2023 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, 2023

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 001-41199

Amylyx Pharmaceuticals, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**46-4600503**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
43 Thorndike St. Cambridge, Massachusetts	**02141**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 682-0917

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 per share	AMLX	Nasdaq Global Select Stock 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 15(d) of the Act. YES ☐ NO ☒

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

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

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

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

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

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

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

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

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

The aggregate market value of voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Market as of June 30, 2023, was $1.31 billion.

The number of shares of Registrant's Common Stock outstanding as of February 12, 2024 was 67,782,139.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2024 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2023. Portions of such definitive proxy statement for the 2024 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

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From time to time, we may use our website or our LinkedIn profile at www.linkedin.com/company/amylyx to distribute material information. Our financial and other material information is routinely posted to and accessible on the Investors section of our website, available at www.amylyx.com. Investors are encouraged to review the Investors section of our website because we may post material information on that site that is not otherwise disseminated by us. Information that is contained in and can be accessed through our website or our LinkedIn page is not incorporated into, and does not form a part of, this Annual Report on Form 10-K.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" or the negative of these terms or other comparable terminology. These statements are not guarantees of future results or performance and involve substantial risks and uncertainties. Forward-looking statements in this Annual Report include, but are not limited to, express or implied statements about:

- our ability to maintain existing regulatory approvals of AMX0035 and obtain additional regulatory approvals of AMX0035 and any other current or future product candidates;
- our ability to continue to successfully commercialize and market AMX0035 and to successfully commercialize and market any other current or future product candidates, if approved, and the timing of any commercialization and marketing efforts;
- our ability to contract with third-party suppliers, manufacturers and other service providers and their ability to perform adequately and to produce sufficient quantities of clinical and commercial supplies;
- the market size, opportunity, demand and growth potential for AMX0035 and any other current or future product candidates, if approved;
- our ability to build and maintain our own sales and marketing capabilities, or seek collaborative partners, to commercialize AMX0035 and any other current or future product candidates, if approved;
- our ability to obtain funding for our operations;
- the initiation, timing, progress and results of our research and development activities, preclinical studies and clinical trials, including our global Phase 3 clinical trial of AMX0035 for the treatment of amyotrophic lateral sclerosis, or ALS, known as the PHOENIX trial, our Phase 3 global clinical trial of AMX0035 for the treatment of progressive supranuclear palsy, or PSP, known as the ORION trial, and our Phase 2 clinical trial of AMX0035 for the treatment of Wolfram syndrome, or WS, known as the HELIOS trial;
- our ability to retain the continued service of our key executives and to identify, hire and retain additional qualified professionals;
- our ability to successfully complete our ongoing clinical trials of AMX0035 and to advance any other current or future product candidates into, and successfully complete, preclinical studies and clinical trials;
- our ability to successfully recruit and enroll suitable patients in our clinical trials;
- the timing or likelihood of the accomplishment of various scientific, clinical, regulatory filings and approvals and other product development objectives, including the timing of a potential resubmission of a Marketing Authorisation Application, or MAA, for AMX0035 for the treatment of ALS in the European Union, or the EU, pending the results of our global Phase 3 PHOENIX clinical trial;
- the pricing and reimbursement of AMX0035 in the U.S., Canada and in any other jurisdictions in which AMX0035 is approved, if any, and of any other current or future product candidates, if approved;
- the rate and degree of market acceptance of AMX0035 and any other current or future product candidates, if approved, by physicians, patients, third-party payors and others in the medical community;
- the implementation of our business model and strategic plans for our business, products, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products, product candidates and technology;
- developments relating to our competitors and our industry, including any regulatory developments;
- our estimates regarding expenses, revenue, capital requirements, cash runway and future needs for additional financing;

- our financial performance, including our ability to maintain profitability;
- fluctuations of our quarterly and annual operating results and the related effects on our stock price;
- the effect of global economic uncertainty and financial market volatility caused by economic effects of rising inflation and interest rates, global health crises, geopolitical events, changes in international trade relationships and military conflicts, such as the ongoing conflict between Russia and Ukraine and the conflict in Israel, on any of the foregoing or other aspects of our business or operations; and
- other statements about future events, including those listed under the section titled "Risk Factors."

Any forward-looking statements in this Annual Report reflect our current views with respect to future events and with respect to our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those described under Part I, Item 1A, "Risk Factors" and elsewhere in this Annual Report. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

All of our forward-looking statements are as of the date of this Annual Report only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Annual Report or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission, or the SEC, could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Annual Report, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Annual Report that modify or impact any of the forward-looking statements contained in this Annual Report will be deemed to modify or supersede such statements in this Annual Report.

We may from time to time provide estimates, projections and other information concerning our industry, the general business environment, and the markets for certain diseases, including estimates regarding the potential size of those markets and the estimated incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events, circumstances or numbers, including actual disease prevalence rates and market size, may differ materially from the information reflected in this Annual Report. Unless otherwise expressly stated, we obtained this industry, business information, market data, prevalence information and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data, and similar sources, in some cases applying our own assumptions and analysis that may, in the future, prove not to have been accurate.

TRADEMARKS

Solely for convenience, our trademarks and trade names in this report are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that we will not assert, to the fullest extent under applicable law, our rights thereto.

PART I

Item 1. Business.

Overview

Amylyx Pharmaceuticals, Inc. (also referred to as Amylyx, we, our or us) is a commercial-stage biotechnology company with a mission to end the suffering caused by neurodegenerative diseases. We have been working in amyotrophic lateral sclerosis, or ALS, and neurodegenerative diseases for over a decade and have been making significant progress in transforming the treatment of these diseases.

Since our founding in 2013, we have transformed from a research-stage company focused on addressing the needs of patients suffering from neurodegenerative diseases to a commercial enterprise with development programs across several indications.

Our first commercial product, AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO], also known as RELYVRIO in the U.S. and ALBRIOZA in Canada) is the first and only ALS therapy of which we are aware that has been shown to slow disease progression, help maintain functional independence, and extend overall survival in the same clinical trial, with a generally well-tolerated side effect profile and oral administration. AMX0035 was commercially launched as RELYVRIO in the U.S. in October 2022 and commercially launched as ALBRIOZA in Canada in July 2022. Since the launch of RELYVRIO and ALBRIOZA through December 31, 2023, we have generated net product revenue of $403.0 million. We believe AMX0035 has the potential to become a widely-used ALS medication and provides an opportunity to transform ALS from a disease for which symptom management is the standard of care to a disease with meaningful interventions. In addition, we believe AMX0035 has the potential to be a foundational therapy for neurodegenerative diseases, meaning that it could be used alone or in conjunction with other therapies to change the treatment paradigm across a broad range of neurodegenerative diseases.

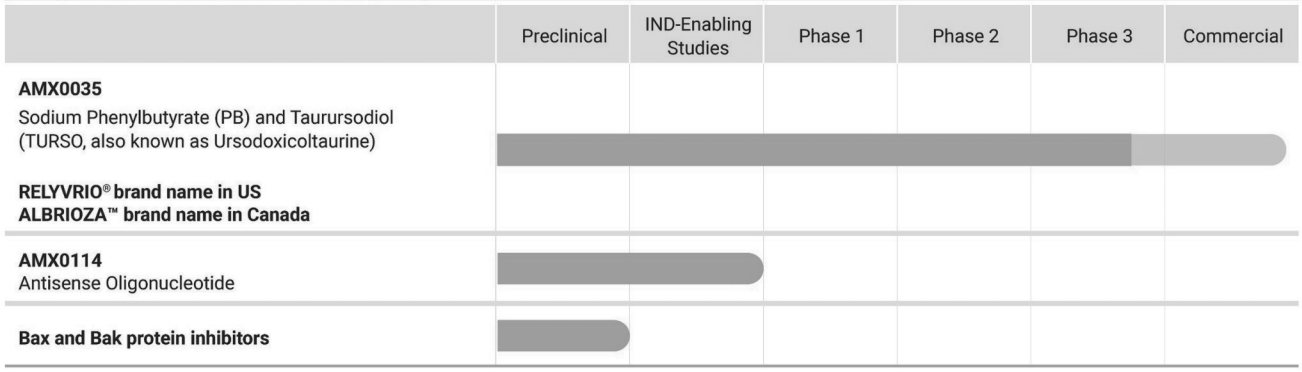
We are committed to bringing the benefits of AMX0035 to the more than 200,000 people living with ALS worldwide. We are building a global infrastructure to commercialize AMX0035 in additional jurisdictions where it may be approved and engaging with key stakeholders around the world to explore opportunities for access including in the EU and Japan.

We continue to focus on the global PHOENIX Phase 3 clinical trial of AMX0035 for the treatment of ALS, a 48-week, randomized, double-blind, placebo-controlled trial at clinical sites in the U.S. and Europe, and expect to report topline results during or before the second quarter of 2024. If the data from PHOENIX are supportive, it will be the first time that two clinical trials have demonstrated a benefit in ALS. We believe that supportive PHOENIX data will further accelerate the commercial launch of AMX0035 and the transformation of the treatment of ALS.

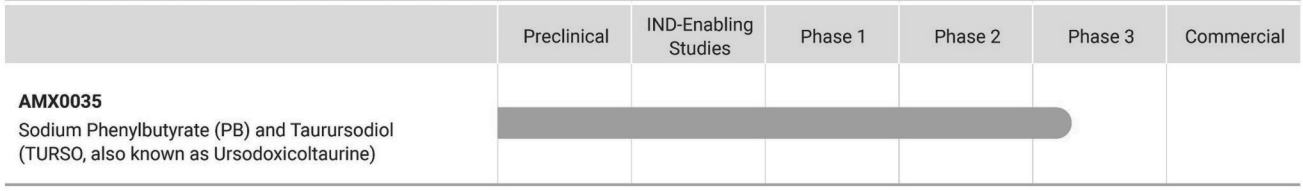
In addition to ALS, we believe there is strong scientific rationale to use AMX0035 to treat other neurodegenerative diseases. AMX0035 was designed to slow or mitigate neurodegeneration by targeting endoplasmic reticulum, or ER, stress and mitochondrial dysfunction, two connected central pathways that lead to neurodegeneration. We believe that our proprietary combination of PB and TURSO and their respective mechanisms of action will allow us to synergistically target abnormal cell death to better prevent neurodegeneration than treatment targeted at either mechanism of action alone. We are actively advancing clinical trials to evaluate AMX0035 in progressive supranuclear palsy, or PSP, and Wolfram syndrome, or WS.

Consistent with our commitment to ongoing research to identify additional potential treatments for ALS and other neurodegenerative diseases, we also are developing AMX0114, an antisense oligonucleotide, for the treatment of people living with ALS. Our current pipeline is represented in the table below.

Amyotrophic Lateral Sclerosis (ALS)

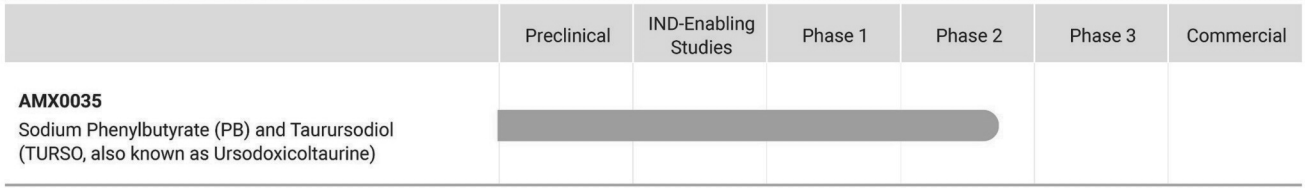


Progressive Supranuclear Palsy (PSP)



Wolfram Syndrome (WS)

Alzheimer's Disease (AD)



Our Company and Team

Amylyx was founded on one simple, unanswered question: What causes neurons to die? Co-CEOs Josh Cohen and Justin Klee began their journey of uncovering the answer, building a world-class company dedicated to ending the suffering caused by relentless progressive neurodegenerative diseases, 11 years ago in 2013. We have assembled a team with deep scientific, clinical, business and leadership experience, bolstered by expertise in biotechnology to help realize our goal. Our Chief Financial Officer, James Frates, brings over 20 years of experience as the Chief Financial Officer of Alkermes. Our Chief Medical Officer, Camille L. Bedrosian, brings nearly 30 years of experience in building successful clinical development and translation research programs in the pharmaceutical industry, including as Chief Medical Officer at Ultragenyx, Alexion, and ARIAD Pharmaceuticals. Our Chief Technical Operations Officer, Tom Holmes, brings more than 25 years of leadership experience at Biogen in supply chain, pharmaceutical manufacturing and program management. Our Chief Legal Officer and General Counsel, Gina M. Mazzariello, brings more than 20 years of corporate and commercial legal experience in the healthcare industry, including holding leadership positions at Boehringer Ingelheim USA, Inc. Our Chief Human Resources Officer, Linda Arsenault, brings over 30 years of people leadership and strategic business acumen including most recently from Sunovion where she was the Chief Human Resources Officer. This team brings a diverse set of skills uniquely suited to drive successful commercialization of AMX0035 in ALS while continuing to advance our pipeline, including studying AMX0035 in other indications, and to explore new approaches and compounds in-house and in partnership with leading clinicians and researchers.

Our Strategy

Our mission is to one day end the suffering caused by neurodegenerative diseases. Key elements of our strategy to achieve this mission include:

- ***Effectively and efficiently commercializing RELYVRIO for ALS in adults in the U.S. and ALBRIOZA for ALS in Canada, obtaining additional regulatory approvals of AMX0035, and commercializing AMX0035 in other key territories, if approved.*** In 2022, AMX0035 was approved by the FDA and commercially launched in the U.S. as RELYVRIO and approved with conditions and commercially launched as ALBRIOZA in Canada. We believe our commercial capabilities, coupled with our understanding of the ALS patient and medical community, enabled us to successfully commercialize, to date, RELYVRIO for ALS in the U.S. and ALBRIOZA for ALS in Canada. We remain committed to bringing the benefits of AMX0035 to the more than 200,000 people living with ALS worldwide. Assuming the data from the PHOENIX trial are supportive, we plan to seek approval for AMX0035 for the treatment of ALS in the EU and the United Kingdom, or UK, as quickly as possible. In addition, we continue to interact with key stakeholders around the world, including Japan, to explore opportunities for access.
- ***Maximizing the therapeutic potential of AMX0035 by expanding into additional neurodegenerative diseases.*** We believe our preclinical data and clinical data from the CENTAUR trial showing functional and survival benefits for ALS patients treated with AMX0035 support its potential mechanism of targeting ER stress and mitochondrial dysfunction. Based on our extensive understanding of neurodegenerative disease pathways, we believe AMX0035 may provide benefit across multiple diseases characterized by neurodegeneration. We conducted our Phase 2 PEGASUS clinical trial in AD to obtain safety data along with initial efficacy and biomarker data, which is helping us evaluate the development of AMX0035 for the treatment of AD within our clinical development strategy. We are also pursuing development of AMX0035 for the treatment of PSP with our Phase 3 ORION clinical trial and WS with our Phase 2 HELIOS clinical trial. As we select additional indications for AMX0035, we will prioritize those indications which we believe, if successful, will most rapidly lead to marketed products and to patient benefit, if approval is received.
- ***Continuing to collaborate with a network of patient advocacy organizations, key opinion leaders, research institutions, and healthcare professionals to inform our patient-centric approach.*** We have partnered with a network of key constituents, which we believe will continue to help us to develop therapies in an efficient and impactful manner. What we learn from the experiences and insights from these groups, which include people living with neurodegenerative diseases, their families, and organizations continues to inform our approach to discovering and developing treatments for people living with ALS and advancing research that addresses unmet needs in additional neurodegenerative diseases. It is a standard practice for Amylyx to partner and consistently engage with these key constituents throughout the pre-clinical to commercialization continuum as we continue to advance our pipeline to better serve and benefit the patients and clinicians.
- ***Deploying a strategic approach to design, acquire and develop new therapies.*** We follow a scientifically rigorous approach to evaluating new opportunities to broaden our portfolio. We plan to target assets that allow us to leverage our experience with neurodegenerative pathways and AMX0035's mechanism of action, focusing

primarily on preventing neuron death. When evaluating assets, we consider not only our ability to apply our experience with AMX0035, but also a variety of factors, including unmet medical need, biological rationale, feasibility of clinical development, potential for regulatory approval, costs of development, competitive landscape and commercial potential. For example, in July 2022, we announced that we entered into a two-year sponsored research agreement with Sunnybrook Research Institute to expedite the identification of novel drug candidates that inhibit Bax and Bak for the development of therapeutics for neurodegenerative diseases, specifically ALS. We are also developing AMX0114, an antisense oligonucleotide, for people living with ALS.

Neurodegenerative Disease

The prevention of neurodegeneration represents one of today's most significant unmet medical needs. The development of therapies that preserve neuron health has historically been limited by unique challenges, including an imperfect understanding of underlying biology and a lack of translation of activity observed in preclinical studies to results in clinical trials. Many neurodegenerative diseases only have symptom-modifying treatment options, with no approved therapies that meaningfully alter the disease course. Others that have approved disease altering therapies still have an unmet need for additional options to further slow disease progression and/or improve survival outcomes. There remains an urgent need for novel approaches to address most neurodegenerative diseases, especially for progressive and severe conditions such as ALS, PSP, WS and AD.

Background and Rationale for AMX0035 in Neurodegenerative Disease

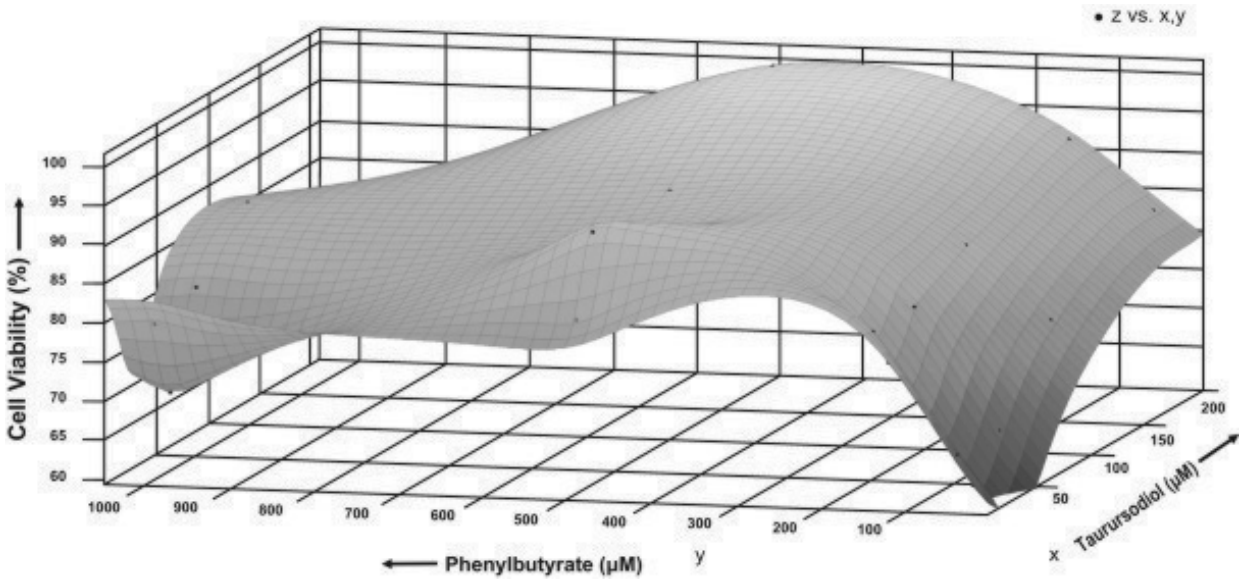
Unlike most other cells in the body that regularly die and are replaced as part of healthy function, mature neurons are normally resistant to cell death and generally cannot regenerate. Neuron death is only triggered when multiple stress factors are activated beyond the neuron's recovery capacity, a circumstance commonly seen in neurodegenerative disorders. Most neurodegenerative disorders have complex pathophysiology, with multiple pathways contributing and converging to eventually cause neuron death. A large fraction of these pathological changes in neurons can be linked to dysfunction in the ER and mitochondria that affect metabolism and secretion of lipids and proteins, calcium homeostasis, and energy production. Dysfunction in these two essential cellular structures is implicated across many neurodegenerative disorders, highlighting the central role they play in maintaining neuron health and survival and providing the rationale for AMX0035, which was designed to rescue ER and mitochondrial function, and to protect and preserve neurons.

AMX0035, a dual unfolded protein response, or UPR, -Bax apoptosis inhibitor, is a proprietary oral fixed-dose combination of two small molecules: PB, which is a small molecular chaperone that reduces the UPR, preventing cell death resulting from the UPR, and TURSO, which is a Bax inhibitor that reduces cell death through apoptosis.

Through the resolution of the UPR and by inhibiting translocation of the Bax to the outer mitochondrial membrane, we have shown in multiple models that AMX0035 can keep neurons alive under a variety of different conditions and stresses, including in *in vitro* models of neurodegeneration, ER stress, mitochondrial dysfunction, oxidative stress and disease-specific models of a variety of other conditions, as well as *in vivo* models of ALS, AD and multiple sclerosis, or MS.

We designed AMX0035 to reduce neuron cell death through simultaneous mitigation of ER stress and mitochondrial dysfunction. PB has been shown to reduce ER stress through upregulation of a protein known as DJ-1 that is a master chaperone regulator, recruitment of other chaperone proteins, and as a small molecular chaperone. TURSO is a bile acid that has been shown to recover mitochondrial bioenergetic deficits through incorporation into the mitochondrial membrane, reducing BAX translocation to the mitochondrial membrane, reducing mitochondrial permeability, and increasing the apoptotic threshold of the cell. Through our research, we identified the specific ratios at which the combination of PB and TURSO target these critical, connected pathways and show synergistic activity in improving neuronal cell viability *in vitro*. In 2022, preclinical data showing the combined potential synergistic effect of PB and TURSO, compared to the individual compounds, were published in the peer-reviewed medical journal *Annals of Clinical and Translational Neurology*. These data on the transcriptomic and metabolomic profiles of primary skin fibroblasts from adults with sporadic ALS and adults without ALS showed that combined PB and TURSO had a greater and more distinct effect on genes and metabolites involved in ALS-relevant pathways compared to either sodium phenylbutyrate or taurursodiol (also known as ursodoxicoltaurine) alone. We then developed AMX0035 as an optimized oral formulation to be tested *in vivo* and clinically.

Our preclinical studies have shown that PB and TURSO, in combination, can inhibit a number of pathological pathways associated with neurodegenerative diseases in cell culture and animal models. For example, in an *in vitro* model of neurodegeneration, we tested the potential abilities of PB and TURSO individually and in combination to prevent oxidative-induced neuronal death, or cell viability, which was measured using a PrestoBlue reagent. In this experiment, hydrogen peroxide was applied to rat primary cortical neurons in a concentration sufficient to kill approximately 40% of the neurons. Particular doses of PB and TURSO individually protected against some of the neuron death, and cell viability reached approximately 80%. However, when these rat primary cortical neurons were dosed with particular ratios of PB and TURSO in combination, nearly 100% of oxidative-induced neuron death was prevented. The results of this *in vitro* model are shown in the graphic below.



Additionally, we have observed benefit from the administration of particular ratios of PB and TURSO across *in vitro* models of ER stress, mitochondrial dysfunction, oxidative stress, and disease specific models of ALS, AD, Parkinson's disease, MS, Friedreich's Ataxia, primary mitochondrial myopathies and a variety of other conditions. We have also conducted *in vivo* models of PB and TURSO, in combination, including models of ALS, AD and MS. Additionally, academic groups have conducted studies with monotherapy treatment with TURSO and/or PB in models of ALS, AD, MS, Parkinson's Disease, Huntington's Disease, PSP, Multi-System Atrophy, X-linked adrenoleukodystrophy, and a variety of other models. We believe this body of evidence collectively supports the use of this combination to treat neurodegenerative indications and led us to pursue the development of AMX0035 in other disease indications.

AMX0035 for the Treatment of ALS

Overview of ALS

We initially developed AMX0035 for the treatment of ALS, a relentlessly progressive and fatal neurodegenerative disease. ALS is caused by motor neuron death in the brain and spinal cord, leading to deteriorating muscle function, the inability to move, speak, swallow, and eat, respiratory paralysis, and, eventually, death. In the later stages of the disease, a person might require constant care, a wheelchair to enable mobility, and mechanical support to communicate, eat and breathe. ALS remains universally fatal with approximately half of patients passing away less than a median of 3 years from symptom onset.

Despite being classified as a rare disease by the U.S. Food and Drug Administration, or the FDA, and the European Medicines Agency, or the EMA, ALS is considered one of the more common adult-onset neuromuscular diseases worldwide. At least 200,000 people worldwide are diagnosed with ALS. We estimate, based on public sources, that there are approximately 30,000 ALS patients in the U.S. More than 30,000 ALS patients are estimated to be located in the EU and the UK, and an estimated 3,000 ALS patients are located in Canada.

Over 90% of patients have no family history of ALS, known as "sporadic" ALS. While other development approaches seek to address genetic instances of ALS, AMX0035 is designed to target all instances of ALS, regardless of whether it is sporadic or genetic. Most people who develop ALS are between the ages of 40 and 70, with a median age of 55 at the time of diagnosis. However, cases of the disease do occur in people in their twenties and thirties.

Medical costs for patients newly diagnosed with ALS in the U.S. are substantial and increase rapidly with each disability milestone. Care of patients with ALS is intensive and requires a team of medical professionals, special equipment, and assistance with daily activities. Caregivers are often forced to miss work or give up employment opportunities to provide care, leading to increased financial strain. The disease also impacts the patient's family, who generally provide the bulk of caregiving, which often entails the provision of 24-hour care. The constant adaptation of caregivers to the demands of the ALS disease progression requires significant physical effort and mental exhaustion particularly during the advanced stages of the disease.

Given half of the patients diagnosed with ALS pass away less than a median of 3 years from symptom onset, a high proportion of the patient population has been recently diagnosed. A therapy that is able to extend independence and slow the loss of physical function of people living with ALS has the potential to increase the number of people who are able to continue living with their disease.

Significant Unmet Need in ALS

ALS is a heterogeneous disease that arises from multiple mechanistic underpinnings, leading patients to experience variable onset and delayed diagnosis, persistent progression and loss of muscle function, and shortened survival.

There is a significant unmet need for ALS therapies that target multiple pathogenic pathways, are disease-modifying, and can provide both functional and survival benefit to patients. AMX0035 treatment by itself and coupled with two other FDA-approved therapeutic agents for ALS, riluzole, an anti-glutamatergic agent, and edaravone, a free-radical scavenger, have been shown to modulate the course of ALS. In pivotal clinical trials, riluzole demonstrated longer time to tracheostomy or death compared to placebo and edaravone demonstrated longer retention of function compared to placebo. However, a need remains for ALS therapies that demonstrate both retention of function and longer survival, allowing patients to maintain greater independence for longer.

Due to the multi-pathway pathophysiology of ALS, experts agree that successful treatment will likely require concurrent targeting of multiple key neuronal death pathways. There is a strong rationale for treatments that target identified convergence points of these critical pathways, including in the ER and mitochondria, and we believe that a therapy that targets multiple pathways simultaneously, like AMX0035, aligns with the emerging ALS treatment paradigm.

Clinical Development of AMX0035 for ALS

We designed our Phase 2 CENTAUR trial with input from leading ALS experts from NEALS to detect a significant difference between AMX0035 and placebo. The study also provided the option for participants to continue with available approved therapies, riluzole and edaravone, for the duration of the trial. The FDA granted orphan drug designation for AMX0035 for the treatment of patients with ALS in September 2017. In December 2019, we announced positive topline results from our CENTAUR trial. The trial met its primary endpoint, and we published detailed trial data in the *New England Journal of Medicine* in September 2020 and in the *Journal of Muscle and Nerve* in October 2020. The EMA granted orphan designation to AMX0035 for the treatment of patients with ALS in April 2020. We submitted a New Drug Submission, or NDS, in Canada in the second quarter of 2021, a New Drug Application, or NDA, in the U.S. in the fourth quarter of 2021 and a MAA in Europe in the first quarter of 2022.

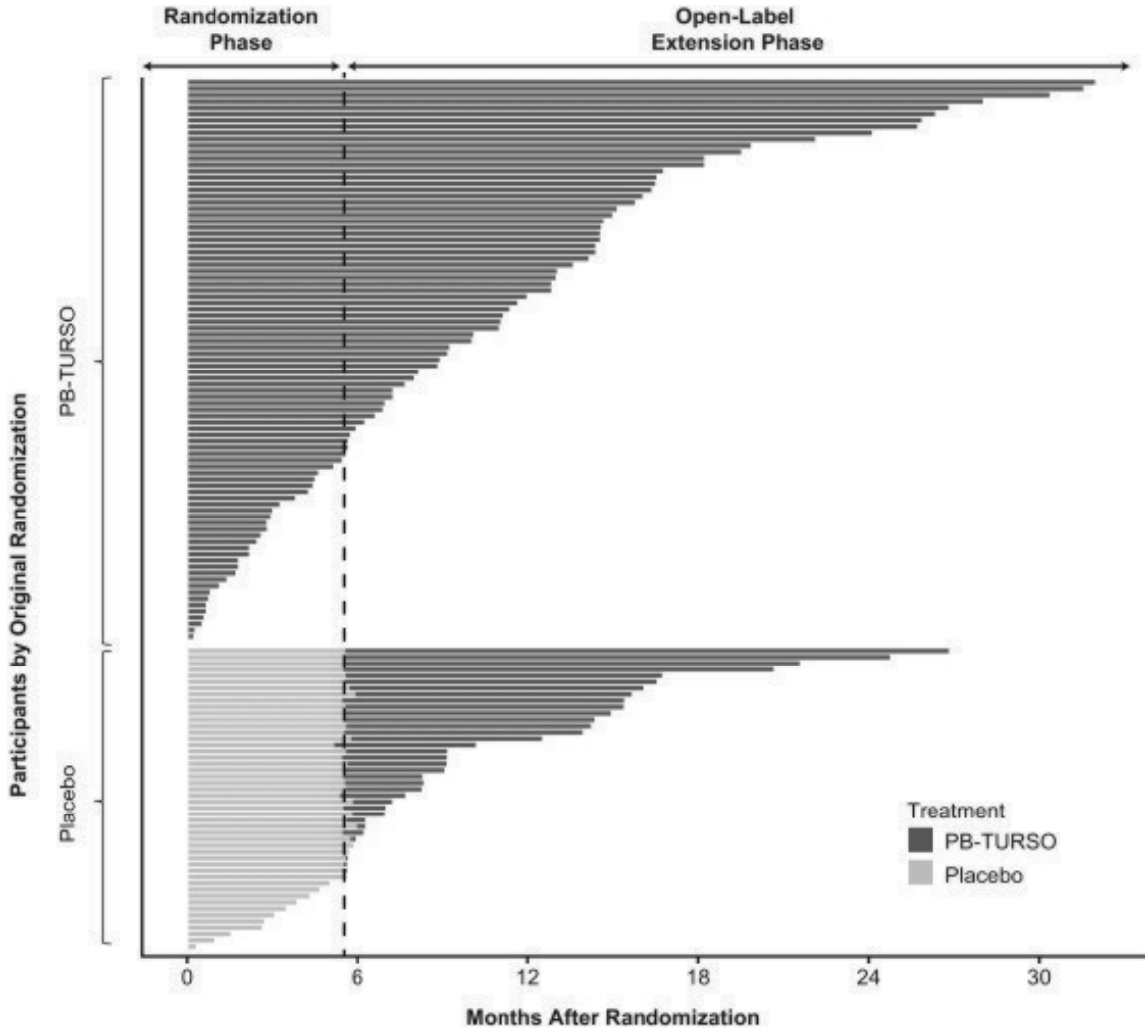
In June 2022, AMX0035 received marketing authorization with conditions as ALBRIOZA by Health Canada for the treatment of ALS, and we launched ALBRIOZA commercially in Canada in July 2022. In September 2022, AMX0035 received approval as RELYVRIO by the FDA for the treatment of ALS in adults, and we launched RELYVRIO commercially in the U.S. in October 2022.

