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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

OR

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

Commission File Number 001-40971

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.)**
85 Bolton Street Cambridge, MA	**02140**
(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. ☐

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

The registrant was not a public company as of June 30, 2021, the last business day of its most recently completed second fiscal quarter, and therefore, cannot calculate the aggregate market value of its voting and non-voting common equity held by non-affiliates as of such date. The registrant's common stock began trading on the Nasdaq Stock Market on October 29, 2021.

The number of shares of Registrant's Common Stock outstanding as of March 21, 2022 was 29,217,236.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement for the 2022 annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days after the registrant's fiscal year ended December 31, 2021, are incorporated by reference in Part III of this Form 10-K.

Table of Contents

		Page
PART I		
Item 1.	Business	1
Item 1A.	Risk Factors	41
Item 1B.	Unresolved Staff Comments	93
Item 2.	Properties	93
Item 3.	Legal Proceedings	93
Item 4.	Mine Safety Disclosures	93
PART II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	94
Item 6.	Reserved	95
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	96
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	105
Item 8.	Financial Statements and Supplementary Data	105
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	106
Item 9A.	Controls and Procedures	106
Item 9B.	Other Information	107
Item 9C.	Disclosure Regarding Foreign Jurisdictions that Prevent Inspections	107
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	108
Item 11.	Executive Compensation	108
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	108
Item 13.	Certain Relationships and Related Transactions, and Director Independence	108
Item 14.	Principal Accounting Fees and Services	108
PART IV		
Item 15.	Exhibits, Financial Statement Schedules	109
Item 16.	Form 10-K Summary	110

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 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 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 effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and clinical trials and any future studies or trials; 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 and commercialization of our product candidates.
- We are heavily dependent on the success of AU-011, our only product candidate to date.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals for AU-011, 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 not yet successfully initiated or completed any pivotal clinical trials nor 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.
- We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, 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 manufacturing organizations, or CMOs, for the production of clinical supply of AU-011 and may continue to rely on CMOs for the production of commercial supply of AU-011, if approved. This reliance on CMOs 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 AU-011 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 AU-011 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 leveraging our novel targeted oncology platform to develop a potential new standard of care across multiple cancer indications, with an initial focus on ocular and urologic oncology. Our proprietary platform enables the targeting of a broad range of solid tumors using Virus-Like Particles, or VLPs, that can be conjugated with drugs or loaded with nucleic acids to create Virus-Like Drug Conjugates, or VDCs. Our VDCs are largely agnostic to tumor type and can recognize a surface marker, known as heparan sulfate proteoglycans, or HSPGs, that are specifically modified and broadly expressed on many tumors. AU-011, our first VDC candidate, is being developed for the first line treatment of primary choroidal melanoma, a rare disease with no drugs approved. We have completed a Phase 1b/2 trial using intravitreal administration that has demonstrated a statistically significant growth rate reduction in patients with prior active growth and high levels of tumor control with visual acuity preservation in a majority of patients, as assessed using clinical endpoints in alignment with the feedback from U.S. Food and Drug Administration, or the FDA. These data supported advancement into a Phase 2 dose escalation trial, where we are currently evaluating suprachoroidal, or SC, administration of AU-011. We plan to present six to twelve month safety and efficacy data from this trial in 2022 and, take a decision on the route of administration to, initiate a pivotal trial in the second half of 2022. We are also developing AU-011 for additional ocular oncology indications and plan to file an IND in the United States in the second half of 2022 for choroidal metastases. Leveraging our VDCs' broad tumor targeting capabilities, we also plan to initiate a Phase 1a trial in non-muscle invasive bladder cancer, or NMIBC, our first non-ophthalmic solid tumor indication, in the second half of 2022 and present Phase 1a data from this trial in 2023.

VDCs are a novel class of drugs with a dual mechanism of action that promotes cancer cell death by both the delivery of the cytotoxic payload to generate acute necrosis and by activating a secondary immune mediated response. VDCs are analogous to ADCs, another technology that employs a targeting moiety and a cytotoxic payload. In contrast to the limited tumor specificity of individual ADCs, the tumor targeting specificity of VDCs is driven by the selective binding of the VLPs to modified 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.

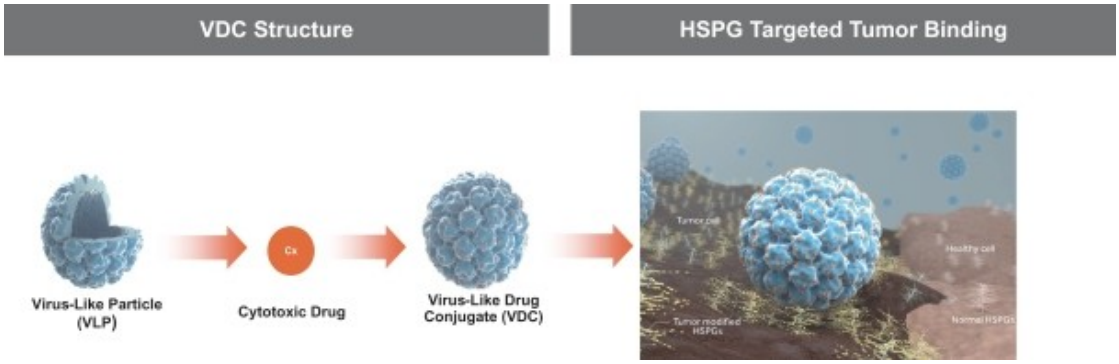

Figure 1. Structure of our VDCs and HSPG Targeted Tumor Binding. The cytotoxic drug payload is covalently bound to the VLP to form the VDC. The capsid proteins that make up the VLP can recognize HSPGs modified by tumor cells and function analogously to the antibody of an ADC.

We believe that our VDC platform has the potential to serve as a backbone for a broad portfolio of targeted oncology therapeutics and has the following potential key advantages:

1. A single VDC can deliver hundreds of cytotoxic molecules conjugated to its capsid proteins.
2. Based on the ability of VLPs to selectively recognize specifically modified and overexpressed HSPGs present on a large number of tumor types, VDCs have the potential to be used broadly across a wide range of cancers with limited off-target toxicity.
3. The VDCs have a high number of HSPG binding sites and this multi-valency permits the strong and selective binding to tumor cells.
4. VDCs have a dual mechanism of action, first by acute necrosis of the tumor cells, and subsequently by creating a highly immunogenic milieu that induces an antitumor specific immune response potentially leading to a more robust and durable therapy.

Our goal is to leverage our platform to develop a new class of targeted therapies that bring therapeutic benefit to multiple cancer indications, initially focusing on the field of ocular oncology, a field representing a potential $1.5 billion market opportunity. Our next area of focus, bladder cancer, is one of the most expensive cancers to treat on a per patient basis, and the global market for bladder cancer is expected to reach $4.0 billion by 2028 across the United States, EU5 and Japan. To date, we have produced a VDC, AU-011, that we are advancing in multiple indications, as shown in the pipeline below.

Program		Preclinical	Phase 1	Phase 2	Pivotal	Upcoming Milestones
Ocular Oncology	**Primary Choroidal Melanoma** *(Ph1b/2 Intravitreal and Ph2 Suprachoroidal)*					• **2022** – Phase 2a safety and efficacy data • **2H 2022** – Initiate Phase 2b (pivotal trial)
	Choroidal Metastasis *(Breast, lung and other cancer metastasis in the eye)*					• **2H 2022** – IND
	Other Cancers of the Ocular Surface *(e.g., SCC, Melanoma)*					
Other Solid Tumors	**Non-Muscle Invasive Bladder Cancer**					• **2H 2022** – Initiate Phase 1 trial • **2023** – Phase 1a data
	Other HSPG-Expressing Tumors *(e.g., Cutaneous Melanoma, HNSCC)*					

We are initially developing AU-011 for the treatment of primary choroidal melanoma, a vision- and life-threatening ocular cancer for which there are currently no drugs approved. Choroidal melanoma is the most common intraocular cancer in adults, with an incidence of 11,000 patients/year in the United States and Europe. It is estimated that 96% of patients are diagnosed early without clinical evidence of metastatic disease. However, despite the current treatments with radiotherapy the long-term prognosis is poor with death occurring in more than 50% of cases and irreversible vision loss within 5 to 10 years in approximately 70% of cases. We intend to develop AU-011 as a first line therapy to treat early-stage disease which includes small melanomas and indeterminate lesions representing approximately 9,000 patients/year in the United States and Europe. AU-011 has also been granted Orphan Drug designation for treatment of uveal melanoma by the EMA.

AU-011 consists of an HPV-derived VLP conjugated to hundreds of infrared laser-activated molecules. The VDC is designed in a way that prevents the conjugation from interfering with tumor binding enabling its selectivity to specifically modified HSPGs on tumor cells but not to normal cells. Laser activation of AU-011 is designed to result in precise tumor cell killing with minimal damage to surrounding healthy tissues. In the absence of AU-011 activation or binding to the tumor cell membrane, there is no cytotoxic effect. Multiple laser treatments, following a single dose of AU-011, increase antitumor activity because of the reoxygenation of the tumor and the photostability of AU-011. Finally, acute necrosis triggers immunogenic cell death leading to the generation of an adaptive, long-term antitumor immune response.

In our completed Phase 1b/2 trial, AU-011, administered by intravitreal injection, was well-tolerated and demonstrated high levels of local tumor control while preserving vision at twelve months in patients that had prior active tumor growth. The therapeutic regimen of AU-011 achieved tumor shrinkage or a near-zero growth rate in the majority of patients and was associated with preservation of visual acuity in 71% of patients at twelve months. We are currently conducting a Phase 2 dose escalation trial of AU-011 with SC administration. We intend to initiate the first pivotal trial in the second half of 2022. Because our mechanism of action preserves key ocular structures, we also intend to develop AU-011 for additional ocular oncology indications, beginning with choroidal metastases.

In addition, we are developing AU-011 for the treatment of NMIBC. Bladder cancer is the most common malignancy involving the urinary system and is the eighth most common cause of cancer death in men in the United States. While metastatic bladder cancer has several approved therapies, there are very limited options for the treatment of high-risk NMIBC. We are planning to initiate clinical development of AU-011 with intramural administration, a novel route of administration, for the treatment of patients with intermediate high-risk NMIBC. This novel route of administration is intended to place high levels of the drug at the base of the tumor where laser activation of AU-011 can cause necrosis and prevent residual tumor cells from further growth and recurrence. We have generated preclinical *in vivo* data that supports that our dual mechanism of action can lead to cytotoxicity and long-term antitumor immunity which may further reduce the risk of metastases. We believe this immune response can play an even larger role in bladder cancer, given that bladder cancer has a well-documented response to immune activation. We are conducting IND-enabling studies with AU-011 and intend to begin clinical trials in the second half of 2022 and present Phase 1a data from this trial in 2023.

Our team

Our team consists of biopharmaceutical experts who have extensive experience in the development of drugs in oncology and ophthalmology. Our CEO and founder, Elisabet de los Pinos, PhD, MBA, was previously part of the marketing team that led the European commercialization of Alimta® for the treatment of lung cancer at Eli Lilly. Cadmus Rich, MD, MBA, CPE, our Chief Medical Officer, an ophthalmologist, has extensive experience in leading ophthalmology research and development at companies including Inotek, IQVIA and Alcon/Novartis. He has led or participated in over 75 development programs including the submission and approval over ten devices and pharmaceutical products in the United States, Europe, China, Japan and Latin America. Julie Feder, our CFO, previously served as CFO at Verastem Oncology, the Clinton Health Access Initiative and was instrumental in the integration of Genzyme and Sanofi. Mark De Rosch, PhD, our COO, was previously the Chief Regulatory Officer at Epizyme during which time Epizyme received FDA accelerated approval of its first product in two oncology indications. Dr. De Rosch also led Regulatory Affairs at Nightstar Therapeutics, a gene therapy company developing treatments for inherited retinal diseases prior to Nightstar's acquisition by Biogen in 2019. Christopher Primiano, our CBO, led multiple strategic transactions during his prior tenure as CBO and General Counsel at Karyopharm Therapeutics, Inc., a commercial oncology company. The Chairman of our Board of Directors is David Johnson, a biopharmaceutical business leader with more than 25 years of experience in drug development and the former Chief Executive Officer at VelosBio Inc., a clinical-stage oncology company developing novel ADCs and bispecific antibodies that was acquired by Merck in 2020 for $2.75 billion. Prior to founding VelosBio Inc. he was the Chief Executive Officer at Acerta Pharma B.V. leading to its acquisition by AstraZeneca plc for $7 billion.

Our Strategy

Our goal is to leverage our proprietary platform to develop a new class of targeted therapies that deliver meaningful therapeutic benefit to a range of cancer indications with high unmet need in which we believe we can establish a new standard of care. The key elements of our strategy include:

- **Advance AU-011 through late-stage clinical development and, if approved, commercialization for the first line treatment of primary choroidal melanoma.** In our Phase 1b/2 trial for AU-011 using intravitreal administration, we observed in patients that had prior active tumor growth high levels of local tumor control while preserving vision at twelve months. We are currently evaluating SC administration of AU-011 in a Phase 2 trial in patients with choroidal melanoma and we plan to present the six to 12 month safety and efficacy data from this trial in 2022 at the American Academy of Ophthalmology Annual Meeting. We believe SC administration will increase tumor exposure to the drug while reducing exposure in the vitreous. We expect to take a decision on the route of administration and decide on either the IVT or SC route of administration to initiate a pivotal trial by the end of 2022. We have received orphan drug designation for treatment of uveal melanoma and fast track designation from the FDA for the treatment of choroidal melanoma and have aligned with FDA, EMA and the UK MHRA on the design and endpoints of this trial. If approved, this would represent the first therapy for primary choroidal melanoma as a first line treatment option for early-stage disease, reserving radiotherapy for a second line treatment option. If approved, we intend to independently commercialize AU-011 in ocular cancers using a limited sales force to target the approximately 50 ocular oncologists in the United States and approximately 50 ocular oncologists in Europe, who are a focused call point that treat most patients.
- **Continue developing AU-011 for additional ocular oncology indications, starting with choroidal metastases**. We intend to be at the forefront of ocular oncology innovation and believe we can apply our mechanism of action for AU-011, which has the potential to treat tumors while preserving key ocular structures, to multiple other ocular oncology indications. Beyond small primary choroidal melanoma and indeterminate lesions, we intend to develop AU-011 in multiple other ocular oncology indications, starting with choroidal metastases. We plan to file an IND with the FDA in the second half of 2022 for choroidal metastases. In addition, we plan to develop AU-011 for tumors of the ocular surface, including both melanomas and squamous cell carcinomas. Every year, approximately 4,500 patients are diagnosed with cancers of the ocular surface. We plan to leverage the sales force infrastructure we intend to build for primary choroidal melanoma for these additional ocular oncology indications.
- **Pursue development of AU-011 for our first non-ophthalmic solid tumor indication in NMIBC.** Our novel approach has the potential benefit of treating early-stage solid tumors, particularly NMIBC, while generating long-term antitumor immunity to prevent metastasis. We believe that local administration into the bladder, and the ability to use a focused laser to activate AU-011, provides the opportunity to apply our technology platform to this area of high unmet medical need. Bladder cancer represents an attractive indication given its sensitivity to immune response, high unmet medical need and expense in treating. AU-011's pro-immunogenic mechanism of action has shown robust activity in preclinical models as a single agent and synergy with checkpoint inhibitors in this indication. Our preclinical data supports initiation of a Phase 1 clinical trial, which we expect to begin in the second half of 2022, subject to FDA acceptance of our IND, with plans to present Phase 1 data from this trial in 2023.
- **Broaden the application of our proprietary technology platform to expand our pipeline of product candidates.** Due to the expression of specifically modified HSPGs across a wide range of solid tumors, we plan to evaluate our technology platform in other oncology indications. We also plan to expand the use of our proprietary technology platform by continuing to explore the potential to deliver other therapeutic agents, including nucleic acid therapies and non-light activated molecules, to broadly treat solid tumors.
- **Evaluate and selectively enter into strategic collaborations to maximize the potential of our pipeline and accelerate the development of our programs.** While we continue to retain worldwide rights to AU-011, we may opportunistically evaluate and enter into strategic collaborations around AU-011 or future product candidates, geographies, or disease areas. We believe our technology platform has the potential to enable the development of a broad scope of product candidates that reaches beyond AU-011. By selectively entering into collaborations, we believe our potential to expand and accelerate the development of our programs and maximize worldwide commercial potential may be enhanced.

Targeting a broad range of solid tumors with our proprietary technology platform

Our technology platform represents a novel approach of targeting a broad range of solid tumors using VLPs that can be loaded or conjugated with drugs creating a new class of targeted therapies. Our VDCs are analogous to ADCs, another technology that employs a targeting moiety and a payload. ADCs typically utilize a monoclonal antibody to traffic a cytotoxic payload preferentially to tumor cells. There are currently 11 FDA-approved ADCs, six of which have gained regulatory approval since 2019. The class achieved approximately $4 billion in sales in 2020 and is expected to garner over $27 billion in sales in 2026.

Despite the successful adoption of this modality, there remains room for improvement. Key challenges related to ADCs include the limited number of payloads that can be conjugated onto the ADC along with toxicities that have been reported. Only two to five toxin drug conjugate molecules per antibody can be delivered, potentially reducing potency, which can necessitate higher doses of toxic drug to be delivered. These higher doses and the expression of ADC target receptors on healthy tissue can lead to systemic toxicity. We believe our VDCs can expand upon the foundation built by ADCs, given VDCs are endowed with specific attributes designed to overcome the shortcomings of ADCs.

The key finding that launched our technology development efforts was the observation that human papilloma virus, or HPV, binds to specifically modified HSPGs on the tumor cell membrane. HSPGs are a large family of molecules found in the extracellular matrix and on the membranes of cells. Tumors cells specifically modify HSPGs with key sulfation modifications that provide high binding specificity to a number of ligands. Tumor modified HSPGs regulate many aspects of tumor progression, including proliferation, invasion, angiogenesis and metastases. Our scientific founder, John Schiller, PhD, and his colleagues at the National Institutes of Health, or NIH, identified that these specific modifications enable HSPG-selective binding of HPV on tumor cells, as illustrated below.

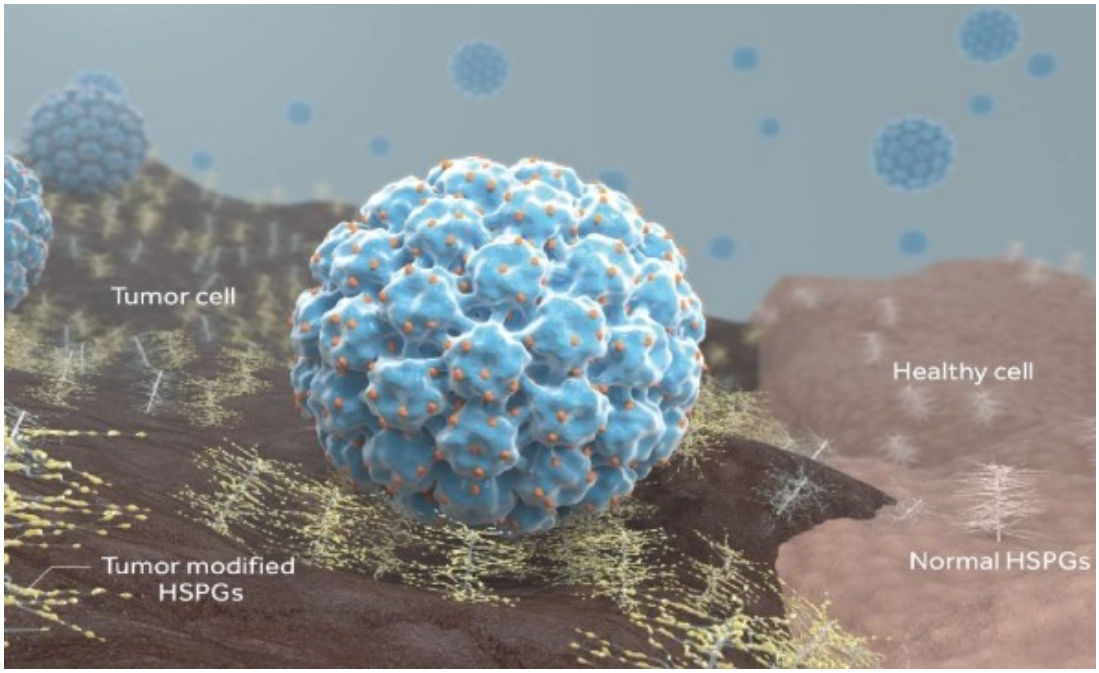

Figure 2. VDCs bind to specifically modified HSPGs on the tumor cell surface with multivalent binding and do not bind to normal healthy cells.

This NIH team discovered that HSPG-selective binding of HPV was determined by the properties of the proteins that make up the viral capsid, or shell, not by the nucleic acids contained within the shell. Dr. Schiller pioneered the development of VLPs into a highly effective HPV vaccine to prevent cancer, work for which he received the Lasker-DeBakey Clinical Medical Research Award. He discovered that these capsid proteins could be recombinantly manufactured and could self-assemble into empty VLPs without any viral genome. Our technology platform is based on HPV derived VLPs that were further engineered to reduce cross-reactivity with pre-existing immunity against HPV, enabling the use of VLPs as oncology therapeutics. This platform leverages the tumor-specific targeting mechanism of HPV VLPs to enable their use to deliver cytotoxic payloads directly to a wide range of solid tumors. VLPs have also demonstrated the ability to deliver nucleic acids, potentially expanding our platform on which to base a novel class of oncology therapies.

We believe that our technology platform has the potential to serve as a backbone for a broad portfolio of therapeutics. There are four key potential advantages of VDCs compared to ADCs:

1. A single VDC can deliver hundreds of cytotoxic molecules conjugated to its capsid proteins.
2. The VDCs have a high number of HSPG binding sites and, it is this multi-valency that permits the strong binding of the VDCs with tumor cells.
3. Based on the ability of VLPs to selectively recognize specifically modified and overexpressed HSPGs present on a large number of tumor types, VDCs have the potential to be used broadly across a wide range of cancers with limited off-target toxicity.
4. Tumor treatment with VDCs results in a dual mechanism of action, both directly with acute necrosis of the tumor cells, and indirectly by creating a highly immunogenic milieu inducing an antitumor specific immune response leading to a more robust and durable therapy.

Choroidal melanoma overview

Choroidal melanoma is the most common intraocular cancer in adults, with an incidence of 11,000 patients/year 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. It is estimated that 96% of patients are diagnosed early without clinical evidence of metastatic disease. There are approximately 2,000 new cases treated each year in the United States and 1,600 new cases treated each year in Europe. However, despite the current treatments with radiotherapy, the long-term prognosis is poor with death occurring in more than 50% cases and irreversible vision loss within 5 to 10 years in approximately 70% of cases. We intend to develop AU-011 as a first line therapy to treat early-stage disease which includes small melanomas and indeterminate lesions representing approximately 9,000 patients in the United States and Europe. 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. Most choroidal melanomas result from transformation of a benign choroidal nevus. In early stage lesions, most of the tumor is composed of benign nevi 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. There are 3,900 patients every year in the United States that are diagnosed with indeterminate melanocytic lesions that have risk factors and that are referred to the ocular oncologist.

Our goal is to develop AU-011 as a first line treatment option that can enable early treatment intervention of primary choroidal melanoma while preserving vision and reserving radiotherapy for a second line treatment option. Earlier diagnosis and early treatment intervention of lesions in the eye before the onset of metastatic disease may dramatically change outcomes for patients.

Current treatment options for choroidal melanoma

There are no FDA-approved therapies for choroidal melanoma. There are three primary treatments that are routinely used 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.

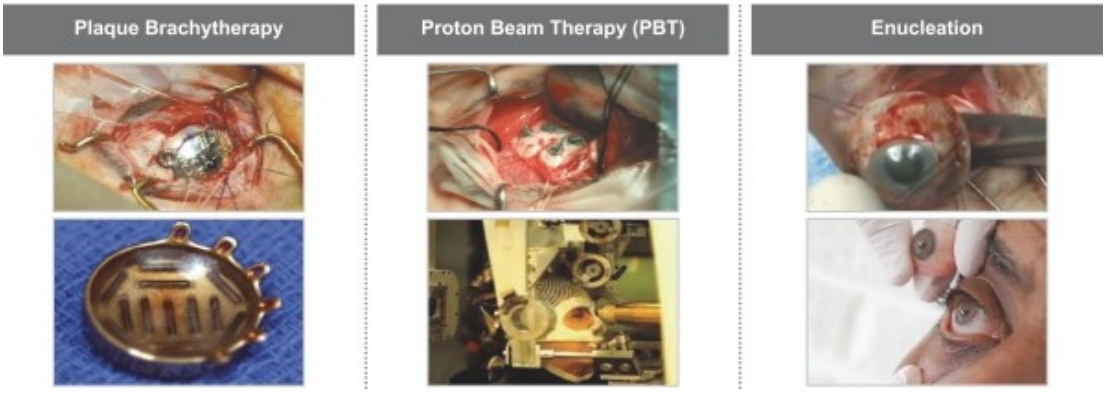

Figure 3. Three primary treatments for choroidal melanoma.

The limited options available to treat patients with choroidal melanoma pose challenges to clinicians and patients. The existing treatments are far from innocuous: all of them are invasive procedures that are associated with irreversible loss of visual acuity and other deleterious side effects. Because 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. We believe that there is an urgent unmet medical need for an effective vision preserving therapy and that the availability of such a therapy may encourage treatment of early stage ocular lesions and increase the awareness of the importance of early diagnosis for this life-threatening disease.

Our solution AU-011

AU-011 is a VDC consisting of an HPV-derived VLP and IRDye 700DX, a laser 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 specifically modified HSPGs found on the surface of tumors cells, including ocular melanoma cells.

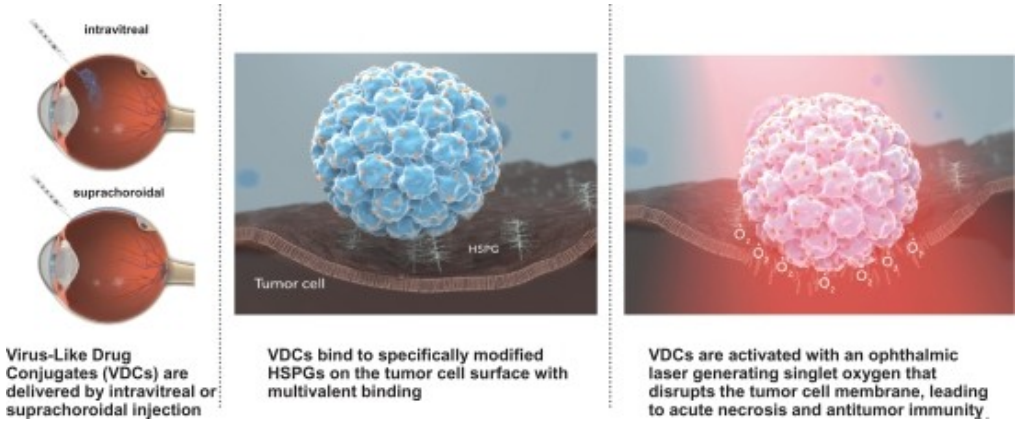

Figure 4. AU-011, administered by intraocular injection, binds to tumor cells. Activation using an ophthalmic laser leads to rupture of the tumor cell membrane, acute necrosis and a secondary immune activation leading to long term antitumor immunity.

Goal of Treatment with AU-011

In ocular oncology, the goal of early stage local treatment is to achieve tumor control—to prevent the tumor from growing further while preserving the delicate ocular structures such as the retina. We believe that treatment early in the disease course can also limit the risk of metastasis for patients. 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, tumor control has been achieved and the treatment is considered successful. Ocular oncologists measure the antitumor activity after plaque brachytherapy by evaluating tumor control as well as systemic disease to detect the presence of metastasis.

