APPLIED THERAPEUTICS, INC.

2024 ANNUAL REPORT

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2024

OR

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

For the transition period from to

Commission file number 001-38898

Applied Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**81-3405262**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
545 Fifth Avenue, Suite 1400, New York, NY	**10017**
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code **(212)-220-9226**

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock $0.0001 par value	**APLT**	The Nasdaq Global Market

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

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

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

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

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

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

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

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

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

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

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

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

The approximate aggregate market value of voting stock held by non-affiliates of the registrant, based upon the last sale price of the registrant's common stock on the last business day of the registrant's most recently completed second fiscal quarter, June 28, 2024, as reported on The Nasdaq Global Market, was approximately $478,467,415. This calculation excludes approximately 12,390,722 shares held by directors, executive officers and 10% or greater shareholders of the registrant. Exclusion of these shares does not constitute a determination that each such person is an affiliate of the registrant.

As of April 11, 2025, the total number of shares outstanding of the registrant's Common Stock was 141,575,526 shares, net of treasury shares.

Documents Incorporated by Reference: Portions of the registrant's definitive proxy statement for the registrant's 2025 annual meeting, to be filed within 120 days after the close of the registrant's fiscal year, are incorporated by reference into Part III of this Annual Report on Form 10-K.

APPLIED THERAPEUTICS, INC.
2024 FORM 10-K ANNUAL REPORT

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this "Annual Report") may contain "forward-looking statements" within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 about us and our industry that involve substantial risks and uncertainties. All statements other than statements of historical fact contained in this Annual Report, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "aim," "anticipate," "assume," "believe," "contemplate," "continue," "could," "design," "due," "estimate," "expect," "forecast," "goal," "intend," "may," "objective," "opportunity," "plan," "predict," "project," "positioned," "potential," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, including risks described in the section titled "Risk Factors" in this Annual Report:

- our plans to develop, market and commercialize our product candidates;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials and our research and development programs;
- our ability to take advantage of expedited regulatory pathways for any of our product candidates;
- our plans to address the Complete Response Letter and the Warning Letter received from the FDA (each term as defined below) and the impact of the Complete Response Letter and the Warning Letter to our current and future clinical trials or NDA submissions (as defined below);
- our estimates regarding expenses, future revenue, capital requirements, team, growth and needs for additional financing;
- our ability to successfully acquire or license additional product candidates on reasonable terms and advance product candidates into, and successfully complete, clinical studies;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to obtain and timing of regulatory approval of our current and future product candidates;
- the anticipated indications for our product candidates, if approved;
- our expectations regarding the potential market size and the rate and degree of market acceptance of such product candidates;
- our ability to fund our working capital requirements and expectations regarding the sufficiency of our capital resources;
- the implementation of our business model and strategic plans for our business and product candidates;
- our intellectual property position and the duration of our patent rights;
- developments or disputes concerning our intellectual property or other proprietary rights;
- disputes, lawsuits, class actions and derivative actions against or involving us;
- our expectations regarding government and third-party payor coverage and reimbursement;
- our ability to compete in the markets we serve;
- the impact of government laws and regulations and liabilities thereunder, including sudden changes in applicable legal or regulatory standards;
- developments relating to our competitors and our industry; and
- other factors that may impact our financial results.

The foregoing list of risks is not exhaustive. Other sections of this Annual Report include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

In light of the significant uncertainties in these forward-looking statements, you should not rely upon forward-looking statements as predictions of future events. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur at all. You should refer to the sections titled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

Unless the context otherwise requires, the terms "Applied," "Applied Therapeutics," "the Company," "we," "us," "our", "the registrant" and similar references in this Annual Report on Form 10-K refer to Applied Therapeutics, Inc.

PART I

ITEM 1. BUSINESS.

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against molecular targets in indications of high unmet medical need. We focus on previously identified disease processes where other molecules have failed to yield successful products due to poor efficacy and tolerability. Our unique approach to drug development leverages recent technological advances to design improved drugs, employs early use of biomarkers to confirm biological activity and focuses on potentially accelerated regulatory pathways. Our first molecular target is aldose reductase, or AR, an enzyme that converts glucose to sorbitol under oxidative stress conditions, and is implicated in multiple diseases. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. The detrimental consequences of AR activation have been well established by decades of prior research. Our AR program currently includes multiple potent and selective inhibitors of AR, which are engineered to have specific tissue permeability profiles to target different disease states, including diabetic complications, heart disease and rare metabolic diseases. The result of this multifaceted approach to drug development is a portfolio of highly specific and selective product candidates that we believe may be able to move more quickly through the development process.

Our lead candidate, AT-007 (also called govorestat) is a novel central nervous system, or CNS, penetrant aldose reductase inhibitor ("ARI") that we are developing for the treatment of rare metabolic diseases, including Galactosemia and CMT-SORD, also known as Charcot-Marie-Tooth-SORD or Sorbitol Dehydrogenase ("SORD") Deficiency. Galactosemia is a devastating rare pediatric metabolic disease that affects how the body processes a simple sugar called galactose, and for which there is no known cure or approved treatment available. The U.S. Food and Drug Administration, or FDA, has granted both orphan drug designation and rare pediatric disease designation to AT-007 for the treatment of Galactosemia and in June 2021, the FDA granted Fast Track Designation to AT-007 for the treatment of Galactosemia.

In February 2024, the FDA accepted a New Drug Application ("NDA") for AT-007 for the treatment of Classic Galactosemia. On November 27, 2024, the FDA issued a complete response letter ("Complete Response Letter") for the NDA for the treatment of Classic Galactosemia, indicating that the agency was unable to approve the NDA in its current form, citing deficiencies in the clinical application. On the same day, the FDA also issued a warning letter to us ("Warning Letter") and to a clinical investigator related to the Phase 2/3, ACTION-Galactosemia Kids study ("Clinical Investigator Warning Letter"). Following receipt of the Complete Response Letter, we withdrew a pending Marketing Authorization Application ("MAA") to the European Medicines Agency ("EMA") for AT-007 for the treatment of Classic Galactosemia, as we believed more time was needed to acquire further data to support a European MAA. We are actively working to address the issues raised in the Complete Response Letter and Warning Letter.

We are also studying a rare disease caused by deficiency in the enzyme Sorbitol Dehydrogenase, called SORD Deficiency. AR is the first enzyme in the polyol pathway, converting glucose to sorbitol. AR is then followed by Sorbitol Dehydrogenase, which converts sorbitol to fructose. Patients with SORD Deficiency accumulate very high levels of sorbitol in their cells and tissues as a result of the enzyme deficiency, which is thought to result in tissue toxicities such as peripheral neuropathy and motor neuron disease. Recent research in drosophila and cell models of SORD Deficiency demonstrated that treatment with an ARI that blocks sorbitol production may provide benefit in this disease. Preclinical studies on AT-007 have demonstrated significant reduction in sorbitol levels in fibroblasts from SORD deficient patients. Treatment with AT-007 in the drosophila model of SORD prevented the disease phenotype and protected from neuronal degeneration. On October 25, 2021, we reported data from a pilot open-label study in 8 SORD Deficiency patients. AT-007 reduced blood sorbitol levels by approximately 66% from baseline through 30 days of treatment. AT-007 was generally safe and well tolerated in treated patients. Both the FDA and EMA granted orphan status designation to AT-007 for the treatment of SORD Deficiency. In May 2022, the first patient was randomized to a Phase 2/3 study in patients with SORD Deficiency. On February 16, 2023, we announced that in an interim analysis of the Phase 2/3 INSPIRE trial, AT-007 reduced sorbitol levels over 90 days of treatment in patients with SORD Deficiency. On February 15, 2024, we announced preliminary results from an analysis of 12-month group-level data from the Phase 2/3 INSPIRE trial. In July 2024, we concluded the double-blind placebo-controlled portion of the Phase 2/3 INSPIRE trial and began transitioning patients to the open-label treatment phase prior to all patients completing 24 months of treatment. We are continuing to analyze the data from the Phase 2/3 INSPIRE trial and the extent to which

these data may support a potential submission for regulatory approval, including under the accelerated approval pathway. Following this analysis, we plan to meet with the FDA to discuss whether an NDA could be submitted based on the current data to date and/or with potential additional supporting data.

We also plan to initiate a clinical development program on AT-007 in another rare pediatric disease, called phosphomannomutase 2 ("PMM2")-congenital disorder of glycosylation ("CDG"), or PMM2-CDG. PMM2-CDG is a glycosylation disorder caused by deficiencies in the enzyme phosphomannomutase 2. The clinical presentations of PMM2-CDG include developmental delay, severe encephalopathy with axial hypotonia, abnormal eye movements, psychomotor retardation, cerebellar hypoplasia, and ataxia. Liver disease with elevated ALT and/or AST as well as abnormal coagulation are common features of PMM2-CDG. Many patients present with cardiomyopathy in infancy and many infants die in the first few years of life. AR is thought to be over-activated in this disease as a compensatory consequence of PMM2 deficiency, and a CNS penetrant ARI may be a compelling clinical option. Initial data in fibroblast cell lines derived from PMM2-CDG patients demonstrates that AT-007 treatment increases phosphomannomutase 2 activity. A young child with PMM2-CDG is being treated in a single-patient investigator initiated trial with AT-007 at the University of North Carolina School of Medicine. Data has been presented at medical conferences in 2022 supporting a favorable treatment effect of AT-007 on biomarkers and organ function in this patient. The FDA has granted rare pediatric disease designation and orphan designation for AT-007 in PMM2-CDG. We plan to request a pre-IND meeting with the FDA to discuss the clinical development program for AT-007 in patients with PMM2-CDG deficiency.

In January 2023 we announced a partnership with Advanz Pharma for commercialization of AT-007 (govorestat) in Europe, and entered into an Exclusive License and Supply Agreement with Advanz Pharma ("Advanz Agreement"). Advanz Pharma is a pharmaceutical company with a strategic focus on commercialization of specialty, hospital, and rare disease medicines in Europe. Under the terms of the Advanz Agreement, Advanz Pharma receives exclusive commercial rights in the European Economic Area, Switzerland, and the UK for AT-007 in Galactosemia and SORD Deficiency, with certain rights to future indications for AT-007 in Europe, if AT-007 receives marketing authorization. We will receive certain near-term development milestone payments upon clinical trial completion and marketing authorization in Europe as well as commercial sales milestones, which in the aggregate amount to over €130 million, including €10 million upfront, which was paid upon signing. If AT-007 receives marketing authorization, we will also receive royalties on any future net sales of AT-007 in Europe of 20%. We will continue to be responsible for the development, manufacturing and supply of AT-007, and Advanz Pharma will be responsible for packaging, distribution and commercialization in Europe.

AT-001 (also called caficrestat) is a novel ARI with broad systemic exposure and peripheral nerve permeability that we were developing for the treatment of diabetic cardiomyopathy, or DbCM, a fatal fibrosis of the heart, for which no treatments are available. We completed a Phase 1/2 clinical trial evaluating AT-001 in approximately 120 patients with type 2 diabetes, in which no drug-related adverse effects or tolerability issues were observed. In September 2019, we announced the initiation of a Phase 2/3 trial of AT-001 in DbCM. The study, called ARISE-HF, was designed to evaluate AT-001's ability to improve or prevent the decline of functional capacity in patients with DbCM at high risk of progression to overt heart failure. Although we did experience enrollment delays in 2020 associated with the Covid-19 pandemic, modifications were made to the trial to include additional sites and geographies to address Covid-19-related issues. On January 4, 2024, we reported topline results from the ARISE-HF study. AT-001 (caficrestat) demonstrated a strong trend in stabilizing cardiac functional capacity, while the placebo group declined over 15 months. The placebo-treated group declined by a mean of -0.31 ml/kg/min over 15 months of treatment, while the AT-001 1500mg twice daily treated group remained primarily stable, with a mean change of -0.01 ml/kg/min over 15 months. While a trend favored active treatment, the difference between active and placebo treated groups (0.30 ml/kg/min) was not statistically significant (p=0.210). Approximately 38% of study subjects were on SGLT2 or GLP-1 therapies for treatment of diabetes, while 62% were not. In a pre-specified subgroup analysis of the primary endpoint in patients not concomitantly treated with SGLT2 or GLP-1 therapies, the placebo group declined by a mean of -0.54 ml/kg/min, while the 1500mg BID AT-001 treated group improved by a mean of 0.08 ml/kg/min over 15 months of treatment, with a difference between groups of 0.62 ml/kg/min (p=0.040). Additionally, in this subgroup analysis, the number of patients who experienced a clinically significant worsening in cardiac functional capacity of 6% or more was substantially higher in the placebo group (46%) as compared to the 1500mg BID AT-001 treated group (32.7%), odds ratio 0.56 (p=0.035). A 6% change in cardiac functional capacity has been shown to predict long-term survival and hospitalization for heart failure. The effect of AT-001 was dose dependent, with the low dose (1000mg BID) demonstrating an intermediate effect between the high dose and placebo. AT-001 was generally safe and well tolerated, with no substantial differences

in serious adverse events between AT-001 treated groups as compared to placebo. We are currently not expending additional internal resources on AT-001 due to our focus on rare diseases.

AT-003 is a novel ARI designed to cross through the back of the eye when dosed orally, and has demonstrated strong retinal penetrance, for the treatment of diabetic retinopathy, or DR. DR is an ophthalmic disease that occurs in diabetic patients and for which treatments are currently limited to high-cost biologics requiring intravitreal administration. DR has been linked to AR activity, including elevations in sorbitol and subsequent changes in retinal blood vessels, which distorts vision and leads to permanent blindness. We are currently not expending additional internal resources on AT-003 due to our focus on rare diseases.

AT-104 is a preclinical dual selective PI3k inhibitor. Due to recent regulatory changes impacting development of the PI3k inhibitor class of compounds, the Company has discontinued its early stage preclinical PI3k program and further development of AT-104. The compound and all rights associated with the technology were returned to Columbia University.

Since inception in 2016, our operations have focused on developing our product candidates, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials. We do not have any product candidates approved for sale and have not generated any revenue.

We have incurred significant operating losses since inception in 2016. 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 loss was $105.6 million for the year ended December 31, 2024. As of December 31, 2024, we had an accumulated deficit of $574.2 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future in connection with our ongoing activities. As of December 31, 2024, we had cash and cash equivalents of $79.4 million.

Our management team and scientific advisory board are composed of accomplished scientists and clinicians with decades of experience developing drugs for a wide range of diseases. Our view is that with a unique and focused approach to drug development, we may be able to significantly shorten development programs and bring lifesaving drugs to patients in urgent need more quickly.

In May 2019, we completed our initial public offering ("IPO") whereby we sold 4,000,000 shares of common stock at a public offering price of $10.00 per share, resulting in aggregate net proceeds of $34.6 million, after deducting underwriting discounts and commissions and offering expenses. In November 2019, we completed a private placement of 1,380,344 shares of our common stock (the "Private Placement"), which resulted in net proceeds of approximately $18.4 million. In January 2020, we completed a secondary public offering of 2,471,489 shares of our common stock, including 411,223 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares (the "Secondary Public Offering"), pursuant to which we received $134.1 million of proceeds, net of underwriting discounts and commissions and offering expenses. In February 2021, we issued and sold 3,000,000 shares of common stock (the "February Offering") at a public offering price of $23.00 per share, with an additional 450,000 shares sold pursuant to the underwriters' full exercise of their option to purchase additional shares in the February Offering. We received aggregate net proceeds, net of underwriting discounts and commissions and offering costs of $74.4 million. In June 2022, we completed an underwritten public offering of 20,000,000 shares of our common stock, 10,000,000 pre-funded warrants to purchase shares of common stock (the "Pre-Funded Warrants"), and 30,000,000 accompanying warrants to purchase shares of our common stock (the "Common Warrants"). The shares and accompanying Common Warrants were offered at a price to the public of $1.00 per share, and the Pre-Funded Warrants and accompanying Common Warrants were offered at a price to the public of $0.9999, resulting in aggregate net proceeds of approximately $27.8 million, after deducting underwriting discounts and commissions and offering expenses. In April 2023, we completed a sale of a total of 9,735,731 shares of common stock and 22,000,000 pre-funded warrants to purchase common stock in a private placement. The shares were offered to a select group of accredited investors at a price of $0.946 per share and the pre-funded warrants were offered to select group of accredited investors at a price of $0.945 per pre-funded warrant, resulting in aggregate net proceeds of approximately $27.5 million, after deducting underwriting discounts and commissions and offering expenses. In August 2023, we entered into a sales agreement (the "Leerink ATM Agreement") with Leerink Partners LLC, pursuant to which we may offer and sell, from time to time, shares of common stock having an aggregate offering price of up to $75.0 million through Leerink Partners LLC as sales agent. In 2023 we sold an aggregate of 17,615,976 shares of our common stock, pursuant to the Leerink ATM Agreement with an average sale price of $2.04 per share, resulting in net proceeds of $36.9 million, after deducting underwriting discounts,

commissions and offering expenses. In October 2023, we entered into an exchange agreement (the "Exchange Agreement") with entities affiliated with Venrock Healthcare Capital Partners (the "Exchanging Stockholders"), pursuant to which we exchanged an aggregate of 5,658,034 shares of common stock, owned by the Exchanging Stockholders for Pre-Funded warrants to purchase an aggregate of 5,658,034 shares of common stock (subject to adjustment in the event of stock splits, recapitalizations and other similar events affecting common stock), with an exercise price of $0.001 per share. In 2023 common warrant holders exercised 10,250,000 warrants at an exercise price of $1 resulting in proceeds of $10.3 million. In 2023, warrant holders exercised 4,250,000 pre-funded warrants at an exercise price of $0.001. On January 31, 2024, the Company sold an additional 1,000,000 shares of the company's common stock pursuant to the Leerink ATM Agreement with an average sale price of $3.13 per share, resulting in net proceeds of $3.0 million, after deducting underwriting discounts, commissions and offering expenses. On February 16, 2024, the Company sold an additional 2,000,000 shares of the company's common stock pursuant to the Leerink ATM Agreement with an average sale price of $4.90 per share, resulting in net proceeds of $9.5 million, after deducting underwriting discounts, commissions and offering expenses. In March 2024, we completed a sale of a total of 12,285,714 shares of common stock and 2,000,000 Pre-Funded Warrants to purchase common stock in a private placement. The shares were offered to a select group of accredited investors at a price of $7.00 per share and Pre-Funded Warrants were offered to select group of accredited investors at a price of $6.999 per Pre-Funded Warrant, resulting in aggregate gross proceeds of approximately $100.0 million, after deducting underwriting discounts and commissions and offering expenses. In 2024, common warrant holders exercised 9,025,000 warrants at an exercise price of $1 resulting in proceeds of $9.0 million. In 2024, warrant holders exercised 26,441,577 pre-funded warrants at an exercise price of $0.001.

We may pursue several potential financing options. Other options for structured finance which we may continue to explore include a PIPE, debt, convertible debt, and synthetic royalty financing. Synthetic royalty financing, in particular, has become a favorable option for many companies for funding ongoing clinical development in late-stage and pre-approval programs. From time to time, we may also engage with potential partners. Additionally, we are in dialogue with several potential partners regarding business development opportunities related to one or more of our programs. There can be no assurances that our discussions with any of the current counterparties will be successful, and we expect to continue to pursue additional opportunities.

Our Strategy

Our goal is to bring potentially transformative therapies to market across a range of fatal or debilitating diseases for which no treatments are available. The critical components of our strategy include:

- ***Leveraging our unique approach to develop our pipeline of novel ARIs.*** We target molecules and pathways that have a role in relevant disease processes, but have previously failed to yield successful products due to poor efficacy and tolerability. Our unique approach to drug development employs early use of biomarkers to confirm biological activity, and focuses on accelerated regulatory pathways. We develop product candidates with increased potency and selectivity by leveraging recent technological advances in high throughput crystallography and in silico structural design. Our strategy is also informed by use of biomarkers to confirm biological activity and target engagement. Evidence of biological activity through biomarkers in clinical trials further bolsters clinical development in our target indications. AR is our first molecular target that has been implicated in multiple diseases and for which sorbitol levels can be assessed as a potential biomarker of enzyme activity. Prior AR-targeting compounds produced nonselective inhibitors and failed to demonstrate adequate safety and efficacy. In the future we may seek to apply our strategy to a wide range of targets across multiple disease indications.
- ***Advancing the development of our ARI product candidates.*** Phase 2/3 studies have been completed for AT-007 in Galactosemia and for AT-001 for the treatment of DbCM. And a study for SORD Deficiency has been conducted that may support registration. Patients in the Phase 2/3 INSPIRE study for SORD Deficiency have been transitioned to open-label extension.
- ***Taking advantage of regulatory pathways designed for accelerated drug development in indications with high unmet need and seeking strategic partnerships in other indications***.We plan to leverage the accelerated approval pathway using biomarker-based surrogate endpoints to shorten clinical development timelines, where possible.
- ***Expanding our pipeline to products targeting other molecules and pathways outside of AR.*** We may continue leveraging our relationships with academic institutions and universities to acquire or license additional technologies that are consistent with our strategy of applying new technologies to targeted molecular pathways.

Our Pipeline

The following table shows the status of our current ARI programs:

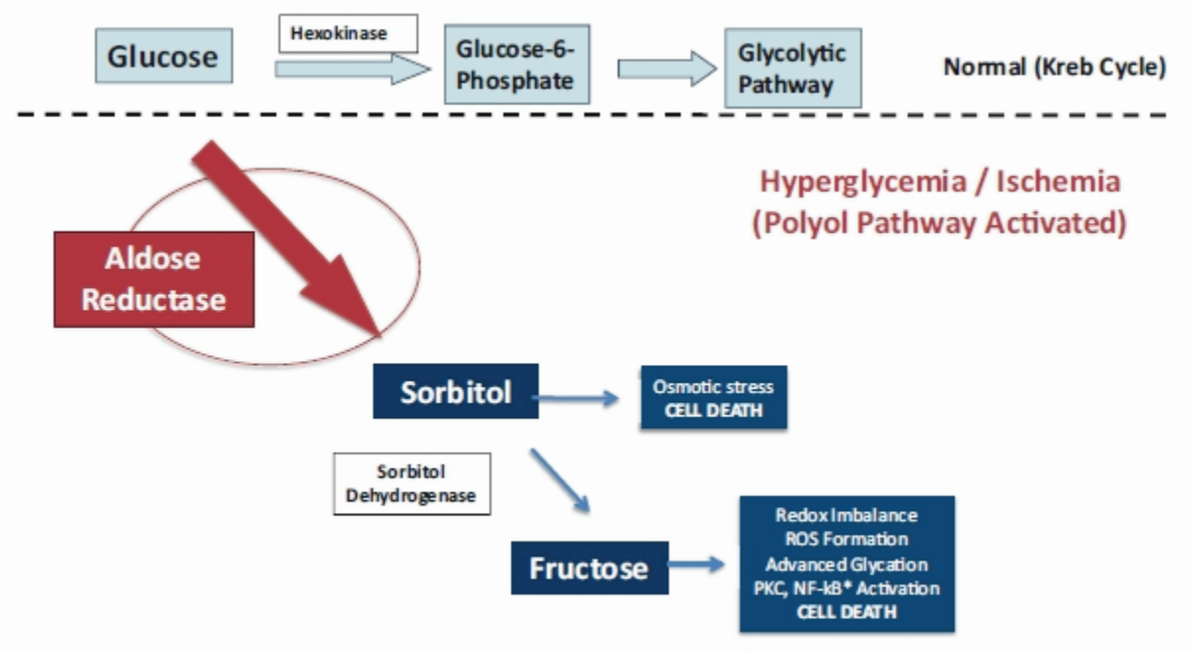
We seek to protect our proprietary and intellectual property position for our product candidates, our core technology, and other know-how through U.S. and foreign patent protection. To the extent that our platform is not patentable, we rely on trade secret protection and confidentiality agreements to protect our interests. For more information, see the section titled “Business – Intellectual Property".

Our Product Candidates

Our Aldose Reductase Program

AR is the first enzyme and a rate-limiting step in the polyol pathway, an alternative glucose metabolism pathway. AR is a redox-regulated enzyme that is activated by an altered redox state within the cell, which occurs during hyperglycemia and ischemia. AR activation is associated with downstream consequences of hyperglycemia, such as diabetic complications, as well as consequences of ischemia in the heart, such as acute myocardial infarction and chronic heart failure. As shown in the figure below, AR activity produces excess sorbitol, which contributes to osmotic dysregulation within cells and tissues, such as nerve and retina, and is thought to be toxic to many cell types, including cardiomyocytes. Sorbitol is also further metabolized to fructose, which is also thought to contribute to a cascade of metabolic dysregulation and inflammatory damage to cells, such as: reactive oxygen species, or ROS, generation; advanced glycation end products, or AGE; protein kinase C, or PKC, activation; and methylglyoxal overproduction. Under non-oxidative, or healthy patient conditions, AR remains largely inactive and less than 3% of a healthy person's glucose is processed by the polyol pathway. However, when the oxidative environment of the cell changes due to hyperglycemia or ischemia, AR is both activated and upregulated, and greater than 30% of the patient's glucose is then shunted through the polyol pathway, resulting in significant downstream damage to cells and tissues. The detrimental consequences of AR activation have been characterized by decades of prior research. These include broad effects, such as mitochondrial dysfunction and cell death, as well as tissue-specific changes, such as neuronal degeneration in peripheral nerves, collagen crosslinking and fibrosis in cardiac tissue, and damage to blood vessels in the lens of the eye.

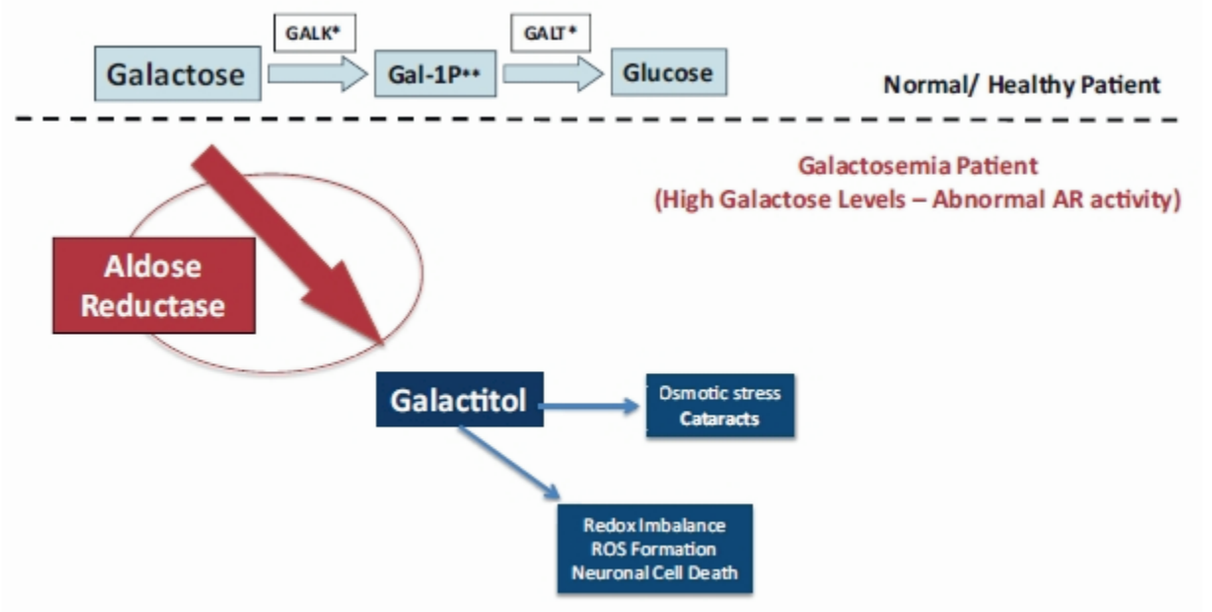
AR Is Believed to Cause Damage to Tissues Under Conditions of Oxidative Stress



* NF-kB is a protein complex that controls transcription of DNA, cytokine production and cell survival.

Additionally, as shown in the figure below, abnormal AR activity is associated with conversion of galactose to galactitol in patients with Galactosemia. Galactitol, like sorbitol, does not cross the cell membrane and is thought to cause damage to cells across a wide range of tissues, including neurons in the brain, retinal cells in the eye and peripheral nerve tissue.

Galactitol Accumulation and Tissue Specific Damage



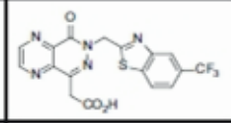
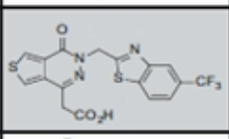
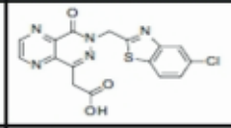
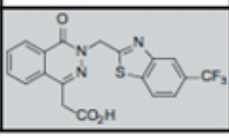
* GALK, or galactokinase, and GALT, or galactose-1-phosphate uridyl transferase, are enzymes that metabolize galactose.

** Galactose-1-phosphate is referred to as Gal-1P.

During the 1980s and 1990s, AR was a significant target of drug development due to its established role in a wide range of debilitating indications. Although these programs failed to produce effective drugs with a favorable risk/benefit profile, the prior ARI clinical development programs supported the role of AR in the pathogenesis of several diabetic complications and provided useful information on optimal patient criteria and trial design.

By applying new techniques in crystallography to better understand how the enzyme works, and applying in silico design and medicinal chemistry approaches, we have developed compounds with logarithmically improved potency and increased selectivity. Our technology includes specific compounds that are in various stages of preclinical and clinical development, and is coupled with an understanding of how the enzyme works and a knowledge base of structural approaches to drug the target while controlling drug characteristics, such as PK, solubility and tissue permeability.

The following table summarizes the current status of our AR program and compound differentiation:

Compound	Structure	IC_{50}[1]	Maximum Tolerated Dose in Animals	LogD[2]	Tissue Penetration (in rats)			
					Systemic/ Heart	Nerve	Retina	CNS
AT-001		30pM	>2,000 mg/kg	-1.00	✓	✓	✓	X
AT-007		100pM	>1,000 mg/kg	-0.09	✓	✓	✓	✓
AT-003		54pM	>1,000 mg/kg	-1.53	✓	✓	✓	X
Zopolrestat (prior Pfizer compound)		10nM	100 mg/kg	+0.06	✓	✓	X	X

(1) IC_{50} is the amount of a compound required to inhibit 50% of enzyme activity.
(2) LogD is a log of partition of a chemical compound between the lipid and aqueous phases. LogD often predicts retinal permeability, with compounds with negative LogD passing through the back of the eye.

AT-007 for the Treatment of Rare Metabolic Disease (Galactosemia, SORD Deficiency, PMM2-CDG)

Overview

AT-007 is a novel CNS penetrant ARI currently being investigated and proposed for the treatment of CNS rare diseases, including Galactosemia, SORD Deficiency, and PMM2-CDG deficiency.

Galactosemia

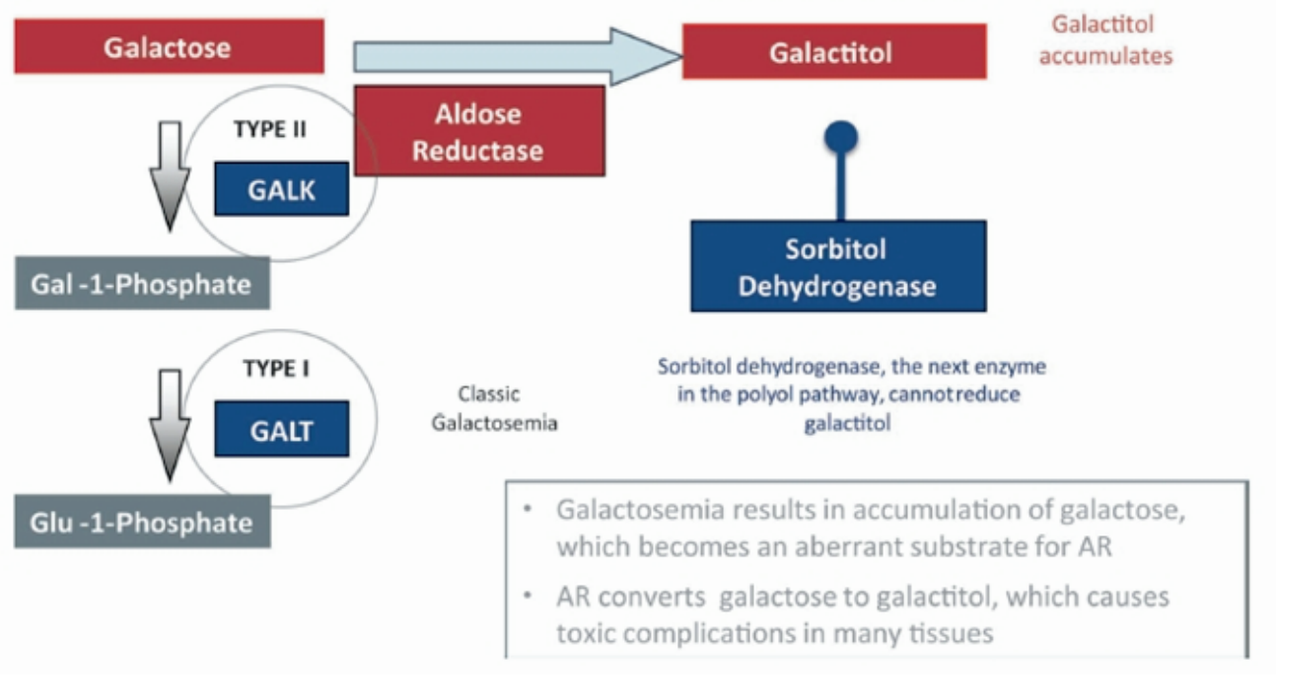
Galactosemia is a devastating rare pediatric metabolic disease that affects how the body processes a simple sugar called galactose, and for which there is no known cure or approved treatment available. High levels of galactose circulating in the blood and tissues of Galactosemia patients enable AR to convert galactose to a potentially toxic metabolite, galactitol, which is thought to result in long-term complications ranging from CNS dysfunction to cataracts. AT-007 was specifically designed to be CNS penetrant to address AR activity in the brain and potentially prevent CNS consequences of the disease. We believe we have evidence that in patients with Galactosemia, plasma galactitol level statistically correlate with clinical outcome assessments, further supporting the role of galactitol in long-term disease complications. In adult and pediatric Galactosemia patients, our analyses indicate that AT-007 treatment may result in a statistically significant reduction in plasma galactitol versus placebo. In a study in children with Galactosemia aged 2-17, our analyses suggest that galactitol reduction from AT-007 treatment was associated with evidence of clinical benefit on activities of daily living, behavioral symptoms, cognition, fine motor skills and tremor over 18 months of treatment. According to our analyses, change in clinical outcome measures correlated with galactitol level.

Diagnosis and Standard of Care

Galactosemia is caused by severe deficiency in the GALK or GALT enzymes that metabolize galactose. Galactose is a sugar produced endogenously by the body, and is also a metabolite of lactose. Galactosemia is often fatal in infants within the first weeks of life if they are exposed to dietary lactose in the form of breast milk or dairy-based formula. As such, there is mandatory newborn screening for Galactosemia in the United States and many countries in Europe. While prompt identification of infants with Galactosemia and immediate implementation of a lactose-restricted diet prevents many fatalities, long-term consequences of disease can persist, thought to be due to endogenous generation of galactose within the body. We are specifically developing AT-007 for patients with severe enzyme deficiencies in GALT, which is referred to as Classic Galactosemia. In these patients, despite dietary restriction, Galactosemia manifests as a combination of CNS and systemic toxicities in tissues, including cognitive dysfunction and intellectual deficiencies, speech and motor pathologies, pre-senile cataracts and tremor, as well as ovarian insufficiency in females.

There are no approved treatments available for Galactosemia. Due to endogenous production of galactose within the body, infants with Galactosemia develop significant complications even with immediate implementation of, and strict adherence to, a dairy-free diet. CNS complications include cognitive impairment, low IQ, speech and motor deficiencies, and seizures. In addition, nearly all females develop ovarian insufficiency. Further to the damage that occurs in childhood, many adults also develop persistent cataracts, seizures, and experience progressive worsening of tremor, cognitive, behavioral and psychiatric issues.

AR Activity Is Believed to Cause Potentially Toxic Accumulation of Galactitol in Galactosemia



We have demonstrated that inhibiting AR activity shifts galactose metabolism to an alternative enzyme called galactose dehydrogenase, which allows galactose to be metabolized to galactonate, a benign substance that is removed in the urine.

Market Opportunity

The global incidence of Galactosemia is estimated to be 1 in 50,000 to 1 in 90,000, depending on ethnicity. The U.S. Galactosemia population is approximately 3,300 patients, based on newborn screening data identifying 2,500

infants through 2014, and the estimated birth rate of 80 patients per year. The EU population (including the UK) is slightly larger than the US population, estimated at approximately 4,000 patients, leading to a combined US + EU market opportunity of approximately 7,300 patients. When additional markets, such as Japan and Canada are considered, we believe the overall market opportunity for Galactosemia is approximately 8,000 patients worldwide.

Preclinical Studies

A rat model of classic Galactosemia displays similar biochemical and functional abnormalities to those associated with Galactosemia in humans.

We found that treatment with AT-007 significantly reduced galactitol levels in target tissues, including blood, brain and liver, without increasing galactose or Gal-1P levels, and prevented complications associated with galactitol accumulation in tissues, including cataract formation and CNS dysfunction. Based on our analyses, the effects of AT-007 were dose dependent and corresponded with galactitol reduction.

Clinical Development

ACTION-Galactosemia Phase 1/2 Study

We have evaluated AT-007 in a Phase 1/2 clinical trial in healthy volunteers and adults with Galactosemia. The Phase 1 portion of the study in healthy volunteers evaluated safety, tolerability, CNS penetrance and PK of AT-007 at doses of 5mg/kg to 40mg/kg for up to seven days of consecutive treatment. The Phase 2 portion in adults with Galactosemia evaluated safety, tolerability, PK and pharmacodynamic reduction in the biomarker galactitol. Patients received AT-007 5mg/kg, 20mg/kg, 40mg/kg or placebo, for 28 days.

AT-007 treatment resulted in a statistically significant and robust reduction in plasma galactitol versus placebo in adult Galactosemia patients. Reductions in galactitol were dose dependent, with higher concentrations of AT-007 resulting in a greater magnitude of reduction in galactitol. At the higher doses tested (20mg/kg and 40mg/kg), AT-007 significantly reduced plasma galactitol by approximately 50% from baseline. Results were statistically significant (p value of less than 0.01) vs. placebo. Galactitol reduction was rapid and sustained over time. No substantial change from baseline was observed in placebo treated patients. AT-007 was well tolerated in both Galactosemia patients and healthy volunteers.

ACTION-Galactosemia Kids

In June 2020, we initiated the ACTION-Galactosemia Kids pediatric Galactosemia study. The study was placed on partial clinical hold in August 2020 while we worked with the FDA to redesign and operationally modify the study to seamless design to ensure continuous treatment and the opportunity to receive clinical benefit. The study re-started in February 2021 and was unblinded in April 2023, and patients who were randomized to active treatment transitioned to an expanded access program. The open-label extension for patients that were initially randomized to placebo is ongoing. The pediatric clinical trial was a 2-part study to evaluate safety, pharmacokinetics, and reduction in the toxic biomarker, galactitol (Part A), as well as impact on functional outcomes in children with Galactosemia over time (Part B). Three age cohorts were studied in parallel: age 2-6, age 7-12, and age 13-17. The biomarker portion of the study demonstrated a reduction in plasma galactitol compared to placebo. The clinical outcomes portion of the study measured several aspects of the Galactosemia phenotype including behavior, cognition, motor and speech problems. Our analyses indicate that AT-007 treatment demonstrated consistent long-term clinical outcomes benefit across a range of functional measures in the ACTION-Galactosemia Kids trial, and improved activities of daily living, behavior, cognition, fine motor skills, adaptive skills and tremor vs. placebo. Consistent with prior reported data, improvement in galactitol levels was rapid and sustained throughout the trial with no material impact on Gal-1p or galactose, further supporting the potential role of galactitol as a metabolite that may drive disease pathogenesis. AT-007 continued to be generally safe and well-tolerated in all age groups; there were no treatment-related serious adverse events (SAEs) reported

Although the primary composite endpoint (OWLS Oral Expression Test, OWLS Listening and Comprehension Test, BASC-Behavioral Symptoms Index, and BASC-Activities of Daily Living domain) failed to reach statistical

significance, we believe the data show a strong trend of improvement of govorestat patients versus placebo patients that strengthened over the course of the 18-month study period. Specifically, our analyses indicate that the behavior and social function (BASC-3; behavioral symptoms index and activities of daily living) components of the primary endpoint showed a positive treatment effect of govorestat versus placebo, which improved over time. However, the speech and language components did not, which may have contributed to the primary composite endpoint failing to reach statistical significance. Imbalances at baseline, and implementation of speech therapy during the trial may have also contributed to a lack of observed treatment effect on speech and language components.