In October 2023, the Committee for Medicinal Products for Human Use, or CHMP, of the EMA confirmed its initial negative opinion on the MAA for AMX0035, for the treatment of adults with ALS in the EU. The decision followed the conclusion of the CHMP's formal re-examination procedure of an initial negative opinion adopted in June 2023. In January 2024, the European Commission confirmed the adoption of the CHMP's negative opinion. We continue to focus on the completion of the global PHOENIX Phase 3 clinical trial of AMX0035 for the treatment of ALS, which was initiated prior to our MAA submission in November 2021. If PHOENIX is supportive, we plan to seek approval in the EU again as quickly as possible.

CENTAUR, Our Phase 2 Trial of AMX0035 in ALS

In September and October 2020, we published detailed results from the Phase 2, randomized, double-blind, placebo-controlled CENTAUR trial. The CENTAUR trial was conducted at 25 NEALS centers and evaluated adult patients with ALS. Key inclusion criteria were definite ALS defined by the revised El Escorial criteria, which entails having various clinical signs and symptoms, defined as upper and lower motor neuron signs, in at least three defined body regions, less than 18 months from symptom onset and slow vital capacity, or SVC, greater than 60%. These criteria were chosen to select a homogenous, rapidly progressing patient population to potentially increase the likelihood of observing a treatment effect. Participants were allowed to continue on their selected standard of care, including treatment with riluzole and/or edaravone. Eligible participants (n=137) were randomized two-to-one to treatment with AMX0035, one sachet (each containing one gram of TURSO and three grams of PB) given once daily for the first three weeks, and if tolerated, the dose was then increased to twice-daily for the remainder of a 24 week treatment period, or matching placebo. Two participants did not have follow-up efficacy assessments and were not included in the efficacy population (modified intention to treat, or mITT, n=135). These two participants were included in the safety population (intention to treat, or ITT, n=137). Upon completion of the 24-week, parallel group phase of the trial, participants were eligible to enroll in the Open Label Extension, or OLE, trial in which all participants were followed up to 35 months while participants and physicians remained blinded to the original treatment group. Of participants completing the CENTAUR trial randomization phase, 92% elected to enroll in the OLE. The

first protocol of the OLE was completed in March 2021. Actual duration of patient treatments across the randomization phase and the OLE, both with the PB-TURSO combination and via placebo, are shown in the graphic below:

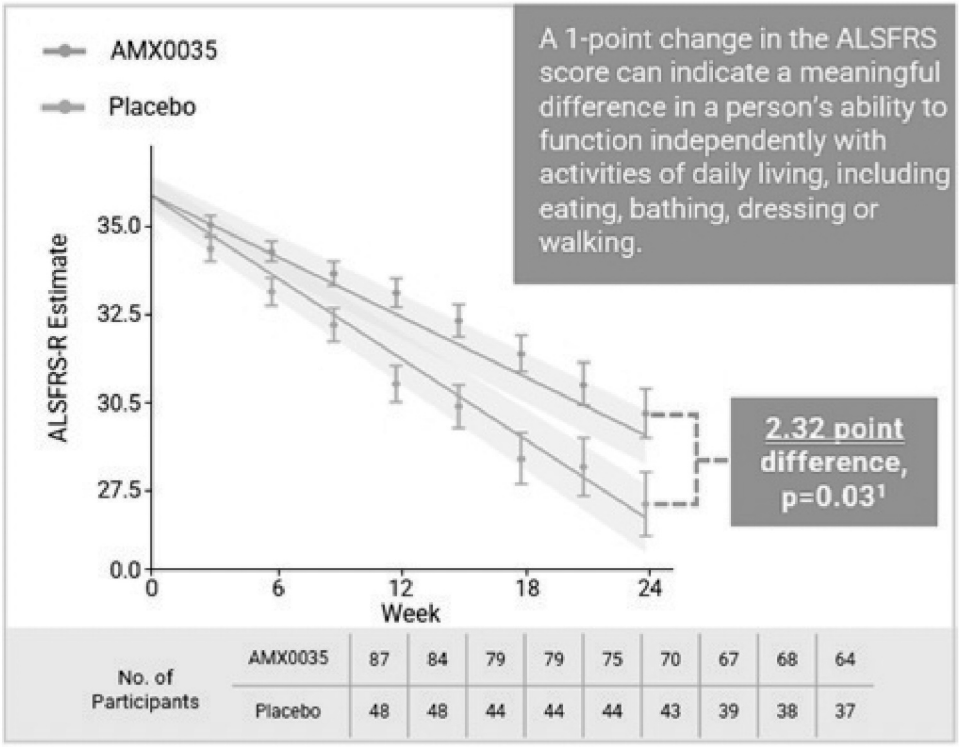


The primary efficacy outcome measure for the CENTAUR trial was the rate of decline in the ALSFRS-R total score. The ALSFRS-R scale is the most widely used ALS rating scale in ALS clinical practice and in ALS clinical trials. It measures patients' functional ability and is broken down into four domains: bulbar (which includes speech, salivation and swallowing), fine motor (which includes handwriting, cutting food/handling utensils, dressing and hygiene), gross motor (which includes turning in bed, walking, and climbing stairs) and breathing (which includes dyspnea, orthopnea and respiratory insufficiency). A decrease of one point on the ALSFRS-R scale can reflect severe limitations in a patient's independence, and a two-point increase on the ALSFRS-R scale would be associated with:

- eating successfully with some difficulty instead of needing a feeding tube;
- being short of breath only while walking instead of having difficulty breathing while sitting or lying down; and
- being able to dress independently instead of needing assistance.

The CENTAUR trial met its primary endpoint with a statistically significant reduction in clinical decline among participants randomized to AMX0035 (n=87) compared to placebo (n=48) (p-value of 0.03) over 24 weeks. These results showed that patients receiving AMX0035 scored an average of 2.32 points higher on the ALSFRS-R as compared to patients receiving placebo after 24 weeks, a difference of 25%, as shown in the graph below. In a survey of ALS clinicians and researchers conducted and sponsored by NEALS, with the objective of determining what percentage reduction in ALSFRS-R would be considered clinically meaningful, a difference of greater than or equal to 20% in ALSFRS-R total score was

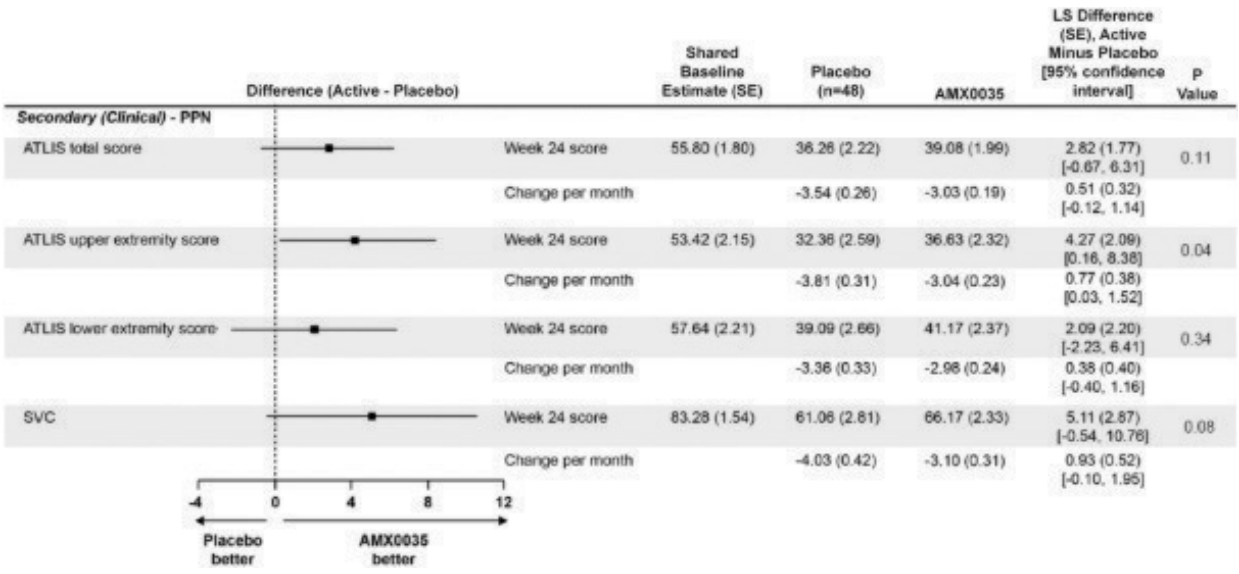
considered clinically meaningful by a majority of clinicians and researchers surveyed. More recent publications by ALS experts have shared the viewpoint that a single point difference can be considered clinically meaningful.



[1.] Two participants did not have follow-up efficacy assessments and were not included in the efficacy population (modified intention to treat n=135).

Secondary efficacy outcomes measuring disease free progression were the decline in muscle strength as measured by Accurate Test of Limb Isometric Strength, or ATLIS, testing and lung function measured by SVC, both expressed as percent of predicted values and key study events including death, permanent ventilation and hospitalization. Neurofilament was also measured as a biologic measure. The analysis also indicated statistically significant preservation of upper limb strength with AMX0035 treatment measured on ATLIS (p=0.042), while the lower limb measure did not reach statistical significance (p=0.34). An average of these two, referred to as the total ATLIS score, trended in favor of AMX0035 (p=0.11). There was also a trend in favor of AMX0035 therapy preserving lung function as measured by SVC, with a numerical difference of 5.11% although this was not statistically significant (p=0.076). These efficacy data are summarized in the table below. In addition, a time-to-event analysis was conducted on key study events including death, permanent ventilation and hospitalization events over the 24-week randomized phase of the trial. Because enrollment of patients in the CENTAUR trial was limited to patients who, in the investigator's opinion, would be able to complete a 6-month follow up, few events of this nature were expected during the initial, 24-week randomized phase of the trial. As a result, we observed a positive, but not statistically significant, difference between the trial's treatment and control groups during the 24-week randomized phase of

the study. There was no statistically significant difference between the rate of decline in plasma levels of the neurofilament observed in the trial's treatment and control groups during the 24-week randomized phase of the study.



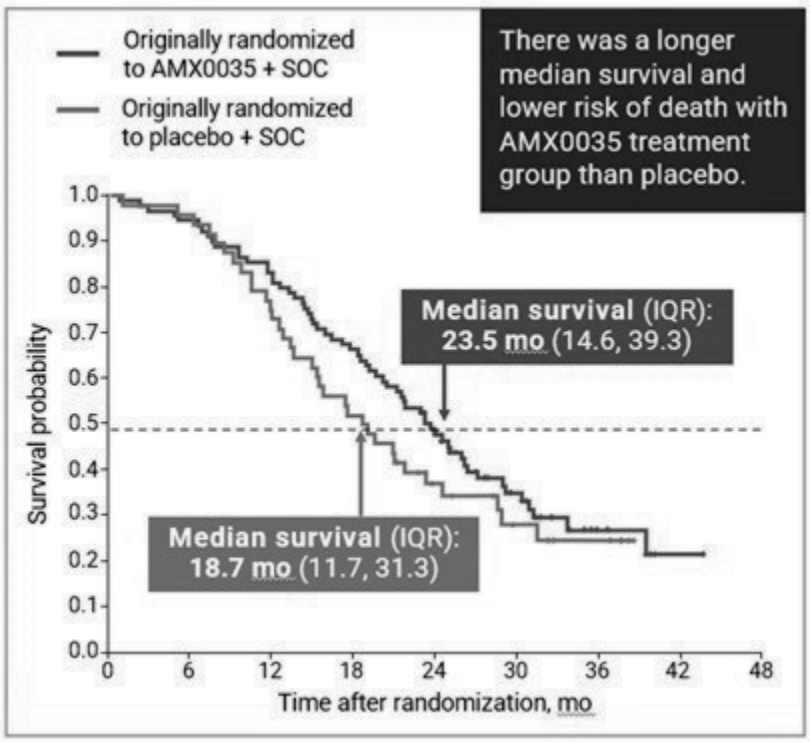
			Shared Baseline Estimate (SE)	Placebo (n=48)	AMX0035	LS Difference (SE), Active Minus Placebo [95% confidence interval]	p Value
***Secondary (Clinical)* - PPN**							
ATLIS total score		Week 24 score	55.80 (1.80)	36.26 (2.22)	39.08 (1.99)	2.82 (1.77) [-0.67, 6.31]	0.11
		Change per month		-3.54 (0.26)	-3.03 (0.19)	0.51 (0.32) [-0.12, 1.14]	
ATLIS upper extremity score		Week 24 score	53.42 (2.15)	32.36 (2.59)	36.63 (2.32)	4.27 (2.09) [0.16, 8.38]	0.04
		Change per month		-3.81 (0.31)	-3.04 (0.23)	0.77 (0.38) [0.03, 1.52]	
ATLIS lower extremity score		Week 24 score	57.64 (2.21)	39.09 (2.66)	41.17 (2.37)	2.09 (2.20) [-2.23, 6.41]	0.34
		Change per month		-3.36 (0.33)	-2.98 (0.24)	0.38 (0.40) [-0.40, 1.16]	
SVC		Week 24 score	83.28 (1.54)	61.06 (2.81)	66.17 (2.33)	5.11 (2.87) [-0.54, 10.76]	0.08
		Change per month		-4.03 (0.42)	-3.10 (0.31)	0.93 (0.52) [-0.10, 1.95]	

Phosphorylated neurofilament heavy chain was measured in plasma in the CENTAUR trial. There were no statistically significant differences between groups in this outcome. A limitation of this outcome is that it was measured in plasma rather than cerebrospinal fluid and the ultimate relevance of this outcome in ALS is still under investigation by the field.

It is important to note that most (77%) participants were receiving riluzole or edaravone at or before study entry, with a greater proportion receiving edaravone in the placebo group (50%) compared with the AMX0035 group (25%). Pre-specified analyses were conducted to determine if the use of concomitant medications impacted results. These analyses found that AMX0035's effect on the primary outcome was consistent regardless of baseline use of concomitant medications (riluzole and/or edaravone).

Overall survival, or OS, was analyzed for all subjects randomized in the CENTAUR trial (ITT analysis) and compared patients originally randomized to AMX0035 (n=89) with those randomized to placebo (n=48). In this post hoc analysis, the vital status of each participant was measured by a participant locating service which used sources such as the U.S. social security death index up to March 1, 2021 even if he or she did not continue into the OLE, stopped study drug, dropped out of the study or was lost to follow-up. Over the duration of follow up, the risk of death was 36% lower among those originally randomized to AMX0035 compared with those originally randomized to placebo (hazard ratio, or HR, of 0.64; a 95% confidence interval, or CI, ranging from 0.42 to 1.00; and a p-value of 0.048). Median survival duration was 23.5

months (IQR of 14.6 to 39.3 months) in the group previously randomized to AMX0035 and 18.7 months (IQR of 11.7 to 31.3 months) in the group previously randomized to placebo as seen in the graph below.



We also conducted three additional post hoc analyses of AMX0035 survival data and one additional post hoc biomarker analysis. These analyses consisted of the following: an analysis utilizing a statistical method, known as the rank-preserving structural failure time model (RPSFTM), to adjust for the effect of treatment crossover; an analysis comparing observed survival in the CENTAUR trial to predicted survival using the European Network for the Cure of ALS survival prediction model derived from an ALS natural history database; an analysis comparing observed survival from the CENTAUR treatment group to survival of matched treatment naïve participants from historical clinical trials of ALS; and finally an analysis performed on neuroinflammatory biomarkers using plasma samples from participants in CENTAUR.

In May 2022, the post hoc analysis using RPSFTM, a method frequently employed in oncology to account for placebo crossover, estimated a 9.7-month longer median survival duration for participants originally randomized to AMX0035 than participants originally randomized to placebo. In addition, participants randomized to receive AMX0035 and who continued into the OLE phase showed an 15-month longer median survival duration than participants who never received AMX0035 in a subgroup analysis.

The European Network to Cure ALS, or ENCALS, has collected data on more than 10,000 people living with ALS and used this data to create a prognostic model based on baseline factors to predict patient survival time. Amylyx collaborated with the originators of this model to predict treatment naïve overall survival time for each individual participant in CENTAUR. The predicted (treatment naïve) survival data generated using this model were compared against the actual observed survival data in the CENTUR study. In this post hoc analysis, participants randomized to AMX0035 had a 9.9-month longer median survival compared to the prediction arm.

In October 2023, the post hoc analyses comparing the long term survival of participants in the CENTAUR study versus a propensity score-matched, AMX0035 naïve propensity score-matched, AMX0035 were published in the peer-reviewed medical journal, *Annals of Clinical and Translational Neurology*. In this analysis, we observed a median overall survival of 10.4 months longer in the AMX0035 group. Participants treated with AMX0035 at the start of the clinical trial, which means that they both started AMX0035 six months earlier and were on it for longer than participants starting on placebo, saw a greater survival benefit.

In December of 2023, post hoc analyses performed on neuroinflammatory biomarkers using plasma samples from CENTAUR trial participants were published in *Journal of Neurology, Neurosurgery and Psychiatry*. The results

demonstrated a significant reduction in plasma concentrations of YKL-40 (also known as chitinase-3-like protein 1) and the systemic inflammatory biomarker C-reactive protein (CRP), two plasma neuroinflammatory biomarkers in ALS, over 24 weeks, with reductions observed as early as Week 12 in participants from the CENTAUR trial.

We also performed sensitivity analyses on the CENTAUR trial data, including a joint rank test, which showed no bias in the estimate of the primary functional outcome by loss of data due to participant death. Sensitivity analyses were also performed to account for missing data and death or death-equivalent events. These sensitivity analyses yielded results similar to the primary analysis. In sensitivity analyses designed to account for concomitant medication use, the treatment effect size was consistent between primary analysis and analyses corrected for concomitant medication use.

AMX0035 was generally well-tolerated with an adverse event rate substantially similar to placebo. Adverse events, or AEs, were reported in 97% (86 out of 89) of participants receiving AMX0035 and 96% (46 out of 48) of participants receiving placebo, with the nature of the AEs being substantially similar in both groups. The most commonly occurring (greater than or equal to 5%) AEs in either treatment group are shown in the table below. Because of the progressive neurodegenerative nature of ALS, many of these AEs (e.g., muscle weakness, falls, dyspnea, fatigue) were likely attributable to the underlying ALS disease. Events occurring in greater than or equal to 5% of patients in either treatment group and more frequently (greater than or equal to 2% of patients) in patients who received AMX0035 compared with those who received placebo were predominantly gastrointestinal events, which were non-serious and mostly mild in intensity and declined considerably in occurrence after three weeks on treatment. A total of 19% of the patients in the AMX0035 treatment group and 8% of the patients in the placebo group discontinued their participation in the trial due to AEs.

The most commonly occurring AEs were diarrhea, abdominal pain, nausea, upper respiratory tract infection, constipation, muscular weakness, fall, headache, dizziness and viral upper respiratory tract infection. Health Canada also noted the occurrence of hypersalivation. Consistent with the known safety profile of TURSO, diarrhea and nausea occurred more frequently in patients who received AMX0035 compared with those who received placebo. In contrast, muscular weakness, fall, constipation and headache occurred more frequently in patients who received placebo. The observed AEs from the CENTAUR trial are summarized in the chart below.

Adverse Events (AEs)[1] Occurring in ≥5% of Patients in either Treatment Group (Safety Population, n=137)

MedDRA System Organ Class Preferred Term	Placebo + SOC (n=48)	AMX0035 + SOC (n=89)	Overall (n=137)
Gastrointestinal disorders	29 (60.4%)	60 (67.4%)	89 (65.0%)
Musculoskeletal and connective tissue disorders	21 (43.8%)	38 (42.7%)	59 (43.1%)
Injury, poisoning and procedural complications	23 (47.9%)	35 (39.3%)	58 (42.3%)
Nervous system disorders	19 (39.6%)	33 (37.1%)	52 (38.0%)
Infections and infestations	21 (43.8%)	28 (31.5%)	49 (35.8%)
Respiratory, thoracic and mediastinal disorders	10 (20.8%)	29 (32.6%)	39 (28.5%)
Investigations	10 (20.8%)	26 (29.2%)	36 (26.3%)
General disorders and administration site conditions	13 (27.1%)	20 (22.5%)	33 (24.1%)
Skin and subcutaneous tissue disorders	8 (16.7%)	16 (18.0%)	24 (17.5%)
Psychiatric disorders	9 (18.8%)	14 (15.7%)	23 (16.8%)
Renal and urinary disorders	8 (16.7%)	10 (11.2%)	18 (13.1%)
Metabolism and nutrition disorders	4 (8.3%)	10 (11.2%)	14 (10.2%)
Cardiac disorders	0 (0.0%)	7 (7.9%)	7 (5.1%)
Eye disorders	1 (2.1%)	5 (5.6%)	6 (4.4%)

(1) Includes serious adverse events.

Serious adverse events, or SAEs, occurred nominally less frequently in the AMX0035 treatment group (12.4% of patients) compared with the placebo treatment group (18.8% of patients). This difference was largely driven by a higher incidence of respiratory events, including respiratory failure in the placebo treatment group (8.3% of patients), compared with the AMX0035 treatment group (3.4% of patients). ALS disease progression often leads to respiratory failure, and it is the most common cause of death in patients with ALS. The observed SAEs from the CENTAUR trial are summarized in the chart below.

Serious Adverse Events (SAEs)

	AMX0035 + SOC (n=89)	Placebo + SOC (n=48)	Overall (N=137)
At least 1 serious AE – n (%)	11 (12)	9 (19)	20 (15)
Number of distinct events	14	10	24
At least 1 fatal AE – n (%)	5 (6)	2 (4)	7 (5)
At least 1 serious AE considered related to treatment – n (%)	1 (1)	1 (2)	2 (2)
Drug withdrawn due to serious AE – n (%)	1 (1)	3 (6)	4 (3)
Due to serious AE considered related	0	0	0
Due to serious AE considered unrelated	1 (1)	3 (6)	4 (3)

Overall, a total of seven patients, two (4% of patients) who received placebo and five (6% of total patients) who received AMX0035), died during the conduct of the 24-week, double-blind study. None of the deaths was considered by the investigator to be related to AMX0035. Consistent with the most common cause of death in patients with ALS, the majority (four of seven patients) of deaths during the study were from respiratory failure (two patients in each group). Other causes of death (in the AMX0035 group) included post-extubational supraglottic and infraglottic aspiration (attributed to aspiration pneumonia), diverticulitis, and subdural hematoma secondary to a fall. Death equivalent was defined as either tracheostomy or permanent assisted ventilation, or PAV. PAV was defined as more than 22 hours daily of non-invasive mechanical ventilation for more than one week (seven days). One patient in the placebo group (2% of patients) and none in the AMX0035 group experienced a death equivalent event (i.e., tracheostomy/PAV) during the 24-week study.

In March 2022, we announced the launch of a U.S. EAP that the FDA authorized for people with ALS who meet certain eligibility criteria for participation. The EAP was discontinued alongside the commercial launch of RELYVRIO in the U.S.

We believe AMX0035 is the first drug candidate in ALS to demonstrate a statistically significant benefit both in function as measured by a prespecified mean rate change in ALSFRS-R and in a longer-term analysis of OS, both important outcomes for people with ALS. In summary, patients in our CENTAUR trial showed a statistically significant improvement in function and a statistically significant improvement in overall survival and AMX0035 was shown to be generally well-tolerated.

Clinical Development Plan of AMX0035 in ALS

Our global PHOENIX Phase 3 clinical trial of AMX0035 for the treatment of ALS, a 48-week, randomized, double-blind, placebo-controlled trial at clinical sites in the U.S. and Europe, is designed to provide further data evaluating the safety and efficacy of AMX0035 for the treatment of ALS. Enrollment in this trial was completed in March 2022 in the U.S. and in February 2023 in Europe. We announced the completion of enrollment in the PHOENIX trial, which enrolled 664 participants, in February 2023. We expect to report topline results from the PHOENIX trial during or before the second quarter of 2024.

The primary endpoints in our PHOENIX trial will be a composite measure of survival and ALSFRS-R total score progression over 48 weeks and safety and tolerability over 48 weeks. The secondary endpoints of our PHOENIX trial will be SVC, ALSAQ-40 (a questionnaire which provides a subjective health measure to specifically assess quality of life for patients with ALS), EQ5D-5L (a standard qualify of life measure), decline in King's (a staging measurement in ALS based on the number of central nervous system, or CNS, regions involved and requirement for gastrostomy or noninvasive ventilation) and MiToS stages (a functional staging measure that can be derived prospectively from the ALSFRS-R subscore using standard methods), ventilation free survival, and long-term survival. Key inclusion criteria for the PHOENIX trial

include ALS patients with clinically definite or clinically probable ALS by El Escorial criteria (2-4 body areas with clinical signs consistent with ALS), <24 months from symptom onset, SVC >55%, and riluzole/edaravone use permitted.

European participants completing the 48-week trial had the option to enroll in an open label extension phase. During this phase, all participants received AMX0035, and continued safety and efficacy measures were assessed.

Because marketing approvals we have obtained to date may be limited, subject to restrictions or post-approval requirements, we may need to provide post-marketing support in those same jurisdictions. For example, as part of our approval for RELYVRIO in the U.S., we have post-marketing requirements to conduct carcinogenicity studies in mice and rats, drug-drug interaction studies, and studies in patients with kidney or liver impairment. In addition, one of the conditions of the marketing authorization in Canada for AMX0035 is the provision of data from our ongoing PHOENIX trial and other additional planned or ongoing studies. The outcomes of the PHOENIX trial could have a material effect on our business.

We also have studies planned to further assess the safety and efficacy of AMX0035 in people living with ALS, including in real-world settings. These collaborative studies include a single center experience and a payer database observational study among others.

Commercialization of AMX0035 in ALS

We believe the global commercial opportunity for AMX0035 in ALS is driven by its being the first and only ALS therapy of which we are aware that helps to slow disease progression, maintains functional independence and extends overall survival in the same trial. AMX0035 is generally well-tolerated, with a manageable side effect profile and convenient oral administration. AMX0035 has been shown to have a significant impact on clinically meaningful endpoints, including reducing time to first hospitalization and permanent ventilation in ALS patients. From launch to December 31, 2023, we generated net product revenue from sales of AMX0035 of $403.0 million.

AMX0035 for the Treatment of Other Potential Indications

Based on our extensive understanding of disease pathways, we believe AMX0035 may provide benefit across multiple diseases, including AD, WS, Parkinson’s Disease, Huntington’s Disease, PSP, Multi-System Atrophy, primary lateral sclerosis, ischemic stroke, MS, Friedreich’s ataxia, Leigh’s syndrome and Leber’s hereditary optic neuropathy.

We are prioritizing these conditions on an indication-by-indication basis, based on the strength of the data supporting AMX0035’s potential; the urgency of the unmet need; the practicality of conducting clinical trials in these conditions; the efficiency of clinical development activities; and the commercial potential. For some of these indications, given the data already produced by the company on AMX0035, we believe it may be possible to move directly into Phase 3 evaluations of safety and efficacy which could allow for a rapid development pathway. We will prioritize those indications which we believe have the greatest chance of providing patients with benefit and the most rapid pathway to market.

Clinical Development of AMX0035 for Progressive Supranuclear Palsy

We initiated the ORION trial, a global, pivotal Phase 3 trial of AMX0035 for the treatment of PSP in December 2023. ORION is a global, randomized, double-blind, placebo-controlled Phase 3 clinical trial designed to assess the efficacy and safety of AMX0035 compared to placebo. Approximately 600 participants will be enrolled in approximately 100 sites across the United States, Canada, the EU, the United Kingdom, and Japan, making what we expect to be this the largest PSP clinical trial to date.

The primary efficacy endpoint will evaluate change in disease progression from baseline to Week 52 as measured by total score on the 28-item Progressive Supranuclear Palsy Rating Scale (PSPRS), an established and validated endpoint in PSP clinical trials.

Secondary efficacy endpoints are disease progression as measured by a modified 10-item PSPRS score and motor aspects of activities of daily life as measured by the Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part 2 (MDS-UPDRS Part II). Exploratory outcomes include changes in activities of daily living, cognitive function, quality of life, overall survival, brain regional volumes, fluid biomarkers of neuronal injury/inflammation, and caregiver burden.

Safety and tolerability will be evaluated by assessing the frequency of treatment emergent adverse events (TEAEs) and serious adverse events (SAEs). Topline results are anticipated in either 2025 or 2026. Participants completing the 52-

week randomized, placebo-controlled phase of the trial will have the option to enroll in an Open Label Extension where all participants will receive AMX0035 for up to an additional year.

ORION was designed and planned in collaboration with key global academic leaders, people living with PSP and their caregivers, and industry advocacy organizations.

PSP is a sporadic, rare and adult-onset neurodegenerative disorder that affects walking and balance, eye movement, swallowing, and speech. The disease is reported to affect seven in 100,000 people worldwide. People living with PSP have a life expectancy of six to eight years after initial diagnosis, and PSP typically begins in late-middle age and rapidly progresses over time. There are currently no approved therapies for the treatment of PSP.

Preclinical data support the potential of both sodium phenylbutyrate, PB, and taurursodiol, TURSO, the two small molecules in the fixed-dose combination of AMX0035, for the potential treatment of PSP. In a variety of *in vitro* experiments, sodium phenylbutyrate upregulated and recruited chaperone proteins, stabilized protein folding, and reduced ER stress and the unfolded protein response, which can lead to apoptosis if the stress is overwhelming. It has been shown in PSP that the unfolded protein response is activated in disease-affected regions in PSP and genetic evidence indicates this activation is not a protective response but a risk factor for the development of PSP. TURSO stabilized the mitochondrial membrane by reducing the translocation of cell death regulator Bax, leading to improved mitochondrial function and energy production, and an increased cell apoptotic threshold. In PSP, impairment of mitochondrial function has been shown in cybrid cell lines from patients with PSP as well as neurons derived from patients with PSP.

PSP is characterized by abnormal tau inclusions and is consequently also known as a tauopathy. Similar to other neurodegenerative diseases, pathophysiologic changes underlying PSP are multifactorial with several genetic and environmental factors likely contributing to tau dysfunction and aggregation. Multiple pathways, including genetic mutations, endoplasmic reticulum stress and the activation of unfolded protein response, mitochondrial dysfunction, and neuroinflammation have been implicated as contributors to tau dysfunction and aggregation. Based on preclinical data and biomarker analyses from the Phase 2 PEGASUS trial of AMX0035 in AD, AMX0035 was shown to significantly lower levels of tau and other markers of neurodegeneration.

Clinical Development of AMX0035 for WS

We announced that the FDA granted orphan drug designation to AMX0035 for the treatment of WS in November 2020. In March 2023, we completed site activation for a Phase 2 clinical trial of AMX0035 for the treatment of WS and in April 2023, we announced that the first participant was dosed. The trial is an exploratory open-label proof of biology study assessing the effect of AMX0035 safety and tolerability, and various measures of endocrinological, neurological and ophthalmologic function. We anticipate topline results from the trial in 2024.

Researchers from the Washington University School of Medicine in St. Louis, in collaboration with Amylyx, published preclinical data exploring the potential of AMX0035 as a novel therapeutic approach for WS. These data were published in the peer-reviewed *Journal of Clinical Investigation*, characterizing a pathogenic variant in the WFS1 gene (WFS1 c.1672C>T, p.R558C), identifying a platform for further genotype-phenotype analysis, and providing initial proof-of-concept for the therapeutic development of AMX0035 in WS. The study demonstrated that iPSC-derived WS models can provide a model of genotype-phenotype relationships that correlate with clinical observations. Study highlights related to AMX0035 included:

- Administration of AMX0035 improved WFS1 protein expression, increased insulin secretion, and inhibited cell death in β cells with the WFS1 c.1672C>T, p.R558C variant. AMX0035 also prevented cellular death in patient-derived neuronal progenitor cells. Gene enrichment analysis revealed that treatment with AMX0035 ameliorated organelle dysfunction, mitophagy, ER stress, and apoptosis.
- Furthermore, AMX0035 delayed the onset of the diabetic phenotype *in vivo* in the Wfs1-knockout mouse model of WS.