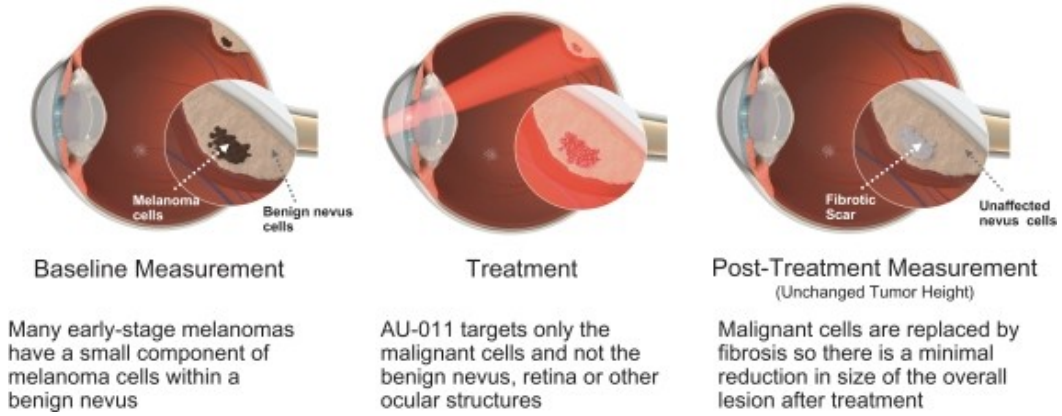

Figure 5. Goal of treatment with AU-011 is local tumor control with targeted killing of melanoma cells.

We believe that patients with earlier stage tumors stand to derive the most benefit from AU-011. These tumors are not only the most likely to respond to our therapy but, based on historic data, these patients also have the highest likelihood of not having already developed life-threatening metastatic disease, and as such, AU-011 has the potential to confer the greatest long-term benefit.

Phase 1b/2 demonstrated robust antitumor activity

A total of 56 patients out of 57 patients enrolled with a clinical diagnosis of choroidal melanoma were treated with AU-011, due to one patient not having met predefined active growth criteria. Tumor growth measurements were obtained by one centralized reading center.

The tumor control rate at twelve months across all treatment doses and initial tumor sizes was 54% based on the predefined criteria of tumor control failure as an increase in thickness of greater than 0.5 mm or an increase in diameter of more than 1.0 mm.

The key two subgroups were patients with well-documented active growth (n=20) and those with well-documented active growth treated at the highest therapeutic regimen (n=14). The 20 patients with well-documented active growth treated at all doses had a tumor control rate of 60%. The 14 patients with well-documented active growth treated at the highest therapeutic regimen had a tumor control rate of 64%.

When compared to each patient's rate of tumor growth within the prior two years before enrollment, the growth rate after treatment with AU-011 at any dose demonstrated a statistically significant reduction both when assessing all patients with active growth as well as patients on the maximum therapeutic regimen.

Phase 1b/2 demonstrated preservation of visual acuity

We believe that showing preservation of visual acuity will be critical in our application for regulatory approval of AU-011 to show that it can both halt tumor growth and preserve visual acuity. Visual acuity was measured at regular intervals as a key efficacy endpoint. In the Phase 1b/2 trial we defined the loss of visual acuity as the loss of three lines of vision, or 15 letters, using best corrected visual acuity, or BCVA, which the FDA considers a clinically meaningful vision loss. We found moderate loss of visual acuity immediately following treatment, which we believe was associated with short-term reversible adverse events such as ocular inflammation and corneal abrasions. Upon resolution of the short-term adverse events, visual acuity recovered in the majority of patients, and we observed a vision preservation rate of 86% across all 56 treated patients in the trial over the twelve months follow up period and 71% for the 14 patients enrolled with active growth and treated with two cycles of AU-011 therapy.

Only four out of 14 patients with small tumors with active growth had a long-term loss of more than 15 letters of vision that did not recover back to less than the 15 letters at 12 months. These were related to persistent adverse events, such as pigmentary changes, macular edema or subretinal fluid. Of the four patients that had persistent vision loss, two lost greater than 30 letters and the other two had a loss of 17 and 18 letters which is close to the threshold of 15 letters.

Importantly, 17 of the 20 patients with small tumors with active growth had tumors close to the fovea or optic nerve and were considered high risk for severe vision loss with radiotherapy. In this patient population, the vision preservation rate was 76% (13/17 patients) highlighting a potential important benefit AU-011 may have over the current standard of care.

Phase 1b/2 safety and tolerability data

Treatment with AU-011 was generally reported to be well-tolerated at all doses including when two cycles of therapy were administered. Adverse events were generally mild or moderate, transient and manageable with standard of care treatments in most patients. Expected AEs of vitreous inflammation, anterior chamber inflammation and increased intraocular pressure were manageable with steroid treatment and ocular antihypertensives.

Intraocular inflammation represented the most common treatment related AE, which was expected given the viral-like component of our drug and the pro-immunogenic mechanism of action. These inflammatory events included anterior chamber inflammation in approximately 71% of patients and posterior inflammation in 91% of patients. Posterior inflammation originated in and around the tumor, suggesting that this inflammation may, at least in part, be related to potential antitumor activity of AU-011. This inflammation was not prophylactically treated, which allowed the immune response to initiate before starting steroid therapy. Cases of anterior inflammation were treated with topical steroid drops, while posterior inflammation was treated with topical, oral, intravitreal or periocular steroids. Approximately 46% of patients also had transient increases in intraocular pressure that were managed with topical anti-hypertensives. One patient had a Grade III vitreous opacity that was removed with surgery.

Adverse events of pigmentary changes around the tumor margin were reported in approximately 38% of patients and were the cause of the only two drug-related serious adverse events, or SAEs, of vision loss. In these two subjects the edge of the tumor was within 1.0 mm of the fovea and the pigmentary changes occurred in the fovea causing the vision loss of greater than 30 letters. Two SAEs that were not related to treatment were reported in two patients, one event each of papillary renal cell carcinoma and diverticulitis.

A high proportion of patients (43/56; 77%) in the trial were at high risk for vision loss with radiotherapy because their tumors were close to the fovea or optic disk (<3.0 mm). If these patients had been treated with radiotherapy, historical studies suggest that a large proportion would have a worse visual acuity prognosis, with many having vision of <20/200 or legal blindness within five years. Approximately 90 percent of high-risk patients with tumors near the fovea or optic nerve had a significant vision loss with plaque brachytherapy as the plaque led to irreversible damage to the fovea or optic nerve. In contrast, most of the high-risk patients in our trial were successfully treated with AU-011 without a significant impact on their visual acuity, highlighting the potential benefit relative to the current standard of care.

We believe that AU-011 has the potential to deliver meaningful clinical benefit to patients with early-stage choroidal melanoma as a first-line treatment while decreasing the likelihood of irreversible loss of visual acuity and other severe comorbidities that are often associated with radiotherapy.

Suprachoroidal delivery

As part of our overall development strategy, we are evaluating and developing the SC route of administration to optimize the delivery of AU-011 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 full posterior segment of the eye.

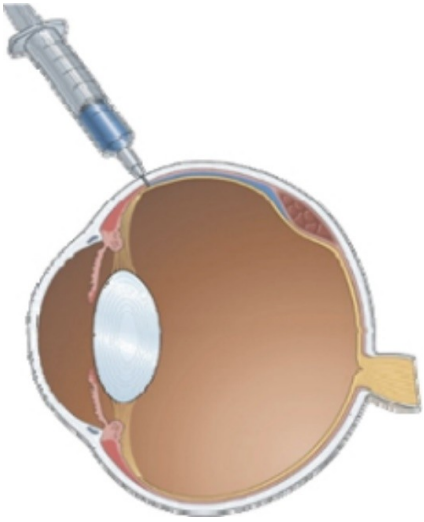

Figure 6. Suprachoroidal administration with SCS Microinjector™.

Our preclinical data supports the SCS as an attractive site for intraocular drug delivery for choroidal melanoma as it provides an optimization of the therapeutic index due to increased bioavailability at the tumor and lower exposure to key ocular structures.

Phase 2 suprachoroidal administration trial

We are currently conducting a Phase 2 dose escalation trial of AU-011 with SC administration in 22 patients with choroidal melanoma. The primary objective of this portion of the trial is to determine the maximum tolerated dose and treatment regimen. We believe SC administration can result in a better target product profile with reduced inflammation because of significantly lower exposure of the drug to the vitreous and potentially higher clinical activity than intravitreal administration because of increased drug exposure to the tumor in the choroid.

The results from the initial patient cohorts with an average of six months follow-up demonstrated that SC administration was generally well tolerated with no serious treatment related adverse events reported. To date, drug and laser related adverse events have included four patients with mild anterior uveitis, two patients each with both punctate keratitis and eye pain, and one patient each with conjunctiva hyperemia, conjunctival edema, cystoid macular edema, eyelid edema, pupils unequal retinal pigment epitheliopathy, salivary gland enlargement and vision blurred. One moderate adverse event of anterior scleritis related to the injection procedure was also observed. All of the events resolved spontaneously or with standard of care treatment. Of note, no inflammation in the vitreous has been observed in this trial through the two cycles of the highest tested dose (40 µg). Given the tolerability profile with the 40 µg dose, we increased the highest dose to 80 µg per treatment and plan to explore a new treatment regimen with three cycles of treatment. Currently 2 cycles of 80 µg have been confirmed to be safe and the third cycle of treatment is underway. We plan to present the six to 12 month safety and efficacy data from this trial in the second half of 2022.

All Treated Subjects (n=16) Drug/Laser Related Adverse Events	Grade I	Grade II	Grade III	Total
Anterior chamber cell/inflammation	25%	0	0	25%
Conjunctival edema	6.3%	0	0	6.3%
Conjunctival hyperemia	6.3%	0	0	6.3%
Eye pain	6.3%	6.3%	0	12.5%
Eyelid edema	6.3%	0	0	6.3%
Punctate keratitis	12.5%	0	0	12.5%
Pupils unequal	6.3%	0	0	6.3%
Retinal pigment epitheliopathy	6.3%	0	0	6.3%
Salivary gland enlargement*	0	6.3%	0	6.3%
Vision blurred	6.3%	0	0	6.3%

Table presents percentage of subject with AEs related to AU-011 or laser by severity and overall; subjects with more than 1 AE are counted in the highest severity group
Data cutoff December 31, 2021 *Likely related to COVID vaccine per investigator

Figure 7. Adverse events among the 13 patients enrolled in the Phase 2 suprachoroidal trial to date.

Pivotal trial plan in choroidal melanoma

In alignment with the FDA and EMA, we plan on conducting two pivotal trials with AU-011. We anticipate to start the first pivotal trial in the second half of 2022 in patients with high-risk indeterminate lesions and small choroidal melanoma who have active growth prior to enrollment. We intend to randomize a minimum of 70 patients in this trial to three arms 2:1:2 to receive therapeutic regimen AU-011, low dose regimen AU-011 or a sham control. Patients will be selected based on having a small amount of active growth within two years of trial enrollment, and a tumor size of 0.5 mm to 3.0 mm in thickness and less than 10 mm in diameter.

Pivotal Trial

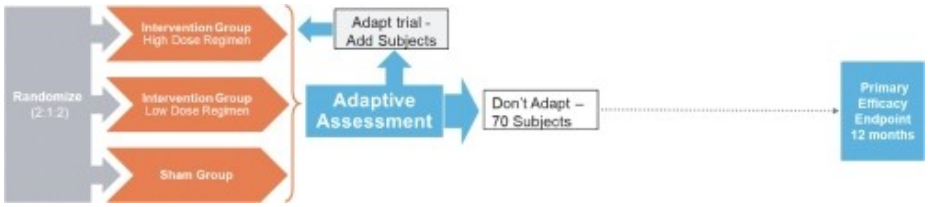

Figure 8. Preliminary design of the pivotal trial.

The key primary endpoint agreed with the FDA is contemplated to be the tumor thickness growth rate over 12 months, comparing the growth rates between the AU-011 high dose group and the sham group. The first key secondary endpoint will be a composite time to event analysis that will evaluate the number of events of disease progression or visual acuity failure between the AU-011 high dose group and the sham group. We will also evaluate time to disease progression and change from baseline in BCVA letter score. There will be a minimum follow up for all patients of 12 months.

The trial has a power of >95% to meet the primary and the first key secondary endpoint. Since there is no drug approved for the treatment of choroidal melanoma, we have agreed with FDA that a statistically significant difference on these endpoints will provide support from a regulatory perspective to meet the requirement of clinical effectiveness.

Given that choroidal melanoma is a rare disease and, based on the limited natural history data of the growth rate of these early-stage tumors, this trial will follow an adaptive design with the ability to perform a sample size re-estimation. With this adaptive design, the sample size will be increased if either (1) the observed growth rate in the sham arm is lower than assumed or (2) the estimated treatment effect comparing the sham arm and the high dose arm is less than expected. With this strategy, we believe we will improve the probability of success of the trial.

We also plan to conduct a second pivotal trial, which will be a Phase 3 randomized trial, that is expected to start enrolling when the first pivotal trial completes enrollment. This Phase 3 trial is planned to be an identical design to the Phase 2b pivotal trial described above with the same primary and secondary endpoints. The final sample size of this second pivotal trial will be determined by the final sample size of the Phase 2b pivotal trial.

If warranted by the data, we plan to submit the results of the first pivotal trial to support approval of AU-011 for the treatment of primary indeterminate lesions and small choroidal melanoma. Based on the results of the first pivotal trial, if positive, and the fact that there are no therapies approved for the treatment of this rare disease, the FDA and EMA may agree to grant approval based on the first pivotal trial with the condition that the second Phase 3 pivotal trial should be completed as a post-approval commitment. However, the FDA and/or EMA may require both trials for approval, which will be addressed subsequent to submission of the data from the first pivotal trial.

Registry Trial

We have agreement with the FDA that we will monitor all patients for a total of five years after dosing to evaluate the long-term tumor response, visual acuity preservation and safety, as well as the risk of metastatic disease and mortality, which we are doing in a Phase 4 registry trial. To date, all 57 patients in the Phase 1b/2 trial with intravitreal administration have completed the Phase 1b/2 trial and 41 (72%) have entered the registry trial. There are also 7 patients from the Ph2a portion of the SC trial that have entered the registry trial. The data collected with an average follow up of more than two years from initial enrollment in the Phase 1b/2 trial or the Phase 2 SC trial and follow up in the registry demonstrates durability of tumor control, visual acuity preservation and related safety profile from treatment of AU-011. All subjects in the registry trial treated only with AU-011 had stable vision and only 2 local progressions of disease after more than two years of average follow-up. For those patients who progressed in tumor size in the Phase 1b/2 trial and who received standard of care with radiotherapy, two patients lost visual acuity and one additional patient had to have their eye enucleated because of tumor recurrence after radiotherapy, reaffirming our belief that there is a high unmet medical need in this patient population.

Only one of 40 patients in the registry had onset of metastatic disease which is an encouraging result as usually the metastatic risk for small melanomas is approximately 12% up to 10 years' follow up.

Matched case control studies

The ability to demonstrate tumor control with long term visual acuity preservation could provide a favorable benefit-risk profile of AU-011 for the first line treatment of patients with early-stage choroidal melanoma compared to an invasive radiotherapy procedure. To demonstrate the long-term value of visual acuity preservation for patients treated with AU-011, we are conducting two Matched Case Control, or MCC, studies that will provide data comparing AU-011 to radiotherapy. A retrospective MCC study has been performed to provide an estimate of the vision benefit of AU-011 versus radiotherapy and to help estimate the treatment effect and powering of the prospective MCC study that was initiated in 2021. These studies are discussed below.

Retrospective matched case control study analysis

To estimate the vision preservation of AU-011 compared to radiotherapy we are conducting a retrospective MCC analysis comparing the group of patients in our Phase 1b/2 trial who had tumors at high risk for vision loss due to its location close to the fovea or optic disk and were treated with AU-011 (n=43) to patients with tumors of similar size and location previously treated with radiotherapy at the Wills Eye Hospital Ocular Oncology Service led by Dr. Carol Shields. This analysis will match up to 5:1 patients using the key baseline characteristics that impact long term visual acuity – tumor location, tumor size and baseline visual acuity – and will compare the visual acuity after treatment with each therapy in terms of a change from baseline in vision and absolute vision at years one, two and three. Results from our Phase 1b/2 trial with intravitreal administration show visual acuity preservation in a majority of patients after two cycles of treatment with AU-011 at twelve months. In addition, data from our ongoing registry trial to date do not show a change or decline in vision for patients treated with AU-011 with long term follow up, while two patients that failed treatment with AU-011 and were treated with radiotherapy are having vision loss. We believe that the results of the retrospective study will further validate these results and strengthen our thesis that the mechanism of AU-011 enables durable preservation of visual acuity providing an important advantage to radiotherapy. The results of the retrospective study are expected to be published with Dr. Carol Shields in the first half of 2022 and will be used to estimate the assumptions to power a prospective Matched Case Control study that we plan to start shortly thereafter.

Prospective matched case control study

Based on the results of the retrospective MCC analysis we are initiating a prospective matched case control trial where we will compare, after one, two, and three years, the visual acuity of patients treated with AU-011 versus patients treated with radiotherapy. Like the retrospective MCC analysis, patients will be matched based on similar tumor size, location, and baseline vision at the beginning of the trial.

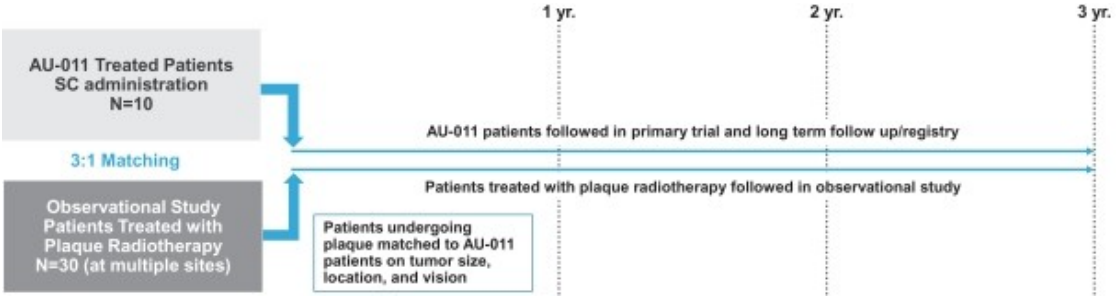

Figure 9. Matched case control prospective trial comparing visual acuity outcomes after treatment with AU-011 or plaque radiotherapy.

The patients are planned to be matched on average 3:1 (Radiotherapy: AU-011) to increase the power. The matching and analysis will be masked and performed independently. The objective is to show the vision benefit of AU-011 compared to radiotherapy using prospective data for both groups. Based on initial results in the retrospective MCC study, we believe these results may support the benefit/risk discussion of our regulatory submission and to serve as support for pricing and reimbursement discussions.

Choroidal metastases from other tumors

We can apply our mechanism of action for AU-011, which we believe has the ability to preserve key ocular structures, in multiple other ocular oncology indications. Beyond primary choroidal melanoma, we are developing AU-011 in additional ocular oncology indications, starting with choroidal metastases. Choroidal metastases are a common intraocular malignancy that are caused by multiple primary cancers in the body that metastasize to the eye due to the high blood flow and perfusion that provides an environment receptive to metastases and tumor growth. Approximately 22,000 patients have choroidal metastases globally every year. and approximately half (~47%) of the patients with choroidal metastases have primary breast tumors. Other common primary cancers include lung (approximately 21%), gastrointestinal (4%), kidney (2%), cutaneous melanoma (2%) and prostate cancer (2%), and approximately 17% of cases with an unknown primary tumor type. The majority of these malignancies are solitary small tumors in the choroid associated with subretinal fluid and, as opposed to choroidal melanoma, they can occur in and adversely affect vision in both eyes. These lesions are typically treated with radiation, which has the same comorbidities as previously described for the treatment of choroidal melanoma. Given their poor prognosis, the quality of life and, in particular, maintenance of vision, for patients with metastatic cancer is critical and as such there is a significant unmet need for an effective vision sparing ocular treatment that enables patients to avoid additional surgical interventions.

We are planning to initiate clinical development in this indication in the second half of 2022, subject to FDA acceptance of an IND.

AU-011 for the treatment of non-muscle-invasive bladder cancer

We are developing AU-011 for the treatment of non-muscle-invasive bladder cancer, or NMIBC. We are planning to initiate clinical development with AU-011 with intramural administration, a novel route of administration for the treatment of patients with intermediate and high-risk bladder cancer lesions. This novel route of administration is based on the direct administration of AU-011 into the lamina propria of the bladder wall at the tumor edge. It is intended to place high levels of AU-011 at the base of the tumor where laser activation can cause localized necrosis preventing residual tumor cells from further growth and recurrence. We are conducting IND-enabling studies with AU-011 to demonstrate the feasibility of this approach and intend to begin clinical trials in the second half of 2022.

Bladder cancer disease background

Bladder cancer is the most common malignancy involving the urinary system and is the eighth most common cause of cancer death in men in the United States. Estimates are that there will be 61,300 new cases of bladder cancer and 17,000 deaths in 2021 in the United States. Globally, bladder cancer accounts for approximately 570,000 cases, with 422,000 cases comprised of NMIBC, and 165,000 deaths each year. Patients with bladder cancer classically present with painless blood in the urine, however, because this symptom is like those of benign disorders such as urinary tract infections, cystitis, prostatitis and the passage of kidney stones, the diagnosis of bladder cancer is often delayed while these other, more common, conditions are ruled out. Furthermore, symptoms are often intermittent. Delays in diagnosis can lead to a worsened prognosis due to the presence of more advanced stage disease by the time a confirmation of bladder cancer is made.

Our solution AU-011

We are currently developing AU-011 for the treatment of NMIBC with IND-enabling studies and plan to initiate a Phase 1a trial in the second half of 2022, subject to FDA acceptance of an IND, to evaluate the feasibility of intramural administration and to assess distribution, safety and initial proof of mechanism with evaluation of local acute cellular necrosis after laser activation. We believe AU-011 represents a potential targeted therapy that can be activated using a similar laser as that currently utilized in our choroidal melanoma program, following a well-characterized approach with commercially available devices used by urologists.

AU-011 has been observed to be highly selective, through both its specific binding to modified HSPGs on cancer cells, combined with focused laser activation leading to cytotoxicity and subsequent immune activation. We believe the immune response could play an even larger role in bladder cancer, given that bladder cancer has a well-documented response to immune activation. This immune sensitivity is substantiated by the effectiveness of immune modulatory agents like BCG. We have observed in preclinical experiments that AU-011 was able to target bladder cancer cells in both *in vitro* and *in vivo* tumor models. Laser activation of AU-011 resulted in cell killing of bladder tumor cells while sparing other normal surrounding cells as a single agent. This cell killing induced a pro-immunogenic antitumor response that resulted in complete elimination of tumors in a mouse xenograft model and durable responses as well as the prevention of tumor re-implantation. This highlights the value of AU-011 to generate antitumor immunity and prevent tumor recurrence. Based on our preclinical data, AU-011 was also observed to be highly synergistic with checkpoint inhibitors that have already been approved for the treatment of a subset of NMIBC and metastatic bladder cancer patients.

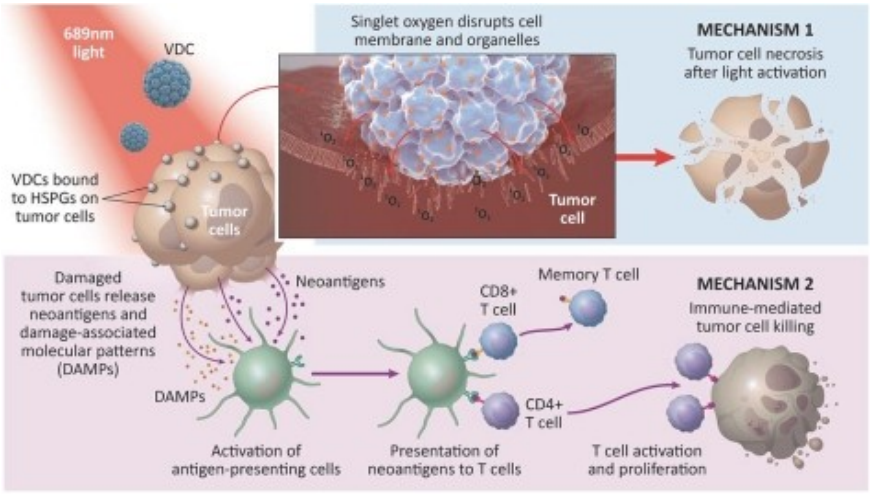

Figure 10. Overview of AU-011's dual mechanism of action with acute tumor cell necrosis and secondary antitumor immunity.

Clinical plans in NMIBC

We intend to conduct a Phase 1 trial in intermediate and high risk NMIBC patients that are either candidates for TURBT or cystectomy beginning in the second half of 2022, subject to FDA acceptance of our IND. We plan to evaluate the safety, tolerability and feasibility of AU-011 using the intramural route of administration. After removal of the tumors, we plan to further assess the tumor tissue with histopathology to evaluate the presence of acute cellular necrosis as an early sign of antitumor response.

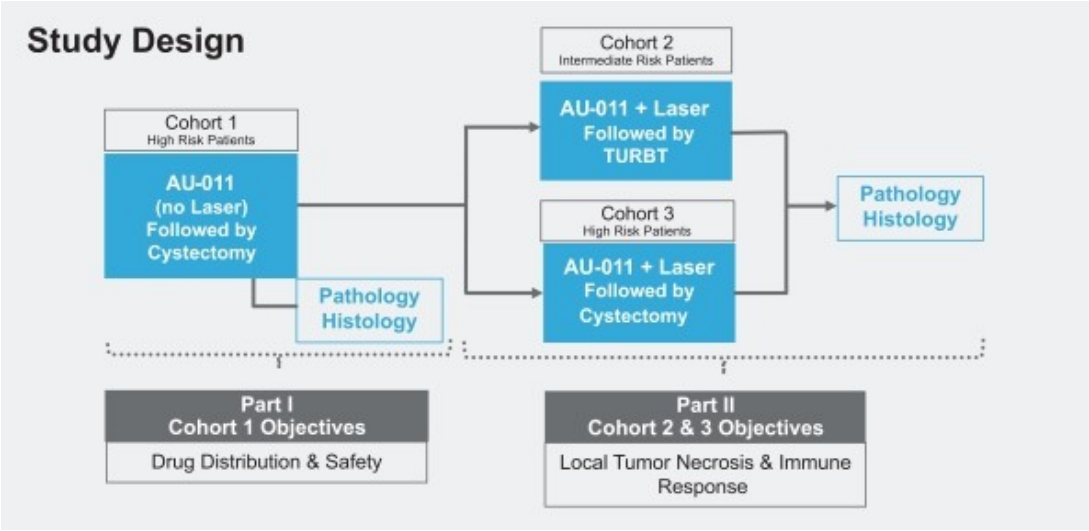

Figure 11. Phase 1 window of opportunity trial to establish route of administration and tumor necrosis.

In this Phase 1 trial, we intend to evaluate the tumor distribution of AU-011 after intramural administration in intermediate to high-risk subjects with NMIBC. In cohort 1, we will assess AU-011 local and systemic exposure without laser activation. In cohorts 2 and 3 we will assess AU-011 and laser activation in patients with intermediate risk that are planned to receive TURBT and high risk patients that are unresponsive to BCG and that are planned to receive cystectomy. In these cohorts, we plan to administer AU-011 followed by laser activation, and one week later the tumor will be removed by TURBT (cohort 2) or the entire bladder by cystectomy (cohort 3), and we will assess tumor response in the form of necrosis and the immune response by pathology and immunohistochemistry. This Phase 1a trial is planned to be conducted in association with the National Cancer Institute at approximately three selected private sites in the United States and is planned to be initiated in the second half of 2022.

Shortly after this initial trial, we are planning to conduct a Phase 1b/2 dose escalation and expansion trial in the treatment of NMIBC. We believe this Phase 1b/2 trial will help establish the treatment regimen and we are planning to involve multiple leading sites in the treatment of bladder cancer.