In addition, we believe that there were consistent improvements, which improved over time, in multiple other relevant clinical outcomes measured by secondary endpoints including subcomponents of the BASC test, cognition, fine motor skills and tremor. Our analyses also indicate that caregivers, through the caregiver global impression of change, and exit interviews, observed a clinically meaningful effect by indicating a larger improvement in different symptoms over the course of the 18-month treatment period versus patients treated with placebo.

The reductions in the level of galactitol seen early in the treatment course and sustained throughout the treatment period were associated with an improvement in many clinical outcome assessments after 18 months of treatment with govorestat. This observed correlation provides further evidence of the association of galactitol levels and patients clinical presentation. Consistent with prior reported data, improvement in galactitol levels appears to have been sustained throughout the trial with no impact on Gal-1p or galactose, further supporting the potential major role of galactitol in disease pathogenesis. AT-007 continued to be safe and well-tolerated in all age groups; there were no treatment-related serious adverse events (SAEs) reported.

In February 2024, the FDA accepted a New Drug Application (NDA) for AT-007 for the treatment of Classic Galactosemia. On November 27, 2024, the FDA issued the Complete Response Letter for the NDA for the treatment of Classic Galactosemia, indicating that the agency was unable to approve the NDA in its current form, citing deficiencies in the clinical application. On the same day, the FDA also issued the Warning Letter to Applied and another warning letter to a clinical investigator related to the Phase 2/3, ACTION-Galactosemia Kids study. Following receipt of the Complete Response Letter, we also withdrew a pending Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for AT-007 for the treatment of Classic Galactosemia, as we believed more time was needed to acquire further data to support a European MAA. We are actively working to address the issues raised in the Complete Response Letter and Warning Letter. Patients with Classic Galactosemia continue to receive AT-007 in the OLE part of ACTION-Galactosemia Kids and in the Expanded Access Program. Those in the Expanded Access Program have received over 3 years of continuous treatment with AT-007. Through this observation period, AT-007 continued to be safe and well-tolerated.

CMT-SORD (or Charcot Marie Tooth-SORD or SORD Deficiency)

SORD Deficiency is a newly characterized genetic cause of Charcot-Marie-Tooth Type 2 Disease (“CMT2”) and distal hereditary neuropathy, in which patients are deficient in the enzyme Sorbitol Dehydrogenase (“SORD”). SORD is the enzyme which follows AR in the polyol pathway and converts sorbitol to fructose. Patients who are deficient in SORD cannot metabolize sorbitol normally, and sorbitol levels accumulate to unnaturally high levels. Sorbitol, like galactitol, is thought to be toxic to cells, especially neurons, resulting in progressive neuronal degeneration. Patients with SORD Deficiency develop progressive neuropathy, which greatly impacts mobility and motility, and significantly affects quality of life.

Diagnosis and Standard of Care

Patients with CMT-SORD are diagnosed based on neurological symptoms and grossly elevated urine sorbitol, along with confirmatory genetic testing. Genetic testing for CMT-SORD is available through several commercial labs and hospital systems however up to 25% of the CMT-SORD patients have genetics that cannot be fully characterized. As such, measurement of sorbitol is being used for the identification of patients with CMT-SORD. There are currently no drugs approved to treat CMT-SORD.

Market Opportunity

Genetic studies indicate that approximately 7-9% of CMT2 cases are caused by SORD Deficiency, estimating the US population around 3,300 patients. The EU population (including the UK) is estimated to be approximately 4,400

patients. When additional markets, such as Japan and Canada are considered, we believe the overall Market opportunity for SORD Deficiency is approximately 8,400 patients worldwide.

Preclinical Studies

Substrate reduction through AR inhibition in patient fibroblasts and a drosophila model of disease have demonstrated preclinical proof of concept in SORD Deficiency, significantly reducing sorbitol levels and normalizing the drosophila disease phenotype. Preclinical studies in fibroblasts derived from CMT-SORD (SORD Deficient) patients have demonstrated significant reduction in sorbitol levels with AT-007 treatment. Preclinical studies in the drosophila model of disease have demonstrated a positive impact on the disease phenotype with AT-007 treatment, including mobility (climbing) and prevention of neuronal degeneration and muscle atrophy.

Clinical Development

In 2021 we conducted an open-label pilot study in 8 patients with CMT-SORD. AT-007 treatment significantly reduced sorbitol levels by approximately 66% from baseline, and was safe and well tolerated. In December 2021 we initiated a Phase 2/3 study (Phase 2/3 INSPIRE trial) in patients with SORD Deficiency. The Phase 2/3 INSPIRE trial was designed to demonstrate biomarker efficacy at 3 months through reduction in sorbitol, and long-term clinical efficacy of treatment, with an interim clinical outcomes assessment at 12 months. The study is a multicenter placebo-controlled trial conducted in the US and Europe in approximately 50 SORD patients aged 18 and older. In February 2023, we announced that in a pre-specified interim analysis of the Phase 2/3 INSPIRE trial, AT-007 reduced sorbitol levels over 90 days of treatment compared to placebo in patients with SORD Deficiency. On February 15, 2024, we announced preliminary results from an analysis of 12-month group-level data from the Phase 2/3 INSPIRE trial. In July 2024, we concluded the double-blind placebo-controlled portion of the Phase 2/3 INSPIRE trial and began transitioning patients to the open-label treatment phase prior to all patients completing 24 months of treatment. Applied is continuing to analyze the data from this trial and the extent to which these data may support a potential submission for regulatory approval. Following this analysis, we plan to meet with the FDA to discuss whether an NDA can be submitted based on the current data package and/or potential additional supporting data.

PMM2-CDG

PMM2-CDG is a glycosylation disorder in which patients have only partial function of the phosphomannomutase enzyme (PMM2). As a result, patients do not process sugars properly to support protein glycosylation, which results in systemic problems and multi-organ failure. PMM2-CDG is a severe disease, resulting in and high mortality in children, with no FDA approved treatments. PMM2-CDG is an ultra-rare disease, with only approximately 1,000 patients identified worldwide.

Recently, AR inhibition was demonstrated to positively impact protein glycosylation in PMM2-CDG patient fibroblasts and a C. elegans model of disease. It is believed that AR inhibition results in increased protein glycosylation by shifting the balance of sugar production to support PMM2 activity. In preclinical studies in PMM2-CDG patient fibroblasts, AT-007 significantly improved PMM2 activity. Based on this data, we have received both orphan designation and rare pediatric disease designation from the FDA.

Diagnosis and Standard of Care

The diagnosis of PMM2-CDG is based on genetic testing as well as on low levels of phosphomannomutase (PMM) enzyme activity, and the low level of Transferrin glycosylation.

There is no FDA-approved treatment available for PMM2-CDG deficiency.

Clinical Development

We plan to request a pre-IND meeting with the FDA to discuss the clinical development program for PMM2-CDG.

AT-001 for the Treatment of Diabetic Cardiomyopathy

Overview

We were developing AT-001, a novel ARI with broad systemic exposure and peripheral nerve permeability being developed for the treatment of DbCM, a fatal fibrosis of the heart, for which no treatments are available. We completed a Phase 1/2 clinical trial evaluating AT-001 in approximately 120 patients with type 2 diabetes, in which no drug-related adverse effects or tolerability issues were observed. This trial also demonstrated target engagement and proof of biological activity, as measured by reduction in sorbitol, a biomarker of AR activity and NTproBNP. A Phase 2/3 study in DbCM patients at high risk of progression to overt heart failure (ARISE-HF) was recently completed. We are currently not expending additional internal resources on AT-001 due to our focus on rare diseases.

Diagnosis and Standard of Care

DbCM is a fatal fibrosis of the heart that occurs in both type 1 and type 2 diabetic patients, which leads to decreased contractility and decreased heart function, eventually resulting in fulminant heart failure. DbCM is caused by metabolic derangements in cardiomyocytes that result in cell death and fibrosis. AR activity has been shown to be a large contributor to these metabolic derangements, and the downstream effect of AR activation is responsible for the cardiomyocyte cell death and fibrosis. DbCM is characterized by increased weight of the heart and decreased contractility, which are identified by echocardiographic screening, as well as by exclusion of other forms of heart disease. Diagnostic criteria include echographia evaluation as well as measurement of NT-proBNP and Troponin, two circulating markers of heart disease. Epidemiological studies have shown that approximately 17% to 24% of diabetic patients with type 2 diabetes display DbCM in the absence of any other forms of heart disease. These patients do not have hypertension, atherosclerosis, valvular heart disease or ischemia, and the only cause of the cardiomyopathy is the underlying diabetes. Stages of DbCM range from asymptomatic, or stage 1, to acute heart failure, or stage 4. Most patients are not diagnosed until stage 2, where symptoms manifest as extreme shortness of breath during exercise, referred to as decreased exercise tolerance. Exercise tolerance in these patients (as measured by maximum amount of oxygen a person can utilize during intense exercise known as peak VO2) is approximately 25% lower than diabetic patients without DbCM, and decreases by an additional 30% as the patients progress to overt heart failure in later stages of diseases. Patients quickly progress at a steady state of decline to stage 3, which includes marked cavity dilation and severe limitations in daily activities. The final stage of DbCM, stage 4, is represented by acute heart failure resulting in death. The current standard of care is to target glucose control in these patients, as well as hemodynamic modulation of blood flow, through use of beta blockers and diuretics. Both approaches are largely ineffective, and DbCM often results in death within five to ten years of diagnosis. Approximately 24% of DbCM patients progress to overt heart failure or death within 1.5 years of diagnosis, and 37% within five years of diagnosis.

Market Opportunity

According to a retrospective epidemiological study, approximately 17% of patients suffering from diabetes develop DbCM. A study completed in France that utilized echocardiographic screening estimates the proportion of diabetic patients to develop DbCM at approximately 24%. The International Diabetes Foundation estimated that there were approximately 451 million patients globally with diabetes in 2017, which is expected to increase to 693 million by 2045. This includes 58.0 million diabetes patients in Europe in 2017, which is expected to increase to 67.0 million in 2045, and 46.0 million in North America, which is expected to increase to 62.0 million in 2045. Based on an estimated prevalence of 17% of diabetic patients who develop DbCM, we estimate that currently there are approximately 77.0 million patients with DbCM globally, with approximately 8.0 million in North America and 10.0 million in Europe. Initially, our development program will target patients at high risk of progression to overt heart failure, which we estimate constitute approximately 50% of all DbCM patients. We believe these patients represent a symptomatic population that is more likely to be responsive to treatment.

Prior AR-Based Approaches to Treat DbCM

AR activity has been implicated as a strong contributing factor to pathogenesis in DbCM. Pfizer Inc. was developing an ARI, Alond (zopolrestat), for the treatment of DPN and DbCM in a Phase 2 clinical trial that demonstrated favorable outcomes on heart function in DbCM patients, but the clinical trial was discontinued due to an unfavorable risk/benefit profile, with several patients experiencing liver toxicity and significant elevations in both aspartate aminotransferase and alanine aminotransferase, which are enzymes central to identification of liver toxicity and

damage. In this trial, patients with early-stage DbCM were identified by echocardiographic screening and were randomized to three treatment groups, which consisted of placebo, 500 mg zopolrestat per day or 1,000 mg zopolrestat per day dosed for one year. Due to liver toxicity seen in another trial with zopolrestat, the 1,000 mg treatment arm was reduced to 500 mg, and the two doses were collapsed into one treatment arm. While patients on placebo displayed decreased heart function over the year of the trial as their disease progressed, patients on zopolrestat displayed a stabilization of heart function and even improvement in heart function in some patients based on hemodynamic endpoints. We believe this data validates the approach of using an ARI to improve outcomes for patients with DbCM and using our compounds, which demonstrate improved potency and have been well tolerated, may lead to greater clinical utility.

We have demonstrated that when compared to zopolrestat, AT-001 has significantly higher in vitro enzymatic inhibitory activity and greater specificity for AR. Liver toxicity associated with "old" ARIs such as zopolrestat has been shown to be due to off-target inhibition of a structurally related enzyme, Aldehyde Reductase, which is required for normal liver function. AT-001 demonstrates increased selectivity for AR, and does not inhibit Aldehyde Reductase at any concentration tested. This increased selectivity led to lack of toxicity in cultured hepatocytes, or liver cells, whereas zopolrestat demonstrated significant toxicity in hepatocytes. Thus, we believe that not only is AT-001 a more potent AR inhibitor than prior drugs, but that we have overcome the safety and toxicity limitations from prior compounds, which were due to lack of selectivity and off-target inhibition of Aldehyde Reductase.

Preclinical Efficacy Studies

In a preclinical model of DbCM AT-001 prevented cardiac damage and dysfunction and normalized cardiac energetics. In a diabetic rat model, AT-001 prevented cardiac damage induced by ischemia/repurfusion.

Clinical Development

Until recently, development in cardiovascular disease indications often required large outcome-based trials that examined survival and re-hospitalization as primary endpoints. These trials were extremely large, expensive and time-consuming, and were often confounded by comorbidities in the patient population. As a result, very few cardiovascular programs resulted in approved drugs. There has been a recent effort from the Division of Cardiovascular and Renal Products at the FDA, as well as at the European Medicines Agency, or EMA, to streamline drug development for cardiovascular disease to increase the probability of demonstrating a meaningful clinical effect in patients. Specifically, in cardiomyopathies, where there is a direct functional link between hemodynamic endpoints, heart contractility and quality of life, there is a unique opportunity to demonstrate benefit of therapy in a smaller number of patients and shorter treatment period than was previously required. Recent clinical development programs in hereditary cardiomyopathies have pioneered smaller trials examining exercise tolerance and/or heart functional capacity as a primary endpoint.

Consistent with these developments, at our pre-IND meeting, the FDA indicated that we would not be required to examine survival and re-hospitalization endpoints, and confirmed that exercise tolerance would qualify as an appropriate primary endpoint in our DbCM trial. This was also recently publicly confirmed by the FDA in a whitepaper entitled "Draft Guidance for Industry: Treatment for Heart Failure: Endpoints for Drug Development." Accordingly, we designed our pivotal Phase 2/3 clinical trial to target functional capacity, or exercise tolerance, as measured by Peak VO2 on Cardiopulmonary Exercise Testing (CPET) in DbCM patients at high risk of progression to overt heart failure.

Phase 1/2 Trial in Adult Type 2 Diabetic Patients

We have evaluated AT-001 in a placebo-controlled Phase 1/2 clinical trial in approximately 120 type 2 diabetes patients. The primary objectives of this trial were to explore the safety, tolerability and PK profile of AT-001. Because AR converts glucose to sorbitol, and AR activity is elevated in diabetic patients, sorbitol normalization was also examined as a pharmacodynamic, or PD, biomarker of target engagement, which provided proof of biological activity in patients.

The Phase 1/2 clinical trial allowed use of concomitant treatments for glucose control, as well as other standard of care treatments for diabetes, such as statins and ACE inhibitors. The FDA permitted us to directly evaluate diabetic patients due to positive data from the preclinical studies, as well as the urgency to develop drugs quickly due to high unmet need. AT-001 was dosed as an active pharmaceutical ingredient, or API, powder in a rapid release capsule and the trial examined both once-daily and twice-daily, or BID, dosing regimens.

AT-001 was safe and well tolerated at all doses tested. Additionally, there were no observed adverse interactions with any concomitant diabetes medications used by patients during the trial. Because AR converts glucose to sorbitol, and AR activity is elevated in diabetic patients, sorbitol normalization to healthy subject levels can be used as a PD biomarker of target engagement and proof of biological activity. Treatment with AT-001 normalized sorbitol levels in diabetic patients to those of healthy volunteers, and prevented post-prandial elevations in sorbitol. Decrease in sorbitol levels was dose-dependent, with higher doses of AT-001 resulting in greater reduction in sorbitol levels. Reduction in sorbitol levels lasted for approximately 10-12 hours post dose, suggesting that twice-daily oral dosing produced optimal pharmacodynamic impact. Placebo-treated patients did not demonstrate any reduction in sorbitol levels, and conversely demonstrated post-prandial increase in sorbitol levels.

Within the Phase 1/2 study, approximately 30 patients with early stage DbCM, assessed by echocardiographic abnormalities and elevations in the cardiac stress biomarker, NTproBNP, were treated with AT-001 or placebo for 28 days. Treatment with AT-001 (twice daily or three times daily) resulted in sustained reduction in sorbitol, and significant reduction in NTproBNP, demonstrating that inhibition of AR decreases cardiac stress. This data supported dose selection and advancement into a Phase 2/3 trial for DbCM.

In September 2019, we initiated a Phase 2/3 trial for AT-001 in DbCM called ARISE-HF. ARISE-HF was a global study in approximately 675 patients with DbCM at high risk of progression to overt heart failure. The study evaluated the treatment effect of AT-001 high dose (1500 mg twice daily) and low dose (1,000mg twice daily) compared to placebo on cardiac functional capacity over 15 months of treatment. On January 4, 2024, we announced topline results from the ARISE-HF study. AT-001 (caficrestat) demonstrated a strong trend in stabilizing cardiac functional capacity, while the placebo group declined over 15 months. The placebo-treated group declined by a mean of -0.31 ml/kg/min over 15 months of treatment, while the AT-001 1500mg twice daily treated group remained primarily stable, with a mean change of -0.01 ml/kg/min over 15 months. While a trend favored active treatment, the difference between active and placebo treated groups (0.30 ml/kg/min) was not statistically significant (p=0.210). Approximately 38% of study subjects were on SGLT2 or GLP-1 therapies for treatment of diabetes, while 62% were not. In a pre-specified subgroup analysis of the primary endpoint in patients not concomitantly treated with SGLT2 or GLP-1 therapies, the placebo group declined by a mean of -0.54 ml/kg/min, while the 1500mg BID AT-001 treated group improved by a mean of 0.08 ml/kg/min over 15 months of treatment, with a difference between groups of 0.62 ml/kg/min (p=0.040). Additionally, in this subgroup analysis, the number of patients who experienced a clinically significant worsening in cardiac functional capacity of 6% or more was substantially higher in the placebo group (46%) as compared to the 1500mg BID AT-001 treated group (32.7%), odds ratio 0.56 (p=0.035). A 6% change in cardiac functional capacity has been shown to predict long-term survival and hospitalization for heart failure. The effect of AT-001 was dose dependent, with the low dose (1000mg BID) demonstrating an intermediate effect between the high dose and placebo. AT-001 was generally safe and well tolerated, with no substantial differences in serious adverse events between AT-001 treated groups as compared to placebo.

AT-003 for the Treatment of Diabetic Retinopathy

Overview

We are developing AT-003, an ARI designed to cross through the back of the eye when dosed orally, which has demonstrated strong retinal penetrance, for the treatment of DR. DR is an ophthalmic disease that occurs in diabetic patients, and for which treatments are currently limited to intravitreal administration. DR has been linked to AR activity, including elevations in sorbitol and subsequent changes in retinal blood vessels, which distorts vision and leads to permanent blindness. We are currently in late stages of preclinical development and intend to advance AT-003 into a Phase 1 clinical trial for the treatment of DR.

Diagnosis and Current Standard of Care

DR is diagnosed by routine dilated eye exam by an ophthalmologist. Annual or biennial ophthalmic exams to screen for DR are a recommended standard of care for diabetic patients under current treatment guidelines. Vascular endothelial growth factor, or VEGF, inhibitors, Lucentis (ranibizumab) and Eylea (aflibercept), are approved to treat severe or late-stage DR, but are limited by high cost, the need for intravitreal injection into the eye and the lack of therapeutic benefit in many patients. A need exists for safe, effective and tolerable treatments for DR early in the disease process that provide a benefit to a wide range of patients. AR is an attractive target for DR drug development since AR activity is upstream of VEGF activity in DR pathogenesis. AR has been shown to cause DR by inducing hyperosmolarity

in retinal cells due to elevated sorbitol, as well as through fructose-mediated detrimental downstream effects, such as AGE generation and PKC activation. AR knock-out rats are protected from DR development, and several prior ARIs demonstrated efficacy on DR endpoints in clinical trials, but were not approved due to dose-limiting safety concerns.

Market Opportunity

A recent retrospective epidemiological analysis of diabetic patients globally confirmed that DR affects approximately 35% of diabetics, and is a leading cause of blindness worldwide. Based on the 2017 diabetes numbers, the global market for DR is approximately 158 million patients, with anticipated increase to 243 million by 2045. The current market is approximately 16.0 million in North America and 20.0 million in Europe.

Preclinical Studies

AT-003 displayed significant retinal penetration when dosed orally in diabetic rats. AT-003 was observed to be well tolerated over a seven-day dosing period in all doses tested, up to 1,000 mg/kg daily, with no adverse effects observed. Efficacy of AT-003 is currently being explored in two animal models of DR - an ischemic injury model (acute damage) and chronic diabetic treatment model.

Clinical Development Plan

Similar to AT-001, we plan to explore the safety, tolerability, PK profile and biomarker effects of AT-003 in a Phase 1a/1b clinical trial in diabetic patients. Assuming positive data in this trial, we plan to initiate a pivotal Phase 2/3 clinical trial of AT-003 in patients with DR to prevent disease progression versus placebo, as measured by subjective metrics, including fluoroscein angiography and optical coherence tomography, which are scans used in the examination and management of retinal diseases.

Exclusive License Agreement with Columbia University

On October 26, 2016, we entered into a license agreement with Columbia University (the "2016 Columbia Agreement"). Pursuant to the 2016 Columbia Agreement, Columbia University granted us a royalty-bearing, sublicensable license that is exclusive with respect to certain patents, and non-exclusive with respect to certain know-how, in each case to develop, manufacture, and commercialize ARI products, including AT-001, AT-003 and AT-007. The license grant is worldwide with the exception of a single patent family covering AT-001 and AT-003 for which the license grant excludes China, Taiwan, Hong Kong and Macao. Under the 2016 Columbia Agreement, we are obligated to use commercially reasonable efforts to research, discover, develop and market licensed products for commercial sale in the licensed territory, and to comply with certain obligations to meet specified development and funding milestones within defined time periods. Columbia University retains the right to conduct, and grant third parties the right to conduct, non-clinical academic research using the licensed technology; *provided* that such research is not funded by a commercial entity or for-profit entity or results in rights granted to a commercial or for-profit entity. As the technology licensed to us under the 2016 Columbia Agreement was developed as a result of a U.S. government grant, the licenses granted to us under the agreement are subject to the terms of such grant, and to standard rights of the U.S. government under the Bayh-Dole Act, including the grant to the government of a non-exclusive, worldwide, freedom to operate license under any patents, and the requirement, absent a waiver, to manufacture products substantially in the United States.

As consideration for entering into the 2016 Columbia Agreement, we made a nominal upfront payment to Columbia University and, following the occurrence of certain trigger events, issued to Columbia University shares equal to 5% of our outstanding common stock on a fully diluted basis at the time of issuance. We will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2016 Columbia Agreement. We will also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on our, our affiliates' and our sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, we are required to make specified annual minimum royalty payments to Columbia University in the mid six figures beginning on the 10th anniversary of the effective date of the agreement. When we grant sublicenses under the 2016 Columbia Agreement we are required to pay to Columbia University a portion of the net sublicensing revenue received from such third parties, at percentages between 10% and 20%, depending on the stage of development at the

time such revenue is received from such third parties. The Advanz Agreement includes a sublicense under the 2016 Columbia Agreement.

Columbia University is responsible for the prosecution and maintenance of the licensed patents, in consultation with us, and subject to a requirement to give due consideration to our comments, at our expense. We have the first right, but not the obligation, to control the enforcement of licensed patents exclusively licensed to us against third parties. We are required to indemnify Columbia University for any third-party claims that arise from or relate to the 2016 Columbia Agreement.

The 2016 Columbia Agreement will terminate upon the expiration of all our royalty payment obligations in all countries. We may terminate the 2016 Columbia Agreement for convenience upon 90 days' written notice to Columbia University. At its election, Columbia University may terminate the 2016 Columbia Agreement, or convert the licenses granted to us into non-exclusive, non-sublicensable licenses, in the case of (a) our uncured material breach upon 30 days' written notice (which shall be extended to 90 days if we are diligently attempting to cure such material breach), (b) our failure to achieve the specified development and funding milestone events, or (c) our insolvency. The 2016 Columbia Agreement may not be assigned by us without Columbia University's consent, except to any successor to all or substantially all of our business to which the 2016 Columbia Agreement relates and upon notice to Columbia University.

In January 2019, we entered into a second license agreement with Columbia University (the "2019 Columbia Agreement"). Pursuant to the 2019 Columbia Agreement, Columbia University granted us a royalty-bearing, sublicensable license that is exclusive with respect to certain patents, and non-exclusive with respect to certain know-how, in each case to develop, manufacture and commercialize PI3k inhibitor products. The license grant is worldwide. Under the 2019 Columbia Agreement, we are obligated to use commercially reasonable efforts to research, discover, develop and market licensed products for commercial sale in the licensed territory, and to comply with certain obligations to meet specified development and funding milestones within defined time periods. Columbia University retains the right to conduct, and grant third parties the right to conduct, non-clinical academic research using the licensed technology; provided that such research is not funded by a commercial entity or for-profit entity or results in rights granted to a commercial or for-profit entity. As consideration for entering into the 2019 Columbia Agreement, we made a nominal upfront payment to Columbia University. We will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2019 Columbia Agreement. We will also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on our, our affiliates' and our sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, we are required to make specified annual minimum royalty payments to Columbia University, which is contingent upon the approval of the licensed products, in the mid-six figures beginning on the tenth anniversary of the effective date of the 2019 Columbia Agreement.

In July 2022, following regulatory changes impacting development of the class of PI3k inhibitors and the Company's decision to discontinue its early stage preclinical PI3k program, the Company and Columbia entered into an agreement terminating the 2019 Columbia Agreement (the "2022 Columbia Termination Agreement") as of July 25, 2022. Under the terms of the 2022 Columbia Termination Agreement, the Company assigned certain regulatory documents regarding the preclinical PI3k inhibitor AT-104 to Columbia and granted Columbia a non-exclusive royalty free license (with rights to sublicense any future Columbia licensee) under certain know-how, technical information and data relating to AT-104 that was developed by the Company during the term of the 2019 Columbia Agreement.

In March 2019, and in connection with the 2016 Columbia Agreement, the Company entered into a research services agreement (the "2019 Columbia Research Agreement") with Columbia University with the purpose of analyzing structural and functional changes in brain tissue in an animal model of Galactosemia, and the effects of certain compounds whose intellectual property rights were licensed to the Company as part of the 2016 Columbia Agreement on any such structural and functional changes. The 2019 Columbia Research Agreement had a term of 12 months from its effective date and expired in accordance with its terms.

On October 3, 2019, and in connection with the 2019 Columbia Agreement, the Company entered into a research services agreement ("PI3k Columbia Research Agreement" and collectively with the 2016 Columbia Agreement, 2019 Columbia Agreement and 2019 Columbia Research Agreement, "Columbia Agreements") with

Columbia University with the purpose of analyzing PI3k inhibitors for the treatment of lymphoid malignancies. The PI3k Columbia Research Agreement had a term of 18 months from its effective date and expired in accordance with its terms.

License Agreement with University of Miami

On October 28, 2020, we entered into a license agreement (the "2020 Miami License Agreement") with the University of Miami relating to certain technology that is co-owned by the University of Miami (UM), the University of Rochester (UR) and University College London (UCL Business Ltd. (UCL)). UM was granted an exclusive agency from UR and UCL to license each of their rights in the technology. Pursuant to the 2020 Miami License Agreement, UM, on behalf of itself and UR and UCL, granted us a royalty-bearing, sublicensable license that is exclusive with respect to certain patent applications and patents that may grant from the applications, and non-exclusive with respect to certain know-how, in each case to research, develop, make, have made, use, sell and import products for use in treating and/or detecting certain inherited neuropathies, in particular those caused by mutation in the sorbitol dehydrogenase (SORD) gene. The license grant is worldwide. Under the 2020 Miami License Agreement, we are obligated to use commercially reasonable efforts to develop, manufacture, market and sell licensed products in the licensed territory, and to comply with certain obligations to meet specified development milestones within defined time periods. UM retains for itself UR and UCL the right to use the licensed patent rights and licensed technology for their internal non-commercial educational, research and clinical patient care purposes, including in sponsored research and collaboration with commercial entities. As the technology licensed to us under the 2020 Miami License Agreement was developed as a result of a U.S. government grant, the licenses granted to us under the agreement are subject to the terms of such grant, and to standard rights of the U.S. government under the Bayh-Dole Act, including the grant to the government of a non-exclusive, worldwide, freedom to operate license under any patents, and the requirement, absent a waiver, to manufacture products substantially in the United States.

Under the terms of the 2020 Miami License Agreement, we are obligated to pay the University an up-front non-refundable license fee of $1.1 million, and a second non-refundable license fee of $0.5 million due on the first anniversary of the date of the license. We will be required to make further payments to UM of up to an aggregate $2.2 million for the achievement of specified patenting and development milestones, and up to an aggregate of $4.1 million for achievement of late stage regulatory milestones. We will also be required to pay royalties ranging from 0.88% - 5% on ours, our affiliates' and our sublicensees' net sales of licensed products. When we sublicense the rights granted under the 2020 Miami License Agreement to one or more third parties, we are required to pay to UM a portion of the non-royalty sublicensing revenue received from such third parties ranging from 15% – 25%. The Advanz Agreement includes a sublicense under the 2020 Miami License Agreement.

The 2020 Miami License Agreement terminates upon the expiration of all issued patents and filed patent applications or 10 years after the first commercial sale of the last product or process for which a royalty is due, unless earlier terminated. In addition, the 2020 Miami License Agreement may be terminated by us at any time upon 60 days prior written notice to UM, and may be terminated by either us or UM upon material breach of an obligation if action to cure the breach is not initiated within 60 days of receipt of written notice.

On October 28, 2020, we entered into an option agreement with the University of Miami (the "2020 Miami Option Agreement") concerning certain research activities and technology relating to SORD neuropathy that may be pursued and developed by UM. Under the 2020 Miami Option Agreement, if UM conducts such research activities, then UM is obligated to grant us certain option rights to access and use the research results and to obtain licenses to any associated patent rights upon us making specified payments to UM within specified time limits. If we elect to obtain option rights, we will be required to make payments to UM in the low-six figures to the low-seven figures, depending upon the rights we elect to obtain, and we will be obligated to make certain milestone payments in the high-six figures to mid-seven figures if UM conducts and completes certain research activities within specified time periods and we elect to receive rights to use the results of that research.

On December 14, 2020, we entered into a research agreement with the University of Miami (the "2020 Miami Research Agreement"), pursuant to which the University of Miami agreed to conduct a research study relating to SORD neuropathy and deliver a final report on the study to us. The term of the research agreement was from December 14, 2020 through December 30, 2021. The consideration for the 2020 Miami Research Agreement was $0.3 million. Due to COVID-19 pandemic disruptions certain research under the 2020 Miami Research Agreement was not completed. In

January 2022, we amended the 2020 Miami Research Agreement to extend the term of the agreement to August 31, 2022, whereby the research study was completed.

License Agreement with Advanz Pharma

On January 3, 2023, we entered into an Exclusive License and Supply Agreement ("the Advanz Agreement") with Mercury Pharma Group Limited (trading as Advanz Pharma Holdings). Pursuant to the Advanz Agreement, we granted Advanz Pharma the exclusive right and license to commercialize drug products containing AT-007 (also known as govorestat), our proprietary Aldose Reductase Inhibitor (ARI) ("Licensed Product"), for use in treatment of Sorbitol Dehydrogenase Deficiency ("SORD") and Galactosemia (each a "Licensed Indication") in the European Economic Area, Switzerland and the United Kingdom ("Territory"). We also granted Advanz Pharma a right of negotiation and "most-favored nation" rights with respect to acquiring the European commercialization rights for any additional indications for which the Licensed Product may be developed in the future (or any other products we may develop solely to the extent used for the Licensed Indications).

Advanz Pharma is required to use commercially reasonable efforts to launch and commercialize the Licensed Products in the major markets in the Territory in each Licensed Indication following, and subject to, receipt of marketing authorization therein. Under the Advanz Agreement, Advanz Pharma agreed to pay us (i) an upfront payment of EUR 10 million (approx. USD $10.7 million), and certain development milestone payments upon clinical trial completions and receipt of marketing authorization in the territory, as well as certain commercial milestone payments, totaling EUR 134 million (approx. USD $142.2 million) in the aggregate, and (ii) royalties of 20% of net sales of the Licensed Product. Such royalty rate will be payable on a country-by-country basis until the later of (i) the expiration of the licensed patents covering the composition of matter of AT-007, or (ii) 10 years after the European Medicines Agency's grant of marketing authorization for the Licensed Product. The royalties are subject to certain deductions, including certain secondary finishing costs, certain step-in establishment costs and a portion of fees for any potential third-party patent licenses if applicable in the future. Following the initial term of the license, as described above, the royalty rate shall be reduced to 10% and shall continue in perpetuity unless the Agreement is terminated in various circumstances in accordance with its terms.

Certain of the patents licensed to Advanz Pharma under the Advanz Agreement are sub-licensed from the University of Miami and Columbia University, and thus remain subject to certain obligations of the Company (including royalty obligations) to such institutions. For more information on these arrangements see "Exclusive License Agreement with Columbia University" and "License Agreements with the University of Miami".

Sales and Marketing

Due to the delay in the anticipated Galactosemia commercial launch, external non-essential commercial expenditures have been suspended, including sales and marketing. In the year ended December 31, 2024 our commercial spending was lower than originally anticipated. However, it was higher than in the year ended December 31, 2023 in anticipation of a potential approval.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We depend on third-party contract manufacturing organizations, or CMOs, for all of our requirements of raw materials, drug substance and drug product for our preclinical research and our clinical trials for AT-007, AT-001 and AT-003. We have not entered into long-term agreements with our current CMOs. We intend to continue to rely on CMOs for later-stage development and commercialization of our current products, as well as the development and commercialization of any other product candidates that we may identify. Although we rely on CMOs, we have personnel and third-party consultants with extensive manufacturing experience to oversee the relationships with our contract manufacturers.

We believe the synthesis of the drug substance for AT-007 and AT-001 are reliable and reproducible from readily available starting materials, and the synthetic routes are amenable to large-scale production and do not require unusual equipment or handling in the manufacturing process. We have obtained adequate supplies of the drug substance for AT-007 and AT-001 to satisfy our immediate clinical and preclinical demands.

Drug product formulation development for AT-007 and AT-001 have been completed. We have contracted with a third-party manufacturer capable of both formulation development and drug product manufacturing through commercialization. We may identify a second drug product manufacturer in the future to add additional capacity and redundancy to our supply chain.

Competition

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, the expertise of our executive and scientific team, research, clinical capabilities, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Product candidates that we successfully develop and commercialize may compete with existing therapies and new therapies that may become available in the future.

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

There are currently no therapies approved to treat Galactosemia. Two companies have announced plans for preclinical or conceptual programs to develop gene therapies in Galactosemia. We believe these potential AAV gene therapies are several years away from entering the clinic, and there are no publicly available data to date in preclinical or clinical studies demonstrating efficacy or safety. Additionally, due to safety issues associated with AAV gene therapy in general and the fact that Galactosemia is a debilitating but not life-threatening disease, we expect there may be concerns about the benefit-risk assessment for gene therapies among parents or physicians.

There are currently no therapies approved for SORD Deficiency. There are no drugs in development to our knowledge outside of AT-007, and we believe that the IP licensed from University of Miami is sufficiently broad to encompass the entire class of aldose reductase inhibitors for treatment of SORD Deficiency.

There are currently no therapies approved to treat PMM2-congenital disorder of glycosylation. Recently, Glycomine, Inc., a biotech company also focused in developing new therapies for orphan diseases, received an FDA Fast Track Designation for its product candidate, a non-AR treatment for PMM2-CDG.

There are currently no therapies approved to treat DbCM. Sponsors of sodium-glucose cotransporter-2, or SGLT2, inhibitors are pursuing broad cardiovascular labels in type 2 diabetes patients, which may include a subset of DbCM patients as part of the larger diabetic population at risk for heart failure. Many of these programs are sponsored by large pharmaceutical companies with a strong presence in cardiology and metabolic disease. There have been prior studies demonstrating effectiveness in DbCM of off-label use of sildenafil, although we do not believe this represents a commercially viable competitive threat.

There are no disease modifying therapies approved to treat DPN outside of Japan, India and China. In these limited markets, epalrestat, another ARI, is approved to prevent worsening of DPN, and despite challenges in compliance due to frequent dosing three to five times daily, the drugs are generic and offer a low cost alternative. A more effective therapy with improved tolerability and dosing may offer an advantage. A re-formulation of proprietary crystalline epalrestat, BNV-222, is in development for DPN in Russia in a 12-month Phase 2/3 clinical trial, which completed enrollment in 2016, but has not yet reported any results.

There are several therapies approved to treat severe or late-stage forms of DR, or proliferative DR, such as diabetic macular edema and proliferative DR, including anti-VEGF therapies, Lucentis and Eylea, which represents approximately 20% of the larger DR population. There are currently no therapies approved to treat non-proliferative DR, an earlier stage of the disease upstream of vessel or capillary proliferation. However, there are significant additional clinical development efforts for other mechanistic interventions in early-stage or for non-proliferative DR.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates, new therapeutic approaches and potential indications, and other inventions that are important to our business. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important for the development and implementation of our business. We also rely on the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how that is not patentable, we rely on confidentiality agreements to protect our interests. We require our employees, consultants and advisors to enter into confidentiality agreements prohibiting the disclosure of confidential information and requiring disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Our patent portfolio includes patents and patent applications that are exclusively licensed from Columbia University, exclusively licensed from University of Miami, and patent applications that are owned by us. Our patent portfolio includes patents and patent applications that cover our product candidates AT-007, AT-001, and AT-003, and the use of these candidates for therapeutic purposes in certain territories. Our proprietary technology has been developed primarily through relationships with academic research centers and contract research organizations.

For our product candidates, we will, in general, initially pursue patent protection covering compositions of matter and methods of use. Throughout the development of our product candidates, we seek to identify additional means of obtaining patent protection that would potentially enhance commercial success, including through additional methods of use, process of making, formulation and dosing regimen-related claims.

In total, our patent portfolio, including patents licensed from Columbia University, patents licensed from University of Miami and patents owned by us, comprises ten different patent families, filed in various jurisdictions worldwide, including families directed to composition of matter for AR inhibitors, and families directed to methods of treating Galactosemia and complications associated with Galactosemia, SORD Deficiency and PMM2-CDG using AR inhibitors. Our patent portfolio includes issued patents in the United States, Europe, Japan, Australia, Canada, and other jurisdictions. Our patent portfolio is outlined below:

Composition of Matter Patents

AT-007. We have exclusively licensed a patent family from Columbia University that includes five issued patents in the United States that claim the composition of matter of, certain methods of use of and certain dosage forms of AT-007, and 80 issued patents in other jurisdictions including Europe, Japan, Australia, India, Israel, China, Mexico, South Africa, Singapore, Russia and Brazil, that claim the composition of matter of and certain methods of use with respect to AT 007. In addition, we have pending patent applications in the United States, Europe, Japan, Canada, Australia, Russia, Brazil, Israel, Mexico, New Zealand, Singapore, South Africa, and Hong Kong. The 20-year term of patents in this family runs through June 2037, absent any available patent term adjustments or extensions.

AT-001 and AT-003. We have exclusively licensed from Columbia University a patent family that includes six issued patents in the United States, 82 issued patents in Europe, Japan, Canada, and Australia, a pending application in the United States and a pending application in Europe that claim the composition of matter of and certain methods of use with respect to AT-001 and AT-003. The 20-year term of the patents in this family runs through July 2031, absent any available patent term adjustments or extensions.

Methods for Treating Galactosemia

We own a family of patent applications that claims methods for treating Galactosemia and preventing complications associated with Galactosemia using AT-007 and other inhibitors of AR. This family currently includes granted patents in the United States, Mexico, Japan, Europe, China, Russia, Australia and Hong Kong and pending patent application in the United States, Europe, Japan, Australia, Brazil, Canada, China, Israel, Mexico, New Zealand, Russia, Singapore, South Africa, and Hong Kong. The 20-year term of patents in this family run through July 2038, absent any available patent term adjustments or extensions.

Methods for Treating SORD Deficiencies

We own a family of patent applications that claims methods for treating SORD Deficiency using AT-007 and other inhibitors of AR. This family currently includes pending patent applications in the United States, Europe, Japan, Australia, Brazil, Canada, China, Israel, Mexico, New Zealand, Russia, Singapore, South Africa, Hong Kong and South Korea. No patents have issued to date, but we expect that the 20-year term of any patents that do issue in this family will run through 2041, absent any available patent term adjustments or extensions.