WS is an autosomal recessive neurodegenerative disease characterized by childhood-onset diabetes, optic nerve atrophy, and neurodegeneration. Common manifestations of WS include diabetes mellitus, optic nerve atrophy, central diabetes insipidus, sensorineural deafness, neurogenic bladder, and progressive neurologic difficulties. The prognosis of WS

is poor, and many people with the disease die prematurely with severe neurological disabilities. WS is a rare, pediatric, life-threatening disease thought to be caused by variants in the WS WFS1 gene, or WFS1, and, in a small fraction of patients, pathogenic variants in the CDGSH iron sulfur domain protein 2 CISD2 gene, or CISD2. There are currently no drugs approved for WS.

WS appears to be a disease of ER stress. WFS1 encodes and produces the vital wolframin protein, which appears to be involved in ER regulatory processes. WFS1 deficiency leads to chronic ER stress and the UPR. WFS1 also negatively regulates activating transcription factor 6 (ATF6), a UPR molecule, resulting in cell death. Furthermore, a recent study suggested that WFS1 impacts mitochondrial function by transporting Ca2+ from the ER to the mitochondria through the mitochondria-associated ER membrane, or MAM.

AMX0035 targets pathways central to WS, including the UPR, and has shown beneficial effects in a variety of models of WS, including cellular models and patient-derived cell line models. For example, to test the potential effects of AMX0035 in the modulation of ER stress in the context of WS, the effects of PB, TURSO and AMX0035 were tested in an *in vitro* model of wild-type and WFS1-deficient pancreatic beta cell lines. In these cells, when compared with the control group, only AMX0035, but not PB or TURSO alone, was able to significantly prevent tunicamycin-induced cell death in WFS1-deficient pancreatic beta cell lines as measured by caspase 3 / 7 activity ($p = 0.017$). Additionally, a combination of PB and TURSO was studied *in vitro* in human patient-derived neural progenitor cells harboring mutations in WFS1, which cause WS. Both PB and TURSO, when applied alone, were observed to inhibit cell death in each of three different human cell lines as compared to control conditions, and the application of PB and TURSO in combination was observed to result in significantly lower levels of cell death in three separate patient-derived WS cell lines differentiated to produce patient-derived neural progenitor cells, as compared to either the control or treatment with PB or TURSO alone. Thus, in relevant models of WS, use of AMX0035 was observed to have synergistic effects lowering cell death as compared to either the control group or treatment with PB or TURSO alone. For these reasons, we believe AMX0035 is a promising clinical candidate for WS.

Clinical Development of AMX0035 for AD

In 2021, we completed and reported the results from our Phase 2 PEGASUS trial evaluating the safety, tolerability and activity of AMX0035 in patients with late mild cognitive impairment, or MCI, or early-to-moderate dementia. The purpose of this trial was to collect biomarker data relevant to both AD and other neurodegenerative diseases and help inform our decisions on the development of AMX0035 in AD.

The PEGASUS trial was a randomized, placebo-controlled Phase 2 trial in 95 participants in the U.S. Patients were randomized three-to-two to treatment with AMX0035, one sachet (each containing one gram of TURSO and three grams of PB) given twice-daily over 24 weeks, or matching placebo.

The primary investigator for the PEGASUS trial, Dr. Steven Arnold, presented topline results from the PEGASUS trial at the Clinical Trials on Alzheimer's Disease conference, or CTAD, which was held during the fourth quarter of 2021. Based on these topline results, AMX0035 was generally well-tolerated with approximately 80% of patients completing dosing in the trial in the AMX0035 arm. Safety results are depicted in the figure below. As in the CENTAUR trial, a higher percentage of patients in the AMX0035 arm had gastrointestinal adverse events. However, no SAEs were attributed to AMX0035 in the PEGASUS trial.

	AMX0035 (n=51)	Placebo (n=44)	Overall (N=95)
Treatment-emergent AEs, n (%)	34 (67)	26 (59)	60 (63)
GI disorders	20 (39)	6 (14)	26 (27)
Drug withdrawn due to AE, n (%)	4 (8)	1 (2)	5 (5)
Serious TEAEs	3 (6)	1 (2)	4 (4)
Treatment-related serious TEAEs	0	0	0
Deaths	0	0	0

The 6-month trial was not powered to evaluate differences between the AMX0035 and placebo arms in cognition, function or imaging.

The exploratory objectives of the trial were to measure the effect of AMX0035 treatment on biochemical markers of amyloid-ß1-42, amyloid-ß1-40, total tau (t-tau), tau phosphorylated at threonine 181 (ptau 181), neuronal injury markers, mitochondrial redox and function markers, and neuroinflammation, as assessed in cerebrospinal fluid, or CSF, from all volunteers.

While functional MRI analyses remain ongoing, no significant differences between dosing groups were observed for any efficacy endpoints in this trial ($p>0.05$). Key efficacy results are included in the figure below:

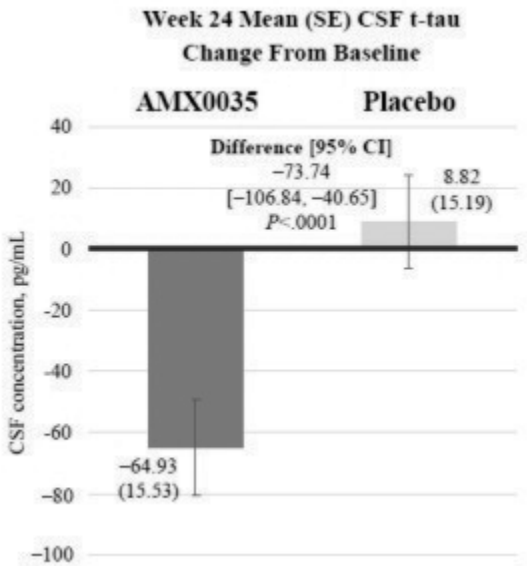
Week 24 Change from Baseline

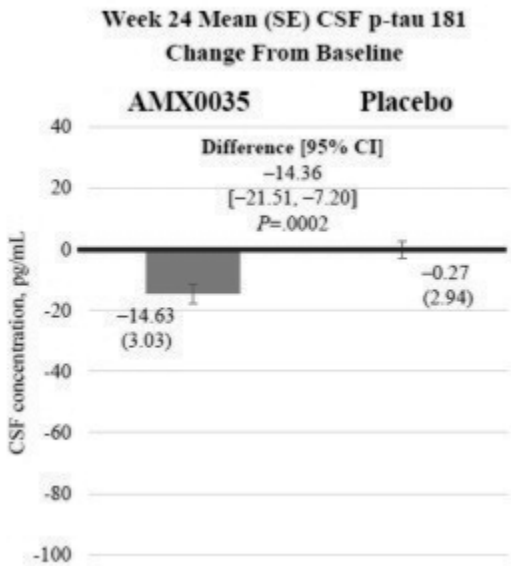
Outcome	LS Mean AMX0035	LS Mean Placebo	LS Mean Difference	Difference 95% Confidence Interval
GST	0.24	0.17	0.07	(–0.08, 0.21)
FAQ	2.61	1.59	1.02	(–0.96, 2.99)
Hippocampal Volume (longitudinal assessment)	-75.18	-70.78	-4.40	(-73.92, 65.11)

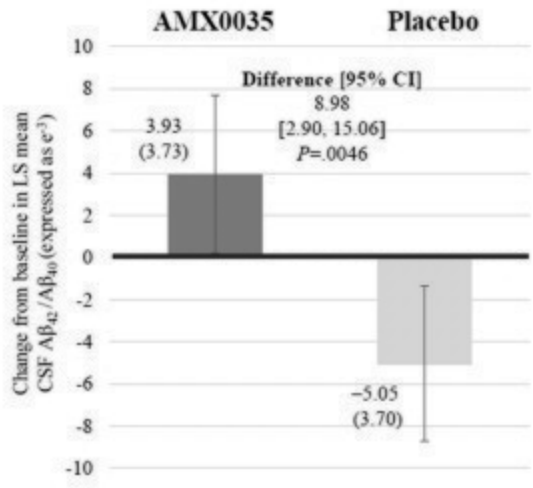
Week 24 Change from Baseline

Outcome	LS Mean AMX0035	LS Mean Placebo	LS Mean Difference	Difference 95% Confidence Interval
MoCA	-2.18	-0.70	-1.48	(–2.86, –0.10)
ADAS-Cog 14 Total Score	2.26	1.52	0.74	(2.70, 4.19)
DSRS	2.34	1.81	0.52	(–1.23, 2.27)
NPI-Q	0.15	–0.46	0.61	(–0.69, 1.91)

[a] Hippocampal volume component is based on standard ADNI MRI algorithm but was also assessed via additional MRI algorithms included in the Statistical Analysis Plan and yielded similar findings.







Significant impacts on multiple biomarkers of interest in AD were observed in the trial. In CSF, the AMX0035-group showed significant reductions of tau protein 181 ($p<0.001$) and phosphorylated tau protein ($p<0.001$) compared with the placebo group, modulation of the amyloid beta 42/40 ratio ($p<0.05$) and increase of 8-hydroxy-2' -deoxyguanosine, ($p<0.01$). These topline results from the PEGASUS trial are still subject to further audit and verification procedures and additional biomarker results are not yet available.

We believe the biomarker and imaging outcomes from the trial have substantially improved and will continue to inform our knowledge of the impact of AMX0035 on the neurodegenerative pathways relevant to the progression of AD. We continue to use these results to evaluate and inform our clinical development strategy of AMX0035 in AD and other potential indications. We are currently evaluating these data and discussing the results of the PEGASUS trial with scientific advisors as we consider potential next steps for the development of AMX0035 for the treatment of AD within our clinical development strategy.

Clinical Development of New Formulation for AMX0035 in ALS

We are working on a new taste-masked formulation of AMX0035. This formulation may allow for new intellectual property.

Clinical Development of AMX0114 for ALS

We believe that a cure for ALS will require a combination approach, targeting multiple cellular pathways implicated in disease pathogenesis. As part of this effort, we are investigating AMX0114, an antisense oligonucleotide, designed to target the gene encoding calpain-2, a key contributor to the axonal (Wallerian) degeneration pathway.

Axonal degeneration has been recognized as a key early contributor to the clinical presentation and pathogenesis of ALS and other neurodegenerative diseases. Activation of the calcium-dependent protease calpain-2 is proposed as a critical effector of axonal degeneration. Calpain-2 has been implicated in the pathogenesis of ALS based on findings of elevated levels of calpain-2 and its cleavage products in postmortem ALS tissue, therapeutic benefit of calpain-2 modulation in animal models of ALS, and the role of calpain-2 in cleaving neurofilament, a broadly researched biomarker in ALS.

Preclinical studies completed to date have shown that AMX0114 achieves potent, dose-dependent, and durable knockdown of *CAPN2* mRNA expression and calpain-2 protein levels in human motor neurons. Moreover, treatment with AMX0114 reduced extracellular neurofilament light chain (NfL) levels following neurotoxic insult in iPSC-derived human motor neurons, and treatment with AMX0114 improved survival of iPSC-derived human motor neurons harboring ALS-linked, pathogenic TDP-43 mutations.

AMX0114 is being advanced through Investigational New Drug, or IND, -enabling studies and we expect to file an IND and enter the clinic in 2024.

Development of a Composite Diagnostic Biomarker for ALS

People living with ALS spend approximately one-third of their disease course searching for a diagnosis. One of the key drivers of diagnostic delay in ALS is the lack of reliable, validated biomarkers to aid in diagnosis. Techniques to support earlier diagnosis are critical to advance care and treatment for ALS and mitigate the significant psychological stress that people living with ALS and their families experience during a lengthy diagnostic process.

We are working to develop a novel composite biomarker with the aim of facilitating earlier diagnosis of ALS. A pilot study is underway, which will provide information about the performance of putative biomarkers, identify candidate biomarkers, and inform the design of subsequent validation studies.

Patient Advocacy

The patient advocacy landscapes for ALS and other neurodegenerative diseases are large and complex integrated networks, and encompass groups at the international, multiregional and country-specific level. We have built credible and trusted partnerships across these complex networks at the international level, with our current emphasis being on ALS advocacy groups in the U.S., Canada, Europe, and APAC.

Working with key advocacy groups is critical to our mission, as people living with these neurodegenerative diseases and their families are at the center of everything we do. This starts with transparent communication and awareness about our science, data and development plans. We seek ensure that these advocacy groups are informed, able to answer questions from their constituents, and advocate appropriately for access and policies to benefit their community.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid technological advancement, significant competition and an emphasis on proprietary products. We face potential competition from many different sources, including major and specialty pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize, including AMX0035, may compete with current therapies and new therapies that may become available in the future. We believe that the key competitive factors affecting the success of any of our product candidates will include efficacy, safety profile, dosing, cost, effectiveness of promotional support and intellectual property protection.

Many of our competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing, and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. These competitors may also vie for a similar pool of qualified scientific and management talent, sites and patient populations for clinical trials, as well as for technologies complementary to, or necessary for, our programs.

Supply and Manufacturing

We rely, and expect to continue to rely for the foreseeable future, on third-party contract manufacturing organizations, or CMOs, for the production of AMX0035 and AMX0114 in compliance with current Good Manufacturing Process, or cGMP, requirements, for commercial supply as well as for use in clinical trials under the guidance of members of our organization. For AMX0035, we utilize two active pharmaceutical ingredients, or APIs, PB and TURSO, which are manufactured and released to us from third-party manufacturers. We have long term, single-source supply agreements in place for these APIs, including authorization to reference the relevant drug master files with these vendors. We have single-source arrangements for the manufacturing and packaging of bulk drug at established CMOs for commercial supply, clinical trials, and other potential needs. We manufacture AMX0035 bulk drug at Patheon Inc., or Patheon, a subsidiary of Thermo Fisher Scientific Inc., located in Whitby, Canada. We have scaled-up our third-party manufacturing capabilities in a manner that we believe will continue to support commercial demand and have entered into agreements covering the manufacture of AMX0035 through 2025. Following manufacturing, bulk drug is then sent to PCI Pharma Services in Rockford, IL, for primary and secondary packaging. As we look to markets outside of the U.S., we plan to add additional manufacturing and distribution sites to support local market demand. In addition, we utilize a risk-based approach to bring on additional manufacturing sites as needed.

We have built a team of pharmaceutical industry technical operations leaders. This team has significant technical, manufacturing, analytical, quality, regulatory, including cGMP, and project management experience to oversee our third-party manufacturers and maintain quality and regulatory compliance. In addition, members of this team have been involved in commercializing and launching rare disease products across the globe. We plan to continue to build our technical operations team as commercialization continues.

We also have a Quality Management System consistent with a regulated industry that outlines Standard Operating Policies and Procedures that govern the oversight of our CMOs.

Manufacturing Agreement with Patheon

In November 2019, we entered into a master manufacturing services agreement, or the Manufacturing Agreement, with Patheon, Inc., or Patheon, pursuant to which Patheon provides cGMP manufacturing, quality control, quality assurance, stability testing, packaging and related services to us. We have executed an initial product agreement under the Manufacturing Agreement, which covers AMX0035. The Manufacturing Agreement has an initial term ending in December 2025, and will automatically renew if there is a product agreement in effect, with the renewal period ending upon the termination of the last product agreement in effect. The product agreement covering AMX0035 has an initial term ending in December 2025 and automatically renews for successive terms of two years, unless either party gives prior notice of its intent not to review.

We may terminate the Manufacturing Agreement or any product agreement: upon 30 days' prior written notice if any government or regulatory authority permanently prevents us from selling AMX0035 in Canada, the EU or the U.S., if approved, or upon 90 days' prior written notice, if we no longer intend to order manufacturing services due to AMX035's discontinuance in the market. Patheon may terminate any product agreement under the Manufacturing Agreement upon 30 days' prior written notice, if we project zero volume for twelve successive months during the term of such product agreement. Additionally, Patheon may terminate the Manufacturing Agreement or any product agreement if payment in full of any overdue, undisputed invoice is not received within 30 days of Patheon's suspension of manufacturing services for nonpayment or, in certain circumstances, upon nine months' prior written notice if we assign any rights under the Manufacturing Agreement or a product agreement. In addition, either party may terminate the Manufacturing Agreement or any product agreement for cause, including the other party's uncured material breach and upon written notice, in the case of the other party's insolvency or bankruptcy.

Supply Agreement with CU Chemie

In October 2019, we entered into a supply agreement with CU Chemie Uetikon, GmbH, or CU Chemie, a division of the SEQENS group, pursuant to which CU Chemie agreed to supply to us, on a non-exclusive basis, bulk drug substance of PB, for use in the manufacture of AMX0035. The agreement has an initial term of five years and will automatically renew for successive terms of two years, unless earlier terminated. After the expiration of the initial term, either party may terminate the agreement for convenience upon three months' prior written notice. Additionally, either party may terminate the agreement in the case of the other party's uncured material breach or upon the insolvency or bankruptcy of the other party.

Supply Agreement with ICE

In August 2023, we entered into a commercial supply agreement with ICE S.p.A., or ICE (formerly Prodotti Chimici e Alimentari S.p.A.), pursuant to which ICE agreed to supply to us, on an exclusive basis, bulk drug substance of tauroursodeoxycholic acid , which we use in the manufacture of AMX0035. The agreement contains certain minimum purchase requirements. The agreement has an initial term ending in December 2028 and can be renewed as determined by a joint steering committee. Either party may terminate the agreement in the case of the other party's insolvency or bankruptcy, or in case of the other party's uncured breach.

Intellectual Property

While the PB and TURSO molecules individually are not proprietary to us, we own patents and patent applications covering AMX0035, including the fixed-dose combination of AMX0035 itself.

Intellectual property is of vital importance in our field and to pharmaceuticals generally. Our commercial success depends in part on our ability to obtain intellectual property that protects AMX0035 and its uses, and any future product

candidates. We seek to protect and enhance proprietary technology, inventions and improvements that are commercially important to the development of our business and AMX0035, in particular, by seeking, maintaining and defending U.S. and foreign patent rights.

We are actively building our intellectual property portfolio in our therapeutic area, including around AMX0035 and AMX0114. Our current patent portfolio includes eight patent families. In those eight families, we currently own a total of 122 issued patents and pending patent applications directed to our technologies, including AMX0035. Currently, our patent portfolio includes six issued U.S. patents, 58 issued foreign patents, 14 pending U.S. patent applications and 44 pending foreign patent applications. Our issued patents and pending applications cover the relative amounts of a phenylbutyrate compound and a bile acid (such as TUDCA) and some of our issued and pending claims cover the specific ratio of those two drugs.

Our earliest in time patent family relates to compositions of a bile acid and a phenylbutyrate compound (including TURSO and 4-PBA) and methods of treating neurodegenerative disease, and its associated causes at a cellular level, using those compositions. This family includes four issued U.S. patents and 58 issued foreign patents (including rights in countries in which our issued European patent was validated). The foreign jurisdictions in which we have been issued patents include Albania, Austria, Australia, Bosnia and Herzegovina, Belgium, Bulgaria, China, Croatia, Cyprus, Czech Republic, Denmark, Estonia, the EU, Finland, France, Germany, Greece, Hong Kong, Hungary, Ireland, Iceland, Italy, Japan, Lithuania, Latvia, Macao, Macedonia, Malta, Monaco, Montenegro, Netherlands, Norway, Poland, Portugal, Romania, San Marino, Serbia, Slovenia, Slovakia, South Korea, Spain, Sweden, Switzerland, Turkey, and UK. We also have patent applications pending in Australia, Canada, the EU, Macao, Japan, South Korea, the U.S. and other jurisdictions. In this family, we have composition of matter claims issued in the U.S. (U.S. Patent No. 11,071,742, which was issued on July 27, 2021) and Australia. These issued patents and others that issue from this family may first begin to expire as early as December 2033.

Our second patent family is directed to specific compositions of a phenylbutyrate compound and a bile acid (including TURSO and 4-PBA) and methods of manufacturing those compositions. This family includes two issued U.S. patents. We also have patent applications pending in this family in the U.S., EU, and other jurisdictions. In this family, we have composition of matter claims pending in applications filed in the U.S., Argentina, Australia, Brazil, Canada, China, the EU, Hong Kong, Israel, Japan, South Korea, Mexico, and Taiwan. The issued patents and others that issue from this family may first begin to expire as early as July 2040.

Our third patent family is directed to methods of treating particular symptoms of ALS and/or reducing the associated adverse events with combinations of a phenylbutyrate compound and a bile acid (including TURSO and 4-PBA). We have patent applications pending in this family in the U.S., EU, and other jurisdictions. Currently, we do not have any composition of matter claims pending in this family. Although no patents have yet issued from this family, we expect the term on patents issuing from this family to extend until at least August 2040.

Our fourth patent family is directed to methods of treating Alzheimer's disease and other tauopathies (including progressive supranuclear palsy) with combinations of a phenylbutyrate compound and a bile acid (including sodium phenylbutyrate and TURSO). We have patent applications pending in this family in Argentina, Taiwan, as well as a Patent Cooperation Treaty (PCT) application. Although no patents have yet issued from this family, we expect the term on patents issuing from this family to extend until at least November 2042.

Our fifth patent family is directed to methods of co-administering other therapeutic drugs (including substrates of cytochrome P450, drugs with a narrow therapeutic index, and substrates of Organic Anion Transporter 1 (OAT1)) with combinations of a phenylbutyrate compound and a bile acid (including sodium phenylbutyrate and TURSO). We have patent applications pending in this family in the U.S., Argentina, Taiwan, as well as a Patent Cooperation Treaty (PCT) application. Although no patents have yet issued from this family, we expect the term on patents issuing from this family to extend until at least March 2042.

Our sixth patent family is directed to pharmacokinetic characteristics following the administration of TURSO and sodium phenylbutyrate. We have patent applications pending in this family in the U.S., Argentina, Taiwan, as well as a Patent Cooperation Treaty (PCT) application. Although no patents have yet issued from this family, we expect the term on patents issuing from this family to extend until at least May 2042.

Our seventh patent family is directed to methods of co-administering other therapeutic drugs (including inhibitors of bile salt efflux pump (BSEP)) with combinations of a phenylbutyrate compound and a bile acid (including sodium phenylbutyrate and TURSO). We have patent applications pending in this family in the U.S., Argentina, Taiwan, as well as a

Patent Cooperation Treaty (PCT) application. Although no patents have yet issued from this family, we expect the term on patents issuing from this family to extend until at least May 2042.

Our eighth patent family is directed to oligonucleotides targeting the Calpain-2 transcript. We have patent applications pending in this family in the U.S., as well as a Patent Cooperation Treaty (PCT) application. Although no patents have yet issued from this family, we expect the term on patents issuing from this family to extend until at least May 2043.

We cannot be sure that patents will be granted with respect to any of our pending patent applications nor with respect to any patent applications that may be filed by us in the future. Further, we cannot be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products. Finally, we cannot be sure that our granted patents, and any future patents granted to us, will be found valid and/or enforceable following a litigation or administrative procedure.

In January 2021, Bruschettini S.r.l. and Lederer & Keller Patentanwälte Partnerschaft mbB each filed oppositions at the European Patent Office to our issued European Patent, EP2978419. At a high level, this patent claims various methods of treating neurodegenerative disease (and or the causes or conditions thereof) with a bile acid and a phenylbutyrate compound. The Opposition Division maintained European Patent, EP2978419 as granted in oral proceedings on June 2, 2022. The decision of the Opposition Division has become final and EP2978419 is maintained as granted. EP2978419 has been opted-out from the jurisdiction of the Unified Patent Court effective April 26, 2023.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing of the first non-provisional application to which priority is claimed. In the U.S., patent term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. In the U.S., the term of a patent that covers an FDA-approved drug may also be eligible for a patent term extension of up to five years under the Hatch-Waxman Act, which is designed to compensate for the patent term lost during the FDA regulatory review process. The length of the patent term extension is calculated based on the length of time it takes for regulatory review. A patent term extension under the Hatch-Waxman Act cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Moreover, a patent can only be extended once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. Following the approval of RELYVRIO in the U.S., we have applied for patent term extensions for certain of our issued U.S. patents covering our product and/or their methods of use.

We also rely on trademarks, trade secrets, know-how, continuing technological innovation, confidentiality agreements, and invention assignment agreements to develop and maintain our proprietary position. The confidentiality agreements are designed to protect our proprietary information and the invention assignment agreements are designed to grant us ownership of technologies that are developed for us by our employees, consultants, or other third parties. We seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology, or IT, systems. While we have confidence in our agreements and security measures, either may be breached, and we may not have adequate remedies. In addition, our trade secrets may otherwise become known or independently discovered by competitors.

Our commercial success also depends in part on our ability to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. A comprehensive discussion on risks relating to intellectual property is provided in Item 1A of this Annual Report entitled “Risk Factors—Risks Related to Our Intellectual Property.”

We have conducted searches of the patent landscape at certain points and in certain jurisdictions with respect to AMX0035, and based on these searches and our analyses, we have not identified any issued patents that we believe are valid and could be successfully asserted to block our ability to commercialize AMX0035.

European Patent EP3016654, entitled “Tauroursodeoxycholic acid (TUDCA) for Use in the Treatment of Neurodegenerative Disorders,” is owned by Bruschettini S.r.l. The patent relates to use of TURSO in the treatment of ALS in a mammal. An opposition has been filed to the grant of EP3016654 at the European Patent Office (EPO), asking the EPO to revoke EP3016654. The EPO issued a preliminary opinion on November 18, 2019 finding that at least the main claim of EP3016654 lacked novelty. Oral proceedings were held before an Opposition Division of the EPO on June 11, 2021. At the

end of the oral proceedings, the Opposition Division announced the decision revoking all claims of EP3016654. A written decision has been issued; however Bruschettini has appealed the decision of the Opposition Division to the Board of Appeal. A response to Bruschettini's appeal has been filed on June 7, 2022 requesting that the appeal should be dismissed and that the decision of the Opposition Division to revoke all claims of EP3016654 be upheld. The Board of Appeal has issued summons to attend oral proceedings on May 24, 2023. The oral proceedings will be held on June 5, 2024.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries, including Canada and member states of the EU impose requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation of Drug Products

In the U.S., 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 applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning 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 U.S. generally involves the following:

- 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 must become effective before human clinical trials may begin;
- Approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- Performance of adequate and well-controlled human clinical trials in accordance with current Good Clinical Practices, or cGCP, requirements to establish the safety and efficacy of the proposed drug product for each indication;
- Submission to the FDA of an NDA, including payment of application user fees;
- A determination by the FDA within 60 days of its receipt of an NDA to accept the marketing application for review;
- Satisfactory completion of an FDA advisory committee review, if applicable;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current Good Manufacturing Practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- Satisfactory completion of FDA audits of clinical trial sites to assure compliance with cGCPs and the integrity of the clinical data; and
- FDA review and approval of the NDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as *in vitro* and animal studies to assess potential safety and efficacy. The conduct of preclinical studies is subject to federal regulations and requirements, including good laboratory practice regulations for safety/toxicology studies.

An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin. Some preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. 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 initiate.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with cGCP 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 representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it is initiated at that institution. The IRB also must review and approve the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completion.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their www.clinicaltrials.gov website. Information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Although sponsors are obligated to disclose the results of their clinical trials after completion, disclosure of the results can be delayed in some cases for up to two years after the date of completion of the trial. Failure to timely register a covered clinical study or to submit study results as provided for in the law can give rise to civil monetary penalties and also prevent the non-compliant party from receiving future grant funds from the federal government. The NIH's Final Rule on ClinicalTrials.gov registration and reporting requirements became effective in 2017, and both the NIH and FDA recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors.

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

- 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 early indication of its effectiveness.
- Phase 2: The drug 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.
- 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 efficacy and safety 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.

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if SAEs occur. Written IND safety reports must be submitted to the FDA and investigators for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected

fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

Phase 1, Phase 2 and Phase 3 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. 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. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check points based on access to certain data from the trial.

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

Expanded Access to an Investigational Drug for Treatment Use

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

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

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 trial; or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

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

NDA Submission and 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 FDA will initially review an NDA for completeness before it accepts it for "filing." Under the FDA's procedures, the agency has 60 days from its receipt of the NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that the application is sufficiently complete to permit substantive review. Under the Prescription Drug User Fee Act, or PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA, for a new molecular entity to review and act on the submission, and six months from the filing date of a new molecular entity NDA with priority review. Accordingly, this review process typically takes 12 months and eight months, respectively from the date the NDA is submitted to the FDA. The FDA does not always meet its PDUFA goal dates for standard or priority NDAs, and the review process is often extended by FDA requests for additional information or clarification. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. This finding can be substantiated based on two adequate and well-controlled studies, or in certain circumstances on a single, large, multicenter, adequate and well-controlled study that is very persuasive or from a single adequate and well-controlled study together with confirmatory evidence. FDA regulations and guidance also allow for greater flexibility and tolerance for uncertainty in the context of rare and fatal diseases. The FDA also assesses whether the facility in which the product is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, as amended, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before initiation of the Phase 3 or Phase 2/3 study. The initial Pediatric Study Plan must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the Pediatric Study Plan. A sponsor can submit amendments to an agreed-upon initial Pediatric Study Plan at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs. PREA does not apply to a drug for an indication for which orphan drug designation has been granted.

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 may refer an application for a novel drug or a drug that presents difficult questions of safety or efficacy to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which 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.

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

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required

specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with cGCP requirements.

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 FDA to reconsider the application. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. 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. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Drug Designation and Exclusivity

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

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product is entitled to orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications to market the same product for the same indication for seven years, except in certain limited circumstances. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what it was designated for, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan drug has exclusivity. U.S. lawmakers have also recently raised the possibility that regulatory or legislative changes might need to be made to the Orphan Drug Act to foster competition. This includes the introduction of legislation that, if adopted into law, would require us to demonstrate to the FDA that AMX0035 would be economically unviable when facing competition to maintain our exclusivity.

Expedited Development and Priority Review Programs

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track Designation, Breakthrough Therapy Designation, Priority Review Designation and accelerated approval, and the purpose of these programs is to either expedite the development or review of important new drugs to get them to patients earlier than under standard FDA development and review procedures.

The FDA has a FastTrack program that is intended to expedite or facilitate the process for reviewing new drugs that meet certain criteria. Specifically, new drugs are eligible for Fast Track Designation if they are intended to treat a serious or life threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast Track Designation applies to both the product and the specific indication for which it is being studied. The sponsor can request the FDA to designate the product for Fast Track status any time before receiving NDA approval, but ideally no later than the pre-NDA meeting. Fast Track Designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as priority review, discussed below.

Additionally, a drug may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. The benefits of Breakthrough Therapy Designation include the same benefits as Fast Track Designation, plus intensive guidance from the FDA to ensure an efficient drug development program. A product may also be eligible for priority review if it treats a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review and to shorten the FDA's goal for taking action on an NDA for a new molecular entity from ten months to six months from the date of filing.

A product may also be eligible for accelerated approval if it treats a serious or life-threatening disease or condition, generally provides a meaningful advantage over available therapies and demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. As a condition of accelerated approval, the FDA may require that a sponsor perform adequate and well-controlled post-marketing confirmatory trials with due diligence and, under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date accelerated approval is granted. Under FDORA, the FDA also has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for products considered for accelerated approval, which could adversely impact the timing of the commercial launch of the product.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. Fast Track Designation, Breakthrough Therapy designation and Priority Review designation do not change the standards for approval, but may expedite the development or review process. Drugs granted accelerated approval also must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

U.S. Non-Patent Exclusivity

Data exclusivity provisions under the FDCA can delay the submission or the approval of certain follow-on applications. The FDCA provides a five-year period of data exclusivity within the U.S. to the first applicant to gain approval of an NDA for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an ANDA for a generic version of the drug or a 505(b)(2) NDA for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such a follow-on application may be submitted after four years if it contains a certification of patent invalidity or non-infringement.

The FDA has previously taken the position that NCE exclusivity is not available for fixed-dose combination products if one of the active moieties in the combination product had been previously approved in a drug product. In October 2014, however, the FDA reversed that position when it issued final guidance stating that an application for a fixed-dose combination product will be eligible for 5-year NCE exclusivity if it contains a drug substance with a single, new active moiety, even if the fixed-combination also contains a drug substance with a previously approved active moiety.