Other HSPG-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. We plan to select our next solid tumor indication for clinical development with AU-011 based on its status as a tumor type with high HSPG expression, such as cutaneous melanoma and head and neck cancer.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid innovation of new technologies, fierce competition and strong defense of intellectual property. While we believe that AU-011 and our knowledge, experience and scientific resources provide us with competitive advantages, 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 therapies in the oncology field. 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 AU-011 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 the treatment of primary choroidal melanoma or for the treatment of choroidal metastases, which are our first two planned ocular oncology indications. The standard of care as a first line treatment for patients is plaque brachytherapy or proton beam therapy. Verteporfin (Visudyne) is currently used off label in some cases of early stage disease alone or in combination with transpupillary thermotherapy. It is possible that there may be other companies with compounds in pre-clinical 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 treatment of the primary cancer in the eye before it metastasizes. Immunocore Holdings PLC, or Immunocore, recently received FSA approval for KIMTRAK® (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 the early stage disease in the eye.

Urologic oncology

There are multiple companies that have drugs in clinical development for the treatment of intermediate and high risk NMIBC patients that are unresponsive to BCG. ImmunityBio, Inc. has presented Phase 2/3 data for their drug Anktiva in combination with BCG in patients with BCG unresponsive high grade NMIBC and they plan to submit a BLA in 2022. Sesen Bio, Inc. presented Phase 3 data for their lead candidate, Viceneum, as a treatment for BCG-unresponsive NMIBC, but in August 2021 the FDA sent Sesen Bio, Inc. a Complete Response Letter, indicating that the agency would not approve the application. The agency recommended additional clinical and statistical data analyses, and had concerns related to the company's Chemistry, Manufacturing and Controls (CMC). FerGene, Inc. announced positive data of their pivotal Phase 3 clinical trial evaluating nadofaragene firadenovec (rAd-IFN/Syn3), an investigational gene therapy, for the treatment of high-grade, BCG-unresponsive NMIBC, however, they have announced delays due to chemistry, manufacturing and controls problems, so it is uncertain when they marketing application will be submitted (last update on BLA filing was May 2020). UroGen Pharma Ltd. has a drug Jelmyto, a gel reformulation of mytomicin that is currently approved to treat low grade upper tract urothelial cancer, which is currently in Phase 3 development for the treatment of NMIBC. CG Oncology, Inc. has a drug (CG0070) that is being investigated in a global Phase 3 clinical trial as a monotherapy for the treatment of BCG-unresponsive NMIBC.

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, as 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. As of December 31, 2021, we have paid NIH approximately $0.4 million in aggregate milestones under the NIH License Agreement. In addition to milestones under the agreement, we reimburse the 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.

During the years ended December 31, 2021 and 2020, we paid $0.03 million and $0.02 million, respectively, in fees associated with the NIH License Agreement.

LI-COR Exclusive License and Supply Agreement

In January 2014, we entered into an Exclusive License and Supply Agreement, or the LI-COR Exclusive License Agreement, with LI-COR, Inc., or LI-COR, for the license of IRDye 700DX and related licensed patents for the treatment and diagnosis of ocular cancers, ocular pre-cancer and indeterminate lesions in humans, and as amended in January 2016, July 2017, April 2018 and April 2019. The LI-COR Exclusive License 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 LI-COR low-single digit royalties on net sales.

The term of the LI-COR 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 expiry of the last to expire patent licensed under the agreement is December 2023.

Clearside License Agreement

In July 2019, we entered into a license agreement, or the Clearside License Agreement, with Clearside Biomedical, Inc., or Clearside, for the license of Clearside's suprachoroidal 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.

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 belzupacap sarotalacan (AU-011), (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 AU-011, 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 January 19, 2022, 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 LI-COR under one issued United States patent; an exclusive license from NIH under four issued United States patents and three issued foreign patents; an exclusive license from INSERM-TRANSFERT (Inserm) under three issued United States patents, and six granted foreign patents; and exclusive rights under a Cooperative Research and Development Agreement (CRADA) with the United States Department of Health and Human Services (DHHS), as represented by the National Cancer Institute, and Institute, Center, or Division of the NIH, under three issued United States patents, three pending non-provisional United States patent applications, eight foreign patents, and eleven pending foreign patent applications.

In addition, as of January 19, 2022, we solely own four issued United States patents, one pending non-provisional United States patent application, six pending foreign patent applications, and one pending United States provisional application. We intend to pursue, when possible, additional patent protection, including composition of matter, method of use and process claims related to AU-011.

Patent families

We license one patent family from LI-COR 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 two patent families, all of which are generally directed to the AU-011 product and related methods of use and production.

The first family, licensed from LI-COR, includes one issued United States patent. 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 AU-011). This patent has a standard expiration date of October 23, 2023, subject to potential extensions.

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 cancer cells using a therapeutic agent formulated with a papilloma virus-like particle, (2) methods that include administering to a subject (e.g., a subject having a melanoma) a papilloma virus-like particle having a fluorescent dye and exposing the dye to an excitation wavelength of light, and (3) methods for detecting cancer cells using a papilloma virus-like particle having a detectable label. This patent has 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 AU-011, (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. This patent has 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 AU-011, (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 subject having cancer. This patent has 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 three issued United States patents, one issued European patent, an issued patent in each of Australia, Canada, Hong Kong, Republic of Korea and Mexico, two issued patents in Japan, and two pending patent applications in the United States, and one pending patent application in each of Australia, Brazil, China and Europe. Patents in this family include claims directed to (1) tumor-targeting papilloma virus-like particles containing near infrared phthalocyanine dye molecules that become toxic or produce a toxic molecule upon light activation, (2) methods that include delivering the papilloma virus-like particles to an ocular tumor, and/or (3) methods of producing tumor-targeting bioconjugates that include the papilloma virus-like particles and near infrared phthalocyanine dye molecules. This patent has a standard expiration date of September 18, 2034, subject to potential extensions.

The sixth patent family, which we own, includes a pending patent application in each of the United States, Australia, Canada, China, Europe, Japan and Korea with claims directed to an ophthalmic composition that includes a near-isotonic solution of virus-like particle 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 seventh patent family, which we co-own with DHHS/NIH and have exclusive rights under a CRADA, includes a pending patent application in each of the United States, Australia, Brazil, Canada, China, Europe, Israel and 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 eighth patent family, which we own, includes a pending United States provisional application with claims directed to a method for treating a bladder tumor by administering a therapeutic agent to a region of the lamina propria of the bladder wall that is proximate to the bladder tumor. Patents issuing from applications claiming priority to this provisional application would have a standard expiration date of September 2042 (assuming an international PCT application claiming priority to this U.S. provisional application is filed in September 2022).

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 initially focused our product development, the FDA regulates biologics under the 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, AU-011, 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.

Preclinical and clinical trials for biologics

Before testing any drug or biologic in humans, the product candidate must undergo rigorous preclinical testing. Preclinical 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 preclinical studies is subject to federal and state regulations and requirements, including GLP requirements for safety and toxicology studies. The results of the preclinical 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 study 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.

While we plan to conduct any international clinical trials under our INDs, 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.

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 biologics license application, or 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 (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 Prescription Drug User Fee Act, or 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. The FDA may withdraw approval of a drug or biologic approved under Accelerated Approval if, for example, the sponsor fails to conduct the confirmatory trials in a timely manner or the 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.

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 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.

Orphan Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation, or 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.

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 and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

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 current GMP 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 the Department of Health and Human Services, or HHS, 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.

Further, due to the COVID-19 pandemic, millions of individuals have lost/will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our products. It is unclear what effect, if any, the American Rescue Plan will have on the number of covered individuals.

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;
- the federal false claims and civil monetary penalties laws, including the False Claims Act and Civil Monetary Penalties Law, 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;
- 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 HHS information related to physician (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) payments and other transfers of value and the ownership and investment interests of such physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include payments and other transfers of value made in the previous year to certain nonphysician providers, including physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 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;
- 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 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; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; 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 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of January 1, 2019) 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.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states on procedural grounds without specifically ruling on the constitutionality of the ACA. Thus, the ACA will remain in effect in its current form. Prior to the Supreme Court's decision, President Biden issued an Executive Order that initiated a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how other healthcare reform measures of the Biden administration or other efforts, if any, to challenge repeal or replace the ACA, will impact our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year and, due to subsequent legislative amendments, will remain in effect through 2030 unless additional Congressional action is taken. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic.

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

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. For example, at the federal level, in a recent executive order, the Biden administration expressed its intent to pursue certain policy initiatives to reduce drug prices. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

Regulation in the European Union

Drug Development

In the European Union, our product candidates may be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained.

Similar to the United States, the various phases of preclinical and clinical research in the European Union are subject to significant regulatory controls. Although the EU Clinical Trials Directive 2001/20/EC, or the Directive, has sought to harmonize the EU clinical trials regulatory framework, setting out common rules for the control and authorization of clinical trials in the European Union, the EU Member States have transposed and applied the provisions of the Directive differently. This has led to significant variations in the Member State regimes. Under the current regime, before a clinical trial can be initiated it must be approved in each of the EU countries where the trial is to be conducted by two distinct bodies: the national competent authority, or CA, and one or more independent ethics committees, or ECs. Under the current regime, all suspected unexpected serious adverse reactions to the investigated drug that occur during the clinical trial have to be reported to the CA and ECs of the Member State where they occurred.

The EU clinical trials legislation currently is undergoing a transition process mainly aimed at harmonizing and streamlining clinical trial authorization, simplifying adverse-event reporting procedures, improving the supervision of clinical trials and increasing their transparency. In April 2014, the EU adopted a new Clinical Trials Regulation (EU) No 536/2014, or the Regulation, which is set to replace the current Clinical Trials Directive 2001/20/EC. It is expected that the new Regulation will become fully applicable at the end of January 2022. The new Regulation will be directly applicable in all 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 instance by providing for a streamlined application procedure via a single point and strictly defined deadlines for the assessment of clinical study applications.

We are in the process of applying to renew our status with EMA as a small and medium-sized enterprise, or SME. If we obtain SME status with EMA, it will provide access to administrative, regulatory and financial support, including fee reductions for scientific advice and regulatory procedures.

Much like the Anti-Kickback Statue 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 European Union. The provision of benefits or advantages to induce or reward improper performance generally is usually governed by the national anti-bribery laws of European Union 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 European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual 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.

Drug Review and Approval

In the European Economic Area, or EEA, which is comprised of the Member States of the European Union together with Norway, Iceland and Liechtenstein, medicinal products can only be commercialized after obtaining a marketing authorization, or MA. There are two types of marketing authorizations.

- 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, and 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 EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the European Union. Under the centralized procedure the maximum timeframe for the evaluation of a 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 a 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 make the final decision to grant a marketing authorization, 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 a MA application under the accelerated assessment procedure is of 150 days, excluding stop-clocks, 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 EMA 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 marketing authorization. This may apply to medicinal products for human use that fall under the jurisdiction of the EMA, including those that aim at the treatment, the prevention, or the medical diagnosis of seriously debilitating or life-threatening diseases.

A conditional marketing authorization may be granted when the CHMP finds that, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, all the following requirements are met:

- the risk-benefit balance of the medicinal product is positive;
- it is likely that the applicant will be in a position to provide the comprehensive clinical data post-authorization;
- unmet medical needs will be fulfilled; and
- the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data is still required.

The granting of a conditional marketing authorization is restricted to situations in which only the clinical part of the application is not yet fully complete. Incomplete preclinical or quality data may only be accepted if duly justified and only in the case of a product intended to be used in emergency situations in response to public health threats. Conditional marketing authorizations are valid for one year, on a renewable basis. The MA holder will be required to complete ongoing trials or to conduct new trials with a view to confirming that the benefit-risk balance is positive. In addition, specific obligations may be imposed in relation to the collection of pharmacovigilance data.

Compassionate Use

Compassionate use programs allow for the use of unauthorized medicines for a specific group of patients under strict conditions. The EMA provides recommendations on how a medicine should be used in a compassionate use program and the type of patient who may benefit from treatment, however the individual Member States implement their own rules in respect of the administration of such programs. Competent authorities of the Member States can also ask the EMA for an opinion on how to administer, distribute and use certain medicines for compassionate use.

Compassionate use programs are only available for a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorized medicinal product. The medicinal product provided through a compassionate use program must either be the subject of an MA application or must be undergoing clinical trials.

New Chemical Entity Exclusivity

In the EEA, new chemical entities (including both small molecules and biological medicinal products), sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization, 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 marketing authorization can be submitted, and the innovator's data may be referenced, no generic or biosimilar product can be marketed 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 marketing authorization 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 a marketing authorization 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 EEA, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions with either (i) affect not more than 5 in 10,000 persons in the European Union, or (ii) where 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, no satisfactory method of diagnosis, prevention or treatment of the condition must have been authorized (or, if such a method exists, the product in question would be of significant benefit to those affected by the condition).

In the EEA, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following marketing approval 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 drug 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, marketing authorization may only be granted to a "similar medicinal product" for the same therapeutic indication 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 marketing authorization holder for the authorized product consents to a second orphan medicinal product application; or (iii) the marketing authorization 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 drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Pediatric Investigation Plan

In the EEA, companies developing a new medicinal product must agree upon a pediatric investigation plan, or PIP, with the EMA's Pediatric Committee, or PDCO, and must conduct pediatric clinical trials in accordance with that PIP, unless a waiver applies. The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which marketing authorization is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months' supplementary protection certificate, or SPC, extension, provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

PRIME Designation

In March 2016, the EMA launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation, where the marketing authorization application will be made through the centralized procedure. Eligible products must target conditions for which where is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the European Union or, if there is, the new medicine will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the EMA's CHMP or Committee for Advanced Therapies are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. Where, during the course of development, a medicine no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

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 Member States. The holder of a 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 European Union. Although general requirements for advertising and promotion of medicinal products are established under European Union directives, the details are governed by regulations in each Member State and can differ from one country to another.

Pricing and Reimbursement

In the European Union, pricing and reimbursement schemes vary widely from country to country. The delivery of healthcare in the European Union, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than European Union, 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 European Union 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. European Union 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 Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on health care 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 European Union 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 drugs. Inclusion of orphan drugs in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any drug. 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 Union Data Collection

The collection and use of personal data, including clinical trial data, in the European Economic Area, or the EEA, governed by the GDPR, which became effective May 25, 2018. The GDPR applies to any company established in the EEA and to companies established outside the EEA that process personal data in connection with the offering of goods or services to data subjects in the EU or the monitoring of the behavior of data subjects in the European Union. The GDPR enhances data protection obligations for data controllers of personal data, including stringent requirements relating to the consent of data subjects, expanded disclosures about how personal data is used, requirements to conduct privacy 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 data processors. The GDPR also imposes strict rules and restrictions on the transfer of personal data outside of the EEA to countries that do not ensure an adequate level of protection, like the United States. Failure to comply with the requirements of the GDPR and the related national data protection laws of the EEA Member States may result in fines up to 20 million euros or 4% of a company's global annual revenues for the preceding financial year, whichever is higher. Moreover, the GDPR grants data subjects the right to request deletion of personal information in certain circumstances, and claim material and non-material damages resulting from infringement of the GDPR.

Regulation in the United Kingdom

Brexit and the Regulatory Framework in the United Kingdom

The UK's withdrawal from the EU on January 31, 2020, commonly referred to as Brexit, has created significant uncertainty concerning the future relationship between the UK and the EU. The impact of Brexit on the ongoing validity in the UK of current EU authorizations for medicinal products, whether granted through the centralized procedure, decentralized procedure or mutual recognition, and on the future process for obtaining marketing authorization for pharmaceutical products manufactured or sold in the UK remains uncertain. On December 24, 2020, the EU and UK reached an agreement in principle on the framework for their future relationship, the EU-UK Trade and Cooperation Agreement, or the Agreement. The Agreement primarily focuses on ensuring free trade between the EU and the UK in relation to goods, including medicinal products. Although the body of the Agreement includes general terms which apply to medicinal products, greater detail on sector-specific issues is provided in an Annex to the Agreement. The Annex provides a framework for the recognition of GMP inspections and for the exchange and acceptance of official GMP documents. The regime does not, however, extended to procedures such as batch release certification. Among the changes that will now occur are that Great Britain (England, Scotland and Wales) will be treated as a third country. Northern Ireland will, with regard to EU regulations, continue to follow the EU regulatory rules. As part of the Agreement, the EU and the UK will recognize Good Manufacturing Practice (GMP) inspections carried out by the other party and the acceptance of official GMP documents issued by the other party. The Agreement also encourages, although it does not oblige, the parties to consult one another on proposals to introduce significant changes to technical regulations or inspection procedures. Among the areas of absence of mutual recognition are batch testing and batch release. The UK has unilaterally agreed to accept EU batch testing and batch release for a period of at least two years until January 1, 2023. However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. This means that medicinal products that are tested and released in the UK must be retested and re-released when entering the EU market for commercial use. As regards marketing authorizations, Great Britain will have a separate regulatory submission process, approval process and a separate national MA. Northern Ireland will, however, continue to be covered by the marketing authorizations granted by the European Commission.

Clinical Trials

The UK has implemented Directive 2001/20/EC into national law through the Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended), and therefore UK legislation currently is broadly aligned with the position in the European Union, where Member State regimes are derived from Directive 2001/20/EC. The extent to which the regulation of clinical trials in the UK will mirror the new European Union Regulation once that comes into effect is unknown at present.

Great Britain Marketing Authorizations

As a result of the Northern Irish Protocol, centralized European Union MAs will continue to be recognized in Northern Ireland. A separate MA is, however, required in order to place medicinal products on the market in Great Britain.

On January 1, 2021, all medicinal products with a current centralized MA were automatically converted to Great Britain MAs. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, the UK medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain MA. This is known as the EC Decision Reliance Procedure, or ECDRP. Under the ECDRP, submission of an MA application can be submitted to the MHRA at any time after the approval of a European Union MA; however, a delay in submission may affect the delivery of a decision within the specified timelines. Where a submission is made within five days of a positive opinion issued by the CHMP, the MHRA will aim to determine the Great Britain MA as soon as possible after European Commission approval, and by day 67 at the latest provided that the European Commission decision has been received.

The MHRA also offers a 150-day assessment timeline for all high quality applications for a UK, Great Britain or Northern Ireland MA. The 150-day timeline does not include a “clock-off” period which may occur if issues arise or points require clarification following an initial assessment of the application. Such issues should be addressed within a 60-day period, although extensions may be granted in exceptional cases.

Early Access to Medicines Scheme

The Early Access to Medicines Scheme, or EAMS, applies in relation to patients with life threatening or seriously debilitating conditions and aims to give such patients access to unauthorized medicines, when there is a clear unmet medical need. Under EAMS, the MHRA will undertake a two-step evaluation process of a medicine, which includes a promising innovative medicine designation (an indication that a product may be eligible for EAMS based on early clinical data) and a scientific opinion on the risks and benefits of the medicine based on data gathered from the patients who will benefit from the medicine. A positive EAMS scientific opinion is valid for one year (which can be renewed) and regular updates must be provided to the MHRA following such positive opinion.

Orphan Designation

Since January 1, 2021, a separate process for orphan drug designation to the European Union process has applied Great Britain. There is now no pre-marketing authorization orphan designation (as there is in the European Union) in Great Britain and the application for orphan designation will be reviewed by the MHRA at the time of an application for a UK or Great Britain MA. The criteria for orphan designation remain the same as in the European Union, save that they apply to Great Britain only (e.g. there must be no satisfactory method of diagnosis, prevention or treatment of the condition concerned in Great Britain, as opposed to the European Union).

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 the Health Information Technology for Economic and Clinical Health Act (HITECH Act), 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.

Employees and human capital resources

As of February 28, 2022, we had 52 full-time employees, of which 14 have M.D. (or its equivalent) Ph.D. or J.D. degrees. Within our workforce, 40 employees are engaged in research and development and 12 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.

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 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 $35.3 million and $22.2 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $152.1 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 AU-011 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 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. 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. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

Our ability to become profitable depends upon our ability to generate revenue. To date, we have not generated any revenue from any product sales. We have no products approved for commercial sale, and 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, AU-011 in primary choroidal melanoma and, additional oncology indications, other research programs from our VDC technology platform and any future product candidates;
- obtaining marketing approval for AU-011 and any future product candidates for which we complete clinical trials;
- transferring our manufacturing process to a commercial contract development and manufacturing organization for AU-011 and any future product candidates, including establishing and maintaining commercially viable supply and manufacturing relationships with third parties;
- launching and commercializing AU-011 and any future product candidates for which we obtain marketing approvals, either directly or with a collaborator or distributor;
- obtaining market acceptance of AU-011 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 AU-011 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 AU-011 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 AU-011 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 AU-011. 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 AU-011 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 preclinical 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 AU-011 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, will be sufficient to fund our operating expenses and capital expenditures into 2024. Advancing the development of AU-011 and other research programs will require a significant amount of capital. Our existing cash and cash equivalents will not be sufficient to fund AU-011 through regulatory approval, and we anticipate needing to raise additional capital to complete the development of and commercialize AU-011. 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 in general or more recently due to the COVID-19 pandemic 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 AU-011 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.

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 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 AU-011 in indeterminate lesions and primary choroidal melanoma and additional oncology indications, other research programs from our VDC technology platform, and any other future programs;
- establishing and maintaining relationships with contract research organizations, or CROs, and clinical sites for the clinical development of AU-011, 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 a commercial 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 AU-011, 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 AU-011 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 AU-011. We can provide no assurance that AU-011 will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of AU-011 or if AU-011 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 AU-011 is, and will remain, subject to comprehensive regulation by the FDA and foreign regulatory authorities. Failure to obtain regulatory approval for AU-011 in the United States, Europe and other major markets around the world will prevent us from commercializing and marketing AU-011 in such jurisdictions.

Even if we were to successfully obtain approval from the FDA and foreign regulatory authorities for AU-011, any approval might contain significant limitations related to use, including limitations on the stage or type of cancer AU-011 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 AU-011. Furthermore, even if we obtain regulatory approval for AU-011, 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 AU-011, 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 AU-011, 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 Investigational New Drug application, or IND, Premarket Approval, or PMA, 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 AU-011 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 don't 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 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, due to the COVID-19 pandemic, 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 not yet successfully initiated or completed any pivotal clinical trials nor commercialized any pharmaceutical products, which may make it difficult to evaluate our future prospects.

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 AU-011 program in indeterminate lesions and primary choroidal melanoma. We have not yet demonstrated an ability to successfully initiate or 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. Furthermore, we may conduct our first pivotal trial based on an adaptive design, which could increase the time spent on or costs associated with this trial. We are in the process of transferring our intended commercial manufacturing process to our intended external contract development and manufacturing organization, or CDMO, commercial manufacturing site. During this transfer process, some modifications may be needed to ensure manufacturability and ability to scale-up the process to commercial batch sizes. 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 may be required, which may result in delayed regulatory approval. We do not anticipate a change in formulation. 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, our commercial opportunity could be limited.

We expect to focus our resources on the development of AU-011 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.

AU-011 is a biologic that requires the use of multiple devices, which may result in additional regulatory risks.

AU-011 is a novel biologic for which the intended use requires activation by a laser, which is regulated as a medical device. We plan to file a single BLA for the review and approval of this combination in our initial target indication of indeterminate lesions and small choroidal melanoma, but subsequent indications and delivery systems may require different or additional applications for marketing authorization. In addition, consistent with recent FDA guidance as seen with the approval of Xipere, Clearside Biomedical's SCS Microinjector® is also expected to be regulated as a medical device and suprachoroidal administration of AU-011 with this device is expected to constitute a combination product. As such, we may also include the SCS Microinjector in our BLA. There may be additional regulatory risks for biologic-device combination products. We may experience delays in obtaining regulatory approval of AU-011 given the increased complexity of the review process when approval of the product and a delivery device is sought under a single marketing application. 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. 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 AU-011 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. For example, we are planning to use Phase 2 drug product to initiate our first pivotal study and transitioning to the intended commercial drug product as soon as it available to conduct the second planned pivotal study. 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 the 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.

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. Furthermore, our ability to enroll patients may be significantly delayed by the evolving COVID-19 pandemic, and we cannot accurately predict the extent and scope of such delays at this point. 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 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 AU-011 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 trails 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, including the impacts of the ongoing COVID-19 pandemic, that may limit patients, principal investigators or staff or clinical site availability.

We may in the future conduct 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 may in the future choose to conduct one or more clinical trials outside the United States, including in Europe. The acceptance of study 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 U.S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction.

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 U.S. 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 U.S., 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. AU-011 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, AU-011 may not be effective at slowing or arresting tumor growth or may not preserve visual acuity in later stage trials. Even if AU-011 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 AU-011 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 any other product candidates then under development and/or cause the FDA or other regulatory authorities to require additional testing before approving any other product candidates.

As an organization, we have never conducted pivotal clinical trials, and we may be unable to do so for any product candidates we may develop.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA, the European Medicines Agency (EMA), or other regulatory agencies to market AU-011 or any future product candidate. Carrying out later-stage clinical trials is a complicated process. As an organization, we have not previously conducted any later stage or pivotal clinical trials. In order to do so, we will need to expand our clinical development 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 the trials on our behalf. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to approval of AU-011 or future product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

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

From time to time, we may publicly disclose preliminary, 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 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 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 AU-011 when studied in a controlled environment with a placebo or active control.

AU-011 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 AU-011 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 AU-011 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, subjects 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 subjects. 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 subjects 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 AU-011 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 subjects 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 boards, 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 clinical research organizations, or 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;
- clinical trials of our product candidates may be delayed due to complications associated with the evolving COVID-19 pandemic;
- 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 AU-011 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, including those caused by the ongoing COVID-19 pandemic, 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 expense. Additionally, our product candidates, if approved, could be subject to post-market study 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. 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 addition 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 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 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.

We may be unable to obtain orphan drug designations 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. Orphan drug designation must be requested before submitting an NDA or BLA. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has orphan drug designation 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 AU-011 for the treatment of uveal melanoma, and we may seek additional orphan drug designations for some or all of our current or future product candidates in orphan indications in which there is a medically plausible basis for the use of these products. Even if we obtain orphan drug designation, 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.

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 AU-011 for the treatment of choroidal melanoma, and we may seek additional fast track designations 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 our current 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. These confirmatory trials must be completed with due diligence. 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.

Risks Related to Our Reliance on Third Parties

We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, 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, medical institutions and clinical investigators, to conduct some aspects of our research, preclinical testing and clinical trials. We plan to use a clinical CRO for at least part of the potentially pivotal trial for AU-011 for the treatment of 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 contract manufacturing organizations, or CMOs, for the production of clinical supply of AU-011 and may continue to rely on CMOs for the production of commercial supply of AU-011, if approved. This reliance on CMOs 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 pre-clinical 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 AU-011.

We or our third-party suppliers or manufacturers may encounter shortages in the raw materials or active pharmaceutical ingredient, or API, necessary to produce AU-011 and future product candidates we may develop in the quantities needed for our clinical trials or, if AU-011 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 AU-011 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 AU-011 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 CMOs 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 CMO 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 CMO 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 AU-011 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 CMOs and third-party suppliers are expected to comply with and respect the intellectual property and proprietary rights of others. If a CMO 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 CMOs 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;
- 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 AU-011 or any future product candidates for use in clinical trials or for commercial supply, including as a result of the COVID-19 pandemic;
- 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.

AU-011 and any other product candidates that we may develop may compete with other product candidates and products for access to manufacturing facilities. Additionally, three vaccines for COVID-19 were granted Emergency Use Authorization by the FDA in late 2020 and early 2021, and one of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, may make it more difficult to obtain materials or manufacturing slots for the products needed for our clinical trials, which could lead to delays in these trials. 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 AU-011 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 AU-011 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 AU-011 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 AU-011 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 virus-like drug conjugates, or 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 AU-011 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 AU-011 and any future product candidates may require significant resources and may not be successful. If AU-011 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 AU-011 and any future product candidates will depend on a number of factors, including:

- the efficacy of AU-011 and our virus-like particle, or VLP, technology, and any future product candidates;
- the prevalence and severity of adverse events associated with AU-011 and any future product candidates or those products with which they may be co-administered;
- the clinical indications for which AU-011 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 AU-011 and any future product candidates that may be more restrictive than other competitive products;
- changes in the standard of care for the targeted indications for AU-011 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 AU-011 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 AU-011 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 AU-011 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 AU-011 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 AU-011 and any future product candidates, as well as competitive products;
- our ability to offer AU-011 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 AU-011 or competing products and treatments;
- the actions of companies that market any products with which AU-011 and any future product candidates may be co-administered;
- the approval of other new products;
- adverse publicity about AU-011 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 European Union (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 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 that are unresponsive to Bacillus Calmette-Guerin, such as Sesen Bio, Inc., FerGene, Inc., UroGen Pharma Ltd., CG Oncology, Inc. and ImmunityBio, Inc. 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 "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.