We have exclusively licensed a patent family from University of Miami that includes an issued patent in the United States that claims methods of treating inherited neuropathy associated with mutation in the SORD gene using inhibitors of AR and pending applications in the United States, Europe, Japan, Australia, Brazil, Canada, China, Israel, Mexico, New Zealand, India, Russia, Singapore, South Africa, South Korea and Hong Kong, that claims methods for treating inherited neuropathy using a variety of therapeutic modalities including inhibitors of AR. This patent family is owned by University of Miami, University of Rochester and UCL Business Ltd. and licensed to us by University of Miami pursuant to an exclusive agency granted to University of Miami, by University of Rochester and UCL Business Ltd. The 20-year term of patents in this family will run through 2040, absent any available patent term adjustments or extensions.

Methods for Treating PMM2-CDG

We own a family of patent applications that claim methods for treating PMM2-CDG using AT-007 and other inhibitors of AR. This family currently includes pending patent application in the United States, Europe, Japan, Australia, Brazil, Canada, China, Israel, Mexico, New Zealand, Singapore, South Africa and Hong Kong. No patents have issued to date, but we expect that the 20-year term of any patents that do grant in this family will run through 2040, absent any available patent term adjustments or extensions.

We expect to file future patent applications on innovations that are developed in the course of advancing our pipeline through preclinical and clinical development.

Patent Term and Term Extensions

Individual patents have terms for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, utility patents issued for applications filed in the United States are granted a term of 20 years from the earliest effective filing date of a non-provisional patent application. In addition, in certain instances, the term of a U.S. patent can be extended to recapture a portion of the United States Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the restoration period cannot extend the patent term beyond 14 years from FDA approval. In addition, only one patent applicable to an approved drug is eligible for the extension, and only those claims covering the approved drug, a method for using it, or a method of manufacturing may be extended. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. All taxes, annuities or maintenance fees for a patent, as required by the USPTO and various foreign jurisdictions, must be timely paid in order for the patent to remain in force during this period of time.

The actual protection afforded by a patent may vary on a product by product basis, from country to country, and can depend upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions and the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Our patents and patent applications may be subject to procedural or legal challenges by others. We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see the section titled “Risk Factors — Risks Related to Our Intellectual Property.”

Trademarks and Know-How

In connection with the ongoing development and advancement of our products and services in the United States and various international jurisdictions, we seek to create protection for our marks and enhance their value by pursuing trademarks and service marks where available and when appropriate. In addition to patent and trademark protection, we rely upon know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by using confidentiality agreements with our commercial partners, collaborators, employees and consultants, and invention assignment agreements with our employees and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed by our employees and through relationships with third parties. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our contractors, commercial partners, collaborators, employees, and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For more information, see the section titled "Risk Factors — Risks Related to Our Intellectual Property."

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local levels, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, import and export of pharmaceutical products, such as those we are developing. The processes for obtaining regulatory approvals in the United States and in foreign countries, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources. The regulation of pharmaceutical products by government authorities can be affected by a variety of factors, including government budget, funding and staffing levels, payment of user fees and reauthorization of user fee programs, ability to hire and retain key personnel, as well as statutory, regulatory and policy changes.

United States Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the drug development process, approval process or after approval, may subject an applicant to delays and a variety of administrative or judicial sanctions, such as the FDA's refusal to approve a pending New Drug Application, or NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which contains results of nonclinical studies (e.g., laboratory evaluations of the chemistry, formulation, stability and toxicity of the product candidate), together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, and must become effective before human clinical trials may begin ;
- approval by an independent institutional review board, or IRB, or ethics committee at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials, in accordance with the FDA's good clinical practice, or GCP, requirements to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of an NDA for marketing approval, which must include data from preclinical testing and clinical trials;
- satisfactory completion of an FDA advisory committee review, if applicable;

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with cGMP requirements, and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- satisfactory completion of one or more FDA inspections of selected clinical investigators, clinical trial sites and/or the clinical trial sponsor to assure compliance with GCP requirements and the integrity of the clinical data;
- payment of user fees; and
- review and approval by the FDA of the NDA, including prescribing information, labeling, and packaging of the drug product, agreement on post-marketing commitments, if applicable, prior to any commercial marketing or sale of the drug in the United States.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. Adherence to federal regulations, such as GLPs and the Animal Welfare Act enforced by the Department of Agriculture, is required during the conduct of these tests. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold or a partial clinical hold.

In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must continue to oversee the clinical trial while it is being conducted and reapprove the study at least annually. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined. In Phase 1, the drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an initial indication of its effectiveness. In Phase 2, the drug typically is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more expensive Phase 3 clinical trials. In Phase 3, the drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the safety and efficacy of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted, at least annually, to the FDA, and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions, findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product, and any clinically important increase in the case of a serious suspected

adverse reaction over that listed in the protocol or investigator brochure. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements, or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. The Prescription Drug User Fee Act, or PDUFA, performance goals currently in effect provide that the FDA should review and act on 90% of standard NDAs for a new molecular entity within ten months of the date of "filing." This review typically takes 12 months from the date the NDA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision. However, the FDA may miss or extend these goal action dates; for example, the FDA may further extend the review process for three additional months to consider new information provided by the applicant to address any outstanding deficiency identified by the FDA following the original submission.

In addition, under the Pediatric Research Equity Act, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements generally do not apply to products with orphan designation.

The FDA also may require submission of a risk evaluation and mitigation strategy, or REMS, plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries or other risk minimization tools.

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

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

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. 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 an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCP requirements.

The testing and approval process for an NDA requires substantial time, effort and financial resources, and takes several years to complete. Data obtained from preclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval of an NDA on a timely basis, or at all.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. An NDA may be resubmitted with the deficiencies addressed, but resubmission does not guarantee approval. Data from clinical trials are not always conclusive, and the FDA's interpretation of data may differ from the sponsor's. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an Approval Letter. An Approval Letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. Failure to satisfy FDA post-marketing requirements can result in FDA enforcement action, up to and including withdrawal of NDA approval, and the FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Orphan drug designation must be requested before submitting an NDA. If the FDA grants orphan drug designation, the common name of the therapeutic agent and its designated 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 the FDA approves a sponsor's marketing application for a designated orphan drug for use in the rare disease or condition for which it was designated, the sponsor is eligible for a seven-year period of marketing exclusivity, during which the FDA may not approve another sponsor's marketing application for the same drug for the same disease or condition as the approved orphan drug, except in limited circumstances, such as if a subsequent sponsor demonstrates its product is clinically superior. During a sponsor's orphan drug exclusivity period, competitors, however, may receive approval for different drugs for the same disease or condition, or for the same drug as the for a different disease or condition. Orphan drug exclusivity could block the approval of one of our product candidates for seven years if a competitor obtains approval for the same drug for the same disease or condition before we do. Further, if a designated orphan drug receives marketing approval for an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, priority review, accelerated approval and breakthrough therapy designation, which are intended to facilitate the process for the development and FDA review of certain qualifying drug candidates that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted. The FDA may do so if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. Even if a product receives fast track designation, the designation can be rescinded and provides no assurance that a product will be reviewed or approved more expeditiously than would otherwise have been the case, or that the product will be approved at all.

The FDA may give a priority review designation to drugs that are intended to treat serious conditions, and if approved, would provide a significant improvement in safety or efficacy compared to available therapy, or provide a safe and effective treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months from FDA filing of the application. If criteria are not met for priority review, the standard FDA review period is ten months from FDA filing. Under the current PDUFA agreement, these six and ten-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review. However, even if priority review is awarded, the FDA may miss or extend the PDUFA goal action date. Priority review designation does not change the scientific or medical standard for approval or the quality of evidence necessary to support approval. Priority review may be available also for sponsors with a priority review voucher, or PRV.

The application for a product candidate for a rare pediatric disease, or RPD, may be eligible for a PRV that can be used to obtain a priority review for a subsequent human drug or biologic application after the date of approval of the rare pediatric disease drug product. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA or Biologics License Application (BLA). A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA or BLA. If a PRV is received, it may be sold or transferred an unlimited number of times. The FDA's rare pediatric disease priority voucher program began to sunset on December 20, 2024, upon Congress' failure to pass a continuing resolution package that included its reauthorization. Under the amended statutory sunset provisions, after December 20, 2024, the FDA may award a PRV for an approved rare pediatric disease product application only if the sponsor has rare pediatric disease designation for the drug and if that designation was granted by December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease PRVs. Congress may vote to reauthorize this program, but its future remains unknown at this time.

In addition, a product designed to treat serious or life-threatening disease or condition and that provide meaningful therapeutic benefit over available therapies may be eligible for accelerated approval, which permits approval on the basis of either an intermediate clinical endpoint or a surrogate endpoint that is reasonably likely to predict clinical benefit. Specifically, to qualify, the FDA must determine that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform a post-marketing study or studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures. Recent amendments to the FDCA included new requirements relating to post-approval studies and enhanced enforcement and withdrawal authorities for the FDA. Specifically, the FDA is now permitted to require that such post-approval studies be underway prior to approval or within a specific time period after the date accelerated approval is granted, and the agency has issued guidance as to what constitutes such a study being "underway".

Breakthrough therapy designation is for a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation provides sponsors of with more frequent interaction and communication with the FDA with the intent of identifying the most efficient path possible for clinical development and FDA approval. Breakthrough therapy designation can be rescinded if the FDA determines the program no longer meets the qualifying criteria for breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or may not meet the PDUFA goal action dates and timelines associated with these programs. These programs and designations provide no assurance that a product will be reviewed or approved more expeditiously than would otherwise have been the case, or that the product will be approved at all. Actual or potential changes in regulatory interpretations or agency resources may impact FDA's use or implementation of one or more expedited review and approval programs. We may explore some of these opportunities for our product candidates as appropriate.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications, manufacturing changes or other labeling claims, are subject to further testing requirements and prior FDA review and approval. There also are continuing annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as application fees for supplemental applications with clinical data.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, including a boxed warning, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution 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.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other regulatory requirements.

The FDA may also subject a drug to official lot release, which requires manufacturers to submit several items to the FDA with respect to each lot of a drug before it is released to distribution. These items include samples of each lot, a summary of the manufacturing history of the lot and the results of any tests performed on the lot.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market.

Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, problems with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies

or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or clinical holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications. The FDA and other agencies actively enforce the laws and regulations prohibiting their promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Federal and State Fraud and Abuse, Data Privacy and Security, and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws and regulations restrict business practices in the biopharmaceutical industry. These laws may impact, among other things, our current and future business operations, including our clinical research activities and proposed sales, marketing and education programs and constrain the business or financial arrangements and relationships with healthcare providers and other parties through which we may market, sell and distribute any products for which we obtain marketing approval. These laws include anti-kickback and false claims laws and regulations, data privacy and security, and transparency laws and regulations, including, without limitation, those laws described below.

The federal Anti-Kickback Statute prohibits any person or entity from, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term “remuneration” has been broadly interpreted to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to, among others, arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. 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 civil False Claims Act or the civil monetary penalties laws. The Anti-Kickback Statute has not been interpreted uniformly by federal courts, the government has pursued novel enforcement theories under the statute, and certain changes to the regulations implementing the statute have been stayed by courts, all of which make ensuring compliance with the law difficult.

Federal civil and criminal false claims laws and civil monetary penalties laws, including the federal civil False Claims Act, which can be enforced by individuals through civil whistleblower or qui tam actions, prohibits any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their respective implementing regulations, impose specified requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities, which include certain healthcare providers, healthcare clearinghouses and health plans, that create, receive, maintain or transmit individually identifiable health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which are not pre-empted by HIPAA, differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members.

In addition, government entities and private litigants have asserted claims under state consumer protection statutes against pharmaceutical companies for alleged false or misleading statements in connection with the marketing, promotion and/or sale of pharmaceutical products. We may also be subject to state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, and state and local laws that require the registration of pharmaceutical sales representatives. State legislatures are increasingly focused on pharmaceutical company activities, and we may be subject to additional new state or federal legislative requirements in the future that could impact our ability to commercialize our product candidates, if they are approved.

Because of the breadth of these laws and the narrowness of available statutory exceptions and regulatory safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to significant criminal, civil and administrative penalties including damages, fines, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, disgorgement, exclusion from

participation in government healthcare programs and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, implementation of corporate compliance programs, reporting of payments or transfers of value to healthcare professionals, and additional data privacy and security requirements.

Coverage and Reimbursement

The future commercial success of our product candidates, if approved, will depend in part on the extent to which third-party payors, such as governmental payor programs at the federal and state levels, including Medicare and Medicaid, private health insurers and other third-party payors, provide coverage of and establish adequate reimbursement levels for our product candidates. Third-party payors generally decide which products they will pay for and establish reimbursement levels for those products. In particular, in the United States, no uniform policy for coverage and reimbursement exists. Private health insurers and other third-party payors often provide coverage and reimbursement for products based on the level at which the government, through the Medicare program, provides coverage and reimbursement for such products, but also on their own methods and approval process apart from Medicare determinations. Therefore, coverage and reimbursement can differ significantly from payor to payor.

In the United States, the European Union, or EU, and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of products, particularly for new and innovative products, which often has resulted in average selling prices lower than they would otherwise be. Further, the increased emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the EU will put additional pressure on product pricing, reimbursement and usage. These pressures can arise from rules and practices of managed care groups, judicial decisions and laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical coverage and reimbursement policies and pricing in general.

Third-party payors are increasingly imposing additional requirements and restrictions on coverage and limiting reimbursement levels for products, particularly for new and innovative products and therapies, which may result in lower average selling prices. For example, federal and state governments reimburse products at varying rates generally below average wholesale price. These restrictions and limitations influence the purchase of products. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of products, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our product candidates, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party payor reimbursement may not be available to enable us to realize an appropriate return on our investment in product development.

Legislative or executive proposals to reform healthcare or reduce funding or costs under government insurance programs may result in lower reimbursement for our product candidates, if approved, or exclusion of our product candidates from coverage and reimbursement. The U.S. Congress continues to examine various Medicare and Medicaid policy proposals that may result in a downward pressure on the prices of prescription products in these programs, including, for example, through the Medicare price negotiation authority for non-rare disease high-cost prescription drugs included as part of the Inflation Reduction Act of 2022 (IRA) that was enacted in August 2022. However, it is unclear how the IRA will be effectuated or changed under the new Trump Administration or the degree of impact that the IRA will ultimately have upon our business. Further, a budget resolution passed by the House of Representatives in February 2025 proposed significant spending reductions for Medicaid and other federal programs, which, if enacted as part of a future U.S. federal budget, could impact our future business prospects. The cost containment measures that third-party payors and providers are instituting and any healthcare reform could significantly reduce our revenues from the sale of any approved product candidates.

Healthcare Reform

The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates. The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates profitably, if approved. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts, which include major legislative and executive branch initiatives to reduce the cost of care through changes in the healthcare system, including limits on the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded healthcare programs, and increased governmental control of drug pricing.

There have been several U.S. government initiatives over the past few years to fund and incentivize certain comparative effectiveness research, including creation of the Patient-Centered Outcomes Research Institute under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the PPACA. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates.

The PPACA became law in March 2010 and substantially changed the way healthcare is financed by third-party payors, and significantly impacts the U.S. pharmaceutical industry. Among other measures that may have an impact on our business, the PPACA establishes an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; a new Medicare Part D coverage gap discount program; and a new formula that increases the rebates a manufacturer must pay under the Medicaid Drug Rebate Program. Additionally, the PPACA extends manufacturers' Medicaid rebate liability, expands eligibility criteria for Medicaid programs, and expands entities eligible for discounts under the Public Health Service Act.

In addition to these provisions, the Affordable Care Act established a number of bodies whose work may have a future impact on the market for certain pharmaceutical products. These include the Patient-Centered Outcomes Research Institute, established to oversee, identify priorities in, and conduct comparative clinical effectiveness research and the Center for Medicare and Medicaid Innovation within the Centers for Medicare and Medicaid Services, to test innovative payment and service delivery models to lower Medicare and Medicaid spending. At this time, we are unsure of the full impact that the PPACA will have on our business.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the PPACA and we expect such challenges and amendments to continue. In his first administration, President Trump implemented certain directives designed to delay the implementation of certain PPACA provisions or otherwise circumvent requirements for health insurance mandated by the PPACA, while Congress has considered legislation that would repeal or repeal and replace all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of the PPACA have been signed into law. For example, a case challenging the PPACA's requirement that private insurers cover certain preventative services is currently pending before the U.S. District Court for the Northern District of Texas. In March 2023, the judge struck down the requirement and, on appeal, in June 2024 the U.S. Court of Appeals for the Fifth Circuit held, among other things, that the PPACA's requirement that group health plans and health insurance issuers cover certain preventative services without cost-sharing is unconstitutional. The parties have petitioned to appeal the case to the U.S. Supreme Court, which granted certiorari in January 2025. It is unclear how this decision, subsequent decisions and appeals, or any potential future litigation and other efforts to repeal and replace the PPACA will impact the PPACA, or our business.

Further, there has been increasing legislative, executive branch, and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. For example, the Inflation Reduction Act of 2022, enacted on August 16, 2022, seeks to reduce prescription drug costs by, among other provisions, allowing Medicare to negotiate prices for certain non-rare disease high-cost prescription drugs in Medicare Parts B and D, imposing an excise tax on pharmaceutical manufacturers that refuse to negotiate pricing with Medicare, requiring inflation rebates to limit annual drug price

increases in Medicare, redesigning the Medicare Part D formula, and limiting the cost-sharing for insulin products. However, the current administration has taken action to limit or change healthcare policies pursued by the Biden Administration. For example, President Trump rescinded an executive order issued by former President Biden, pursuant to which the Center for Medicare and Medicaid Innovation (CMMI) created three drug pricing experiments, and it is unclear whether CMMI will continue to pursue some or any of these models. It is unclear whether additional drug pricing and other healthcare reform measures will be enacted, or prior measures repealed, and if enacted or repealed, what effect they would have on our business.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine which drugs and suppliers will be included in their healthcare programs. These measures could reduce future demand for our products or put pressure on our pricing.

Additionally, in May 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or 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 I 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 drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our product candidates. For example, in the EU, we must obtain authorization of a clinical trial application, or CTA, in each member state in which we intend to conduct a clinical trial. Whether or not we obtain FDA approval for a drug, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the drug in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Facilities

We are currently in a five-year lease for the space for our principal executive offices in New York, New York and a three-year lease for the offices in Englewood Cliffs, New Jersey. We believe that our facilities are adequate to meet our current needs.

Employees and Human Capital Resources

Investing in, developing, and maintaining human capital is critical to our success. As of December 31, 2024, we had 35 full-time employees, 18 of whom were primarily engaged in research and development activities. A total of eleven employees have an M.D. or Ph.D. degree. We emphasize a number of measures and objectives in managing our human capital assets, including, among others, employee safety and wellness, talent acquisition and retention, employee engagement, development and training, ranges of experience and compensation and pay equity. None of our employees are represented by a labor union and we consider our employee relations to be good.

Our human capital resource objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees and advisors. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel and increase our success and stockholder value thereby.

The success of our business is fundamentally connected to the well-being of our employees. Accordingly, we are committed to their health, safety and wellness.

Information About Our Executive Officers

The following table sets forth information regarding our executive officers:

Name	Age	Position(s)
Executive Officers		
John H. Johnson	67	Executive Chairman and Chair of the Board of Directors
Les Funtleyder	55	Interim Chief Executive Officer and Chief Financial Officer
Catherine Thorpe	62	Interim Chief Accounting Officer
Constantine Chinoporos	58	Chief Operating Officer and Chief Business Officer
Dale Hooks	58	Chief Commercial Officer
Riccardo Perfetti, M.D., Ph.D	65	Chief Medical Officer

John Johnson, age 67, has served as our Executive Chairman and Chair of our Board of Directors since December 2024. Mr. Johnson is a recognized leader in the pharmaceutical and biotechnology industry with over 40 years of experience. Mr. Johnson has served as a member of the Board and Compensation Committee and Chair of the Nominating and Corporate Governance Committee at Verastem, Inc. (Nasdaq: VSTM) since April 2020. Since March 2022, Mr. Johnson has served as CEO and Board Director of Reaction Biology. Mr. Johnson joined the Board and Nominating and Corporate Governance Committee of Xeris Biopharma Holdings, Inc. (Nasdaq: XERS) in October 2021 and has served on the Board and Compensation Committee, as well as Chair of the Quality, Compliance, and Portfolio Committee, at Axogen, Inc. (Nasdaq: AXGN) since January 2021. Previously, Mr. Johnson was Company Group Chairman of Biopharmaceuticals at Johnson & Johnson from 2005 to 2007, CEO of Strongbridge Biopharma plc until its acquisition by Xeris Biopharma Holding Inc. in 2021, and President of Eli Lilly's Worldwide Oncology Unit from 2009 to 2011. Mr. Johnson also led ImClone Systems, Inc. (Nasdaq: IMCL) as CEO and Director from 2007 to 2008. Additionally, Mr. Johnson served on the Board of Melinta Therapeutics, Inc. and as CEO in 2019, and was involved with the Pharmaceutical Research and Manufacturers of America and Biotechnology Industry Organization from 2013 to 2014.

Les Funtleyder, age 55, has served as our Interim Chief Executive Officer since December 2024, has served as our Chief Financial Officer since November 2023, has served as director of the Company since June 2016 and previously served as our interim Chief Financial Officer from December 2018 to April 2019. Mr. Funtleyder also serves as a healthcare portfolio manager at E Squared Capital Management, LLC since January 2014. Mr. Funtleyder currently serves on the board of directors of public and private healthcare companies and foundations, including Reviva Pharmaceuticals (Nasdaq: RVPH) where he also serves as a member of the governance committee and as chair of the audit committee. Mr. Funtleyder previously served as the director of strategic investments and communications of OPKO Health Inc. (Nasdaq: OPK), a publicly traded healthcare company. Mr. Funtleyder is also an adjunct professor at Columbia University Medical Center and an adjunct professor at Columbia University School of Public Health. Mr. Funtleyder received his B.A. from Tulane University and MPH from Columbia University Mailman School of Public Health. We believe that Mr. Funtleyder's extensive experience managing and investing in the healthcare industry qualifies him to serve on our board of directors.

Catherine Thorpe, age 62, has served as our Interim Chief Accounting Officer since June 2023 and our Interim Principal Financial Officer from June 2023 until November 2023. While serving in this role, Ms. Thorpe also serves as the Managing Partner of CFGI Stamford Office. Ms. Thorpe has occupied various roles at CFGI, a specialized financial consulting firm, since 2018. From February 2016 to April 2018, she was the Internal Audit Leader at Datto, Inc., a cybersecurity and data backup company. Prior to that, she was a Managing Director at GE Capital from 2007 to 2016, and from July 1984 to December 1991 and from September 2004 to January 2007 she was a Manager at PricewaterhouseCoopers. Ms. Thorpe holds a bachelor's degree in accounting from Simmons University and is a Certified Public Accountant.

Constantine Chinoporos, age 58, has served as our Chief Operating Officer since December 2023. Prior to joining us he was a Chief Business Officer at Albireo Pharmaceuticals, from December 2021 until their acquisition by Ipsen in March 2023. He served as Chief Business Officer at Boston Pharmaceuticals from November 2015 to October 2021. Prior to that, he held senior positions in business and corporate development, corporate finance, and alliance management at Sanofi S.A., Genzyme, and Eli Lilly. He currently serves as a strategic advisor to Apollo Therapeutics, a role which he has held since February 2023. Mr. Chinoporos received an undergraduate degree in History as well as an MBA from Cornell University.

Dale Hooks, age 58, has served as our Chief Commercial Officer since April 2024. Mr. Hooks has over 30 years of experience in the biopharma industry, leading numerous product launches and managing global brands. Mr. Hooks previously served as Vice President of Global Commercial Operations at Reata Pharmaceuticals, Inc. from February 2019 to November 2023. Prior to joining Reata, Mr. Hooks was the Chief Commercial Officer at Clovis Oncology, Inc. from January 2016 to October 2018, where he was responsible for building their global commercial organization. From 1992 to 2014, Mr. Hooks held positions of increasing responsibility at Genentech, Galderma, Novartis, and GSK. Mr. Hooks has a B.S. degree in Marketing and Finance from Stephen F. Austin University and an M.B.A. from the University of North Carolina at Chapel Hill.

Riccardo Perfetti, M.D., Ph.D., age 65, has served as our Chief Medical Officer since August 2018. Prior to joining us, Dr. Perfetti served as a Senior Medical Officer, Vice President and Head of Global Medical Affairs, Diabetes and Cardiovascular Business Unit at Sanofi S.A., a publicly traded pharmaceutical company from October 2007 to September 2018. Prior to joining Sanofi, Dr. Perfetti served in various roles at Amgen Inc., a publicly traded biopharmaceutical company, including as a Director and Global Development Leader in diabetes, obesity, metabolism and endocrinology from December 2004 to August 2007. Dr. Perfetti was previously an associate professor of medicine at University of California in Los Angeles and a professor of medicine at the National Institutes of Health, or NIH. Dr. Perfetti practiced as an endocrinologist at Cedars-Sinai Medical Center and also served as Director of the Diabetes Research Laboratory and Director of the Outpatient Diabetes Program. Dr. Perfetti received his M.D. and Ph.D. in Endocrinology from University La Sapienza in Rome, Italy and received post-graduate training in endocrinology and molecular biology at NIH.

Other Information

We were incorporated in Delaware in January 2016 and completed the IPO in May 2019. Our principal executive offices are located at 545 5th Avenue, Suite 1400, New York, New York 10017, and our telephone number is (212) 220-9226.

We maintain a website at www.appliedtherapeutics.com. The contents of our website are not incorporated in, or otherwise to be regarded as part of this Annual Report. Unless the context otherwise requires, the terms, “Applied Therapeutics,” the “Company,” “we,” “us,” “our” and the “ registrant” refer to Applied Therapeutics, Inc.

Investors and others should note that we announce material financial information to our investors using our investor relations website (http://ir.appliedtherapeutics.com), SEC filings, press releases, public conference calls and webcasts.

ITEM 1A. RISK FACTORS.

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks described below, together with other information appearing elsewhere in this Annual Report, including our financial statements and the related notes and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth 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.

Risk Factor Summary

The following is a summary of the risk factors included in this Item 1A and is qualified entirely by the disclosure included in the rest of this Item 1A:

Risks Related to Our Financial Position and Capital Needs

- We have incurred and expect to continue to incur substantial operating losses and our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.
- The report of our independent registered public accounting firm included a "going concern" explanatory paragraph.
- We identified a material weakness in our internal control over financial reporting as of December 31, 2024 and this or other material weaknesses could continue to materially impair our ability to report accurate financial information in a timely manner.
- Our operating history makes evaluating our business and future viability more difficult.
- We need substantial funding to operate, and failure to secure it may harm our development programs.
- Raising additional capital may cause adverse effects.

Risks Related to the Development and Commercialization of Our Product Candidates

- The Warning Letter from FDA could impede our current and future clinical trials or NDA submissions.
- Our success is substantially dependent on the successful clinical development, regulatory approval and commercialization of our product candidates and may be adversely affected upon failure to do so.
- We received the Complete Response Letter from the FDA indicating that our new drug application or NDA for govorestat for the treatment of Classic Galactosemia was not approvable at this time, and do not know if govorestat or any of our product candidates will ever receive regulatory approval.
- We or Advanz Pharma may fail to perform under our partnership agreements for AT-007 (govorestat) commercialization, potentially leading to liabilities and unachieved benefits.
- Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials and our results may not be sufficient for the necessary regulatory approvals.
- Clinical drug development involves a lengthy and expensive process and the development of additional product candidates is risky and uncertain.
- We may be unable to obtain or maintain regulatory approvals, designations, or accelerated pathways for our product candidates.
- Clinical trials are expensive, time consuming and subject to factors outside our control.
- Our product candidates may cause undesirable side effects, affecting regulatory approval, commercial potential or result in significant negative consequences following any potential marketing approval.

- Interim, "top-line" and preliminary data from our clinical trials may be subject to change.
- Market opportunities for our products may be smaller or approval may narrow our patient population.
- We may face substantial competition.
- We may face risks related to strategic collaborations to develop our product candidates
- We may experience sudden changes in the regulatory standards that govern the acceptability of our clinical studies to support approval.
- Even if approved, our products may not achieve market acceptance necessary for commercial success.
- We may face risks from potential international operations if we commercialize any product candidate.
- We may be adversely affected by product liability lawsuits.
- Our insurance policies may be inadequate and potentially expose us to unrecoverable risks.

Risks Related to Regulatory Compliance

- We are subject to healthcare laws and regulations, which are subject to change and carry substantial penalties for noncompliance.
- Coverage and adequate reimbursement may not be available for our product candidates.
- Healthcare reform measures may have a negative impact on our business and results of operations.

Risks Related to Our Dependence on Third Parties

- One of our clinical investigators received a warning letter from the FDA following a site inspection.
- Third-parties may conduct our preclinical studies and clinical trials in an unsatisfactory manner.
- We intend to rely on third parties to produce supplies of our product candidates.
- We and our third-party affiliates are subject to environmental, health and safety laws and regulations.

Risks Related to Our Intellectual Property

- Breaches of our license agreements may result in the adverse effects to our ability to continue the development and commercialization of our product candidates.
- Insufficient patent protection could let competitors develop similar products.
- Obtaining and maintaining our patent rights is expensive, complicated and labor intensive and patent terms may be inadequate to protect our competitive position on our product candidates.
- We may be subject to claims alleging violations of intellectual property rights.
- Changes in patent law could impair our ability to protect our product candidates.
- We may be unable to protect our intellectual property rights.
- Intellectual property rights do not necessarily address all potential threats to our business.

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

- We face securities-related class-action and shareholder derivative litigation that could be costly, divert resources, and damage our reputation, business, or financial condition if an adverse judgment occurs.
- Recent leadership changes, including our founder and CEO's departure, may cause uncertainty.
- We may experience difficulties resulting from the expansion of our organization.
- We may be subject to security breaches in our information technology systems.

- Our employees and the third-parties we deal with may engage in misconduct or improper activities.

Risks Related to Ownership of Our Common Stock

- The market price of our common stock is volatile, has fluctuated substantially and significantly declined.
- Failure to regain compliance with the continued listing requirements of Nasdaq could result in our common stock being delisted and the price of our common stock could be negatively impacted.
- We do not anticipate paying any cash dividends on our capital stock in the foreseeable future.

General Risk Factors

- We may be affected by unfavorable research or reports.
- We may use our cash and cash equivalents ineffectively or in ways with which you do not agree.
- We face risks and costs from losing "emerging growth company" status and must meet new requirements.
- We may use defensive and forum selection provisions in our governing documents and Delaware law.

Risks Related to Our Financial Position and Capital Needs

We have incurred significant operating losses since inception and anticipate that we will continue to incur substantial operating losses for the foreseeable future and may never achieve or maintain profitability.

Since inception in January 2016, we have incurred significant operating losses. Our net loss was $105.6 million and $119.8 million for the years ended December 31, 2024, and 2023 respectively. As of December 31, 2024, we had an accumulated deficit of $574.2 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Since inception, we have devoted substantially all of our efforts to research and preclinical and clinical development of our product candidates, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials. To date, we have never obtained regulatory approval for, or commercialized, any drugs. It could be several years, if ever, before we have a commercialized drug. The net losses we incur may fluctuate significantly from quarter to quarter and year-to-year. We anticipate that our expenses will increase substantially if, and as, we:

- continue the ongoing and planned development of our product candidates;
- initiate, conduct and complete any ongoing, anticipated or future preclinical studies and clinical trials for our current and future product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any current or future product candidate for which we may obtain marketing approval;
- seek to discover and develop additional product candidates;
- continue to build a portfolio of product candidates through the acquisition or in-license of drugs, product candidates or technologies;
- maintain, protect and expand our intellectual property portfolio;
- meet the requirements and demands of being a public company;
- defend against any product liability claims or other lawsuits related to our products;
- hire additional executive, clinical, regulatory and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Furthermore, we have recently incurred and likely will continue to incur additional costs associated with the Complete Response Letter we received from the FDA in November 2024 for the new drug application (NDA) we submitted for govorestat for the treatment of Classic Galactosemia, the Warning Letter related to the Phase 2/3, ACTION-Galactosemia Kids study, the departure of our founder and CEO and securities-related class action litigation and derivative litigation, including significant legal, accounting, investor relations and other expenses.

To become and remain profitable, we must succeed in developing and eventually commercializing drugs that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our current and future product candidates, obtaining regulatory approval, procuring commercial-scale manufacturing, marketing and selling any products for which we obtain regulatory approval (including through third parties), as well as discovering or acquiring and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are sufficient to offset our expenses and achieve profitability.

Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of expenses or when, or if, we will be able to achieve profitability. If we are required by regulatory authorities to perform studies in addition to those currently expected, or if there are any additional delays in the initiation and completion of our clinical trials or the development and approval of any of our product candidates, our expenses will likely increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. Any additional decline in the value of our common stock could also cause you to lose all or part of your investment.

The report of our independent registered public accounting firm included a "going concern" explanatory paragraph.

The report of our independent registered public accounting firm on our financial statements for the year ended December 31, 2024 includes an explanatory paragraph regarding the existence of substantial doubt about our ability to continue as a going concern. Our cash and cash equivalents were $79.4 million at December 31, 2024. We will need to obtain substantial additional funding in connection with our continuing operations and planned research and clinical development activities. Additionally, we may encounter unforeseen expenses, including in connection with reevaluating our product candidates and potential new trials. Given our planned expenditures for the next several years, we have concluded, and our independent registered public accounting firm has agreed with our conclusion that there is still a substantial doubt regarding our ability to continue as a going concern for a period of 12 months beyond the filing of this Annual Report on Form 10-K. Any such inability to continue as a going concern may result in our stockholders losing their entire investment. There is no guarantee that we will become profitable or secure additional financing on acceptable terms.

We identified a material weakness in our internal control over financial reporting as of December 31, 2024 and this or other material weaknesses could continue to materially impair our ability to report accurate financial information in a timely manner.

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of its disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act for the year ended December 31, 2024. Based on such evaluation, the principal executive officer and principal financial officer has concluded that our disclosure controls and procedures were not effective as of December 31, 2023 due to the identified material weakness in internal control over financial reporting as discussed below.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act). Our management, under the supervision and with the participation of the principal executive officer and principal financial officer, conducted an assessment of the effectiveness of internal control over financial reporting as of December 31, 2024, based on the framework and criteria established in Internal Control-Integrated Framework (2013) (the "COSO framework") issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). Based on this assessment, management

concluded that, as of December 31, 2023, its internal control over financial reporting was not effective due to the existence of the material weakness described below.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that a reasonable possibility exists that a material misstatement of the annual or interim financial statements would not be prevented or detected on a timely basis. Our management identified a deficiency in our internal control over financial reporting that gave rise to a material weakness. The deficiency primarily related to deficiencies in the principles associated with the information and communication component of the COSO framework. This material weakness resulted in not having effective communication process to ensure that relevant and reliable information was communicated timely across the organization to enable management to effectively carry out their financial reporting and internal control roles and responsibilities.

As further described in Item 9A below, our management has been engaged in developing and implementing a remediation plan to address the material weakness described above. However, the material weakness will not be fully remediated until management can demonstrate the full effectiveness of controls over a sufficient period of time, and we can give no assurance on the success of such measures or the outcome of our assessment of these measures at this time.

If the steps we take to remediate the material weakness are ineffective, the material weakness could result in material misstatements to our annual or interim consolidated financial statements that might not be prevented or detected on a timely basis, or in delayed filings of our required periodic reports. This might lead to investors losing confidence in the accuracy and completeness of our financial reports, the market price of our common stock could be adversely affected, and we could become subject to litigation or investigations by Nasdaq, the SEC or other regulatory authorities, which could require additional financial and management resources.

Furthermore, if we identify any new material weaknesses in the future, any such newly identified material weakness could limit our ability to prevent or detect a misstatement of our accounts or disclosures that could result in a material misstatement of our annual or interim financial statements. In such case, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting and our stock price may decline as a result. We cannot assure you that the measures we have taken to date, or any measures we may take in the future, will be sufficient to remediate our existing material weakness or avoid potential future material weaknesses.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results in a timely manner or prevent fraud, which would adversely affect investor confidence in our company and harm our business.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations in a timely manner, or at all. Testing by us conducted in connection with Section 404(a) of the Sarbanes Oxley Act may reveal material weaknesses in our internal controls over financial reporting related to our limited finance, accounting and IT staffing levels. For example, in connection with the audit of our financial statements for the year ended December 31, 2023, we identified a material weakness in our internal control over financial reporting related to deficiencies in our controls over the financial statement close process, which was fully remediated as of March 31, 2024. In addition, as further described in Item 9A below, in connection with the audit of our financial statements for the year ended December 31, 2024, we identified a material weakness related to deficiencies in the principles associated with the information and communication component of the COSO framework. While we are implementing our remediation plan, we cannot provide assurances that the measures that have been taken to date, and are continuing to be implemented, will be sufficient to remediate the material weakness identified or to avoid potential future materials weaknesses. Subsequent testing by our independent registered public accounting firm in connection with Section 404(b) of the Sarbanes Oxley Act may reveal continued or additional deficiencies in our internal controls over financial reporting that are deemed to be significant deficiencies or material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Ineffective internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

We are required to disclose material changes made in our internal controls over financing reporting and procedures on a quarterly basis and our management are required to assess the effectiveness of these controls annually. We are also required to make a formal assessment of the effectiveness of our internal control over financial reporting, and once we cease to be a non-accelerated filer, we will be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, for as long as we are a smaller reporting company under the JOBS Act or a non-accelerated filer, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act.

To achieve compliance with Section 404(a) of the Sarbanes-Oxley Act, we engage 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 implement our remediation plan, continue to dedicate internal resources, potentially engage additional outside consultants to assess the adequacy of our internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are designed and operating effectively and implement a continuous reporting and improvement process for internal control over financial reporting.

We determined that, as of December 31, 2024, our disclosure controls and procedures were not effective due to the identified material weakness in internal control and financial reporting as described herein. The effectiveness of our internal controls in future periods is subject to the risk that our controls may become further inadequate because of changes in conditions. We may be unable to timely remediate our material weakness and may discover additional weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls over financial reporting, we may not be able to produce timely and accurate financial statements. If that were to happen, our investors could lose confidence in our reported financial information, the market price of our stock could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities including equivalent foreign authorities.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are a clinical-stage company with limited operational history, and our operations to date have been largely focused on raising capital, organizing and staffing our company, identifying and developing our product candidates, and undertaking preclinical and clinical development for our product candidates. As an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product or conduct sales and marketing activities necessary for successful commercialization, or arrange for a third-party to conduct these activities on our behalf. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In connection with our efforts to address the issues referenced in the Warning Letter, including reevaluating govorestat for the treatment of Classic Galactosemia and Sorbitol Dehydrogenase SORD Deficiency, we expect to encounter significant additional expenses, including expenses that we had not expected, as well as additional unforeseen expenses, difficulties, complications, delays, and other known or unknown factors in achieving our business objectives. If we are successful in our clinical trials for a product candidate, we will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

Additionally, we expect our financial condition to continue to fluctuate from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

We will require substantial additional funding to finance our operations. If we are unable to raise capital when needed, we could be forced to delay, reduce or terminate certain of our development programs or other operations.

As of December 31, 2024, we had $79.4 million in cash and cash equivalents. We will need to obtain substantial additional funding in connection with our continuing operations and planned research and clinical development activities. Additionally, we may encounter unforeseen expenses, including in connection with reevaluating our product candidates and potential new trials. There is no assurance that we will be able to obtain such additional financing on favorable terms or at all, or to fund our operations beyond that point. Our future capital requirements will depend on many factors, including:

- the timing, progress and results of our ongoing preclinical studies and clinical trials of our product candidates;
- FDA requirements for the approval of govorestat for any indication;
- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials of other product candidates that we may pursue;
- our ability to establish collaborations on favorable terms, if at all;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities if we are successful in reaching commercialization of any product candidate, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval, if any;
- the cost of any milestone and royalty payments with respect to any approved product candidates;
- 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;
- the costs of operating as a public company; and
- the extent to which we acquire or in-license other product candidates and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. 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.

In addition, our ability to access additional capital has and will be affected by the decrease in our common stock trading price and the Complete Response Letter for the govorestat NDA for Classic Galactosemia and the Warning Letter we received from the FDA which may have damaged our reputation, as well as overall macroeconomic trends which have caused the price of our common stock to fluctuate significantly and/or decline significantly. As a result, adequate additional financing may not be available to us when needed or on attractive terms. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce, or altogether terminate our research and development programs or future commercialization efforts.

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

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through public or private equity or debt financings, including through third-party funding, marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these

approaches. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest in our company may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt and equity financings, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as redeeming our shares, making investments, incurring additional debt, making capital expenditures, declaring dividends or placing limitations on our ability to acquire, sell or license intellectual property rights.

If we raise additional capital through future collaborations, strategic alliances or third-party licensing arrangements, we may have to relinquish valuable rights to our intellectual property, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional capital when needed, we may be required to delay, limit, reduce or terminate our drug development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise develop and market ourselves.

Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.

We have incurred substantial losses since inception and do not expect to become profitable in the near future, if ever. In general, under Section 382 of the United States Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses ("NOLs") to offset future taxable income. An ownership change for these purposes is generally defined as a greater than 50% change, by value, in the equity ownership of a corporation over a 3-year period. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of subsequent changes in our stock ownership (some of which shifts are outside our control). As a result, if, and to the extent that we earn net taxable income, our ability to use our pre-change NOLs to offset such taxable income may be subject to limitations.

For NOLs arising in tax years beginning after December 31, 2017, the Code limits a taxpayer's ability to utilize NOL carryforwards to 80% of taxable income. In addition, NOLs arising in tax years ending after December 31, 2017, can be carried forward indefinitely, but carryback is generally prohibited. NOLs generated in tax years beginning before January 1, 2018, are not subject to the 80% taxable income limitation, and NOLs generated in tax years ending before January 1, 2018, continue to have a two-year carryback and 20-year carryforward period. Deferred tax assets for NOLs are measured at the applicable tax rate in effect when the NOL is expected to be utilized. The limitations in the carryforward and carryback periods, as well as the limitation on use of NOLs arising in tax years beginning after December 31, 2017, may significantly impact our ability to utilize our NOLs to offset taxable income in the future.

In order to realize the future tax benefits of our NOL carryforwards, we must generate taxable income, of which there is no assurance. Accordingly, we have provided a full valuation allowance for deferred tax assets as of December 31, 2024 and 2023.

Risks Related to the Development and Commercialization of Our Product Candidates

We received a Warning Letter from the FDA for our NDA filed in December 2023 for our AT-007-1002 study. Failure to resolve the matters addressed in the Warning Letter could negatively impact our company's ability to undertake clinical trials in the future or timely complete future NDA submissions.

In November 2024, we received a Warning Letter from the FDA relating to our AT-007-1002 study. The letter identified issues related to electronic data capture and also referred to a dosing error in the dose-escalation phase of our study resulting in slightly lower levels than targeted in a limited number of patients. We responded to the Warning Letter in a timely manner and our response contained various remediation measures. We are closely working with our clinical team, consultants, and employees to develop and implement a plan that addresses FDA's concerns. Such actions have and will continue to increase our expenses, and the extent of those costs is still unknown.

If we are unable to sufficiently establish to the FDA that current or future clinical trials conducted by us would be in accordance with FDA regulations, we may be subject to enforcement action by the FDA including being subject to the FDA's Application Integrity Policy. This policy would require third-party validation of the integrity of the raw data

underlying any of our future filings to the FDA before those filings would be accepted for consideration. Such a requirement would be onerous and require significant additional time and expense, including unforeseen costs, for the clinical development and potential approval of any product candidates that we are currently developing and may wish to develop in the future. These requirements would make it difficult for us to attempt to restart the development of any of our former product candidates or commence the development of any new product candidates. Further, we could be subject to additional actions from the FDA that may negatively impact our ability to enter into clinical trials or submit an NDA in the future.

We recently received a Complete Response Letter from the FDA for our NDA for govorestat (AT-007) for the treatment of Classic Galactosemia, one of our lead product candidates, and we are currently evaluating our development program for Classic Galactosemia and SORD Deficiency, and do not currently know if govorestat will ever receive regulatory approval for any indication, which is necessary before it can be commercialized.

If we do not receive regulatory approval for govorestat (AT-007) for the treatment of Classic Galactosemia or SORD Deficiency or any other indication and we are not able to commercialize govorestat, we may not generate revenue for several years, if at all, and we may never generate sufficient revenue to achieve and sustain profitability. We need approval from the FDA prior to marketing our product candidates in the U.S. In December 2023, we submitted our first NDA to the FDA seeking approval for govorestat. In February 2024, the FDA accepted the filing of the NDA and the NDA was granted Priority Review status. In November 2024, the FDA issued a Complete Response Letter for the NDA. The Complete Response Letter indicates that the FDA completed its review of the application and determined that is unable to approve the NDA in its current form, citing deficiencies in the clinical application and failure to reach statistical significance on primary endpoints. Following receipt of the Complete Response Letter, we also withdrew the Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for govorestat for the treatment of Classic Galactosemia, as we believed more time was needed to acquire further data to support a European MAA. We are in the planning stages of determining our next steps with respect to our govorestat development program. Further clinical development of govorestat for any indications may require us to complete additional and more extensive clinical trials, which will be costly and time consuming. The amount and timing of the increased costs related to our clinical trials is difficult to predict due to the uncertainty inherent in the timing of clinical trial initiations, the rate of patient enrollment and the detailed design of future trials. If we continue our clinical development program for govorestat, we may not obtain necessary approvals from the FDA even if our trials demonstrate favorable results. The data we collect from any additional clinical trials may not demonstrate sufficient safety and efficacy to support regulatory approval of govorestat in which case we would experience potentially significant delays in, or be required to abandon, development of that product candidate. If we continue our clinical development program for govorestat, we will have fewer resources to devote to the research and development of our other product candidates and development stage programs. If we decide to terminate any further development of govorestat, we will be dependent upon the success of our other product candidates in our pipeline or other compounds we may in-license and the size of the potential markets for such other product candidates may not be as significant as the potential markets for govorestat, and we may not be able to monetize it.

Our other indications and development stage programs are in various stages of development. In light of recent regulatory developments, we will be closely examining the ongoing SORD Deficiency clinical development program and will continue to work with the FDA on the data needed to support an appropriate regulatory pathway for the drug, including ongoing work to provide the FDA with support for the potential use of the accelerated approval pathway for govorestat for the treatment of SORD Deficiency. We plan to meet with the FDA to discuss whether an NDA can be submitted based on the current data package and/or potential additional supporting data. However, there is no guarantee that the FDA will agree with this strategy, and the agency may require additional costly preclinical or clinical trials to support an NDA. There is also the risk that these additional trials will not be successful.

Our future success is substantially dependent on the successful clinical development, regulatory approval and commercialization of our product candidates. If we are not able to obtain required regulatory approvals, we will not be able to commercialize our product candidates and our ability to generate product revenue will be adversely affected.

We have invested a significant portion of our time and financial resources in the development of AT-007, AT-001 and AT-003. Our business is dependent on our ability to successfully complete development of, obtain regulatory approval for, and, if approved, successfully commercialize our product candidates in a timely manner. We may face unforeseen challenges in our drug development strategy, such as the Complete Response Letter received from the FDA

for the NDA we submitted for govorestat, and we can provide no assurances that our drug design will prove to be effective, that we will be able to take advantage of expedited regulatory pathways for any of our product candidates, or that we will ultimately be successful in our future clinical trials.

We have not obtained regulatory approval for any product candidate, our NDA seeking approval of AT-007 for Classic Galactosemia received a Complete Response Letter and was not approved, and it is possible that any product candidates we may seek to develop in the future will not obtain regulatory approval. Neither we nor any future collaborator is permitted to market any product candidates in the United States or abroad until we receive regulatory approval from the FDA or applicable foreign regulatory agency. The time required to obtain approval or other marketing authorizations by the FDA and comparable foreign regulatory authorities is unpredictable and typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions.

Prior to obtaining approval to commercialize any product candidate in the United States or abroad, we must demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that such product candidate is safe and effective for its intended uses. The FDA requires "substantial evidence" to make a finding of effectiveness for any approval, including accelerated approval. Substantial evidence generally requires two adequate and well-controlled studies; however, in certain circumstances, substantial evidence may be based on a single, large, multicenter, adequate and well-controlled study together with confirmatory evidence to be sufficient.

Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe that the preclinical or clinical data for our product candidates are promising and meet the applicable approval standards, the FDA and other regulatory authorities may disagree, or it may no longer be acceptable to the FDA upon submission due to changes in regulatory standards. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or it may object to elements of our clinical development program, requiring their alteration.

Of the large number of products in development across the pharmaceutical industry, only a small percentage successfully complete the FDA or comparable foreign regulatory authorities approval processes and receiving marketing authorization. The lengthy approval or marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval or marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

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

In addition, the FDA or comparable foreign regulatory authorities may change their policies, adopt additional regulations, revise existing regulations or guidance or take other actions, which may prevent or delay approval of our future product candidates under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained.

The development of our product candidates also may be delayed by other events beyond our control. For example, actions to limit federal agency budgets or personnel may result in reductions to the FDA's budget, employees, and operations, as well as changes to FDA regulatory programs, all of which may lead to slower response times and longer review periods, potentially affecting our ability to progress development of our product candidates, undergo regulatory inspections or obtain regulatory approval for our product candidates.

Furthermore, even if we obtain regulatory approval for our product candidates, we will still need to develop a commercial organization, establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payors, including government health administration authorities. If we are unable to successfully commercialize our product candidates, we may not be able to generate sufficient revenue to continue our business.

Changes in funding for the FDA and other government agencies and the implementation of tariffs could prevent new products and services from being developed or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, payment of user fees and reauthorization of user fee programs, staffing and other resource limitations, ability to hire and retain key personnel, as well as statutory, regulatory and policy changes. In addition, funding of other government agencies that support research and development activities that pertain to FDA review, such as research to understand new technologies or establish new standards, is subject to the political process, which is inherently fluid and unpredictable. Such government agencies also have been subject to reductions in funding and downsizing of agency staffing levels, which could materially impact our business and operations.

The current administration has implemented or proposed policies that may affect the FDA review process, including efforts to downsize the federal workforce, remove job elimination protections for federal workers, limit certain communications, and potentially impact user fee reauthorization. If political pressure or global health concerns prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In addition, a portion of our supply chain is located in countries that may be subject to new or increased tariffs, which could lead to increased costs to us. This exposure to international trade policies poses a risk to our operations and our financial condition.

We or Advanz Pharma may fail to perform under any of the agreements entered into in connection with the partnership for the potential commercialization of AT-007, which may subject us to liabilities, and we may fail to achieve anticipated benefits of the partnership.

In January 2023, we announced a partnership with Advanz Pharma ("Advanz") for the potential commercialization of AT-007 (govorestat) in Europe, and entered into an Exclusive License and Supply Agreement ("Advanz Agreement") with Advanz. Under the terms of the Advanz Agreement, Advanz receives exclusive commercial rights in the European Economic Area, Switzerland, and the UK (Territory) for AT-007 in Galactosemia and SORD Deficiency, with certain rights to future indications for AT-007 in the Territory. In return, we have the right to receive certain near-term development milestone payments upon clinical trial completion and marketing authorization in Europe as well as commercial sales milestones, which in the aggregate are expected to amount to over €130 million. We also have the right to receive royalties on any future net sales of AT-007 in the Territory of 20%. The royalty rate will be payable on a country-by-country basis until the later of (i) the expiration of the licensed patents covering the composition of matter of AT-007, or (ii) 10 years after the European Medicines Agency's grant of marketing authorization for AT-007. The royalties are subject to certain deductions, including certain secondary finishing costs, certain step-in establishment costs and a portion of fees for any potential third-party patent licenses if applicable in the future. Following the initial term of the license, as described above, the royalty rate shall be reduced to 10% and shall continue in perpetuity unless the Advanz Agreement is terminated in various circumstances in accordance with its terms. We will continue to be responsible for the development, manufacturing and supply of AT-007, and Advanz will be responsible for packaging, distribution and commercialization in the Territory. The Advanz Agreement includes a sublicense under the 2016 Columbia Agreement and the 2020 Miami License Agreement.

Our partnership with Advanz is subject to various risks, including, but not limited to, the following:

- If Advanz breaches the contractual obligations owed to us pursuant to the Advanz Agreement or any related agreements, we could be exposed to commercial, regulatory or other liabilities.

- We may be subject to liabilities in connection with the development, manufacturing and supply of AT-007 under the Advanz Agreement, including with respect to the 2016 Columbia Agreement and the 2020 Miami License Agreement.
- We may not be able to adequately protect our intellectual property or may become involved in intellectual property enforcement actions, which may cause us to incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights, and such litigation may divert the attention of our management and scientific personnel and adversely affect our development and commercialization efforts.
- We may have limited control over the commercialization efforts of Advanz, and Advanz may fail to successfully sell and market AT-007.
- Our ability to receive certain economic benefits from the partnership, including the milestone payments and royalties, depends on certain contingencies beyond our control.
- In certain circumstances, Advanz may exercise certain step-in rights, including the ability for Advanz to perform its own supply arrangements, and in some cases, specified development rights in the Territory and assignment of certain contract rights. In all such circumstances, Advanz must continue to pay royalties and milestone payments, but may recoup certain of its manufacturing and development establishment costs, and deduct such costs from royalties owed.

Any of these factors could cause us to incur higher costs, disrupt the supply of our product candidates or approved products, delay or prevent the approval of our product candidates or prevent or disrupt the commercialization of our approved products. As a result, we may not achieve some or all economic benefits expected from the partnership.

The development of additional product candidates is risky and uncertain, and we can provide no assurances that we will be able to replicate our approach to drug development for other disease indications.

Efforts to identify, acquire or in-license, and then develop, product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our efforts may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development, approved products or commercial revenues for many reasons, including the following:

- the methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render any product candidates we develop obsolete;
- any product candidates we develop may be covered by third parties' patents or other exclusive rights;
- a product candidate may be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by physicians, patients, the medical community or third-party payors.

We have limited financial and management resources and, as a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater market potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in circumstances under which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. In addition, we may not be successful in replicating our approach to drug development for other disease indications. If we are unsuccessful in identifying and developing additional product candidates or are unable to do so, our business may be harmed.

Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials and we cannot assure you that any ongoing, planned or future clinical trials will lead to results sufficient for the necessary regulatory approvals.

Success in preclinical testing and earlier clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical studies and Phase 1 clinical trials are primarily designed and operate to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical studies and earlier clinical trials does not ensure that later efficacy trials will be successful, nor does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through earlier clinical trials.

In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. As an organization, we have limited experience designing clinical trials and may be unsuccessful in designing and executing a clinical trial to support regulatory approval 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 clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

Clinical drug development involves a lengthy and expensive process. We may incur additional costs and encounter substantial delays or difficulties in our clinical trials.

We may not commercialize, market, promote or sell any product candidate without obtaining marketing approval from the FDA or other comparable regulatory authority, and we may never receive such approvals, particularly following the recent Complete Response Letter received from the FDA for the NDA for govorestat for the treatment of Classic Galactosemia. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans and will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is uncertain as to outcome.

A failure of one or more clinical trials can occur at any stage of testing. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

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

- delays in reaching a consensus with regulatory authorities on the design or implementation of our clinical trials;
- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites;
- FDA requirements for the approval of govorestat for any indication;
- 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, participants may drop out of these clinical trials at a higher rate than we anticipate or fail to return for post-treatment follow-up or we may fail to recruit suitable patients to participate in a trial;
- clinical trials of our product candidates may produce negative or inconclusive results;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations, trial sites or manufacturing facilities;

- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- deviations from GCP or clinical trial protocols, data integrity issues and other issues that could affect the data or other results of a clinical trial, the safety or efficacy of a product candidate or a product candidate's review or approval by regulatory authorities;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols; or
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenue from future drug sales or other sources. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional testing to bridge our modified product candidate to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates, if approved, or allow our competitors to bring competing drugs to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

- receive a new warning letter from the FDA, which can damage our reputation and prevent the continuance of our clinical trials;
- be delayed in obtaining marketing approval, or not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including in the form of a risk evaluation and mitigation strategy, or REMS;
- be subject to additional post-marketing testing requirements;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a new or modified REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- be sued; or
- experience damage to our reputation.

Our product development costs will also increase if we experience delays in testing or obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, need to be restructured or be completed on schedule, if at all.

Further, we, the FDA or an IRB may suspend our clinical trials at any time if it appears that we or our collaborators are failing to conduct a trial in accordance with regulatory requirements, including the FDA's GCP regulations, that we are exposing participants to unacceptable health risks, or if the FDA finds deficiencies in our investigational new drug applications, or INDs, or the conduct of these trials. In November 2024, the FDA issued a Complete Response Letter for our NDA seeking approval of govorestat for the treatment of Classic Galactosemia citing deficiencies in the clinical application. We cannot predict with any certainty the schedule for commencement and completion of future clinical trials. If we experience delays in the commencement or completion of our clinical trials, or if we terminate a clinical trial prior to completion, the commercial prospects of our product candidates could be negatively impacted, and our ability to generate revenues from our product candidates may be delayed.

All of our current product candidates that have proceeded to clinical trials target inhibition of aldose reductase. There can be no assurance that aldose reductase inhibitors will ever receive regulatory approval.

All of our current product candidates that have proceeded to clinical trials target inhibition of the aldose reductase enzyme. The FDA may not agree with this proposed mechanism of action for the indications we are pursuing, which could impact the amount of evidence the FDA requires to support marketing approval. There are no currently approved aldose reductase inhibitors on the market outside of Japan, India, and China, and there can be no assurance that aldose reductase inhibitors will ever receive regulatory approval in other countries, including the United States. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. Our current product candidates may face similar or different challenges that prevent their successful commercialization.

We may not be able to obtain or maintain rare pediatric disease designation or exclusivity for our product candidates, which could limit the potential profitability of our product candidates.

We have obtained orphan drug designation and rare pediatric disease designation, from the FDA for AT-007 for the treatment of Galactosemia and PMM2-CDG. The FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is defined as a disease or condition that either affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

For the purposes of the rare pediatric disease program, a "rare pediatric disease" is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years or a rare disease or conditions within the meaning of the Orphan Drug Act. Under the FDA's rare pediatric disease priority review voucher, or RPD-PRV, program, upon the approval of an NDA for the treatment of a rare pediatric disease, the sponsor of such application may be eligible for an RPD-PRV that can be used to obtain priority review for a subsequent NDA or Biologics License Application (BLA). A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its application. If an RPD-PRV is received, it may be sold or transferred an unlimited number of times. However, the FDA's rare pediatric disease priority voucher program began to sunset on December 20, 2024, upon Congress' failure to pass a continuing resolution package that included its reauthorization. Under the amended statutory sunset provisions, after December 20, 2024, the FDA may award an RPD-PRV for an approved rare pediatric disease product application only if the sponsor has rare pediatric disease designation for the drug and if that designation was granted by December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease PRVs. Congress may vote to reauthorize this program, but its future remains unknown at this time.

A breakthrough therapy designation by the FDA for a product candidate may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.

We may seek a breakthrough therapy designation for one or more product candidates. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate 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. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the NDA.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe that 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 product candidates considered for approval under conventional FDA procedures and it would 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

the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened. We also are unable to predict the potential changes in regulatory interpretations or agency funding or staffing that may impact the FDA's use or implementation of the Breakthrough Therapy designation.

We have sought, and may in the future seek, fast track designation from the FDA for our product candidates. Even if granted, fast track designation may not actually lead to a faster development, regulatory review or approval process.

If a product candidate is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to address unmet needs for this condition, the sponsor may apply for FDA fast track designation. If fast track designation is obtained, the FDA may prioritize interactions with the sponsor concerning the designated development program and initiate review of sections of an NDA before the application is complete, known as "rolling review." Fast track designation would not ensure that we would experience a faster development, regulatory review or approval process compared to conventional FDA procedures or that we would ultimately obtain regulatory approval. Additionally, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. We also are unable to predict the potential changes in regulatory interpretations or agency funding or staffing that may impact the FDA's use or implementation of the fast track designation.

We may seek approval from the FDA under the accelerated approval pathway. If we are unable to obtain accelerated approval, we may be required to conduct additional preclinical studies or clinical trials, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approvals. Even if we receive accelerated approval from the FDA for a product candidate, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw accelerated approval.

We intend to seek efficient pathways to approval for our product candidates, which may include the accelerated approval pathway. Under the accelerated approval provisions of the Federal Food, Drug, and Cosmetic Act, or the FDCA, and the FDA's implementing regulations, the FDA may grant accelerated approval to a product designed to treat a serious or life-threatening condition that provides meaningful therapeutic advantage over available therapies and demonstrates an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval development pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. Products approved under the accelerated approval pathway are still required to meet the evidentiary standards for approval, including substantial evidence of effectiveness based on adequate and well-controlled studies.

If granted, accelerated approval is contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical profile or risks and benefits for accelerated approval. The FDA has indicated its general expectation that any such confirmatory studies be initiated or substantially underway prior to the submission of an application for accelerated approval, and issued guidance as to what constitutes such a study being "underway." If such post-approval studies fail to confirm the drug's clinical profile or risks and benefits, the FDA may withdraw its approval of the drug. The Food and Drug Omnibus Reform Act, or FDORA, which was signed into law on December 29, 2022, made amendments to the accelerated approval program, among them new requirements relating to post-approval studies and enhanced enforcement and withdrawal authorities for the FDA, including in the event that a sponsor fails to comply with applicable requirements under the program. We can provide no assurances that our biomarker-based approach will be successful in demonstrating a predictive benefit in relevant clinical outcomes we are evaluating. If our approach is not successful, we may be required to conduct longer, different, or additional clinical trials, which also may fail to confirm clinical benefit.

If we choose to pursue accelerated approval, we intend to seek feedback from the FDA or will otherwise evaluate our ability to seek and receive such accelerated approval. There can be no assurance that, after our evaluation of the feedback from the FDA or other factors, we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Submitting an application for accelerated approval, does not assure that the application will be accepted or that approval will be granted on a timely basis, or at all. The FDA also could require us to conduct further studies or trials prior to considering our application or granting approval of any type. We might not be able to fulfill the FDA's requirements in a timely manner, which would cause delays, or approval might not be granted because our submission is deemed incomplete by the FDA. A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate may result in a longer time period to commercialize such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we receive accelerated approval from the FDA, we will be subject to rigorous post-marketing requirements, including the completion of confirmatory post-market clinical trial(s) to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw accelerated approval for multiple reasons, including if we fail to conduct any required post-market study with due diligence, a post-market study does not confirm the predicted clinical benefit, other evidence shows that the product is not safe or effective under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false or misleading.

A failure to obtain accelerated approval or any other form of expedited development, review or approval for a product candidate that we may choose to develop would result in a longer time period prior to commercializing such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be delayed, made more difficult or rendered impossible by multiple factors outside our control.

Identifying and qualifying patients to participate in our clinical trials is critical to our success. We may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development and approval of our product candidates. Even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data, the number and nature of competing treatments and ongoing clinical trials of competing therapies for the same indication, the proximity of patients to clinical sites and the eligibility criteria for the trial. Because our focus includes rare disorders, there are limited patient pools from which to draw in order to complete our clinical trials in a timely and cost-effective manner. Accordingly, enrollment of our clinical trials could take significantly longer than projected, which would delay any potential approval of our product candidates. Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

Our efforts to build relationships with patient communities may not succeed, particularly following the Complete Response Letter for govorestat for Classic Galactosemia and Warning Letter relating to our AT-007-1002 study received from the FDA in November 2024, which could result in delays in patient enrollment in our clinical trials. Any negative results we may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in other clinical trials of that same product candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates or could render further development impossible. In addition, we may rely on CROs and clinical trial sites to ensure proper and timely conduct of our future clinical trials and, while we intend to enter into agreements governing their services, we will be limited in our ability to ensure their actual performance.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their doctor. Often, it is not possible to determine whether or not the product candidate being studied

caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm these determinations, if they occur.

In addition, 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 observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects or patients. Many times, side effects are only detectable after investigational drugs are tested in large-scale pivotal trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates have side effects or cause serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would harm our business, prospects, operating results and financial condition.

Interim, "top-line" and preliminary data from our clinical trials that we have announced or published, has changed and may continue to change as more patient data becomes available and are subject to audit and verification procedures that has resulted and could in the future result in material changes in the final data.

We have published interim, "top-line" or preliminary data from our clinical trials and may continue to do it from time to time. Interim data from clinical trials that we have completed and may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues, more patient data become available, and/or additional analyses are conducted, as has occurred in the past. Preliminary or "top-line" data remain subject to new or further audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data and results are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

For example, in February 2024, we announced results from a group-level, interim analysis of 12-month data in the Phase 2/3 INSPIRE trial studying AT-007 for SORD Deficiency. Our review and analyses of these data are ongoing.

The incidence and prevalence for target patient populations of our product candidates have not been established with precision. If the market opportunities for our product candidates are smaller than we believe they are or any approval we obtain is based on a narrower definition of the patient population, our business may suffer.

We currently focus our drug development on product candidates for the treatment of diseases with high unmet medical need. Our eligible patient population and pricing estimates may differ significantly from the actual market addressable by our product candidates. Our estimates of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and analyses. These estimates have been derived from a variety of sources, including the scientific literature, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of the diseases we are targeting. The number of patients may turn out to be lower than expected. Likewise, the potentially addressable patient population for each of our product candidates may be limited or may not be receptive to treatment with our product candidates, and new patients may become increasingly difficult to identify or access. If the market opportunities for our product candidates are smaller than we estimate, we may not be able to achieve our forecast revenue, which could hinder our business plan and adversely affect our business and results of operations.

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

The development and commercialization of new drugs is highly competitive. We face competition with respect to our current product candidates and may face competition with respect to any other product candidates that we may seek to develop or commercialize in the future from pharmaceutical and biotechnology companies, academic institutions, government agencies and other public and private research institutions.

Our competitors may have an advantage over us due to their greater size, resources and institutional experience. In particular, these companies have greater experience and expertise in securing reimbursement, government contracts

and relationships with key opinion leaders, conducting testing and clinical trials, obtaining and maintaining regulatory approvals and distribution relationships to market products and marketing approved drugs. These companies also have significantly greater research and marketing capabilities than we do. If we are not able to compete effectively against existing and potential competitors, our business and financial condition may be harmed.

As a result of these factors, our competitors may obtain regulatory approval of their drugs before we are able to, which may limit our ability to develop or commercialize our product candidates. Our competitors may also develop therapies that are safer, more effective, more widely accepted or less expensive than ours, and may also be more successful than we are in manufacturing and marketing their drugs. These advantages could render our product candidates obsolete or non-competitive before we can recover the costs of such product candidates' development and commercialization.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third-parties compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

We may explore strategic collaborations that may never materialize or we may be required to relinquish important rights to and control over the development and commercialization of our product candidates to any future collaborators.

Over time, our business strategy includes acquiring or in-licensing additional product candidates for treatments of diseases with high unmet medical need. As a result, we expect that we may periodically explore a variety of possible strategic collaborations in an effort to gain access to additional product candidates or resources. These strategic collaborations may include partnerships with large strategic partners, particularly for the development of DPN treatments using AT-001. At the current time however, we cannot predict what form such a strategic collaboration might take. We are likely to face significant competition in seeking appropriate strategic collaborators, and strategic collaborations can be complicated and time consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any strategic collaborations because of the numerous risks and uncertainties associated with establishing them.

Future collaborations could subject us to a number of risks, including:

- we may be required to undertake the expenditure of substantial operational, financial and management resources;
- we may be required to issue equity securities that would dilute our stockholders' percentage ownership of our company;
- we may be required to assume substantial actual or contingent liabilities;
- we may not be able to control the amount and timing of resources that our strategic collaborators devote to the development or commercialization of our product candidates;
- strategic collaborators may select indications or design clinical trials in a way that may be less successful than if we were doing so;
- strategic collaborators may delay clinical trials, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing;
- strategic collaborators may not pursue further development and commercialization of products resulting from the strategic collaboration arrangement or may elect to discontinue research and development programs;
- strategic collaborators may not commit adequate resources to the marketing and distribution of our product candidates, limiting our potential revenues from these products;

- disputes may arise between us and our strategic collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management's attention and consumes resources;
- strategic collaborators may experience financial difficulties;
- changes in the collaborator's strategic focus or available funding;
- strategic collaborators may not properly maintain, enforce or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- business combinations or significant changes in a strategic collaborator's business strategy may adversely affect a strategic collaborator's willingness or ability to complete its obligations under any arrangement;
- strategic collaborators could decide to move forward with a competing product candidate developed either independently or in collaboration with others, including our competitors;
- collaborators may not pursue development of our product candidates or may elect not to continue or renew development programs based on results of clinical trials or other studies;
- strategic collaborators could terminate the arrangement or allow it to expire, which would delay the development and may increase the cost of developing our product candidates;
- collaborators may not perform their obligations as expected; and
- other factors, such as an acquisition or business combination, that divert resources or create competing priorities.

Even if any product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, third-party payors or others in the medical community necessary for commercial success.

Even if any product candidates receive marketing approval, they may fail to gain market acceptance by physicians, patients, third-party payors and others in the medical community. If such product candidates do not achieve an adequate level of acceptance, we may not generate significant drug revenue and may not become profitable. The degree of market acceptance of any product candidate, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the convenience and ease of administration compared to alternative treatments and therapies;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the efficacy and potential advantages compared to alternative treatments and therapies;
- the effectiveness of sales and marketing efforts;
- the strength of our relationships with patient communities;
- the cost of treatment in relation to alternative treatments and therapies, including any similar generic treatments;
- our ability to offer such drug for sale at competitive prices;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of the drug together with other medications.

Our efforts to educate physicians, patients, third-party payors and others in the medical community on the benefits of our product candidates may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our product candidates.

Because we expect sales of our product candidates, if approved, to generate substantially all of our revenues for the foreseeable future, the failure of our product candidates to find market acceptance would harm our business.

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

Even if we obtain regulatory approvals for our product candidates, such approvals will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates may also be subject to a risk evaluation and mitigation strategy (REMS), limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 trials, and surveillance to monitor the quality, safety and efficacy of the drug. Such regulatory requirements may differ from country to country depending on where we have received regulatory approval.

In addition, drug manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

If we or our contract manufacturers or partners fail to comply with applicable regulatory requirements following approval of our product candidates, a regulatory authority may, among other actions:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or comparable foreign marketing application or any supplements thereto submitted by us or our partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant civil, criminal and administrative penalties.

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

Further, if we are not able to maintain regulatory compliance with the FDCA, Cures Act, or other applicable requirements, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

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. For example, on June 28, 2024, the U.S. Supreme Court, in *Loper Bright Enterprises v. Raimondo,* overturned long-standing precedent regarding the deference courts owe to agencies' interpretation of ambiguous statutes in their rulemaking. While the impact of the *Loper Bright* decision on our business and regulatory strategy is unknown, the decision generally may, among other things, increase the frequency of challenges to decisions and rulemaking of health regulators, including FDA determinations of drug approval and market exclusivity and the Centers for Medicare & Medicaid Services' rules regarding reimbursement, and also impact the speed at which such health regulators make decisions and issue regulations. Furthermore, beginning in February 2025, the Trump administration has downsized and terminated significant numbers of employees at the FDA and the NIH, along with other federal agencies. We cannot predict the effect that any such restructuring may have on our business.

In addition, we cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the U.S. administration may impact our business and industry. It is difficult to predict how executive actions, including executive orders, may be implemented and the extent to which they will affect the FDA's ability to exercise its regulatory authority. If legislative, administrative or executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be successful in commercializing them, if and when they are approved.

To successfully commercialize any product candidate that may result from our development programs, we will need to build out our sales and marketing capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract sales force to market any product candidate we may develop will be expensive and time-consuming and could delay any drug launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may seek to enter into collaborations with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any current or future collaborators do not commit sufficient resources to commercialize our product candidates, or we are unable to develop the necessary capabilities on our own, we may be unable to generate sufficient revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded marketing and sales operations to recruit, hire, train and retain marketing and sales personnel. We will likely also face competition if we seek third parties to assist us with the sales and marketing efforts of our product candidates. Without an internal team or the support of a third-party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Even if we obtain and maintain approval for our product candidates from the FDA, we may never obtain approval outside the United States, which would limit our market opportunities.

Approval of a product candidate in the United States by the FDA does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable foreign regulatory authorities also must approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for any product candidates, if approved, is also subject to approval. Obtaining approval for our product candidates in the European Union from the European Commission following the opinion of the European Medicines Agency, or the EMA, is a lengthy and expensive process. Even if a product candidate is approved, the EMA may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time-consuming additional clinical trials or reporting as conditions of approval. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. Following receipt of the Complete Response Letter for govorestat for the treatment of

Classic Galactosemia, we also withdrew the MAA to the EMA for govorestat for the treatment of Classic Galactosemia, which may result in further delays, difficulties and costs to support a European MAA for govorestat.

Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Also, regulatory approval for our product candidates may be withdrawn. If we fail to comply with the applicable regulatory requirements, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects could be harmed.

If we commercialize our product candidates outside the United States, a variety of risks associated with international operations could harm our business.

If we obtain regulatory and marketing approval in the United States for any product candidate, we intend to seek approval to market our product candidates outside the United States. If we market approved products outside the United States, we expect that we will be subject to additional risks in commercialization, including:

- different regulatory requirements for approval of therapies in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, international hostilities, or natural disasters including earthquakes, typhoons, floods and fires.

We have no prior experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by many of the individual countries in which we may operate, with which we will need to comply. Many biopharmaceutical companies have found the process of marketing their products in foreign countries to be challenging.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and may face an even greater risk if we commercialize any product candidate that we may develop. If we cannot successfully defend ourselves against claims that any such product candidates caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidate that we may develop;
- loss of revenue;
- substantial monetary awards to trial participants or patients;
- significant time and costs to defend the related litigation;
- withdrawal of clinical trial participants;
- increased insurance costs;

- the inability to commercialize any product candidate that we may develop; and
- injury to our reputation and significant negative media attention.

Any such outcomes could negatively impact our business, financial condition, results of operations and prospects.

Our insurance policies may be inadequate and potentially expose us to unrecoverable risks.

Although we maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. Insurance availability, coverage terms and pricing continue to vary with market conditions. We endeavor to obtain appropriate insurance coverage for insurable risks that we identify; however, we may fail to correctly anticipate or quantify insurable risks, we may not be able to obtain appropriate insurance coverage and insurers may not respond as we intend to cover insurable events that may occur. We have observed rapidly changing conditions in the insurance markets relating to nearly all areas of traditional corporate insurance. Such conditions have resulted in higher premium costs, higher policy deductibles, and lower coverage limits. For some risks, we may not have or maintain insurance coverage because of cost or availability.

Risks Related to Regulatory Compliance

Our relationships with customers, physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations.

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

If the physicians or other providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs. Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have an adverse effect on our ability to compete in the marketplace.

We may obtain health information from third parties, including research institutions from which we obtain clinical trial data, that are subject to privacy and security requirements under HIPAA, and depending on the facts and

circumstances, we could be subject to significant penalties if we obtain, use or disclose individually identifiable health information in a manner that is not authorized or permitted by HIPAA.

Coverage and adequate reimbursement may not be available for our product candidates, which could make it difficult for us to sell profitably, if approved.

Market acceptance and sales of any product candidates that we commercialize, if approved, will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from third-party payors, including government health administration authorities, managed care organizations and other private health insurers. Third-party payors decide which therapies they will pay for and establish reimbursement levels. While no uniform policy for coverage and reimbursement exists in the United States, third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor-by-payor basis. Therefore, one payor's determination to provide coverage for a drug does not assure that other payors will also provide coverage, and adequate reimbursement, for the drug. Additionally, a third-party payor's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each payor determines whether or not it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its formulary it will be placed. The position on a payor's list of covered drugs, or formulary, generally determines the co-payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our product candidates, if approved, unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products.

Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand for, or the price of, any drug for which we obtain marketing approval. If coverage and adequate reimbursement are not available, or are available only at limited levels, we may not be able to successfully commercialize any product candidates that we develop.

Due to general uncertainty with respect to the current legal, regulatory and policy environment, we are unable to predict the impact of any future legislative, regulatory, third-party payor or policy actions. If enacted, we and any third parties we might engage may be unable to adapt to any changes implemented as a result of such measures, and we could face difficulties in maintaining or increasing profitability or otherwise experience a material adverse impact on our business, financial condition and results of operations.

Healthcare reform measures may have a negative impact on our business and results of operations.

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes, as well as judicial challenges, regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval. The increased emphasis on managed healthcare in the U.S. and on country-specific and national pricing and reimbursement controls in the EU will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing coverage and/or reimbursement controls and measures, could have a material adverse impact on our net product revenues and results of operations.

In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, since 2003, Medicare coverage for drug purchases by the elderly have been subject to a reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Managed Medical Assistant (MMA) program

applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

Further, in March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or, collectively, the PPACA, was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the United States. Some of the provisions of the PPACA have yet to be fully implemented, while certain provisions have been subject to executive, judicial and Congressional challenges. For example, a case challenging the PPACA's requirement that insurers cover certain preventative services is currently pending before the U.S. District Court for the Northern District of Texas. In March 2023, the judge struck down the requirement, and, on appeal, in June 2024 the U.S. Court of Appeals for the Fifth Circuit held, among other things, that the PPACA's requirement that group health plans and health insurance issuers cover certain preventative services without cost-sharing is unconstitutional. The parties have petitioned to appeal the case to the U.S. Supreme Court, which granted certiorari in January 2025. It is unclear how this decision, subsequent decisions and appeals, or any potential future litigation, executive orders or other actions by the current administration, and other efforts to repeal and replace the PPACA will impact the PPACA. Congress may consider additional legislation to repeal or repeal and replace other elements of the PPACA. We continue to evaluate the effect that the PPACA and its possible repeal and replacement may have on our business and the potential profitability of our product candidates.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the Bipartisan Budget Act (BBA), which will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

The current Trump administration has taken additional action to limit or change healthcare policies pursued by the prior Biden Administration. For example, President Trump rescinded an executive order issued by former President Biden, pursuant to which the Center for Medicare and Medicaid Innovation (CMMI) created three drug pricing experiments, and it is unclear whether CMMI will continue to pursue some or any of these models or that other changes may occur under the current administration. Beginning in February 2025, the Trump administration has downsized and terminated significant numbers of employees at the FDA and the NIH, along with other federal agencies. We cannot predict the impact that any such restructuring may have on our business.

Additional changes that may affect our business include the expansion of programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015. At this time, the full impact of the introduction of the Medicare quality payment program on overall physician reimbursement is unclear.

Further, in the United States there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. While some of the proposed measures will require authorization through additional legislation to become effective, the U.S. Congress have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. For example, the Inflation Reduction Act of 2022 also seeks to reduce prescription drug costs by, among other provisions, allowing Medicare to negotiate prices for certain high-cost prescription drugs in Medicare Parts B and D, imposing an excise tax on pharmaceutical manufacturers that refuse to negotiate pricing with Medicare, requiring inflation rebates to limit annual drug price increases in Medicare, redesigning the Medicare Part D formula, and limiting cost-sharing for insulin products. It is unclear how the IRA will be effectuated or changed under the new Trump Administration or the degree of impact that the IRA may ultimately have upon our business, or whether additional drug pricing and other healthcare reform measures will be enacted, and if enacted, what effect they would have on our business. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our current or any future product candidates or additional pricing pressures. We cannot predict the likelihood, nature or extent of government regulation that may arise

from future legislation or administrative action in the United States or any other jurisdiction. If we or any third parties we may engage are slow or unable to adapt to changes in existing or new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our current or any future product candidates we may develop may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

At the state level, legislatures and regulatory agencies have increasingly passed legislation and implemented regulations designed to control drug pricing, including restrictions on pricing or reimbursement at the state government level, limitations on discounts to patients, advance notices of price increases, marketing cost disclosure and transparency measures, and, in some cases, policies to encourage importation from other countries (subject to federal approval) and bulk purchasing.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug, which could have an adverse effect on demand for our product candidates if they are approved. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates.

Risks Related to Our Dependence on Third Parties

One of our clinical investigators received a warning letter from the FDA following a site inspection. Failure to resolve the matters addressed in the warning letter and any similar issues at other clinical trial sites could negatively impact the continuance of our govorestat clinical program, our ability to rely on the data collected in our clinical trials for regulatory submissions and approval, and our ability to undertake clinical trials in the future or timely complete future NDA submissions.

In November 2024, one of our clinical investigators received a warning letter (Clinical Investigator Warning Letter) from the FDA relating to our AT-007-1002 study, following a site inspection in April 2024. The inspection was conducted as a part of the FDA's Bioresearch Monitoring Program. The Clinical Investigator Warning Letter identified issues with the clinical investigator's compliance with the FDA requirements and regulations governing clinical investigations. Specifically, the Clinical Investigator Warning Letter cited deviations from the investigational plan. If we are unable to sufficiently establish to the FDA that our current or future clinical trials are and will be conducted in accordance with FDA requirements, Applied (and our clinical investigators) may be subject to additional FDA enforcement action including being subject to the FDA's Application Integrity Policy. For more information on the Warning Letter we received from the FDA and the implications of being subject to the FDA's Application Integrity Policy, please see "Risks Related to Our Operations, Employee Matters and Managing Growth – We received a Warning Letter from the FDA for our NDA filed in December 2023 for our AT-007-1002 study. Failure to resolve the matters addressed in the Warning Letter could negatively impact our company's ability to undertake clinical trials in the future or timely complete future NDA submissions."