The FDCA also provides three years of market exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity period covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving follow-on applications that do not reference the protected clinical data. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of regulatory market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods for all formulations, dosage forms, and indications of the active moiety and patent terms. This six-month exclusivity may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining.

Post-approval Requirements

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

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

FDA regulations require that products be manufactured in specific facilities and in accordance with cGMP regulations which require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs, including those supply products, ingredients and components thereof, 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. In addition, the Drug Supply Chain Security Act, or DSCSA, was enacted in 2013 with the aim of building an electronic system to identify and trace certain prescription drugs and biologics distributed in the United States. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that culminated in November 2023. The FDA established a one-year stabilization period from November 2023 to November 2024 for trading partners to continue to build and validate interoperable systems and processes to meet certain requirements of the DSCSA. The law's requirements include the quarantine and prompt investigation of a suspect product, to determine if it is illegitimate, notifying trading partners and the FDA of any illegitimate product, and compliance with product tracking and tracing 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 requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval of a drug is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market, such as if, based on new evidence of clinical experience not contained in the application or not available to the FDA until after the application was approved, there is a lack of substantial evidence that the approved product will have the effect it is purported or represented to have under the conditions of use prescribed, recommended, or suggested in its labeling. Sponsors may also voluntarily withdrawal their approved products from the market for similar reasons. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution

or other restrictions under a REMS program. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Other potential consequences include, among other things:

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

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

Other U.S. Healthcare Laws

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of drug products for which we obtain marketing approval. Arrangements with third-party payors, healthcare providers and physicians, as well as patients and other third-parties, in connection with the clinical research, sales, marketing and promotion of products, once approved, and related activities, may expose a pharmaceutical manufacturer to broadly applicable fraud and abuse and other healthcare laws and regulations. In the U.S., these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below:

- the Anti-Kickback Statute, or AKS, which makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, that is intended to induce or reward, referrals including the purchase, recommendation, order or prescription of a particular drug for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. The AKS has been interpreted to apply to arrangements between therapeutic product manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the AKS is violated. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA;
- the federal civil and criminal false claims laws, including the FCA, which can be enforced by private citizens through "qui tam" or "whistleblower" actions, and civil monetary penalty laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Pharmaceutical and other healthcare companies have been, and continue to be, prosecuted under these laws, among other things, for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product and for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses. Similar to the AKS, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation.
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit

program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Like the AKS, the Patient Protection and Affordable Care Act, or the ACA, amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the creation, use, receipt, maintenance or disclosure of individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions;
- the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Centers for Medicare and Medicaid Services, or CMS, under the Open Payments Program, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), to certain non-physician providers such as physician assistants and nurse practitioners, and to teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- federal price reporting laws, which require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- analogous state and foreign laws and regulations, such as state and foreign anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; 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 that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensations and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of a pharmaceutical manufacturer's business activities could be subject to challenge under one or more of such laws. Efforts to ensure that business arrangements comply with applicable healthcare laws involve substantial costs. It is possible that governmental and enforcement authorities will conclude that a pharmaceutical manufacturer's business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against a pharmaceutical manufacturer, and it is not successful in defending itself or asserting its rights, those actions could have a significant impact on its business, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, imprisonment, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, reporting obligations and oversight if we become subject to integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the results of operations. In addition, commercialization of any drug product outside the U.S. will also likely be subject to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

In the U.S., numerous federal and state laws and regulations, including state data breach notification laws, state and federal health information privacy laws, and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of health-related and other personal information. For example California recently enacted the California Consumer Privacy Act, or CCPA, which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California State Attorney General has submitted various versions of final regulations. Since July 1, 2020, the California State Attorney General has had the authority to commence enforcement actions against violators. Further, a California privacy law, the California Privacy Rights Act, or CPRA, was passed by California voters on November 3, 2020 and entered into force on January 1, 2023. The CPRA creates additional obligations with respect to processing and storing personal information. We will continue to monitor developments related to the CPRA and anticipate additional costs and expenses associated with CPRA compliance. Other U.S. states also are considering omnibus privacy legislation (with one additional law already passed in Colorado, Connecticut, Utah and Virginia) and industry organizations regularly adopt and advocate for new standards in these areas. While the CCPA, as modified by the CPRA contain an exception for certain activities involving PHI under HIPAA, we cannot yet determine the impact the CCPA, CPRA or other such future laws, regulations and standards may have on our business, as these laws either do not yet apply to us or are not yet in effect.

In the event we decide to conduct clinical trials or continue to enroll subjects in our ongoing or future clinical trials, we may be subject to additional privacy restrictions, under state and federal law or other obligations. We also may become subject to laws in other countries, including the General Data Protection Regulation in Europe.

Current and Future U.S. Healthcare Reform Legislation

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

Since its enactment, there have been numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA. For example, President Biden has issued multiple executive orders that have sought to reduce prescription drug costs. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs. In addition, other legislative changes have been proposed and adopted in the U.S. since the ACA was enacted. The Budget Control Act of 2011 and subsequence legislation, among other things, created measures for spending reductions by Congress that include aggregate reductions of Medicare payments to providers of 2% per fiscal year, which remain in effect through 2031. The American Taxpayer Relief Act of 2012 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 American Rescue Plan Act of 2021 eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

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The Inflation Reduction Act of 2022, or IRA, includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries from $7,050 to $2,000 starting in 2025, thereby effectively eliminating the coverage gap; impose new manufacturer financial liability on certain drugs under Medicare Part D, allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation; and delay until January 1, 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation that challenges the constitutionality of the IRA's Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general is not yet known.

Canadian Review and Approval Process

In Canada, our small molecule product candidates and our research and development activities are primarily regulated by the Food and Drugs Act and the rules and regulations thereunder, which are enforced by Health Canada. Health Canada regulates, among other things, the research, development, testing, approval, manufacture, packaging, labeling, storage, recordkeeping, advertising, promotion, distribution, marketing, post-approval monitoring and import and export of pharmaceutical products. The drug approval process under Canadian laws requires licensing of manufacturing facilities, carefully controlled research and testing of products, government review and approval of experimental results prior to granting approval for commercial sale of drug products. Regulators also typically require that rigorous and specific standards such as cGMP, Good Laboratory Practices, or GLP, and Continuing Good Clinical Practices, or cGCP, are followed in the manufacture, nonclinical development and clinical development, respectively, of any drug product. The processes for obtaining regulatory approvals in Canada, along with subsequent compliance with applicable statutes and regulations, require the expenditure of substantial time and financial resources. For further information, see "Risk Factors."

The principal steps required for drug approval in Canada are as follows:

Nonclinical Safety Pharmacology and Toxicology Studies

Non-clinical studies are conducted *in vitro* and in animals to evaluate pharmacokinetics, metabolism and possible toxic effects to provide evidence of the safety of the drug candidate prior to its administration to humans in clinical studies and throughout development. Such studies are conducted in accordance with applicable laws and GLP.

Clinical Trials

Similar regulations apply in Canada regarding clinical trials as in the U.S. In Canada, Research Ethics Boards, or REBs, are used to review and approve clinical trial plans when trials are performed in Canada. For clinical trials that involve the administration of an investigational new drug to human subjects, an application must be made to Health Canada and approved before the trial can commence at a Canadian site. Trials are performed under the supervision of qualified investigators, in most cases a physician, in accordance with cGCP requirements. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated and a statistical analysis plan. The protocol and the informed consent forms that are signed by subjects, are reviewed and approved by the REB affiliated with the site where the trial will be conducted. Human

clinical trials for new drugs are typically conducted in three sequential phases, Phase 1, Phase 2 and Phase 3, as discussed above in the context of government regulation in the U.S. Similar to the FDA, Health Canada also accepts foreign clinical trial data in support of marketing applications. Additionally, the manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements.

New Drug Submission

In Canada, upon successful completion of Phase 3 clinical trials or earlier stage trials if agreeable to Health Canada, the company sponsoring a new drug then assembles all the nonclinical and clinical data and other testing relating to the product's pharmacology, chemistry, manufacture, and controls, and submits it to Health Canada as part of an NDS The NDS is then reviewed by Health Canada.

Health Canada will not approve the new drug unless compliance with cGMP—a quality system regulating manufacturing—is satisfactory, and the NDS contains data that provide substantial evidence that the drug is safe and effective in the indication and at the dosage studied. If Health Canada is satisfied that the NDS contains sufficient information, then marketing authorization for the new drug may be granted. In Canada, the marketing authorization for a new drug is called a Notice of Compliance, or NOC.

The testing required to generate data for inclusion in an NDS, and approval process for an NDS, requires substantial time, effort and financial resources, and may take several years to complete. This is necessary to help ensure the efficacy, safety and quality of the product. Data obtained from nonclinical and clinical testing are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Health Canada may not grant approval of an NDS on a timely basis, or at all. In Canada, NDSs are subject to user fees and these fees are typically increased annually to reflect inflation.

Health Canada has authority to grant conditional marketing approval following the review of an NDS for a new drug that would treat a serious, life-threatening or severely debilitating disease or condition. A Notice of Compliance with conditions (NOC/c) can be granted when there is promising evidence of clinical effectiveness based on the available data that the drug has the potential to provide (i) effective treatment, prevention or diagnosis of a disease or condition for which no drug is presently marketed in Canada or (ii) a significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies, preventatives or diagnostic agents for a disease or condition that is not adequately managed by a drug marketed in Canada. When a NOC/c is granted, the company to which the NOC/c is issued must make certain commitments to Health Canada, which typically include a requirement to provide confirmatory data to Health Canada to support the safe use and efficacy of the new drug.

Even if Health Canada approves a product candidate, it may limit the approved indications for use of the product candidate, 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 restrictions or other risk management mechanisms.

Health Canada 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, notification, and review and approval before the change can be implemented. Further, should new safety information arise, additional testing and/or regulatory notification may be required, or Health Canada may require an update to the product label that impacts the scope of the approved indications or other conditions for clinical use.

European Union Approval Process

The process governing approval of medicinal products in the EU generally follows the same lines as in the U.S. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of an MAA and granting of a marketing authorization by these authorities before the product can be marketed and sold in the

EU Following the UK's departure from the EU, a separate marketing authorization is required in order to place medicinal products on the market in Great Britain (under the Northern Ireland Protocol, the EU regulatory framework continues to apply in Northern Ireland and centralized EU authorizations continue to be recognized). In January 2024, developers of new medicinal products can now submit applications under the Medicines and Healthcare products Regulatory Agency's, or MHRA, International Recognition Procedure, or IRP. IRP will be open to products that already received an approval from one of MHRA's specified Reference Regulators which includes the United States and Canada.

Clinical Trial Approval

In April 2014, the EU adopted the new Clinical Trials Regulation (EU) No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022. The transitory provisions of the new Regulation provide that, by January 31, 2025, all ongoing clinical trials must have transitioned to the new Regulation. The new Regulation overhauls the system of approvals for clinical trials in the EU. Specifically, it is directly applicable in all Member States (meaning that no national implementing legislation in each Member State is required), and aims at simplifying and streamlining the approval of clinical trials in the EU. The main characteristics of the new Regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all Member States of the EU, or EU Member States, in which an application for authorization of a clinical trial has been submitted (Concerned Member States) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications.

PRIME Designation in the EU

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

Fixed-Dose Combination Guideline

As with the FDA, the EMA has also issued guidelines to address review and approval of fixed-dose combination products. This EMA's Guideline on clinical development of fixed combination medicinal products came into force on October 1, 2017. The basic scientific requirements for any fixed combination medicinal product are justification of the pharmacological and medical rationale for the combination, and establishment of the evidence base for the relevant contribution of all active substances to the desired therapeutic effect (efficacy and/or safety) and a positive benefit-risk for the combination in the targeted indication. For products that involve initial combination of two active ingredients, the EMA has indicated that the design of clinical efficacy/safety studies to support a fixed combination medicinal product application for initial treatment will depend on its rationale, specifically to achieve superior efficacy or improved safety compared to use of the single active substances. In situations when it has been established that monotherapy will not be adequate, appropriate or ethical to reach the desired therapeutic effect, initial use of combination therapy should be easily justified (e.g., HIV).

Marketing Authorization

To obtain a marketing authorization for a product in the European Economic Area (i.e., the EU as well as Iceland, Liechtenstein and Norway), or EEA, an applicant must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the EEA. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP (for example, when this data is not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients). Products that are granted a marketing authorization with the results of the pediatric clinical trials conducted in accordance with the PIP (even where such results are negative) are eligible for six months' supplementary protection certificate, or SPC, extension (provided an application for such extension is made at the same time as filing the SPC application for the product, or at any point up to 2 years before the SPC expires).

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the EEA. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (*i.e.* gene therapy, somatic-cell therapy and tissue-engineered medicinal products)and products with a new active substance indicated for the treatment of certain diseases, including HIV, AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of public health, the centralized procedure is optional. The centralized procedure may at the request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Clock stops may extend the timeframe of evaluation of an MAA considerably beyond 210 days. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days (excluding clock stops) but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Where the CHMP gives a positive opinion, the EMA provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because either (i) the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence; (ii) in the present state of scientific knowledge, comprehensive information cannot be provided; or (iii) it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Conditional Marketing Authorization

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates intended for treating, preventing or diagnosing seriously debilitating or life-threatening diseases (including medicines designated as orphan medicinal products) or in a public health emergency, if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data post-authorization, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization. A conditional marketing authorization can be converted into a standard centralized marketing authorization (no longer subject to specific obligations) once the marketing authorization holder fulfils the obligations imposed and the complete data confirm that the medicine's benefits continue to outweigh its risks.

Regulatory Data Protection in the EU

In the EU, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. Data exclusivity, if granted, prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the EU. During an additional two-year period of market exclusivity, a generic or biosimilar MAA can be submitted and authorized, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be an innovative medical product so that the innovator gains the prescribed period of data exclusivity, another company

nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA (for a centrally authorized product) or by the competent authority of the relevant EU Member State (for a nationally authorized product). To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least nine months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State (for a nationally authorized product) within three years after authorization, or if the product is removed from the market for three consecutive years, ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (1) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (2) either (i) such condition affects no more than five in ten thousand persons in the EU when the application is made, or (ii) without incentives it is unlikely that the marketing of the product in the EU would generate sufficient return to justify the necessary investment in its development; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the product will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure and a reduction or elimination of registration and marketing authorization fees. During the period of market exclusivity, a marketing authorization may only be granted for a "similar medicinal product" with the same orphan indication if: (i) the marketing authorization holder for the original orphan medicinal product consents to the authorization of the second orphan medicinal product; (ii) the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities of the product; or (iii) it is established that the second product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The period of market exclusivity may, in addition, be reduced to six years if at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation because, for example, the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Regulatory Requirements After a Marketing Authorization has been Obtained

Where an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2017/1572, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of

active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.

- The marketing and promotion of authorized medicinal products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of medicinal products and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and are also subject to EU Member State national laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

The aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

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

Data Protection Regulation in the European Economic Area and United Kingdom

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to the EU General Data Protection Regulation, or EU GDPR and similar processing of personal data regarding individuals in the UK is subject to the UK General Data Protection Regulation, or UK GDPR, and the UK Data Protection Act 2018. In this Annual Report, GDPR refers to both the EU GDPR and the UK GDPR, unless specified otherwise. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA/UK, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million (£17.5 million) or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the EU (commonly referred to as "Brexit") on January 31, 2020, and the EU and the UK have concluded a trade and cooperation agreement, or TCA, which was provisionally applicable since January 1, 2021 and has been formally applicable since May 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP, inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not provide for wholesale mutual recognition of UK and EU pharmaceutical regulations. At present, Great Britain has implemented EU legislation on the marketing, promotion and sale of medicinal products through the Human Medicines Regulations 2012 (as amended) (under the Northern Ireland Protocol, the EU regulatory framework continues to apply in Northern Ireland). Except in respect of the new EU Clinical Trials Regulation, the regulatory regime in Great Britain therefore largely aligns with EU regulations, however it is possible that these regimes will diverge more significantly in future now that Great Britain's regulatory system is independent from the EU and the TCA does not provide for mutual recognition of UK and EU pharmaceutical legislation. However, notwithstanding that there is no wholesale recognition of EU pharmaceutical legislation under the TCA, under a new framework mentioned below which will be put in place by the MHRA, the UK's medicines regulator, from January 1, 2024, the MHRA has stated that it will take into account decisions on the approval of marketing authorization from the EMA (and certain other regulators) when considering an application for a Great Britain marketing authorization.

On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". This new framework fundamentally changes the existing system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA will be responsible for approving all medicinal products

destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA will no longer have any role in approving medicinal products destined for Northern Ireland. A single UK-wide marketing authorization will be granted by the MHRA for all medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK. The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, so the UK government and the EU will enact legislative measures to bring it into law. On June 9, 2023, the MHRA announced that the medicines aspects of the Windsor Framework will apply from January 1, 2025.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. All existing EU marketing authorizations for centrally authorized products were automatically converted (grandfathered) into Great Britain marketing authorization's free of charge on January 1, 2021. Since January 1, 2024, a new framework for the approval of marketing authorizations has been put in place, whereby the MHRA may have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators when determining an application for a new Great Britain marketing authorization. There is now no pre-marketing authorization orphan designation in Great Britain. Instead, the MHRA reviews applications for orphan designation in parallel to the corresponding MAA. The criteria are essentially the same, but have been tailored for the Great Britain market, i.e., the prevalence of the condition in Great Britain (rather than the EU) must not be more than five in 10,000. Should an orphan designation be granted, the period of market exclusivity will be set from the date of first approval of the product in Great Britain.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional cost effectiveness assessments that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, EU Member States have the option to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense.

As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced EU Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Japanese Approval Process

Japan Government Regulation of Drug Products

Regulatory framework of pharmaceutical products in Japan is based on various laws and regulations, consisting mainly of Pharmaceutical and Medical Device Act ("PMD Act"). The Ministry of Health, Labour and Welfare ("MHLW") is the principal regulatory authority overseeing development, manufacture and commercialization of drugs and medical devices and to instruct as well as supervise drug and medical device companies to secure product quality and safety. The Pharmaceuticals and Medical Devices Agency ("PMDA") is the regulatory agency working together with the MHLW to assure safety, efficacy and quality of products. PMDA is authorized to conduct scientific reviews of clinical trial and marketing authorization applications for drug and medical devices; and monitors their post-marketing safety. The PMDA is also responsible for providing compensation for patients suffering from adverse drug reactions caused by drugs and medical devices.

Overall, being a member of the International Conference on Harmonization ("ICH"), Japan has pharmaceutical regulations fundamentally similar to those of the United States and the EU. Non-clinical studies are performed to demonstrate the health safety of new chemical or biological substances. Non-clinical studies must be conducted in compliance with the principles of Japanese good laboratory practice, or GLP, which reflect the Organization for Economic Co-operation and Development requirements. Currently, Japan and EU have a mutual recognition agreement for GLP, and data generated compliant with EU requirements will be accepted by the Japanese authorities. There is no similar agreement with the United States.

Clinical trials in Japan must be conducted in accordance with Japanese regulations based on ICH guidelines governing good clinical practices, or GCP. If the sponsor of the clinical trial is not established within Japan, it must appoint an entity within the country to act as its caretaker who should be authorized to act on the sponsor's behalf. The sponsor must take out a clinical trial insurance policy, and, according to the industry agreement, should put in place a common compensation policy for the injuries from the trial. Prior to the commencement of human clinical studies, the sponsor must complete an evaluation of the safety of the investigative product and submit a clinical trial notification and clinical trial protocol to the authorities in advance, upon agreement of the IRB of the participating institutions. When the authorities do not comment on the notification, the sponsor may proceed with the clinical trial. Any substantial changes to the trial protocol or other information submitted must be cleared by the IRB and notified to the authorities. Medicines used in clinical trials must be manufactured in accordance with GMP.

To market a drug in Japan, we must obtain regulatory approval. To obtain regulatory approval of an investigational drug, we must submit a new drug application. The evaluation of new drug applications is based on an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety, and efficacy. The volume and quality of the clinical data are key determinants of the approval decision. Clinical trial data generated overseas is accepted as part of the data package consistent with the ICH recommendation. Typically, a clinical trial in Japanese participants is required to ensure that data are extrapolatable for the Japanese population. A data compliance review, on-site inspection for good clinical practice, and audit and detailed data review for compliance with current good manufacturing practices are undertaken by the PMDA. Once the review organization completes its review, the matter is considered by the advisory committee of experts, and the government grants approval upon positive recommendation from the committee.

Orphan Drug Designation and Exclusivity

If the product is designed for treating certain "intractable diseases" or those whose patient size is limited to be less than 50,000 patients, we may be able to obtain designation as an orphan drug product if it demonstrates addressing high medical need. Drugs designated as orphan drugs are entitled to receive financial aid, tax relief on research expenses, reduction of application and consultation fees, PMDA's guidance and advice, priority review, and extension of the reexamination period up to a maximum of 10 years for drugs. New drug creation premium will also be applied at the time of calculation of drug price for the product.

Expedited Development and Priority Review Programs

The whole approval process takes 12 months under the standard review regime. MHLW has introduced several expedited development or review programs for especially important and innovative drugs, at least including:

Special Approval System for products required to prevent the spread of diseases that may seriously affect public health, such as COVID-19. This is intended to be used in limited circumstances where there are no other available therapy and the product has been approved for use in certain foreign countries. There are an expedited approval review process, special exceptions made for GMP review, national certification, containers, and packaging and labelling, etc.

License for Pharmaceutical Business

Separate from the approval requirement, it is also mandatory to possess a license of an appropriate class for the manufacturer to commercially distribute the product in Japan. To receive such license, the manufacturer or seller must, at the very least, employ certain manufacturing, marketing, quality, and safety personnel. The licensing requirements for drug manufacturing/marketing businesses include the appointment of a general marketing compliance officer of drugs, etc., who is a pharmacist, and compliance with Good Quality Practice (GQP) for quality control and Good Vigilance Practice (GVP) for post-marketing safety surveillance.

Non-Japanese companies who possess only the product approval may designate an appropriate license holder in Japan to commercially distribute the product, rather than distributing it on its own. The license is valid for five years. PMD Act requires a license for marketing authorization when importing to Japan and selling pharmaceutical products manufactured in other countries. It also requires each manufacturing site of a foreign manufacturer to be certified as a manufacturing site of pharmaceutical products to be marketed in Japan.

Regulatory Exclusivity

Marketing authorization holders must perform post-marketing surveys on new drugs so that efficacy and safety can be reconfirmed by reexamination by the MHLW for a specified period after marketing approval, in general, for at least six years. The concept of the risk management plan has been incorporated in reexamination. In this aspect, applications for generic drugs cannot be filed until completion of the reexamination. Branded products are protected from generics during this period.

Regardless of the type of drugs, MHLW may extend the reexamination period to a period not exceeding 10 years, if the minister believes that the extension is particularly necessary. In general, drugs containing new active ingredients will earn 8 years reexamination period, and drugs with new routes of administration will earn 6 years. There is no specific period for pediatric drugs in this regard, but the reexamination period may be extended (not exceeding 10 years) as needed to collect clinical data required for the reexamination of dosage or administration for pediatric use.

Intellectual Property Right Protection

The patent term is 20 years from the time of application as a rule. However, if the patent cannot be implemented because of laws and regulations to ensure safety of drugs and regenerative medicine products, etc. the patent term can be extended for a maximum of 5 years. There is also the Orange Book which lists information about drug approval; however, this is not US-style patent linkage. The MHLW will not approve generic drugs until the substance patent or the application patent of the original drug expires and production of the active ingredient becomes possible.

Pricing Decision

Pricing approval for the product is required in order to be applied for redemption of health insurance. Once approved and marketable, drugs are also subject to regular post-marketing vigilance of safety and quality under the standards of Good Manufacturing Practice. In Japan, the National Health Insurance system maintains a Drug Price List specifying which pharmaceutical products are eligible for reimbursement, and the MHLW sets the prices of the products on this list. Upon marketing approval, the manufacturer or seller begins negotiations regarding the reimbursement price with the MHLW, which is generally determined within 60 to 90 days. Historically, Japan performs scheduled biannual price adjustments as a cost-reduction method but recently there have been additional adjustments in the years in between. New products judged innovative or useful, that are indicated for pediatric use, or that target orphan or small population diseases, however, may be eligible for a pricing premium. The government has also promoted the use of generics, where available.

Rest of the World Regulation

For other countries outside of Canada, the EU and the U.S., such as countries in the Middle East, Africa, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Additionally, the clinical trials must be conducted in accordance with GCP requirements and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Coverage and Reimbursement

Successful commercialization of new drug products depends in part on the extent to which reimbursement for those drug products will be available from government health administration authorities, private health insurers, and other organizations. In the U.S., government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drug products they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford a drug

product. Sales of drug products depend substantially, both domestically and abroad, on the extent to which the costs of drugs products are paid for by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drug products. Third-party payors are increasingly challenging the price, examining the medical necessity, and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA and foreign approvals. These studies could result in delays or disadvantageous coverage for products we develop. Our product candidates may not be considered medically necessary or cost-effective. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on its investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the U.S. Other countries allow companies to fix their own prices for drug products, but monitor and control company profits. Accordingly, in markets outside the U.S., the reimbursement for drug products may be reduced compared with the U.S.

In the U.S., the principal decisions about reimbursement for new drug products are typically made by CMS, an agency within the HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a drug product is:

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

We cannot be sure that coverage or reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Future coverage and reimbursement may be subject to increased restrictions, such as prior authorization requirements, and to changes in the rates of reimbursement for orphan drug products both in the U.S. and in international markets. Reimbursement may impact the demand for, or the price of, any product for which we obtain regulatory approval.

The MMA established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. While all Medicare drug plans must give at least a standard level of coverage set by Medicare, Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each Part D prescription drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for

some of the costs of prescription drugs may increase demand for drugs for which we obtain marketing approval. Any negotiated prices for any of our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

For a drug product to receive federal reimbursement under the Medicaid or Medicare Part B programs or to be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the average manufacturer price, or AMP, and Medicaid rebate amounts reported by the manufacturer. As of 2010, the ACA expanded the types of entities eligible to receive discounted 340B pricing, although under the current state of the law these newly eligible entities (with the exception of children's hospitals) will not be eligible to receive discounted 340B pricing on orphan drugs. As the required 340B discount is determined based on average manufacturer price, or AMP, and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase. The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by HHS, the Agency for Healthcare Research and Quality and the NIH, and periodic reports on the status of the research and related expenditures are made to Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidates, if any such drug or the condition that they are intended to treat are the subject of a trial. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's drug could adversely affect the sales of our product candidate. If third-party payors do not consider our drugs to be cost-effective compared to other available therapies, they may not cover our drugs after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our drugs on a profitable basis.

These laws and future state and federal healthcare reform measures may be adopted in the future, any of which may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Outside of the U.S., the pricing of pharmaceutical products is subject to governmental control in many countries. For example, in the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional cost effectiveness assessments that compare the cost effectiveness of a particular therapy to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. Other countries may allow companies to fix their own prices for products, but monitor and control product volumes and issue guidance to physicians to limit prescriptions. Efforts to control prices and utilization of pharmaceutical products will likely continue as countries attempt to manage healthcare expenditures.

Employees and Human Capital

As of December 31, 2023, we had 384 full-time employees. Of our workforce, 151 employees are directly engaged in research and development with the rest providing administrative, business and operations support. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider the relationship with our employees to be good.

Our human capital is integral to helping us achieve our goal to end the suffering caused by neurodegenerative diseases. The objectives for our human capital resources include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards and cash-based performance bonus awards.

Available Information

We file Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, proxy statements and other information with the SEC. Our filings with the SEC are available on the SEC's website at www.sec.gov. We also maintain a website at http://www.amylyx.com. We make available, free of charge, in the Investors section of our website, documents we file with or furnish to the SEC, including our Annual Reports on Form 10-K, Quarterly Reports on

Form 10-Q, Current Reports on Form 8-K and any exhibits and amendments to those reports. We make this information available as soon as reasonably practicable after we electronically file such materials with, or furnish such information to, the SEC. The other information found on our website is not part of this or any other report we file with, or furnish to, the SEC.

Environmental, Social, and Governance (ESG)

The values that drive our mission to one day end the suffering caused by neurodegenerative diseases are at the heart of how we do business. Our commitment to audacity, curiosity, engagement, accountability, and authenticity compels us to be responsible members of the global community. We are committed to better understanding our impact on the world, what we are doing well, and where we can improve. In 2023, we formed an ESG Committee to lead the effort to help us formalize our environmental, social, and governance journey as we grow. This Committee reports to the Executive Leadership Team and is comprised of a cross-functional team of employees. As a virtual company, we recognize the importance of working with vendors and suppliers whose practices demonstrate a commitment to sustainability. With our recent rapid growth, we have now implemented a procurement function and are introducing a process to evaluate new vendors' sustainability efforts.

Environmental

As a company, we have grown quickly. Many of our employees choose to work remotely, but we have implemented features such as recycling programs and automatic lighting at our facilities. Amylyx expects its contract manufacturing, packaging and supply partners to maintain a similar ESG program, compliant with local laws and regulations, and retains the ability to conduct periodic audits to review these programs. That said, we acknowledge that there is work to do in this area, and looking at our environmental impact will be part of our future work.

Social

Our commitment to people is stated in our core values and reflected in our actions. We are dedicated to the discovery and development of potential treatments for people living with neurodegenerative diseases.

People living with the diseases we focus on are our true north, and we continue to work closely with the ALS and other neurodegenerative disease communities. This includes seeking their input on our clinical trial designs and recruitment materials as well as regularly engaging these individuals and caregivers for their feedback on multiple topics, including barriers to access to multidisciplinary care and to approved treatment. To ensure we continue to listen to and understand the needs of the neurodegenerative communities, we invite individuals to share their perspectives monthly at our all-company meetings. We are also proud to feature people living with ALS and their caregivers in our promotional and other external materials. As we advance novel drug candidates in our pipeline, we are committed to ensuring equal access for all to clinical trials and, in particular, to clinical trials comprised of people with diversity of gender, age, socioeconomic background, color, ethnicity, and more.

In regions where our product is approved and commercially available, we have a dedicated team that can provide a number of services, including education and access support. For eligible patients, we offer financial support programs to help with affordability.

We believe the best way to get helpful medicines to the most people who are qualified to receive them is to move through regulatory processes, following each country's rules. In some cases, however, we may be able to provide an investigational drug for use even if it is not yet approved or is still being studied, providing access to treatment to certain individuals who otherwise would have no access.

As an employer, diversity is also important, including having representation of diverse views and backgrounds at the highest levels of the organization. Three of our seven senior executives are women. Our board is committed to increasing diversity as we add additional members over time. At present, of our six board members, two are women, one who is ethnically diverse. We have posted a board diversity matrix on our website.

We care about the health and wellbeing of our employees. We offer:

- Flexible and remote work arrangements to all employees
- Unlimited time off
- Medical, dental, life, and disability insurance

- 401(k) plan with a company contribution
- Paid parental leave
- An employee assistance program

Governance

Our Board of Directors is responsible for overseeing the business and management of the Company. As part of our governance practices, we are committed to high standards of ethics, which are reflected in our Code of Business Conduct and Ethics, which applies to our directors, officers, employees and designated agents. This Code is posted on our corporate website. We have an independent chairman, and four of our six board members are independent. Our Audit, Nominating and Corporate Governance, and Compensation Committees are comprised solely of independent directors.

Item 1A. Risk Factors.

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

Summary of Risk Factors

Risks Related to Our Financial Position and Need for Capital

- We have in the past incurred significant losses and may in the future incur additional losses if we are unable to continue to generate sufficient revenue from our approved products to cover our expenses.
- We have a limited history of recognizing revenue from product sales and may not be able to achieve or maintain long-term sustainable profitability.
- We have a limited operating history and currently only have one commercial product, AMX0035, branded as RELYVRIO in the U.S. and ALBRIOZA in Canada, which may make it difficult to evaluate the prospects for our future viability.