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 the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, or HHS. 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.

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.

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, that the level of reimbursement will be sufficient. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, 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.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States, particularly in light of the most recent presidential election, 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 AU-011 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 AU-011 and any future product candidates has not been established with precision. AU-011 is a virus-like drug conjugate product candidate being developed for the first line treatment of primary 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 AU-011 is approved for sale, acceptance by the medical community and patient access, product pricing and reimbursement. The number of patients with choroidal melanoma, choroidal metastases and NMIBC for which AU-011 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. AU-011 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. Such laws include, but are not limited to:

- The federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, the purchase, lease, order, arrangement, or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it 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 money penalties;
- The federal civil and criminal false claims laws and Civil Monetary Penalties Law, such as the federal False Claims Act, which impose criminal and civil penalties and authorize civil whistleblower or qui tam actions, against individuals or entities for, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; knowingly making, using or causing to be made or used, a false statement of record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. 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, which created new federal criminal statutes that prohibit a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious, or fraudulent statements or representations in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to 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;

- The United States Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the government information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other health care professionals beginning in 2022 (physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists & anesthesiologist assistants, and certified nurse-midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members;
- Federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs; and
- Federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

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 European Union General Data Protection Regulation, which became effective May 2018 also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. 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. In the United States, there have been, and continue to be, a significant number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education and Reconciliation Act, or collectively, the ACA, was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the United States pharmaceutical industry. The ACA, among other things, subjects biological products to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (increased to 70% pursuant to the Bipartisan Budget Act of 2018, effective as of 2019) 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. Since then, the ACA risk adjustment program payment parameters have been updated annually.

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. On June 17, 2021, the U.S. Supreme Court dismissed on procedural grounds the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an Executive Order that initiated a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how other healthcare reform measures of the Biden administrations or other efforts, if any, to challenge repeal or replace the ACA, will impact our business.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, President Biden signed an Executive Order on July 9, 2021, affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. The FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Further, on November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. The MFN Model regulations mandate participation by identified Part B providers and would have applied to all U.S. states and territories for a seven-year period beginning January 1, 2021, and ending December 31, 2027. On December 28, 2020, the U.S. District Court for the Northern District of California issued a nationwide preliminary injunction against implementation of the interim final rule. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the MFN Model interim final rule shall not commence earlier than sixty (60) days after publication of that regulation in the Federal Register. Further, authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. If implemented, importation of drugs from Canada and the MFN Model may materially and adversely affect the price we receive for any of our product candidates. Additionally, on December 2, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. On November 30, 2020, HHS published a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Further, implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. 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 it will continue to seek new legislative measures to control drug costs. For example, based on a recent executive order, the Biden administration expressed its intent to pursue certain policy initiatives to reduce drug prices.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, and, due to subsequent legislative amendments, will remain in effect through 2030, unless additional Congressional action is taken. Pursuant to the Coronavirus Aid, Relief, and Economic Security Act, also known as the CARES Act, as well as subsequent legislation, these reductions have been suspended from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic.

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

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. 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.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future, including repeal, replacement or significant revisions to the ACA. 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. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

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 virus-like particles to target tumors and VDCs like AU-011, 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 AU-011 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 AU-011 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 AU-011, we may still not be able to make use or sell AU-011 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 AU-011 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 AU-011 or any future product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize AU-011 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 AU-011 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 AU-011 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 AU-011 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 our AU-011 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, AU-011 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 AU-011 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, AU-011 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, 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 AU-011 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 AU-011 or a future product candidate, or forced to modify AU-011 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 AU-011 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 AU-011 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 AU-011 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 AU-011 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 U.S., or from selling or importing products made using our inventions in and into the U.S. 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 LI-COR maintains its manufacture of IRDye 700DX® dye molecules (used in AU-011) 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 AU-011. 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 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 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 Cambridge, Massachusetts, 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.

The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. The COVID-19 pandemic continues to evolve, and has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. The extent to which the ongoing COVID-19 pandemic impacts our operations or those of our third party partners, including our preclinical studies or clinical trial operations, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the pandemic, the emergence of new variants that may be more severe or contagious, acceptance of vaccines and the actions of government authorities, health systems, and private companies to contain the spread of COVID-19 or treat its impact, among others. The continued spread of COVID-19 globally could adversely impact our preclinical or clinical trial operations in the United States, including our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19. For example, similar to other biopharmaceutical companies, we may experience delays in initiating IND-enabling studies, protocol deviations, enrolling our clinical trials, or dosing of patients in our clinical trials as well as in activating new trial sites. COVID-19 may also affect employees of third-party CROs located in affected geographies that we rely upon to carry out our clinical trials. Any negative impact COVID-19 has to patient enrollment or treatment or the execution of our product candidates could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

Additionally, timely enrollment in planned clinical trials is dependent upon clinical trial sites which could be adversely affected by global health matters, such as pandemics. Some factors from the ongoing COVID-19 pandemic that will delay or otherwise adversely affect enrollment in the clinical trials of our product candidates, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on pandemic concerns, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials;
- limitations on travel that could interrupt key trial and business activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites, as well as any government-imposed travel restrictions or quarantines or employer-required isolation requirements that will impact the ability or willingness of patients, employees or contractors to travel to our clinical trial sites or secure visas or entry permissions, a loss of face-to-face meetings and other interactions with potential partners, any of which could delay or adversely impact the conduct or progress of our prospective clinical trials;
- the potential negative affect on the operations of our third-party manufacturers;
- interruption in global shipping affecting the transport of clinical trial materials, such as drug product and conditioning drugs and other supplies used in our clinical trials;
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments;
- operations, staffing shortages, travel limitations or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors;
- changes in local regulations as part of a response to the COVID-19 pandemic, which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether; and
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines.

We have taken temporary precautionary measures intended to help minimize the risk of the virus to our employees, including temporarily requiring certain of our employees to work remotely, suspending all non-essential travel worldwide for our employees and discouraging employee attendance at industry events and in-person work-related meetings, which could negatively affect our business. We cannot presently predict the scope and severity of the planned and potential shutdowns or disruptions of businesses and government agencies, such as the SEC, or the FDA. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. Since April 2021, the FDA has conducted limited inspections and employed remote interactive evaluations, using risk management methods, to meet user fee commitments and goal dates. Ongoing travel restrictions and other uncertainties continue to impact oversight operations both domestic and abroad and it is unclear when standard operational levels will resume. The FDA is continuing to complete mission-critical work, prioritize other higher-tiered inspectional needs (e.g., for-cause inspections), and carry out surveillance inspections using risk-based approaches for evaluating public health. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. During the COVID-19 public health emergency, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the ongoing COVID-19 pandemic and may experience delays in their regulatory activities.

These and other factors arising from COVID-19 could worsen in countries that are already afflicted with COVID-19 or could continue to spread to additional countries. Any of these factors, and other factors related to any such disruptions that are unforeseen, could have a material adverse effect on our business and our results of operation and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize our programs and product candidates.

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 wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

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 security incidents, 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). It is critical that we do so in a secure manner 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 those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, 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 security incidents 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 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 or acquisition of information. Cyberattacks 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 security incidents 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 security breaches, may not be adequate to prevent or detect service interruption, system failure or data loss.

Significant disruptions of our information technology systems or security 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, the COVID-19 pandemic has resulted in a significant number of our employees and partners working remotely, which increases the risk of a data breach or issues with data and cybersecurity. To the extent that any disruption or security incident results in a loss of, or damage to, our data or applications, or inappropriate disclosure of 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 security incidents. 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 security 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 security 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 breach. In addition, our efforts to contain or remediate a security 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 security breaches may adversely affect our business. Unauthorized access to our information technology systems 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 security 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 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 the Health Insurance Portability and Accountability Act, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH. Depending on the facts and circumstances, we could be subject to significant penalties if we violate HIPPA. 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.

The CCPA became effective on January 1, 2020, and gives California residents expanded rights to access and delete their personal data, opt out of certain personal data sharing and receive detailed information about how their personal data is used. The CCPA requires covered businesses to provide new disclosures to California residents. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although there are limited exemptions for clinical trial data and the CCPA's implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, the CCPA may increase our compliance costs and potential liability. It is anticipated that the CCPA will be expanded on January 1, 2023, when the California Privacy Rights Act of 2020, or CPRA, becomes operative. The CPRA will, among other things, give California residents the ability to limit use of certain sensitive information, establish restrictions on the retention of personal data, expand the types of data breaches subject to the CCPA's private right of action and establish a new California Privacy Protection Agency to implement and enforce the new law. In addition, other states have enacted or proposed data privacy laws. For example, Virginia recently passed its Consumer Data Protection Act and Colorado recently passed the Colorado Privacy Act, both of which differ from the CPRA and go into effect in 2023. 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's GDPR and the EU member state implementing legislation, may also apply to health-related and other personal data that we process, including, without limitation, personal data relating to clinical trial participants. European data protection laws impose strict obligations on the ability to process health-related and other personal data of European data subjects, including in relation to security (which requires the adoption of administrative, physical and technical safeguards designed to protect such information), collection, use and transfer or personal data. European data protection laws may affect our use, collection, analysis, and transfer (including cross-border transfer) of such personal data. These include, without limitation, several requirements relating to transparency related to communications with data subjects regarding the processing of their personal data, obtaining the consent of the individuals to whom the personal data relates, limitations on the retention of personal data, increased requirements pertaining to health data, establishing a legal basis for processing, 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 transfer of personal data outside of Europe (including from the European Economic Area (EEA), Switzerland and United Kingdom (UK).

European data protection laws prohibit, without an appropriate legal basis, the transfer of personal data to countries outside of Europe, such as to the United States, which are not considered relevant authorities to provide an adequate level of data protection. A decision by the Court of Justice of the EU, or the "Schrems II" ruling, invalidated the EU-U.S. Privacy Shield Framework, and raised questions about whether the European Commission's Standard Contractual Clauses, or SCCs, one of the primary alternatives to the Privacy Shield, can lawfully be used for personal data transfers from Europe to the United States or most other countries. Similarly, the Swiss Federal Data Protection and Information Commissioner recently opined that the Swiss-U.S. Privacy Shield is inadequate for transfers of personal data from Switzerland to the United States. The UK, whose data protection laws are similar to those of the EU, has similarly determined that the EU-U.S. Privacy Shield is not a valid mechanism for lawfully transferring personal data from the UK to the U.S. Use of the SCCs must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular, applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place. However, the nature of these additional measures is currently uncertain. Additionally, the European Commission recently adopted new SCCs that will repeal the SCCs adopted under the Data Protection Directive. This means we may need to update our contracts that involve the transfer of personal data outside of the EEA to the new SCCs. As supervisory authorities issue further guidance on personal data export mechanisms, including on the new SCCs, and/or start taking enforcement action, our compliance costs could increase, we may be subject to complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we conduct clinical trials, this could negatively impact our business.

Further, the UK's decision to leave the EU, often referred to as Brexit, and ongoing developments in the UK have created uncertainty regarding data protection regulation in the UK. Following December 31, 2020, and the expiry of transitional arrangements between the UK and EU, the data protection obligations of the GDPR continue to apply to UK-related Processing of personal data in substantially unvaried form under the so-called "UK GDPR" (i.e., the GDPR as it continues to form part of UK law by virtue of section 3 of the EU (Withdrawal) Act 2018, as amended). However, going forward, there is increasing risk for divergence in application, interpretation and enforcement of the data protection laws as between the UK and EEA. Furthermore, the relationship between the UK and the EEA in relation to certain aspects of data protection law remains uncertain, including with respect to regulation of data transfers between the EU member states and the UK. On June 28, 2021, the European Commission issued an adequacy decision under the GDPR which allows transfers (other than those carried out for the purposes of the UK immigration control) of personal data from the EEA to the UK to continue without restriction for a period of four years ending June 27, 2025. After that period, the adequacy decision may be renewed, but, only if the UK continues to ensure an adequate level of data protection. During these four years, the European Commission will continue to monitor the legal situation in the UK and could intervene at any point if the UK deviates from the level of data protection in place at the time of issuance of the adequacy decision. If the adequacy decision is withdrawn or not renewed, transfers of personal data from the EEA to the UK will require a valid 'transfer mechanism' and we may be required to implement new processes and put new agreements in place, such as SCCs, to enable transfers of personal data from the EEA to the UK to continue.

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 or 4% of their worldwide annual turnover (revenue). Additionally, regulators could prohibit our use of personal data subject to 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.

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. 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 or security breaches. Moreover, clinical trial participants or subjects 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.

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.

We do not yet maintain product liability insurance, and we anticipate that we will need to increase our insurance coverage when we begin 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, 2021, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 60.8% 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 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, 2021, we had federal gross operating loss carryforwards of approximately $138.7 million, and state gross operating loss carryforwards of $113.6 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 net operating losses 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. For a further description of our dividend policy, please refer to the section entitled "Dividend Policy."

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 AU-011 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.

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 (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 (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 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 fourth 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 (the "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 fourth 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.

General Risks

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.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, in 2008, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets and the current COVID-19 pandemic has caused significant volatility and uncertainty in the U.S. and international markets. See "Risks Related to our Business and Industry—The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates." In addition, the current military conflict between Russia and Ukraine could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions that may be initiated by nations including the U.S., the European Union or Russia (e.g., potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with which we conduct business. A severe or prolonged economic downturn or political unrest could result in a variety of risks to our business, including, 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 economic climate and financial market conditions could adversely impact 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 or Section 404, as amended, (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 $1.07 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 their 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 on Form 10-K entitled “Risk Factors” and the following:

- results of preclinical studies and results or enrollment of clinical trials of AU-011 or our future product candidates, or those of our potential future competitors or our existing or future collaborators;
- the impact of the COVID-19 pandemic on our employees, trials, collaboration partners, suppliers, our results of operations, liquidity and financial condition;
- 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 AU-011 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;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters, pandemics and other calamities; and
- general economic, industry and market conditions.

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 insubstantial 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 will be required to devote substantial time to new 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are located in Cambridge, Massachusetts, where we lease and occupy approximately 14,354 square feet of office space at 85 Bolton St, Cambridge, MA 02140. The current term of our Cambridge lease expires in July 2023.

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, 2021, 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".

Holders of record

As of March 21, 2022, we had approximately 132 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.

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

On November 2, 2021, upon the closing of our IPO, all 308,332,857 shares of our then-outstanding convertible preferred stock automatically converted into 22,550,561 shares of our common stock. The issuance of such common stock was exempt from the registration requirements of the Securities Act, pursuant to Section 3(a)(9) of the Securities Act, involving an exchange of securities exchanged by the issuer with its existing security holders exclusively where no commission or other remuneration is paid or given directly or indirectly for soliciting such exchange. No underwriters were involved in this issuance of shares.

During the period between January 1, 2021 and September 30, 2021, we issued to certain of our employees, advisors and directors, options to purchase an aggregate of 1,883,480 shares of our common stock at an average exercise price of $6.13 per share. We deemed these issuances to be exempt from registration under the Securities Act in reliance on Rule 701 of the Securities Act as sales and offers under compensatory benefit or Section 4(a)(2) of the Securities Act as sales and offers not involving a public offering.

Use of Proceeds from Initial Public Offering of Common Stock

On November 2, 2021, the Company completed its initial public offering, or the IPO, in which it issued and sold 5,400,000 shares of its common stock at a public offering price of $14.00 per share. The Company received net proceeds from the IPO of $67.8 million, after deducting underwriters' discounts, commissions and offering-related costs. In connection with the IPO, the Company granted the underwriters a 30-day option to purchase an additional 810,000 shares. On November 8, 2021, the underwriters exercised the option in full and the Company issued 810,000 shares of common stock for aggregate net proceeds of $10.5 million after deducting underwriter discounts and commissions of $0.8 million.

The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1, as amended (File No. 333- 260156), which was declared effective by the SEC on October 28, 2021. Cowen and Company, LLC, SVB Leerink LLC, Evercore Group L.L.C. and BTIG, LLC acted as underwriters for the IPO.

No expenses incurred by the Company in connection with the IPO were paid directly or indirectly to (i) any of its officers or directors or their associates, (ii) any persons owning 10% or more of any class of its equity securities, or (iii) any of its affiliates, other than payments in the ordinary course of business to officers for salaries and to non-employee directors as compensation for board or board committee service.

There has been no material change in the planned use of proceeds from the IPO from those disclosed in the Prospectus. We plan to invest the funds received in cash equivalents and other marketable securities in accordance with our investment policy.

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.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes thereto included in Part II, Item 8 "Financial Statements and Supplementary Data". This discussion contains forward-looking statements that reflect our plans, estimates and beliefs and involve numerous risks and uncertainties, including but not limited to those described in Part I, Item 1A "Risk Factors" of this Annual Report on Form 10-K. Actual results may differ materially from those contained in any forward-looking statements. You should carefully read "Special Note Regarding Forward-Looking Statements" and Part I, Item 1A, "Risk Factors."

Overview

We are a clinical-stage biotechnology company leveraging our novel targeted oncology platform to develop a potential new standard of care across multiple cancer indications, with an initial focus on ocular and urologic oncology. Our proprietary platform enables the targeting of a broad range of solid tumors using Virus-Like Particles, or VLPs, that can be conjugated with drugs or loaded with nucleic acids to create Virus-Like Drug Conjugates, or VDCs. Our VDCs are largely agnostic to tumor type and can recognize a surface marker, known as heparan sulfate proteoglycans, or HSPGs, that are specifically modified and broadly expressed on many tumors. AU-011, our first VDC candidate, is being developed for the first line treatment of primary choroidal melanoma, a rare disease with no drugs approved. We have completed a Phase 1b/2 trial using intravitreal administration that has demonstrated a statistically significant growth rate reduction in patients with prior active growth and high levels of tumor control with visual acuity preservation in a majority of patients, as assessed using clinical endpoints in alignment with the feedback from U.S. Food and Drug Administration, or the FDA. These data supported advancement into a Phase 2 dose escalation trial, where we are currently evaluating suprachoroidal, or SC, administration of AU-011. We plan to present six to twelve month safety and efficacy data from this trial in 2022 and, take a decision on the route of administration to, initiate a pivotal trial in the second half of 2022. We are also developing AU-011 for additional ocular oncology indications and plan to file an IND in the United States in the second half of 2022 for choroidal metastases. Leveraging our VDCs' broad tumor targeting capabilities, we also plan to initiate a Phase 1a trial in non-muscle invasive bladder cancer, or NMIBC, our first non-ophthalmic solid tumor indication, in the second half of 2022 and present Phase 1a data from this trial in 2023.

We were incorporated as a Delaware corporation in 2009 and our headquarters are located in Cambridge, 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, 2021, we have raised an aggregate of approximately $218.6 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. In November 2021, we issued and sold 6,210,000 shares of our common stock, including the full exercise of the underwriters' option to purchase additional shares at a price to the public of $14.00 per share for aggregate gross proceeds of $86.9 million in our IPO. We received approximately $78.3 million in net proceeds after deducting underwriting discounts, commissions and offering expenses.

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 $35.3 million and $22.2 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $152.1 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 AU-011;
- progress the preclinical and clinical development of new indications;
- establish our manufacturing capability, including developing our contract development and manufacturing 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, 2021, we had cash and cash equivalents of $149.1 million. In November 2021, we issued and sold 6,210,000 shares of our common stock, including the full exercise of the underwriters' option to purchase additional shares at a price to the public of $14.00 per share for aggregate gross proceeds of $86.9 million in our IPO. We received approximately $78.3 million in net proceeds after deducting underwriting discounts, commissions and offering expenses. We believe that the net proceeds from the IPO, together with our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into 2024. 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.

Impact of the COVID-19 Pandemic

The ongoing COVID-19 pandemic continues to present substantial public health and economic challenges around the world, and to date has led to the implementation of various responses, including government-imposed quarantines, stay-at-home orders, travel restrictions, mandated business closures and other public health safety measures.

We continue to closely monitor the impact of the COVID-19 pandemic on all aspects of our business, including how it has and will continue to impact our operations and the operations of our suppliers, vendors and business partners, and may take further precautionary and preemptive actions as may be required by federal, state or local authorities. In addition, we have taken steps to minimize the current environment's impact on our business and strategy, including devising contingency plans and securing additional resources from third party service providers. For the safety of our employees and families, we have introduced enhanced safety measures for scientists to be present in our labs and increased the use of third party service providers for the conduct of certain experiments and studies for research programs. To date, we've only encountered minor delays in our manufacturing process due to a supply chain constraint with one of our vendors.

Beyond the impact on our pipeline, the extent to which COVID-19 ultimately impacts our business, results of operations and financial condition will depend on future developments, which remain highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, the emergence of new variants, new information that may emerge concerning the severity of COVID-19 or the effectiveness of actions taken to contain COVID-19 or treat its impact, including vaccination campaigns, among others. If we or any of the third parties with whom we engage, however, were to experience any additional shutdowns or other prolonged business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially or negatively affected, which could have a material adverse impact on our business, results of operations and financial condition. Although to date, our business has not been materially impacted by COVID-19, it is possible that our clinical development timelines could be negatively affected by COVID-19, which could materially and adversely affect our business, financial condition and results of operations. See *Item 1A "Risk Factors" of this Annual Report on Form 10-K* for a discussion of the potential adverse impact of the COVID-19 pandemic on our business, financial condition and results of operations.

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 AU-011 program, and include:

- employee-related expenses, including salaries, related-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 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 AU-011, including the potential cost of CMOs 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 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 AU-011 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 AU-011 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 AU-011 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 being a public company, 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 changes in the fair value of our warrant liability, gain/loss on disposal of fixed assets, and interest income on our invested cash balances.

Income Taxes

Since our inception, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in any year or for our earned research and development tax credits, due to the uncertainty of realizing a benefit from those items. As of December 31, 2021, we had federal gross operating loss carryforwards of approximately $138.7 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 $94.5 million do not expire. The state gross operating loss carryforwards of $113.6 million, which may be available to offset future taxable income and which would begin to expire in 2030. As of December 31, 2021, we had federal and state research and experimentation credit carryforwards of $4.7 million and $1.4 million, respectively, which may be available to offset future income tax liabilities and which would begin to expire in 2029 and 2028, respectively. Due to the degree of uncertainty related to the ultimate use of the deferred tax assets, we have fully reserved these tax benefits, as the determination of the realization of the deferred tax benefits was not determined to be more likely than not.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

	Year ended December 31,		
	2021	2020	Change
	(in thousands)		
Operating expenses:			
Research and development	$ 25,161	$ 18,042	$ 7,119
General and administrative	10,089	4,164	5,925
Total operating expenses	35,250	22,206	13,044
Loss from operations	(35,250)	(22,206)	(13,044)
Other income (expense):			
Change in fair value of warrant liability	(11)	3	(14)
Interest income (expense), including amortization of discount	13	(3)	16
Loss from disposal of assets	(3)	—	(3)
Total other expense	(1)	—	(1)
Net loss and comprehensive loss	$ (35,251)	$ (22,206)	$ (13,045)

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2021 and 2020:

	Year ended December 31,		
	2021	2020	Change
	(in thousands)		
Preclinical	$ 1,548	$ 2,211	$ (663)
Clinical trials	3,417	3,057	360
Manufacturing development	8,070	4,965	3,105
Personnel/overhead expenses	12,126	7,809	4,317
Total research and development expenses	$ 25,161	$ 18,042	$ 7,119

Research and development expenses increased to $25.2 million for the year ended December 31, 2021, from $18.0 million for the year ended December 31, 2020, primarily due to ongoing manufacturing development costs for AU-011 and higher personnel expenses from growing headcount due to the progression of clinical trials.

General and Administrative Expenses

General and administrative expenses increased to $10.1 million for the year ended December 31, 2021, from $4.2 million for the year ended December 31, 2020, due to an increase in personnel expenses due to an increase in headcount, as well as general increases in audit, legal, consulting, insurance, regulatory, and facilities expenses related to operating as a public company.

Liquidity and Capital Resources

To date we have funded our operations primarily through the sale of convertible preferred stock, and common stock. Through December 31, 2021, we have raised an aggregate of approximately $218.6 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. In November 2021, we issued and sold a total of 6,210,000 shares in our IPO of our common stock, including the full exercise of the underwriters' option to purchase additional shares, at a price to the public of $14.00 per share for aggregate gross proceeds of $86.9 million. We received approximately $78.3 million in net proceeds after deducting underwriting discounts, commissions and offering expenses.

Cash Flows

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

	Year ended December 31,	
	2021	2020
	(in thousands)	
Net cash used in operating activities	$ (32,410)	$ (24,321)
Net cash used in investing activities	(2,125)	(771)
Net cash provided by financing activities	166,259	10,036
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 131,724	$ (15,056)

Operating Activities

During the year ended December 31, 2021, net cash used in operating activities was $32.4 million, primarily due to our net loss of $35.3 million and increase in prepaid expenses and other assets related to clinical trials, partially offset by the non-cash charge related to stock compensation expense, an increase in accrued expenses and other liabilities related to personnel expenses, and clinical trials and increase in accounts payable related to the timing of vendor invoicing and payments.

During the year ended December 31, 2020, net cash used in operating activities was $24.3 million, primarily due to our net loss of $22.2 million and decreases in accrued expenses and other liabilities related to personnel expenses and clinical trials as well as decrease in accounts payable related to the timing of vendor invoicing and payments.

Investing Activities

Net cash used in investing activities for the years ended December 31, 2021 and 2020 was $2.1 million and $0.8 million, respectively, due to purchases of property and equipment.

Financing Activities

During the year ended December 31, 2021, net cash provided by financing activities was $166.3 million from the net proceeds from the IPO, the sale of Series E convertible preferred stock, the second tranche of the Series D-2 convertible preferred stock, and proceeds from stock options exercises.

During the year ended December 31, 2020, net cash provided by financing activities was $10.0 million from the net proceeds from the sale of Series D-2 convertible preferred stock and proceeds from stock options exercises.

Funding Requirements

Our plan of operation is to continue implementing our business strategy, continue research and development of AU-011 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;
- our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payers;
- addressing any potential interruptions or delays resulting from factors related to the COVID-19 pandemic;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in businesses, products, and technologies.

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, 2021, we had cash and cash equivalents of $149.1 million. Based on our research and development plans, we believe that our existing cash and cash equivalents, will be sufficient to fund our operations into 2024. 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 resulting from the ongoing COVID-19 pandemic and otherwise. 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, 2021.

		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(1)	$ 1,002	$ 625	$ 377	$ —	$ —
Total	$ 1,002	$ 625	$ 377	$ —	$ —

(1) Amounts in the table above reflect payments due for our lease of office space in Cambridge, Massachusetts that expires July 2023.

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, CMOs 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. 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.

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 Securities and Exchange Commission, or 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. In the periods prior to the IPO, the determination of fair value of our common stock required significant judgment. In the periods following the IPO, the fair value of our common stock is determined based on the quoted market price of our common stock.

Prior to our IPO, there was no public market for our common stock, and consequently, the estimated fair value of our common stock was determined by our Board of Directors as of the date of each option grant, with input from management, considering third-party valuations of our common stock as well as our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the grant.

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 Jumpstart Our Business Startups Act of 2012, or 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. However, we did early adopt ASU No. 2016-02, Leases (*Topic 842*) effective January 1, 2021 as disclosed in Note 2 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K . 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 $1.07 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 EGC, 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 EGCs, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivity, which is affected by changes in the general level of the U.S interest rates. As of December 31, 2021, our cash and cash equivalents of $149.1 million included $24.1 million of money market funds that invest in the U.S. Treasury obligations and government funds with commercial banks and financial institutions. Our exposure to interest rate sensitivity is impacted by changes in the underlying U.S. bank interest rates but is minimal. We have not entered into investments for trading or speculative purposes.

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, 2021.

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 Securities and Exchange Commission's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

As of December 31, 2021, our management, under the supervision of our Chief Executive Officer and Chief Financial Officer, performed an evaluation of the effectiveness of our disclosure controls and procedures. Based on this evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2021.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives 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 the 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.