We rely on third parties to produce clinical and commercial supplies of our product candidates.

We do not own or operate facilities for drug manufacturing, storage and distribution, or testing. We are dependent on third parties to manufacture the clinical supplies of our current and any future product candidates. The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMP requirements, for manufacture of both active drug substance and finished drug product. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure and/or maintain regulatory approval for our product candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a third-party

manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates.

We also intend to rely on third-party manufacturers to supply us with sufficient quantities of our product candidates to be used, if approved, for commercialization. We do not yet have a commercial supply agreement for commercial quantities of drug substance or drug product. If we are not able to meet market demand for any approved product, it would negatively impact our ability to generate revenue, harm our reputation, and could have an adverse effect on our business and financial condition.

Further, our reliance on third-party manufacturers entails risks to which we may not be subject if we manufactured product candidates ourselves, including:

- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- our third-party manufacturers may not be able to execute our manufacturing procedures and other logistical support requirements appropriately;
- our third-party manufacturers may fail to comply with cGMP requirements and other inspections by the FDA or other comparable regulatory authorities;
- our inability to negotiate manufacturing agreements with third parties under commercially reasonable terms, if at all;
- breach, termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- reliance on single sources for drug components;
- lack of qualified backup suppliers for those components that are currently purchased from a sole or single-source supplier;
- diminished numbers of FDA inspectors available to conduct pre-approval inspections may slow the pre-approval inspection process and delay review and/or approval of our applications;
- our third-party manufacturers may not devote sufficient resources to our product candidates;
- we may not own, or may have to share, the intellectual property rights to any improvements made by our third-party manufacturers in the manufacturing process for our product candidates;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier; and
- carrier disruptions or increased costs that are beyond our control.

In addition, if we enter into a strategic collaboration with a third-party for the commercialization of our current or any future product candidates, we will not be able to control the amount of time or resources that they devote to such efforts. If any strategic collaborator does not commit adequate resources to the marketing and distribution of our product candidates, it could limit our potential revenues.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize our current or any future product candidates once approved. Some of these events could be the basis for FDA action, including injunction, request for recall, seizure, or total or partial suspension of production.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental, health and safety laws and regulations, which can be expensive and restrict how we do, or interrupt our, business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the generation, storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds and wastes. We and our manufacturers and suppliers are subject to environmental, health and safety laws and regulations governing, among other matters, the use, manufacture, generation, storage, handling, transportation, discharge and disposal of these hazardous materials and wastes and worker health and safety. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination or injury, which could result in an interruption of our commercialization efforts, research and development efforts and business operations, damages and significant cleanup costs and liabilities under applicable environmental, health and safety laws and regulations. We also cannot guarantee that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials and wastes generally comply with the standards prescribed by these laws and regulations. We may be held liable for any resulting damages, costs or liabilities, which could exceed our resources, and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental, health and safety laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. Failure to comply with these environmental, health and safety laws and regulations may result in substantial fines, penalties or other sanctions. We do not currently carry environmental insurance coverage.

We rely on third-parties to conduct, supervise and monitor our preclinical studies and clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We do not currently have the ability to independently conduct any clinical trials. We have relied and intend to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our preclinical studies and clinical trials, and we expect to have limited influence over their actual performance. We rely upon CROs to monitor and manage data for our clinical programs, as well as the execution of future preclinical studies. We expect to control only certain aspects of our CROs' activities. Nevertheless, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the good laboratory practices, or GLPs, and GCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities in the form of International Conference on Harmonization guidelines for any of our product candidates that are in preclinical and clinical development. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. Although we rely on CROs to conduct GCP-compliant clinical trials, we remain responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with its investigational plan and protocol and applicable laws and regulations. If we or our CROs fail to comply with GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat clinical trials, which would delay the regulatory approval process.

In particular, one of our clinical investigators for the ACTION-Galactosemia Kids (AT-007-1002) received the Clinical Investigator Warning Letter following an inspection conducted by the FDA at her clinical site in April 2024. The Clinical Investigator Warning Letter identified issues with the clinical investigator's compliance with the FDA requirements and regulations governing clinical investigations. Specifically, the Clinical Investigator Warning Letter cited deviations from the investigational plan. For more information, please see "Risks Related to Our Dependence on Third Parties". Failure to resolve the matters addressed in the warning letter and any similar issues at other clinical trial sites could negatively impact the continuance of our govorestat clinical program, our ability to rely on the data collected in our clinical trials for regulatory submissions and approval, and our ability to undertake clinical trials in the future or timely complete future NDA submissions."

Further, we experienced issues related to data collection, management, and retention with one of our vendors for AT-007-1002 that were raised in the Warning Letter to Applied. This vendor had a role in the Phase 2/3 INSPIRE trial (AT-007-1005) for SORD Deficiency; we are still investigating whether any issues with this vendor have impacted the INSPIRE trial.

In addition, a clinical trial site for the SORD Deficiency trial outside of the United States is in the process of responding to an inspection by local authorities, and we are evaluating the potential impact of such inspection on the data.

Our reliance on third parties to conduct clinical trials results in less direct control over the management of data developed through clinical trials than would be the case if we were relying entirely upon our own staff. Communicating with CROs and other third parties can be challenging, potentially leading to mistakes as well as difficulties in coordinating activities. Such parties may:

- have staffing difficulties;
- fail to comply with contractual obligations;
- experience legal or regulatory compliance issues; or
- undergo changes in priorities or become financially distressed.

These factors may adversely affect the willingness or ability of third parties to conduct our clinical trials and may subject us to unexpected cost increases that are beyond our control. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or fail to comply with regulatory requirements, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, any product candidate that we develop. As a result, our financial results and the commercial prospects for any product candidate that we develop would be harmed, our costs could increase, and our ability to generate revenue could be delayed. While we have and will have agreements governing their activities, our CROs will not be our employees, and we will not control whether or not they devote sufficient time and resources to our future clinical and preclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our business. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology.

If our relationship with any of these CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. Switching or adding additional CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can negatively impact our ability to meet our desired clinical development timelines. While we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a negative impact on our business, financial condition and prospects.

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

Risks Related to Our Intellectual Property

Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues. If we breach our license agreements with Columbia University or any of the other agreements under which we acquired, or will acquire, the intellectual property rights to our product candidates, we could lose the ability to continue the development and commercialization of the related product.

The licensing of intellectual property is of critical importance to our business and to our current and future product candidates, and we expect to enter into additional such agreements in the future. In particular, our current product candidates AT-007, AT-001 and AT-003 are dependent on our license agreement with The Trustees of

Columbia University in the City of New York, or Columbia University. Pursuant to that license agreement with Columbia University, or the 2016 Columbia Agreement, Columbia University granted us an exclusive license under two important patent families, and a nonexclusive license to certain know-how, owned by Columbia University to develop, manufacture or commercialize certain compounds, including AT-001, AT-003 and AT-007, for the diagnosis and treatment of human and animal diseases and conditions. The license grant is worldwide, with the exception of the patent family that covers AT-001 and AT-003. The license grant for the patent family that covers AT-001 and AT-003 excludes patent rights in China, Taiwan, Hong Kong and Macao, which Columbia University has exclusively licensed to a third-party. We cannot prevent Columbia University's third-party licensee from developing, manufacturing or commercializing certain compounds, including AT-001 and AT-003, but not including AT-007, in China, Taiwan, Hong Kong and Macao, and we cannot develop, manufacture or commercialize AT-001 or AT-003 in these territories, which could have a negative effect on our business.

We do not have the right to control the preparation, filing, prosecution and maintenance of patents and patent applications covering the technology that we license under either of the Columbia Agreements. Therefore, we cannot always be certain that these patents and patent applications will be prepared, filed, prosecuted and maintained in a manner consistent with the best interests of our business. Although we have a right to have our comments considered in connection with the prosecution process, if Columbia University fails to prosecute and maintain such patents, or loses rights to those patents or patent applications as a result of its control of the prosecution activities, the rights we have licensed may be reduced or eliminated, and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected.

If we fail to meet our obligations under the Columbia Agreement in any material respect and fail to cure such breach in a timely fashion, then Columbia University may terminate the Columbia Agreement. If the Columbia Agreement is terminated, and we lose our intellectual property rights under the Columbia Agreement, this may result in complete termination of our product development and any commercialization efforts for the product candidates that are subject to the agreement, including AT-007, AT-001, and AT-003. While we would expect to exercise all rights and remedies available to us, including seeking to cure any breach by us, and otherwise seek to preserve our rights under the Columbia Agreement, we may not be able to do so in a timely manner, at an acceptable cost or at all. Furthermore, license agreements we enter into in the future may not provide exclusive rights to use intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories included in all of our licenses.

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

Our success depends, in large part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates and our technology. We and our licensors have sought, and intend to seek, to protect our proprietary position by filing patent applications in the United States and abroad related to our product candidates and our technology that are important to our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has, in recent years, been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or product candidates or which effectively prevent others from commercializing competitive technologies and product candidates. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file a patent application relating to any particular aspect of a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by such third-party, or by the U.S. Patent and Trademark Office, or USPTO, itself, to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, enforce or license all necessary or desirable patent applications at a reasonable cost or in a timely

manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

We or our licensors have not pursued or maintained, and may not pursue or maintain in the future, patent protection for our product candidates in every country or territory in which we may sell our products, if approved. 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 infringing our patents in all countries outside the United States, or from selling or importing products that infringe our patents in and into the United States or other jurisdictions.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if the patent applications we license or own do issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our 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 in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

Furthermore, our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our owned and in-licensed patent rights and technology was funded in part by the U.S. government. As a result, the government may have certain rights, or march-in rights, to such patent rights and technology. When new technologies are developed with government funding, the government generally obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for noncommercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of such rights could harm our competitive position, business, financial condition, results of operations and prospects.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In addition, periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or patent applications will have to be paid to the USPTO and various government patent agencies outside the United States over the lifetime of our owned and licensed patents and/or applications and any patent rights we may own or license in the future. We rely on our service providers or our licensors to pay these fees. The USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, nonpayment of fees and failure to properly legalize and submit formal documents. If we or our licensors fail to maintain the patents and patent applications covering our products or technologies, we may not be able to stop a competitor from marketing products that are the same as or similar to our product candidates, which would have an adverse effect on our

business. 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 noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market and this circumstance could harm our business.

In addition, if we fail to apply for applicable patent term extensions or adjustments, we will have a more limited time during which we can enforce our granted patent rights. In addition, if we are responsible for patent prosecution and maintenance of patent rights in-licensed to us, any of the foregoing could expose us to liability to the applicable patent owner.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of product candidates such as AT-007, AT-001, and AT-003, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we have or will obtain patent rights. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent; provided that the patent is not enforceable for more than 14 years from the date of drug approval, which is limited to the approved indication (or any additional indications approved during the period of extension). Furthermore, only one patent per approved product can be extended and only those claims covering the approved product, a method for using it or a method for manufacturing it may be extended. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their drug earlier than might otherwise be the case.

Third-parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a negative impact on the success of our business.

Our commercial success depends, in part, upon our ability and the ability of others with whom we may collaborate to develop, manufacture, market and sell our current and any future product candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and complex litigation regarding patents and other intellectual property rights. We may in the future become party to, or be threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and any future product candidates and technology, including interference proceedings, post grant review and inter partes review before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of their merit. There is a risk that third parties may choose to engage in litigation with us to enforce or to otherwise assert their patent rights against us. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize our current and any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this is a high burden and requires us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future. Other companies and research institutions have filed, and may file in the future, patent applications related to AR inhibitors and their therapeutic use. Some of these patent applications have already been allowed or issued, and others may issue in the future. While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the United States and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third-party patents or patent applications,

or we may incorrectly conclude that a third-party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes that our product candidate infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from nonpracticing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit.

If we are found to infringe a third-party's valid and enforceable intellectual property rights, we could be required to obtain a license from such third-party to continue developing, manufacturing and marketing our product candidate(s) and technology. Under any such license, we would most likely be required to pay various types of fees, milestones, royalties or other amounts. Moreover, we may not be able to obtain any required license on commercially reasonable terms or at all.

The licensing or acquisition of third-party intellectual property rights is a competitive area, and more established companies may also pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have an adverse effect on our business, financial condition, results of operations and prospects. Furthermore, even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors and other third-parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product candidate. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent or other intellectual property right. We may be required to indemnify collaborators or contractors against such claims. A finding of infringement could prevent us from manufacturing and commercializing our current or any future product candidates or force us to cease some or all of our business operations, which could harm our business. Even if we are successful in defending against such claims, litigation can be expensive and time-consuming and would divert management's attention from our core business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have an adverse effect on the price of our common stock.

Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business, financial condition, results of operations and prospects.

We may be subject to claims asserting that our employees, consultants or advisors have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting ownership of what we regard as our own intellectual property.

Certain of our employees, consultants or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although it is our policy to require our employees and contractors who may be involved in the conception or development of

intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own, and we cannot be certain that our agreements with such parties will be upheld in the face of a potential challenge or that they will not be breached, for which we may not have an adequate remedy. The assignment of intellectual property rights may not be self-executing or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property.

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

Competitors may infringe, misappropriate or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming and are likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our owned or licensed patents at risk of being invalidated or interpreted narrowly and could put our owned or licensed patent applications at risk of not issuing. The initiation of a claim against a third-party might also cause the third-party to bring counterclaims against us, such as claims asserting that our patent rights are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or lack of statutory subject matter. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the USPTO, or made a materially misleading statement, during prosecution. Third parties may also raise similar validity claims before the USPTO in post-grant proceedings such as ex parte reexaminations, inter partes review, post-grant review, or oppositions or similar proceedings outside the United States, in parallel with litigation or even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. We cannot be certain that there is or will be no invalidating prior art, of which we and the patent examiner were unaware during prosecution. For the patents and patent applications that we have licensed, we may have limited or no right to participate in the defense of any licensed patents against challenge by a third-party. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of any future patent protection on our current or future product candidates. Such a loss of patent protection could harm our business.

We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. Our business could be harmed if in litigation the prevailing party does not offer us a license, or if the license offered as a result is not on commercially reasonable terms. Any litigation or other proceedings to enforce our intellectual property rights may fail, and even if successful, may result in substantial costs and distract our management and other employees.

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

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have an adverse effect on our ability to compete in the marketplace.

Changes in U.S. patent law or the patent law of other countries or jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our current and any future product candidates.

Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith America Invents Act, or the America Invents Act, the United States transitioned to a first inventor to file system in which, assuming that other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third-party was the first to invent the claimed invention. The America Invents Act also includes a number of significant changes that affect the way patent applications are prosecuted and also may affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business, financial condition, results of operations, and prospects.

In addition, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could weaken our ability to obtain new patents or to enforce patents that we own, have licensed or might obtain in the future. Similarly, changes in patent law and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we own or have licensed or that we may obtain in the future.

We may not be able to protect our intellectual property rights throughout the world, which could negatively impact our business.

Filing, prosecuting and defending patents covering our current and any future product candidates in all countries throughout the world would be prohibitively expensive. Competitors may use our technologies in jurisdictions where we or our licensors have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents, and any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Since we rely on third parties to help us discover, develop and manufacture our current and any future product candidates, or if we collaborate with third parties for the development, manufacturing or commercialization of our current or any future product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third-party illegally or unlawfully obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for our product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into nondisclosure 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, advisors and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets. 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 a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. 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 trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We also seek to preserve the integrity and confidentiality of our 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.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. We have selected trademarks for some of our later stage product candidates and filed applications to register those trademarks for our current or any future product candidates. For other earlier stage product candidates, we have not yet selected trademarks or begun the process of applying to register trademarks. Our pending trademark applications, and any future trademark applications may not be approved. Third parties may oppose our trademark applications or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe our trademarks, and we may not have adequate resources to enforce our trademarks.

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

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

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

- others may be able to make compounds or formulations that are similar to our product candidates but that are not covered by the claims of any patents, should they issue, that we own or license;
- we or our licensors might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or license;
- we or our licensors might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or license may not provide us with any competitive advantages, or may be held invalid or unenforceable as a result of legal challenges;
- our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as in countries where we do not have patent rights, and then use the information learned from such activities to develop competitive drugs for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

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

We are involved in a securities-related class action and derivative litigation and defending against these claims could result in substantial costs and divert management time and resources, damages and have a material adverse effect on our results of operations. These lawsuits, and any other lawsuits to which we are subject, will be costly to defend or pursue and are uncertain in their outcome.

The stock markets have from time-to-time experienced significant price and volume fluctuations that have affected the market prices for the common stock of pharmaceutical companies. These broad market fluctuations may cause the market price of our common stock to decline. In addition, the market price of our common stock may vary significantly based on specific events, such as receipt of complete response letters, warnings letters, such as the Complete Response Letter and Warning Letter we received from the FDA in November 2024, negative clinical results, a negative vote or decision by an FDA advisory committee, or other negative feedback from the FDA, EMA, or other regulatory agencies. This risk is especially relevant for us because biotechnology and biopharmaceutical companies often experience significant stock price volatility in connection with their investigational drug or medical device product candidate development programs and the regulatory review of their marketing applications. For example, in November 2024, we experienced a significant decline in our stock price based, in large part, on the Complete Response Letter and Warning Letter we received from the FDA.

Following receipt of the Complete Response Letter and Warning Letter, a putative class action lawsuit was filed against us and certain of our current and former officers and directors on December 17, 2024, in the United States District Court for the Southern District of New York and is captioned *Alexandru v. Applied Therapeutics, Inc.*, *et al.*, No. 24-cv-09715. On December 27, 2024, another purported stockholder filed a putative class action lawsuit against us and a former officer and director in the United States District Court for the Southern District of New York (*Ikram v. Applied Therapeutics, Inc., et al.,* No. 1:24-cv-09973). On March 11, 2025 the court consolidated the actions (*In re Applied Therapeutics Securities Litigation,* No. 1:24-cv-9715). In addition, on January 31, 2025, certain of our current and former officers and directors were named as defendants in a shareholder derivative action filed in the United States District Court for the Southern District of New York (*Hassine v. Shendelman, et al.,* No. 1:25-cv-00935). The complaint seeks to implement reforms to the Company's corporate governance and internal procedures and to recover on behalf of the Company for any liability the Company might incur as a result of the individual defendants' alleged misconduct, as well as declaratory, equitable, and monetary relief, including attorneys' fees and other costs. The derivative action is based substantially on the same facts alleged in the consolidated action described above. Please refer to "*Legal Proceedings*" in this Annual Report on Form 10-K for additional information about these pending legal proceedings.

The outcome of litigation is necessarily uncertain, and we cannot predict the outcome of these pending legal proceedings. An unfavorable outcome in any such proceeding could have an adverse impact on our business, financial condition, results of operations and cash resources. In addition, we may be exposed to additional litigation or government investigation even if no wrongdoing occurred and we ultimately prevail. Continuing or additional litigation, or responding to any related investigation or enforcement action, as well as a material final judgment or decree against us, would be expensive, divert management's attention and resources, and could adversely affect our business, financial condition, results of operations and cash resources. Moreover, if our stock price is volatile, we could face additional securities class action lawsuits in the future.

We recently experienced the departure of our founder and CEO and changes to our board and our executive management. These changes may create uncertainty and, more generally, if we are unable to attract and retain qualified management, clinical and scientific personnel, our business will be harmed.

We have experienced recent changes to our senior management team and board, including the departures of our founder, President, Chief Executive Officer, Secretary and member of the board, Dr. Shoshana Shendelman, on December 19, 2024, and member of the board, Joel Marcus, on December 6, 2024. Les Funtleyder, our Chief Financial Officer, is serving as Interim Chief Executive Officer while our board conducts a search for a permanent Chief Executive Officer. On December 19, 2024, our board also appointed John H. Johnson as Executive Chairman and as Chairman of the Board. Changes in our board and senior management and uncertainty regarding pending changes may disrupt our business and investor relationships, and impair our ability to recruit and retain other needed personnel. Any such disruption or impairment could have an adverse effect on our business.

Recruiting and retaining other senior executives, qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize our product candidates. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors 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.

Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team, including Mr. Johnson, and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations. Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees.

If we determine to bring in-house some functions that we are currently outsourcing and if we commercialize any of our product candidates we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2024, we had 35 full-time employees. As the clinical development of our product candidates progresses, we also expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of research, drug development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a significant disruption of our product development programs and our ability to operate our business effectively, and adversely affect our business and operating results.

Our internal computer systems, cloud-based computing services and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage or interruption from computer viruses, data corruption, cyber-based attacks (including phishing attempts, denial of service attacks, and malware or ransomware incidents, attacks enhanced or facilitated by artificial intelligence), unauthorized access, natural disasters, terrorism, war, international hostilities and telecommunication and electrical failures. While we have not experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, federal, state and international laws and regulations, such as the European Union's General Data Protection Regulation, which took effect in May 2018, can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties and significant legal liability, if our information technology security efforts fail. In addition, our software systems include cloud-based applications that are hosted by third-party service providers with security and information

technology systems subject to similar risks. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

Risks of unauthorized access and cyber-attacks have increased as most of our personnel, and the personnel of many third-parties with which we do business, have adopted remote working arrangements as a result of the COVID-19 pandemic, and may increase as a result of recent hostilities between Russia and Ukraine. Improper or inadvertent employee behavior, including data privacy breaches by employees, contractors and others with permitted access to our systems, may also pose a risk that sensitive data may be exposed to unauthorized persons or to the public. If a system failure or security breach occurs and interrupts our operations or the operations at one of our third-party vendors, it could result in intellectual property and other proprietary or confidential information being lost or stolen or a material disruption of our drug development programs. For example, the loss of clinical trial data from 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. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, loss of trade secrets or inappropriate disclosure of confidential or proprietary information, including protected health information or personal data of employees or former employees, access to our clinical data, or disruption of the manufacturing process, we could incur liability and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber-attacks by hackers or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or reputation or result in legal or regulatory proceedings. In addition, if a ransomware attack or other cyber-attack occurs, either internally or at our third-party vendors, we could be prevented from accessing our systems or data, which may cause interruptions or delays in our business, cause us to incur remediation costs or subject us to demands to pay ransom, or adversely affect our business reputation.

Additionally, the increased prevalence and use of artificial intelligence may heighten the risk that we may be subject to cybersecurity incidents in the future. Although we don't currently rely on or use artificial intelligence in our operations, if any of our third-party vendors who use artificial intelligence are compromised, it could have a negative impact to our business through leaks of our confidential information and/or our financial information and adversely affect our business or reputation or result in legal or regulatory proceedings.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in other jurisdictions, provide accurate information to the FDA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could result in significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government-funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, contractual damages, reputational harm and the curtailment or restructuring of our operations, any of which could have a negative impact on our business, financial condition, results of operations and prospects.

Any future acquisitions or strategic collaborations may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and/or subject us to other risks.

From time to time, we may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses, as deemed appropriate to carry out our business plan. Any potential acquisition or strategic partnership may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent or unknown liabilities;
- assimilation of operations, intellectual property and drugs of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing drug programs and initiatives in pursuing such a strategic partnership, merger or acquisition;
- retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we engage in future acquisitions or strategic partnerships, we may issue dilutive securities, assume or incur debt obligations, incur large one-time expenses, and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition opportunities, and this inability could impair our ability to grow or obtain access to technology or drugs that may be important to the development of our business.

Risks Related to Ownership of Our Common Stock

The market price of our common stock is volatile and has fluctuated substantially, which could result in substantial losses for purchasers of our common stock.

The stock market in general and the market for biopharmaceutical and pharmaceutical companies in particular, has experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price at which you purchased it. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this Annual Report, the market price for our common stock has been, and is likely to continue to be influenced by the following:

- the commencement, enrollment, results of, or any delays in our planned or future clinical trials of our product candidates or those of our competitors;
- the success of competitive drugs or therapies;
- the Complete Response Letter we received from the FDA for the NDA we submitted for govorestat;
- the departure of our founder and CEO and changes to our senior management team and board;
- regulatory or legal developments in the United States and other countries;
- the success of competitive products or technologies;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

- our inability to obtain or delays in obtaining adequate drug supply for any approved drug or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, including coverage and adequate reimbursement for any approved drug;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, political, and market conditions and overall fluctuations in the financial markets in the United States and abroad; and
- investors' general perception of us and our business.

These and other market and industry factors have caused the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from selling their shares at or above the price paid for the shares and may otherwise negatively affect the liquidity of our common stock. Furthermore, we believe our stock has been, and may in the future be, adversely affected as a result of actions by third-parties. Short sellers and others, some of whom post anonymously on social media, may be positioned to profit if our stock declines and their activities can negatively affect our stock price.

Some companies that have experienced volatility in the trading price of their shares have been the subject of lawsuits and/or securities class action litigation. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our business practices. Defending against litigation is costly and time-consuming, and could divert our management's attention and our resources. Furthermore, during the course of litigation, there could be negative public announcements of the results of hearings, motions or other interim proceedings or developments, which could have a negative effect on the market price of our common stock.

If we fail to regain compliance with the continued listing requirements of Nasdaq, our common stock may be delisted and the price of our common stock and our ability to access the capital markets could be negatively impacted.

On February 7, 2025, we received a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market, or Nasdaq, notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Market, referred to as the minimum bid price rule. In accordance with Nasdaq Listing Rules, we have an initial period of 180 calendar days, or until August 6, 2025, to regain compliance with the minimum bid price rule. If at any time before August 6, 2025 the bid price for our common stock closes at $1.00 or more per share for a minimum of 10 consecutive business days, the Nasdaq Listing Qualifications Department staff will provide written notification to us that we are in compliance with the minimum bid price rule, unless the staff exercises its discretion to extend this 10-day period pursuant to the Nasdaq Listing Rules. If we do not regain compliance with the minimum bid price rule by August 6, 2025, we may be eligible for an additional 180 calendar day compliance period. We intend to monitor the closing bid price of our common stock and may, if appropriate, consider available options to regain compliance with the minimum bid price rule.

There are many factors that may adversely affect our minimum bid price, including those described throughout this section titled "Risk Factors." Many of these factors are outside of our control. As a result, we may not be able to sustain compliance with the minimum bid price rule in the long term. Any potential delisting of our common stock from the Nasdaq Global Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq Global Market would also make it more difficult for our stockholders to sell our common stock in the public market.

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.

You should not rely on an investment in our common stock to provide dividend income. 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. Investors seeking cash dividends should not purchase our common stock.

Future sales of common stock by holders of our common stock, or the perception that such sales may occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public market could occur at any time, subject to certain restrictions described below. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of December 31, 2024, we had outstanding 137,228,741 shares of common stock. A substantial number of such shares are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold in the future.

We further have registered all shares of common stock that we may issue in the future or have issued to date under our equity compensation plans. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and certain lock-up agreements. Sales of a large number of the shares issued under these plans in the public market could have an adverse effect on the market price of our common stock.

General Risk Factors

If research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or financial analysts publish about us or our business. Equity research analysts may discontinue research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. We do not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research about us. If one or more equity research analysts cease coverage of us or fail to publish reports on us regularly, demand for our shares could decrease, which in turn could cause the trading price or trading volume of our common stock to decline.

We have broad discretion in the use of our cash and cash equivalents and may use them ineffectively, in ways with which you do not agree or in ways that do not increase the value of your investment.

Our management has broad discretion in the application of our cash and cash equivalents, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in additional operating losses that could have a negative impact on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

We no longer qualify as an "emerging growth company," and as a result, we have to comply with increased disclosure and compliance requirements.

While we still qualify as a "smaller reporting company," as defined in Regulation S-K of the Securities Act of 1933, we no longer qualify as an emerging growth company ("EGC") as defined in the Jumpstart Our Business Startups Act because in 2024, we reached the five-year anniversary of the first sale of our common stock pursuant to an effective registration statement under the Securities Act of 1933. As such, we are no longer exempt from certain disclosure and compliance requirements that apply to other public companies but did not previously apply to us due to our status as an EGC. These requirements include, but are not limited to:

- compliance with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, including critical audit matters;
- the requirement that we provide more detailed disclosures regarding executive compensation, although we are still able to take advantage of exemptions provided to smaller reporting companies; and
- the requirement that we obtain stockholder approval of any golden parachute payments not previously approved.

We anticipate increased expenses, including exchange listing and SEC requirements, director and officer insurance premiums, legal, audit and tax fees, regulatory compliance programs, and investor relations costs associated with being a public company and ceasing to be an emerging growth company.

We have incurred 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 now that we are no longer an EGC, we incur and will continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the SEC and The Nasdaq Stock Market LLC 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 comply with these requirements. Moreover, these rules and regulations increase our legal and financial compliance costs and 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.

Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. 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.

Provisions in our corporate charter documents 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.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;

- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a stockholder rights plan, or so-called "poison pill," that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 66$^2/_3$% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our governing documents designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, with respect to any state actions or proceedings under Delaware statutory or common law, the Court of Chancery of the State of Delaware is the exclusive forum for:

- any derivative action or proceeding brought on our behalf;
- any action asserting a breach of fiduciary duty;
- any action asserting a claim against us or any of our directors, officers, employees or agents arising under the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws;
- any action or proceeding to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; and
- any action asserting a claim against us or any of our directors, officers, employees or agents that is governed by the internal-affairs doctrine.

In addition, our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States are, to the fullest extent permitted by law, the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act.

These exclusive-forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find an exclusive-forum provision in our amended and restated certificate of incorporation or our amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could harm our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

None.

ITEM 1C. CYBERSECURITY.

We have established policies and procedures for assessing, identifying and managing material risk from cybersecurity threats, and have integrated these processes into our overall risk management systems and processes. We leverage well-known and established third parties as industry partners to support our key business processes and utilize the services of reputable external advisory firms for running important functions such as cybersecurity assessments and technical security management activities, including network security management. Our Chief Financial Officer and Chief Operating Officer are jointly responsible for managing cybersecurity risks and implementing the required policies across the Company. Our Chief Executive Officer is responsible for making strategic decisions and approving external communication releases related to cybersecurity risks or incidents. Our Chief Executive Officer and Chief Financial Officer work closely with our third-party IT manager to stay informed about and monitor the prevention, detection, mitigation and remediation of any potentially significant cybersecurity incidents, including making determinations on the materiality of a cybersecurity incident.

One of the key functions of our Board of Directors is informed oversight of our risk management processes, including risks from cybersecurity threats. Our Board of Directors is responsible for monitoring and assessing strategic risk exposure, and our executive officers are responsible for the day-to-day management of the material risks we face. Our Board of Directors administers its cybersecurity risk oversight function directly as a whole, as well as through the Audit Committee of the Board of Directors (the "Audit Committee"). The Audit Committee oversees our risk management program, which focuses on the most significant risks we face. Audit Committee meetings include discussions of specific risk areas throughout the year, including, among others, those relating to cybersecurity. Our Chief Financial Officer or Chief Operating Officer reports on our enterprise risk profile on an annual basis or more frequently as needed. Our Audit Committee also engages with external counsel on legal matters related to cybersecurity incident management and reporting.

To date, risks from cybersecurity threats, including those resulting from any previous cybersecurity incidents, have not materially affected us, including our operations or financial standing. We do not believe that cybersecurity threats resulting from any previous cybersecurity incidents of which we are aware are reasonably likely to materially affect us. For additional information regarding risks from cybersecurity threats, please refer to Item 1A, “Risk Factors,” in this annual report on Form 10-K.

ITEM 2. PROPERTIES.

Our corporate headquarters are located at 545 Fifth Ave, Suite 1400 and 1401, New York, NY 10017 where we lease office space pursuant to a lease agreement amended on September 11, 2024 and expires on October 31, 2029. We also occupy space for offices in Englewood Cliffs, New Jersey pursuant to a lease which commenced on November 1, 2020 for a three year period and subsequently renewed through 2026. We believe that our existing facilities are suitable and adequate to meet our current needs. We intend to add new facilities or expand existing facilities as we add employees, and we believe that suitable additional or substitute space will be available as needed to accommodate any such expansion of our operations.

ITEM 3. LEGAL PROCEEDINGS.

Securities Class Action Litigation

On December 17, 2024, a purported stockholder filed a putative class action lawsuit against the Company and certain current and former Company officers and directors in the United States District Court for the Southern District of New York (*Alexandru v. Applied Therapeutics, Inc., et al.*, No. 1:24-cv-09715). The complaint alleges that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Rule 10b-5 promulgated thereunder by making false and/or misleading statements between January 3, 2024 to December 2, 2024 in connection with the Company's NDA to the FDA for govorestat for the treatment of Classic Galactosemia, and seeks unspecified damages. On December 27, 2024, another purported stockholder filed a putative class action lawsuit against the Company and a former Company officer and director in the United States District Court for the Southern District of New York (*Ikram v. Applied Therapeutics, Inc., et al.*, No. 1:24-cv-09973). The complaint alleges claims substantially similar to those alleged in the *Alexandru* action and also seeks unspecified damages. On February 18, 2025, several purported stockholders filed motions seeking to consolidate the *Alexandru* and *Ikram* actions and seeking appointment as lead plaintiff in the consolidated action. On March 11, 2025, the court consolidated the Alexandru and Ikram actions (In re Applied Therapeutics Securities Litigation, No. 1:24-cv-9715) and appointed a lead plaintiff and lead counsel. The deadline for lead plaintiff to file a consolidated amended complaint is May 2, 2025.

Shareholder Derivative Litigation

On January 31, 2025, a purported stockholder filed a derivative action in the United States District Court for the Southern District of New York (*Hassine v. Shendelman, et al.*, No. 1:25-cv-00935). The complaint purports to assert derivative claims against certain current and former Company officers and directors for breach of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement, waste of corporate assets, violations of Section 14(a) of the Exchange Act, and contribution under Sections 10(b) and 21D of the Exchange Act. The complaint seeks to implement reforms to the Company's corporate governance and internal procedures and to recover on behalf of the Company for any liability the Company might incur as a result of the individual defendants' alleged misconduct, as well as declaratory, equitable, and monetary relief, including attorneys' fees and other costs. The derivative action is based substantially on the same facts alleged in the consolidated action described above.

On March 4, 2025, plaintiff and the Company filed a joint stipulation seeking to temporarily stay the derivative action. On March 5, 2025, the court so-ordered the stipulation, thereby temporarily staying the derivative action.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

PART II

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

Market Information

On May 16, 2019, our common stock began trading on the Nasdaq Global Market under the symbol "APLT." Prior to that time, there was no public market for our common stock.

Stockholders

As of December 31, 2024, there were approximately 30 stockholders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street names by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never paid or declared any cash dividends on our common stock, and we do not anticipate paying any cash dividends on our common stock in the foreseeable future. We intend to retain all available funds and any future earnings to fund the development and expansion of our business. Any future determination to pay dividends will be at the discretion of our board of directors and will depend upon a number of factors, including our results of operations, financial condition, future prospects, contractual restrictions, restrictions imposed by applicable law and other factors that our board of directors deems relevant.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

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 financial statements and the related notes included elsewhere in this Annual Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Annual Report, our actual results could differ materially from the results described in or implied by these forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against molecular targets in indications of high unmet medical needs. We focus on previously identified disease processes where other molecules have failed to yield successful products due to poor efficacy and tolerability. Our unique approach to drug development leverages recent technological advances to design improved drugs, employs early use of biomarkers to confirm biological activity and focuses on potentially accelerated regulatory pathways. Our first molecular target is aldose reductase, or AR, an enzyme that converts glucose to sorbitol under oxidative stress conditions, and is implicated in multiple diseases. Prior attempts to inhibit this enzyme were hindered by nonselective, nonspecific inhibition, which resulted in limited efficacy and significant off-target safety effects. The detrimental consequences of AR activation have been well established by decades of prior research. Our AR program currently includes multiple potent and selective inhibitors of AR, which are engineered to have specific tissue permeability profiles to target different disease states, including diabetic complications, heart disease and rare metabolic diseases. The result of this multifaceted approach to drug development is a portfolio of highly specific and selective product candidates that we believe may be able to move quickly through the development process.

Our lead candidate, AT-007 (also called govorestat) is a novel central nervous system, or CNS, penetrant ARI that we are developing for the treatment of rare metabolic diseases, including Galactosemia and SORD Deficiency. Galactosemia is a devastating rare pediatric metabolic disease that affects how the body processes a simple sugar called galactose, and for which there is no known cure or approved treatment available. The U.S. Food and Drug Administration, or FDA, has granted both orphan drug designation and rare pediatric disease designation to AT-007 for the treatment of Galactosemia and in June 2021, the FDA granted Fast Track Designation to AT-007 for the treatment of Galactosemia.

We submitted a New Drug Application (NDA) in December 2023 to the US FDA, and the FDA accepted the filing of the NDA for govorestat (AT-007) for the treatment of Classic Galactosemia in February of 2024. On November 27, 2024, the FDA issued a Complete Response Letter (Complete Response Letter) for the NDA for the treatment of Classic Galactosemia, indicating that the agency was unable to approve the NDA in its current form, citing deficiencies in the clinical application. On the same day, the FDA also issued warning letters to both Applied and a clinical investigator (Warning Letter and the Clinical Investigator Warning Letter, respectively) related to the Phase 2/3, ACTION-Galactosemia Kids study. Following receipt of the Complete Response Letter, we also withdrew a pending Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for AT-007 for the treatment of Classic Galactosemia, as we believed more time was needed to acquire further data to support a European MAA. We are actively working to address the issues raised in the Complete Response Letter and Warning Letter.

We are also studying AT-007 in a rare disease caused by deficiency in the enzyme Sorbitol Dehydrogenase (SORD). Aldose Reductase is the first enzyme in the polyol pathway, converting glucose to sorbitol. AR is then followed by Sorbitol Dehydrogenase, which converts sorbitol to fructose. Patients with SORD Deficiency accumulate very high levels of sorbitol in their cells and tissues as a result of the enzyme deficiency, which is thought to result in tissue toxicities such as peripheral neuropathy and motor neuron disease. Recent research in drosophila and cell models of SORD Deficiency demonstrated that treatment with an ARI that blocks sorbitol production may provide benefit in this disease. Preclinical studies on AT-007 have demonstrated significant reduction in sorbitol levels in fibroblasts from SORD deficient patients. Treatment with AT-007 in the drosophila model of SORD prevented the disease phenotype and protected from neuronal degeneration. On October 25, 2021, we reported data from a pilot open-label study in eight SORD Deficiency patients. AT-007 reduced blood sorbitol levels by approximately 66% from baseline through 30 days of treatment. AT-007 was generally safe and well tolerated in treated patients. In December 2021, we initiated a Phase

2/3 study in patients with SORD Deficiency. In July 2024, we concluded the double-blind placebo-controlled portion of the Phase 2/3 INSPIRE trial and began transitioning patients to the open-label treatment phase prior to all patients completing 24 months of treatment. Applied is continuing to analyze the data from the Phase 2/3 INSPIRE trial and the extent to which these data may support a potential submission for regulatory approval, including under the accelerated approval pathway. Following this analysis, we plan to meet with the FDA to discuss whether an NDA can be submitted based on the current data package and/or potential additional supporting data.

We also plan to initiate a clinical development program on AT-007 in another rare pediatric disease, called PMM2-CDG. PMM2-CDG is a glycosylation disorder caused by deficiencies in the enzyme phosphomannomutase 2, which leads to CNS symptoms similar to Galactosemia, including low IQ, tremor, and speech and motor problems. Aldose Reductase is over-activated in this disease as a compensatory consequence of PMM2 deficiency, and a CNS penetrant ARI may be a compelling clinical option. Initial data in fibroblast cell lines derived from PMM2-CDG patients demonstrates that AT-007 treatment increases phosphomannomutase 2 activity. The FDA has granted rare pediatric disease designation and orphan designation for AT-007 in PMM2-CDG.

AT-001 (also called caficrestat) is a novel ARI with broad systemic exposure and peripheral nerve permeability that we are developing for the treatment of diabetic cardiomyopathy, or DbCM, a fatal fibrosis of the heart, for which no treatments are available. We completed a Phase 1/2 clinical trial evaluating AT-001 in approximately 120 patients with type 2 diabetes, in which no drug-related adverse effects or tolerability issues were observed. In September 2019, we announced the initiation of a Phase 2/3 trial of AT-001 in DbCM. The study, called ARISE-HF, was designed to evaluate AT-001's ability to improve or prevent the decline of functional capacity in patients with DbCM at high risk of progression to overt heart failure. Although we did experience enrollment delays in 2020 associated with the Covid-19 pandemic, modifications were made to the trial to include additional sites and geographies to address Covid-19-related issues. On January 4, 2024, we reported topline results from the ARISE-HF study. AT-001 (caficrestat) demonstrated a strong trend in stabilizing cardiac functional capacity, while the placebo group declined over 15 months. The placebo-treated group declined by a mean of -0.31 ml/kg/min over 15 months of treatment, while the AT-001 1500mg twice daily treated group remained primarily stable, with a mean change of -0.01 ml/kg/min over 15 months. While a trend favored active treatment, the difference between active and placebo treated groups (0.30 ml/kg/min) was not statistically significant (p=0.210). Approximately 38% of study subjects were on SGLT2 or GLP-1 therapies for treatment of diabetes, while 62% were not. In a pre-specified subgroup analysis of the primary endpoint in patients not concomitantly treated with SGLT2 or GLP-1 therapies, the placebo group declined by a mean of -0.54 ml/kg/min, while the 1500mg BID AT-001 treated group improved by a mean of 0.08 ml/kg/min over 15 months of treatment, with a difference between groups of 0.62 ml/kg/min (p=0.040). Additionally, in this subgroup analysis, the number of patients who experienced a clinically significant worsening in cardiac functional capacity of 6% or more was substantially higher in the placebo group (46%) as compared to the 1500mg BID AT-001 treated group (32.7%), odds ratio 0.56 (p=0.035). A 6% change in cardiac functional capacity has been shown to predict long-term survival and hospitalization for heart failure. The effect of AT-001 was dose dependent, with the low dose (1000mg BID) demonstrating an intermediate effect between the high dose and placebo. AT-001 was generally safe and well tolerated, with no substantial differences in serious adverse events between AT-001 treated groups as compared to placebo.