Risks Related to Commercialization of AMX0035 or Future Product Candidates

- We have limited sales and marketing experience. If we are unable to continue to successfully commercialize AMX0035 or any other current or future product candidates in the U.S., Canada or elsewhere, if and when approved, we may be unable to generate meaningful additional product revenue.
- AMX0035 may fail to maintain the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for continued commercial success or to remain profitable.
- If the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities approve generic versions of AMX0035 or any other current or future product candidate of ours that receives regulatory approval, or such authorities do not grant our products appropriate periods of non-patent exclusivity before approving generic versions of such products, the sales of such products could be adversely affected.
- If we fail to obtain coverage and reimbursement for AMX0035 or any other current or future product candidates in new geographies, it could make it difficult for us to sell AMX0035 or any other current or future product candidates profitably.

Risks Related to the Discovery and Development of Our Current and Future Product Candidates

- We currently depend on the success of AMX0035. If we are unable to maintain, or obtain additional, regulatory approvals for, and successfully commercialize, AMX0035, or experience significant delays in doing so, our business may be materially harmed.
- The delay or denial of regulatory approval, inability to maintain regulatory approval, inability to complete post-marketing requirements, or the requirement to resubmit any marketing application with additional data or information for AMX0035 in any jurisdiction could delay or suspend commercialization of AMX0035 and adversely impact our ability to generate revenue, our business and our results of operations, and could cause us to delay or even cease operations.
- AMX0035 is a fixed-dose combination drug product and certain regulatory authorities may require a demonstration that each component makes a contribution to the claimed effects in addition to demonstrating that the combination is safe and effective for the intended population.
- We have concentrated our research and development efforts on the treatment of neurodegenerative and CNS disorders, a field that has seen very limited success in product development.
- The regulatory approval processes of the FDA, Health Canada, the EMA and other comparable foreign authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to maintain or obtain regulatory approval for AMX0035 or any other current or future product candidates, our business will be substantially harmed. A finding that our global Phase 3 PHOENIX trial is insufficient to support current or additional marketing authorizations in ALS could lead the FDA or Health Canada to restrict or withdraw prior

regulatory approvals for RELYVRIO or ALBRIOZA, respectively, or we could decide, after consultation with regulatory authorities, to voluntarily withdraw RELYVRIO or ALBRIOZA from the marketplace, or we may not be successful in obtaining marketing authorisation for AMX0035 from the EMA or other comparable foreign authorities.

- Competitive products may reduce or eliminate the commercial opportunity for AMX0035 for our current or future indications. If our competitors develop technologies or product candidates more rapidly than we do, or their technologies or product candidates are more effective or safer than ours, our ability to develop and successfully commercialize AMX0035 may be adversely affected.

Risks Related to Our Dependence on Third Parties

- We have entered and may in the future enter into collaborations with third parties for the development and commercialization of AMX0035 or any other current or future product candidates, and our prospects with respect to AMX0035 and our other current or future product candidates will depend in significant part on the success of those collaborations.
- Our use of third parties to manufacture AMX0035 in compliance with cGMP may increase the risk that we will not have sufficient cGMP-compliant quantities of AMX0035 or necessary quantities of such materials on time or at an acceptable cost.

Risks Related to Our Intellectual Property

- Our commercial success depends on our ability to protect our intellectual property and proprietary technology.

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

- We are currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability, an ongoing military conflict between Russia and Ukraine and the conflict in Israel, and high inflation and rising interest rates, any of which could have a material adverse effect on our business, financial condition and results of operations.
- We depend heavily on our executive officers, principal consultants and others, and the loss of their services would materially harm our business.
- A pandemic, epidemic, or outbreak of an infectious disease may materially and adversely affect our business, including our preclinical studies, clinical trials, third parties on whom we rely, our supply chain, our ability to raise capital, our ability to conduct regular business and our financial results.

Risks Related to Our Common Stock

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

Risks Related to Our Financial Position and Need for Capital

We have in the past incurred significant losses and may in the future incur additional losses if we are unable to continue to generate sufficient revenue from our approved products to cover our expenses.

Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have invested substantial resources into our product development efforts and toward the commercialization of RELYVRIO, which has been approved by the FDA, and ALBRIOZA, which has received marketing authorization with conditions from Health Canada, but we have only been generating revenue from product sales in the U.S., Canada for a limited period. We will continue to incur significant research and development and other expenses related to clinical development, commercialization, approvals in additional jurisdictions and for additional indications, and ongoing operations. Since our inception, we have devoted the majority of our financial resources and efforts to research and development, including preclinical studies and our clinical trials, preparation for commercialization and commercialization activities. Our financial condition and operating results, including our revenues, expenses and net income (loss), may fluctuate significantly from quarter to quarter and year to year. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. Additionally, net losses and negative cash flows have had, and may in the future have, an adverse effect on our stockholders' equity and working capital. As of December 31, 2023, we had an accumulated deficit of $304.9 million. We may again in the future incur significant losses and our financial results will be highly dependent upon continued successful commercial sales of RELYVRIO in the U.S and ALBRIOZA in Canada.

We anticipate that our expenses may increase substantially if and as we:

- further build out our sales, marketing, pharmacovigilance and distribution infrastructure and scale-up manufacturing capabilities for AMX0035 and any product candidate for which we may obtain approval;
- conduct clinical trials of AMX0035 for the treatment of ALS, PSP, WS, AD and potential other additional indications;
- seek to identify additional product candidates;
- initiate and continue research, preclinical and clinical development efforts for any current or future product candidates;
- maintain regulatory approvals in the U.S. and Canada for RELYVRIO and ALBRIOZA for the treatment of ALS, respectively, and seek to obtain regulatory approvals in the EU and other geographies for AMX0035 for the treatment of ALS, PSP, WS, AD and any other indications that successfully complete clinical development;
- experience any delays or encounter any issues with any of the above, including but not limited to completion of post-marketing requirements, the potential that regulators require additional data to support the approval of AMX0035 for ALS, failed studies, negative or mixed clinical trial results, safety issues or other regulatory challenges;
- add operational, financial and management information systems and personnel, including personnel to support commercialization of AMX0035 and product candidate development and to help us comply with our obligations as a public company;
- hire and retain additional personnel, such as clinical, quality control, scientific, commercial and administrative personnel;
- maintain, expand and protect our intellectual property portfolio;
- add equipment and physical infrastructure to support our research and development; and
- acquire or in-license other product candidates and technologies.

We are continuing to build out our infrastructure, including sales and marketing, distribution and manufacturing capabilities, to support commercialization of AMX0035 in the U.S. and Canada. As of December 31, 2023, we had 384 full-time employees.

Our expenses could increase beyond our expectations if we are required by the FDA, Health Canada, the EMA, or other regulatory authorities to perform clinical trials or conduct other studies in addition to those that we currently expect, or if

there are any delays in establishing appropriate manufacturing arrangements for or in completing our clinical trials or the development of AMX0035 or any other current or future product candidates we may develop.

We have a limited history of recognizing revenue from product sales and may not be able to achieve or maintain long-term sustainable profitability.

Our ability to generate revenue and achieve profitability depends on our ability to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize our products, including our commercialization of RELYVRIO in the U.S. and ALBRIOZA in Canada. Our ability to recognize revenues from product sales depends heavily on our success in:

- manufacturing and delivering supply of AMX0035;
- satisfying any post-marketing requirements;
- obtaining reimbursement for our products from private insurance or government payors;
- completing research, preclinical, and clinical development of other product candidates, including AMX0114, and for AMX0035 in additional indications;
- seeking and obtaining U.S. and foreign marketing approvals for AMX0035 in additional indications and for other product candidates for which we complete clinical trials;
- obtaining and maintaining market acceptance of our product and product candidates, if approved, as a treatment option;
- launching and commercializing product candidates for which we obtain marketing approval;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure;
- negotiating favorable terms in any collaboration, licensing, or other arrangements into which we may enter;
- maintaining, defending, protecting, and expanding our portfolio of IP rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel.

Other than RELYVRIO in the U.S. and ALBRIOZA in Canada, we have not yet launched any other approved products for commercial sale. We anticipate continuing to incur significant costs associated with the commercialization of RELYVRIO and ALBRIOZA, and even if another product candidate we are developing is approved for commercial sale, we anticipate incurring significant costs associated the commercialization of any such approved product candidate. Even though we have begun to generate revenues from the sale of RELYVRIO and ALBRIOZA, we may not be able to achieve or maintain long-term sustainable profitability unless AMX0035 is approved in other jurisdictions or for additional indications or other of our current or future product candidates is approved in the future. Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenues, the extent of any future losses or if we might sustain profitability.

Our failure to remain profitable may depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we suffer losses as we have in the past, investors may not receive any return on their investment and may lose their entire investment.

We have a limited operating history and currently only have one commercial product, AMX0035, branded as RELYVRIO in the U.S. and ALBRIOZA in Canada, which may make it difficult to evaluate the prospects for our future viability.

We are still in the relatively early stages of our transition from a clinical-stage to a commercial-stage company in the past few years. Our operations to date have been primarily limited to organizing, staffing and financing our company, raising capital, conducting research and development activities, including preclinical studies and clinical trials and, more recently, preparing for and commercializing AMX0035. We have not yet demonstrated an ability to generate significant revenues on a long term sustained basis, or to conduct sales and marketing activities necessary for successful longer term product commercialization. In June 2022, AMX0035 received marketing authorization with conditions from Health Canada for the treatment of ALS, with one such condition being the provision of data from the PHOENIX trial and other additional planned or ongoing studies.

In September 2022, AMX0035 received marketing authorization from the FDA for the treatment of ALS in adults. In January 2024, the European Commission confirmed the adoption of the CHMP's negative opinion on the MAA for conditional marketing authorisation of AMX0035 for ALS in the EU. We continue to focus on the completion of our global PHOENIX Phase 3 clinical trial, and will provide additional data on the efficacy and safety profile of AMX0035 in people living with ALS. If PHOENIX is supportive, we plan to seek approval in the EU as quickly as possible, although there is no guarantee we will receive such approval.

In addition, we have post-marketing requirements as part of our approval of RELYVRIO in the U.S. and ALBRIOZA has been approved in Canada with conditions, which if not met, could impair our ability to continue commercializing AMX0035. At a second meeting of the FDA's Peripheral and Central Nervous System Drugs Advisory Committee, or the Advisory Committee, on September 7, 2022, relating to AMX0035 for the treatment of ALS, we stated that if our PHOENIX trial is not successful then we will do what is right for patients, which includes voluntarily removing the product from the market. We will work in consultation with regulatory authorities when the PHOENIX data are available. We could also be required by regulatory authorities to withdraw AMX0035 from the marketplace. As part of our approval of RELYVRIO in the U.S., we have post-marketing requirements to conduct carcinogenicity studies in mice and rats, drug-drug interaction studies in human volunteers, and studies in subjects with kidney or liver impairment. The outcomes of these studies including the PHOENIX trial and any potential withdrawal could have a material adverse effect on our business.

Additionally, we may not satisfy all of the conditions imposed by Health Canada for marketing authorization of ALBRIOZA for the treatment of ALS. If we fail to do so, we may be subject to additional conditions imposed by Health Canada or we may have to cease commercialization of ALBRIOZA, which may impact our prospect for profitability.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early commercial stage, especially pharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history with these activities.

Our quarterly and annual operating results may fluctuate in the future. As a result, we may fail to meet or exceed the expectations of research analysts or investors, which could cause our stock price to decline and negatively impact our financing or funding ability, as well as negatively impact our ability to exist as a standalone company.

Our financial condition and operating results have varied in the past and will continue to fluctuate from quarter-to-quarter and year-to-year in the future due to a variety of factors, many of which are beyond our control. Factors relating to our business that may contribute to these fluctuations include the following, as well as other factors described elsewhere in this Annual Report:

- our ability to manufacture and deliver supply of AMX0035;
- our ability to maintain market acceptance of our product and product candidates, if approved, as a treatment option;
- delays or failures in advancement of existing or future development candidates into the clinic or product candidates in clinical trials;
- the feasibility of developing, manufacturing, and commercializing our product and product candidates;
- our ability to manage our growth;
- the outcomes of research programs, clinical trials or other product development or approval processes;
- our ability to successfully develop AMX0035 for additional indications and to commercialize AMX0035 for such additional indications, if approved;
- risks associated with the international aspects of our business including the conduct of clinical trials in multiple locations and potential commercialization in such locations;
- our ability to accurately report our financial results in a timely manner;
- our dependence on, and the need to attract and retain, key management and other personnel;
- our ability to obtain, protect and enforce our IP rights;

- our ability to prevent the theft or misappropriation of our IP, know-how or technologies;
- advantages that our competitors and potential competitors may have in securing funding, obtaining the rights to critical IP or developing competing technologies or products;
- our ability to obtain additional capital that may be necessary to expand our business;
- business interruptions such as power outages, strikes, acts of terrorism or natural disasters; and
- the ultimate impact of global economic and geopolitical events.

Due to the various factors mentioned herein, and others, the results of any of our prior quarterly or annual periods should not be relied upon as indications of our future operating performance.

Our financial results may fluctuate significantly from quarter-to-quarter and year-to-year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline. Our stock price may also decline as a result of unexpected clinical trial results in one or more of our ongoing or future clinical trials.

We may require substantial additional funding in the future to meet our financial needs and to pursue our business objectives. If we are unable to raise capital if and when needed, we could be forced to delay, reduce or eliminate our product discovery and development activities or commercialization efforts.

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to continue to commercialize AMX0035 in jurisdictions in which it has received regulatory approval and to continue the clinical development of AMX0035 in additional indications and the preclinical and clinical development of additional product candidates. If we are unable to obtain additional marketing approvals for AMX0035 or any other current or future product candidates that we develop, we may require significant additional amounts of cash in order to continue to develop AMX0035 and any other current or future product candidates and fund our operations. In addition, other unanticipated costs may arise in the course of our development and commercialization efforts. Because the design and outcome of our ongoing and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of any product candidate we develop.

Our future capital requirements depend on many factors, including:

- the scope, progress, results and costs of researching and developing AMX0035 for the treatment of ALS in additional jurisdictions where approved, if any, and in PSP, WS, AD and potential additional indications, as well as any other product candidates we are currently developing or may in the future develop;
- the timing of, and the costs involved in, maintaining marketing approvals for AMX0035 for the treatment of ALS, and obtaining marketing approvals for AMX0035 for the treatment of ALS and for the treatment of PSP, WS, AD and potential additional indications, and obtaining approvals for other product candidates we are developing or may in the future develop and pursue;
- the number of other product candidates that we may pursue and their development requirements;
- the costs of commercialization activities for AMX0035 for any approved indications, or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing sufficient product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt and maintenance of regulatory approval on a jurisdiction-by-jurisdiction basis, additional revenue received from commercial sales of AMX0035 for any approved indications or any other current or future product candidates;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies;
- our headcount growth and associated costs as we expand our research and development efforts, increase our office space, and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights, including enforcing and defending intellectual property related claims; and

- the ongoing costs of operating as a public company.

We cannot be certain that additional funding will be available on acceptable terms, or at all. As a result of the challenges caused by economic uncertainty in various global markets due to geopolitical instability and conflict, including the ongoing conflicts in Ukraine and Israel, the global credit and financial markets have experienced in recent periods significant volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, high rates of inflation and interest rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly or more dilutive.

We have no committed source of additional capital and if we are unable to raise additional capital, if needed, in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of AMX0035 or any other current or future product candidates or other research and development initiatives. We may need to seek collaborators for AMX0035 and any other current or future product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to AMX0035 and any other current or future product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves. Any of the above events could significantly harm our business, prospects, financial condition, and results of operations and cause the price of our common stock to decline.

We believe that the revenue we generate from commercial sales of AMX0035 in the U.S. and Canada and our existing cash, cash equivalents, and short-term investments, will be sufficient to meet our anticipated operating and capital expenditure requirements for at least twelve months after the date of this Annual Report. However, our estimate may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

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

We expect our expenses to continue to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue on a sustained basis and demonstrate sustained profitability from product sales, we may be required to finance our future cash needs through public or private equity offerings, royalty-based or debt financings, collaborations, licensing arrangements or other sources, or any combination of the foregoing. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. In addition, debt financing, if available, may result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. Securing financing could also require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development and commercialization of AMX0035 or any future product candidates.

If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

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

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

investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

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

Events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. Although we do not currently have investments with any financial institution that has experienced such events, if any financial institution with which we have a relationship were to be placed into receivership, we may be unable to access such funds. In addition, if any parties with whom we conduct business are unable to access funds pursuant to instruments or lending arrangements with such a financial institution, such parties' ability to pay their obligations to us or to enter into new commercial arrangements requiring additional payments to us could be adversely affected.

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

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

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

Risks Related to Commercialization of AMX0035 or Future Product Candidates

We have limited sales and marketing experience. If we are unable to continue to successfully commercialize AMX0035 or any other current or future product candidates in the U.S., Canada or elsewhere, if and when approved, and we may be unable to generate meaningful additional product revenue.

AMX0035 is the first product that we have commercialized. We currently sell ALBRIOZA in Canada and RELYVRIO in the U.S. through specialized teams, given the relative rarity of ALS and certain of the other indications we are targeting. We are continuing to build the global marketing and sales team for the marketing, sales and distribution of AMX0035 and any future product candidates, if approved. In order to continue to successfully commercialize AMX0035 for the treatment of ALS, and to commercialize AMX0035 for the treatment of PSP, WS, AD and other indications, or to commercialize any of our other current or future product candidates that may be approved, we must build, on a territory-by-territory basis, marketing, sales, distribution, managerial and other capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, we have recruited and trained a U.S. commercial organization which is expensive and time-consuming. Factors that may inhibit our efforts to commercialize AMX0035 or any other current or future product candidates, if approved, on our own include:

- the inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability to supply the market with our drug product, including manufacturing or distribution challenges we may face;
- the inability of sales personnel to obtain access to physicians to prescribe AMX0035 or any other product that we are currently developing or may in the future develop and gets approved;
- any views or opinions expressed by ALS or community organizations about the safety or efficacy of AMX0035;
- the lack of complementary or symptomatic treatments to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines;
- the availability of adequate coverage by and reimbursement from government and third-party payors; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or profitability from these revenue streams is likely to be lower than if we were to market and sell any product candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market AMX0035 or any of our other current or future product candidates or may be unable to do so on terms that are favorable to us. We likely will have limited control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market AMX0035 or any other current or future product candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we may not be successful in commercializing AMX0035 or any other current or future product candidates.

Our efforts to educate the ALS and other neurodegenerative disease medical communities and payors on the benefits of AMX0035 or any future 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 AMX0035 or any future product candidates, and the indications we are targeting. Even if AMX0035 or any future product candidates are approved in any jurisdiction, if we are unable to successfully market our products successfully, we will not be able to generate significant revenues from such products.

If we are unable to expand our marketing, manufacturing and distribution capabilities or enter into agreements with third parties to market and sell AMX0035 or other current or future product candidates for which we obtain marketing approval, we will be unable to generate any additional product revenue.

To successfully commercialize any products that may result from our development activities, we need to continue to expand our marketing, pharmacovigilance, manufacturing and distribution capabilities, either on our own or with others. The development of our own marketing and distribution effort has been, is, and will continue to be, expensive and time-consuming and could delay any further product launches. Moreover, we cannot be certain that we will be able to continue to develop this capability successfully. We may enter into collaborations regarding any approved product candidates with other entities to utilize their established marketing and distribution capabilities, however, we may be unable to enter into such agreements on favorable terms, if at all. If any future collaborators do not commit sufficient resources to commercialize AMX0035 or any other current or future product candidates, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many companies that currently have extensive, experienced and well-funded sales, distribution and marketing operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of AMX0035 and any other current or future product candidates, if approved. 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.

The market for AMX0035 for ALS, PSP, WS, AD and other neurodegenerative diseases and for any other product candidates we are currently developing or may in the future develop may be smaller than we expect.

We focus our research and product development on treatments of neurodegenerative diseases. We base our market opportunity estimates on a variety of factors, including our estimates of the number of people who have these diseases, the potential scope of our approved product labels, the subset of people with these diseases who have the potential to benefit from treatment with AMX0035 or any other current or future product candidates, various pricing scenarios, and our understanding of reimbursement policies for rare diseases in particular countries. These estimates are based on many assumptions and may prove incorrect, and new studies may reduce the estimated incidence or prevalence of these diseases. Estimating market opportunities can be particularly challenging for rare indications, such as the ones we currently address, as epidemiological data is often more limited than for more prevalent indications and can require additional assumptions to assess potential patient populations. As we continue to commercialize RELYVRIO in the U.S., ALBRIOZA in Canada and begin to market AMX0035, if approved, in other jurisdictions, and learn more about market dynamics and engage with regulators on additional potential marketing approvals, our view of our products' initial potential market opportunity will become more refined. For example, we are finding that the market for ALS in the U.S. may be different than our initial estimations because a large percentage of ALS patients in the U.S. are treated outside of larger treatment centers, making it difficult to identify and access these patients. Additionally, we have primarily focused on the annual incidence of ALS, which means the initial market opportunity for AMX0035 may be smaller than the total addressable market opportunity that could be achieved over time. If we are unable to identify patients and successfully commercialize AMX0035 or any other current or future product candidates with attractive market opportunities, our future product revenues may be smaller than anticipated, and our business may suffer.

Patient identification efforts also influence the ability to address a patient population. If efforts in patient identification are unsuccessful or less impactful than anticipated, for instance, because of a lack of diagnostic initiatives, inadequate disease awareness among healthcare professionals, difficulties in identifying and accessing patients outside of larger treatment centers or otherwise, we may not address the entirety of the opportunity we are seeking. As a result, patients may be difficult to identify and access, the addressable patient population in the U.S., Canada, the EU and elsewhere may turn out to be lower than expected, or patients may not be otherwise amenable to treatment with our products, all of which would adversely affect our business, financial condition, results of operations and prospects.

AMX0035 may fail to maintain the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for continued commercial success or to remain profitable.

Even if AMX0035 for the treatment of any indication, or any other current or future product candidate of ours, is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians may be reluctant to add AMX0035 or another product to their patients' treatment regimen, or may cease to add AMX0035 or such product to their patients' treatment regimen. Further, patients often acclimate to the treatment regime they are currently taking and do not want to add additional treatments unless their physicians recommend it. Further, patients may be unable to add AMX0035 or such other product to their treatment regimen due to lack of coverage and adequate reimbursement. In addition, even if we are able to demonstrate our product candidates' safety and efficacy to Health Canada, the FDA, the EMA and other regulators, safety or efficacy concerns in the medical community may hinder market acceptance. Our ability to proactively educate health care professionals and patients may be limited based on the marketing restrictions in a given jurisdiction, specifically as they relate to the particular labeling approved by the applicable health authority.

Efforts to educate the medical community and third-party payors on the benefits of our current and any future product candidates may require significant resources, including management time and financial resources, and may not be successful. If AMX0035 or any other current or future product candidate is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not remain profitable. The degree of market acceptance of AMX0035 and any other future product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to competitive therapies and our ability to successfully publicize these advantages or highlight them in any marketing materials;
- the prevalence and severity of any side effects;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy or as a single agent or in combination;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;

- the product's convenience, tolerability and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- limitations or warnings, including distribution or use restrictions contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the product; and
- availability and adequacy of coverage and reimbursement from government payors, managed care plans and other third-party payors.

Any failure by AMX0035 or any other current or future product candidate of ours that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects.

Off-label use for the treatment of ALS with PB, which is available as a generic drug, along with the potential sale in some jurisdictions of TURSO, expose us to additional risks that could reduce or eliminate the commercial opportunity for AMX0035.

We are developing and advancing AMX0035 as a combination of TURSO and PB. PB has been approved by the FDA and other regulatory authorities for the treatment of patients with certain urea cycle disorders.

TURSO is being marketed in preparations without approval for the treatment of ALS in some jurisdictions, including the U.S. We face the risk that healthcare professionals may prescribe PB for the treatment of ALS and recommend that patients obtain a commercial preparation of TURSO not approved, labeled, or marketed for the treatment of ALS on the belief that this combination could replicate the benefits of AMX0035. Patient-directed treatment with TURSO for ALS may also arise in certain jurisdictions if the Phase 3 clinical trial to assess the safety and efficacy of TURSO in patients with ALS conducted by Humanitas Mirasole SpA in the EU reports positive results. While these practices are not recommended by the medical community and have not been approved by any regulatory authority, they may nonetheless impact our sales of RELYVRIO in the U.S., ALBRIOZA in Canada and AMX0035, if approved in other jurisdictions, and/or public perception of AMX0035 in the U.S. or abroad.

If the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities approve generic versions of AMX0035 or any other current or future product candidate of ours that receives regulatory approval, or such authorities do not grant our products appropriate periods of non-patent exclusivity before approving generic versions of such products, the sales of such products could be adversely affected.

In the U.S., once an NDA is approved, the product covered thereby becomes a "reference listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications, or ANDAs, in the U.S. In support of an ANDA, a generic manufacturer generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration, and adequate labeling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning, in part, that it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Moreover, many states allow or require substitution of therapeutically equivalent generic drugs at the pharmacy level even if the branded drug is prescribed. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug may be lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the listed drug is invalid, unenforceable or will not be infringed by the generic product. In that case, the applicant may submit its application four years following approval of the listed drug and seek to launch its generic product even if we still have patent protection for our product unless an infringement suit is timely filed by the NDA or patent holder in which case the FDA cannot approve the ANDA for 30 months unless a court decision in

favor of the generic manufacturer is issued earlier. For fixed dose combination products, the FDA has taken the position that a combination product will be eligible for NCE exclusivity (also known as data exclusivity) if it contains a new active moiety, even if the fixed-combination also contains a drug substance with a previously approved active moiety.

We have received NCE exclusivity from the FDA for RELYVRIO and such exclusivity expires in September 2027. In addition, in connection with our Health Canada marketing authorization with conditions, ALBRIOZA was added to the Register of Innovative Drugs, which provides an eight year period of market exclusivity. The regulatory authorities in Europe may reach different conclusions from the FDA or Health Canada with respect to exclusivity for AMX0035.

If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to the invalidity or non-infringement of any patents listed for our products in the Orange Book. If an infringement suit is timely filed by the NDA or patent holder, the FDA cannot finally approve the ANDA for 30 months unless a court decision in favor of the generic manufacturer is issued earlier. Three-year exclusivity is given to a drug if it contains an active moiety that has previously been approved, and the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are determined by the FDA to be essential to the approval of the NDA. This form of data exclusivity is known as New Clinical Investigation, or NCI, exclusivity. If AMX0035 is approved for future uses or if current and future candidates are approved with only NCI exclusivity, generic manufacturers may file their ANDAs anytime following approval of AMX0035 and seek to launch their generic products following the expiration of the three year market exclusivity period, even if we still have patent protection for our product.

In addition, in the U.S. the FDCA provides a period of seven years of orphan drug exclusivity for drugs that treat small patient populations less than 200,000 patients or for which there are more than 200,000 patients but there is no reasonable expectation that the cost of developing and making the drug for such disease or condition will be recovered from sales in the U.S. of such drug. AMX0035 has been granted orphan drug designation for the treatment of ALS, and with the approval of AMX0035 (RELYVRIO) by the FDA in September 2022 for the treatment of ALS in adults, the product was granted orphan drug exclusivity and the FDA cannot approve a generic or a brand product that contains the same active moiety for the same orphan indication as AMX0035, for a period of seven years, subject to certain exceptions. This period runs concurrent with the NCE exclusivity period.

Canada's data protection regime provides an eight year period of market exclusivity for "innovative drugs", which is independent from patent protection. An innovative drug is a drug that contains a medicinal ingredient not previously approved by Health Canada and that is not a variation of a previously approved medicinal ingredient such as a salt, ester, enantiomer, solvate or polymorph. If a drug qualifies as an "innovative drug" in Canada, generic/and manufacturers are not permitted to seek approval for their product on the basis of a direct or indirect comparison to an innovative drug for the first six years of the data protection period, and Health Canada cannot issue a Notice of Compliance, or NOC or marketing approval, for eight years. One of the components of ALBRIOZA (ursodoxicoltaurine) is an innovative drug, and therefore ALBRIOZA was added to the Register of Innovative Drugs upon its approval. The data protection period for ALBRIOZA runs until June 10, 2030 which is eight years from the date its NOC was issued.

There is no regulatory provision in Canada that provides orphan drug exclusivity to approved products for rare diseases.

In the EU, innovative medicinal products (including both small molecules and biological medicinal products), sometimes referred to as new active substances, or NAS, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. The data exclusivity, if granted, prevents generic or biosimilar applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization, for a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. This 10-year market exclusivity period may be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. However, even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained a marketing authorization based on an application with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials. We have applied for NAS status for AMX0035 in the EU. Irrespective of the NAS status, we expect that AMX0035 will be eligible for orphan market exclusivity if the orphan designation is maintained upon grant of a marketing authorisation in the EU. The current orphan medicines regime in the EU

entitles an orphan medicine to a 10-year period of market exclusivity, which can be extended to 12 years if the sponsor complies with an agreed upon paediatric investigation plan. However, the European Commission introduced a legislative proposal in April 2023 that, if implemented, could reduce the current exclusivity period for certain orphan medicines.

Competition that AMX0035 or any future products, if approved, may face from generic versions of such products could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

AMX0035 and any other current or future product candidates, if approved, could be subject to post-marketing restrictions, requirements or withdrawal from the market and we, or any future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval, which may result in significant expenses.

AMX0035 or any other current or future product candidates for which we, or any future collaborators, obtain regulatory approval, as well as the manufacturing processes, post-approval studies, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA, Health Canada, the EMA and other applicable regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and notify the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the U.S. We and our contract manufacturers will also be subject to user fees and periodic inspection by regulatory authorities to monitor compliance with these requirements and the terms of any product approval we may obtain. Even if regulatory approval of a product candidate is granted, the approval may be subject to limitations on the indications or uses for which the product may be marketed or to the conditions of approval, including the requirement in the U.S. to implement a Risk Evaluation and Mitigation Strategy, or REMS.

The FDA, Health Canada, the EMA and other regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. For example, as part of our approval of RELYVRIO in the U.S., we have post-marketing requirements to conduct carcinogenicity studies in mice and rats, drug-drug interaction studies in human volunteers, and studies in subjects with kidney or liver impairment. Additionally, the FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. Regulatory authorities impose stringent restrictions on manufacturers' communications regarding off-label use. However, companies generally may share truthful and not misleading information that is otherwise consistent with a product's approved labeling. If we, or any future collaborators, do not market AMX0035 or any of our other current or future product candidates for which we, or they, receive regulatory approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing if it is alleged that we are doing so. Violation of laws and regulations relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws, including the False Claims Act and any comparable foreign laws. In the EU, the direct-to-consumer advertising of prescription-only medicinal products is prohibited. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public, if approved, and may also impose limitations on our promotional activities with health care professionals.

Post-marketing requirements in Canada are similar to those in the U.S. Following the approval of our New Drug Submission, or NDS with conditions, Health Canada requires that we submit a Risk Management Plan, or RMP. Health Canada may, as part of the RMP, require that we conduct additional clinical trials. For example, one of the conditions of the marketing authorization in Canada of AMX0035 (ALBRIOZA) is the provision of data from our ongoing PHOENIX trial and other additional planned or ongoing studies. Standard pharmacovigilance activities are also required for any marketed drug product. Any labelling changes or changes in the product supply chain would require a submission to Health Canada for approval before the change may be implemented. Our advertising may be scrutinized by competitors or by health care providers, and complaints could be made to Health Canada or other agencies. Reimbursement in Canada is complex and requires submissions to both public and private payors to gain access to prescription drug formulary lists. In addition, if there are any patents associated with AMX0035, the product will be subject to price regulation by the Patented Medicine Prices Review Board, or the PMPRB.