Changes in Internal Control over Financial Reporting

There were no material changes in our internal control over financial reporting during the quarter ended December 31, 2021, 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.

2022 Annual Stockholder Meeting

The Company currently plans to hold its 2022 Annual Meeting of Stockholders (the "Annual Meeting") on June 15, 2022 at 10:30 a.m. local time virtually. Pursuant to the provisions of the Company's Bylaws, for any stockholder to propose business (other than pursuant to and in compliance with Exchange Act Rule 14a-8) or make a nomination before the annual meeting, the stockholder must have given timely notice in writing to the secretary and any such nomination or proposed business must constitute a proper matter for stockholder action. Under the Company's Bylaws, to be timely, a stockholder's notice must be received by the secretary at the principal executive offices of the Company later than the close of business on the 90th day before the 2022 Annual Meeting nor earlier than the close of business on the 10th day following the day on which public announcement of the date of 2022 Annual Meeting is first made by the Company. Because the Company did not hold an annual meeting last year, the Company has determined that the date by which stockholders must deliver such notice for the purposes of the 2022 Annual Meeting is April 2, 2022, which is 10 days after the filing of this Annual Report on Form 10-K. Pursuant to Rule 14a-8, for a stockholder to submit a proposal for inclusion in the Company's proxy materials for the 2022 Annual Meeting, the stockholder must comply with the requirements set forth in Rule 14a-8 including with respect to the subject matter of such proposal and must deliver the proposal and all required documentation to the Company a reasonable time before the Company begins to print and send its proxy materials for the meeting. For the purposes of the 2022 Annual Meeting of Stockholders, the Company has determined that April 18, 2022 is a reasonable time before the Company plans to begin printing and mailing its proxy materials. The public announcement of an adjournment or postponement of the 2022 Annual Meeting date will not commence a new time period (or extend any time period) for giving such notice under the Company's Bylaws or submitting a proposal pursuant to Rule 14a-8.

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 the Company's 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 the Company's fiscal year ended December 31, 2021.

Item 11. Executive Compensation.

The information required under this item is incorporated herein by reference to the Company's 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 the Company's fiscal year ended December 31, 2021.

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 the Company's 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 the Company's fiscal year ended December 31, 2021.

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

The information required under this item is incorporated herein by reference to the Company's 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 the Company's fiscal year ended December 31, 2021.

Item 14. Principal Accounting Fees and Services.

The information required under this item is incorporated herein by reference to the Company's 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 the Company's fiscal year ended December 31, 2021.

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 Registrant
3.2*	Amended and Restated Bylaws of Registrant
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 10.3 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 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#	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 2021)
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 Julie Feder, dated August 10, 2018 (incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 2021)
10.10#	Employment Offer Letter between the Registrant and Cadmus Rich, dated October 14, 2017 (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 25, 2021)
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 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	Lease Agreement with Bolton Street Partners, LLC, dated June 9, 2011, as amended (incorporated by reference to Exhibit 10.14 of the Registrant's Registration Statement on Form S-1 (File No. 333-260156) filed on October 8, 2021)
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 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.
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 Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, 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 23, 2022 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 23, 2022
/s/ Julie Feder **Julie Feder**	Chief Financial Officer	March 23, 2022
/s/ David Johnson **David Johnson**	Chairman of the Board of Directors	March 23, 2022
/s/ Giovanni Mariggi **Giovanni Mariggi**	Director	March 23, 2022
/s/ Antony Mattessich **Anthony Mattessich**	Director	March 23, 2022
/s/ Raj Parekh **Raj Parekh**	Director	March 23, 2022
/s/ Sapna Srivastava **Sapna Srivastava**	Director	March 23, 2022
/s/ Karan Takhar **Karan Takhar**	Director	March 23, 2022

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Report of Independent Registered Public Accounting Firm (PCAOB ID 42)	F-2
Consolidated Balance Sheets	F-3
Consolidated Statements of Operations and Comprehensive Loss	F-4
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)	F-5
Consolidated Statements of Cash Flows	F-6
Notes to Consolidated Financial Statements	F-7

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, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' deficit and cash flows for the years then ended, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated 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 consolidated 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 consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. 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 23, 2022

Aura Biosciences, Inc.

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

	December 31,	
	2021	**2020**
Assets		
Current assets:		
Cash and cash equivalents	$ 149,063	$ 17,393
Restricted cash and deposits	23	19
Prepaid expenses and other current assets	4,618	1,043
Total current assets	153,704	18,455
Restricted cash and deposits, net of current portion	125	75
Right of use assets - operating lease	950	—
Property and equipment, net	5,251	3,574
Total Assets	$ 160,030	$ 22,104
Liabilities, Convertible Preferred Stock, and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	2,401	611
Short-term operating lease liability	615	—
Accrued expenses and other current liabilities	4,256	2,050
Total current liabilities	7,272	2,661
Deferred rent	—	8
Long-term operating lease liability	360	—
Warrant liability	83	72
Total Liabilities	7,715	2,741
Commitments and Contingencies (Note 12)		
Convertible preferred stock (Note 7)	—	128,076
Stockholders' Equity (Deficit):		
Common stock, $0.00001 par value, 150,000,000 and 232,697,999 authorized at December 31, 2021, and December 31, 2020, and 29,211,643 and 381,123 shares issued and outstanding at December 31, 2021, and December 31, 2020, respectively	—	—
Additional paid-in capital	304,452	8,173
Accumulated deficit	(152,137)	(116,886)
Total Stockholders' Equity (Deficit)	152,315	(108,713)
Total Liabilities, Convertible Preferred Stock, and Stockholders' Deficit	$ 160,030	$ 22,104

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 for share and per share data)

	Year Ended December 31,	
	2021	2020
Operating Expenses:		
Research and development	25,161	18,042
General and administrative	10,089	4,164
Total operating expenses	35,250	22,206
Total operating loss	(35,250)	(22,206)
Other income (expense):		
Change in fair value of warrant liability	(11)	3
Interest income (expense), including amortization of discount	13	(3)
Loss on disposal of assets	(3)	—
Total other expense	(1)	—
Net loss and comprehensive loss	$ (35,251)	$ (22,206)
Net loss attributable to common stockholders—basic and diluted (Note 13)	$ (46,193)	$ (30,132)
Net loss per share attributable to common stockholders—basic and diluted	(8.95)	(82.06)
Weighted average common stock outstanding—basic and diluted	5,159,973	367,204

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

Aura Biosciences, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Convertible Preferred Stock														Common Stock		Additional Paid-In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Series A		Series A-1		Series A-2		Series B		Series C-1 and C-2		Series D-1 and D-2		Series E						
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
Balance, December 31, 2019	1,701,141	$3,368	3,298,732	$7,837	4,324,998	$5,373	22,531,819	$20,806	91,327,903	$41,099	57,878,742	$39,686	—	$—	340,591	$-	$7,274	$(94,680)	$(87,406)
Issuance of Series D convertible preferred stock, net of issuance costs of $93	—	—	—	—	—	—	—	—	—	—	14,469,710	9,907	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	736	—	736
Stock options exercises	—	—	—	—	—	—	—	—	—	—	—	—	—	—	40,532	—	163	—	163
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(22,206)	(22,206)
Balance, December 31, 2020	1,701,141	$3,368	3,298,732	$7,837	4,324,998	$5,373	22,531,819	$20,806	91,327,903	$41,099	72,348,452	$49,593	—	$—	381,123	$-	$8,173	$(116,886)	$(108,713)
Issuance of Series D convertible preferred stock, net of issuance costs of $18	—	—	—	—	—	—	—	—	—	—	10,128,771	6,982	—	—	—	—	—	—	—
Issuance of Series E convertible preferred stock, net of issuance costs of $237	—	—	—	—	—	—	—	—	—	—	—	—	102,671,041	80,246	—	—	—	—	—
Issuance of common stock - as a result of IPO, net of issuance costs $8,620	—	—	—	—	—	—	—	—	—	—	—	—	—	—	6,210,000	—	78,320	—	78,320
Conversion of convertible preferred stock to common stock upon closing of IPO	(1,701,141)	(3,368)	(3,298,732)	(7,837)	(4,324,998)	(5,373)	(22,531,819)	(20,806)	(91,327,903)	(41,099)	(82,477,223)	(56,575)	(102,671,041)	(80,246)	22,550,561	—	215,304	—	215,304
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2,307	—	2,307
Stock options exercises	—	—	—	—	—	—	—	—	—	—	—	—	—	—	69,959	—	348	—	348
Net loss	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(35,251)	(35,251)
Balance, December 31, 2021	—	$—	—	$—	—	$—	—	$—	—	$—	—	$—	—	$—	29,211,643	$-	$304,452	$(152,137)	$152,315

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,	
	2021	2020
Cash flows from operating activities:		
Net loss	$ (35,251)	$ (22,206)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation expense	831	831
Change in fair value of warrant liability	11	(3)
Stock-based compensation expense	2,307	736
Gain on disposal of property and equipment	3	—
Operating lease expense	4	—
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(3,575)	(165)
Accounts payable	1,054	(1,721)
Accrued expenses and other liabilities	2,206	(1,793)
Net cash used in operating activities	(32,410)	(24,321)
Cash flows from investing activities:		
Purchases of property and equipment	(2,125)	(771)
Net cash used in investing activities	(2,125)	(771)
Cash flows from financing activities:		
Proceeds from issuance of common stock upon IPO, net of issuance costs	78,697	—
Proceeds from exercise of stock options	349	163
Proceeds from issuance of Series E convertible preferred stock, net of issuance costs	80,246	—
Proceeds from issuance of Series D convertible preferred stock, net of issuance costs	6,982	9,907
Other	(15)	(34)
Net cash provided by financing activities	166,259	10,036
Net increase (decrease) in cash, cash equivalents and restricted cash	131,724	(15,056)
Cash, cash equivalents and restricted cash at beginning of period	17,487	32,543
Cash, cash equivalents and restricted cash at end of period	$ 149,211	$ 17,487
Supplemental disclosure of cash flow information:		
Purchases of property and equipment in accounts payable and accrued expenses and other liabilities	$ 386	$ —
Initial measurement of operating lease right-of-use assets and liabilities	$ 536	$ —
Right-of-use assets obtained in exchange for operating lease liabilities	$ 516	$ —
Remeasurement of operating lease right-of-use assets and liabilities for lease modification	$ 390	$ —
Deferred offering costs in accounts payable	$ 377	$ —

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

	Year ended December 31,	
	2021	2020
Cash and cash equivalents, end of period	$ 149,063	$ 17,393
Short-term restricted cash, end of period	23	19
Long-term restricted cash, end of period	125	75
Cash, cash equivalents and restricted cash at end of period	$ 149,211	$ 17,487

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

1. Description of Business

Aura Biosciences, Inc. (the “Company” or “Aura”) is a clinical-stage biotechnology company leveraging its novel targeted oncology platform to develop a potential new standard of care across multiple cancer indications, with an initial focus on ocular and urologic oncology. Within these consolidated financial statements, unless the context otherwise requires, references to the Company or Aura refer to Aura Biosciences, Inc. The Company’s proprietary platform enables the targeting of a broad range of solid tumors using Virus-Like Particles, or VLPs, that can be conjugated with drugs or loaded with nucleic acids to create Virus-Like Drug Conjugates, or VDCs. The Company’s VDCs are largely agnostic to tumor type and can recognize a surface marker, known as HSPGs, that are specifically modified and more broadly expressed on many tumors. The Company is developing AU-011, its first VDC product candidate for the first line treatment of primary choroidal melanoma, a rare disease with no drugs approved. The Company is also developing AU-011 for additional ocular oncology indications and in non-muscle invasive bladder cancer. Aura’s team combines expertise in cancer cell biology, ophthalmology, and targeted therapies together with experience in the development and commercialization of orphan products for significant unmet medical needs. Aura’s headquarters are located in Cambridge, 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 and collaborative partners, competition, customer demand, management of growth, and the effectiveness of marketing by the Company.

Reverse Stock Split

On October 22, 2021, the Company effected a reverse stock split of the Company’s common stock on a 1-for-13.7 basis, or the Reverse Stock Split. In connection with the Reverse Stock Split, the conversion ratio for the Company’s convertible preferred stock was proportionately adjusted such that the common stock issuable upon conversion of such preferred stock was decreased in proportion to the Reverse Stock Split. Accordingly, all common stock share and per share amounts, for all periods presented in these consolidated financial statements, have been retroactively adjusted, to reflect this reverse stock split and adjustment of the convertible preferred stock conversion ratios.

Initial Public Offering

On November 2, 2021, the Company completed its initial public offering or the IPO, in which it issued and sold 6,210,000 shares of common stock, including the full exercise of the underwriters’ option to purchase additional shares at a price to the public of $14.00 per share for aggregate gross proceeds of $86.9 million. The Company received approximately $78.3 million in net proceeds after deducting underwriting discounts, commissions and offering expenses.

Liquidity and Going Concern

Through December 31, 2021, the Company has funded its operations primarily with proceeds from the initial closing and additional closings of its convertible preferred stock financings, through its license agreements, and through its IPO. On November 2, 2021, the Company completed its IPO, in which it issued and sold 6,210,000 shares of common stock, including the full exercise of the underwriters' option to purchase additional shares at a price to the public of $14.00 per share for aggregate gross proceeds of $86.9 million. The Company received approximately $78.3 million in net proceeds after deducting underwriting discounts, commissions and offering expenses. The Company has incurred recurring losses and negative operating cash flows from operations since its inception, including net losses of $35.3 million and $22.2 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, the Company had cash and cash equivalents of $149.1 million and an accumulated deficit of $152.1 million. The Company expects to continue to generate operating losses for the foreseeable future.

As of the issuance date of these consolidated financial statements for the year ended December 31, 2021, the Company expects that its cash and cash equivalents 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 ("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 operating exclusively in the United States.

Cash and Restricted Cash

Cash consists of standard checking accounts. As of December 31, 2021 and 2020, the restricted cash account is comprised of a $0.1 million security deposit held by the lessor for the Company's facility lease, and a $0.02 million deposit that is collateral for the Company's corporate credit card.

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.

Fair Value Measurements

Accounting Standards Codification 820, Fair Value Measurement ("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. Upon sale or retirement, the cost and accumulated depreciation is eliminated from their respective accounts and the resulting gain or loss is included in income or loss for the period. Repair and maintenance expenditures are charged to expense as incurred. The estimated useful lives of the Company's respective assets are as follows:

	Estimated Useful Life
Leasehold improvements	2 years
IT equipment	3 years
Laboratory equipment	5 years
Office furniture	7 years

Costs for capital assets not yet placed into service are capitalized as construction-in-progress and depreciated in accordance with the above guidelines 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.

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 material impairments during the years ended December 31, 2021 or 2020.

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

Prior to January 1, 2021, the Company accounted for leases in accordance with ASC 840, Leases ("ASC 840"). At lease inception, the Company determined if an arrangement was an operating or capital lease. For operating leases, the Company recognized rent expense, inclusive of rent escalation, holidays and lease incentives, on a straight-line basis over the lease term. The difference between rent expense recorded and the amount paid was charged to deferred rent. The Company presented lease incentives as deferred rent and amortized the incentives as a reduction to rent expense on a straight-line basis over the lease term. The Company classified deferred rent as current and noncurrent liabilities based on the portion of the deferred rent that was scheduled to mature within the proceeding twelve months.

Effective January 1, 2021, the Company accounts for leases in accordance with ASU No. 2016-02, *Leases* (Topic 842) (“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.

The Company adopted the new leasing standard effective January 1, 2021, using the modified retrospective transition approach which uses the effective date, or January 1, 2021, as the date of initial application. As a result, prior periods are presented in accordance with the previous guidance in ASC 840. ASC 842 provides several optional practical expedients in transition. The Company has elected to apply the package of practical expedients requiring no reassessment of whether any expired or existing contracts are or contain leases, the lease classification of any expired or existing leases, or the capitalization of initial direct costs for any existing leases.

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 sheet 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, 2021 and 2020.

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, 2021, and 2020, 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, these costs were recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering.

Convertible Preferred Stock Classification

The Company records all convertible preferred stock upon issuance at its respective fair value or original issuance price less issuance costs. The Company classifies its convertible preferred stock outside of stockholders' deficit as the redemption of such shares is outside the Company's control. The Company does not adjust the carrying values of the convertible preferred stock to redemption value unless and until it becomes probable that the instrument will become redeemable. As of December 31, 2020, the Company's convertible preferred stock was not adjusted to redemption value. After the closing of the IPO, all of the Company's outstanding shares of convertible preferred stock automatically converted into shares of common stock.

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 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. As of December 31, 2021, the Company has no performance-based awards. 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.

Before the IPO, as there has been no public market for the Company's common stock, the estimated fair value of its common stock was been determined by its Board of Directors, with input from management, considering third-party valuations of the common stock as well as the Board of Directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the option grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation. The Company's common stock valuations were prepared using either an option pricing method, or OPM, or a hybrid method, both of which used market approaches to estimate the Company's enterprise value. The hybrid method is a probability-weighted expected return method, or PWERM, where the equity value in one or more of the scenarios is calculated using an OPM. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock. A discount for lack of marketability of the common stock is then applied to arrive at an indication of value for the common stock. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preferences at the time of the liquidity event, such as a strategic sale or a merger.

In addition to considering the results of these third-party valuations, the Company's Board of Directors considered various objective and subjective factors to determine the fair value of the Company's common stock as of each grant date, including:

- The prices at which the Company sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to its common stock at the time of each grant;
- The progress of Aura's research and development programs, including the status and results of preclinical studies for its product candidates;
- The Company's stage of development and commercialization and its business strategy;
- External market conditions affecting the biotechnology industry and trends within the biotechnology industry;
- The Company's financial position, including cash on hand, and its historical and forecasted performance and operating results;
- The lack of an active public market for Aura's common stock and convertible preferred stock;
- The likelihood of achieving a liquidity event, such as an IPO, or sale of the Company in light of prevailing market conditions; and
- The analysis of an IPO and the market performance of similar companies in the biotechnology industry.

The assumptions underlying these valuations represented management’s best estimate, which involved inherent uncertainties and the application of management’s judgment. As a result, if the Company had used different assumptions or estimates, the fair value of its common stock and stock-based compensation expense could have been materially different.

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.

Warrants

The Company accounts for warrants on capital stock based on guidelines provided in ASC Topic 815, Derivatives and Hedging—Contracts in Entity’s Own Equity (“ASC 815”), which provides guidance on contracts that are settled in the Company’s own shares as either a liability or as an equity instrument depending on the warrant agreement. The Company's warrants are all classified as equity instruments. As such, the Company uses the Black-Scholes pricing model, depending on the applicable terms of the warrant agreement, to value the warrants.

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 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 income per share is computed using the more dilutive of (a) the two-class method, or (b) 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 number 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.

The Company's convertible preferred stock contractually entitles the holders of such shares to participate in dividends. Accordingly, in periods in which the Company reports a net loss, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. The Company reported a net loss attributable to common stockholders for the years ended December 31, 2021 and 2020, respectively.

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. For the years ended December 31, 2021 and 2020, comprehensive loss was equal to net loss.

Recently Adopted Accounting Pronouncements

Upon adoption of ASC 842, the Company recorded lease liabilities and their corresponding right-of-use assets based on the present value of lease payments over the remaining lease term. The adoption of ASC 842 resulted in the recognition of operating lease liabilities of $0.6 million and operating lease right-of-use assets of $0.5 million and the derecognition of deferred rent liabilities of $0.02 million on the Company's consolidated balance sheet as of January 1, 2021. The adoption impact relates to the Company's existing operating lease for operating and laboratory space. The adoption of ASC 842 did not have a material impact on the Company's consolidated statements of operations and comprehensive loss or consolidated statements of cash flows.

Recently Issued Accounting Pronouncements Not Yet Adopted

The Company reviewed recently issued accounting pronouncements for the year end December 31, 2021 and noted no pronouncements would have a material impact on the Company's consolidated financial statements.

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, 2021 and 2020 (in thousands):

Description	December 31, 2021	Quoted prices active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant other observable inputs (Level 3)
Assets				
Money market funds	$ 24,063	$ 24,063	$ —	$ —
Total financial assets	$ 24,063	$ 24,063	$ —	$ —
Liability				
Warrant Liability	$ 83	$ —	$ —	$ 83
Total financial liabilities	$ 83	$ —	$ —	$ 83

Description	December 31, 2020	Quoted prices active markets for identical assets (Level 1)	Significant other observable inputs (Level 2)	Significant other observable inputs (Level 3)
Liability				
Warrant Liability	$ 72	$ —	$ —	$ 72
Total financial liabilities	$ 72	$ —	$ —	$ 72

At December 31, 2021, the fair value of the warrant liability was determined based on Level 3 inputs and utilizing the Black-Scholes option pricing model (see Note 10).

During the years ended December 31, 2021 and 2020, there were no transfers into or out of Level 3.

The following table set forth a summary of changes in the fair value of the common stock warrants, which represents a recurring fair value measurement that is classified within Level 3 of the fair value hierarchy. Changes in fair value are recognized in other (expense) income as “Change in fair value of warrant liability” in the Company’s consolidated statements of operations and comprehensive loss (in thousands):

Common Stock (12,686 warrants)	
Fair value at December 31, 2019	$ 75
Change in fair value	(3)
Fair value at December 31, 2020	72
Change in fair value	11
Fair value at December 31, 2021	$ 83

4. Property and Equipment, Net

At December 31, 2021 and 2020, property and equipment consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Assets under construction	$ 2,365	$ 1,154
IT equipment	85	—
Leasehold improvements	13	—
Lab equipment	5,489	4,708
Office furniture	63	64
	$ 8,015	$ 5,926
Less—accumulated depreciation	(2,764)	(2,352)
Property and equipment, net	$ 5,251	$ 3,574

For the years ended December 31, 2021 and 2020, depreciation expense was $0.8 million.

5. Prepaid Expenses and Other Current Assets

At December 31, 2021 and 2020, prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Prepaid insurance	$ 2,734	$ 51
Prepaid research and development expenses	1,754	915
Prepaid license agreements	64	61
Other	66	16
Prepaid expenses and other current assets	$ 4,618	$ 1,043

6. Accrued Expenses and Other Current Liabilities

At December 31, 2021 and 2020, accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Accrued research and development expenses	$ 1,686	$ 750
Accrued compensation	2,147	1,023
Other	423	277
Accrued expenses and other current liabilities	$ 4,256	$ 2,050

7. Convertible Preferred Stock

As of December 31, 2020, the Company had 1,701,141 authorized, issued and outstanding shares of Series A convertible preferred stock, 3,298,732 authorized, issued and outstanding shares of Series A-1 convertible preferred stock, 4,325,021 authorized shares and 4,324,998 issued and outstanding shares of Series A-2 convertible preferred stock and, 22,705,646 authorized shares and 22,531,819 issued and outstanding shares of Series B convertible preferred stock, 58,109,711 authorized, issued and outstanding shares of Series C-1 convertible preferred stock, 33,218,192 authorized, issued and outstanding shares of Series C-2 convertible preferred stock, 57,878,742 authorized, issued and outstanding shares of Series D-1 convertible preferred stock and 24,598,481 authorized shares and 14,469,710 issued and outstanding shares of Series D-2 convertible preferred stock. All series of convertible preferred stock are collectively referred to as Preferred Stock, each with a par value of $0.00001 per share.

Series D-2 Offering

On June 25, 2020, the Company entered into the Series D-2 Purchase Agreement (the "Series D-2 Agreement") with certain investors to sell up to 24,598,481 shares of Series D-2 convertible preferred stock at a purchase price of $0.6911 per share. The Series D-2 Agreement provides for two closings, the first on October 1, 2020 and the second upon the achievement or waiver of certain milestone events. The Company sold 14,469,710 shares of the Series D-2 convertible preferred stock on October 1, 2020 at the first tranche closing for gross proceeds of $10.0 million.

On March 5, 2021, the Company completed the second tranche of the Series D-2 convertible preferred stock offering and issued 10,128,771 shares of the Series D-2 convertible preferred stock, $0.00001 par value per share, at a purchase price of $0.6911 per share for gross proceeds of $7.0 million.

Costs incurred in connection with the Series D-2 convertible preferred stock offering totaled $0.1 million and were recorded as a reduction to the Series D-2 convertible preferred stock. The majority of offering costs were incurred during the year ended December 31, 2020. Offering costs incurred during the year ended December 31, 2021 was $0.02 million.

The Company evaluated the tranche rights pursuant to the Series D-2 Agreement and determined the tranche rights did not represent a freestanding financial instrument as they are not legally detachable from the Series D-2 convertible preferred stock issued in the first tranche.

As of December 31, 2021, all the Series D-2 convertible preferred stock have been converted to shares of common stock upon closing of the IPO.

Series E Offering

On March 18, 2021, the Company completed its Series E Stock offering and issued 102,671,041 shares of Series E convertible preferred stock, $0.00001 par value per share, at a purchase price of $0.7839 per share for gross proceeds of $80.5 million.

Costs incurred in connection with the Series E convertible preferred stock offering totaled $0.2 million during the year ended December 31, 2021 and were recorded as a reduction to Series E convertible preferred stock.

As of December 31, 2021, all Series E convertible preferred stock have been converted to shares of common stock upon closing of the IPO.

The rights and privileges of the Company's Preferred Stock for the year ended December 31, 2020, and the period January 1, 2021 through November 2, 2021, are as follows:

Voting

Except as otherwise required by law or by other provisions, holders of the Preferred Stock vote together with the holders of common stock as a single class. Holders of Preferred Stock may cast the number of votes equal to the number of shares of common stock to which such shares of Preferred Stock are convertible into.

Dividends

Series C, D and E Dividend:

From and after the date of the issuance of any shares of Series C-1, Series C-2, Series D-1, Series D-2, and Series E, dividends at the annual rate of seven percent (7%) per annum of the original share price per share accrue on such shares of Series C-1, Series C-2, Series D-1, Series D-2, and Series E. Dividends accrue from day to day, whether or not declared, and are cumulative, but not compounding. Such dividends are only payable when and if declared by the Board or in the event of a Deemed Liquidation Event (as defined in the amended and restated Certificate of Incorporation). No other dividends may be declared or paid on any other class of stock unless the holders of the shares of Series E then outstanding first receive, or simultaneously receive, their applicable dividend. For the year ended December 31, 2020, $5.9 million, $2.6 million, $3.9 million, and $0.2 million of cumulative dividends on Series C-1, Series C-2, Series D-1, and Series D-2, respectively, are included in the liquidation preference amount indicated on the consolidated balance sheet. For the year ended December 31, 2020, there were no Series E convertible preferred stock shares issued or outstanding.

Series B Dividends:

From and after the date of the issuance of any shares of Series B, dividends at the annual rate of $0.0869645 per share accrue on such shares of Series B. Dividends accrue from day to day, whether or not declared, and are cumulative, but not compounding. Such dividends are only payable when and if declared by the Company's Board or in the event of a Deemed Liquidation Event (as defined in the amended and restated Certificate of Incorporation). No other dividends may be declared or paid on any other class of stock unless the holders of the shares of Series B then outstanding first receive, or simultaneously receive, their applicable dividend. For the year ended December 31, 2020, $9.4 million of cumulative dividends on Series B are included in the liquidation preference amount indicated on the consolidated balance sheet.

Series A Dividends:

From and after the date of the issuance of Series A, Series A-1, and Series A-2, if the Company declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Company, the dividend payable to the holders of Series A, Series A-1, and Series A-2 convertible preferred stock shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest dividend. No other dividends, or dividends on common stock payable in shares of common stock, may be declared or paid unless the holders of Series A, Series A-1, and Series A-2 then outstanding first receive, or simultaneously receive, their applicable dividend. As of December 31, 2020, no dividends have been declared on the common stock or the convertible preferred stock.