As we advance our product candidates forward in additional indications, such as SORD Deficiency, PMM2-CDG and retinopathy, we anticipate potential moderate growth in our clinical development and operations teams to support the additional clinical trials, as well as the addition of a medical affairs team to support the late stage indications and preparations for commercialization.

AT-003 is a novel ARI designed to cross through the back of the eye when dosed orally, and has demonstrated strong retinal penetrance, for the treatment of diabetic retinopathy, or DR. DR is an ophthalmic disease that occurs in diabetic patients and for which treatments are currently limited to high-cost biologics requiring intravitreal administration. DR has been linked to AR activity, including elevations in sorbitol and subsequent changes in retinal blood vessels, which distorts vision and leads to permanent blindness.

AT-104 is a preclinical dual selective PI3K inhibitor. Due to regulatory changes impacting development of the PI3K inhibitor class of compounds, the Company discontinued its early stage preclinical PI3K program and further development of AT-104. The compound and all rights associated with the technology were returned to Columbia University.

Since inception in 2016, our operations have focused on developing our product candidates, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials. We do not have any product candidates approved for sale and have not generated any product revenue.

We have incurred significant operating losses since inception in 2016. 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 loss was $105.6 million for the year ended December 31, 2024. As of December 31, 2024, we had an accumulated deficit of $574.2 million. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future in connection with our ongoing activities. Furthermore, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses. As of December 31, 2024, we had cash and cash equivalents of $79.4 million.

April 2023 Offering

On April 26, 2023, we completed the April 2023 Private Placement, in which we sold a total of 9,735,731 shares of common stock, at a purchase price of $0.946 per share, and 22,000,000 Pre-Funded Warrants to purchase common stock, at a purchase price of $0.945 per Pre-Funded Warrant, in a private placement to a select group of accredited investors (the "2023 Purchasers"), pursuant to a Securities Purchase Agreement, dated as of April 23, 2023, by and between us and the 2023 Purchasers. The April 2023 Private Placement resulted in net proceeds to us of approximately $27.5 million, after deducting underwriting discounts, commissions and offering expenses. The Pre-Funded Warrants are immediately exercisable from the date of issuance and do not have an expiration date. They have an exercise price of $0.001. Holders may not exercise any Pre-Funded Warrants that would cause the aggregate number of shares of common stock beneficially owned by the holder to exceed 9.99% of our outstanding common stock immediately after exercise. The Pre-Funded Warrants are subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the common stock and also upon any distributions for no consideration of assets to our stockholders. In the event of certain corporate transactions, the holders of the Pre-Funded Warrants will be entitled to receive, upon exercise of the Pre-Funded Warrants, the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants immediately prior to such transaction. The Pre-Funded Warrants do not entitle the holders thereof to any voting rights or any of the other rights or privileges to which holders of common stock are entitled.

Leerink ATM Agreement

On August 11, 2023, we entered into the Leerink ATM Agreement with Leerink Partners LLC, pursuant to which we may offer and sell, from time to time, shares of common stock having an aggregate offering price of up to $75.0 million through Leerink Partners LLC as sales agent. Under the Leerink ATM Agreement, the sales agent may sell shares of common stock by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended. We will pay the sales agent a commission rate of up to 3% of the gross offering proceeds of any shares sold and has agreed to provide the sales agent with indemnification and contribution against certain liabilities. The Leerink ATM Agreement contains customary representations and warranties.

During the year ended December 31, 2024, we sold an aggregate 3,000,000 shares of our common stock, pursuant to Leerink ATM Agreement with an average sale price of $4.31 per share, resulting in net proceeds of $12.4 million, after deducting underwriting discounts, commissions and offering expenses.

During the year ended December 31, 2023, we had sold an aggregate of 17,615,976 shares of our common stock, pursuant to the Leerink ATM Agreement with an average sale price of $2.04 per share, resulting in net proceeds of $36.9 million, after deducting underwriting discounts, commissions and offering expenses.

Venrock Warrant Exchange

On October 12, 2023, we entered into the Exchange Agreement with entities affiliated with Venrock Healthcare Capital Partners, pursuant to which we exchanged an aggregate of 5,658,034 shares of common stock, owned by the Exchanging Stockholders for pre-funded warrants to purchase an aggregate of 5,658,034 shares of common stock

(subject to adjustment in the event of stock splits, recapitalizations and other similar events affecting common stock), with an exercise price of $0.001 per share.

March 2024 Private Placement

On March 1, 2024, we completed the March 2024 Private Placement, during which we sold a total of 12,285,714 common shares, at a purchase price of $7.00 per share, and 2,000,000 Pre-Funded Warrants at a purchase price of $6.999 per Pre-Funded Warrant, in a private placement to a select group of purchasers (the "2024 Purchasers") pursuant to a Securities Purchase Agreement ("Securities Purchase Agreement"). The March 2024 Private Placement resulted in gross proceeds to us of approximately $92.3 million, after deducting placement agent commissions and other offering expenses.

The Pre-Funded Warrants are immediately exercisable from the date of issuance and do not have an expiration date. They have an exercise price of $0.001. Holders may not exercise any Pre-Funded Warrants that would cause the aggregate number of shares of common stock beneficially owned by the holder to exceed 9.99% of our outstanding common stock immediately after exercise. The Pre-Funded Warrants are subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the common stock and also upon any distributions for no consideration of assets to our stockholders. In the event of certain corporate transactions, the holders of the Pre-Funded Warrants will be entitled to receive, upon exercise of the Pre-Funded Warrants, the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants immediately prior to such transaction. The Pre-Funded Warrants do not entitle the holders thereof to any voting rights or any of the other rights or privileges to which holders of common stock are entitled.

The securities issued have the benefit of the Registration Rights Agreement (the "Registration Rights Agreement"), dated as of February 27, 2024, by and among us and the 2024 Purchasers, requiring us to prepare and file a registration statement with the SEC as soon as reasonably practicable, but in no event later March 28, 2024 ("Filing Deadline"), and to use commercially reasonable efforts to have the registration statement declared effective within 30 days of the Filing Deadline, subject to extension under the terms of the Registration Rights Agreement. We satisfied our obligations under the Registration Rights Agreement by filing a registration statement on Form S-3 on May 12, 2023, which became effective on April 25, 2024. We are using the net proceeds to fund research and development and registration of its pipeline candidates, and for working capital and general corporate purposes.

Components of Our Results of Operations

Revenue

Since inception, we have not generated any product revenue and do not expect to generate any revenue from the sale of products until after we receive regulatory approval. We have generated revenue solely from licensing of intellectual property and sale of research and development services. If our development efforts for 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.

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 product candidates, 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 incurred under agreements with contract research organizations, or CROs, as well as contract manufacturing organizations, or CMOs, and consultants that conduct and provide supplies for our preclinical studies and clinical trials;

- costs associated with preclinical activities and development activities;
- costs associated with our technology and our intellectual property portfolio; and
- costs related to compliance with regulatory requirements.

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.

Research and development costs also include costs incurred in connection with certain licensing arrangements. Before a compound receives regulatory approval, we record upfront and milestone payments made by us to third parties under licensing arrangements as expense. Upfront payments are recorded when incurred, and milestone payments are recorded when the specific milestone has been achieved. Once a compound receives regulatory approval, we will record any milestone payments in identifiable intangible assets, commence amortization and, unless the asset is determined to have an indefinite life, we amortize the payments on a straight-line basis over the remaining agreement term or the expected product life cycle, whichever is shorter.

Research and development activities are central to our business model. We expect that our research and development expenses will remain a significant expense for the foreseeable future as we continue clinical development for our product candidates 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. Historically, we have incurred research and development expenses that primarily relate to the development of AT-007 and AT-001 programs. As we advance our product candidates, we expect to allocate our direct external research and development costs across each of the indications or product candidates.

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

	Year Ended December 31,	
(in thousands)	**2024**	**2023**
Product pipeline research and development expenses		
AT-001	$ 4,600	$ 19,540
AT-007	29,360	24,319
Personnel-related expenses	6,512	6,387
Stock-based compensation	7,340	3,005
Other expenses	932	654
Total research and development expenses	$ 48,744	$ 53,905

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, and commercial 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 expenses for rent and maintenance of facilities and other operating costs.

Commercial expenses consist of payroll expense for commercial personnel, as well as marketing, market research, market access, and other focused investments to support launch of drug candidates, and generate evidence of commercial potential and value proposition. Commercial expenses are included in general and administrative expenses.

We expect that our general and administrative expenses will remain a significant expense in the future as we may increase our general and administrative headcount to support our continued research and development and potential commercialization of our product candidates.

Other Income (Expense), Net

Other income (expense), net consists of interest income (expense), net, other income (expense), net and change in fair value of warrant liabilities. Interest income (expense), net consists primarily of our interest income on our cash and cash equivalents and marketable securities. Other income (expense), net consists primarily of realized gains and losses on sales of marketable securities. Changes in fair value of warrant liabilities consists of mark to market changes on our common warrants that are classified as liabilities.

Results of Operations

The following table summarizes our results of operations:

	Year Ended December 31,	
(in thousands)	**2024**	**2023**
REVENUE:		
License revenue	$ —	$ 9,219
Research and development services revenue	455	774
Total revenue	455	9,993
COSTS AND EXPENSES:		
Research and development	48,744	53,905
General and administrative	56,010	20,623
Total costs and expenses	104,754	74,528
LOSS FROM OPERATIONS	(104,299)	(64,535)
OTHER INCOME (EXPENSE), NET:		
Interest income	3,534	1,372
Change in fair value of warrant liabilities	(4,782)	(56,573)
Other expense	(77)	(27)
Total other expense, net	(1,325)	(55,228)
Net loss	$ (105,624)	$ (119,763)

Revenue

Revenue for the year ended December 31, 2024 was $0.5 million, compared to $10.0 million for the year ended December 31, 2023. For the year ended December 31, 2024 , the decrease of $9.5 million was primarily related to:

- a decrease in license revenue of $9.2 million, due to the Company not executing any new license arrangements during the year ended December 31, 2024; and
- a decrease in research and development services revenue of $0.3 million primarily due to the recognition of less deferred revenue amortization related to the Advanz agreement.

Research and Development Expenses

The following table summarizes our research and development expenses:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**Increase/(Decrease)**
Clinical and pre-clinical	$ 27,816	$ 39,841	$ (12,025)
Drug manufacturing and formulation	1,087	2,429	(1,342)
Personnel expenses	6,512	6,283	229
Stock-based compensation	7,340	3,005	4,335
Regulatory and other expenses	5,989	2,347	3,642
Total research and development expenses	$ 48,744	$ 53,905	$ (5,161)

Research and development expenses for the year ended December 31, 2024, were $48.7 million, compared to $53.9 million for the year ended December 31, 2023. The decrease of approximately $5.2 million was primarily related to:

- a decrease in clinical and pre-clinical expense of $12.0 million, primarily due to decreased expense related to AT-001, partially offset by increased expense related to AT-007 during the year ended December 31, 2024;
- a decrease in drug manufacturing and formulation costs of $1.3 million primarily due to decreased manufacturing activities for AT-001 and AT-007;
- an increase in personnel expenses of $0.2 million primarily related to severance expense and salary increases during 2024, partially offset by an overall decrease in accrued bonuses;
- an increase in stock-based compensation of $4.3 million primarily related to the acceleration of former executive equity awards and additional award grants to employees during 2024; and
- an increase in regulatory and other expenses of $3.6 million primarily related increased regulatory expenses related to the Galactosemia study.

General and Administrative Expenses

The following table summarizes our general and administrative expenses:

	Year Ended December 31,		
(in thousands)	2024	2023	Increase/(Decrease)
Legal and professional fees	$ 14,923	$ 6,780	$ 8,143
Commercial expenses	18,381	123	$ 18,258
Personnel expenses	8,385	3,714	$ 4,671
Stock-based compensation	8,227	4,355	$ 3,872
Insurance expenses	1,503	2,274	$ (771)
Other expenses	4,591	3,377	$ 1,214
Total general and administrative expenses	$ 56,010	$ 20,623	$ 35,387

General and administrative expenses were $56.0 million for the year ended December 31, 2024, compared to $20.6 million for the year ended December 31, 2023. The increase of approximately $35.4 million was primarily related to:

- an increase in legal and professional fees of $8.1 million related to higher external legal fees to support planned commercialization;
- an increase in commercial expenses of $18.3 million related to planned commercialization;
- an increase in personnel expenses of $4.7 million, primarily related to severance paid to former executives and an increase in headcount, partially offset by an overall decrease in accrued bonuses;
- an increase in stock-based compensation of $3.9 million related to acceleration of former executive stock based compensation, an overall increase in headcount and additional award grants to employees in 2024 ;
- a decrease in insurance expenses of $0.8 million related to decreased director and officers' liability insurance costs; and
- an increase in other expenses of $1.2 million due to an overall increase in data storage costs to support planned commercialization.

Interest Income

Interest income was $3.5 million for the year ended December 31, 2024, as compared to $1.4 million for the year ended December 31, 2023. Interest income increased due to higher interest rates and cash balances in the current period.

Change in Fair Value of Warrant Liabilities

Change in the fair value of warrant liabilities was $4.8 million for the year ended December 31, 2024, as compared to $56.6 million for the year ended December 31, 2023. The decrease in the fair value of warrant liabilities is primarily related to an overall decrease in our common share price and a change in the number of warrants outstanding at December 31, 2024 compared to December 31, 2023. Warrants outstanding at December 31, 2024 was 10,725,000 compared to 19,750,000 at December 31, 2023.

Other Expense

Other expense was $0.1 million for the year ended December 31, 2024, compared to $27,000 for the year ended December 31, 2023. The increase is primarily due to fluctuation in foreign exchange rates.

Liquidity and Capital Resources

Since our inception and through December 31, 2024, we have not generated any product revenue and have incurred significant operating losses and negative cash flows from our operations. The accompanying financial statements have been prepared assuming the continuation of the Company as a going concern. The exclusive licensing agreement with Advanz Pharma for commercialization rights to AT-007 in Europe may provide additional sources of capital after the potential resubmission of the NDA and the marketing authorization application in Europe. However, there are no guarantees that this will materialize, and additional delays or unexpected data could disrupt this potential source of liquidity. Broadly, we have not yet established an ongoing source of product revenue sufficient to cover our operating costs and we are dependent on debt and equity financing to fund our operations. As of December 31, 2024, our cash and cash equivalents were $79.4 million. We will need to obtain substantial additional funding in connection with our continuing operations and planned research and clinical development activities. Additionally, we may encounter unforeseen expenses, including in connection with reevaluating our product candidates and potential new trials. The report of our independent registered public accounting firm on our financial statements for the year ended December 31, 2024 includes an explanatory paragraph regarding the existence of substantial doubt about our ability to continue as a going concern. Given our planned expenditures for the next several years, we have concluded and our independent registered public accounting firm has agreed with our conclusion that there is still a substantial doubt regarding our ability to continue as a going concern for a period of 12 months beyond the filing of this Form 10-K.

Cash Flows

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

	Year Ended December 31,	
(in thousands)	**2024**	**2023**
Net cash used in operating activities	$ (84,305)	$ (55,173)
Net cash provided by investing activities	—	13,872
Net cash provided by financing activities	113,805	74,542
Net increase in cash and cash equivalents	$ 29,500	$ 33,241

Operating Activities

During the year ended December 31, 2024, operating activities used cash of $84.3 million, due to our net losses of $105.6 million,an increase in prepaid expenses of $0.6 million, a decrease in operating lease liability of $0.4 million, and a decrease of $0.8 million in other liabilities. This is offset by an increase of $2.7 million in accounts payable, $13.5 million in stock-based compensation expense, $1.2 million in accrued expenses and other current liabilities, $0.6 million amortization of insurance premium, $4.8 million in changes in fair value of our warrant liabilities, and $0.4 million in amortization of operating lease right-of-use assets.

During the year ended December 31, 2023, operating activities used cash of $55.2 million, due to our net losses of $119.8 million, a decrease in operating lease liability of $0.4 million, a decrease in financed insurance premium of $1.5 million, and a decrease of $2.8 million in accounts payable. This is partially offset by an increase of $1.9 million in prepaid expense, $0.7 million in accrued expenses and other liabilities, $7.4 million in non-cash stock-based

compensation expense, $2.1 million of amortization of insurance premium, $56.6 million in changes in fair value of our warrant liabilities, $0.4 million in amortization of operating lease right-of-use assets, and $0.3 million of other liabilities.

Investing Activities

There was no cash provided by investing activities for the year ended December 31, 2024.

Net cash provided by investing activities for the year ended December 31, 2023, was $13.9 million relating to the proceeds from the sale of available-for-sale securities of $4.9 million and maturities of available-for-sale securities of $8.9 million.

Financing Activities

During the year ended December 31, 2024, net cash provided by financing activities was $113.8 million, primarily from proceeds from the issuance of shares and pre-funded warrants of $104.7 million, $9.0 million from the exercise of common warrants, $0.3 million from exercise of stock options for common stock under the equity incentive plan, partially offset by repayment of short-term borrowings of $0.3 million.

During the year ended December 31, 2023, net cash provided by financing activities was $74.5 million, primarily from proceeds from the issuance of shares and pre-funded warrants of $64.5 million, $10.3 million from the exercise of common warrants, proceeds from financed insurance premium of $1.5 million, $0.1 million from exercise of stock options for common stock under the equity incentive plan, partially offset by repayment of short-term borrowings of $1.9 million.

Funding Requirements

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 product candidates. We believe that our expenses may increase significantly if and as we:

- continue the ongoing and planned development of our product candidates for regulatory approval;
- initiate, conduct and complete any ongoing, anticipated or future preclinical studies and clinical trials for our current and future product candidates;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- establish a sales, marketing, manufacturing and distribution infrastructure to commercialize any current or future product candidate for which we may obtain marketing approval;
- seek to discover and develop additional product candidates;
- continue to build a portfolio of product candidates through the acquisition or in-license of drugs, product candidates or technologies;
- maintain, protect and expand our intellectual property portfolio;
- hire additional clinical, regulatory and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

Due to the numerous risks and uncertainties associated with the development of our product candidates and programs, and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of our product candidates. Our future funding requirements, both near and long-term, will depend on many factors, including:

- the initiation, scope, progress, timing, costs and results of our ongoing and planned clinical trials for our product candidates;
- the outcome, timing, effort and cost of meeting regulatory requirements established by the FDA including the costs incurred to respond to CRL and warning letter and other federal, state, local and foreign regulatory authorities;

- the cost of filing, prosecuting, defending and enforcing our patent claims and other intellectual property rights;
- the cost of defending potential intellectual property disputes, including patent infringement actions;
- the achievement of milestones or occurrence of other developments that trigger payments under the Columbia Agreements or other agreements we may enter into;
- the extent to which we are obligated to reimburse, or entitled to reimbursement of, clinical trial costs under future collaboration agreements, if any;
- the effect of competing technological and market developments;
- the cost and timing of completion of clinical or commercial-scale manufacturing activities;
- the costs of operating as a public company;
- the extent to which we in-license or acquire other products and technologies;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates in regions where we choose to commercialize our product candidates, if approved; and
- the initiation, progress, timing and results of the commercialization our product candidates, if approved, for commercial sale.

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.

Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through offerings of securities, PIPE, debt financings, collaborations or other strategic transactions. The terms of financing may adversely affect the holdings or the rights of our stockholders. Funding may not be available to us on acceptable terms, or at all. If we are unable to obtain funding, we may be required to delay, limit, reduce or terminate some or all of our research and product development, product portfolio expansion or future commercialization efforts. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

Contractual Obligations and Commitments

We lease certain assets under noncancelable operating leases, which expire through 2029. The leases relate primarily to office space. As of December 31, 2024, aggregate future minimum commitments under these office leases are $2.8 million through 2029, excluding any related common area maintenance charges or real estate taxes.

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

While our significant accounting policies are described in greater detail in Note 1 to our financial statements appearing elsewhere in this Annual Report, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Revenue Recognition

Under ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)*, or ASC 606, as amended by ASU 2016-08, 2016-10, 2016-12 and 2016-20, we recognize revenue in an amount that reflects the consideration to which we expect to be entitled in exchange for the transfer of promised goods or services to customers. To determine revenue

recognition for contracts with customers that are within the scope of ASC 606, the Company performs the following steps: (1) identifies the contract with the customer, (2) identifies the performance obligations in the contract, (3) determines the transaction price, (4) allocates the transaction price to the performance obligations in the contract, and (5) recognizes revenue when (or as) the entity satisfies a performance obligation.

We have entered into an agreement ("Advanz Agreement") to license our intellectual property, or IP, related to Galactosemia and SORD to develop, manufacture and/or commercialize drug products with Mercury Pharma Group Limited, trading as Advanz Pharma Holdings, (“Advanz Pharma”). The agreement contains multiple performance obligations, including licenses of IP, research and development services, and the manufacturing and supply material right. Payments to us under this agreement may include nonrefundable fees, payments for research activities, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

The transaction price is the amount of consideration that we expect to be entitled to in exchange for transferring promised goods or services to the customer based on the contract terms at inception of a contract. We estimate an amount of variable consideration, if any, by using either the expected value or the most likely amount method depending on which method we expect to better predict the amount of consideration to which we will be entitled, and only to the extent that it is probable that that a significant reversal in the amount of cumulative revenue recognized will not occur in the future when the uncertainty is resolved. The determination of whether it is probable that a significant reversal of revenue will occur in the future depends on the likelihood and magnitude of the reversal. Factors that could increase the likelihood or magnitude of a reversal of revenue include (a) the susceptibility of the amount of consideration to factors outside the entity’s influence, such as the outcome of clinical trials, the timing of initiation of clinical trials by the counterparty and the approval of drug product candidates by regulatory agencies, (b) situations in which the uncertainty is not expected to be resolved for a long period of time, and (c) the level of the Company’s predictive experience in the field with similar types of contracts. At the end of each reporting period, we will update the estimated transaction price and allocate the updated consideration to the separate performance obligations in the same manner as described below.

At inception of a contract, we allocate the transaction price to the distinct performance obligations based upon their relative standalone selling prices. Standalone selling price is the price at which an entity would sell a promised good or service separately to a customer. The best evidence of standalone selling price is an observable price of a good or service when sold separately by an entity in similar circumstances to similar customers. Since we typically do not have such evidence, we estimate standalone selling price so that the amount that is allocated to each performance obligation equals the amount that we expect to receive for transferring the promised goods or services. The methods that the Company uses to make such estimates include (1) the adjusted market assessment approach, under which we forecast and analyze Galactosemia and SORD sales in the appropriate market, the phase of clinical development as well as considering recent similar license arrangements within the same phase of clinical development, therapeutic area, type of agreement, etc. and (2) the expected cost of satisfying the performance obligations plus a margin, or the expected cost plus a margin approach.

We recognize revenue when, or as, we satisfy a performance obligation by transferring a promised good or service to a customer and the customer obtains control of the good or service. Revenue related to the grant of a license of functional IP that is distinct from the other promised goods or services in the contract and therefore represents a performance obligation is recognized at the point in time that we have the right to payment for the license, the customer has legal title to the license and can direct the use of the license (for example, to grant sublicenses) to benefit from its right to use the intellectual property, the customer has the significant risks and rewards of ownership of the license and the customer has accepted the asset ("license") by signing the license agreement.

Recognition of revenue related to research and development services that are a distinct performance obligation is deferred at inception of a contract and is recognized as the services are performed to satisfy the performance obligation based on the costs incurred as a percentage of the estimated total costs to be incurred to satisfy the performance obligation. The Advanz Agreement requires that Advanz Pharma receive regular updates and data on any research and development services as the services are performed. In accordance with ASC 606-10-25-27, we determined that Advanz Pharma simultaneously benefits from the research and development services that are satisfied over time. We believe this method most faithfully depicts performance in transferring the promised services while research and development services are ongoing.

Contingencies

From time to time, we have been and may be party to various disputes and claims arising from normal business activities. We continually assesses litigation to determine if an unfavorable outcome would lead to a probable loss or reasonably possible loss which could be estimated. We accrue for all contingencies at the earliest date at which we deem it probable that a liability has been incurred and the amount of such liability can be reasonably estimated. If the estimate of a probable loss is a range and no amount within the range is more likely than another, we accrue the minimum of the range. In the cases where we believe that a reasonably possible loss exists, we discloses the facts and circumstances of the litigation, including an estimable range, if possible. Legal defense costs associated with loss contingencies are expensed in the period incurred.

Accrued Research and Development Expenses

We expense all costs incurred in performing research and development activities. Research and development expenses include materials and supplies, preclinical expenses, manufacturing expenses, contract services and other outside expenses. As part of the process of preparing our 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 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. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Research and development costs also include costs incurred in connection with certain licensing arrangements. Before a compound receives regulatory approval, we record upfront and milestone payments made by us to third parties under licensing arrangements as expense. Upfront payments are recorded when incurred, and milestone payments are recorded when the specific milestone has been achieved. Once a compound receives regulatory approval, we will record any milestone payments in Identifiable intangible assets, less accumulated amortization and, unless the asset is determined to have an indefinite life, we will amortize the payments on a straight-line basis over the remaining agreement term or the expected product life cycle, whichever is shorter.

Warrant Liabilities

We account for our common warrant liabilities by measuring the fair value at inception and are then subsequently measured on a recurring basis, with changes in fair value recognized in other income (expense) within our statement of operations.

We utilized a Black-Scholes option pricing model to estimate the fair value of our warrant liabilities, which utilizes certain unobservable inputs and is therefore considered a Level 3 fair value measurement. Certain inputs used in this Black-Scholes pricing model may fluctuate in future periods based upon factors that are outside of our control, including a potential change in control. A significant change in one or more of these inputs used in the calculation of the fair value may cause a significant change to the fair value of our warrant liabilities, which could also result in material non-cash gains or losses being reported in the Company’s statement of operations.

The inputs we utilized to value our warrant liabilities are highly subjective. The assumptions used in calculating the fair value of our warrant liabilities represent our best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, the fair value of the warrant liabilities may be materially different in the future.

Stock-Based Compensation

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

Stock-Based Compensation–Stock Options

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.We have based our estimate of expected volatility on our historical volatility. Our historical volatility is calculated based on a period of time commensurate with the expected term assumption.We use the simplified method as allowed by the SEC Staff Accounting Bulletin No.107, Share-Based Payment, to calculate the expected term for options granted 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. Forfeitures are recognized as a reduction of stock-based compensation expense as they occur.

Stock-Based Compensation–Restricted Stock Units

We account for restricted stock units in accordance with the authoritative guidance for stock-based compensation. The fair value of restricted stock units is measured at the grant date based on the closing market price of our common stock on the date of grant and is recognized as expense on a straight-line basis over the period of vesting. Forfeitures are recognized as a reduction of stock-based compensation expense as they occur.

Stock-Based Compensation–Employee Stock Purchase Plan

We estimate the grant-date fair value of stock to be issued under our Employee Stock Purchase plan ("ESPP") using the Black-Scholes model. The fair value of ESPP is recognized as expense over the requisite service period which is generally the offering period.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Recently Issued Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 1 to our financial statements appearing elsewhere in this Annual Report.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities and foreign currency sensitivities.

Interest Rate Sensitivity

Our exposure to market risk relates to our cash and cash equivalents of $79.4 million as of December 31, 2024. The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive without significantly increasing risk. Some of the financial instruments in which we invest could be subject to market risk where the interest rates may cause the value of the instruments to fluctuate. To minimize this risk, we intend

to maintain a portfolio which may include cash, cash equivalents and short-term investment securities available-for-sale in a variety of securities.

We do not believe that our cash has significant risk of default or illiquidity. While we believe our cash and cash equivalents does not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash at one or more financial institutions that are in excess of federally insured limits. Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations during the periods presented.

Foreign Currency Sensitivity

Our primary operations are transacted in U.S. Dollars, however, certain service agreements with third parties are denominated in currencies other than the U.S. Dollar, primarily the Euro. As such, we are subject to foreign exchange risk and therefore, fluctuations in the value of the U.S. Dollar against the Euro may impact the amounts reported for expenses and obligations incurred under such agreements. We do not participate in any foreign currency hedging activities and we do not have any other derivative financial instruments. We did not recognize any significant exchange rate loss during the year ended December 31, 2024. A hypothetical 10% change in foreign exchange rates during any of the periods presented would not have a material impact on our financial condition or results of operations.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

The information required by this item is set forth in the financial statements filed with this report and are herein incorporated by reference.

Report of Independent Registered Public Accounting Firm

The Stockholders and the Board of Directors of Applied Therapeutics, Inc.

Opinion on the Financial Statements

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

The Company's Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations, will require additional capital to fund operations, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

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

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the

critical audit matter below, providing a separate opinion on the critical audit matter or on the account or disclosure to which it relates.

Valuation of liability-classified warrants

Description of the Matter	As discussed in Note 8 to the financial statements, the Company has issued warrants to purchase shares of its common stock in connection with financing activities. The Company accounts for certain warrants as liabilities on the balance sheet that are measured at fair value at inception and re-measured at fair value on a recurring basis. The Company's warrant liability as of December 31, 2024 totaled $6.3 million, and expense of $4.8 million was recognized in the statement of operations during the year ended December 31, 2024 for changes in the fair value of liability-classified warrants. The fair value of the liability-classified warrants was estimated using a Black-Scholes model that utilized various assumptions, including expected term, volatility, risk free rate, expected dividend yield, and the probability of a change in control. Auditing the fair value of the warrant liability was challenging due to the judgmental nature of selecting an appropriate valuation model and the model's assumptions, especially expected volatility and the probability of a change in control. These assumptions are highly subjective and require the evaluation of possible future events. Further, the identified material weakness relating to the Company's information and communication affected the liability-classified warrants and our audit procedures.
How We Addressed the Matter in Our Audit	To test the Company's estimate of fair value of the liability-classified warrants, our audit procedures included, among others, assessing the Company's use of the Black-Scholes model, involving our valuation specialists to assist in evaluating the appropriateness of the use of the model and the accuracy of the underlying calculation. We also tested the significant assumptions described above used to estimate the fair value and tested the completeness and accuracy of the underlying data. For the volatility assumption, we compared the Company's estimated volatility to the historical equity volatility of the Company with a lookback term commensurate with the remaining term of the warrants. We also compared the Company's volatility assumption to the implied volatility based on the longest dated traded or quoted Company share options. We assessed the Company's estimated probability of a change in control through various procedures which included performing inquiries with Company executives and members of the Board of Directors and assessing consistency of the information with evidence obtained in other areas of our audit. We also performed sensitivity analyses on the key assumptions. The nature and extent of our audit procedures considered the material weakness described above.

We have served as the Company's auditor since 2017.

New York, New York
April 14, 2025

Applied Therapeutics, Inc.

Balance Sheets

(in thousands except share and per share data)

	As of December 31, 2024	As of December 31, 2023
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 79,398	$ 49,898
Current portion of security deposits	—	254
Prepaid expenses and other current assets	4,248	4,234
Total current assets	83,646	54,386
Noncurrent portion of security deposits	253	—
Operating lease right-of-use asset	2,792	447
TOTAL ASSETS	$ 86,691	$ 54,833
LIABILITIES AND STOCKHOLDERS'EQUITY/(DEFICIT)		
CURRENT LIABILITIES:		
Current portion of operating lease liabilities	$ 406	$ 429
Accounts payable	4,433	1,742
Accrued expenses and other current liabilities	16,143	15,286
Warrant liabilities	6,314	53,725
Total current liabilities	27,296	71,182
NONCURRENT LIABILITIES:		
Noncurrent portion of operating lease liabilities	2,389	38
Clinical holdback - long-term portion	—	759
Total noncurrent liabilities	2,389	797
Total liabilities	29,685	71,979
Commitments and Contingencies (Note 15)		
STOCKHOLDERS' EQUITY/(DEFICIT):		
Common stock, $0.0001 par value; 250,000,000 shares authorized as of December 31, 2024 and 200,000,000 shares authorized as of December 31, 2023; 137,228,741 shares issued and outstanding as of December 31, 2024 and 84,869,832 shares issued and outstanding as of December 31, 2023	35	8
Preferred stock, par value $0.0001; 10,000,000 shares authorized as of December 31, 2024 and December 31, 2023; 0 shares issued and outstanding as of December 31, 2024 and December 31, 2023	—	—
Additional paid-in capital	631,181	451,432
Accumulated deficit	(574,210)	(468,586)
Total stockholders' equity/(deficit)	57,006	(17,146)
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY/(DEFICIT)	$ 86,691	$ 54,833

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statements of Operations

(in thousands except share and per share data)

	Year Ended December 31,	
	2024	**2023**
REVENUE:		
License revenue	$ —	$ 9,219
Research and development services revenue	455	774
Total revenue	455	9,993
COSTS AND EXPENSES:		
Research and development	48,744	53,905
General and administrative	56,010	20,623
Total costs and expenses	104,754	74,528
LOSS FROM OPERATIONS	(104,299)	(64,535)
OTHER INCOME (EXPENSE), NET:		
Interest income	3,534	1,372
Change in fair value of warrant liabilities	(4,782)	(56,573)
Other expense	(77)	(27)
Total other expense, net	(1,325)	(55,228)
Net loss	$ (105,624)	$ (119,763)
Net loss per share attributable to common stockholders—basic and diluted	$ (0.76)	$ (1.42)
Weighted-average common stock outstanding—basic and diluted	139,534,746	84,244,494

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statements of Comprehensive Loss

(in thousands)

	Year Ended December 31,	
	2024	**2023**
Net Loss	$ (105,624)	$ (119,763)
Other comprehensive loss		
Unrealized loss on marketable securities	—	(51)
Other comprehensive loss, net of tax	—	(51)
Comprehensive loss, net of tax	$ (105,624)	$ (119,814)

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statements of Stockholders' Equity (Deficit)

(in thousands, except share and per share data)

	Common Stock		Treasury Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
BALANCE, December 31, 2022	48,063,358	$ 5	—	$ —	$ 352,828	$ (348,823)	$ 51	$ 4,061
Exchange of common stock for prefunded warrants	—	—	5,658,034	(12,900)	12,900	—	—	—
Issuance of common stock, prefunded warrants and reissuance of treasury stock, net of issuance costs of $4.0 million	21,693,673	2	(5,658,034)	12,900	51,500	—	—	64,402
Exercise of common warrants	10,250,000	1	—	—	26,754	—	—	26,755
Exercise of pre-funded warrants	4,250,000	—	—	—	—	—	—	—
Exercise of stock options	85,619	—	—	—	90	—	—	90
Restricted stock units released for common issued under Equity Incentive Plan	527,182	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	7,360	—	—	7,360
Net loss	—	—	—	—	—	(119,763)	—	(119,763)
Other comprehensive income (loss)	—	—		—	—	—	(51)	(51)
BALANCE, December 31, 2023	84,869,832	8	—	—	451,432	(468,586)	—	(17,146)
Issuance of common stock and pre-funded warrants, net of issuance costs of $8.2 million	15,285,714	2	—	—	104,746	—	—	104,748
Exercise of common warrants	9,025,000	1	—	—	61,217	—	—	61,218
Exercise of pre-funded warrants	26,441,577	24	—	—	(24)	—	—	—
Exercise of stock options	327,492	—	—	—	343	—	—	343
Restricted stock units released for common stock issued under Equity Incentive Plan	1,279,126	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	13,467	—	—	13,467
Net loss	—	—		—	—	(105,624)	—	(105,624)
BALANCE, December 31, 2024	137,228,741	$ 35	—	$ —	$ 631,181	$ (574,210)	$ —	$ 57,006

The Notes to Financial Statements are an integral part of these statements.

Applied Therapeutics, Inc.

Statements of Cash Flows

(in thousands)

	Year Ended December 31,	
	2024	2023
OPERATING ACTIVITIES:		
Net loss	$ (105,624)	$ (119,763)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	13,467	7,360
Amortization of insurance premium	566	2,111
Amortization of operating lease right-of-use assets	425	353
Amortization of leasehold improvements	1	1
Change in net operating lease liability	(442)	(367)
Change in fair value of warrant liabilities	4,782	56,573
Changes in operating assets and liabilities:		
Financed insurance premium	—	(1,546)
Prepaid expenses	(580)	1,872
Accounts payable	2,691	(2,792)
Accrued expenses and other current liabilities	1,168	730
Other liabilities	(759)	295
Net cash used in operating activities	(84,305)	(55,173)
INVESTING ACTIVITIES:		
Proceeds from sale of available-for-sale securities	—	4,944
Proceeds from maturities of available-for-sale securities	—	8,928
Net cash provided by investing activities	—	13,872
FINANCING ACTIVITIES:		
Proceeds from issuance of common stock, pre-funded warrants and reissuance of treasury stock, net of issuance costs	104,748	64,514
Proceeds from financed insurance premium	—	1,546
Repayments of short-term borrowings	(311)	(1,858)
Exercise of stock options for common stock under Equity Incentive Plan	343	90
Exercise of Warrants	9,025	10,250
Net cash provided by financing activities	113,805	74,542
NET INCREASE IN CASH AND CASH EQUIVALENTS	29,500	33,241
Cash and cash equivalents at beginning of period	49,898	16,657
Cash and cash equivalents at end of period	$ 79,398	$ 49,898
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:		
Operating lease right-of-use asset obtained in exchange for operating lease liabilities	$ 2,770	$ (57)
Offering costs in accrued expenses	$ —	$ 112
Conversion of warrant liabilities to equity for warrant exercises	$ 52,193	$ 16,505
Unrealized gain (loss) on marketable securities	$ —	$ (51)

The Notes to Financial Statements are an integral part of these statements.

NOTES TO AUDITED FINANCIAL STATEMENTS

1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Operations and Business

Applied Therapeutics, Inc. (the "Company") is a clinical-stage biopharmaceutical company developing a pipeline of novel product candidates against validated molecular targets in indications of high unmet medical need. In particular, the Company is currently targeting treatments for rare metabolic diseases such as Galactosemia, Sorbitol Dehydrogenase ("SORD") deficiency, and diabetic complications including diabetic cardiomyopathy. The Company was incorporated in Delaware on January 20, 2016 and is headquartered in New York, New York.

Basis of Presentation

The Company's fiscal year ends on December 31 and its first three quarters end on March 31, June 30 and September 30. The accompanying financial statements are prepared in conformity with accounting principles generally accepted in the United States of America ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Liquidity and Going Concern

Under ASC Topic 205-40, *Presentation of Financial Statements - Going Concern*, management is required at each reporting period to evaluate whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity's ability to continue as a going concern within one year after the date that the financial statements are issued. In making its assessment, management considered the Company's current financial condition and liquidity sources including current funds available, forecasted future cash flows and condition and unconditional obligations due over the next twelve months. As of December 31, 2024, financing through the Company's March 2024 Private Placement, Leerink ATM Agreement and warrant exercises has resulted in net proceeds of $113.8 million, after deducting placement agent commissions and other offering expenses (see Note 7 and Note 8). The Company continues to actively pursue several potential long-term financing options, including equity capital, debt, convertible debt, and synthetic royalty financing. Additionally, the Company is in active dialogue with several potential partners regarding business development opportunities related to one or more of its programs. There can be no assurances that the Company's discussions with any of the current counterparties will be successful, and the Company expects to continue to pursue additional opportunities.

As reflected in the accompanying financial statements, the Company incurred a net loss of $105.6 million for the year ended December 31, 2024 and has an accumulated deficit of $574.2 million as of December 31, 2024. The exclusive licensing agreement with Advanz Pharma for commercialization rights to AT-007 in Europe may provide additional source of capital to the Company after the potential resubmission of NDA and the marketing authorization application in Europe. However, there are no guarantees that this will materialize timely or at all, and delays or unexpected data could disrupt this potential source of liquidity. Broadly, the Company has not yet established an ongoing source of revenues sufficient to cover its operating costs and is dependent on debt and equity financing to fund its operations. As of December 31, 2024, the Company has cash and cash equivalents of $79.4 million. Given the Company's planned expenditures for the next twelve months, the Company concluded that substantial doubt exists regarding its ability to continue as a going concern within one year after the date these audited financial statements are issued. The accompanying financial statements have been prepared on a going concern basis, which contemplates the realization of assets and satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts or the amounts and classification of liabilities that might result from the outcome of this uncertainty.