In addition, later discovery of previously unknown adverse events or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on the manufacturing of such products;
- restrictions on the labeling or marketing of such products;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- exclusion from federal health care programs such as Medicare and Medicaid;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for AMX0035 or any future approved products withdrawn or restricted by regulatory authorities, or we may voluntarily do so, and our ability to market AMX0035 or any future approved products, to develop AMX0035 in the U.S., Canada or additional jurisdictions or for additional indications, and to develop and seek approval for additional product candidates could become limited, which could adversely affect our ability to achieve or sustain profitability. As a result, the cost of compliance with post-approval regulatory requirements may have a negative effect on our operating results and financial condition.

If we fail to obtain coverage and reimbursement for AMX0035 or any other current or future product candidates in new geographies, it could make it difficult for us to sell AMX0035 or any other current or future product candidates profitably.

The success of AMX0035 and any of our other current or future product candidates, if approved, depends on the availability of adequate coverage and reimbursement from third-party payors. Because AMX0035 and any other current or future product candidates represent new approaches to the treatment of the diseases they target, we cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, AMX0035 and any other current or future product candidates or for any product that we may develop. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell any such product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to any current or future product candidates we may develop (e.g., for the administration of our product candidate to patients) is also important. Inadequate reimbursement for such services may lead to physician and payor resistance and adversely affect our ability to market or sell AMX0035 or any other current or future product candidates we may develop. In addition, we may need to develop new reimbursement models, in order to realize adequate value. Payors may not be able or willing to adopt such new models and patients may be unable to afford that portion of the cost that such models may require them to bear. If we determine such new models are necessary, but we are unsuccessful in developing them, or if payors do not adopt such models, our business, financial condition, results of operations and prospects could be adversely affected. For additional information on coverage and reimbursement, see the section entitled “Business—Government Regulation—Coverage and Reimbursement” in this Annual Report.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors, such as private health insurers and health maintenance organizations, are critical to new product acceptance. Government authorities and other third-party payors decide which drugs and treatments they will cover and the reimbursement amount. Coverage and reimbursement by a third-party payor may depend upon a number of factors.

In the U.S., no uniform policy of coverage and reimbursement for products exists among third-party payors. As a result, obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our products on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement from third-party payors will be obtained. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products, which uncertainty may be heightened where the product is subject to post-marketing conditions or requirements to provide additional clinical data. In the U.S., the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. Future coverage and reimbursement may be subject to increased restrictions, such as prior authorization requirements, both in the U.S. and in international markets. Orphan drugs are typically placed on the highest cost-sharing tier and a substantial percentage are subject to prior authorization requirements. Reimbursement agencies in the EU may be more conservative than CMS.

Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Canada, the EU and other countries has and will continue to put pressure on the pricing and usage of drug products such as AMX0035 and any other current or future product candidates we may develop, if approved. We may also incur additional challenges when seeking reimbursement from public and private payers where AMX0035 or any future product candidate has been approved subject to post-marketing conditions. In many countries, particularly the countries of the EU, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. For example, in Canada, price negotiations with provincial authorities can take more than 18 months before there are agreed-upon pricing and reimbursement rates. Prior to these negotiations, a review by CADTH and INESSS are conducted to assess the value that a medicine will provide to the health system. For patented medicines, the PMPRB has jurisdiction over the price at which the medicine is sold, and PMPRB's assessment of an acceptable price can impact negotiations with payors. Such negotiations may also result in additional studies and rationale required for combination products before reimbursement will be granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay or might even prevent our commercial launch of the product, possibly for lengthy periods of time. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the U.S. Other countries allow companies to fix their own prices for products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for product candidates. Accordingly, in markets outside the U.S., the reimbursement for AMX0035 and any other current or future product candidates we may develop may be reduced compared with the U.S. and may be insufficient to generate commercially reasonable revenues and profits.

Additionally, third-party payors may not cover, or provide adequate reimbursement for, long-term follow-up evaluations required following the use of product candidates. Patients are unlikely to use AMX0035 or any other current or future product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of AMX0035 or any future product candidates. Because AMX0035 and any other current or future product candidates may have a higher cost of goods than conventional therapies and may require long-term follow-up evaluations, the risk that coverage and reimbursement rates may be inadequate for us to sustain profitability may be greater. While we have received a positive response from some providers in Canada following Health Canada's approval with conditions of AMX0035 for the treatment of ALS, there is significant uncertainty related to insurance coverage and reimbursement. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for AMX0035 and any other current or future product candidates.

Moreover, increasing efforts by governmental and other third-party payors in the U.S., Canada, the EU, and other foreign jurisdictions to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for AMX0035 or any other current or future product candidates. There has been increasing legislative and enforcement interest in the U.S. with respect to specialty drug pricing practices. We expect to experience pricing pressures in connection with the sale of AMX0035 or any other current or future product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, cost containment initiatives and additional legislative changes.

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

Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (i) changes to our manufacturing arrangements; (ii) additions or modifications to product labeling; (iii) the recall or discontinuation of our products; or (iv) additional record-keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. For more information, see the section entitled "*Business – Government Regulation – Current and Future U.S. Healthcare Reform Legislation*" in this Annual Report.

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for AMX0035 or any other current or future product candidates;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

These laws and future state and federal healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for AMX0035 or any other current or future product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. 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, sustain profitability or commercialize our product candidates.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our product candidates. There has been increasing legislative and enforcement interest in the U.S. with respect to specialty 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, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. The effect of these reform efforts on our business and the healthcare industry in general is not yet known.

Additional state and federal healthcare reform measures are expected to be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for certain pharmaceutical products or additional pricing pressures.

While some of these and other proposed measures may require additional authorization to become effective, Congress and the Biden administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

Governments outside the U.S. may impose strict price controls, which may adversely affect our revenues, if any.

In some countries, including Canada and certain Member States of the EU, the pricing of prescription drugs is, in part, subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. In such countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. The EU provides options for the EU Member States to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. EU Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for drug products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may

further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In some countries, we may be required to conduct a clinical trial or other trials that compare the cost-effectiveness of AMX0035 or any other current or future product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval, which is time-consuming and costly. We cannot be sure that such prices and reimbursement will be acceptable to us. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our strategic partners and the potential profitability of AMX0035 or any other current or future product candidates in those countries would be negatively affected.

Our relationships with healthcare providers, physicians, patients and third-party payors may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors in the U.S. and elsewhere play a primary role in the recommendation and prescription of pharmaceutical products. Arrangements with third-party payors and customers can expose pharmaceutical manufacturers to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, or FCA, which may constrain the business or financial arrangements and relationships through which such companies conduct research, sell, market and distribute pharmaceutical products. In particular, the promotion, sales and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs and other business arrangements generally. Activities subject to these laws also involve the improper use of information obtained in the course of patient recruitment for clinical trials. For more information, see the section entitled "*Business – Government Regulation - Other U.S. Healthcare Laws*" in this Annual Report.

In the U.S., to help patients afford our approved product, we offer programs to assist them or support third-party organizations' programs to assist patients, including patient assistance programs and co-pay coupon programs for eligible patients. Government enforcement agencies have shown increased interest in pharmaceutical companies' product and patient assistance programs, including reimbursement support services, and a number of investigations into these programs have resulted in significant civil and criminal settlements. In addition, at least one insurer has directed its network pharmacies to no longer accept co-pay coupons for certain specialty drugs the insurer identified. Our co-pay coupon programs could become the target of similar insurer actions. In September 2014, the HHS Office of Inspector General, or OIG, issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal anti-kickback statute and/or civil monetary penalty laws if they do not take appropriate steps to exclude Part D beneficiaries from using co-pay coupons. Accordingly, companies exclude these Part D beneficiaries from using co-pay coupons and the same is true for our Amylyx Care Team. It is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, such as RELYVRIO in the U.S., and therefore could have a material adverse effect on our sales, business, and financial condition.

Third party patient assistance programs that receive financial support from companies have also become the subject of enhanced government and regulatory scrutiny. The OIG has established guidelines that suggest that it is lawful for pharmaceutical manufacturers to make donations to charitable organizations who provide co-pay assistance to Medicare patients. However, donations to patient assistance programs have received some negative publicity and have been the subject of multiple government enforcement actions, related to allegations regarding their misuse to promote branded pharmaceutical products over other less costly alternatives. Specifically, in recent years, there have been multiple settlements resulting out of government claims challenging the legality of third party patient assistance programs under a variety of federal and state laws. We have in the past and may, from time to time, make charitable grants to independent charitable foundations that help financially needy patients with their premium, co-pay, and co-insurance obligations. If we choose to do so, and if we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the provision of charitable donations or operation of these programs, we could be subject to damages, fines, penalties, or other criminal, civil, or administrative sanctions or enforcement actions. We cannot ensure that our compliance controls, policies, and procedures will be sufficient to protect against acts of our employees, business partners, vendors or charitable foundations that may violate the laws or regulations of the jurisdictions in which we operate. Regardless of whether we have complied with the law, a government investigation, including of any business partners, vendors or charitable foundations,

could impact our business practices, harm our reputation, divert the attention of management, increase our expenses, and reduce the availability of foundation support for our patients who need assistance.

The distribution of pharmaceutical products is also subject to additional requirements and regulations, including extensive recordkeeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government-funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws and the delay, reduction, termination or restructuring of our operations. Further, defending against any such actions can be costly and time-consuming, and may require significant financial and personnel resources. Therefore, even if we successfully defend against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business is found to not comply with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in the Medicaid Drug Rebate Program, the 340B program, the U.S. Department of Veterans Affairs, Federal Supply Schedule, or FSS, pricing program, and the Tricare Retail Pharmacy program, which require us to disclose average manufacturer pricing, and, in the future may require us to report the average sales price for certain of our drugs to the Medicare program. Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts. Furthermore, regulatory and legislative changes, and judicial rulings relating to these programs and policies (including coverage expansion), have increased and will continue to increase our costs and the complexity of compliance, have been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS or another agency challenges the approach we take in our implementation. For example, in the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect or has changed as a result of recalculation of the pricing data, we are generally obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements increase our costs and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program and give rise to an obligation to refund entities participating in the 340B program for overcharges during past quarters impacted by a price recalculation.

Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. Additionally, our agreement to participate in the 340B program or our Medicaid drug rebate agreement could be terminated, in which case federal payments may not be available under Medicaid or Medicare Part D for our covered outpatient drugs. Additionally, if we overcharge the government in connection with our arrangements with FSS or Tricare Retail Pharmacy, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the FCA and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Further, legislation may be introduced that, if passed, would, among other things, further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting, and any additional future changes to the definition of average manufacturer price or the Medicaid

rebate amount could affect our 340B ceiling price calculations and negatively impact our results of operations. Additionally, certain pharmaceutical manufacturers are involved in ongoing litigation regarding contract pharmacy arrangements under the 340B program. For example, on November 3, 2023, the U.S. District Court of South Carolina issued an opinion in Genesis Healthcare Inc. v. Becerra et al. that may lead to an expansion of the scope of patients eligible to access prescriptions at 340B pricing. The outcome of this and other judicial proceedings on the 340B program and the potential impact on the way in which manufacturers extend discounts to covered entities through contract pharmacies under the 340B program remain uncertain.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other information processing worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to the GDPR, and similarly, processing of personal data regarding individuals in the UK, including personal health data, is subject to the UK GDPR, and together with the EU GDPR, the GDPR. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining the consent of the individuals to whom the personal data relates, providing detailed information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA/UK that are not considered by the European Commission and the UK government as providing "adequate" protection to personal data, including the U.S., and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the U.S. Such transfers of personal data outside of the EEA and UK are prohibited unless a valid GDPR transfer mechanism (for example, the European Commission approved Standard Contractual Clauses, or SCCs, and the UK International Data Transfer Agreement/Addendum, or UK IDTA) has been put in place. Where relying on the SCCs /UK IDTA for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data. The international transfer obligations under the EEA/UK data protection regimes will require significant effort and cost, and may result in us needing to make strategic considerations around where EEA/UK personal data is transferred and which service providers we can utilize for the processing of EEA/UK personal data. Any inability to transfer personal data from the EEA and UK to the United States in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position. The GDPR also permits data protection authorities to require the destruction of improperly gathered or used personal information and or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or €20 million (£17.5 million under the UK GDPR), whichever is greater and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Although the UK is regarded as a third country under the EU GDPR, the European Commission has now issued a decision recognizing the UK as providing adequate protection under the EU GDPR, or Adequacy Decision, and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. The UK Government has introduced a Data Protection and Digital Information Bill, or UK Bill, into the UK legislative process to reform the UK's data protection regime, and if passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regimes and threaten the UK Adequacy Decision from the European Commission, which may lead to additional compliance costs for us and could increase our overall risk. It is unclear how UK data protection laws and regulations will develop in the medium to longer term, and how data transfers to and from the UK will be regulated in the long term. Although the EU GDPR and the EU GDPR currently impose substantially similar obligations, it is possible that over the time the UK GDPR could become less aligned with the EU GDPR. In addition, EU member states have adopted national laws to supplement the EU GDPR, which may partially deviate from the EU GDPR, and the competent authorities in the EU Member States may interpret EU GDPR obligations slightly differently from country to country, such that we do not expect to operate in a uniform legal landscape in the EEA with respect to data protection regulations. The potential of the respective provisions and enforcement of the EU GDPR and UK GDPR further diverging in the future creates additional regulatory challenges and uncertainties for us. The lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to the handling of European personal data and our privacy and data security compliance programs could require us to implement different compliance measures for the UK and EEA.

Similar legal requirements are either in place or are being proposed in the U.S. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General are all aggressive in reviewing consumers' privacy and data security protections. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act—which went into effect on January 1, 2020 and which was recently amended by the California Privacy Rights Act —is creating similar risks and obligations as those created by GDPR. Though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects, or the Common Rule, it does apply to other personal information that we may otherwise handle, such as personal information collected in a business to business context and personal information collected from employees, applicants and retirees residing in California. Similar broad consumer privacy laws have already been passed in numerous states, and laws in Virginia, Colorado and Connecticut already have entered into force. In addition, bills for broad consumer privacy laws are being considered in numerous other states and at the federal level.

Compliance with the above requirements and any other data privacy and data security laws and regulations is a rigorous and time-intensive process and requires significant resources and an ongoing review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

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

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

Risks Related to the Discovery and Development of Our Current and Future Product Candidates

We currently depend on the success of AMX0035, our most advanced product candidate. If we are unable to maintain, or obtain additional, regulatory approvals for, and successfully commercialize, AMX0035, or experience significant delays in doing so, our business may be materially harmed.

We currently only have one commercial product, AMX0035, which is marketed as RELYVRIO in the U.S. and ALBRIOZA in Canada, and our current business and future success depends significantly on our ability to maintain regulatory approvals for and continue to successfully commercialize AMX0035 for ALS, and to develop, maintain and obtain additional regulatory approvals for and successfully commercialize AMX0114 for ALS and AMX0035 in additional jurisdictions and for other indications, such as PSP, WS, AD and other neurological diseases. To date, we have obtained limited clinical trial data supporting AMX0035, having only completed a clinical trial of 137 patients with ALS and a clinical trial in 95 patients with AD. We are conducting a global Phase 3 clinical trial of AMX0035 in ALS, a Phase 2 clinical trial of AMX0035 in WS, and a global Phase 3 clinical trial of AMX0035 in PSP, and intend to conduct additional clinical trials for other indications and product candidates in the future. We are also conducting IND-enabling studies of AMX0114 in ALS and plan to initiate clinical trials in 2024.

We received approval from the FDA for RELYVRIO for the treatment of ALS in adults and marketing authorization with conditions from Health Canada for ALBRIOZA for the treatment of ALS, but we have not yet obtained marketing authorization from the EU following adoption of a negative opinion on our application. If the results of our PHOENIX trial are supportive, we plan to resubmit a MAA for AMX0035 for the treatment of ALS in the EU again as quickly as possible. Accordingly, we are investing the majority of our efforts and financial resources in the further development and commercialization of AMX0035 for the treatment of ALS and other diseases. Successful continued development and additional regulatory approvals of AMX0035 for our initial and potential additional indications is critical to the future success of our business. We will need to have sufficient funds for, and successfully enroll and complete, our clinical development of AMX0035 for the treatment of ALS, PSP, WS, AD and other indications.

The future regulatory and commercial success of AMX0035 or any other current or future product candidates are subject to a number of risks, including the following:

- successful completion of preclinical studies and clinical trials;
- successful patient enrollment in clinical trials;
- successful data from our preclinical studies and clinical trials that supports an acceptable risk-benefit profile of AMX0035 or any other current or future product candidates in the intended populations;
- satisfaction of applicable regulatory requirements, including to satisfy applicable rules governing fixed dose combination products;
- the interpretation of our preclinical and clinical data by regulatory authorities to support marketing approvals;
- potential unforeseen safety issues or adverse side effects;
- receipt and maintenance of marketing approvals from applicable regulatory authorities, including with any expected NCE and new clinical investigation data exclusivity and orphan drug market exclusivity;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for AMX0035 or any other current or future product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of AMX0035 or any other current or future product candidates;
- entry into collaborations to further the development of AMX0035 or any other current or future product candidates;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, including of RELYVRIO in the U.S., ALBRIOZA in Canada and AMX0035, if and when approved in other jurisdictions, whether alone or in collaboration with others;
- successfully conducting commercial sales of RELYVRIO in the U.S., ALBRIOZA in Canada and AMX0035 or any future product candidates, if and when approved in other jurisdictions;
- acceptance of AMX0035, or any other products, if and when approved, by patients, the medical community and third-party payors;
- appropriately identifying patients with the neurological diseases targeted by AMX0035 or any other current or future product candidates;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- maintaining a continued acceptable safety profile of the products following approval;
- effectively competing with other therapies;
- ensuring that we promote and distribute our products consistent with all applicable healthcare laws; and
- enforcing and defending intellectual property rights and claims.

Many of these risks are beyond our control, including the risks related to clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, obtain or maintain additional regulatory approvals for, or successfully

commercialize AMX0035 for the indications we are developing it for, or if we experience delays as a result of any of these risks or otherwise, our business could be materially harmed.

In addition, of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of marketing applications to regulatory authorities, and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval for AMX0035 for any indication, or for AMX0114, any such approval may be subject to limitations on the indications or uses or the patient populations for which we may market the product. Additionally, may not realize the full commercial potential of AMX0035 or any other current or future product candidates that receive marketing approval if we are unable to appropriately identify patients with the neurological diseases targeted by AMX0035 or any other current or future product candidates. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development activities, we cannot assure you that we will successfully develop or commercialize AMX0035 or AMX0114 for any indication in any jurisdiction. If we or any of our future collaborators are unable to develop, maintain, or obtain additional, regulatory approvals for, or, if approved, successfully commercialize AMX0035 or AMX0114 for our initial or potential additional indications, we may not be able to generate sufficient revenue to continue our business. In addition, our failure to demonstrate positive results in our clinical trials in any indication for which we are developing AMX0035 or AMX0114, or to satisfy other regulatory requirements could adversely affect our development efforts for AMX0035 in other indications or for AMX0114.

The delay or denial of regulatory approval, inability to complete post-marketing requirements and post-market obligations, or the requirement to resubmit any marketing application with additional data or information for AMX0035 in any jurisdiction could delay or suspend commercialization of AMX0035 and adversely impact our ability to generate revenue, our business and our results of operations, and could cause us delay or even cease operations.

The research, testing, manufacturing, labeling, approval, sale, marketing, distribution and post-market obligations of drug products are subject to extensive regulation by the FDA, Health Canada, the EMA, and other regulatory agencies in the U.S. and other countries, and such regulations differ from country to country. In September 2022, we received approval from the FDA for AMX0035 (RELYVRIO) for the treatment of ALS in adults and, as part of our approval of RELYVRIO in the U.S., we have post-marketing requirements to conduct carcinogenicity studies in mice and rats, drug-drug interaction studies, and studies in patients with kidney or liver impairment. We also received marketing authorization with conditions from Health Canada for AMX0035 (ALBRIOZA) for the treatment of ALS. One of the conditions of the approval in Canada is the provision of data from our ongoing global PHOENIX trial and additional planned or ongoing studies. We have also pursued regulatory approval of AMX0035 for the treatment of ALS in the EU, but we have not yet obtained marketing authorization from the European Commission following adoption of a negative opinion on our application.. If the results of PHOENIX are supportive, we plan to seek approval of AMX0035 for the treatment of ALS in the EU again as quickly as possible, however it is possible that we may be unable to successfully achieve European Commission approval.

The FDA, Health Canada, the EMA or any other foreign regulatory agency can delay, limit, deny or withdraw approval to market AMX0035 for many reasons, including:

- our inability to demonstrate to the satisfaction of, the FDA, Health Canada, the EMA or any other applicable foreign regulatory agency that AMX0035 is safe and effective for the requested indication;
- our inability to gain agreement from applicable foreign regulatory authorities that AMX0035 is appropriate for approval under applicable regulatory pathways;
- the FDA's, Health Canada's, the EMA's or any other applicable foreign regulatory agency's disagreement with the interpretation of data from preclinical and clinical studies and trials, such as the FDA's differing interpretations of certain data, including sensitivity and statistical analyses, from our CENTAUR trial and OLE as presented at the meetings of the FDA's Advisory Committee on March 30, 2022 and September 7, 2022;
- our inability to demonstrate that the clinical and other benefits of AMX0035 outweigh any safety or other perceived risks;
- a finding that our global Phase 3 PHOENIX trial is insufficient to support current or additional marketing authorizations in ALS;
- the FDA's, Health Canada's, the EMA's or any other applicable foreign regulatory agency's requirement for additional preclinical or clinical studies or trials, including studies to satisfy applicable rules governing fixed dose combination products or post-market requirements;

- the FDA's, Health Canada's, the EMA's or any other applicable foreign regulatory agency's having differing requirements for the trial protocols used in our clinical trials;
- the FDA's, Health Canada's, the EMA's or any other applicable foreign regulatory agency's non-approval of the formulation, labeling and/or the specifications of AMX0035;
- the FDA's, Health Canada's, the EMA's or any other applicable foreign regulatory agency's failure to accept the manufacturing processes or third-party manufacturers with which we contract; or
- the potential for approval policies or regulations the FDA, of Health Canada, the EMA or any other applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs in development, only a small percentage successfully complete the FDA, Health Canada, the EMA or other regulatory approval processes and are commercialized.

The FDA or the applicable foreign regulatory agency may also approve AMX0035 for a more limited indication and/or a narrower patient population than we originally request, and the FDA, Health Canada, the EMA or any other applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of AMX0035. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of AMX0035 and would materially adversely impact our business and prospects.

AMX0035 is a fixed-dose combination drug product and certain regulatory authorities may require a demonstration that each component makes a contribution to the claimed effects in addition to demonstrating that the combination is safe and effective for the intended population.

Under the FDA's combination rule, the FDA may not file or approve an NDA for a fixed-dose combination product unless each component of a proposed drug product is shown to make a contribution to the claimed effects and the dosage of each component (amount, frequency, duration) is safe and effective for the intended population. For additional information on FDA's combination rule, see the section entitled "Business—Government Regulation—Combination Rule for Fixed-Dose Combination Products" in this Annual Report.

Similar requirements may be imposed on us by the EMA in the EU and comparable regulatory authorities in other jurisdictions where we intend to seek regulatory approval. See the section entitled "Business—Government Regulation—Fixed-Dose Combination Guideline" in this Annual Report. In the EU, we have only submitted preclinical data to demonstrate the clinical effects of each component in AMX0035, PB and TURSO (also known as TUDCA), in our prior MAA. There can be no assurance that the EMA will conclude in a future MAA that our preclinical data are sufficient for these purposes or, even if they are, that the results from our preclinical studies demonstrate the clinical effects of each component in AMX0035 for the treatment of ALS. We may be required to produce clinical data supporting the contribution of each component when present at the levels included in the fixed-dose combination in order to obtain marketing authorization in the EU.

While the FDA has approved AMX0035 (known as RELYVRIO) as a fixed-dose combination product for the treatment of ALS in adults, we may be required by the FDA and comparable foreign regulatory authorities to satisfy the fixed-dose combination rule for AMX0035 or any other fixed-dose combination products we may develop for the treatment of any other indications we may pursue in advance of approval.

If the FDA, the EMA or other comparable foreign regulatory authorities require us to conduct one or more clinical trials to support such a demonstration, such as a factorial study, the design, duration, and scope of such clinical trials will be decided upon after further discussions with those agencies and other comparable foreign regulatory authorities. As a result, we are unable to predict with certainty the estimated timing or scope of any future clinical trials of AMX0035 we may be required to conduct to satisfy these requirements governing fixed dose combination products in various jurisdictions. Ongoing third-party data in neurology, specifically within ALS, on our products or other products may influence regulatory decision making, including for fixed-dose combinations.

We have concentrated our research and development efforts on the treatment of neurodegenerative and CNS disorders, a field that has seen very limited success in product development.

We have focused our research and development efforts on addressing neurodegenerative and CNS disorders. Historically,

efforts by pharmaceutical companies in the field of neurodegenerative and CNS disorders have experienced limited successes in product development. The development of neurodegenerative and CNS therapies presents unique challenges, including an imperfect understanding of the biology, the presence of the blood brain barrier that can restrict the flow of drugs to the brain, a frequent lack of translatability of preclinical study results in subsequent clinical trials and dose selection, and the product candidate having an effect that may be too small to be detected using the outcome measures selected in clinical trials or if the outcomes measured do not reach statistical significance. There are few approved therapeutic options available for patients with ALS, AD and other neurodegenerative disorders. Our future success is highly dependent on the successful development and commercialization of AMX0035 and any other current or future product candidates for treating neurodegenerative and CNS disorders. Developing and commercializing AMX0035 and any other current or future product candidates for treatment of neurodegenerative and CNS disorders subjects us to a number of challenges, including ensuring that we have selected the optimal doses, executing an appropriate clinical trial to test for efficacy and obtaining and maintaining regulatory approval from Health Canada, the FDA, the EMA and other comparable foreign regulatory authorities.

The regulatory approval processes of the FDA, Health Canada, the EMA and other comparable foreign authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to maintain or obtain regulatory approval for AMX0035 or any other current or future product candidates, our business will be substantially harmed. A finding that our global Phase 3 PHOENIX trial is insufficient to support current or additional marketing authorizations in ALS could lead the FDA or Health Canada to restrict or withdraw prior regulatory approvals for RELYVRIO or ALBRIOZA, respectively, or we could decide, after consultation with regulatory authorities, to voluntarily withdraw RELYVRIO or ALBRIOZA from the marketplace, or we may not be successful in obtaining regulatory approval in the EU.

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the U.S., Canada, or the EU without obtaining regulatory approval from the FDA, Health Canada, or the EMA, respectively. Regulatory authorities in other jurisdictions may have similar requirements. The time required to obtain approval by the FDA, Health Canada, the EMA and other comparable foreign regulatory authorities is unpredictable, and typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of such 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. The FDA in any approval needs to determine that there is substantial evidence of effectiveness. This finding can be substantiated based on two adequate and well-controlled studies, or in certain circumstances on a single, large, multicenter, adequate and well-controlled study that is very persuasive or from a single adequate and well-controlled study together with confirmatory evidence. FDA regulations and guidance also allow for greater flexibility and tolerance for uncertainty in the context of rare and fatal diseases.

One of the conditions of the marketing authorization in Canada is the provision of data from our ongoing global PHOENIX Phase 3 clinical trial. There is no guarantee that Health Canada will accept the data from our PHOENIX trial as satisfying the conditions and grant a marketing authorization without conditions for ALBRIOZA for the treatment of ALS. Health Canada could require us to make further undertakings with respect to confirmatory clinical trials if it is not satisfied with the data from the PHOENIX trial, in order for AMX0035 to continue to be marketed in Canada. Additionally, the data may not support resubmission of the MAA for AMX0035 for the treatment of ALS in the EU.

Our approval of RELYVRIO by the FDA was granted following a positive recommendation for approval at the second virtual meeting of the Advisory Committee held on September 7, 2022. Although the FDA subsequently approved RELYVRIO for the treatment of ALS in adults, at this meeting and the previous Advisory Committee meeting, the FDA presented concerns regarding choices of statistical models for the prespecified primarily analysis and the interpretability of the survival results included in our marketing application. Other regulatory authorities may present similar concerns regarding our data when reviewed to support marketing applications for AMX0035 for the treatment of ALS. If PHOENIX is not supportive, the FDA could restrict or withdraw approval of AMX0035 or we may seek to withdraw AMX0035 from the market. If we experience delays in obtaining regulatory approval or if we fail to obtain or maintain such approvals, the commercial prospects for AMX0035 may be harmed and our ability to generate revenues or obtain additional approvals and the value of our common stock will be materially impaired.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of AMX0035 for our initial and potential additional indications or any future product candidates, including AMX0114, is susceptible to the risk of failure inherent at any stage of development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are

severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA, Health Canada, the EMA or any other comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. Additionally, our expenses could increase if we are required by the FDA, Health Canada, the EMA or any other comparable foreign regulatory authority to perform clinical trials in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of AMX0035 in additional indications and of AMX0114. It is possible that even if AMX0035 or any other current or future product candidate has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of AMX0035 or any other current or future product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by AMX0035 or any other current or future product candidate, or mistakenly believe that AMX0035 or any other current or future product candidates are toxic or not well-tolerated when that is not in fact the case.

AMX0035 and AMX0114 could fail to obtain additional or initial regulatory approvals, and any of our future product candidates could fail to obtain regulatory approvals, for many reasons, including the following:

- the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities may disagree as to the design or implementation of our clinical trials and may require additional data to support regulatory approval;
- we may be unable to demonstrate to the satisfaction of the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication(s) and, if necessary, that a product candidate and any active components thereof are safe and effective for the proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, Health Canada, the EMA and comparable authorities in other countries may disagree with our interpretation of data from clinical trials or preclinical studies and our request may require additional trials or studies to support marketing approval;
- the data collected from clinical trials of AMX0035 or any other current or future product candidates may not be sufficient to support the submission of an NDA or other submission to the FDA or other comparable foreign regulatory authority to obtain regulatory approval in the U.S., Canada, the EU or elsewhere;
- the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities may find deficiencies with clinical trial sites or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of clinical trial results may result in our failing to obtain regulatory approval to market AMX0035 or any future product candidate we develop, which would significantly harm our business, results of operations and prospects. There is no assurance that the endpoints and trial designs used for the approval of currently approved drugs for the treatment of neurodegenerative diseases will be acceptable for future approvals, including for AMX0035 and AMX0114. The FDA, Health Canada, the EMA and other comparable foreign authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be obtained for any product candidate that we develop. Even if we believe the data collected from past or future clinical trials of AMX0035 or any other current or future product candidates are promising, such data may not be sufficient to support approval by the FDA or any other regulatory authority.

The FDA reviews an NDA to determine whether the product is safe and effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. This finding can be substantiated based on two adequate and well-controlled studies, or in certain circumstances on a single, large, multicenter, adequate and well-controlled study that is very persuasive or from a single adequate and well-controlled study together with confirmatory evidence. The FDA may not agree that this standard is met. Accordingly, there can be no assurance that for AMX0035 or any other current or future product candidates the FDA and other regulatory agencies, including Health Canada and the EMA, will not require additional clinical trials beyond what we may plan to conduct. This may be the case particularly as these regulatory authorities may

consult with one another or as we may be required to apprise the respective agencies of studies we are conducting of AMX0035 for ALS in conjunction with our requests for marketing approval or in response to post-marketing requirements from the respective agency. In September 2022, we received approval for AMX0035 from the FDA for the treatment of ALS in adults, and as a part of our approval, we have post-marketing requirements to conduct carcinogenicity studies in mice and rats, drug-drug interaction studies, and studies in patients with kidney or liver impairment. In July 2022, we received marketing authorization for AMX0035 from Health Canada, with conditions, for the treatment of ALS. One of the conditions of the approval is the provision of data from our PHOENIX trial. There is no guarantee that Health Canada will accept the data from our PHOENIX trial and grant authorization without conditions for AMX0035 for the treatment of ALS. It is typically the case not just in the U.S., but also in Canada and Europe, that marketing approvals are based on two Phase 3 clinical studies. For example, the CHMP of the EMA and the European Commission adopted a negative opinion on our application for conditional marketing authorisation of AMX0035 for the treatment of adults with ALS in the EU relating to the sufficiency of the clinical data in CENTAUR to support approval. Moreover, any finding by another regulatory authority that our global Phase 3 PHOENIX trial is insufficient to support additional marketing authorizations in ALS could lead the FDA or Health Canada to restrict or withdraw prior regulatory approvals for RELYVRIO and ALBRIOZA, respectively. At the second meeting of the Advisory Committee on September 7, 2022, we stated that if our PHOENIX trial is not successful then we will do what is right for patients, which includes voluntarily removing the product from the market. Any such findings by a regulatory authority or decision to voluntarily withdraw AMX0035 from the marketplace would materially harm our ability to generate revenue and remain profitable.