Liquidation Rights

In the event of a Deemed Liquidation Event, as defined in the Company's amended and restated Certificate of Incorporation, the assets of the Company will be distributed first to the holders of Series E convertible preferred stock. The holders of Series E convertible preferred stock will receive, in preference to all other stockholders, and amount equal to the sum of the Series E original issue price (equal to the cash price paid per share of $0.783900), plus unpaid dividends on such shares. Next, the holders of Series D convertible preferred stock will receive, in preference to all other stockholders other than Series E, an amount equal to the sum of the Series D original issue price, plus unpaid dividends on such shares. Next, the holders of Series C will receive, in preference to all stockholders other than the Series E and D convertible preferred stock holders, an amount equal to the sum of the Series C original issue price plus unpaid dividends on such shares. Next, the holders of Series B will receive, in preference to the holders of Series A, Series A-1, Series A-2 and common stock, an amount equal to the sum of the Series B original issue price plus unpaid dividends on such shares. Next, the holders of Series A, Series A-1, and Series A-2 will receive, in preference to the holders of common stock, an amount equal to the greater of their applicable liquidation preference or what they would have received had their shares converted into common stock. If the proceeds available are not sufficient to satisfy the full liquidation preference, the entire proceeds are to be distributed pro-rata among the Series E convertible preferred stock holders in proportion to the full preferential amount the Series E convertible preferred stock holders are entitled to receive.

Conversion

The Series E, together with the Series D, the Series C and the Series B convertible preferred stock, collectively the "Senior Preferred Stock", converts into common stock on a one-for-one basis. Each share of Series B, Series C-1, Series C-2, Series D-1, Series D-2, and Series E convertible preferred stock is convertible into the number of shares of common stock as is determined by dividing the respective original issue price by the conversion price in effect at the time of conversion. The Series E conversion price is set at $0.7839 per share, the Series D-1 and Series D-2 conversion price is set at $0.6911 per share, the Series C-1 conversion price is set at $0.5213 per share, the Series C-2 conversion price is set at $0.36491 per share, and the Series B conversion price is set at $1.24235 per share; none represents a beneficial conversion feature. Subject to certain exceptions, the Senior Preferred Stock has the benefit of anti- dilution protection on a weighted-average basis in the event that the Company sells stock at less than the applicable conversion price per share.

Each share of Series A and Series A-1 was originally convertible into the number of shares of common stock determined by dividing the respective Series A and Series A-1 original issue price by the conversion price in effect at the time of conversion. The Series A conversion price was originally equal to $2.00 per share and the Series A-1 conversion price was originally equal to $2.4847 per share. As Series A-2 was sold at $1.24235 per share, less than the per share prices of Series A and Series A-1, anti-dilution protections were triggered. Pursuant to the anti-dilution protection terms, on February 24, 2015, the Series A conversion price was reduced from $2.00 to $1.8191 per share of common stock and the Series A-1 conversion price was reduced from $2.4847 to $2.1898 per share of common stock and, therefore, the Series A conversion ratio was changed from 1:1 to 1:1.099 and the Series A-1 conversion ratio was changed from 1:1 to 1:1.135. The Company evaluated Series A and Series A-1 with the updated conversion ratios and determined that there was no beneficial conversion feature.

Series A-2 converts into common stock on a one-for-one basis. The Series A-2 conversion price is set at $1.24235 per share and does not represent a beneficial conversion feature.

According to the terms of the Company's amended and restated Certificate of Incorporation, in the event that the applicable conversion price for any series of Senior Preferred Stock is reduced, then the applicable conversion price for each series of Series A convertible preferred stock shall be uniformly and concurrently reduced.

Each share of Preferred Stock will automatically convert into common stock upon (a) the occurrence of an event, specified by vote or written consent of certain stockholders or (b) the completion of a public stock offering involving a price per share of common stock of not less than $1.554975 per share, subject to certain adjustments, where such offering results in aggregate gross proceeds to the Company of at least $50.0 million and the common stock is listed for trading on either the New York Stock Exchange or the Nasdaq Stock Market.

The Company must reserve and keep available out of its authorized but unused capital stock such number of authorized shares of common stock to sufficiently effect the conversion of all outstanding Preferred Stock.

In considering the features of the convertible preferred stock, the Company determined that none of the features, including the conversion features, requires bifurcation during the year ended December 31, 2020.

The conversion ratios for the Series A stock was changed to 13.700 to 1.099, Series A-1 stock was changed to 13.7 to 1.135, and the Series A-2 stock through Series E stock was changed to 13.7 to 1 upon the Company's filing of its amendment to its amended and restated Certificate of Incorporation on October 22, 2021.

Upon closing of the IPO on November 2, 2021, all of the Company's outstanding shares of convertible preferred stock automatically converted into 22,550,561 shares of common stock. In addition, the Company authorized 10,000,000 shares of preferred stock, par value $0.00001 per share, all of which shares of preferred stock will be undesignated.

8. C*ommon Stock*

The Company has 150,000,000 and 232,697,999 authorized shares of common stock, par value $0.00001 per share, of which 29,211,643 and 381,123 shares were issued and outstanding as of December 31, 2021 and 2020, respectively.

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 (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 right. 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, (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 both options to purchase common stock intended to qualify as incentive stock options under Section 422 of 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 will automatically increase on January 1, 2022 and 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.

2021 Employee Stock Purchase Plan

The 2021 Employee Stock Purchase Plan, (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 will automatically increase on January 1, 2022 and 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 March 18, 2021, the Board approved an increase to the 2018 Plan available option pool of 2,346,228 options. As mentioned above, the 2021 Plan was initiated in November 2021. With the transfer of the available options from the 2018 Plan to the 2021 Plan, there were 2,042,774 options available for grant under the 2021 Plan at December 31, 2021.

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 2018 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 2021 Plan for the year ended December 31, 2021:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding at December 31, 2020	1,512,129	$ 3.84	7.77	$ 1,174
Granted	2,970,708	9.03		
Exercised	(69,959)	4.99		
Cancelled/Forfeited	(179,887)	4.59		
Outstanding at December 31, 2021	4,232,991	$ 7.43	8.66	$ 40,437
Exercisable at December 31, 2021	1,174,871	$ 3.95	6.82	$ 15,304
Unvested as of December 31, 2021	3,058,120	$ 8.78	9.30	$ 25,133

The weighted-average grant date fair value of stock options granted during the years ended December 31, 2021 and 2020 was $5.84 and $2.74 per share, respectively. The total intrinsic value of options exercised was $0.1 million and $0.02 million for the years ended December 31, 2021 and 2020, respectively.

The Company has elected to use the Black-Scholes option pricing model to determine the fair value of options granted and generally recognizes the compensation cost of stock-based awards on a straight-line basis over the vesting period of the award.

The determination of the fair value of stock-based payment awards utilizing the Black-Scholes option pricing model is affected by the fair value of the Company's common stock and a number of other assumptions, including expected volatility, expected life, risk-free interest rate, and expected dividends.

The fair value of the stock options issued as of December 31, 2021 and 2020 was measured with the following weighted-average assumptions:

	December 31, 2021	December 31, 2020
Risk-free interest rate, %	1.15%	0.55%
Expected term	6.03	6.02
Expected volatility of the underlying stock, %	73.87%	74.04%
Expected dividend rate, %	—%	—%

Restricted Stock Units

The Company has granted restricted stock units with service vesting based conditions. Unvested shares of restricted common stock may not be sold or transferred by the holder. They are legally issued and outstanding. These restrictions lapse accordingly to the time-based vesting of each award.

A summary of the restricted stock unit activity during the year ended December 31, 2021 is as follows:

	Restricted Stock Units	Weighted-Average Grant Date Fair Value
Granted at December 31, 2020	—	$ —
Granted	232,111	14.00
Forfeited	(191)	14.00
Granted at December 31, 2021	231,920	$ 14.00

As a result of the 2021 Equity Incentive Plan, the Company granted restricted stock units which vest in increments of 25% annually over a period of four years. No restricted stock units vested during the year ended December 31, 2021.

Stock-based Compensation Expense

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

	Year Ended December 31, 2021	2020
Research and development	$ 702	$ 193
General and administrative	1,605	543
Total	$ 2,307	$ 736

As of December 31, 2021, there was $16.5 million of unrecognized compensation expense related to stock options, which is expected to be recognized over a weighted-average period of 3.33 years.

As of December 31, 2021, there was $3.1 million of unrecognized compensation expense related to restricted stock units, which is expected to be recognized over a weighted-average period of 3.82 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 (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 are re-measured to fair value at each balance sheet date and immediately prior to exercise. The Series B Warrants were converted into warrants to purchase 12,686 shares of common stock upon the completion of the IPO in November 2021.

A total of 12,686 of the common stock warrants remained outstanding at December 31, 2021 and 2020.

The warrants were valued using the Black-Scholes option pricing model. The fair value of the warrants and the significant assumptions used were as follows:

Common Stock Warrants	December 31, 2021	December 31, 2020
Fair value	$ 16.98	$ 16.03
Volatility	80.38%	74.00%
Expected term (years)	3.15	4.2
Risk free rate	0.97%	0.27%
Dividend yield	7.00%	7.00%

11. Compensation

In January 2012, the Company adopted the Aura Biosciences 401(K) Profit Sharing Plan and Trust (the "401(k) Plan") for its employees, which is designed to be qualified under Section 401(k) of the Internal Revenue 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 $0.3 million and $0.2 million for the years ended December 31, 2021 and 2020, respectively.

12. Commitments and Contingencies

Lease Commitments

The Company has historically entered into lease arrangements for its facilities. As of December 31, 2021 and 2020, respectively, the Company had one operating lease for its office and laboratory facility with required future minimum payments. The lease does not contain any options to renew, terminate, or purchase the underlying asset, and was set to expire on July 31, 2022. As part of its adoption of ASC 842, the Company recorded a right-of-use asset and operating lease liability for this lease as of the effective date.

On March 31, 2021, the Company executed an amendment to the facility lease which included an extension of the expiration date of the original leased premises, the addition of 4,516 square feet of laboratory space with an expected commencement date of May 1, 2021, and the addition of 1,000 square feet of laboratory space with an expected commencement date of June 15, 2021. The lease term for the original and new spaces will expire on July 31, 2023, with an option to renew for an additional 12 months.

Upon the execution of the amendment, which was deemed to be a lease modification, the Company re-evaluated the assumptions made at the original lease commencement date. The Company determined the amendment consists of two separate contracts under ASC 842. One contract is related to the modification of term for the original space, and the other is related to a new right-of-use for the two additional spaces, which are to be accounted for as new leases. The Company remeasured the lease liability and corresponding right-of-use asset for the original space as of the effective date of the amendment to reflect the extended term and recorded in the second quarter of 2021 an additional right-of-use asset and lease liability upon lease commencement of each of the additional space.

The Company also leases office and laboratory equipment for which the related expense is immaterial.

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 year ended December 31, 2021 (in thousands):

	Year Ended December 31, 2021
Lease Cost	
Amortization of finance right-of-use assets	$ 11
Operating lease costs	524
Variable lease costs	322
Short-term lease costs	4
Total lease costs	$ 861

Cash paid for amounts included in the measurement of lease liability—finance leases	$	15
Cash paid for amounts included in the measurement of lease liability—operating leases	$	519
Weighted-average remaining lease term—operating leases (years)		1.58
Weighted-average discount rate—finance leases		7.94%
Weighted-average discount rate—operating leases		3.51%

The following table reconciles the future minimum commitments to the Company's operating lease liabilities at December 31, 2021 (in thousands):

	Operating lease payments as of December 31, 2021
2022	$ 625
2023	377
Thereafter	—
Total lease payments	1,002
Less: interest	(27)
Total operating lease liabilities at December 31, 2021	975
Less: current portion of lease liabilities	615
Lease liabilities, net of current portion	$ 360

In May 2021, the Company paid in full its finance lease.

Laser Purchasing Commitment

On April 5, 2019, the Company entered into a purchase agreement for equipment with future commitments payable in three installments of €0.2 million each. The first two installments of €0.2 million were paid by the Company in April 2019 and August 2019. Upon receipt of the laser systems, the Company will assess whether the laser systems have an alternative future use and, if so, will capitalize the lasers as a component of fixed assets.

License Agreements

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

LI-COR Exclusive License and Supply Agreement

In January 2014, the Company entered into an Exclusive License and Supply Agreement, or the LI-COR Exclusive License agreement with LI-COR, Inc. (LI-COR) for the license of IRDye 700DC and related licensed patents for the treatment and diagnosis of ocular cancers in humans as amended in January 2016, July 2017, April 2018 and April 2019. The LI-COR Exclusive License 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 LI-COR low-single digit royalties on net sales. The term of the LI-COR 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.

For the years ended December 31, 2021, and December 31, 2020, the Company incurred, respectively, $nil and $0.1 million of expenses related to this agreement.

LI-COR Non-Exclusive License and Supply Agreement

In December 2014, the Company entered into a Non-Exclusive License 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, the Company paid a license issue fee of $0.03 million on the effective date. The Company must also pay LI-COR 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 LI-COR a low-single digit percentage royalty on net sales. LI-COR 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.

Life Technologies Corporation

In December 2014, the Company entered into a non-exclusive, perpetual license agreement with Life Technologies Corporation ("Life Technologies"), which allows for five licensed products. Under this agreement the Company is required to pay an initial license fee of $0.1 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.

For the years ended December 31, 2021 and December 31, 2020, the Company incurred $0.1 million of expenses related to this agreement.

National Institute of Health (NIH)-Biologic Materials License Agreement

In December 2010, the Company entered into a Biologic Materials License Agreement with NIH for a non-exclusive right to use materials described in Schiller et al., Virology 2004 Apr.10, 321(2):205-16. This agreement required a one-time non-refundable license issuance fee of $0.02 million. No future milestone payments or royalties are due under this agreement.

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

In July 2011, the Company entered into a Collaboration Research and Development Agreement (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 first amended in 2012, 2013, 2014, 2015, 2016, 2018 and most recently in September of 2020. During 2011-2021, the Company paid an aggregate of $0.4 million in research collaboration fees, $0.03 million and 0.04 million of which was paid in 2021 and 2020, respectively.

A seventh amendment was made in October 2020, requiring payment of $0.04 million within 30 days of October 1, 2020, and another $0.03 million within 30 days of the 10th anniversary of the CRADA, which was paid in July 2021. This seventh amendment extended the term of the CRADA to September 30, 2022.

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

In September 2013, the Company entered into an exclusive patent license agreement (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. As of December 31, 2021, the Company has paid NIH approximately $0.4 million in aggregate milestones under the NIH license agreement. The Company accrued $0.03 million and $0.02 million in patent licensing reimbursement fees as of December 31, 2021, and 2020, 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 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. There are potential milestone 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 those milestones have not been achieved as of December 31, 2021. 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 did not incur any expense in the years ended December 31, 2021, and 2020.

Clearside

In July 2019, the Company entered into an exclusive license agreement with Clearside Biomedical, Inc. ("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 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.

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 loss per share for the years ended December 31, 2021 and 2020 as follows (in thousands, except share and per share data):

	December 31, 2021	December 31, 2020
Numerator:		
Net loss	$ (35,251)	$ (22,206)
Less: Accruals of dividends of preferred stock	(10,942)	(7,926)
Net loss attributable to common stockholders—basic and diluted	$ (46,193)	$ (30,132)
Denominator:		
Weighted-average common stock outstanding	5,159,973	367,204
Net loss per share attributable to common stockholders—basic and diluted	$ (8.95)	$ (82.06)

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:

	December 31, 2021	December 31, 2020
Convertible preferred stock on an if converted basis	—	14,317,032
Stock options to purchase common stock	4,232,991	1,512,129
Restricted stock units that vest into common stock	231,920	—
Warrants to purchase preferred stock	—	12,686
Warrants to purchase common stock	12,686	—
Total potential dilutive shares	4,477,597	15,841,847

14. Income Taxes

The Company has not recorded any net tax provision for the periods presented due to the losses incurred and the need for a full valuation allowance on net deferred tax assets. The difference between the income tax expense at the U.S. federal statutory rate and the recorded provision is primarily due to the valuation allowance provided on all deferred tax assets. The Company's loss before income tax for the periods presented was generated entirely in the United States:

A reconciliation of the federal statutory income tax rate to the Company's effective tax rate as of December 31, 2021 and 2020 is as follows:

	2021	2020
Tax provision at statutory rate	21.0%	21.0%
State taxes, net of federal benefit	5.3%	5.4%
Federal tax credits	2.6%	3.8%
Permanent items	(0.4)%	(0.3)%
Other	(0.3)%	(0.4)%
Decrease in valuation reserve	(28.2)%	(29.5)%
Total	0.0%	0.0%

Temporary differences that give rise to significant deferred tax assets (liabilities) as of December 31, 2021 and 2020 are as follows (in thousands):

	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 36,287	$ 27,921
Stock-based compensation expense	635	328
Tax credit carryforwards	5,821	4,675
Accrued expenses	517	418
Lease liability	248	—
Other	194	168
Total deferred tax assets	43,702	33,510
Deferred tax liabilities:		
Right of use asset	(241)	
Depreciable assets	(182)	(157)
Valuation allowance	(43,279)	(33,353)
Net deferred tax asset	$ —	$ —

As of December 31, 2021, the Company had federal gross operating loss carryforwards of approximately $138.7 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 $94.5 million do not expire. The Company had state gross operating loss carryforwards of $113.6 million, which may be available to offset future taxable income and which would begin to expire in 2030. As of December 31, 2021, the Company had federal and state research and experimentation credit carryforwards of $4.7 million and $1.4 million, respectively, which may be available to offset future income tax liabilities and which would 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 United States Internal Revenue Code (the "Internal Revenue Code"). Under the Internal Revenue 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 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 provided 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 sheet or consolidated statement 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 $43.3 million has been recorded at December 31, 2021. The increase in the valuation allowance of $9.9 million during the year ended December 31, 2021 was primarily due to the increase in net operating loss generated by the Company.

As of December 31, 2021 and 2020, 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 provision for income taxes in the consolidated statements of operations. 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. 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.

15. Related Parties

During the years ended December 31, 2021 and 2020, the Company incurred $0.04 million and $nil million in expenses to a legal firm whose partner is also an investor and former officer of the Company. As of December 31, 2021, and 2020, none of these amounts were included in accounts payable.

During the years ended December 31, 2021 and 2020, the Company incurred $0.3 million and $0.5 million in expenses to a stockholder that provided research and development related services. Of these amounts, $nil and $0.1 million were in accrued expenses as of December 31, 2021 and 2020.

16. Subsequent Events

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

Exhibit 3.1

TENTH AMENDED AND RESTATED

CERTIFICATE OF INCORPORATION

OF

AURA BIOSCIENCES, INC.

Aura Biosciences, Inc., a corporation organized and existing under the laws of the State of Delaware (the "Corporation"), hereby certifies as follows:

1. The name of the Corporation is Aura Biosciences, Inc. The date of the filing of its original Certificate of Incorporation with the Secretary of State of the State of Delaware was January 13, 2009 (the "Original Certificate"). The name under which the Corporation filed the Original Certificate was Aura Biosciences, Inc.

2. This Tenth Amended and Restated Certificate of Incorporation (the "Certificate") amends, restates and integrates the provisions of the Ninth Amended and Restated Certificate of Incorporation that was filed with the Secretary of State of the State of Delaware on March 17, 2021 (the "Amended and Restated Certificate"), and was duly adopted in accordance with the provisions of Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware (the "DGCL").

3. The text of the Amended and Restated Certificate is hereby amended and restated in its entirety to provide as herein set forth in full.

ARTICLE I

The name of the Corporation is Aura Biosciences, Inc.

ARTICLE II

The address of the Corporation's registered office in the State of Delaware is c/o Corporation Trust Center, 1209 Orange Street, Wilmington, DE 19801 and County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

ARTICLE III

The purpose of the Corporation is to engage in any lawful act or activity for which corporations may be organized under the DGCL.

ARTICLE IV

CAPITAL STOCK

The total number of shares of capital stock which the Corporation shall have authority to issue is one hundred and sixty million (160,000,000), of which (i) one hundred and fifty million (150,000,000) shares shall be a class designated as common stock, par value $0.00001 per share (the "Common Stock"), and (ii) ten million (10,000,000) shares shall be a class designated as undesignated preferred stock, par value $0.00001 per share (the "Undesignated Preferred Stock").

Except as otherwise provided in any certificate of designations of any series of Undesignated Preferred Stock, the number of authorized shares of the class of Common Stock or Undesignated Preferred Stock may from time to time be increased or decreased (but not below the number of shares of such class outstanding) by the affirmative vote of the holders of a majority in voting power of the outstanding shares of capital stock of the Corporation irrespective of the provisions of Section 242(b)(2) of the DGCL.

The powers, preferences and rights of, and the qualifications, limitations and restrictions upon, each class or series of stock shall be determined in accordance with, or as set forth below in, this Article IV.

A. COMMON STOCK

Subject to all the rights, powers and preferences of the Undesignated Preferred Stock and except as provided by law or in this Certificate (or in any certificate of designations of any series of Undesignated Preferred Stock):

(a) the holders of the Common Stock shall have the exclusive right to vote for the election of directors of the Corporation (the "Directors") and on all other matters requiring stockholder action, each outstanding share entitling the holder thereof to one vote on each matter properly submitted to the stockholders of the Corporation for their vote; provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to this Certificate (or on any amendment to a certificate of designations of any series of Undesignated Preferred Stock) that alters or changes the powers, preferences, rights or other terms of one or more outstanding series of Undesignated Preferred Stock if the holders of such affected series of Undesignated Preferred Stock are entitled to vote, either separately or together with the holders of one or more other such series, on such amendment pursuant to this Certificate (or pursuant to a certificate of designations of any series of Undesignated Preferred Stock) or pursuant to the DGCL;

(b) dividends may be declared and paid or set apart for payment upon the Common Stock out of any assets or funds of the Corporation legally available for the payment of dividends, but only when and as declared by the Board of Directors or any authorized committee thereof; and

(c) upon the voluntary or involuntary liquidation, dissolution or winding up of the Corporation, the net assets of the Corporation shall be distributed pro rata to the holders of the Common Stock.

B. UNDESIGNATED PREFERRED STOCK

The Board of Directors or any authorized committee thereof is expressly authorized, to the fullest extent permitted by law, to provide by resolution or resolutions for, out of the unissued shares of Undesignated Preferred Stock, the issuance of the shares of Undesignated Preferred Stock in one or more series of such stock, and by filing a certificate of designations pursuant to applicable law of the State of Delaware, to establish or change from time to time the number of shares of each such series, and to fix the designations, powers, including voting powers, full or limited, or no voting powers, preferences and the relative, participating, optional or other special rights of the shares of each series and any qualifications, limitations and restrictions thereof.

ARTICLE V

STOCKHOLDER ACTION

1. Action without Meeting. Any action required or permitted to be taken by the stockholders of the Corporation at any annual or special meeting of stockholders of the Corporation must be effected at a duly called annual or special meeting of stockholders and may not be taken or effected by a written consent of stockholders in lieu thereof. Notwithstanding anything herein to the contrary, the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article V, Section 1.

2. Special Meetings. Except as otherwise required by statute and subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock, special meetings of the stockholders of the Corporation may be called only by the Board of Directors 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. Only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders of the Corporation.

ARTICLE VI

DIRECTORS

1. General. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors except as otherwise provided herein or required by law.

2. Election of Directors. Election of Directors need not be by written ballot unless the By-laws of the Corporation (the "By-laws") shall so provide.

3. Number of Directors; Term of Office. The number of Directors of the Corporation shall be fixed solely and exclusively by resolution duly adopted from time to time by the Board of Directors. The Directors, other than those who may be elected by the holders of any series of Undesignated Preferred Stock, shall be classified, with respect to the term for which they severally hold office, into three classes. The Class I Directors of the Corporation shall be Giovanni Mariggi, Ph.D. Raj Parekh, Ph.D. and Elisabet de los Pinos, Ph.D.; the Class II Directors of the Corporation shall be David Johnson and Karan Takhar; and the Class III Directors of the Corporation shall be Sapna Srivastava and Antony Mattessich. The Class I Directors shall serve for a term expiring at the annual meeting of stockholders to be held in 2022, the Class II Directors shall serve for a term expiring at the annual meeting of stockholders to be held in 2023, and the Class III Directors shall serve for a term expiring at the annual meeting of stockholders to be held in 2024. At each annual meeting of stockholders, Directors elected to succeed those Directors whose terms expire shall be elected for a term of office to expire at the third succeeding annual meeting of stockholders after their election. Notwithstanding the foregoing, the Directors elected to each class shall hold office until their successors are duly elected and qualified or until their earlier resignation, death or removal.

Notwithstanding the foregoing, whenever, pursuant to the provisions of Article IV of this Certificate, the holders of any one or more series of Undesignated Preferred Stock shall have the right, voting separately as a series or together with holders of other such series, to elect Directors at an annual or special meeting of stockholders, the election, term of office, filling of vacancies and other features of such directorships shall be governed by the terms of this Certificate and any certificate of designations applicable to such series.

Notwithstanding anything herein to the contrary, the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article IV, Section 3.

4. Vacancies. Subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock to elect Directors and to fill vacancies in the Board of Directors relating thereto, any and all vacancies in the Board of Directors, however occurring, including, without limitation, by reason of an increase in the size of the Board of Directors, or the death, resignation, disqualification or removal of a Director, shall be filled solely and exclusively by the affirmative vote of a majority of the remaining Directors then in office, even if less than a quorum of the Board of Directors, and not by the stockholders. Any Director appointed in accordance with the preceding sentence shall hold office for the remainder of the full term of the class of Directors in which the new directorship was created or the vacancy occurred and until such Director's successor shall have been duly elected and qualified or until his or her earlier resignation, death or removal. Subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock to elect Directors, when the number of Directors is increased or

decreased, the Board of Directors shall, subject to Article VI.3 hereof, determine the class or classes to which the increased or decreased number of Directors shall be apportioned; provided, however, that no decrease in the number of Directors shall shorten the term of any incumbent Director. In the event of a vacancy in the Board of Directors, the remaining Directors, except as otherwise provided by law, shall exercise the powers of the full Board of Directors until the vacancy is filled.

5. Removal. Subject to the rights, if any, of any series of Undesignated Preferred Stock to elect Directors and to remove any Director whom the holders of any such series have the right to elect, any Director (including persons elected by Directors to fill vacancies in the Board of Directors) may be removed from office (i) only with cause and (ii) only by the affirmative vote of the holders not less than two-thirds (2/3) of the outstanding shares of capital stock then entitled to vote at an election of Directors. At least forty-five (45) days prior to any annual or special meeting of stockholders at which it is proposed that any Director be removed from office, written notice of such proposed removal and the alleged grounds thereof shall be sent to the Director whose removal will be considered at the meeting.

ARTICLE VII

LIMITATION OF LIABILITY

A Director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of his or her fiduciary duty as a Director, except for liability (a) for any breach of the Director's duty of loyalty to the Corporation or its stockholders, (b) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (c) under Section 174 of the DGCL or (d) for any transaction from which the Director derived an improper personal benefit. If the DGCL is amended after the effective date of this Certificate to authorize corporate action further eliminating or limiting the personal liability of Directors, then the liability of a Director of the Corporation shall be eliminated or limited to the fullest extent permitted by the DGCL, as so amended.

Any amendment, repeal or modification of this Article VII by either of (i) the stockholders of the Corporation or (ii) an amendment to the DGCL, shall not adversely affect any right or protection existing at the time of such amendment, repeal or modification with respect to any acts or omissions occurring before such amendment, repeal or modification of a person serving as a Director at the time of such amendment, repeal or modification.

Notwithstanding anything herein to the contrary, the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote thereon, and the affirmative vote of not less than two-thirds (2/3) of the outstanding shares of each class entitled to vote thereon as a class, shall be required to amend or repeal any provision of this Article VII.

ARTICLE VIII

AMENDMENT OF BY-LAWS

1. Amendment by Directors. Except as otherwise provided by law, the By-laws of the Corporation may be amended or repealed by the Board of Directors by the affirmative vote of a majority of the Directors then in office.

2. Amendment by Stockholders. Except as otherwise provided therein, the By-laws of the Corporation may be amended or repealed at any annual meeting of stockholders, or special meeting of stockholders called for such purpose, by the affirmative vote of at least not less than two-thirds (2/3) of the outstanding shares of capital stock entitled to vote on such amendment or repeal, voting together as a single class.