Risks and Uncertainties

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, risks of failure of preclinical studies and clinical trials, the need to obtain marketing approval for any product candidate that it may identify and develop, the need to successfully commercialize and gain market acceptance of its

product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and reliance on third-party manufacturers.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities and the Company's ability to continue as a going concern as of the date of the financial statements and the reported amounts of revenue and expenses during the reporting period. In preparing the financial statements, management used estimates in the following areas, among others: prepaid and accrued expenses; warrant liabilities valuation; license revenue; research and development services revenue; stock-based compensation expense; the likelihood of realization of deferred tax assets; and the evaluation of the existence of conditions and events that raise substantial doubt regarding the Company’s ability to continue as a going concern. Actual results could differ from those estimates.

Significant Accounting Policies

Fair Value Measurements

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

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

Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

Cash and Cash Equivalents

The Company considers all short-term, highly liquid investments, with an original maturity of three months or less at the date of purchase, to be 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 these accounts and does not believe it is exposed to any significant credit risk on cash and cash equivalents.

Leases

At the inception of an arrangement, the Company determines if an arrangement is, or contains, a lease based on the unique facts and circumstances present in that arrangement. Lease classification, recognition, and measurement are then determined at the lease commencement date. For arrangements that contain a lease the Company (i) identifies lease and non-lease components, (ii) determines the consideration in the contract, (iii) determines whether the lease is an operating or financing lease; and (iv) recognizes lease right-of-use (“ROU”) assets and liabilities. Lease liabilities and their corresponding ROU assets are recorded based on the present value of lease payments over the expected lease term. The interest rate implicit in lease contracts is typically not readily determinable and as such, the Company uses its incremental borrowing rate based on the information available at the lease commencement date, which represents an internally developed rate that would be incurred to borrow, on a collateralized basis, over a similar term, an amount equal to the lease payments in a similar economic environment.

Most leases include options to renew and, or, terminate the lease, which can impact the lease term. The exercise of these options is at the Company's discretion and the Company does not include any of these options within the expected lease term as the Company is not reasonably certain it will exercise these options. The Company has elected to combine lease components (for example fixed payments including rent) with non-lease components (for example, non-dedicated parking and common-area maintenance costs) on our real estate asset classes.

Fixed, or in substance fixed, lease payments on operating leases are recognized over the expected term of the lease on a straight-line basis. Fixed lease expense on operating leases is recognized within operating expenses within the statements of operations. The Company has operating leases for its corporate offices. The Company has elected the short-term lease exemption and, therefore, does not recognize a ROU asset or corresponding liability for lease arrangements with an original term of 12 months or less. Leasehold improvements and assets under financing lease arrangements are amortized over the lesser of the asset's estimated useful life or the term of the respective lease. Maintenance costs are expensed as incurred.

Operating leases are included in operating lease right-of-use asset, current portion of operating lease liabilities, and noncurrent portion of operating lease liabilities in the balance sheets as of December 31, 2024 and 2023.

Contingencies

The Company, from time to time, has been and may be a party to various disputes and claims arising from normal business activities. The Company continually assesses litigation to determine if an unfavorable outcome would lead to a probable loss or reasonably possible loss which could be estimated. The Company accrues for all contingencies at the earliest date at which the Company deems it probable that a liability has been incurred and the amount of such liability can be reasonably estimated. If the estimate of a probable loss is a range and no amount within the range is more likely than another, the Company accrues the minimum of the range. In the cases where the Company believes that a reasonably possible loss exists, the Company discloses the facts and circumstances of the litigation, including an estimable range, if possible. Legal defense costs associated with loss contingencies are expensed in the period incurred.

Clinical hold-back, long-term

As part of the regulatory approval process for taking its products to market, the Company enters into certain Clinical Trial Agreements (CTAs) which include, among other things, the compensation and payment schedule the participating medical institutions and physicians will receive for all costs in connection with the clinical trial (or study) under the terms of the CTA. As individual patients are enrolled in the study by the participating medical institution or physician, the Company pays certain per study fees according to the CTA for the duration of the trial. As invoices are received by the Company from the medical institution or physician, the Company retains an agreed upon percentage of total invoiced costs, generally ranging between 5% - 10%, that is withheld from payment until the end of the study.

These retained amounts are recorded as clinical holdback, a liability, on the accompanying balance sheets, and all expenses incurred in connection with these CTA activities are expensed as services are provided, which are included as research and development expenses on the accompanying statements of operations.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in the statement of stockholders' equity (deficit) as a reduction of proceeds generated as a result of the offering. Should a planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the statement of operations.

As of December 31, 2024 and 2023, the Company did not have any deferred offering costs recorded.

Warrant Liabilities

The Company accounts for common warrant liabilities by measuring the fair value at inception and subsequently remeasuring on a recurring basis, with changes in fair value recognized in other income (expense) within the Company's statement of operations.

The Company utilized a Black-Scholes option pricing model to estimate the fair value of the warrant liabilities, which utilizes certain unobservable inputs and is therefore considered a Level 3 fair value measurement. Certain inputs used in the Black-Scholes pricing model may fluctuate in future periods based upon factors that are outside of the Company's control, including a potential change in control outside of the Company's control. A significant change in one or more of these inputs used in the calculation of the fair value may cause a significant change to the fair value of the Company's warrant liabilities, which could also result in material non-cash gains or losses being reported in the Company's consolidated statement of operations.

The inputs utilized to value the warrant liabilities are highly subjective. The assumptions used in calculating the fair value of the warrant liabilities represent the best estimates, but these estimates involve inherent uncertainties and application of management's judgment. As a result, if factors change and the Company uses different assumptions, the fair value of the warrant liabilities may be materially different in the future.

Treasury Stock

The Company records treasury stock activities under the cost method. Treasury stock is included in authorized and issued shares but excluded from outstanding shares. The re-issuance of treasury stock is accounted for on a first in, first-out basis and any differences between the cost of treasury stock and the re-issuance proceeds are charged or credited to additional paid-in capital.

Revenue Recognition

Under ASU 2014-09, *Revenue from Contracts with Customers (Topic 606)*, or ASC 606, as amended by ASU 2016-08, 2016-10, 2016-12 and 2016-20, the Company recognizes revenue in an amount that reflects the consideration to which it expects to be entitled in exchange for the transfer of promised goods or services to customers. To determine revenue recognition for contracts with customers that are within the scope of ASC 606, the Company performs the following steps: (1) identifies the contract with the customer, (2) identifies the performance obligations in the contract, (3) determines the transaction price, (4) allocates the transaction price to the performance obligations in the contract, and (5) recognizes revenue when (or as) the entity satisfies a performance obligation.

The Company has entered into an agreement to license its intellectual property, or IP, related to Galactosemia and SORD to develop, manufacture and/or commercialize drug products with Mercury Pharma Group Limited, trading as Advanz Pharma Holdings, ("Advanz Pharma"). The agreement contains multiple performance obligations, including licenses of IP, research and development services, and the manufacturing and supply material right. Payments to the Company under this agreement may include nonrefundable fees, payments for research activities, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

The Company identifies agreements as contracts that create enforceable rights and obligations when the agreement is approved by the parties, the Company can identify the rights of the parties and the payment terms, the contract has commercial substance and it is probable that the Company will collect substantially all of the consideration to which it will be entitled in exchange for the goods and services that will be transferred to the customer. The counterparty is considered to be a customer when it has contracted with the Company to obtain goods and services that are the output of the Company's ordinary activities (i.e., development of pharmaceutical products) in exchange for consideration.

A performance obligation is a promise to transfer distinct goods or services to a customer. Performance obligations that are both capable of being distinct and distinct within the context of the contract are considered to be separate performance obligations. Performance obligations are capable of being distinct if the counterparty is able to benefit from the good or service on its own or together with other resources that are readily available to it. Performance obligations are distinct within the context of the contract when each performance obligation is separately identifiable. In assessing whether the Company's promises to transfer goods or services to the customer are separately identifiable, the

Company considers factors in ASC 606, including whether the Company uses the goods or services as inputs to produce or deliver a combined output or outputs specified by the customer, whether one or more of the goods or services significantly modify or customize one of the other goods or services in the contract, and whether the goods or services are highly interdependent or highly interrelated. If a promised good or service is not distinct, it is combined with other promised goods or services until the Company identifies a bundle of goods or services that is distinct, which is accounted for as a single performance obligation. The determination of whether promised goods or services in a contract are distinct may require significant judgment.

The transaction price is the amount of consideration that the Company expects to be entitled to in exchange for transferring promised goods or services to the customer based on the contract terms at inception of a contract. The Company estimates an amount of variable consideration, if any, by using either the expected value or the most likely amount method depending on which method the Company expects to better predict the amount of consideration to which it will be entitled, and only to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur in the future when the uncertainty is resolved. The determination of whether it is probable that a significant reversal of revenue will occur in the future depends on the likelihood and magnitude of the reversal. Factors that could increase the likelihood or magnitude of a reversal of revenue include (a) the susceptibility of the amount of consideration to factors outside the entity's influence, such as the outcome of clinical trials, the timing of initiation of clinical trials by the counterparty and the approval of drug product candidates by regulatory agencies, (b) situations in which the uncertainty is not expected to be resolved for a long period of time, and (c) the level of the Company's predictive experience in the field with similar types of contracts. At the end of each reporting period, the Company will update the estimated transaction price and allocate the updated consideration to the separate performance obligations in the same manner as described below.

At inception of a contract, the Company allocates the transaction price to the distinct performance obligations based upon their relative standalone selling prices. Standalone selling price is the price at which an entity would sell a promised good or service separately to a customer. The best evidence of standalone selling price is an observable price of a good or service when sold separately by an entity in similar circumstances to similar customers. Since the Company typically does not have such evidence, it estimates standalone selling price so that the amount that is allocated to each performance obligation equals the amount that the Company expects to receive for transferring the promised goods or services. The methods that the Company uses to make such estimates include (1) the adjusted market assessment approach, under which the Company forecasts and analyzes Galactosemia and SORD sales in the appropriate market, the phase of clinical development as well as considering recent similar license arrangements within the same phase of clinical development, therapeutic area, type of agreement, etc. and (2) the expected cost of satisfying the performance obligations plus a margin, or the expected cost plus a margin approach.

The Company recognizes revenue when, or as, it satisfies a performance obligation by transferring a promised good or service to a customer and the customer obtains control of the good or service. Revenue related to the grant of a license of functional IP that is distinct from the other promised goods or services in the contract and therefore represents a performance obligation is recognized at the point in time that the Company has the right to payment for the license, the customer has legal title to the license and can direct the use of the license (for example, to grant sublicenses) to benefit from its right to use the intellectual property, the customer has the significant risks and rewards of ownership of the license and the customer has accepted the asset (license) by signing the license agreement.

Recognition of revenue related to research and development services that are a distinct performance obligation is deferred at inception of a contract and is recognized as the services are performed to satisfy the performance obligation based on the costs incurred as a percentage of the estimated total costs to be incurred to satisfy the performance obligation. The Agreement requires that Advanz Pharma receives regular updates and data on any research and development services as the services are performed. In accordance with ASC 606-10-25-27, the Company determined that Advanz Pharma simultaneously benefits from the research and development services that are satisfied over time. The Company believes this method most faithfully depicts its performance in transferring the promised services while research and development services are ongoing.

Milestone payments are considered to be variable consideration and are not included in the transaction price at inception of the contract if it is uncertain that the milestone will be achieved. Rather, when it becomes probable that the milestone will be achieved and, therefore, there will not be a significant reversal of revenue in future periods, the respective amount to be earned is included in the transaction price, allocated to the distinct performance obligations

based on their relative standalone selling price and recognized as revenue, as described above. Sales based milestones and sales-based royalty payments related to a license of IP are recognized as revenue when the respective sales occur.

Research and Development

The Company expenses all costs incurred in performing research and development activities. Research and development expenses include salaries and other related costs, materials and supplies, preclinical expenses, manufacturing expenses, contract services and other outside expenses. As part of the process of preparing the financial statements, the Company is required to estimate accrued research and development expenses. The Company makes estimates of the accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known at that time. In addition, there may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense in which case such amounts are reflected as prepaid expenses and other current assets. In accruing service fees, the Company estimates 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, the Company adjusts the accrual or the amount of prepaid expenses accordingly. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized in prepaid expenses and other current assets. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

Research and development costs also include costs incurred in connection with certain licensing arrangements. Before a compound receives regulatory approval, the Company records upfront and milestone payments made to third parties under licensing arrangements as expense. Upfront payments are recorded when incurred, and milestone payments are recorded when the specific milestone has been achieved. Once a compound receives regulatory approval, the Company will record any milestone payments in identifiable intangible assets, less accumulated amortization and, unless the asset is determined to have an indefinite life, the Company will amortize the payments on a straight-line basis over the remaining agreement term or the expected product life cycle, whichever is shorter.

General and Administrative

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in the Company's 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.

Commercial expenses consist of payroll expense for commercial personnel, as well as marketing, market research, market access, and other focused investments to support launch of drug candidates, generate evidence of commercial potential and value proposition, and maximize potential business development deal leverage. Commercial expenses are included in general and administrative expenses.

Stock-Based Compensation

The Company accounts for its stock-based compensation as expense in the statements of operations based on the awards' grant date fair values. The Company accounts for forfeitures as they occur by reversing any expense recognized for unvested awards.

Stock-Based Compensation–Stock Options

The Company estimates 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. The Company has based its estimate of expected volatility on the Company's historical volatility. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The Company uses the simplified method as allowed by the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin ("SAB") No. 107, *Share-Based Payment*, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The risk-free interest rate is 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 the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

The fair value of stock-based payments is recognized as expense over the requisite service period which is generally the vesting period. Forfeitures are recognized as a reduction of stock-based compensation expense as they occur.

Stock-Based Compensation–Restricted Stock Units

The Company accounts for restricted stock units in accordance with the authoritative guidance for stock-based compensation. The fair value of restricted stock units is measured at the grant date based on the closing market price of the Company's common stock on the date of grant and is recognized as expense on a straight-line basis over the period of vesting. Forfeitures are recognized as a reduction of stock-based compensation expense as they occur.

Stock-Based Compensation–Employee Stock Purchase Plan

The Company estimates the grant-date fair value of stock to be issued under the Company's Employee Stock Purchase plan (ESPP) using the Black-Scholes model. The fair value of ESPP is recognized as expense over the requisite service period which is generally the offering period.

Income Taxes

The Company uses the asset and liability method of accounting for deferred income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities at currently enacted tax rates. These temporary differences primarily relate to net operating loss carryforwards available to offset future taxable income. Valuation allowances are established, if necessary, to reduce a deferred tax asset to the amount that will more likely than not be realized.

The Company recognizes tax liabilities from an uncertain tax position only if it is more likely than not that the tax position will not be sustained upon examination by the taxing authorities, based on the technical merits of the tax position. There are no uncertain tax positions that have been recognized in the accompanying financial statements. The Company is required to file tax returns in the U.S. federal jurisdiction and in the state of New York. The Company's policy is to recognize interest and penalties related to uncertain tax benefits, if any, as part of income tax expense. No such interest and penalties have been accrued as of December 31, 2024 and 2023.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss available to common stockholders by the weighted-average common stock outstanding. Diluted net loss per share is calculated similarly, except that it includes the dilutive effect of the assumed exercise of securities, including outstanding warrants and the effect of shares issuable under the Company's stock-based compensation plan, if such effect is dilutive.

Segment Information

The Company operates in one operating segment for the purposes of assessing performance, making operating decisions, and allocating Company resources. The Company's chief operating decision maker (CODM) is its interim chief executive officer, who considers net loss to evaluate overall expenses associated with conducting research and development activities, which includes evaluating the progress of ongoing clinical trials and the planning and execution of current and future research and development activities. Further, the CODM reviews and utilizes functional expenses

(research and development and general and administrative) as reported in the statements of operations to manage the Company's operations.

Recent Accounting Pronouncements

Any recent pronouncements issued by the FASB or other authoritative standards groups with future effective dates are either not applicable or are not expected to be significant to the financial statements of the Company, unless otherwise discussed.

In November 2023, the FASB issued ASU 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures, which expands annual and interim disclosure requirements for reportable segments, including public entities with a single reportable segment, primarily through enhanced disclosures about significant segment expenses. The Company adopted this standard for the Company's fiscal year 2024 annual reporting period. The adoption of ASU 2023-07 did not have a material impact on the financial statements for the year ended December 31, 2024.

2. LICENSE AGREEMENTS

Columbia University

In October 2016, the Company entered into a license agreement (the "2016 Columbia Agreement") with the Trustees of Columbia University ("Columbia University") to obtain an exclusive royalty-bearing sublicensable license in respect to certain patents. As part of the consideration for entering into the 2016 Columbia Agreement, the Company issued to Columbia University shares equal to 5% of its outstanding common stock on a fully diluted basis at the time of issue. The common stock had a fair value of $0.5 million at the time of issuance. The Company will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2016 Columbia Agreement. The Company will also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on the Company's, its affiliates' and its sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, the Company is required to make specified annual minimum royalty payments to Columbia University, which is contingent upon the approval of the licensed products, in the mid-six figures beginning on the 10th anniversary of the effective date of the 2016 Columbia Agreement. When the Company grants sublicenses under the 2016 Columbia Agreement, the Company will be required to pay Columbia University a portion of the net sublicensing revenue received from such third parties, at percentages between 10% and 20%, depending on the stage of development at the time such revenue is received from such third parties. The Advanz Agreement includes a sublicense under the 2016 Columbia Agreement.

The 2016 Columbia Agreement will terminate upon the expiration of all the Company's royalty payment obligations in all countries. The Company may terminate the 2016 Columbia Agreement for convenience upon 90 days' written notice to Columbia University. At its election, Columbia University may terminate the 2016 Columbia Agreement, or convert the licenses granted to the Company into non-exclusive, non-sublicensable licenses, in the case of (a) the Company's uncured material breach upon 30 days' written notice (which shall be extended to 90 days if the Company is diligently attempting to cure such material breach), (b) the Company's failure to achieve the specified development and funding milestone events, or (c) the Company's insolvency.

In January 2019, the Company entered into a second license agreement with Columbia University (the "2019 Columbia Agreement"). Pursuant to the 2019 Columbia Agreement, Columbia University granted the Company a royalty-bearing, sublicensable license that is exclusive with respect to certain patents, and non-exclusive with respect to certain know-how, in each case to develop, manufacture and commercialize PI3k inhibitor products. The license grant is worldwide. Under the 2019 Columbia Agreement, the Company is obligated to use commercially reasonable efforts to research, discover, develop and market licensed products for commercial sale in the licensed territory, and to comply with certain obligations to meet specified development and funding milestones within defined time periods. Columbia University retains the right to conduct, and grant third parties the right to conduct, non-clinical academic research using the licensed technology; provided that such research is not funded by a commercial entity or for-profit entity or results in rights granted to a commercial or for-profit entity. As consideration for entering into the 2019 Columbia Agreement, the Company made a nominal upfront payment to Columbia University. The Company will be required to make further payments to Columbia University of up to an aggregate of $1.3 million for the achievement of specified development and regulatory milestones, and up to an aggregate of $1.0 million for the achievement of a specified level of aggregate annual net sales, in each case in connection with products covered by the 2019 Columbia Agreement. The Company will also be required to pay tiered royalties to Columbia University in the low- to mid-single digit percentages on the Company's, its affiliates' and its sublicensees' net sales of licensed products, subject to specified offsets and reductions. In addition, the Company is required to make specified annual minimum royalty payments to Columbia University, which is contingent upon the approval of the licensed products, in the mid-six figures beginning on the tenth anniversary of the effective date of the 2019 Columbia Agreement.

In July 2022, following regulatory changes impacting development of the class of PI3k inhibitors and the Company's decision to discontinue its early stage preclinical PI3k program, the Company and Columbia entered into an agreement terminating the 2019 Columbia Agreement (the "2022 Columbia Termination Agreement") as of July 25, 2022. Under the terms of the 2022 Columbia Termination Agreement, the Company assigned certain regulatory documents regarding the preclinical PI3k inhibitor AT-104 to Columbia and granted Columbia a non-exclusive royalty free license (with rights to sublicense any future Columbia licensee) under certain know-how, technical information and data relating to AT-104 that was developed by the Company during the term of the 2019 Columbia Agreement.

In March 2019, and in connection with the 2016 Columbia Agreement, the Company entered into a research services agreement (the "2019 Columbia Research Agreement") with Columbia University with the purpose of analyzing structural and functional changes in brain tissue in an animal model of Galactosemia, and the effects of certain compounds whose intellectual property rights were licensed to the Company as part of the 2016 Columbia Agreement on any such structural and functional changes. The 2019 Columbia Research Agreement had a term of 12 months from its effective date and expired in accordance with its terms.

On October 3, 2019, and in connection with the 2019 Columbia Agreement, the Company entered into a research services agreement (the "PI3k Columbia Research Agreement" and collectively with the 2016 Columbia Agreement, 2019 Columbia Agreement and 2019 Columbia Research Agreement, the "Columbia Agreements") with Columbia University with the purpose of analyzing PI3k inhibitors for the treatment of lymphoid malignancies. The PI3k Columbia Research Agreement had a term of 18 months from its effective date and expired in accordance with its terms.

During the years ended December 31, 2024 and 2023, the Company recorded $0.3 million and $0.2 million, respectively, in expense related to the Columbia Agreements. In aggregate, the Company has incurred $3.2 million in expense from the execution of the Columbia Agreements through December 31, 2024.

As of December 31, 2024 and 2023, the Company had $16,000 and $29,000, respectively, due to Columbia University included in accrued expenses and no amounts included in accounts payable.

University of Miami

2020 Miami License Agreement

On October 28, 2020, the Company entered into a license agreement with the University of Miami (the "2020 Miami License Agreement") relating to certain technology that is co-owned by the University of Miami (UM), the University of Rochester (UR) and University College London (UCL). UM was granted an exclusive agency from UR and UCL to license each of their rights in the technology. Pursuant to the 2020 Miami License Agreement, UM, on

behalf of itself and UR and UCL, granted the Company a royalty-bearing, sublicensable license that is exclusive with respect to certain patent applications and patents that may grant from the applications, and non-exclusive with respect to certain know-how, in each case to research, develop, make, have made, use, sell and import products for use in treating and/or detecting certain inherited neuropathies, in particular those caused by mutation in the sorbitol dehydrogenase (SORD) gene. The license grant is worldwide. Under the 2020 Miami License Agreement, the Company is obligated to use commercially reasonable efforts to develop, manufacture, market and sell licensed products in the licensed territory, and to comply with certain obligations to meet specified development milestones within defined time periods. UM retains for itself, UR, and UCL the right to use the licensed patent rights and licensed technology for their internal non-commercial educational, research and clinical patient care purposes, including in sponsored research and collaboration with commercial entities.

Under the terms of the 2020 Miami License Agreement, the Company was obligated to pay UM an up-front non-refundable license fee of $1.1 million, and a second non-refundable license fee of $0.5 million due on the first anniversary of the date of the license. The Company will be required to make further payments to UM of up to an aggregate $2.2 million for the achievement of specified patenting and development milestones, and up to an aggregate of $4.1 million for achievement of late stage regulatory milestones. The Company will also be required to pay royalties ranging from 0.88% - 5% on the Company's, the Company's affiliates' and the Company's sublicensees' net sales of licensed products. When the Company sublicenses the rights granted under the 2020 Miami License Agreement to one or more third parties, the Company will be required to pay to UM a portion of the non-royalty sublicensing revenue received from such third parties ranging from 15% – 25%. The Advanz Agreement includes a sublicense under the 2020 Miami License Agreement.

The 2020 Miami License Agreement terminates upon the expiration of all issued patents and filed patent applications or 10 years after the first commercial sale of the last product or process for which a royalty is due, unless earlier terminated. In addition, the 2020 Miami License Agreement may be terminated by the Company at any time upon 60 days prior written notice to UM, and may be terminated by either the Company or UM upon material breach of an obligation if action to cure the breach is not initiated within 60 days of receipt of written notice.

During the years ended December 31, 2024 and 2023, the Company recorded $1.3 million and $0.1 million, respectively, in expense related to the Miami License Agreements. In aggregate, the Company has incurred $3.8 million in expense from the execution of the Miami License Agreements through December 31, 2024.

As of December 31, 2024 and 2023, the Company had $0.3 million and $0.4 million, respectively, related to the Miami License Agreement included in accrued expenses and no amounts included in accounts payable.

2020 Miami Option Agreement

On October 28, 2020, the Company entered into an option agreement with the University of Miami (the "2020 Miami Option Agreement") concerning certain research activities and technology relating to SORD neuropathy that may be pursued and developed by UM. Under the 2020 Miami Option Agreement, if UM conducts such research activities, then UM is obligated to grant us certain option rights to access and use the research results and to obtain licenses to any associated patent rights upon us making specified payments to UM within specified time limits. If the Company elects to obtain option rights the Company will be required to make payments to UM in the low-six figures to the low-seven figures, depending upon the rights the Company elects to obtain, and the Company will be obligated to make certain milestone payments in the high-six figures to mid-seven figures if UM conducts and completes certain research activities within specified time periods and the Company elects to receive rights to use the results of that research.

2020 Miami Sponsored Research Agreement

On December 14, 2020, the Company entered into a research agreement with the University of Miami (the "2020 Miami Research Agreement"), under which the University of Miami will conduct a research study relating to SORD neuropathy and deliver a final report on the study to the Company. The term of the research agreement was from December 14, 2020 through December 30, 2021, and was extended through August 31, 2022, whereby the research study was completed. The total consideration for the 2020 Miami Research Agreement was $0.3 million.

During the years ended December 31, 2024 and 2023, the Company recorded no research and development expenses, in relation to the 2020 Miami Research Agreement. As of December 31, 2024 and 2023, the Company had $0 and $0.1 million, respectively, in accrued expenses due to the University of Miami.

Bayh-Dole Act

Some of the intellectual property rights the Company has licensed, including certain rights licensed in the agreements described above, may have been generated through the use of U.S. government funding. As a result, the U.S. government may have certain rights to intellectual property embodied in the Company's current or future product candidates under the Bayh-Dole Act of 1980, or Bayh-Dole Act, including the grant to the government of a non-exclusive, worldwide, freedom to operate license under any patents, and the requirement, absent a waiver, to manufacture products substantially in the United States. To the extent any of the Company's current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

3. FAIR VALUE MEASUREMENTS

The following tables summarize, as of December 31, 2024 and 2023, the Company's financial assets and liabilities that are measured at fair value on a recurring basis, according to the fair value hierarchy described in the significant accounting policies section.

	As of December 31, 2024			
(in thousands)	Level 1	Level 2	Level 3	Total
Cash	$ 6,165	$ —	$ —	$ 6,165
Money market funds	73,233	—	—	73,233
Total cash and cash equivalents	$ 79,398	$ —	$ —	$ 79,398
Total financial assets measured at fair value on a recurring basis	$ 79,398	$ —	$ —	$ 79,398
Warrant liabilities - Common Warrants	—	—	6,314	6,314
Total financial liabilities measured at fair value on a recurring basis	$ —	$ —	$ 6,314	$ 6,314

	As of December 31, 2023			
(in thousands)	Level 1	Level 2	Level 3	Total
Cash	$ 24,887	$ —	$ —	$ 24,887
Money market funds	25,011	—	—	25,011
Total cash and cash equivalents	$ 49,898	$ —	$ —	$ 49,898
Total financial assets measured at fair value on a recurring basis	$ 49,898	$ —	$ —	$ 49,898
Warrant liabilities - Common Warrants	—	—	53,725	53,725
Total financial liabilities measured at fair value on a recurring basis	$ —	$ —	$ 53,725	$ 53,725

On June 27, 2022 the Company issued 30,000,000 warrants to purchase shares of common stock (the "Common Warrants") and 10,000,000 pre-funded warrants to purchase common stock (the "Pre-Funded Warrants") in connection with the June 2022 Offering (see Note 7 for more information on the June 2022 Offering). The Common Warrants were accounted for as liabilities under ASC 815-40, *Derivatives and Hedging, Contracts in Entity's Own Equity* ("ASC 815-40"), as these warrants initially provided for a settlement provision that does not meet the requirements of the indexation guidance under ASC 815-40. The Pre-Funded Warrants were initially recorded at fair value as a liability as the Company could be required to settle the Pre-Funded Warrants in cash under certain circumstances. In December 2022, the Company amended the Pre-Funded Warrants to remove the potential requirement that they could be settled in cash under certain circumstances. Upon the amendment to the Pre-Funded Warrants, the Pre-funded Warrants liability was reclassified to equity, using their fair value as of the amendment date.

The Common Warrants were remeasured using a Black-Scholes option pricing model with a range of assumptions included below as of December 31, 2024 and 2023.

	December 31, 2024	December 31, 2023
Expected term (in years)	1.9	2.4
Volatility	166.19%	109.46%
Risk-free interest rate	4.25%	4.32%
Dividend yield	0.00%	0.00%

As of December 31, 2024, the Company utilized a probability-weighted approach that considered the probability of a change in control at the Company in the Black-Scholes option pricing model, whereby a 20% probability of change in control was used for years three and four and a 10% probability was used for year five in the term of the agreements.

As of December 31, 2023, the Company utilized a probability-weighted approach that considered the probability of a change in control at the Company in the Black-Scholes option pricing model, whereby a 20% probability of change in control was used for years two and three and a 5% probability was used for years four and five in the term of the agreements.

The following table provides a roll forward of the aggregate fair values of the Company's warrant liability, for which fair value is determined using Level 3 inputs (in thousands):

	Warrant Liabilities
Balance as of December 31, 2023	$ 53,725
Warrants exercised	(52,193)
Change in fair value	4,782
Balance as of December 31, 2024	$ 6,314

The inputs utilized by management to value the warrant liabilities are highly subjective. The assumptions used in calculating the fair value of the warrant liabilities represent the Company's best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and the Company uses different assumptions, the fair value of the warrant liability for Common Warrants may be materially different in the future.

4. PREPAID EXPENSES AND OTHER CURRENT ASSETS

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

	December 31, 2024	December 31, 2023
Prepaid research and development expenses	$ 2,511	$ 2,880
Insurance premium asset	—	566
Prepaid insurance expenses	443	72
Prepaid commercial and patient advocacy	506	284
Prepaid manufacturing costs	327	—
Other prepaid expenses and current assets	461	432
Total prepaid expenses & other current assets	$ 4,248	$ 4,234

5. ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

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

	December 31, 2024	December 31, 2023
Accrued pre-clinical and clinical expenses	$ 2,753	$ 10,142
Short-term insurance financing note	—	310
Deferred revenue	212	667
Accrued professional fees	2,914	1,307
Accrued compensation and benefits	4,017	2,066
Accrued commercial expenses	5,309	19
Accrued patent expenses	335	396
Other	603	379
Total accrued expenses & other current liabilities	$ 16,143	$ 15,286

6. STOCK-BASED COMPENSATION

Equity Incentive Plans

In 2016, the Company adopted, and its stockholders approved, the 2016 Equity Incentive Plan, as amended (the "2016 Plan"), which provides for the granting of options at the discretion of the board of directors (the "Board") or any subcommittee of the Board to its employees, officers and independent contractors. Under the terms of the 2016 Plan, options may not be granted at an exercise price less than fair market value of the Company's common stock on the date of the grant.

In May 2019, the Company's board of directors adopted its 2019 Equity Incentive Plan ("2019 Plan"), which was subsequently approved by its stockholders and became effective on May 13, 2019. As a result, no additional awards under the Company's 2016 Equity Incentive Plan, as amended (the "2016 Plan") will be granted and all outstanding stock awards granted under the 2016 Plan that are repurchased, forfeited, expired or are cancelled will become available for grant under the 2019 Plan in accordance with its terms. The 2016 Plan will continue to govern outstanding equity awards granted thereunder.

The 2019 Plan provides for the issuance of incentive stock options ("ISOs") to employees, and for the grant of nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards and other forms of stock awards to the Company's employees, officers and directors, as well as non- employees, consultants and affiliates to the Company. Under the terms of the 2019 Plan, stock options may not be granted at an exercise price less than fair market value of the Company's common stock on the date of the grant. The 2019 Plan is administered by the Compensation Committee of the Company's Board.

Initially, subject to adjustments as provided in the 2019 Plan, the maximum number of the Company's common stock that may be issued under the 2019 Plan is 4,530,000 shares, which is the sum of (i) 1,618,841 new shares, plus (ii) the number of shares (not to exceed 2,911,159 shares) that remained available for the issuance of awards under the 2016 Plan, at the time the 2019 Plan became effective, and (iii) any shares subject to outstanding stock options or other stock awards granted under the 2016 Plan that are forfeited, expired, or reacquired. The 2019 Plan provides that the number of shares reserved and available for issuance under the 2019 Plan will automatically increase each January 1, beginning on January 1, 2020, 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 Board. Subject to certain changes in capitalization of the Company, the aggregate maximum number of shares of common stock that may be issued pursuant to the exercise of ISOs shall be equal to 13,000,000 shares of common stock. Stock options awarded under the 2019 Plan expire 10 years after grant and typically vest over four years.

As of December 31, 2024, there were 3,643,533 shares of common stock available for issuance under the 2019 Plan. On January 1, 2025, there were 10,504,970, shares that became issuable for future grants subject to the adjustments provided in the 2019 Plan.

On December 19, 2024, the board of directors appointed John Johnson as Executive Chairman of the Board. Concurrently, with his appointment, the Board granted 1,000,000 restricted stock units and 2,000,000 stock options as inducement grants in accordance with Nasdaq Listing Rule 5635(c)(4) separate from 2019 Plan.

Stock-Based Compensation Expense

Total stock-based compensation expense recorded for employees, directors and non-employees under (in thousands):

	Year Ended December 31,	
(in thousands)	**2024**	**2023**
Research and development	$ 7,340	$ 3,005
General and administrative	8,227	4,355
Total stock-based compensation expense	$ 15,567	$ 7,360

Stock Option Activity

During the year ended December 31, 2024, the Company granted 2,150,000 stock options. For the years ended December 31, 2024 and 2023, amortization of stock compensation of options amounted to $2.1 million and $5.0 million, respectively.

On December 19, 2024, the Company's Chairman and Chief Executive Officer ("CEO") resigned. The board approved a modification of the former Executive Chairman and CEO stock options, whereby all unvested stock options became immediately vested and exercisable. This resulted in additional stock option expense of $29,000, which is included in amortized stock compensation of options totaling $2.1 million for the year ended December 31, 2024. There were no stock option modifications for the year ended December 31, 2023.

As of December 31, 2024, the total unrecognized stock-based compensation balance for unvested options was $2.0 million, which is expected to be recognized over 1.9 years. The weighted-average fair value of options granted during the year ended December 31, 2024 was $0.89. There were no stock options granted for the year ended December 31, 2023.

The following table summarizes the information about options outstanding at December 31, 2024:

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2023	4,695,619	$ 2.01	5.7	$ 7,044
Options granted	2,150,000	1.02		
Options exercised	(327,492)	1.05		
Forfeited	(58,123)	1.05		
Expired	—	—		
Outstanding at December 31, 2024	6,460,004	$ 1.74	4.72	$ —
Exercisable at December 31, 2024	4,254,654	$ 2.11	2.04	$ —
Nonvested at December 31, 2024	2,205,350	$ 1.02	9.90	$ —

The aggregate intrinsic value is calculated as the difference between the exercise price of all outstanding and exercisable stock options and the fair value of the Company’s common stock at December 31, 2024. The intrinsic value of stock options exercised during each of the years ended December 31, 2024 and 2023 was $0.1 million. The total grant-date fair value of stock options vested during the years ended December 31, 2024 and 2023 was $0.2 million and $0.4 million, respectively.

Valuation of Stock Options Granted to Employees

The fair value of each option award granted is estimated on the date of the grant using the Black-Scholes option valuation model based on the weighted-average assumptions noted in the table below for those options granted in the year ended December 31, 2024. There were no stock options granted during the year ended December 31, 2023.

	Year Ended December 31, 2024
Expected term (in years)	5.27 - 6.00
Volatility	120.97 - 123.97%
Risk-free interest rate	4.43 - 4.47%
Dividend yield	—%

Restricted Stock Unit Activity

During the year ended December 31, 2024, the Company granted 2,650,000 restricted stock units ("RSUs"). For the years ended December 31, 2024 and 2023 amortization of stock compensation of RSUs amounted to $13.4 million and $2.4 million, respectively. On December 19, 2024, the Company's Chairman and CEO resigned. The board approved a modification of the Chairman and CEO restricted stock units, whereby all unvested and unreleased RSUs were cancelled and settled in cash totaling $2.1 million. This resulted in additional RSU expense of $7.7 million, which is included in amortized stock compensation of RSUs totaling $13.4 million for the year ended December 31, 2024. There were no RSU modifications for the year ended December 31, 2023.

As of December 31, 2024, the unamortized compensation costs associated with non-vested restricted stock awards was $10.1 million with a weighted-average remaining amortization period of 2.4 years.

The following table summarizes the information about restricted stock units outstanding at December 31, 2024:

	Shares	Weighted-Average Grant Date Fair Value
Outstanding at December 31, 2023	6,917,422	$ 2.35
Awarded	2,650,000	3.62
Released	(1,279,126)	1.91
Forfeited	(4,178,544)	2.81
Outstanding at December 31, 2024	4,109,752	$ 3.16
Nonvested at December 31, 2024	3,715,191	$ 3.17
Weighted-Average Remaining Recognition Period (in years)	2.4	

2019 Employee Stock Purchase Plan

In May 2019, the Company's Board and its stockholders approved the 2019 Employee Stock Purchase Plan (the "ESPP"), which became effective as of May 13, 2019. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the U.S. Internal Revenue Code of 1986, as amended. The number of shares of common stock initially reserved for issuance under the ESPP was 180,000 shares. The ESPP provides for an annual increase on the first day of each year beginning in 2020 and ending in 2029, equal to the lesser of (i) 1% of the shares of common stock outstanding on the last day of the calendar month before the date of the automatic increase and (ii) 360,000 shares; provided that prior to the date of any such increase, the Board may determine that such increase will be less than the amount set forth in clauses (i) and (ii). As of December 31, 2024, no shares of common stock had been issued under the ESPP. The first offering period commenced on November 15, 2024.

Under the ESPP substantially all employees may voluntarily enroll to purchase shares of the Company's common stock through payroll deductions at a price equal to 85% of the lower of the fair market values of the stock as of the beginning or the end of the each six-month offering period. An employee's payroll deductions under the ESPP are limited to 15% of the employee's compensation, and an employee may not purchase more than $25,000 worth of stock during any calendar year. As of December 31, 2024 a total of 1,387,091 of the Company's common stock were available for future issuance under the ESPP. On January 1, 2025, there were 1,747,091, shares that became issuable for future grants under the ESPP subject to the adjustments provided in the 2019 Plan.

For the year ended December 31, 2024, amortization of stock compensation of the ESPP amounted to $0.1 million. As of December 31, 2024, the unamortized compensation costs related to the ESPP was $0.2 million with a weighted-average remaining amortization period of 0.6 year.

Valuation of ESPP Granted to Employees

The fair value of each ESPP award is estimated on the date of the grant using the Black-Scholes valuation model based on the weighted-average assumptions noted in the table below for those ESPP awards granted in the year ended December 31, 2024. There were no ESPP awards issued during the year ended December 31, 2023.

	Year Ended December 31, 2024
Expected term (in years)	0.62 - 1.13
Volatility	97.1 - 125.70%
Risk-free interest rate	4.34 - 4.44%
Dividend yield	—%

7. STOCKHOLDERS' EQUITY

As of December 31, 2024 and 2023, the authorized capital stock of the Company consists of 250,000,000 and 200,000,000 shares of common stock, respectively, par value $0.0001 per share and 10,000,000 shares of preferred stock, par value $0.0001 per share.

Common Stock

Voting

The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of the stockholders. There is no cumulative voting.