In addition, disruptions caused by any future public health crisis may increase the likelihood that we encounter difficulties or delays in initiating, screening, enrolling, conducting, or completing our ongoing and planned preclinical studies and clinical trials. Clinical site initiation and patient screening and enrollment may be delayed due to prioritization of hospital resources in the event of a future public health crisis. Investigators and patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to such future highly infectious or contagious diseases, could be limited, which in turn could adversely impact our clinical trial operations. Additionally, we may experience interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel, quarantines or social distancing protocols imposed or recommended by federal or state governments, employers and others in connection with any future outbreak of any highly infectious or contagious diseases. As a result of a future public health crisis, we may face delays in meeting our anticipated timelines for our ongoing and planned clinical trials.

In addition, regulatory authorities may subject our clinical or manufacturing operations to inspections, including routine surveillance, bioresearch monitoring and pre-approval inspections. In addition, even if we were to obtain approval, regulatory authorities may approve AMX0035 or any other current or future product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing preclinical studies and clinical trials, or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for AMX0035 or any other current or future product candidates.

In Canada, pre-approval GMP inspections are not performed in association with the NDS. Instead, Health Canada relies on a Drug Establishment License, or DEL, to determine the site's compliance with GMP. DELs can only be held by companies in Canada, and that company becomes the importer of record for the drug. To import, the sites of manufacture, testing and packaging of the Drug Substance and Drug Product are required to be listed on the DEL. Listing is dependent on having an inspection report from a recognized sister regulatory agency such as the EMA or the FDA. As a result of the COVID-19 pandemic, inspection reports can now be up to three years old. The site of manufacture of the drug product for AMX0035 is in Canada and is subject to routine inspections from Health Canada. These Canadian inspections are currently being performed remotely as a result of the COVID-19 pandemic.

We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development of AMX0035 or any other current or future product candidates.

To obtain regulatory approval to commercialize AMX0035 and any other current or future product candidates, we must demonstrate through extensive preclinical studies and clinical trials that such product candidates are safe and effective in humans. Preclinical and clinical testing are expensive and can take many years to complete, and their outcome is inherently uncertain. Failure can occur at any time during the clinical trial process and our future clinical trial results may not be successful, which could impact our ability to obtain additional regulatory approvals for AMX0035, to satisfy any applicable

post-market conditions or requirements or to continue marketing AMX0035 in the U.S. and Canada. We could also be required by regulatory authorities to withdraw AMX0035 from the marketplace. This could impact our development plans for AMX0035 for other indications and any other current or future product candidates and could impact our results of operations.

We may experience delays in completing our clinical trials or preclinical studies and initiating or completing additional clinical trials. We may also experience numerous unforeseen events during our clinical trials that could delay or prevent our ability to receive marketing approval or commercialize AMX0035 or any other current or future product candidates we develop, including:

- regulators, or institutional review boards, or IRBs, or other reviewing bodies may not authorize us or our investigators to commence a clinical trial, or to conduct or continue a clinical trial at a prospective or specific trial site;
- we may not reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the number of subjects or patients required for clinical trials of AMX0035 in an indication or any future product candidate may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, and the number of clinical trials being conducted at any given time may be high and result in fewer available patients for any given clinical trial, or patients may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors, including those manufacturing AMX0035 or any other current or future product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may have to amend clinical trial protocol submitted to regulatory authorities or conduct additional studies to reflect changes in regulatory requirements or guidance, which we may be required to resubmit to an IRB and regulatory authorities for re-examination;
- unforeseen safety events may occur during the course of a clinical trial and these events may result in the temporary suspension or termination of a clinical trial, or require urgent safety measures or restrictions to protect human subjects during the conduct of a clinical trial;
- regulators, IRBs or other reviewing bodies may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies, or the supply or quality of AMX0035 or any other current or future product candidate or other materials necessary to conduct clinical trials of AMX0035 or any other current or future product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the potential for approval policies or regulations of Health Canada, the FDA, the EMA or any other applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval.

Regulators, IRBs of the institutions in which clinical trials are being conducted or data monitoring committees may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Negative or inconclusive impressions of the results from our earlier clinical trials of AMX0035 for the treatment of ALS or AD, or any other clinical trial or preclinical studies in animals that we have conducted, could mandate repeated or additional preclinical studies or clinical trials and could delay marketing approvals or result in changes to or delays in preclinical studies or clinical trials of AMX0035 in other indications. We do not know whether any clinical trials that we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market AMX0035 for our initial or potential additional indications, or any future product candidate. If later stage clinical trials, including our ongoing global Phase 3 PHOENIX trial in ALS, do not produce favorable results with very strong statistical significance, our ability to obtain or maintain any prior-issued regulatory approval for AMX0035 for ALS (including our FDA approval and our marketing

authorization with conditions from Health Canada) or potential additional indications, or any future product candidate, may be adversely impacted.

Our failure to successfully initiate and complete clinical trials of AMX0035 for ALS, PSP, WS, AD or potential additional indications and to demonstrate the efficacy and safety of AMX0035, including each component thereof, necessary to obtain and maintain regulatory approval to market AMX0035, including if our global Phase 3 PHOENIX trial is not successful, would significantly harm our business and ability to continue developing and marketing AMX0035 for any indications. Our product candidate development costs will also increase if we experience delays in testing or obtaining and maintaining regulatory approvals and we may be required to obtain additional funds to complete clinical trials. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays or the need for additional data from our clinical trials also could shorten any periods during which we may have the exclusive right to commercialize AMX0035 or any other current or future product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize such product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of AMX0035 or any future product candidate.

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us or any future collaboration partners from obtaining or maintaining approvals for the commercialization of AMX0035 for our initial or potential additional indications as well as for any future product candidate we develop.

Any product candidate we may develop and the activities associated with its development and commercialization, including its design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, and distribution, are subject to comprehensive regulation by Health Canada, the FDA, the EMA and other regulatory authorities in the U.S. and in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing that product candidate in a given jurisdiction. Although we have invested substantial time and resources to date in pursuit of regulatory approval and toward potential commercialization, we have only received regulatory approval for AMX0035 (RELYVRIO) in the U.S. and marketing authorization with conditions for AMX0035 (ALBRIOZA) in Canada and have not received any other regulatory approvals to market any product candidates from regulatory authorities in any jurisdiction, and it is possible that none of the product candidates we may seek to develop in the future will ever obtain regulatory approval. We have no experience in filing and supporting the applications necessary to gain marketing approvals and rely on third-party CROs or regulatory consultants to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the biologic product candidate's safety, purity, efficacy and potency. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Any product candidates we develop may not be effective, may be only moderately effective, or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, in the U.S., Canada, EU and other foreign jurisdictions, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity, and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA, Health Canada, the EMA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide during the review process that our data are insufficient for approval and require additional preclinical, clinical or other studies. For example, during the review of our NDA for AMX0035 for the treatment of ALS, the FDA requested clarifying information regarding our preclinical and clinical data and during the Advisory Committee meetings noted certain concerns with interpretation of our clinical data. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit, or prevent marketing approval of, or limit the approved labeling for, a product candidate. For example, while we have conducted preclinical studies in various models of neurodegenerative diseases, it is the view of the FDA that the mechanism by which RELYVRIO exerts its therapeutic effects in patients with ALS is unknown. In addition, in the approved labeling for RELYVRIO, the FDA noted that the post hoc, long-term exploratory survival analysis should be interpreted with caution given the limitations of data collected outside of a controlled study. Additionally, the FDA has discretion to refer an application for a novel drug or a drug that presents difficult questions of safety or efficacy to an advisory committee. For example, our approval of RELYVRIO by the FDA was granted following the second virtual meeting of the Advisory Committee held on September 7, 2022. The

Advisory Committee initially met on March 30, 2022 and voted 4 (yes) and 6 (no) on the question of whether the data from our randomized, controlled Phase 2 CENTAUR trial and OLE established a conclusion that AMX0035 is effective in the treatment of patients with ALS. At the second meeting of the Advisory Committee, the Advisory Committee voted 7 (yes) to 2 (no) in response to the question of whether available evidence of effectiveness is sufficient to support approval of AMX0035 for the treatment of ALS, taking into account the unmet need in ALS, the status of the ongoing global PHOENIX trial and the seriousness of ALS. At this meeting and the previous Advisory Committee meeting, the FDA presented concerns regarding choices of statistical models for the prespecified primarily analysis and the interpretability of the survival results. Additionally, one of the conditions of our marketing authorization for ALBRIOZA in Canada is the provision of data from our PHOENIX trial. There is no guarantee that Health Canada will accept the data from our PHOENIX trial as satisfying the conditions and grant a marketing authorization without conditions for ALBRIOZA for the treatment of ALS or that the PHOENIX trial will be successful. Health Canada could require us to make further undertakings with respect to confirmatory clinical trials if it is not satisfied with the data from the PHOENIX trial, in order for AMX0035 to continue to be marketed in Canada. As such, we may be unable to maintain the marketing approvals we are pursuing and any marketing approvals we ultimately obtain, including any conditional approvals, may be denied, limited, withdrawn, or subject to restrictions or post-approval commitments that could render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to maintain or obtain approval of AMX0035 or of any product candidates we may develop, the commercial prospects for those product candidates, including for AMX0035, may be harmed, and our ability to generate revenues will be materially impaired.

The results of early-stage clinical trials and preclinical studies may not be predictive of future results. Initial or preliminary data in our clinical trials may not be indicative of results obtained when these trials are completed or in later stage trials.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any early-stage clinical trials we commence may not be predictive of the results of the later-stage clinical trials. In addition, initial data in clinical trials may not be indicative of results obtained when such trials are completed. There can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of AMX0035 or any other current or future product candidates. In addition, the clinical results seen in the CENTAUR trial may not be repeated in our global Phase 3 PHOENIX clinical trial, which may materially impact our ability to obtain authorization without conditions for ALBRIOZA in Canada, to maintain our approval for RELYVRIO in the U.S., to seek approval in the EU and continue development of AMX0035 for additional indications. There is a high failure rate for drugs and biologics proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results.

Additionally, we have in the past utilized and may in the future utilize an "open-label" clinical trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with AMX0035 or any future product candidates when studied in a controlled environment with a placebo or active control.

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

From time to time, we may publish interim topline or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or topline results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation and business prospects.

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

Patient enrollment is a significant factor in the timing of clinical trials, and the timing of our clinical trials depends, in part, on the speed at which we can recruit patients to participate in our trials, as well as completion of required follow-up periods. We may not be able to initiate or continue clinical trials for AMX0035 or any other current or future product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials to such trial's conclusion as required by Health Canada, the FDA, the EMA or other comparable foreign regulatory authorities. Additionally, certain clinical trials for AMX0035 and any other current or future product candidates may be focused on indications with relatively small patient populations, which may further limit enrollment of eligible patients or may result in slower enrollment than we anticipate. The eligibility criteria of our clinical trials, once established, may further limit the pool of available trial participants. For example the number of patients suffering from ALS, is small and, in some cases, has not been established with precision. If the actual number of patients with these diseases is smaller than we anticipate, we may encounter difficulties in enrolling patients in our clinical trials, thereby delaying or preventing development and approval of AMX0035 or any other current or future product candidates. Even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. For example, ALS patients have significant mobility issues, morbidities and other complications that have historically made retention in ALS trials, more challenging. These challenges are also present with many other neurodegenerative indications, including indications for which we may run clinical trials in the future. In the past, we have had discontinuations in our clinical trials, including in our CENTAUR trial and CENTAUR OLE trial. Discontinuations may occur in current or future trials and could result in delays of completion of our clinical trials and affect our ability to enroll additional patients in our clinical trials and impact the integrity of data from our clinical trials.

Patient enrollment and retention in clinical trials depends on many factors, including the size of the patient population, the severity of the disease under investigation, the nature of the trial protocol, the existing body of safety and efficacy data for the product candidate, the number and nature of competing treatments and ongoing clinical trials of or expanded access to competing therapies for the same indication, the proximity of patients to clinical sites, the eligibility criteria for the trial, the ability to adequately monitor patients during a trial, clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied, and the risk that patients will drop out of a trial before completing all site visits. There are limited patient pools from which to draw in order to complete our clinical trials in a timely and cost-effective manner, including due to the fact that the neurological diseases we target are rare.

Furthermore, our efforts to build relationships with patient communities may not succeed, which could result in delays in patient enrollment in our clinical trials.

Any negative results we may report in clinical trials of AMX0035 or any future product candidate may also 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 AMX0035 in ALS, PSP, WS, AD and additional indications and any other current or future product candidates, or could render further development impossible. Further, if patients drop out of our clinical trials, miss scheduled doses or follow-up visits, or otherwise fail to follow clinical trial protocols, whether as a result of public health epidemics and related illness, the integrity of data from our clinical trials may be compromised or not accepted by Health Canada, the FDA, the EMA or other regulatory authorities, which would represent a significant setback for the applicable program. 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 compel their actual performance.

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

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development activities, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Any of these changes could cause AMX0035 or any other current or future product candidates to perform differently and affect the results of ongoing clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. For example, in seeking approval of AMX0035 in Europe, we submitted data supporting a different formulation of AMX0035 from the formulation evaluated in the CENTAUR trial. Changes to commercial formulations from those studied clinically could lead regulatory authorities to delay the approval of our marketing applications until we can demonstrate through additional clinical data that there is comparability in the bioavailability of the two different formulations or may require us to revert to the prior formulation evaluated clinically. Should we have to conduct comparability testing to bridge earlier clinical data obtained from product candidates produced under earlier manufacturing methods or formulations with the planned commercial

formulation, regulatory authorities may disagree on the interpretation of results from this testing. This could delay completion of clinical trials, require the repetition of one or more clinical trials, increase clinical trial costs, delay approval of AMX0035 or any other current or future product candidates and jeopardize our ability to commence sales and generate revenue.

AMX0035 or any future product candidate may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following regulatory approval, if obtained.

Undesirable side effects caused by AMX0035, or any future product candidate, could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay, denial or withdrawal of regulatory approval by the FDA, Health Canada, the EMA or comparable foreign regulatory authorities. Results of our preclinical studies or clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. In clinical trials of AMX0035 to date, AMX0035 has been generally well-tolerated, with most common treatment-emergent adverse events including diarrhea, abdominal pain, nausea, upper respiratory infection, constipation, headache, fatigue, proteinuria, and decreased appetite. In addition, it has been reported that patients experience a bad taste when taking AMX0035. In animal studies, administration of AMX0035 to rats throughout pregnancy and lactation resulted in increased offspring mortality at all doses tested, which were less than or similar to the clinical doses tested in our clinical trials. However, there can be no guarantee that we would observe a similar tolerability profile of AMX0035 in our global Phase 3 PHOENIX clinical trial or in other future clinical trials for ALS or other indications. Many compounds that initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound.

If unacceptable or severe side effects arise in the development of AMX0035 or any other current or future product candidates, we, the FDA, Health Canada, the EMA or comparable foreign regulatory authorities, the IRBs, or independent ethics committees at the institutions in which our trials are conducted, or the independent safety monitoring committee could suspend or terminate our clinical trials or regulatory authorities could order us to cease clinical trials or deny approval of AMX0035 or any other current or future product candidates for any or all targeted indications. Treatment-emergent side effects that are deemed to be drug-related could also affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Undesirable side effects in one of our clinical trials for AMX0035 in one indication could adversely affect enrollment in clinical trials, regulatory approval and commercialization of AMX0035 in other indications. Additionally, there may be negative findings regarding components of AMX0035 or future product candidates by other parties. For example, Humanitas Mirasole SpA, or Humanitas, is conducting a Phase 3 clinical trial in the EU to assess the safety and efficacy of TURSO in patients with ALS which may lead to additional findings as to the safety profile of TURSO. Any negative findings by third parties may impact the future approvability or labeling of AMX0035 or other product candidates we may develop. In addition, side effects may not be appropriately recognized or managed by the treating medical staff. We have no relationship with Humanitas. If their Phase 3 clinical trial is successful and TURSO is approved by the FDA or any other regulatory agency, TURSO may become a commercialized product competitive with AMX0035, unless our intellectual property protections and any regulatory exclusivities we possess or may possess in the future prevent such commercialization. Inadequate training in recognizing or managing the potential side effects of AMX0035 or any future product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

Bitter taste was frequently observed in our clinical trials of AMX0035. While bitter taste, by itself, does not present a safety risk for patients, it may lead to higher levels of patient non-compliance, which could have the effect of reducing the observed efficacy of AMX0035 in our clinical trials, including our ongoing global Phase 3 PHOENIX trial, or limit its commercial adoption.

Moreover, clinical trials of AMX0035 are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of AMX0035 or any other current or future product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects.

Finally, AMX0035 is a combination of TURSO and PB. PB has been approved by the FDA and other regulatory authorities for the treatment of patients with certain urea cycle disorders and TURSO has been approved in Italy for diseases of cirrhotic liver disorders such as primary biliary cirrhosis. It is possible that one or more of the active moieties in AMX0035 has also been approved by FDA or other regulatory authorities. Even if AMX0035 receives marketing approval and is commercialized in a jurisdiction, we would continue to be subject to the risks that the applicable regulatory authorities could revoke approval of PB or TURSO or any active moiety in AMX0035, if applicable, or that efficacy, manufacturing or supply issues could

arise with PB or TURSO or any active moiety in AMX0035, if applicable. This could result in our own products being removed from the market or being less commercially successful.

Increasing demand for expanded access to AMX0035 could negatively affect our reputation and harm our business.

We are developing AMX0035 for the treatment of ALS, PSP, WS, AD and other potential future indications for which there are currently limited or no available therapeutic options. It is possible for individuals or groups to target companies with disruptive social media campaigns related to a request for access to unapproved drugs for patients with significant unmet medical need. If we experience a similar social media campaign regarding our decision to provide or not provide access to AMX0035 or any of our future product candidates under an expanded access policy, our reputation may be negatively affected and our business may be harmed.

In the past, media attention to individual patients' expanded access requests has resulted in the introduction and enactment of legislation at the local and national level, including the Accelerating Access to Critical Therapies for ALS Act and prior "Right to Try" laws, such as the federal Right to Try Act of 2017, which are intended to allow patients access to unapproved therapies earlier than traditional EAPs and the former of which is intended to support research and development related to ALS, specifically. A possible consequence of both activism and legislation in this area may be the need for us to initiate an EAP beyond that which we have submitted to the FDA or to make AMX0035 or any future product candidates more widely available sooner than anticipated.

In addition, some patients who receive access to drugs prior to their commercial approval through compassionate use, EAPs or right to try access have life-threatening illnesses and have exhausted all other available therapies. The risk for SAEs in this patient population is high, which could have a negative impact on the safety profile of AMX0035 or future product candidates, which could cause significant delays or an inability to successfully commercialize AMX0035 or future product candidates, which could materially harm our business. We may in the future need to restructure or pause any future compassionate use and/or EAP we initiate in order to perform the controlled clinical trials required for regulatory approval and successful commercialization of AMX0035 or future product candidates, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our clinical development activities and the diseases AMX0035 is being developed to treat, and we intend to continue to utilize appropriate social media in connection with our commercialization efforts for RELYVRIO in the U.S. and ALBRIOZA in Canada, and in any other jurisdictions where we obtain regulatory approvals. Social media practices in the biotechnology and pharmaceutical industries continue to evolve and regulations and regulatory guidance relating to such use are evolving and not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us, along with the potential for litigation related to off-label marketing or other prohibited activities and heightened scrutiny by the FDA, the SEC and other regulators. For example, patients may use social media channels to comment on their experience on treatment with AMX0035 or their experience in an ongoing blinded clinical trial or to report an alleged adverse event. If such disclosures occur, there is a risk that trial enrollment may be adversely impacted, that we may fail to monitor and comply with applicable adverse event reporting obligations or that we may not be able to defend our business or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive or confidential information or negative or inaccurate posts or comments about us on any social networking website. In addition, we may encounter attacks on social media regarding our company, management, AMX0035 or future product candidates. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions or incur other harm to our business.

If we fail to develop and commercialize AMX0035 for additional indications or fail to discover, develop and commercialize other current or future product candidates, we may be unable to grow our business and our ability to achieve our strategic objectives would be impaired.

Although the commercialization of AMX0035 for the treatment of ALS is our current primary focus, as part of our longer-term growth strategy, we are currently, and plan to continue to, evaluate AMX0035 in other indications and develop other product candidates. We intend to evaluate internal opportunities from AMX0035 or other potential product candidates, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from neurodegenerative diseases and CNS or other disorders with significant unmet medical needs and limited treatment

options. These other potential product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA, Health Canada, the EMA and/or other applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

Research activities to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research activities may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our potential product candidates obsolete;
- product candidates that we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, 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 patients, the medical community or third-party payors.

If we are unsuccessful in identifying and developing additional product candidates, our potential for growth and achieving our strategic objectives may be impaired.

We may not be successful in our efforts to expand our pipeline by identifying additional product candidates or indications and modifications for which to investigate AMX0035 in the future. We may expend our limited resources to pursue particular product candidates or indication or formulation for AMX0035 and fail to capitalize on such product candidates or indications or formulations of AMX0035 that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we are focused on specific indications and modifications for AMX0035. As a result, we may fail to generate additional clinical development opportunities for AMX0035 for a number of reasons, including, that AMX0035 may in certain indications, on further study, be shown to have harmful side effects, limited to no efficacy, or other characteristics that suggest it is unlikely to receive marketing approval and achieve market acceptance in such additional indications.

We plan to conduct several clinical trials for AMX0035 in parallel over the next several years, including clinical trials in patients with WS, PSP and other indications, which may make our decision as to which indication to prioritize more difficult. As a result, we may forgo or delay pursuit of opportunities with other indications that we believe could have had greater commercial potential or likelihood of success. In addition, we are continuing to evaluate plans to explore the use of AMX0035 in patients with AD, and other product candidates in ALS and additional neurodegenerative diseases. However, we may focus on or pursue one or more of our target indications over other potential indications and product candidates and such development efforts may not be successful, which would cause us to delay the clinical development and approval of AMX0035, and other product candidates. Furthermore, research activities to identify additional indications for AMX0035 require substantial technical, financial, and human resources. We may not successfully develop these additional modifications for chemistry-related, stability-related, or other reasons. We have recently announced the development of AMX0114, an antisense oligonucleotide, targeting Calpain-2 for ALS and other neurodegenerative diseases. We are currently advancing AMX0114 through IND-enabling studies and expect to enter the clinic in 2024. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development activities for specific indications or formulations of AMX0035 or for AMX0114 or other product candidates may not yield any commercially viable products.

Additionally, we may pursue in-licenses or acquisitions of development-stage assets or programs, which entails additional risk to us. Identifying, selecting and acquiring promising product candidates requires substantial technical, financial, and

human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit.

For example, if we are unable to identify programs that ultimately result in approved products, we may spend material amounts of our capital and other resources evaluating, acquiring and developing products that ultimately do not provide a return on our investment.

Competitive products may reduce or eliminate the commercial opportunity for AMX0035 for our current or future indications. If our competitors develop technologies or product candidates more rapidly than we do, or their technologies or product candidates are more effective or safer than ours, our ability to develop and successfully commercialize AMX0035 may be adversely affected.

The clinical and commercial landscape for the treatment of ALS and other neurodegenerative diseases, including AD is highly competitive and subject to rapid and significant technological change. We face competition with respect to our current indications for AMX0035 and will face competition with respect to any future indications of AMX0035 or other drug candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. For example, Humanitas Mirasole SpA is currently conducting a Phase 3 clinical trial in the EU to assess the safety and efficacy of TURSO in patients with ALS, which, if approved, may be commercialized as a competitor to AMX0035. If this study meets its clinical endpoints, this monotherapy treatment could be approved by the FDA, the EMA and other regulatory authorities, and TURSO may become a commercialized product competitive with AMX0035, unless our intellectual property protections and any regulatory exclusivities we possess or may possess in the future prevent such commercialization. There are also a number of large pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drug candidates for the treatment of the indications that we are pursuing. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

Several large pharmaceutical companies market FDA-approved drugs for the treatment of ALS. These drugs include: Riluzole, marketed by Sanofi-Aventis U.S. LLC, and Radicava, marketed by Mitsubishi Tanabe Pharma America, Inc. Additionally, Mitsubishi Tanabe Pharma America, Inc., or MTPA, is developing an oral alternative to Radicava. In the first quarter of 2022, the FDA accepted MTPA's application for priority review of its oral alternative to Radicava and in May 2022, the FDA approved its oral alternative to Radicava. Our potential competitors include pharmaceutical and biotechnology companies, such as Biogen, Inc., UCB S.A. and PTC Therapeutics, Inc., specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. In July 2022, the FDA accepted the NDA and granted Priority Review for tofersen, an investigational antisense drug being evaluated for people with SOD1 ALS. In April 2023 the FDA granted accelerated approval for QALSODY.

Many of our competitors 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. Accordingly, our competitors may be more successful than we may be in obtaining regulatory approval for therapies and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed and sold, than any product candidate we may commercialize and may render AMX0035 or any future product candidates obsolete or non-competitive before we can recover development and commercialization expenses. If AMX0035 is approved for the indications we are currently pursuing, it could compete with a range of therapeutic treatments that are in development. In addition, our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than AMX0035 or any future product candidates that we may develop, which could render such product candidates obsolete and noncompetitive.

Following approval for AMX0035 or any other future product candidate, we may face competition based on many different factors, including the efficacy, safety and tolerability of our products, the ease with which our products can be administered, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Existing and future competing products could present superior treatment alternatives, including being more effective, safer, less expensive or marketed and sold more effectively than any products we commercialize. Competitive products may make any products we commercialize obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

In addition, our competitors may obtain patent protection, regulatory exclusivities or regulatory approval and commercialize products more rapidly than we do, which may impact future approvals or sales of any of our product candidates that receive regulatory approval. We expect to face competition with respect to our commercialization of RELYVRIO in the U.S. and ALBRIOZA in Canada and any future product candidates, if approved. Following approval by Health Canada, the FDA or the EMA for the commercial sale of AMX0035 or any future product candidates, we will also be competing with respect to marketing capabilities and manufacturing efficiency. We expect competition among products will be based on product efficacy and safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capabilities, product price, reimbursement coverage by government and private third-party payors, regulatory exclusivities and patent position. Our profitability and financial position will suffer if our product candidates receive regulatory approval, but cannot compete effectively in the marketplace.

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 other 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 and management personnel and establishing clinical trial sites, as well as in acquiring technologies complementary to, or necessary for, our activities.

Obtaining and maintaining regulatory approval of AMX0035 or any future product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of those product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of AMX0035 and any future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even though the FDA has approved AMX0035 (RELYVRIO) and Health Canada has granted marketing authorization with conditions of AMX0035 (ALBRIOZA), comparable regulatory authorities in the EU and other foreign jurisdictions must also approve the manufacturing, marketing and promotion of AMX0035 in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the U.S., Canada or the EU, including additional preclinical studies or clinical trials, as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the U.S., including Canada, and certain jurisdictions in the EU, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Regulatory authorities in jurisdictions outside of the U.S. have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions and such regulatory requirements can vary widely from country to country. Obtaining other regulatory approvals and compliance with other regulatory requirements could result in significant delays, difficulties and costs for us and could require additional preclinical studies or clinical trials, which could be costly and time-consuming and could delay or prevent the introduction of our products in certain countries. The foreign regulatory approval process involves all of the risks associated with FDA approval. We do not have any product candidates approved for sale in any jurisdiction except the U.S. and Canada, and we do not have experience in obtaining regulatory approval in international markets outside of Canada. If we fail to comply with the regulatory requirements in international markets and/or obtain and maintain applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of AMX0035 or any future product candidates will be harmed.

Even though we have obtained orphan drug designation for AMX0035 for the treatment of ALS in the U.S. and the EU and for the treatment of WS in the U.S., we may not be able to obtain or maintain the benefits associated with orphan drug status, including market exclusivity.

Regulatory authorities in some jurisdictions, including the U.S. and the EU, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 people in the U.S., or a patient population of greater than 200,000 people in the U.S., but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the EU, an orphan designation may be granted in respect of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than five in 10,000 people in the EU when the application is made. Additionally, designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition when, without incentives, it is unlikely that sales of the product in the EU would be sufficient to justify the necessary investment in developing the product. In either case, the applicant for orphan designation must also demonstrate

that no satisfactory method of diagnosis, prevention, or treatment for the condition has been authorized (or, if such a method exists, the new product would be a significant benefit to those affected compared to the product available).

In September 2017, the FDA granted orphan drug status to AMX0035 for the treatment of patients with ALS in the U.S., and with the approval of AMX0035 (RELYVRIO) by the FDA in September 2022 for the treatment of ALS in adults, the product was granted orphan drug exclusivity and the FDA cannot approve a generic or a brand product that contains the same active moiety for the same orphan indication as AMX0035 for a period of seven years, subject to certain exceptions. In addition, in June 2020, the EMA granted orphan medicine status to AMX0035 for the treatment of patients with ALS in the EU. We also received orphan drug status for AMX0035 for the treatment of patients with WS in the U.S. in November 2020. Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug may be entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing authorization application for the same drug for that time period. Another drug may receive marketing approval prior to AMX0035. The applicable period is seven years in the U.S. and ten years in the EU, which may be extended by six months and two years, respectively, in the case of product candidates that have complied with the respective regulatory agency's agreed upon pediatric investigation plan. The exclusivity period in the EU may be reduced to six years if, at the end of the fifth year, it is demonstrated that a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. In the EU, during the ten-year period of orphan marketing exclusivity, neither the competent authorities of the EU Member States, the EMA, or the European Commission are permitted to accept applications or grant marketing authorization for similar medicinal products to the authorized orphan product. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. Legislation has been proposed by the European Commission that, if implemented, has the potential in some cases to shorten the ten-year period of orphan marketing exclusivity. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. In addition, even after a drug is granted orphan exclusivity and approved, the FDA and the EMA can subsequently approve another drug for the same condition before the expiration of the seven-year (or ten-year in the EU) exclusivity period if the FDA or the EMA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, if an orphan designated product receives marketing approval for an indication broader than or different from what is designated, such product may not be entitled to orphan exclusivity. Even though the FDA has granted orphan drug designation to AMX0035 for the treatment of WS, if we receive approval for AMX0035 for a modified or different indication, our current orphan designation may not provide us with exclusivity.

Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review or approval process. Also, regulatory approval for any product candidate may be withdrawn, and other product candidates may obtain approval before us and receive orphan drug exclusivity, which could block us from entering the market.

Even if we obtain orphan drug exclusivity for AMX0035, that exclusivity may not effectively protect us from competition because different drugs can be approved for the same condition before the expiration of the orphan drug exclusivity period. For example, even though AMX0035 is entitled to orphan drug exclusivity, that exclusivity may not prevent the approval of TURSO by the FDA, the EMA or other regulatory authorities as a monotherapy treatment for ALS if those regulatory agencies determine that TURSO is a different drug product from AMX0035. In addition, the regulatory authorities may find that this monotherapy treatment is clinically superior to our fixed dose product and approve it even if we are granted orphan drug exclusivity. U.S. lawmakers have also recently raised the possibility that regulatory or legislative changes might need to be made to the Orphan Drug Act to foster competition. This includes the introduction of legislation that, if adopted into law, would require us to demonstrate to the FDA that AMX0035 would be economically unviable when facing competition to maintain our exclusivity.