ARTICLE IX

AMENDMENT OF CERTIFICATE OF INCORPORATION

The Corporation reserves the right to amend or repeal this Certificate in the manner now or hereafter prescribed by statute and this Certificate, and all rights conferred upon stockholders herein are granted subject to this reservation. Except as otherwise required by this Certificate or by law, whenever any vote of the holders of capital stock of the Corporation is required to amend or repeal any provision of this Certificate, such amendment or repeal shall require the affirmative vote of the majority of the outstanding shares of capital stock entitled to vote on such amendment or repeal, and the affirmative vote of the majority of the outstanding shares of each class entitled to vote thereon as a class at a duly constituted meeting of stockholders called expressly for such purpose.

* * *

THIS TENTH AMENDED AND RESTATED CERTIFICATE OF INCORPORATION is executed as of this 2nd day of November, 2021.

AURA BIOSCIENCES, INC.

By:/s/ Elisabet de los Pinos
Name: Elisabet de los Pinos
Title: Chief Executive Officer and President

Exhibit 3.2

AMENDED AND RESTATED

BY-LAWS

OF

AURA BIOSCIENCES, INC.

(the "Corporation")

ARTICLE I

Stockholders

SECTION 1.Annual Meeting. The annual meeting of stockholders (any such meeting being referred to in these By-laws as an "Annual Meeting") shall be held at the hour, date and place within or without the United States which is fixed by the Board of Directors, which time, date and place may subsequently be changed at any time by vote of the Board of Directors. If no Annual Meeting has been held for a period of thirteen (13) months after the Corporation's last Annual Meeting, a special meeting in lieu thereof may be held, and such special meeting shall have, for the purposes of these By-laws or otherwise, all the force and effect of an Annual Meeting. Any and all references hereafter in these By-laws to an Annual Meeting or Annual Meetings also shall be deemed to refer to any special meeting(s) in lieu thereof.

SECTION 2.Notice of Stockholder Business and Nominations.

(a) Annual Meetings of Stockholders.

(1) Nominations of persons for election to the Board of Directors of the Corporation and the proposal of other business to be considered by the stockholders may be brought before an Annual Meeting (i) by or at the direction of the Board of Directors or (ii) by any stockholder of the Corporation who was a stockholder of record at the time of giving of notice provided for in this By-law, who is entitled to vote at the meeting, who is present (in person or by proxy) at the meeting and who complies with the notice procedures set forth in this By-law as to such nomination or business. For the avoidance of doubt, the foregoing clause (ii) shall be the exclusive means for a stockholder to bring nominations or business properly before an Annual Meeting (other than matters properly brought under Rule 14a-8 (or any successor rule) under the Securities Exchange Act of 1934, as amended (the "Exchange Act")), and such stockholder must comply with the notice and other procedures set forth in Article I, Section 2(a)(2) and (3) of this By-law to bring such nominations or business properly before an Annual Meeting. In addition to the other requirements set forth in this By-law, for any proposal of business to be considered at an Annual Meeting, it must be a proper subject for action by stockholders of the Corporation under Delaware law.

(2) For nominations or other business to be properly brought before an Annual Meeting by a stockholder pursuant to clause (ii) of Article I, Section 2(a)(1) of this By-law, the stockholder must (i) have given Timely Notice (as defined below) thereof in writing to the Secretary of the Corporation, (ii) have provided any updates or supplements to such notice at the times and in the forms required by this By-law and (iii) together with the beneficial owner(s), if any, on whose behalf the nomination or business proposal is made, have acted in accordance with the representations set forth in the Solicitation Statement (as defined below) required by this By-law. To be timely, a stockholder's written notice shall be received by the Secretary at the principal executive offices of the Corporation not later than the close of business on the ninetieth (90th) day nor earlier than the close of business on the one hundred twentieth (120th) day prior to the one-year anniversary of the preceding year's Annual Meeting; provided, however, that in the event the Annual Meeting is first convened more than thirty (30) days before or more than sixty (60) days after such anniversary date, or if no Annual Meeting were held in the preceding year, notice by the stockholder to be timely must be received by the Secretary of the Corporation not later than the close of business on the later of the ninetieth (90th) day prior to the scheduled date of such Annual Meeting or the tenth (10th) day following the day on which public announcement of the date of such meeting is first made (such notice within such time periods shall be referred to as "Timely Notice"). Notwithstanding anything to the contrary provided herein, for the first Annual Meeting following the initial public offering of common stock of the Corporation, a stockholder's notice shall be timely if received by the Secretary at the principal executive offices of the Corporation not later than the close of business on the later of the ninetieth (90th) day prior to the scheduled date of such Annual Meeting or the tenth (10th) day following the day on which public announcement of the date of such Annual Meeting is first made or sent by the Corporation. Such stockholder's Timely Notice shall set forth:

(A) as to each person whom the stockholder proposes to nominate for election or reelection as a director, all information relating to such person that is required to be disclosed in solicitations of proxies for election of directors in an election contest, or is otherwise required, in each case pursuant to Regulation 14A under the Exchange Act (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected);

(B) as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting, and any material interest in such business of each Proposing Person (as defined below);

(C) (i) the name and address of the stockholder giving the notice, as they appear on the Corporation's books, and the names and addresses of the other Proposing Persons (if any) and (ii) as to each Proposing Person, the following information: (a) the class or series and number of all shares of capital stock of the Corporation which are, directly or indirectly, owned beneficially or of record by such Proposing Person or any of its affiliates or associates (as such terms are defined in Rule 12b-2 promulgated under the Exchange Act), including any shares of any class or series of capital stock of the Corporation as to which such

Proposing Person or any of its affiliates or associates has a right to acquire beneficial ownership at any time in the future, (b) all Synthetic Equity Interests (as defined below) in which such Proposing Person or any of its affiliates or associates, directly or indirectly, holds an interest including a description of the material terms of each such Synthetic Equity Interest, including without limitation, identification of the counterparty to each such Synthetic Equity Interest and disclosure, for each such Synthetic Equity Interest, as to (x) whether or not such Synthetic Equity Interest conveys any voting rights, directly or indirectly, in such shares to such Proposing Person, (y) whether or not such Synthetic Equity Interest is required to be, or is capable of being, settled through delivery of such shares and (z) whether or not such Proposing Person and/or, to the extent known, the counterparty to such Synthetic Equity Interest has entered into other transactions that hedge or mitigate the economic effect of such Synthetic Equity Interest, (c) any proxy (other than a revocable proxy given in response to a public proxy solicitation made pursuant to, and in accordance with, the Exchange Act), agreement, arrangement, understanding or relationship pursuant to which such Proposing Person has or shares a right to, directly or indirectly, vote any shares of any class or series of capital stock of the Corporation, (d) any rights to dividends or other distributions on the shares of any class or series of capital stock of the Corporation, directly or indirectly, owned beneficially by such Proposing Person that are separated or separable from the underlying shares of the Corporation, and (e) any performance-related fees (other than an asset based fee) that such Proposing Person, directly or indirectly, is entitled to based on any increase or decrease in the value of shares of any class or series of capital stock of the Corporation or any Synthetic Equity Interests (the disclosures to be made pursuant to the foregoing clauses (a) through (e) are referred to, collectively, as “Material Ownership Interests”) and (iii) a description of the material terms of all agreements, arrangements or understandings (whether or not in writing) entered into by any Proposing Person or any of its affiliates or associates with any other person for the purpose of acquiring, holding, disposing or voting of any shares of any class or series of capital stock of the Corporation;

(D) (i) a description of all agreements, arrangements or understandings by and among any of the Proposing Persons, or by and among any Proposing Persons and any other person (including with any proposed nominee(s)), pertaining to the nomination(s) or other business proposed to be brought before the meeting of stockholders (which description shall identify the name of each other person who is party to such an agreement, arrangement or understanding), and (ii) identification of the names and addresses of other stockholders (including beneficial owners) known by any of the Proposing Persons to support such nominations or other business proposal(s), and to the extent known the class and number of all shares of the Corporation’s capital stock owned beneficially or of record by such other stockholder(s) or other beneficial owner(s); and

(E) a statement whether or not the stockholder giving the notice and/or the other Proposing Person(s), if any, will deliver a proxy statement and form of proxy to holders of, in the case of a business proposal, at least the

percentage of voting power of all of the shares of capital stock of the Corporation required under applicable law to approve the proposal or, in the case of a nomination or nominations, at least the percentage of voting power of all of the shares of capital stock of the Corporation reasonably believed by such Proposing Person to be sufficient to elect the nominee or nominees proposed to be nominated by such stockholder (such statement, the "Solicitation Statement").

For purposes of this Article I of these By-laws, the term "Proposing Person" shall mean the following persons: (i) the stockholder of record providing the notice of nominations or business proposed to be brought before a stockholders' meeting, and (ii) the beneficial owner(s), if different, on whose behalf the nominations or business proposed to be brought before a stockholders' meeting is made. For purposes of this Section 2 of Article I of these By-laws, the term "Synthetic Equity Interest" shall mean any transaction, agreement or arrangement (or series of transactions, agreements or arrangements), including, without limitation, any derivative, swap, hedge, repurchase or so-called "stock borrowing" agreement or arrangement, the purpose or effect of which is to, directly or indirectly: (a) give a person or entity economic benefit and/or risk similar to ownership of shares of any class or series of capital stock of the Corporation, in whole or in part, including due to the fact that such transaction, agreement or arrangement provides, directly or indirectly, the opportunity to profit or avoid a loss from any increase or decrease in the value of any shares of any class or series of capital stock of the Corporation, (b) mitigate loss to, reduce the economic risk of or manage the risk of share price changes for, any person or entity with respect to any shares of any class or series of capital stock of the Corporation, (c) otherwise provide in any manner the opportunity to profit or avoid a loss from any decrease in the value of any shares of any class or series of capital stock of the Corporation, or (d) increase or decrease the voting power of any person or entity with respect to any shares of any class or series of capital stock of the Corporation.

(3) A stockholder providing Timely Notice of nominations or business proposed to be brought before an Annual Meeting shall further update and supplement such notice, if necessary, so that the information (including, without limitation, the Material Ownership Interests information) provided or required to be provided in such notice pursuant to this By-law shall be true and correct as of the record date for the meeting and as of the date that is ten (10) business days prior to such Annual Meeting, and such update and supplement shall be received by the Secretary at the principal executive offices of the Corporation not later than the close of business on the fifth (5th) business day after the record date for the Annual Meeting (in the case of the update and supplement required to be made as of the record date), and not later than the close of business on the eighth (8th) business day prior to the date of the Annual Meeting (in the case of the update and supplement required to be made as of ten (10) business days prior to the meeting).

(4) Notwithstanding anything in the second sentence of Article I, Section 2(a)(2) of this By-law to the contrary, in the event that the number of directors to be elected to the Board of Directors of the Corporation is increased and there is no public announcement naming all of the nominees for director or specifying the size of the

increased Board of Directors made by the Corporation at least ten (10) days before the last day a stockholder may deliver a notice of nomination in accordance with the second sentence of Article I, Section 2(a)(2), a stockholder's notice required by this By-law shall also be considered timely, but only with respect to nominees for any new positions created by such increase, if it shall be received by the Secretary of the Corporation not later than the close of business on the tenth (10th) day following the day on which such public announcement is first made by the Corporation.

(b) General.

(1) Only such persons who are nominated in accordance with the provisions of this By-law shall be eligible for election and to serve as directors and only such business shall be conducted at an Annual Meeting as shall have been brought before the meeting in accordance with the provisions of this By-law or in accordance with Rule 14a-8 under the Exchange Act. The Board of Directors or a designated committee thereof shall have the power to determine whether a nomination or any business proposed to be brought before the meeting was made in accordance with the provisions of this By-law. If neither the Board of Directors nor such designated committee makes a determination as to whether any stockholder proposal or nomination was made in accordance with the provisions of this By-law, the presiding officer of the Annual Meeting shall have the power and duty to determine whether the stockholder proposal or nomination was made in accordance with the provisions of this By-law. If the Board of Directors or a designated committee thereof or the presiding officer, as applicable, determines that any stockholder proposal or nomination was not made in accordance with the provisions of this By-law, such proposal or nomination shall be disregarded and shall not be presented for action at the Annual Meeting.

(2) Except as otherwise required by law, nothing in this Article I, Section 2 shall obligate the Corporation or the Board of Directors to include in any proxy statement or other stockholder communication distributed on behalf of the Corporation or the Board of Directors information with respect to any nominee for director or any other matter of business submitted by a stockholder.

(3) Notwithstanding the foregoing provisions of this Article I, Section 2, if the nominating or proposing stockholder (or a qualified representative of the stockholder) does not appear at the Annual Meeting to present a nomination or any business, such nomination or business shall be disregarded, notwithstanding that proxies in respect of such vote may have been received by the Corporation. For purposes of this Article I, Section 2, to be considered a qualified representative of the proposing stockholder, a person must be authorized by a written instrument executed by such stockholder or an electronic transmission delivered by such stockholder to act for such stockholder as proxy at the meeting of stockholders and such person must produce such written instrument or electronic transmission, or a reliable reproduction of the written instrument or electronic transmission, to the presiding officer at the meeting of stockholders.

(4) For purposes of this By-law, "public announcement" shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or

comparable national news service or in a document publicly filed by the Corporation with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the Exchange Act.

(5) Notwithstanding the foregoing provisions of this By-law, a stockholder shall also comply with all applicable requirements of the Exchange Act and the rules and regulations thereunder with respect to the matters set forth in this By-law. Nothing in this By-law shall be deemed to affect any rights of (i) stockholders to have proposals included in the Corporation's proxy statement pursuant to Rule 14a-8 (or any successor rule), as applicable, under the Exchange Act and, to the extent required by such rule, have such proposals considered and voted on at an Annual Meeting or (ii) the holders of any series of Undesignated Preferred Stock to elect directors under specified circumstances.

SECTION 3.Special Meetings. Except as otherwise required by statute and subject to the rights, if any, of the holders of any series of Undesignated Preferred Stock, special meetings of the stockholders of the Corporation may be called only by the Board of Directors acting pursuant to a resolution approved by the affirmative vote of a majority of the Directors then in office. The Board of Directors may postpone or reschedule any previously scheduled special meeting of stockholders. Only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders of the Corporation. Nominations of persons for election to the Board of Directors of the Corporation and stockholder proposals of other business shall not be brought before a special meeting of stockholders to be considered by the stockholders unless such special meeting is held in lieu of an annual meeting of stockholders in accordance with Article I, Section 1 of these By-laws, in which case such special meeting in lieu thereof shall be deemed an Annual Meeting for purposes of these By-laws and the provisions of Article I, Section 2 of these By-laws shall govern such special meeting.

SECTION 4.Notice of Meetings; Adjournments.

(a) A notice of each Annual Meeting stating the hour, date and place, if any, of such Annual Meeting and the means of remote communication, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting, shall be given not less than ten (10) days nor more than sixty (60) days before the Annual Meeting, to each stockholder entitled to vote thereat by delivering such notice to such stockholder or by mailing it, postage prepaid, addressed to such stockholder at the address of such stockholder as it appears on the Corporation's stock transfer books. Without limiting the manner by which notice may otherwise be given to stockholders, any notice to stockholders may be given by electronic transmission in the manner provided in Section 232 of the Delaware General Corporation Law ("DGCL").

(b) Notice of all special meetings of stockholders shall be given in the same manner as provided for Annual Meetings, except that the notice of all special meetings shall state the purpose or purposes for which the meeting has been called.

(c) Notice of an Annual Meeting or special meeting of stockholders need not be given to a stockholder if a waiver of notice is executed, or waiver of notice by electronic transmission is provided, before or after such meeting by such stockholder or if such stockholder

attends such meeting, unless such attendance is for the express purpose of objecting at the beginning of the meeting to the transaction of any business because the meeting was not lawfully called or convened.

(d) The Board of Directors may postpone and reschedule any previously scheduled Annual Meeting or special meeting of stockholders and any record date with respect thereto, regardless of whether any notice or public disclosure with respect to any such meeting has been sent or made pursuant to Section 2 of this Article I of these By-laws or otherwise. In no event shall the public announcement of an adjournment, postponement or rescheduling of any previously scheduled meeting of stockholders commence a new time period for the giving of a stockholder's notice under this Article I of these By-laws.

(e) When any meeting is convened, the presiding officer may adjourn the meeting if (i) no quorum is present for the transaction of business, (ii) the Board of Directors determines that adjournment is necessary or appropriate to enable the stockholders to consider fully information which the Board of Directors determines has not been made sufficiently or timely available to stockholders, or (iii) the Board of Directors determines that adjournment is otherwise in the best interests of the Corporation. When any Annual Meeting or special meeting of stockholders is adjourned to another hour, date or place, notice need not be given of the adjourned meeting other than an announcement at the meeting at which the adjournment is taken of the hour, date and place, if any, to which the meeting is adjourned and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting; provided, however, that if the adjournment is for more than thirty (30) days from the meeting date, or if after the adjournment a new record date is fixed for the adjourned meeting, notice of the adjourned meeting and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting shall be given to each stockholder of record entitled to vote thereat and each stockholder who, by law or under the Certificate of Incorporation of the Corporation (as the same may hereafter be amended and/or restated, the "Certificate") or these By-laws, is entitled to such notice.

SECTION 5.Quorum. A majority of the shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at any meeting of stockholders. If less than a quorum is present at a meeting, the holders of voting stock representing a majority of the voting power present at the meeting or the presiding officer may adjourn the meeting from time to time, and the meeting may be held as adjourned without further notice, except as provided in Section 4 of this Article I. At such adjourned meeting at which a quorum is present, any business may be transacted which might have been transacted at the meeting as originally noticed. The stockholders present at a duly constituted meeting may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

SECTION 6.Voting and Proxies. Stockholders shall have one vote for each share of stock entitled to vote owned by them of record according to the stock ledger of the Corporation as of the record date, unless otherwise provided by law or by the Certificate. Stockholders may vote either (i) in person, (ii) by written proxy or (iii) by a transmission permitted by Section 212(c) of the DGCL. Any copy, facsimile telecommunication or other reliable reproduction of

the writing or transmission permitted by Section 212(c) of the DGCL may be substituted for or used in lieu of the original writing or transmission for any and all purposes for which the original writing or transmission could be used, provided that such copy, facsimile telecommunication or other reproduction shall be a complete reproduction of the entire original writing or transmission. Proxies shall be filed in accordance with the procedures established for the meeting of stockholders. Except as otherwise limited therein or as otherwise provided by law, proxies authorizing a person to vote at a specific meeting shall entitle the persons authorized thereby to vote at any adjournment of such meeting, but they shall not be valid after final adjournment of such meeting. A proxy with respect to stock held in the name of two or more persons shall be valid if executed by or on behalf of any one of them unless at or prior to the exercise of the proxy the Corporation receives a specific written notice to the contrary from any one of them.

SECTION 7.Action at Meeting. When a quorum is present at any meeting of stockholders, any matter before any such meeting (other than an election of a director or directors) shall be decided by a majority of the votes properly cast for and against such matter, except where a larger vote is required by law, by the Certificate or by these By-laws. Any election of directors by stockholders shall be determined by a plurality of the votes properly cast on the election of directors.

SECTION 8.Stockholder Lists. The Secretary or an Assistant Secretary (or the Corporation's transfer agent or other person authorized by these By-laws or by law) shall prepare and make, at least ten (10) days before every Annual Meeting or special meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for a period of at least ten (10) days prior to the meeting in the manner provided by law. The list shall also be open to the examination of any stockholder during the whole time of the meeting as provided by law.

SECTION 9.Presiding Officer. The Board of Directors shall designate a representative to preside over all Annual Meetings or special meetings of stockholders, provide that if the Board of Directors does not so designate such a presiding officer, then the Chairman of the Board, if one is elected, shall preside over such meetings. If the Board of Directors does not so designate such a presiding officer and there is no Chairman of the Board or the Chairman of the Board is unable to so preside or is absent, then the Chief Executive Officer, if one is elected, shall preside over such meetings, provided further that if there is no Chief Executive Officer or the Chief Executive Officer is unable to so preside or is absent, then the President shall preside over such meetings. The presiding officer at any Annual Meeting or special meeting of stockholders shall have the power, among other things, to adjourn such meeting at any time and from time to time, subject to Sections 4 and 5 of this Article I. The order of business and all other matters of procedure at any meeting of the stockholders shall be determined by the presiding officer.

SECTION 10.Inspectors of Elections. The Corporation shall, in advance of any meeting of stockholders, appoint one or more inspectors to act at the meeting and make a written report thereof. The Corporation may designate one or more persons as alternate inspectors to replace any inspector who fails to act. If no inspector or alternate is able to act at a meeting of

stockholders, the presiding officer shall appoint one or more inspectors to act at the meeting. Any inspector may, but need not, be an officer, employee or agent of the Corporation. Each inspector, before entering upon the discharge of his or her duties, shall take and sign an oath faithfully to execute the duties of inspector with strict impartiality and according to the best of his or her ability. The inspectors shall perform such duties as are required by the DGCL, including the counting of all votes and ballots. The inspectors may appoint or retain other persons or entities to assist the inspectors in the performance of the duties of the inspectors. The presiding officer may review all determinations made by the inspectors, and in so doing the presiding officer shall be entitled to exercise his or her sole judgment and discretion and he or she shall not be bound by any determinations made by the inspectors. All determinations by the inspectors and, if applicable, the presiding officer, shall be subject to further review by any court of competent jurisdiction.

ARTICLE II

Directors

SECTION 1.Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors except as otherwise provided by the Certificate or required by law.

SECTION 2.Number and Terms. The number of directors of the Corporation shall be fixed solely and exclusively by resolution duly adopted from time to time by the Board of Directors. The directors shall hold office in the manner provided in the Certificate.

SECTION 3.Qualification. No director need be a stockholder of the Corporation.

SECTION 4.Vacancies. Vacancies in the Board of Directors shall be filled in the manner provided in the Certificate.

SECTION 5.Removal. Directors may be removed from office only in the manner provided in the Certificate.

SECTION 6.Resignation. A director may resign at any time by giving written notice to the Chairman of the Board, if one is elected, the President or the Secretary. A resignation shall be effective upon receipt, unless the resignation otherwise provides.

SECTION 7.Regular Meetings. Regular meetings (including any annual meeting) of the Board of Directors may be held at such hour, date and place as the Board of Directors may by resolution from time to time determine and publicize by means of reasonable notice given to any director who is not present at the meeting at which such resolution is adopted.

SECTION 8.Special Meetings. Special meetings of the Board of Directors may be called, orally or in writing, by or at the request of a majority of the directors, the Chairman of the Board, if one is elected, or the President. The person calling any such special meeting of the Board of Directors may fix the hour, date and place thereof.

SECTION 9.Notice of Meetings. Notice of the hour, date and place of all special meetings of the Board of Directors shall be given to each director by the Secretary or an Assistant Secretary, or in case of the death, absence, incapacity or refusal of such persons, by the Chairman of the Board, if one is elected, or the President or such other officer designated by the Chairman of the Board, if one is elected, or the President. Notice of any special meeting of the Board of Directors shall be given to each director in person, by telephone, or by facsimile, electronic mail or other form of electronic communication, sent to his or her business or home address, at least twenty-four (24) hours in advance of the meeting, or by written notice mailed to his or her business or home address, at least forty-eight (48) hours in advance of the meeting. Such notice shall be deemed to be delivered when hand-delivered to such address, read to such director by telephone, deposited in the mail so addressed, with postage thereon prepaid if mailed, dispatched or transmitted if sent by facsimile transmission or by electronic mail or other form of electronic communications. A written waiver of notice signed before or after a meeting by a director and filed with the records of the meeting shall be deemed to be equivalent to notice of the meeting. The attendance of a director at a meeting shall constitute a waiver of notice of such meeting, except where a director attends a meeting for the express purpose of objecting at the beginning of the meeting to the transaction of any business because such meeting is not lawfully called or convened. Except as otherwise required by law, by the Certificate or by these By-laws, neither the business to be transacted at, nor the purpose of, any meeting of the Board of Directors need be specified in the notice or waiver of notice of such meeting.

SECTION 10.Quorum. At any meeting of the Board of Directors, a majority of the total number of directors shall constitute a quorum for the transaction of business, but if less than a quorum is present at a meeting, a majority of the directors present may adjourn the meeting from time to time, and the meeting may be held as adjourned without further notice. Any business which might have been transacted at the meeting as originally noticed may be transacted at such adjourned meeting at which a quorum is present. For purposes of this section, the total number of directors includes any unfilled vacancies on the Board of Directors.

SECTION 11.Action at Meeting. At any meeting of the Board of Directors at which a quorum is present, the vote of a majority of the directors present shall constitute action by the Board of Directors, unless otherwise required by law, by the Certificate or by these By-laws.

SECTION 12.Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors may be taken without a meeting if all members of the Board of Directors consent thereto in writing or by electronic transmission and the writing or writings or electronic transmission or transmissions are filed with the records of the meetings of the Board of Directors. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form. Such consent shall be treated as a resolution of the Board of Directors for all purposes.

SECTION 13.Manner of Participation. Directors may participate in meetings of the Board of Directors by means of conference telephone or other communications equipment by means of which all directors participating in the meeting can hear each other, and participation in a meeting in accordance herewith shall constitute presence in person at such meeting for purposes of these By-laws.

SECTION 14.Presiding Director. The Board of Directors shall designate a representative to preside over all meetings of the Board of Directors, provided that if the Board of Directors does not so designate such a presiding director or such designated presiding director is unable to so preside or is absent, then the Chairman of the Board, if one is elected, shall preside over all meetings of the Board of Directors. If both the designated presiding director, if one is so designated, and the Chairman of the Board, if one is elected, are unable to preside or are absent, the Board of Directors shall designate an alternate representative to preside over a meeting of the Board of Directors.

SECTION 15.Committees. The Board of Directors, by vote of a majority of the directors then in office, may elect one or more committees, including, without limitation, a Compensation Committee, a Nominating & Corporate Governance Committee and an Audit Committee, and may delegate thereto some or all of its powers except those which by law, by the Certificate or by these By-laws may not be delegated. Except as the Board of Directors may otherwise determine, any such committee may make rules for the conduct of its business, but unless otherwise provided by the Board of Directors or in such rules, its business shall be conducted so far as possible in the same manner as is provided by these By-laws for the Board of Directors. All members of such committees shall hold such offices at the pleasure of the Board of Directors. The Board of Directors may abolish any such committee at any time. Any committee to which the Board of Directors delegates any of its powers or duties shall keep records of its meetings and shall report its action to the Board of Directors.

SECTION 16.Compensation of Directors. Directors shall receive such compensation for their services as shall be determined by a majority of the Board of Directors, or a designated committee thereof, provided that directors who are serving the Corporation as employees and who receive compensation for their services as such, shall not receive any salary or other compensation for their services as directors of the Corporation.

ARTICLE III

Officers

SECTION 1.Enumeration. The officers of the Corporation shall consist of a President, a Treasurer, a Secretary and such other officers, including, without limitation, a Chairman of the Board of Directors, a Chief Executive Officer and one or more Vice Presidents (including Executive Vice Presidents or Senior Vice Presidents), Assistant Vice Presidents, Assistant Treasurers and Assistant Secretaries, as the Board of Directors may determine.

SECTION 2.Election. At the regular annual meeting of the Board of Directors following the Annual Meeting, the Board of Directors shall elect the President, the Treasurer and the Secretary. Other officers may be elected by the Board of Directors at such regular annual meeting of the Board of Directors or at any other regular or special meeting.

SECTION 3.Qualification. No officer need be a stockholder or a director. Any person may occupy more than one office of the Corporation at any time.

SECTION 4.Tenure. Except as otherwise provided by the Certificate or by these By-laws, each of the officers of the Corporation shall hold office until the regular annual meeting

of the Board of Directors following the next Annual Meeting and until his or her successor is elected and qualified or until his or her earlier resignation or removal.

SECTION 5.Resignation. Any officer may resign by delivering his or her written resignation to the Corporation addressed to the President or the Secretary, and such resignation shall be effective upon receipt, unless the resignation otherwise provides.

SECTION 6.Removal. Except as otherwise provided by law, the Board of Directors may remove any officer with or without cause by the affirmative vote of a majority of the directors then in office.

SECTION 7.Absence or Disability. In the event of the absence or disability of any officer, the Board of Directors may designate another officer to act temporarily in place of such absent or disabled officer.

SECTION 8.Vacancies. Any vacancy in any office may be filled for the unexpired portion of the term by the Board of Directors.