June 2022 Offering

On June 27, 2022, the Company completed the June 2022 Offering, an underwritten public offering of 20,000,000 shares of common stock, 10,000,000 Pre-Funded Warrants, and accompanying Common Warrants to purchase up to 30,000,000 shares of common stock. The shares and accompanying Common Warrants were offered at a price to the public of $1.00 per share and warrant, and the Pre-Funded Warrants and accompanying Common Warrants were offered at a price to the public of $0.9999, resulting in aggregate net proceeds of approximately $27.8 million, after deducting underwriting discounts and commissions and offering expenses. The Pre-Funded Warrants and the Common Warrants are immediately exercisable and will expire five years from the date of issuance. Holders may not exercise any Pre-Funded Warrants or Common Warrants that would cause the aggregate number of shares of common stock beneficially owned by the holder to exceed 9.99% of the Company's outstanding common stock immediately after exercise. Holders of the Pre-Funded Warrants and/or Common Warrants (together with affiliates) who immediately prior to June 27, 2022 beneficially owned more than 9.99% of the Company's outstanding common stock may not exercise any portion of their Pre-Funded Warrants or Common Warrants if the holder (together with affiliates) would beneficially own more than 19.99% of the Company's outstanding common stock after exercise. The Pre-Funded Warrants and Common Warrants are subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the common stock and also upon any distributions for no

consideration of assets to the Company's stockholders. In the event of certain corporate transactions, the holders of the Pre-Funded Warrants and/or Common Warrants will be entitled to receive, upon exercise, the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants and/or Common Warrants immediately prior to such transaction. The Pre-Funded Warrants and Common Warrants do not entitle the holders thereof to any voting rights or any of the other rights or privileges to which the Company's stockholders are entitled.

April 2023 Private Placement

On April 26, 2023, the Company completed its sale of a total of 9,735,731 shares of the Company's common stock, at a purchase price of $0.946 per share, and 22,000,000 Pre-Funded Warrants to purchase common stock, at a purchase price of $0.945 per Pre-Funded Warrant, in a private placement (the "April 2023 Private Placement") to a select group of accredited investors, pursuant to the Securities Purchase Agreement, dated as of April 23, 2023, by and between the Company and the purchasers named therein. The April 2023 Private Placement resulted in net proceeds to the Company of approximately $27.5 million, after deducting underwriting discounts, commissions and offering expenses. The Pre-Funded Warrants are immediately exercisable from the date of issuance and do not have an expiration date. They have an exercise price of $0.001. Holders may not exercise any Pre-Funded Warrants that would cause the aggregate number of shares of common stock beneficially owned by the holder to exceed 9.99% of the Company's outstanding common stock immediately after exercise. The Pre-Funded Warrants are subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the common stock and also upon any distributions for no consideration of assets to the Company's stockholders. In the event of certain corporate transactions, the holders of the Pre-Funded Warrants will be entitled to receive, upon exercise of the Pre-Funded Warrants, the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants immediately prior to such transaction. The Pre-Funded Warrants do not entitle the holders thereof to any voting rights or any of the other rights or privileges to which holders of common stock are entitled.

Leerink ATM Agreement

On August 11, 2023, the Company entered into an ATM Agreement with Leerink Partners LLC (the "Leerink ATM Agreement"), pursuant to which the Company may offer and sell, from time to time, shares of common stock having an aggregate offering price of up to $75.0 million through Leerink Partners LLC as sales agent. Under the Leerink ATM Agreement, the sales agents may sell shares of common stock by any method permitted by law deemed to be an "at the market offering" as defined in Rule 415(a)(4) of the Securities Act of 1933, as amended. The Company will pay the sales agent a commission rate of up to 3% of the gross offering proceeds of any shares sold and has agreed to provide the sales agent with indemnification and contribution against certain liabilities. The Leerink ATM Agreement contains customary representations and warranties.

During the year ended December 31, 2024, the Company sold an aggregate of 3,000,000 shares of common stock, pursuant to Leerink ATM Agreement with an average sale price of $4.31 per share, resulting in net proceeds of $12.4 million, after deducting underwriting discounts, commissions and offering expenses.

During the year ended December 31, 2023, the Company sold an aggregate of 17,615,976 shares of common stock, pursuant to the Leerink ATM Agreement with an average sale price of $2.04 per share, resulting in net proceeds of $36.9 million, after deducting underwriting discounts, commissions and offering expenses.

Venrock Warrant Exchange

On October 12, 2023, the Company entered into an exchange agreement (the "Exchange Agreement") with entities affiliated with Venrock Healthcare Capital Partners (the "Exchanging Stockholders"), pursuant to which the Company exchanged an aggregate of 5,658,034 shares of common stock, owned by the Exchanging Stockholders for pre-funded warrants to purchase an aggregate of 5,658,034 shares of common stock (subject to adjustment in the event of stock splits, recapitalizations and other similar events affecting common stock), with an exercise price of $0.001 per share. The common stock exchanged, and the pre-funded warrants issued were recorded at fair market value of $12.9 million.

March 2024 Private Placement

On March 1, 2024, the Company completed its sale of a total of 12,285,714 shares of the Company's common stock, at a purchase price of $7.00 per share, and 2,000,000 Pre-Funded Warrants to purchase common stock, at a purchase price of $6.999 per Pre-Funded Warrant, in a private placement to a select group of accredited investors (the "March 2024 Private Placement"), pursuant to a Securities Purchase Agreement, dated as of February 27, 2024, by and between the Company and the purchasers named therein (the "2024 Purchasers"). The Private Placement resulted in net proceeds to the Company of approximately $92.3 million, after deducting placement agent commissions and other offering expenses.

The Pre-Funded Warrants are immediately exercisable from the date of issuance and do not have an expiration date. They have an exercise price of $0.001. Holders may not exercise any Pre-Funded Warrants that would cause the aggregate number of shares of common stock beneficially owned by the holder to exceed 9.99% of the Company's outstanding common stock immediately after exercise. The Pre-Funded Warrants are subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the common stock and also upon any distributions for no consideration of assets to the Company's stockholders. In the event of certain corporate transactions, the holders of the Pre-Funded Warrants will be entitled to receive, upon exercise of the Pre-Funded Warrants, the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants immediately prior to such transaction. The Pre-Funded Warrants do not entitle the holders thereof to any voting rights or any of the other rights or privileges to which holders of common stock are entitled.

8. WARRANTS

Warrants Issued with June 2022 Offering

On June 27, 2022, in connection with the sale and issuance common stock as part of the June Offering, the Company issued 10,000,000 Pre-Funded Warrants at an exercise price of $0.0001 per share, and 30,000,000 accompanying Common Warrants at an exercise price of $1.00 per share. Each share of common stock and accompanying Common Warrant was sold at a public offering price of $1.00, less underwriting discounts and commissions, and each Pre-Funded Warrant and accompanying Common Warrant was sold at a public offering price of $0.9999, less underwriting discounts and commissions, as described in the prospectus supplement, dated June 22, 2022, filed with the Securities and Exchange Commission on June 24, 2022.

The June 2022 Pre-Funded Warrants were initially recorded at fair value as a liability as the Company could be required to settle the Pre-Funded Warrants in cash in the event of an acquisition of the Company under certain circumstances. In December 2022, the Company amended the Pre-Funded Warrants to remove the potential requirement that they could be settled in cash under certain circumstances. Beginning December 2022, the Pre-funded Warrants are recorded as equity, using their fair value as of the amendment date.

As of December 31, 2024, warrant holders had exercised 8,500,000 Pre-Funded Warrants on a cash basis and received 8,500,000 shares of common stock. The Company received $850 in cash proceeds for the exercise of these Pre-Funded Warrants.

As of December 31, 2024, the Company had 1,500,000 Pre-Funded Warrants from the June 2022 offering outstanding with a weighted-average exercise price of $0.0001 per share and an average contractual life of 5 years.

The Common Warrants were accounted for as liabilities under ASC 815-40, as these warrants provide for a settlement provision that does not meet the requirements of the indexation guidance under ASC 815-40. These warrant liabilities are measured at fair value at inception and on a recurring basis, with changes in fair value presented within the statements of operations. The Common Warrants were remeasured using a Black-Scholes option pricing model with a range of assumptions as of December 31, 2024 and December 31, 2023 (See Note 3).

As of December 31, 2024, warrant holders had exercised 19,275,000 Common Warrants on a cash basis and received 19,275,000 shares of common stock. The Company received $19.3 million in cash proceeds for the exercise of these Common Warrants.

As of December 31, 2024, the Company had 10,725,000 Common Warrants outstanding with a weighted-average exercise price of $1.00 per share and an average contractual life of 5 years.

Warrants Issued with April 2023 Private Placement

On April 26, 2023, in connection with the sale and issuance of common stock as part of the April 2023 Private Placement, the Company issued 22,000,000 Pre-Funded Warrants at an exercise price of $0.001 per share. Each share of common stock was sold at a public offering price of $0.946, less underwriting discounts and commissions, and each Pre-Funded Warrant was sold at a public offering price of $0.945, less underwriting discounts and commissions, pursuant to a Securities Purchase Agreement, dated as of April 23, 2023, by and between the Company and the Purchasers.

As of December 31, 2024, warrant holders had exercised 22,000,000 Pre-Funded Warrants on a cashless basis and received 21,986,515 shares of common stock.

As of December 31, 2024, the Company had no Pre-Funded Warrants from the April 2023 private placement outstanding.

Venrock Warrant Exchange

On October 12, 2023, the Company entered into an exchange agreement with entities affiliated with Venrock Healthcare Capital Partners, pursuant to which the Company exchanged an aggregate of 5,658,034 shares of common stock, owned by the Venrock Healthcare Capital Partners for pre-funded warrants to purchase an aggregate of 5,658,034 shares of common stock (subject to adjustment in the event of stock splits, recapitalizations and other similar events affecting common stock), with an exercise price of $0.001 per share.

As of December 31, 2024, warrant holders had exercised 1,956,789 Pre-Funded Warrants on a cashless basis and received 1,955,062 shares of common stock.

As of December 31, 2024, the Company had 3,701,245 Pre-Funded Warrants from the Venrock Warrant Exchange outstanding with a weighted-average exercise price of $0.001 per share.

Warrants Issued with March 2024 Private Placement

On March 1, 2024, in connection with the sale and issuance of common stock as part of the March 2024 Private Placement, the Company issued 2,000,000 Pre-Funded Warrants at an exercise price of $0.001 per share. Each share of common stock was sold at a public offering price of $7.00, less underwriting discounts and commissions, and each Pre-Funded Warrant was sold at a public offering price of $6.999, less underwriting discounts and commissions, pursuant to a Securities Purchase Agreement, dated as of February 27, 2024, by and between the Company and the Purchasers.

As of December 31, 2024, the Company had 2,000,000 Pre-Funded Warrants from the March 2024 private placement outstanding with a weighted-average exercise price of $0.001 per share. The pre-funded warrants do not have an expiration date.

A summary of the Company's outstanding common stock warrants as of December 31, 2024 is as follows:

	Equity Classified Warrants	Liability Classified Warrants	Total Warrants
Outstanding as of December 31, 2023	31,783,652	19,750,000	51,533,652
Warrants granted and issued	2,000,000	—	2,000,000
Warrants exercised	(26,456,789)	(9,025,000)	(35,481,789)
Outstanding as of December 31, 2024	7,326,863	10,725,000	18,051,863

9. LEASES

The following table summarizes our lease related costs for the years ended December 31, 2024 and 2023:

(in thousands) Lease Cost	Statement of Operations Location	Year Ended December 31, 2024	2023
Operating Lease Cost	General and administrative	$ 549	$ 505
Total lease cost		$ 549	$ 505

Average lease terms and discount rates for the Company's operating leases were as follows:

Other Information	Year Ended December 31, 2024	December 31, 2023
Weighted-average remaining lease term		
Operating leases	4.8 years	1.1 years
Weighted-average discount rate		
Operating leases	15.05%	6.86%

The following table summarizes the maturities of lease liabilities as of December 31, 2024:

Year	Operating *(in thousands)*
2025	787
2026	803
2027	803
2028	823
2029	702
Thereafter	—
Total lease payments	3,918
Less: interest	1,123
Total lease liabilities	$ 2,795

On September 11, 2024, the Company entered into a lease renewal agreement for its New York office space located at 545 Fifth Avenue, suite 1400, New York, New York 10017 (the "New York Lease") for a five-year term. In conjunction with the execution of the New York lease renewal, the Company leased additional space located in suite 1401 for a five-year term. The lease of suite 1401 commenced on November 26, 2024. The total lease payments for suite 1400 and 1401 is approximately $4.1 million.

10. INCOME TAXES

The Company has not recorded a current or deferred tax provision for the years ended December 31, 2024 and 2023 due to net losses incurred.

A reconciliation of the Company's deferred taxes is as follows (in thousands):

	Year ended December 31,	
	2024	2023
Deferred Tax Assets		
Operating lease liability	$ 871	$ 146
Stock-based compensation	1,505	4,060
License fee	779	501
Net operating loss carryforwards	114,961	94,119
Research and development tax credits	29,844	25,145
Capitalized research and development expense	33,016	26,945
Other	663	445
Total deferred tax assets	$ 181,639	$ 151,361
Valuation allowance	$ (180,769)	$ (151,222)
Net deferred tax assets	$ 870	$ 139
Deferred tax liabilities		
Right of use asset	(870)	(139)
Net deferred tax liabilities	$ (870)	$ (139)
Net deferred tax asset (liability)	$ —	$ —

Deferred tax assets result primarily from unutilized net operating losses, research tax credits, stock-based compensation, operating lease liability, and timing differences as a result of the Company reporting its income tax returns. As of December 31, 2024, the Company had approximately $365.9 million of federal operating loss (“NOLs”) carry forwards. Of this amount, approximately $3.3 million will begin to expire in 2037 and approximately $362.6 million are carried forward indefinitely. The Company had approximately $748.3 million in state and city net operating loss carryforwards available to offset future taxable income.

As of December 31, 2024, the Company had federal research tax credits ("R&D") of approximately $7.0 million which may be used to offset future tax liabilities. Additionally, the Company had a federal orphan drug credit (“ODC”) related to qualifying research of $22.8 million. These tax credit carryforwards will begin to expire at various times beginning in 2037 for federal purposes.

The NOL, R&D and ODC credits carry forwards are subject to review and possible adjustment by the U.S. and state tax authorities. NOL carry forwards and credit carry forwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders, as defined under Sections 382 and 383 Internal Revenue Code. This could limit the amount of NOLs and credits that the Company can utilize annually to offset future taxable income or tax liabilities. As of December 31, 2024, the Company has not performed such an analysis. Subsequent ownership changes and proposed future changes to tax rules in respect of the utilization of losses carried forward may further affect the limitation in future years.

In assessing the realizability of the Company’s deferred tax assets, management considers whether or not it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income. The Company’s assessment is based on the weight of available evidence, including cumulative losses since inception and expected future losses and, as such, the Company does not believe it is more likely than not that the deferred tax assets will be realized. Accordingly, a full valuation allowance has been established and no deferred tax assets and related tax benefit have been recognized in the accompanying financial statements. At December 31, 2024 and 2023, the Company recorded valuation allowances of $180.8 million and $151.2 million, respectively. The increase in valuation allowance is primarily driven by additional net operating losses.

The Company files its income tax returns in the United States, Connecticut, Iowa, Massachusetts, Michigan, Mississippi, New Jersey, New York State, and New York City. All years remain subject to examination for federal and state purpose.

A reconciliation of the U.S. federal statutory corporate tax rate to the Company's effective tax rate for the years ended December 31, 2024 and 2023 is as follows:

	Year Ended December 31,	
	2024	2023
Federal statutory rate	21.0%	21.0%
State and local taxes net of federal tax benefit	7.8	3.4
Credits	4.4	3.1
Permanent differences	—	(0.1)
Change in fair value of warrant liabilities	(1.0)	(9.9)
Change in valuation allowance	(28.0)	(14.2)
Stock-based compensation	(4.3)	(3.3)
Other	0.1	—
Total	0.0%	0.0%

11. BENEFIT PLANS

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code in 2018. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the plan may be made at the discretion of the Company's Board. The Company made approximately $0.4 million in matching contributions to the plan during each of the years ended December 31, 2024 and 2023.

12. NET LOSS PER COMMON SHARE

Basic net loss per common share is computed by dividing the net loss available to common stockholders by the weighted-average number of shares of common stock outstanding during the period which includes shares issuable under pre-funded warrants agreements for little consideration.

Diluted net loss per common share is computed by giving the effect of all potential shares of common stock, including stock options, preferred shares, warrants and instruments convertible into common stock, to the extent dilutive. Basic and diluted net loss per common share was the same for the years ended December 31, 2024 and 2023, as the inclusion of all potential common shares outstanding would have been anti-dilutive due to net losses incurred.

The following table sets forth the computation of basic and diluted net loss per common share (in thousands, except share and per share data):

	Year Ended December 31,	
(in thousands, except for share and per share data)	2024	2023
Numerator:		
Net loss	$ (105,624)	$ (119,763)
Denominator:		
Weighted-average common stock outstanding	139,534,746	84,244,494
Net loss per share attributable to common stockholders - basic and diluted	$ (0.76)	$ (1.42)

The Company excluded the following potential common shares, presented based on amounts outstanding at December 31, 2024 and 2023, from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	As of December 31,	
	2024	2023
Options to purchase common stock	6,460,004	4,695,619
Restricted stock units	4,109,752	3,867,422
Warrants to purchase common stock	10,850,618	19,875,618

13. RELATED PARTIES

In December 2018, the Company entered into an agreement (the "LaunchLabs Agreement") with ARE-LaunchLabs NYC LLC ("Alexandria LaunchLabs"), a subsidiary of Alexandria Real Estate Equities, Inc. for use of specified premises within the Alexandria LaunchLabs space on a month-to-month basis. A shareholder and former member of the Company's board of directors is the founder and executive chairman of Alexandria Real Estate Equities, Inc. During the years ended December 31, 2024 and 2023, the Company made payments to Alexandria LaunchLabs of approximately $0.1 million under the LaunchLabs Agreement, which was recognized in research and development expenses. As of December 31, 2024 and 2023, there was $9,000 and $8,000 due to Alexandria LaunchLabs under the LaunchLabs Agreement, respectively, recorded in accounts payable.

14. REVENUE

On January 3, 2023, the Company entered into an Exclusive License and Supply Agreement (the "Advanz Agreement") with Mercury Pharma Group Limited (trading as Advanz Pharma Holdings) ("Advanz Pharma"). Pursuant to the Advanz Agreement, the Company granted Advanz Pharma the exclusive right and license to commercialize drug products containing AT-007 (also known as govorestat), our proprietary Aldose Reductase Inhibitor (the "Licensed Product"), for use in treatment of Sorbitol Dehydrogenase Deficiency ("SORD") and Galactosemia (each a "Licensed Indication") in the European Economic Area, Switzerland and the United Kingdom (the "Territory"). The Agreement provides that Applied will perform research and development services prior to and subsequent to marketing authorization and manufacture and supply product for Advanz Pharma. The Company also granted Advanz Pharma a right of negotiation and "most-favored nation" rights with respect to acquiring the European commercialization rights for any additional indications for which the Licensed Product may be developed in the future (or any other products we may develop solely to the extent used for the Licensed Indications).

Advanz Pharma is required to use commercially reasonable efforts to launch and commercialize the Licensed Products in the major markets in the Territory in each Licensed Indication following, and subject to, receipt of marketing authorization therein. Under the Advanz Agreement, Advanz Pharma agreed to pay the Company (i) an upfront payment of EUR 10.0 million (approximately USD $10.7 million), and certain development milestone payments upon clinical trial completion and receipt of marketing authorization in the territory, as well as certain commercial milestone payments, totaling EUR 134 million (approximately USD $142.2 million) in the aggregate, and (ii) royalties of 20% of net sales of the Licensed Product. Such royalty rate will be payable on a country-by-country basis until the later of (i) the expiration of the licensed patents covering the composition of matter of AT-007, or (ii) 10 years after the European Medicines Agency's grant of marketing authorization for the Licensed Product. The royalties are subject to certain deductions, including certain secondary finishing costs, certain step-in establishment costs and a portion of fees for any potential third-party patent licenses if applicable in the future. Following the initial term of the license, as described above, the royalty rate will be reduced to 10% and shall continue in perpetuity unless the Advanz Agreement is terminated in various circumstances in accordance with its terms. In addition, the Company is entitled to receive cost sharing consideration for post-marketing authorization studies, if applicable.

In accordance with the Company's ASC 606 assessment, Advanz Pharma is considered to be a customer. The Company identified three performance obligations, the exclusive license to commercialize the Licensed Product, the obligations to provide research and development for pre and post-marketing authorization and the obligation to manufacture and supply Advanz Pharma with the Product, at cost (a material right). The Company determined that the upfront payment of EUR 10 million (approximately USD $10.7 million) is the estimated transaction price at contract inception. The performance-based milestone payments, sales-based milestone payments, sales-based royalties, and post-marketing authorization study cost sharing are each determined to be variable consideration that are fully constrained due to the uncertainty of achievement.

At inception of the Advanz Agreement, the Company determined the estimate of standalone selling price for the license performance obligation by using the adjusted market assessment approach. Under this method, the Company forecasted and analyzed Galactosemia and SORD in the European market, the probability of marketing authorization approval as well as considered recent similar license arrangements within the same phase of clinical development, therapeutic area, type of agreement, forecasted sales for the contract period, probability of success and a market discount rate. To estimate the standalone selling price of the research and development services, the Company forecasted its expected costs of satisfying that performance obligation and added an appropriate margin for that service. To estimate the standalone selling price for the manufacturing supply agreement material right, the Company utilized an adjusted market assessment approach. The Company analyzed the discount Advanz Pharma is expected to obtain by estimating the material right the customer is receiving for the future purchase of manufacturing and supply services. This estimation utilized the estimated number of patients to be treated per year in the Territory; the estimated volume of bottles per patient required per year; typical margin; probability of success; and discounted at market rate.

The Company allocated the total transaction price to each performance obligation on a relative standalone selling price basis and determined whether revenue should be recognized at a point in time or over time. The Company allocated $9.3 million to the license performance obligation; $1.3 million to the research and development performance obligation; and $0.1 million to the manufacturing and supply material right.

Revenue should be recognized when, or as, an entity satisfies a performance obligation by transferring a promised good or service to a customer, i.e., when the customer obtains control of the good or service. The license granted to Advanz Pharma is being accounted for as a distinct performance obligation. The Advanz Pharma license relates to functional IP for which revenue is recognized at a point in time – in the case of this license agreement, the point in time is at inception of the contract because the customer obtained control of the license and was able to use and benefit from its right to use the intellectual property at that point. The Company recognized the transaction price allocated to the license obligation of $9.3 million as license revenue on its statements of operations for the year ended December 31, 2023.

The research and development services performance obligation under the Advanz Agreement represents a separate performance obligation. The research and development services were provided to Advanz Pharma by the Company from inception of the agreement in January 2023 and will continue through completion of post marketing authorization approval studies. Revenue related to the research and development services performance obligation was recognized as services were performed based on the costs incurred during the year ended December 31, 2024 and 2023, as a percentage of the estimated total costs to be incurred for this performance obligation. The Company recognized $0.5 million and $0.7 million of revenue related to the satisfaction of the research and development services performance obligation during years ended December 31, 2024 and 2023, respectively. The Company had deferred revenue of $0.1 million and $0.5 million related to the research and development services performance obligation at December 31, 2024 and 2023, respectively. Operating expenses for costs incurred pursuant to this arrangement are reported in their respective expense line items in the Statements of Operations, net of any payments due to or reimbursements due from Advanz, with such reimbursements being recognized at the time the party becomes obligated to pay.

The manufacturing supply agreement material right performance obligation provided to Advanz Pharma by the Company resulted in an allocation of the transaction price and resulting deferred revenue as of contract inception and December 31, 2024, of approximately $0.1 million. Revenue associated with this performance obligation will be recognized when Advanz Pharma buys supply from the Company after regulatory approval or upon expiration of the material right.

15. Commitments and Contingencies

The Company is involved in various lawsuits, claims and other legal matters from time to time that arise in the ordinary course of conducting business. The Company records a liability when a particular contingency is probable and estimable.

Securities Class Action Litigation

On December 17, 2024, a purported stockholder filed a putative class action lawsuit against the Company and certain current and former Company officers and directors in the United States District Court for the Southern District of New York (*Alexandru v. Applied Therapeutics, Inc., et al.*, No. 1:24-cv-09715). The complaint alleges that defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, and Rule 10b-5 promulgated thereunder by making false and/or misleading statements between January 3, 2024 to December 2, 2024 in connection with the Company's NDA to the FDA for govorestat for the treatment of Classic Galactosemia, and seeks unspecified damages. On December 27, 2024, another purported stockholder filed a putative class action lawsuit against the Company and a former Company officer and director in the United States District Court for the Southern District of New York (*Ikram v. Applied Therapeutics, Inc., et al.*, No. 1:24-cv-09973). The complaint alleges claims substantially similar to those alleged in the *Alexandru* action and also seeks unspecified damages. On February 18, 2025, several purported stockholders filed motions seeking to consolidate the *Alexandru* and *Ikram* actions and seeking appointment as lead plaintiff in the consolidated action. On March 11, 2025, the court consolidated the Alexandru and Ikram actions (In re Applied Therapeutics Securities Litigation, No. 1:24-cv-9715) and appointed a lead plaintiff and lead counsel. The deadline for lead plaintiff to file a consolidated amended complaint is May 2, 2025.

Shareholder Derivative Litigation

On January 31, 2025, a purported stockholder filed a derivative action in the United States District Court for the Southern District of New York (*Hassine v. Shendelman, et al.*, No. 1:25-cv-00935). The complaint purports to assert derivative claims against certain current and former Company officers and directors for breach of fiduciary duty, unjust enrichment, abuse of control, gross mismanagement, waste of corporate assets, violations of Section 14(a) of the Exchange Act, and contribution under Sections 10(b) and 21D of the Exchange Act. The complaint seeks to implement reforms to the Company's corporate governance and internal procedures and to recover on behalf of the Company for any liability the Company might incur as a result of the individual defendants' alleged misconduct, as well as declaratory, equitable, and monetary relief, including attorneys' fees and other costs. The derivative action is based substantially on the same facts alleged in the consolidated action described above. On March 4, 2025, plaintiff and the Company filed a joint stipulation seeking to temporarily stay the derivative action. On March 5, 2025, the court so-ordered the stipulation, thereby temporarily staying the derivative action.

As of December 31, 2024, the Company determined the probability of loss on the aforementioned lawsuits was reasonably possible; however, the Company has not recorded a liability, since the the Company is not currently able to estimate the amount or range of loss, if any, at this stage of the litigation.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE.

None.

ITEM 9A. CONTROLS AND PROCEDURES.

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports we file or submit pursuant to the Securities and Exchange Act of 1934, as amended (the "Exchange Act"), is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and that such information is accumulated and communicated to our management, including our Principal Executive Officer and Principal Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Management, with the participation of the Principal Executive Officer and Principal Financial Officer, evaluated the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act as of the end of the period covered by this Annual Report. Based on that evaluation, our Principal Executive Officer and Principal Financial Officer has concluded that, as of December 31,2024, our disclosure controls and procedures were not effective to provide reasonable assurance that information required to be disclosed by the Company in reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, due to the material weakness in our internal control over financial reporting described below.

After giving full consideration to the material weakness, and the additional analyses and other procedures that we performed to ensure the preparation and fair presentation of our financial statements included in this Annual Report, our management and the board of directors have concluded that such financial statements present fairly, in all material respects, our financial position, results of operations and cash flows for the periods disclosed in conformity with U.S. GAAP.

Management’s Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) under the Exchange Act. Our internal control was designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

Management maintains a comprehensive system of controls intended to ensure that transactions are executed in accordance with management's authorization, assets are safeguarded, and financial records are reliable. Management also takes steps to ensure that information and communication flows are effective, and to monitor performance, including performance of internal control procedures.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2024, based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013). Based on this assessment, management believes that our internal control over financial reporting was not effective as of December 31, 2024 and 2023, due to the material weakness described below.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

As described below and in Part II, Item 1A. of this Annual Report on Form 10-K, in connection with; our assessment of our internal control over financial reporting as of December 31, 2024, we identified a material weakness related to deficiencies in the principles associated with the information and communication component of the COSO framework.

Factors contributing to the material weakness included a failure to appropriately design and operate internal controls to ensure complete and timely communication between our former chief executive officer, senior management and our board of directors. The Company did not have an effective communication process to ensure that relevant and reliable information was communicated timely across the organization to enable management to effectively carry out their financial reporting and internal control roles and responsibilities.

Remediation of Material Weakness

Management has enhanced its resources as described below and implemented several enhanced internal controls that are designed to remediate the material weakness. Our former chief executive officer and chairman of our board of directors resigned from the Company on December 19, 2024. On December 19, 2024, our board of directors appointed a new executive chairman of our board of directors and an interim chief executive officer, with extensive public company experience to improve communication with the board of directors and senior management and compliance with policies within our organization. Management has also instituted additional disclosure controls, including a rigorous disclosure review process that includes the executive team and legal counsel. As part of enhancing resources, the board has instituted a cross-functional quality council comprised of senior leadership of our company and external parties, which provides independent oversight over good practice, quality guidelines and regulations and reports its findings to senior leadership and our board of directors. Management believes its enhanced resources and control activities, including the cross-functional quality council, will support the functioning of the information and communication principles. In addition, we have hired a chief regulatory officer and a head of quality both reporting to the executive chairman.

Management continues to implement enhanced internal controls as part of its plan to remediate the material weakness. However, assurance as to when the remediation efforts will be complete cannot be provided and the material weakness cannot be considered remedied until the applicable controls have operated for a sufficient period of time and management has concluded, through testing, that these controls are operating effectively. Management cannot assure readers that the measures that have been taken to date, and are continuing to be implemented, will be sufficient to remediate the material weakness identified or to avoid potential future material weaknesses.

Changes in Internal Control over Financial Reporting

Other than the material weakness discussed above, there were no changes in our internal control over financial reporting (as such term is defined by Rules 13a-15(f) and 15d-15(f) of the Exchange Act) during the most recent fiscal quarter ended December 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION.

None.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not Applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE.

The information required by Item 10 is incorporated by reference to the information that will be contained in our 2025 Proxy Statement under the captions “Proposal 1 - Election of Directors,” “Principal Stockholders,” “Proposal 2 – Ratification of Independent Registered Public Accounting Firm” and “Audit Committee Report.”

ITEM 11. EXECUTIVE AND DIRECTOR COMPENSATION.

The information required by Item 11 is incorporated by reference to the information that will be contained in our 2025 Proxy Statement under the captions “Executive and Director Compensation,” “Compensation Discussion and Analysis,” “Compensation Committee Report,” “Compensation Committee Interlocks and Insider Participation,” “Compensation of Named Executives,” “Summary Compensation Table,” “Equity Incentive Plans,” “Non-Employee Director Compensation,” “Stock Option Grants,” “Outstanding Equity Awards at Fiscal Year-End,” “Health and Welfare Retirement Benefits,” and “Potential Payments and Benefits Upon Termination or Change-in-Control.”

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.

The information required by Item 12 is incorporated by reference to the information that will be contained in our 2025 Proxy Statement under the caption “Principal Stockholders.”

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.

The information required by Item 13 is incorporated by reference to the information that will be contained in our 2025 Proxy Statement under the caption “Certain Relationships and Transactions.”

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES.

The information required by Item 14 is incorporated by reference to the information that will be contained in our 2025 Proxy Statement under the caption “Independent Registered Public Accounting Firm”.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES.

(a) The following documents are filed as part of this Annual Report

1. Financial Statements:

The following financial statements and schedules of the Registrant are contained in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report:

2. Financial Statement Schedules:

There are no Financial Statement Schedules included with this filing for the reason that they are not applicable or are not required or the information is included in the financial statements or notes thereto.

(b) Exhibits required by Item 601 of Regulation S-K

The information required by this Item is set forth on the exhibit index that follows.

EXHIBIT INDEX

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date
3.1+	Amended and Restated Certificate of Incorporation of the Registrant, as amended.	10-Q	001-38898	3.1	August 7, 2024
3.2	Certificate of Amendment to Amended and Restated Certificate of Incorporation of the Registrant.	10-Q	001-38898	3.2	August 7, 2024
3.3+	Amended and Restated Bylaws of the Registrant.	10-K	001-38898	3.3	March 23, 2023
4.1+	Registration Rights Agreement, dated November 7, 2019, by and among the Registrant and the Purchasers.	8-K	001-38898	10.2	November 12, 2019
4.2+	Form of Common Stock Certificate of the Registrant.	10-Q	001-38898	4.1	August 12, 2019
4.3+	Amended and Restated Investors' Rights Agreement, by and among the Registrant and certain of its stockholders, dated November 5, 2018.	S-1/A	333-230838	4.2	April 29, 2019
4.4+	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC on March 13, 2017.	S-1/A	333-230838	4.3	April 29, 2019
4.5+	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC on November 5, 2018.	S-1/A	333-230838	4.4	April 29, 2019
4.6+	Form of Warrant, issued to affiliates of Brookline Capital Markets, a division of CIM Securities, LLC on April 9, 2019.	S-1/A	333-230838	4.5	April 29, 2019
4.7+	Form of Pre-Funded Warrant to Purchase Common Stock.	8-K	001-38898	4.1	June 27, 2022
4.8+	Form of Common Warrant to Purchase Common Stock.	8-K	001-38898	4.2	June 27, 2022
4.9+	Form of Pre-Funded Common Stock Purchase Warrant.	8-K	001-38898	4.1	February 29, 2024
4.10+	Description of securities registered under Section 12 of the Exchange Act.	10-K	001-38898	4.7	March 13, 2020
10.1*+	Forms of Indemnity Agreement by and between the Registrant and its directors and executive officers.	S-1/A	333-230838	10.1	April 29, 2019

10.2*+	2019 Equity Incentive Plan, as amended.	S-1/A	333-230838	10.2	April 29, 2019
10.3*+	Forms of Option Grant Notice and Option Agreement under 2019 Equity Incentive Plan.	S-1/A	333-230838	10.3	April 29, 2019
10.4*+	Form of Restricted Stock Unit Grant Notice and Unit Award Agreement under 2019 Equity Incentive Plan.	S-1/A	333-230838	10.4	April 29, 2019
10.5*+	2016 Equity Incentive Plan, as amended.	S-1/A	333-230838	10.5	April 29, 2019
10.6*+	Forms of Stock Option Agreement under the 2016 Equity Incentive Plan, as amended.	S-1/A	333-230838	10.6	April 29, 2019
10.7*+	2019 Employee Stock Purchase Plan.	S-1/A	333-230838	10.7	April 29, 2019
10.8†+	Exclusive License Agreement by and between the Registrant and The Trustees of Columbia University in the City of New York, dated October 26, 2016.	S-1	333-230838	10.11	April 12, 2019
10.9†	Exclusive License Agreement by and between the Registrant and Mercury Pharma Group Limited, dated January 3, 2023.	10-K	001-38898-	10.9	March 23, 2023
10.10*+	Employment Agreement, by and between the Registrant and Riccardo Perfetti, dated August 28, 2019.	10-Q	001-38898	10.1	November 13, 2019
10.11*	Employment Agreement, by and between the Registrant and Shoshana Shendelman, dated March 9, 2020.	10-K	001-38898	10.13	March 13, 2020
10.12*	Amendment to Employment Agreement, by and between the Registrant and Riccardo Perfetti, dated March 9, 2020.	10-K	001-38898	10.14	March 13, 2020
10.13*	Employment Agreement, by and between Applied Therapeutics, Inc. and Les Funtleyder, dated November 17, 2023.	8-K	001-38898	10.1	November 17, 2023
10.14*+	Employment letter, by and between Applied Therapeutics, Inc. and Constantine Chinoporos, dated December 28, 2023.	8-K	001-38898	10.1	December 29, 2023
10.15+	Employment letter, by and between Applied Therapeutics, Inc. and Dale Hooks, dated April 9, 2024	8-K	001-38898	10.1	April 15, 2024
10.16+	Separation agreement and general release, by and between Applied Therapeutics, Inc. and Adam Hansard.	8-K	001-38898	10.2	April 15, 2024

10.17*+	Offer Letter, between John H. Johnson and Applied Therapeutics, Inc., dated as of December 19, 2024.	8-K	001-38898	10.1	December 20, 2024
10.18*+	Amendment to Offer Letter, between Les Funtleyder and Applied Therapeutics, Inc, dated as of December 19, 2024.	8-K	001-38898	10.2	December 20, 2024
10.19*+	Separation Agreement, between Shoshana Shendelman and Applied Therapeutics, Inc., dated as of December 19, 2024.	8-K	001-38898	10.3	December 20, 2024
10.20+	Securities Purchase Agreement, dated April 23, 2023, by and among the Company and the 2023 Purchasers.	8-K	001-38898	10.1	April 24, 2023
10.21+	Registration Rights Agreement, dated April 23, 2023, by and among the Company and the 2023 Purchasers.	8-K	001-38898	10.2	April 24, 2023
10.22+	Exchange Agreement, dated as of October 12, 2023, between Applied Therapeutics, Inc. and Venrock Healthcare Capital Partners EG, L.P., Venrock Healthcare Capital Partners III, L.P. and VHCP Co-Investment Holdings III, LLC.	8-K	001-38898	10.1	October 13, 2023
10.23+	Securities Purchase Agreement, dated February 27, 2024, by and among the Company and the 2024 Purchasers.	8-K	001-38898	10.1	February 29, 2024
10.24+	Registration Rights Agreement, dated February 27, 2024, by and among the Company and the 2024 Purchasers.	8-K	001-38898	10.2	February 29, 2024
19.1	Insider Trading Policy.				
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.				
31.1	Rule 13a-14(a)/15d-14(a) Certification under the Exchange Act by John Johnson, Executive Chairman (Principal Executive Officer).				
31.2	Rule 13a-14(a)/15d-14(a) Certification under the Exchange Act by Leslie Funtleyder, Interim Chief Executive Officer and Chief Financial Officer (Principal Financial Officer).				
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 Section 1350 Certifications.				

32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 Section 1350 Certifications.					
97.1*	Applied Therapeutics, Inc. Clawback Policy.	10-K	001-38898	97.1	March 6, 2024	
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File as its XBRL tags are embedded within the Inline XBRL document.					
101.SCH	Inline XBRL Taxonomy Extension Schema Document With Embedded Linkbase Documents.					
104	Cover Page formatted as Inline XBRL and contained in Exhibit 101.					

* Indicates a management contract or compensatory plan.
† Portions of this exhibit have been omitted.
+ Previously filed.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

Applied Therapeutics, Inc.

Dated: April 14, 2025

/s/ *Les Funtleyder*
Name: Les Funtleyder.
Title: Interim Chief Executive Officer and Chief Financial Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Company and in the capacities indicated on the 14th of April 2025.

Name	Title	Date
/s/ John Johnson John Johnson	Executive Chairman and Director (Principal Executive Officer)	April 14, 2025
/s/ Les Funtleyder Les Funtleyder	Interim Chief Executive Officer, Chief Financial Officer and Director (Principal Financial Officer)	April 14, 2025
/s/ Catherine Thorpe Catherine Thorpe	Interim Chief Accounting Officer (Principal Accounting Officer)	April 14, 2025
/s/ Teena Lerner Teena Lerner, Ph.D.	Director	April 14, 2025
/s/ Stacy Kanter Stacy Kanter	Director	April 14, 2025
/s/ Jay S. Skyler Jay S. Skyler, M.D., MACP	Director	April 14, 2025

APPLIED THERAPEUTICS, INC. CORPORATE AND OTHER INFORMATION

Board Of Directors

John H. Johnson
Executive Chairman and Chair of the Board of Directors

Les Funtleyder
Interim Chief Executive Officer, Chief Financial Officer, Treasurer and Secretary

Stacy J. Kanter
Former Head of Global Capital Markets at Skadden, Arps, Slate, Meagher & Flom LLP

Jay S. Skyler, M.D., MACP
Professor of Medicine, Pediatrics and Psychology and Deputy Director of the Diabetes Research Institute at the University of Miami

Teena Lerner, Ph.D.
Founder and Former Chief Executive Officer of Rx Capital Management LP

Executive Officers

John H. Johnson
Executive Chairman

Les Funtleyder
Interim Chief Executive Officer, Chief Financial Officer, Treasurer and Secretary

Catherine Thorpe
Interim Chief Accounting Officer

Constantine Chinoporos
Chief Business Officer and Chief Operating Officer

Dale Hooks
Chief Commercial Officer

Riccardo Perfetti
Chief Medical Officer

Board Committees

Audit Committee
Compensation Committee
Nominating and Corporate Governance Committee

Annual Meeting

The 2025 Annual Meeting of Stockholders will be held online, on the day and time as set forth in the notice of the meeting, proxy statement and form of proxy that will be mailed to stockholders in advance of the meeting.

Form 10-K Report

The Company's Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the Securities and Exchange Commission, is printed as part of this Annual Report. Additional copies are available without charge upon written request to:

Attention: Secretary
Applied Therapeutics, Inc.
545 Fifth Avenue, Suite 1400
New York, NY 10017

Transfer Agent

Computershare Trust Company, N.A
150 Royall Street, Suite 101
Canton, MA 02021
Toll Free: (800) 736-3001
International: +1 (781) 575-3100
www.computershare.com/us

Investor Relations

Maeve Conneighton / Andrew Vulis
(212) 600-1902
appliedtherapeutics@argotpartners.com

Stock Exchange

Applied Therapeutics, Inc.'s common shares are listed on the Nasdaq Global Market under the trading symbol "APLT."

Visit us on the Web
www.appliedtherapeutics.com