SECTION 9.President. The President shall, subject to the direction of the Board of Directors, have such powers and shall perform such duties as the Board of Directors may from time to time designate.

SECTION 10.Chairman of the Board. The Chairman of the Board, if one is elected, shall have such powers and shall perform such duties as the Board of Directors may from time to time designate.

SECTION 11.Chief Executive Officer. The Chief Executive Officer, if one is elected, shall have such powers and shall perform such duties as the Board of Directors may from time to time designate.

SECTION 12.Vice Presidents and Assistant Vice Presidents. Any Vice President (including any Executive Vice President or Senior Vice President) and any Assistant Vice President shall have such powers and shall perform such duties as the Board of Directors or the Chief Executive Officer may from time to time designate.

SECTION 13.Treasurer and Assistant Treasurers. The Treasurer shall, subject to the direction of the Board of Directors and except as the Board of Directors or the Chief Executive Officer may otherwise provide, have general charge of the financial affairs of the Corporation and shall cause to be kept accurate books of account. The Treasurer shall have custody of all funds, securities, and valuable documents of the Corporation. He or she shall have such other duties and powers as may be designated from time to time by the Board of Directors or the Chief Executive Officer. Any Assistant Treasurer shall have such powers and perform such duties as the Board of Directors or the Chief Executive Officer may from time to time designate.

SECTION 14.Secretary and Assistant Secretaries. The Secretary shall record all the proceedings of the meetings of the stockholders and the Board of Directors (including committees of the Board of Directors) in books kept for that purpose. In his or her absence from any such meeting, a temporary secretary chosen at the meeting shall record the proceedings

thereof. The Secretary shall have charge of the stock ledger (which may, however, be kept by any transfer or other agent of the Corporation). The Secretary shall have custody of the seal of the Corporation, and the Secretary, or an Assistant Secretary shall have authority to affix it to any instrument requiring it, and, when so affixed, the seal may be attested by his or her signature or that of an Assistant Secretary. The Secretary shall have such other duties and powers as may be designated from time to time by the Board of Directors or the Chief Executive Officer. In the absence of the Secretary, any Assistant Secretary may perform his or her duties and responsibilities. Any Assistant Secretary shall have such powers and perform such duties as the Board of Directors or the Chief Executive Officer may from time to time designate.

SECTION 15.Other Powers and Duties. Subject to these By-laws and to such limitations as the Board of Directors may from time to time prescribe, the officers of the Corporation shall each have such powers and duties as generally pertain to their respective offices, as well as such powers and duties as from time to time may be conferred by the Board of Directors or the Chief Executive Officer.

ARTICLE IV

Capital Stock

SECTION 1.Certificates of Stock. Each stockholder shall be entitled to a certificate of the capital stock of the Corporation in such form as may from time to time be prescribed by the Board of Directors. Such certificate shall be signed by the Chairman of the Board, the President or a Vice President and by the Treasurer or an Assistant Treasurer, or the Secretary or an Assistant Secretary. The Corporation seal and the signatures by the Corporation's officers, the transfer agent or the registrar may be facsimiles. In case any officer, transfer agent or registrar who has signed or whose facsimile signature has been placed on such certificate shall have ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the Corporation with the same effect as if he or she were such officer, transfer agent or registrar at the time of its issue. Every certificate for shares of stock which are subject to any restriction on transfer and every certificate issued when the Corporation is authorized to issue more than one class or series of stock shall contain such legend with respect thereto as is required by law. Notwithstanding anything to the contrary provided in these Bylaws, the Board of Directors of the Corporation may provide by resolution or resolutions that some or all of any or all classes or series of its stock shall be uncertificated shares (except that the foregoing shall not apply to shares represented by a certificate until such certificate is surrendered to the Corporation), and by the approval and adoption of these Bylaws the Board of Directors has determined that all classes or series of the Corporation's stock may be uncertificated, whether upon original issuance, re-issuance, or subsequent transfer.

SECTION 2.Transfers. Subject to any restrictions on transfer and unless otherwise provided by the Board of Directors, shares of stock that are represented by a certificate may be transferred on the books of the Corporation by the surrender to the Corporation or its transfer agent of the certificate theretofore properly endorsed or accompanied by a written assignment or power of attorney properly executed, with transfer stamps (if necessary) affixed, and with such proof of the authenticity of signature as the Corporation or its transfer agent may reasonably require. Shares of stock that are not represented by a certificate may be transferred on the books

of the Corporation by submitting to the Corporation or its transfer agent such evidence of transfer and following such other procedures as the Corporation or its transfer agent may require.

SECTION 3.Record Holders. Except as may otherwise be required by law, by the Certificate or by these By-laws, the Corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect thereto, regardless of any transfer, pledge or other disposition of such stock, until the shares have been transferred on the books of the Corporation in accordance with the requirements of these By-laws.

SECTION 4.Record Date. In order that the Corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof or entitled to receive payment of any dividend or other distribution or allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of stock or for the purpose of any other lawful action, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date: (a) in the case of determination of stockholders entitled to vote at any meeting of stockholders, shall, unless otherwise required by law, not be more than sixty (60) nor less than ten (10) days before the date of such meeting and (b) in the case of any other action, shall not be more than sixty (60) days prior to such other action. If no record date is fixed: (i) the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held; and (ii) the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

SECTION 5.Replacement of Certificates. In case of the alleged loss, destruction or mutilation of a certificate of stock of the Corporation, a duplicate certificate may be issued in place thereof, upon such terms as the Board of Directors may prescribe.

ARTICLE V

Indemnification

SECTION 1.Definitions. For purposes of this Article:

(a) "Corporate Status" describes the status of a person who is serving or has served (i) as a Director of the Corporation, (ii) as an Officer of the Corporation, (iii) as a Non-Officer Employee of the Corporation, or (iv) as a director, partner, trustee, officer, employee or agent of any other corporation, partnership, limited liability company, joint venture, trust, employee benefit plan, foundation, association, organization or other legal entity which such person is or was serving at the request of the Corporation. For purposes of this Section 1(a), a Director, Officer or Non-Officer Employee of the Corporation who is serving or has served as a director, partner, trustee, officer, employee or agent of a Subsidiary shall be deemed to be serving at the request of the Corporation. Notwithstanding the foregoing, "Corporate Status" shall not include the status of a person who is serving or has served as a director, officer, employee or agent of a

constituent corporation absorbed in a merger or consolidation transaction with the Corporation with respect to such person's activities prior to said transaction, unless specifically authorized by the Board of Directors or the stockholders of the Corporation;

(b) "Director" means any person who serves or has served the Corporation as a director on the Board of Directors of the Corporation;

(c) "Disinterested Director" means, with respect to each Proceeding in respect of which indemnification is sought hereunder, a Director of the Corporation who is not and was not a party to such Proceeding;

(d) "Expenses" means all attorneys' fees, retainers, court costs, transcript costs, fees of expert witnesses, private investigators and professional advisors (including, without limitation, accountants and investment bankers), travel expenses, duplicating costs, printing and binding costs, costs of preparation of demonstrative evidence and other courtroom presentation aids and devices, costs incurred in connection with document review, organization, imaging and computerization, telephone charges, postage, delivery service fees, and all other disbursements, costs or expenses of the type customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, being or preparing to be a witness in, settling or otherwise participating in, a Proceeding;

(e) "Liabilities" means judgments, damages, liabilities, losses, penalties, excise taxes, fines and amounts paid in settlement;

(f) "Non-Officer Employee" means any person who serves or has served as an employee or agent of the Corporation, but who is not or was not a Director or Officer;

(g) "Officer" means any person who serves or has served the Corporation as an officer of the Corporation appointed by the Board of Directors of the Corporation;

(h) "Proceeding" means any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, inquiry, investigation, administrative hearing or other proceeding, whether civil, criminal, administrative, arbitrative or investigative; and

(i) "Subsidiary" shall mean any corporation, partnership, limited liability company, joint venture, trust or other entity of which the Corporation owns (either directly or through or together with another Subsidiary of the Corporation) either (i) a general partner, managing member or other similar interest or (ii) (A) fifty percent (50%) or more of the voting power of the voting capital equity interests of such corporation, partnership, limited liability company, joint venture or other entity, or (B) fifty percent (50%) or more of the outstanding voting capital stock or other voting equity interests of such corporation, partnership, limited liability company, joint venture or other entity.

SECTION 2.Indemnification of Directors and Officers.

(a) Subject to the operation of Section 4 of this Article V of these By-laws, each Director and Officer shall be indemnified and held harmless by the Corporation to the fullest extent authorized by the DGCL, as the same exists or may hereafter be amended (but, in the case

of any such amendment, only to the extent that such amendment permits the Corporation to provide broader indemnification rights than such law permitted the Corporation to provide prior to such amendment), and to the extent authorized in this Section 2.

(1) Actions, Suits and Proceedings Other than By or In the Right of the Corporation. Each Director and Officer shall be indemnified and held harmless by the Corporation against any and all Expenses and Liabilities that are incurred or paid by such Director or Officer or on such Director's or Officer's behalf in connection with any Proceeding or any claim, issue or matter therein (other than an action by or in the right of the Corporation), which such Director or Officer is, or is threatened to be made, a party to or participant in by reason of such Director's or Officer's Corporate Status, if such Director or Officer acted in good faith and in a manner such Director or Officer reasonably believed to be in or not opposed to the best interests of the Corporation and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful.

(2) Actions, Suits and Proceedings By or In the Right of the Corporation. Each Director and Officer shall be indemnified and held harmless by the Corporation against any and all Expenses that are incurred by such Director or Officer or on such Director's or Officer's behalf in connection with any Proceeding or any claim, issue or matter therein by or in the right of the Corporation, which such Director or Officer is, or is threatened to be made, a party to or participant in by reason of such Director's or Officer's Corporate Status, if such Director or Officer acted in good faith and in a manner such Director or Officer reasonably believed to be in or not opposed to the best interests of the Corporation; provided, however, that no indemnification shall be made under this Section 2(a)(2) in respect of any claim, issue or matter as to which such Director or Officer shall have been finally adjudged by a court of competent jurisdiction to be liable to the Corporation, unless, and only to the extent that, the Court of Chancery or another court in which such Proceeding was brought shall determine upon application that, despite adjudication of liability, but in view of all the circumstances of the case, such Director or Officer is fairly and reasonably entitled to indemnification for such Expenses that such court deems proper.

(3) Survival of Rights. The rights of indemnification provided by this Section 2 shall continue as to a Director or Officer after he or she has ceased to be a Director or Officer and shall inure to the benefit of his or her heirs, executors, administrators and personal representatives.

(4) Actions by Directors or Officers. Notwithstanding the foregoing, the Corporation shall indemnify any Director or Officer seeking indemnification in connection with a Proceeding initiated by such Director or Officer only if such Proceeding (including any parts of such Proceeding not initiated by such Director or Officer) was authorized in advance by the Board of Directors of the Corporation, unless such Proceeding was brought to enforce such Officer's or Director's rights to indemnification or, in the case of Directors, advancement of Expenses under these By-laws in accordance with the provisions set forth herein.

SECTION 3.Indemnification of Non-Officer Employees. Subject to the operation of Section 4 of this Article V of these By-laws, each Non-Officer Employee may, in the discretion of the Board of Directors of the Corporation, be indemnified by the Corporation to the fullest extent authorized by the DGCL, as the same exists or may hereafter be amended, against any or all Expenses and Liabilities that are incurred by such Non-Officer Employee or on such Non-Officer Employee's behalf in connection with any threatened, pending or completed Proceeding, or any claim, issue or matter therein, which such Non-Officer Employee is, or is threatened to be made, a party to or participant in by reason of such Non-Officer Employee's Corporate Status, if such Non-Officer Employee acted in good faith and in a manner such Non-Officer Employee reasonably believed to be in or not opposed to the best interests of the Corporation and, with respect to any criminal proceeding, had no reasonable cause to believe his or her conduct was unlawful. The rights of indemnification provided by this Section 3 shall exist as to a Non-Officer Employee after he or she has ceased to be a Non-Officer Employee and shall inure to the benefit of his or her heirs, personal representatives, executors and administrators. Notwithstanding the foregoing, the Corporation may indemnify any Non-Officer Employee seeking indemnification in connection with a Proceeding initiated by such Non-Officer Employee only if such Proceeding was authorized in advance by the Board of Directors of the Corporation.

SECTION 4.Determination. Unless ordered by a court, no indemnification shall be provided pursuant to this Article V to a Director, to an Officer or to a Non-Officer Employee unless a determination shall have been made that such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the Corporation and, with respect to any criminal Proceeding, such person had no reasonable cause to believe his or her conduct was unlawful. Such determination shall be made by (a) a majority vote of the Disinterested Directors, even though less than a quorum of the Board of Directors, (b) a committee comprised of Disinterested Directors, such committee having been designated by a majority vote of the Disinterested Directors (even though less than a quorum), (c) if there are no such Disinterested Directors, or if a majority of Disinterested Directors so directs, by independent legal counsel in a written opinion, or (d) by the stockholders of the Corporation.

SECTION 5.Advancement of Expenses to Directors Prior to Final Disposition.

(a) The Corporation shall advance all Expenses incurred by or on behalf of any Director in connection with any Proceeding in which such Director is involved by reason of such Director's Corporate Status within thirty (30) days after the receipt by the Corporation of a written statement from such Director requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by such Director and shall be preceded or accompanied by an undertaking by or on behalf of such Director to repay any Expenses so advanced if it shall ultimately be determined that such Director is not entitled to be indemnified against such Expenses. Notwithstanding the foregoing, the Corporation shall advance all Expenses incurred by or on behalf of any Director seeking advancement of expenses hereunder in connection with a Proceeding initiated by such Director only if such Proceeding (including any parts of such Proceeding not initiated by such Director) was (i) authorized by the Board of Directors of the Corporation, or (ii) brought to enforce such Director's rights to indemnification or advancement of Expenses under these By-laws.

(b) If a claim for advancement of Expenses hereunder by a Director is not paid in full by the Corporation within thirty (30) days after receipt by the Corporation of documentation of Expenses and the required undertaking, such Director may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim and if successful in whole or in part, such Director shall also be entitled to be paid the expenses of prosecuting such claim. The failure of the Corporation (including its Board of Directors or any committee thereof, independent legal counsel, or stockholders) to make a determination concerning the permissibility of such advancement of Expenses under this Article V shall not be a defense to an action brought by a Director for recovery of the unpaid amount of an advancement claim and shall not create a presumption that such advancement is not permissible. The burden of proving that a Director is not entitled to an advancement of expenses shall be on the Corporation.

(c) In any suit brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall be entitled to recover such expenses upon a final adjudication that the Director has not met any applicable standard for indemnification set forth in the DGCL.

SECTION 6.Advancement of Expenses to Officers and Non-Officer Employees Prior to Final Disposition.

(a) The Corporation may, at the discretion of the Board of Directors of the Corporation, advance any or all Expenses incurred by or on behalf of any Officer or any Non-Officer Employee in connection with any Proceeding in which such person is involved by reason of his or her Corporate Status as an Officer or Non-Officer Employee upon the receipt by the Corporation of a statement or statements from such Officer or Non-Officer Employee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by such Officer or Non-Officer Employee and shall be preceded or accompanied by an undertaking by or on behalf of such person to repay any Expenses so advanced if it shall ultimately be determined that such Officer or Non-Officer Employee is not entitled to be indemnified against such Expenses.

(b) In any suit brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall be entitled to recover such expenses upon a final adjudication that the Officer or Non-Officer Employee has not met any applicable standard for indemnification set forth in the DGCL.

SECTION 7.Contractual Nature of Rights.

(a) The provisions of this Article V shall be deemed to be a contract between the Corporation and each Director and Officer entitled to the benefits hereof at any time while this Article V is in effect, in consideration of such person’s past or current and any future performance of services for the Corporation. Neither amendment, repeal or modification of any provision of this Article V nor the adoption of any provision of the Certificate of Incorporation inconsistent with this Article V shall eliminate or reduce any right conferred by this Article V in respect of any act or omission occurring, or any cause of action or claim that accrues or arises or any state of facts existing, at the time of or before such amendment, repeal, modification or

adoption of an inconsistent provision (even in the case of a proceeding based on such a state of facts that is commenced after such time), and all rights to indemnification and advancement of Expenses granted herein or arising out of any act or omission shall vest at the time of the act or omission in question, regardless of when or if any proceeding with respect to such act or omission is commenced. The rights to indemnification and to advancement of expenses provided by, or granted pursuant to, this Article V shall continue notwithstanding that the person has ceased to be a director or officer of the Corporation and shall inure to the benefit of the estate, heirs, executors, administrators, legatees and distributes of such person.

(b) If a claim for indemnification hereunder by a Director or Officer is not paid in full by the Corporation within sixty (60) days after receipt by the Corporation of a written claim for indemnification, such Director or Officer may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim, and if successful in whole or in part, such Director or Officer shall also be entitled to be paid the expenses of prosecuting such claim. The failure of the Corporation (including its Board of Directors or any committee thereof, independent legal counsel, or stockholders) to make a determination concerning the permissibility of such indemnification under this Article V shall not be a defense to an action brought by a Director or Officer for recovery of the unpaid amount of an indemnification claim and shall not create a presumption that such indemnification is not permissible. The burden of proving that a Director or Officer is not entitled to indemnification shall be on the Corporation.

(c) In any suit brought by a Director or Officer to enforce a right to indemnification hereunder, it shall be a defense that such Director or Officer has not met any applicable standard for indemnification set forth in the DGCL.

SECTION 8.Non-Exclusivity of Rights. The rights to indemnification and to advancement of Expenses set forth in this Article V shall not be exclusive of any other right which any Director, Officer, or Non-Officer Employee may have or hereafter acquire under any statute, provision of the Certificate or these By-laws, agreement, vote of stockholders or Disinterested Directors or otherwise.

SECTION 9.Insurance. The Corporation may maintain insurance, at its expense, to protect itself and any Director, Officer or Non-Officer Employee against any liability of any character asserted against or incurred by the Corporation or any such Director, Officer or Non-Officer Employee, or arising out of any such person's Corporate Status, whether or not the Corporation would have the power to indemnify such person against such liability under the DGCL or the provisions of this Article V.

SECTION 10.Other Indemnification. The Corporation's obligation, if any, to indemnify or provide advancement of Expenses to any person under this Article V as a result of such person serving, at the request of the Corporation, as a director, partner, trustee, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount such person may collect as indemnification or advancement of Expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or enterprise (the "Primary Indemnitor"). Any indemnification or advancement of Expenses under this Article V owed by the Corporation as a result of a person serving, at the request of the Corporation, as a director, partner, trustee, officer, employee or

agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall only be in excess of, and shall be secondary to, the indemnification or advancement of Expenses available from the applicable Primary Indemnitor(s) and any applicable insurance policies.

ARTICLE VI

Miscellaneous Provisions

SECTION 1.Fiscal Year. The fiscal year of the Corporation shall be determined by the Board of Directors.

SECTION 2.Seal. The Board of Directors shall have power to adopt and alter the seal of the Corporation.

SECTION 3.Execution of Instruments. All deeds, leases, transfers, contracts, bonds, notes and other obligations to be entered into by the Corporation in the ordinary course of its business without director action may be executed on behalf of the Corporation by the Chairman of the Board, if one is elected, the President or the Treasurer or any other officer, employee or agent of the Corporation as the Board of Directors or the executive committee of the Board may authorize.

SECTION 4.Voting of Securities. Unless the Board of Directors otherwise provides, the Chairman of the Board, if one is elected, the President or the Treasurer may waive notice of and act on behalf of the Corporation, or appoint another person or persons to act as proxy or attorney in fact for the Corporation with or without discretionary power and/or power of substitution, at any meeting of stockholders or shareholders of any other corporation or organization, any of whose securities are held by the Corporation.

SECTION 5.Resident Agent. The Board of Directors may appoint a resident agent upon whom legal process may be served in any action or proceeding against the Corporation.

SECTION 6.Corporate Records. The original or attested copies of the Certificate, By-laws and records of all meetings of the incorporators, stockholders and the Board of Directors and the stock transfer books, which shall contain the names of all stockholders, their record addresses and the amount of stock held by each, may be kept outside the State of Delaware and shall be kept at the principal office of the Corporation, at an office of its counsel, at an office of its transfer agent or at such other place or places as may be designated from time to time by the Board of Directors.

SECTION 7.Certificate. All references in these By-laws to the Certificate shall be deemed to refer to the Amended and Restated Certificate of Incorporation of the Corporation, as amended and/or restated and in effect from time to time.

SECTION 8.Exclusive Jurisdiction of Delaware Courts or the United States Federal District Courts. Unless the Corporation consents in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on behalf of the

Corporation, (ii) any action asserting a claim of, or a claim based on, a breach of a fiduciary duty owed by any current or former director, officer or other employee of the Corporation to the Corporation or the Corporation's stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or the Certificate or Bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim governed by the internal affairs doctrine. Unless the Corporation consents in writing to the selection of an alternative forum, the federal district courts of the United States of America shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. Any person or entity purchasing or otherwise acquiring any interest in shares of capital stock of the Corporation shall be deemed to have notice of and consented to the provisions of this Section 8.

SECTION 9.Amendment of By-laws.

(a) Amendment by Directors. Except as provided otherwise by law, these By-laws may be amended or repealed by the Board of Directors by the affirmative vote of a majority of the directors then in office.

(b) Amendment by Stockholders. These By-laws may be amended or repealed at any Annual Meeting, or special meeting of stockholders called for such purpose in accordance with these By-Laws, by the affirmative vote of at least seventy-five percent (75%) of the outstanding shares entitled to vote on such amendment or repeal, voting together as a single class; provided, however, that if the Board of Directors recommends that stockholders approve such amendment or repeal at such meeting of stockholders, such amendment or repeal shall only require the affirmative vote of the majority of the outstanding shares entitled to vote on such amendment or repeal, voting together as a single class. Notwithstanding the foregoing, stockholder approval shall not be required unless mandated by the Certificate, these By-laws, or other applicable law.

SECTION 10.Notices. If mailed, notice to stockholders shall be deemed given when deposited in the mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the Corporation. Without limiting the manner by which notice otherwise may be given to stockholders, any notice to stockholders may be given by electronic transmission in the manner provided in Section 232 of the DGCL.

SECTION 11.Waivers. A written waiver of any notice, signed by a stockholder or director, or waiver by electronic transmission by such person, whether given before or after the time of the event for which notice is to be given, shall be deemed equivalent to the notice required to be given to such person. Neither the business to be transacted at, nor the purpose of, any meeting need be specified in such a waiver.

Adopted by the Board on October 7, 2021 and approved by the stockholders on October 22, 2021 subject to and effective upon the effectiveness of the Corporation's Registration Statement on Form S-1 for its initial public offering.

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The summary of the general terms and provisions of the registered securities of Aura Biosciences, Inc. (the "Company," "we," "us," and "our") set forth below does not purport to be complete. It is subject to and qualified in its entirety by reference to our Tenth Amended and Restated Certificate of Incorporation ("certificate of incorporation") and our Amended and Restated Bylaws ("bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.1 is a part, and by applicable law. We encourage you to read our certificate of incorporation, our bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

General

Our authorized capital stock consists of 150,000,000 shares of common stock, par value $0.00001 per share, and 10,000,000 shares of preferred stock, par value $0.00001 per share, all of which shares of preferred stock are undesignated.

Common Stock

The holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Preferred Stock

Outstanding shares of our preferred stock will be converted into shares of our common stock. Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our Company or other corporate action.

No shares of preferred stock are outstanding as of the date of our Annual Report on Form 10-K with which this Exhibit 4.1 is filed as an exhibit.

Registration Rights

Certain of our stockholders are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of our Fifth Amended and Restated Investors' Rights Agreement, dated as of March 18, 2021 (the "Investors' Rights Agreement"). The investors' rights agreement between us and the holders of our preferred stock. The Investors' Rights Agreement includes demand registration rights, short-form registration rights, and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning six months after our initial public offering, certain of our stockholders are entitled to demand registration rights. Under the terms of our Investors' Rights Agreement, we will be required, upon the written request of a majority of holders of the registrable securities then outstanding that would result in an aggregate offering price of at least $5.0 million, to file a registration statement and to use commercially reasonable efforts to effect the registration of all or a portion of these shares for public resale.

Short-Form Registration Rights

Pursuant to the Investors' Rights Agreement, if we are eligible to file a registration statement on Form S-3, upon the written request from any such holder to sell registrable securities at an aggregate price of at least $3.0 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. We are required to effect only two registrations in any twelve-month period pursuant to this provision of the Investors' Rights Agreement.

Piggyback Registration Rights

If we register any of our securities either for our own account or for the account of other security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the Investors' Rights Agreement, we and the underwriters may limit the number of shares included in the underwritten offering to the number of shares which we and the underwriters determine in our sole discretion will not jeopardize the success of the offering.

Indemnification

The Investors' Rights Agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short-form registration rights granted under the Investors' Rights Agreement will terminate upon the earlier of (i) November 2, 2026 (ii) a liquidation event and (iii) with respect to any particular stockholder, when such stockholder is able to sell all of its shares pursuant to Rule 144 or any similar exemption under the Securities Act during any three-month period without registration.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of two-thirds or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and bylaws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, and limitation of liability must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of a majority of the outstanding shares entitled to vote on the amendment, voting together as a single class, except that the amendment of the provisions relating to notice of stockholder business and nominations and special meetings must be approved by not less than two-thirds of the outstanding shares entitled to vote on the amendment, and not less than two-thirds of the outstanding shares of each class entitled to vote thereon as a class, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

Our certificate of incorporation provides for 10,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Exclusive Forum

Our bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for any state law claims for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers and employees to us or our stockholders; (3) any action asserting a claim arising pursuant to the Delaware General Corporation Law or our certificate of incorporation or bylaws (including the interpretation, validity or enforceability thereof); or (4) any action asserting a claim that is governed by the internal affairs doctrine; provided, however, that this provision shall not apply to any causes of action arising under the Securities Act or the Exchange Act. In addition, our bylaws provide that, unless we consent to 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 under the Securities Act (the Federal Forum Provision). Any person or entity purchasing or otherwise acquiring any interest in our securities shall be deemed to have notice of and consented to these forum provisions. These forum provisions may impose additional costs on stockholders and may limit our stockholders' ability to bring a claim in a forum they find favorable, and the designated courts may reach different judgements or results than other courts. In addition, there is uncertainty as to whether our Federal Forum Provision will be enforced, which may impose additional costs on us and our stockholders.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges, or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Nasdaq Global Market Listing

Our common stock is listed on The Nasdaq Global Market under the trading symbol "AURA."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, Massachusetts 02021, and its telephone number is (800) 962-4284.

Exhibit 21.1

List of Subsidiaries of Registrant

1. Aura Biosciences Securities Corporation

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333- 260589) pertaining to the 2009 Amended and Restated Stock Option and Restricted Stock Plan, 2018 Equity Incentive Plan, Aura Biosciences, Inc. 2021 Stock Option and Incentive Plan, and Aura Biosciences, Inc. 2021 Employee Stock Purchase Plan of our report dated March 23, 2022, with respect to the consolidated financial statements of Aura Biosciences, Inc. included in this Annual Report (Form 10-K) of Aura Biosciences, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 23, 2022

Exhibit 31.1

CERTIFICATION

I, Elisabet de los Pinos, certify that:

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

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

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

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

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

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

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

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

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

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

Aura Biosciences, Inc.

Date: March 23, 2022

By: /s/ Elisabet de los Pinos
Elisabet de los Pinos
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION

I, Julie Feder, certify that:

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

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

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

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

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

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

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

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

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

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

Aura Biosciences, Inc.

Date: March 23, 2022

By: /s/ Julie Feder
Julie Feder
Chief Financial Officer

Exhibit 32.1

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

In connection with the Annual Report on Form 10-K of Aura Biosciences, Inc. (the "Company") for the year ended December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned certifies, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that, to the best of her knowledge:

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

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

Aura Biosciences, Inc.

Date: March 23, 2022

By: /s/ Elisabet de los Pinos
Elisabet de los Pinos
President and Chief Executive Officer

Date: March 23, 2022

By: /s/ Julie Feder
Julie Feder
Chief Financial Officer