We may pursue orphan drug designation for AMX0035 for the treatment of additional indications. The incidence and prevalence of the target patient populations for these indications will be based on our estimates and third-party data. If the market opportunity for these target populations is larger than we estimate, we may be unable to receive orphan drug designation. Additionally, if orphan drug designation is granted, we may be unable to maintain any benefits associated with orphan drug designation, including market exclusivity.

Periodically, we make estimates regarding the incidence and prevalence of target patient populations based on various third-party sources and internally generated analysis. Our estimates may be inaccurate or based on imprecise data. As described above, under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 people in the U.S., or a patient population

of greater than 200,000 people in the U.S., but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. If our incidence or prevalence estimates for future indications for which we may seek orphan drug designation are incorrect, we may be unable to receive orphan drug designation.

Even if the FDA grants orphan drug designation for AMX0035 for other indications, exclusive marketing rights in the U.S. may be limited if we seek FDA marketing approval for an indication broader than the orphan designated indication. Additionally, any product candidate that initially receives orphan drug status designation, may lose such designation if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, others may obtain orphan drug status for products addressing the same diseases or conditions as products we are developing, thus limiting our ability to compete in the markets addressing such diseases or conditions for a significant period of time. As a result, our business and prospects could suffer.

We may pursue Priority Review Designation for product candidates that we may develop, but we might not receive such designations, and Priority Review Designations may not lead to a faster development or regulatory review or approval process.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A Priority Review Designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. For example, we received priority review for AMX0035 for the treatment of ALS, and we may in the future request Priority Review Designation for any future product candidates, however, we cannot assume that any application for future indications of AMX0035 or any other product candidate we may develop will meet the criteria for that designation. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a Priority Review Designation does not necessarily mean a faster development or regulatory review or approval process or necessarily confer any advantage with respect to approval compared to standard FDA review and approval. For example, the FDA originally set the PDUFA date for AMX0035 for the treatment of ALS, for June 29, 2022, and then extended the review timeline for our NDA to September 2022. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

We may seek Fast Track Designation by the FDA for a product candidate that we develop, and we may be unsuccessful. If we are successful, the designation may not actually lead to a faster development or regulatory review or approval process.

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

We may seek Breakthrough Therapy Designation by the FDA for a product candidate that we develop, and we may be unsuccessful. If we are successful, the designation may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

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

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe a product candidate we develop 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 Breakthrough Therapy Designation for a product

candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if any product candidate we develop qualifies as a breakthrough therapy, the FDA may later decide that the drug no longer meets the conditions for qualification and rescind the designation.

Product liability lawsuits against us or any of our future collaborators could divert our resources and attention, cause us to incur substantial liabilities and limit commercialization of AMX0035 or any other current or future product candidates.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. The use of AMX0035 by us and any collaborators in clinical trials, and the sale of AMX0035 in the U.S., Canada and in other jurisdictions, if approved, in the future, may expose us to liability claims. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, health care providers, pharmaceutical companies, our collaborators or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities or be required to limit commercialization of AMX0035 or any other current or future product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs, including with respect to potential class action lawsuits;
- substantial monetary awards to, or costly settlements with, patients or other claimants;
- product recalls or a change in the indications for which they may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize AMX0035 or any other current or future product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new drug, and it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If AMX0035 was to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use AMX0035 or any of our future product candidates. If any of our current or future product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies.

Although we maintain product liability insurance coverage in the amount of up to $5.0 million in the aggregate, including clinical trial liability, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage as we commercialize AMX0035 in the U.S., Canada and other jurisdictions, if approved, or any other current or future product candidate that receives regulatory approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of AMX0035 or any other current or future product candidates, which could harm our business, financial condition, results of operations and prospects.

Even if we, or any future collaborators, obtain and maintain regulatory approvals for AMX0035 or any other current or future product candidate, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could impair our ability to generate revenue.

Once regulatory approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for AMX0035 or any other current or future product candidate for which we or they obtain regulatory approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA, Health Canada and EMA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers could fail to conform to cGMPs and be subject to periodic unannounced inspections by the FDA, Health Canada and the EMA to monitor and ensure compliance with cGMPs. Despite our efforts to inspect and verify regulatory compliance, one or more of our third-party manufacturing vendors may be found on regulatory inspection by the FDA, Health Canada, the EMA or other authorities to be not in compliance with cGMP regulations, which may result in shutdown of the third-party vendor or invalidation of drug product lots or processes. In some cases, a product recall may be warranted or required, which would materially affect our ability to supply and market our drug products.

Accordingly, in any jurisdiction where we or any future collaborators, receive regulatory approval for AMX0035 or one or more future product candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the regulatory approvals for AMX0035 or any other current or future products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Laws and regulations governing any international operations we expect to have in the future may preclude us from developing, manufacturing and selling certain products outside of the U.S. and will require us to develop and implement costly compliance programs.

We have operations in the U.S. and Canada and expect to engage in operations in other jurisdictions, including the EU, as well as other potential jurisdictions, and we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we currently or plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders, including export control and trade sanctions laws, also restrict the use and dissemination outside of the U.S., or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the U.S., it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the U.S., which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

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

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Risks Related to Our Dependence on Third Parties

We may seek to establish collaborations and, if we are not able to establish and maintain them on commercially reasonable terms, we may have to alter our development and commercialization plans.

The advancement of AMX0035, and any other current or future product candidates and development programs or activities, as well as the commercialization of RELYVRIO in the U.S. and ALBRIOZA in Canada and the potential commercialization of AMX0035 in other jurisdictions and of any future product candidates will require substantial additional cash to fund expenses. For some indications of AMX0035 or other current or future product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies with respect to development and potential commercialization. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, if we are able to obtain regulatory approval for product candidates from foreign regulatory authorities, we may enter into collaborations with international biotechnology or pharmaceutical companies for the commercialization of such product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the potential differentiation of our product candidate from competing product candidates, design or results of clinical trials, the likelihood of approval by Health Canada, the FDA, the EMA or other comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop AMX0035 or any other current or future product candidates or bring them to market and generate product revenue.

Collaborations are complex and time-consuming to negotiate and document. Further, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Any collaboration agreements that we enter into in the future may contain restrictions on our ability to enter into potential collaborations or to otherwise develop specified product candidates. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the

development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs or activities, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

We have entered and may in the future enter into collaborations with third parties for the development and commercialization of AMX0035 or any other current or future product candidates, and our prospects with respect to AMX0035 and our other current or future product candidates will depend in significant part on the success of those collaborations.

We may rely on collaborations for the development and commercialization of AMX0035 and any other current or future product candidates. For example, we may utilize a variety of distribution, collaboration and other marketing arrangements with one or more third parties to facilitate commercialization of AMX0035 or to identify novel drug candidates for neurodegenerative diseases as with our partnership with Sunnybrook Research Institute. Our likely collaborators for any distribution, development, sales, marketing, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we enter into such collaborations, we may have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of AMX0035 or any other current or future product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving AMX0035 and any other current or future product candidates pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of AMX0035 or any future product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with AMX0035 or any of our other current or future product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, including trade secrets and intellectual property rights, contract interpretation, or the preferred course of development might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

We rely on third parties to assist in conducting our clinical trials. If they do not perform satisfactorily, we may not be able to obtain or maintain regulatory approval or successfully commercialize AMX0035 or any other current or future product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We have relied upon and plan to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials and expect to rely on these third parties to conduct clinical trials of any future product candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects. Clinical trials involve multiple clinical sites, vendors and other third parties and we are dependent on these vendors to ensure appropriate study conduct, statistical analysis and randomization. Errors or deviations they make in any of these activities could impact the usefulness and interpretability of clinical trial results by regulatory authorities. For example, at the Advisory Committee meeting on March 30, 2022, the FDA noted a number of concerns that, in the FDA's view, impacted the interpretability of the results from the CENTAUR trial. Clinical trials from time to time have deviations where a protocol or standard operating procedure is not perfectly carried out and where corrective actions are taken. While we may perceive these events as low risk, our perception of risk and appropriate corrective actions may differ from that of the regulators' view. Deviations from protocols or standard operating procedures during studies could result in negative regulatory opinions and outcomes.

Further, although our reliance on these third parties for clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. Moreover, the FDA, the EMA and competent authorities of the EU Member States require us to comply with Good Clinical Practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA or other regulatory body may require us to perform additional clinical trials before approving AMX0035, including for additional indications, or any other current or future product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA, the EMA or other regulatory body will determine that any of our clinical trials comply with GCPs. For example, our clinical trial sites and investigators have in the past and may in the future engage in protocol deviations which could impact the overall interpretability of the outcomes of our clinical trials. We are also required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, such as ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development activities. These contractors 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 impede their ability to devote appropriate time to our clinical activities. If these third parties, including clinical investigators, do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, clinical data necessary for regulatory approvals for AMX0035 or any other current or future product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize AMX0035 or any other current or future product candidates. In such an event, our financial results and the commercial prospects for AMX0035 or any other current or future product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

In addition, quarantines, shelter-in-place, and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to infectious diseases, such as the measures that were taken by governments during the COVID-19 pandemic, could impact personnel at our CROs, which could disrupt our clinical timelines, which could have a material adverse impact on our business, prospects, financial condition, and results of operations.

We also rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or regulatory approval of AMX0035 or any other current or future product candidates or commercialization of any resulting products, producing additional losses and depriving us of potential product revenue.

Our use of third parties to manufacture AMX0035 in compliance with cGMP may increase the risk that we will not have sufficient cGMP-compliant quantities of AMX0035 or necessary quantities of such materials on time or at an acceptable cost.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of AMX0035, and we currently lack the resources and the capabilities to do so. As a result, we currently rely on third parties for the manufacture and supply of the active pharmaceutical ingredients, or APIs, in AMX0035, and for the blending and packaging of AMX0035 in accordance with applicable law, regulations and standards. Our current strategy is to outsource all manufacturing of AMX0035 and any other current or future product candidates to third parties.

We currently engage third-party manufacturers to provide the APIs of AMX0035 and for the final drug product formulation of AMX0035 that is being used in our clinical trials and for expanded access and commercial supply, and we engage separate third-parties for the blending and packaging of finished clinical materials. We must be able to demonstrate comparability of drug substance across suppliers along with stability data across suppliers. We currently rely on a single manufacturer to supply one of our APIs and a separate manufacturer to supply the other. Although we believe that there are several potential alternative manufacturers who could manufacture each of the APIs in AMX0035, we may incur added costs and delays in identifying and qualifying any such replacement. Moreover, the extent to which geopolitical events or global health crises may impact our ability to procure sufficient supplies for the development of AMX0035, and any other current or future products and product candidates will depend on whether the economic challenges caused by such events continue to impact the global economy and supply chains, among many other factors. There is no assurance that we will be able to timely secure needed supply arrangements on satisfactory terms, or at all. Our failure to secure these arrangements as needed could have a material adverse effect on our ability to complete the development of AMX0035 or any other current or future product candidates or, to commercialize them, if approved. We may be unable to conclude agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms. There may be difficulties in scaling up to commercial quantities and formulation of AMX0035, and the costs of manufacturing could be prohibitive.

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

- the failure of the third-party manufacturer to comply with applicable regulatory requirements, including cGMPs, and reliance on third-parties for manufacturing process development, regulatory compliance and quality assurance;
- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over AMX0035 or any other current or future product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- limitations on supply availability resulting from capacity and scheduling constraints of third-parties, or as a result of economic or political developments, including the ongoing conflicts in Ukraine and Israel and global economic instability;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control;
- the possible termination or non-renewal of the manufacturing agreements by a third-party, at a time that is costly or inconvenient to us; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

If we do not maintain our key manufacturing relationships, or if any of our contract manufacturers fail to perform their obligations, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could adversely impact our ability to commercialize AMX0035 in the U.S. and Canada, and delay or impair our ability to obtain regulatory approval for our products. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us and there could be a substantial delay before new facilities could be qualified and registered with the FDA, Health Canada, the EMA and other foreign regulatory authorities.

Any change in manufacturer may also involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. In addition, we will need to verify that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA, Health Canada, the EMA or another regulatory authority. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

In some cases, the technical skills required to manufacture AMX0035, or any other current or future products or product candidates may be unique or proprietary to the original contract manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. Furthermore, a contract manufacturer may possess or acquire technology related to the manufacture of AMX0035 or any other current or future product candidate that such contract manufacturer owns independently. This would increase our reliance on such contract manufacturer or require us to obtain a license from such contract manufacturer in order to have another contract manufacturer manufacture AMX0035 or any other current or future product candidates. If AMX0035 for any of our initial or potential additional indications or any future product candidate is approved by any regulatory agency, we intend to utilize arrangements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing AMX0035 or any other current or future product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or voluntary recalls of AMX0035 or any other current or future product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of AMX0035 or any other current or future product candidates. The facilities used by our contract manufacturers to manufacture AMX0035 or any other current or future product candidates must be evaluated by the FDA, Health Canada, the EMA and certain other foreign regulatory authorities. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, Health Canada, the EMA or others, we may not be able to secure and/or maintain regulatory approval for our product manufactured at these facilities. 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, Health Canada, the EMA or other comparable foreign regulatory authority finds deficiencies or does not approve these facilities for the manufacture of AMX0035 or any other current or future 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 AMX0035 or any other current or future product candidates, if approved. Furthermore, if we are required to change contract manufacturers, we will be required to verify that the new contract manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations, which could result in further costs and delays. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, Health Canada, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop AMX0035 or any other current or future product candidates and market our products, if approved.

The FDA, Health Canada, the EMA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA, Health Canada, the EMA and corresponding foreign regulators also inspect these facilities to confirm compliance with cGMPs. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, Health Canada, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop AMX0035 or any future product candidates and market our products following approval.

If any third-party manufacturer of AMX0035 or any other current or future product candidates is unable to increase the scale of its production of such product candidates, and/or increase the product yield of its manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials, expanded access and commercialization of AMX0035 in the U.S. and Canada, and any subsequent commercialization of AMX0035 in other jurisdictions, if approved,

or any other current or future product candidates that we may develop, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third party manufacturers are not able to optimize their manufacturing processes to increase the product yield for AMX0035 or any other current or future product candidates, or if they are unable to produce increased amounts of such product candidates while maintaining the quality of the product and compliance with cGMPs, then we may not be able to meet the demands of clinical trials, expanded access or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

We may need to maintain licenses for active ingredients from third parties to develop and commercialize AMX0035 or a future product candidate, which could increase our development costs and delay our ability to commercialize such product candidate.

Should we decide to use API in any of AMX0035 or any other current or future product candidates that are proprietary to one or more third parties, we would need to maintain licenses to those active ingredients from those third parties. If we are unable to gain or continue to access rights to these active ingredients prior to conducting preclinical toxicology studies intended to support clinical trials, we may need to develop alternate product candidates from these programs by either accessing or developing alternate active ingredients, resulting in increased development costs and delays in commercialization of these product candidates. If we are unable to gain or maintain continued access rights to the desired active ingredients on commercially reasonable terms or develop suitable alternate active ingredients, we may not be able to commercialize product candidates from these programs.

Risks Related to Our Intellectual Property

Our commercial success depends on our ability to protect our intellectual property and proprietary technology.

Our commercial success depends in large part on our ability to obtain and maintain intellectual property rights protection through patents, trademarks and trade secrets in the U.S. and other countries with respect to our proprietary product candidate, AMX0035, and any future proprietary product candidates. If we do not adequately protect our intellectual property rights, competitors may be able to erode, negate or preempt any competitive advantage we may have, which could harm our business and ability to sustain profitability. To protect our proprietary position, we have filed patent applications and may file other patent applications in the U.S. or abroad related to AMX0035 or any other current or future product candidates that are important to our business; we may also license or purchase patents or patent applications filed by others. The patent application process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

If the scope of the patent protection we obtain is not sufficiently broad, we may not be able to prevent others from developing and commercializing technology and products similar or identical to ours. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending owned patent applications that mature into issued patents will include claims with a scope sufficient to protect our proprietary therapeutics or otherwise provide any competitive advantage. Other parties have developed or may develop technologies that may be related or competitive with our approach, and may have filed or may file patent applications and may have been issued or may be issued patents with claims that overlap or conflict with our patent applications, either by claiming the same compounds, formulations or methods or by claiming subject matter that could dominate our patent position. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the U.S. Furthermore, patents have a limited lifespan. In the U.S., the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. 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 patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to AMX0035 or any other current or future product candidates. In the event that an alternative combination, or TURSO as a single drug product, is developed and approved for use in indications for which we may seek approval and falls outside the scope of our patent claims, the marketability and commercial success of AMX0035 could be materially harmed.

Even if they are unchallenged, our owned patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our patents by

developing similar or alternative therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to our product candidate but falls outside the scope of our patent protection or license rights. If the patent protection provided by the patent and patent applications we hold or pursue with respect to AMX0035 or any other current or future product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidate could be negatively affected, which would harm our business.

We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patent or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, or licensees whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, or licensees are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies carries uncertainty. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which are dependent upon the current legal and intellectual property context, extant legal precedent and interpretations of the law by individuals. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are characterized by uncertainty.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the U.S., the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patent or pending patent applications, or that we were the first to file for patent protection of such inventions. If third parties have filed prior patent applications on inventions claimed in our patents or applications that were filed on or before March 15, 2013, an interference proceeding in the U.S. can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such prior applications after March 15, 2013, a derivation proceeding in the U.S. can be initiated by such third parties to determine whether our invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents may be challenged in the courts or patent offices in the U.S. and abroad. Also, while we believe that we have disclosed all potentially relevant prior art relating to our patents and patent applications, there is no assurance that we have found all such prior art or disclosed it in every relevant jurisdiction. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all.

Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. If such prior art exists, it may be used to invalidate a patent, or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or to other patent offices around the world. Alternately or additionally, we may become involved in post-grant review procedures, oppositions, derivation proceedings, ex parte reexaminations, inter partes review, supplemental examinations, or interference proceedings or challenges in district court, in the U.S. or in various foreign patent offices, including both national and regional, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenges may result in loss of the patent or in patent or patent application claims being narrowed, invalidated or held unenforceable, in whole or in part, or in denial of the patent application or loss or reduction in the scope of one or more claims of the patent or patent application, any of which could limit our ability to stop

others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products.

Pending and future patent applications may not result in patents being issued that protect our business, in whole or in part, or which effectively prevent others from commercializing competitive products. Competitors may also be able to design around our patents. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the U.S. For example, patent laws in various jurisdictions, including jurisdictions covering significant commercial markets, such as the European Patent Office, or EPO, China and Japan, restrict the patentability of methods of treatment of the human body more than U.S. law does. If these developments were to occur, they could have a material adverse effect on our ability to generate revenue.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting AMX0035 or any other current or future product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance, whether intentional or not, can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell AMX0035;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the U.S. for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns;
- countries other than the U.S. may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates; and
- countries other than the U.S. may, under certain circumstances, force us to grant a license under our patents to a competitor, thus allowing the competitor to compete with us in that jurisdiction or forcing us to lower the price of our drug in that jurisdiction.

Issued patents that we have or may obtain or license may not provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors do not infringe our patents. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

In addition, we rely on the protection of our trade secrets and proprietary, unpatented know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and invention assignment agreements with employees, consultants, collaborators, vendors, and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. It is possible that technology relevant to our business will be independently developed by a person who is not a party to such a confidentiality or invention assignment agreement. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade

secrets by consultants, collaborators, vendors, advisors, former employees and current employees. Furthermore, if the parties to our confidentiality agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a consequence of such breaches or violations. Our trade secrets could otherwise become known or be independently discovered by our competitors. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, our business may be harmed.

It is difficult and costly to protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for our proprietary product candidate, AMX0035, as well as on successfully defending these patents against potential third-party challenges. Our ability to protect our product candidate from unauthorized making, using, selling, offering to sell or importing by third parties is dependent on the extent to which we have rights under valid and enforceable patents that cover these activities.

The patent positions of pharmaceutical, biotechnology and other life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved and have in recent years been the subject of much litigation. Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. Over the past decade, U.S. federal courts have increasingly invalidated pharmaceutical and biotechnology patents during litigation often based on changing interpretations of patent law. Further, the determination that a patent application or patent claim meets all of the requirements for patentability is a subjective determination based on the application of law and jurisprudence. The ultimate determination by the U.S. Patent and Trademark Office, or USPTO, or by a court or other trier of fact in the U.S., or corresponding foreign national patent offices or courts, on whether a claim meets all requirements of patentability cannot be assured. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our owned patents or patent applications.

We cannot provide assurances that any of our patent applications will be found to be patentable, including over our own prior art publications or patent literature, or will issue as patents. Neither can we make assurances as to the scope of any claims that may issue from our pending and future patent applications nor to the outcome of any proceedings by any potential third parties that could challenge the patentability, validity or enforceability of our patents and patent applications in the U.S. or foreign jurisdictions. Any such challenge, if successful, could limit patent protection for our products and current or future product candidates and/or materially harm our business.

In addition to challenges during litigation, third parties can challenge the validity of our patents in the U.S. using post-grant review and inter partes review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent filed March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine-month window from issuance of the patent. A petition for inter partes review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for inter partes review can be filed after the nine-month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas inter partes review proceedings can only raise an invalidity challenge based on published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts, and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or inter partes review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we will be successful in defending the patent, which may result in a loss of the challenged patent right to us.

In the EU, third parties can challenge the validity of our patents by filing an Opposition before the EPO. An adverse determination by the Opposition Board can result in the narrowing or invalidation of a European patent. If any of our European patents are challenged by a third party in such an opposition proceeding, there is no guarantee that we will be successful in defending the patent, which may result in a loss of the challenged patent right to us.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we may not be able to generate sufficient data to support full patent applications that protect the entire breadth of developments in one or more of our programs;
- it is possible that one or more of our pending patent applications will not become an issued patent or, if issued, that the patent(s) claims will have sufficient scope to protect our technology, provide us with commercially viable patent protection or provide us with any competitive advantages;
- if our pending applications issue as patents, they may be challenged by third parties as invalid or unenforceable under U.S. or foreign laws;
- we may not successfully commercialize AMX0035 before our relevant patents expire;
- we may not be the first to make the inventions covered by each of our patents and pending patent applications; or
- we may not develop additional proprietary technologies or product candidates that are separately patentable.

In addition, to the extent that we are unable to obtain and maintain patent protection for AMX0035 or any other current or future product candidates or in the event that such patent protection expires, it may no longer be cost-effective to extend our portfolio by pursuing additional development of a product or product candidate for follow-on indications.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

In addition to patents, we also may rely on trade secrets to protect our proprietary product candidate, especially where we do not believe patent protection is appropriate or obtainable. Trade secrets are difficult to protect. We seek to protect our confidential proprietary information, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements are designed to protect our proprietary information. However, we cannot be certain that such agreements have been entered into with all relevant parties, and we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, our employees, consultants, contractors, outside scientific collaborators and other advisers may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third-party entity illegally obtained and is using any of our trade secrets is expensive and time-consuming, and the outcome is unpredictable, and we may not be able to obtain adequate remedies for such breaches. We also seek to preserve the integrity and confidentiality of our confidential proprietary information by maintaining physical security of our premises and physical and electronic security of our IT systems, but it is possible that these security measures could be breached. In addition, courts outside the U.S. are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Notably, proprietary technology protected by a trade secret does not preempt the patenting of independently developed equivalent technology, even if such equivalent technology is invented subsequent to the technology protected by a trade secret. If any of our confidential proprietary information were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

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

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. The patent term of a U.S. patent may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

Various extensions may be available, but the life of a patent, and the protection it affords, is limited. 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.

In the U.S., the Drug Price Competition and Patent Term Restoration Act of 1984 permits a Patent Term Extension, or PTE, of up to five years beyond the normal expiration of the patent to compensate patent owners for loss of enforceable patent term due to the lengthy regulatory approval process. PTE is limited to the approved indication (or any additional indications

approved during the period of extension). We anticipate applying for PTE in the U.S. Similar extensions may be available in other countries where we are prosecuting patents and we likewise anticipate applying for such extensions.

The granting of such patent term extensions is not guaranteed and is subject to numerous requirements. We might not be granted an extension because of, for example, failure to apply within applicable periods, failure to apply prior to the expiration of relevant patents or failure to otherwise satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the USPTO in the U.S., 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 obtain approval of competing products following our patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate revenue.

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

The U.S. Congress is responsible for passing laws establishing patentability standards. As with any laws, implementation is left to federal agencies and the federal courts based on their interpretations of the laws. Interpretation of patent standards can vary significantly within the U.S. Patent and Trademark Office, and across the various federal courts, including the Supreme Court. Recently, the Supreme Court has ruled on several patent cases, generally limiting the types of inventions that can be patented. Further, there are open questions regarding interpretation of patentability standards that the Supreme Court has yet to decisively address. Absent clear guidance from the Supreme Court, the USPTO has become increasingly conservative in its interpretation of patent laws and standards.

In addition to increasing uncertainty with regard to our ability to obtain patents in the future, the legal landscape in the U.S. has created uncertainty with respect to the value of patents. Depending on any actions by Congress, and future decisions by the lower federal courts and the Supreme Court, along with interpretations by the USPTO, the laws and regulations governing patents could change in unpredictable ways and could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may not be able to enforce our intellectual property rights throughout the world.

Filing, prosecuting, enforcing and defending patents on our product candidate in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the U.S. and the EU do not afford intellectual property protection to the same extent as the laws of the U.S. and the EU. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the U.S. and the EU or from selling or importing products made from our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Proceedings to enforce our patent rights, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings could put our patents at risk of being invalidated or held unenforceable, or interpreted narrowly, and our pending 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. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts

in all jurisdictions in which we may wish to market our products, if approved. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Others may challenge inventorship or claim an ownership interest in our intellectual property which could expose it to litigation and have a significant adverse effect on its prospects.

A third party or former employee or collaborator may claim an inventorship or ownership interest in one or more of our or our licensors' patents or other proprietary or intellectual property rights. A third party could bring legal actions against us and seek monetary damages and/or enjoin clinical testing, manufacturing and marketing of the affected product or products. While we are presently unaware of any claims or assertions by third-parties with respect to inventorship or ownership of our patents or other intellectual property, we cannot guarantee that a third party will not assert a claim or an interest in any of such patents or intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to AMX0035 or any other current or future product candidates. Further, regardless of the outcome, if we become involved in any litigation, it could consume a substantial portion of our resources, and cause a significant diversion of effort by our technical and management personnel.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing AMX0035 or any other current or future product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidate without infringing the intellectual property and other proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds, methods of manufacturing compounds and/or methods of use for the treatment of the disease indications for which we are developing AMX0035 or any other current or future product candidates. If any third-party patents or patent applications are found to cover AMX0035 or any other current or future product candidates or their methods of use or manufacture, we may not be free to manufacture or market such product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates, including patent infringement lawsuits in the U.S. or abroad. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the composition, use or manufacture of AMX0035 or any other current or future product candidates. While we perform periodic searches for relevant patents and patent applications with respect to our proprietary drug candidate, AMX0035, we cannot guarantee that any of our patent searches or analyses including, but not limited to, the identification of relevant patents, the scope of patent claims or the expiration of relevant patents are complete or thorough, nor can we be certain that we have identified each and every patent and pending application in the U.S. and abroad that is relevant to or necessary for the commercialization of AMX0035 or any other current or future product candidates in any jurisdiction. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that AMX0035 or any other current or future product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on intellectual property rights that exist now or arise in the future. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use or manufacture. The scope of protection afforded by a patent is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidate, product or method either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the U.S., proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources, and we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. If we were required to obtain a license to continue to manufacture or market the affected product, we may be required to pay substantial royalties or grant cross-licenses to our patents. We cannot, however, assure you that any such license will be available on acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights. Further, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree. Furthermore, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. In addition, we could be found liable for significant monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing AMX0035 or any other current or future product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our current and former employees and our licensors' current and former employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some which may be competitors or potential competitors. Some of these employees, including members of our senior management, may have executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may sustain damages or lose key personnel, valuable intellectual property rights or the personnel's work product, which could hamper or prevent commercialization of our technology, which in turn could materially affect our commercial development efforts. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

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

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to

overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use for our products in the U.S. 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 potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a usable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

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, or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make products that are competitive to AMX0035, for example a TURSO monotherapy, or any of our future product candidates but that are not covered by the claims of the patents that we own;
- others may independently develop similar or alternative technologies or otherwise circumvent any of our technologies without infringing our intellectual property rights;
- we or any of our collaborators might not have been the first to invent the inventions covered by the patents or patent applications that we own;
- we or any of our collaborators might not have been the first to file patent applications covering certain of the patents or patent applications that we or they own or have obtained a license, or will own or will have obtained a license;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own may not provide us with any competitive advantage, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights, or in countries where research and development safe harbor laws exist, and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- ownership of our patents or patent applications may be challenged by third parties;
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business; and
- patent enforcement is expensive and time-consuming and difficult to predict; thus we may not be able to enforce any of our patents against a competitor.

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

We consider proprietary trade secrets or confidential know-how and unpatented know-how to be important to our business. We may rely on trade secrets or confidential know-how to protect our technology, especially where patent protection is believed by us to be of limited value. We rely on third parties for research and development work, and expect to rely on third parties for future manufacturing of our proprietary product candidate, AMX0035, and any other current or future product candidates. We also expect to collaborate with third parties on the development of AMX0035 and any other current or future product candidates. As a result of the aforementioned collaborations, we must, at times, share trade secrets with our collaborators.

Trade secrets or confidential know-how can be difficult to maintain as confidential. To protect this type of information against disclosure or appropriation by competitors, our policy is to require our employees, consultants, contractors and

advisors to enter into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with us 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. However, current or former employees, consultants, contractors and advisers may unintentionally or willfully disclose our confidential information to competitors, and confidentiality agreements may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. 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 would impair our competitive position and may have an adverse effect on our business and results of operations. Enforcing a claim that a third party obtained illegally and is using trade secrets or confidential know-how is expensive, time consuming and unpredictable. Moreover, the enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction.

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, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

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

A third party may hold intellectual property, including patent rights that are important or necessary to the development of additional future product candidates. It may be necessary for us to use the patented or proprietary technology of one or more third parties to commercialize our current and future product candidates. If we are unable to acquire such intellectual property outright, or obtain licenses to such intellectual property from such third parties when needed or on commercially reasonable terms, our ability to commercialize additional future product candidates, if approved, would likely be delayed.

The risks described elsewhere pertaining to our intellectual property rights also apply to the intellectual property rights that we may in-license, and any failure by us or our licensors to obtain, maintain, defend and enforce these rights could have an adverse effect on our business. In some cases we may not have control over the prosecution, maintenance or enforcement of the patents that we license, and may not have sufficient ability to provide input into the patent prosecution, maintenance and defense process with respect to such patents, and potential future licensors may fail to take the steps that we believe are necessary or desirable in order to obtain, maintain, defend and enforce the licensed patents.

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

We are currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability, ongoing military conflicts, including the conflict between Russia and Ukraine and the conflict in Israel, and high inflation and rising interest rates, any of which could have a material adverse effect on our business, financial condition and results of operations.

U.S. and global markets have recently been experiencing volatility and disruption caused by economic uncertainty, including as a result of the ongoing Russia-Ukraine conflict and the effects of sanctions imposed on Russia as a result of the conflict, as well as the recent conflict in Israel and the Gaza Strip. In February 2022, a full-scale military invasion of Ukraine by Russian troops began. Although the length and impact of the ongoing military conflict is highly unpredictable, the conflict in Ukraine has led to market disruptions, including significant volatility in commodity prices, credit and capital markets, as well as supply chain interruptions, which contributed to record inflation globally. In addition, global markets may experience additional disruptions as a result of the current armed conflict in Israel and the Gaza Strip, with Israel having declared war on Hamas, a U.S. designated Foreign Terrorist Organization, due to recent attacks. We are continuing to monitor inflation, the situations in Ukraine and Israel and global capital markets and assessing their potential impact on our business, including the impact on the supply chains we rely on for the manufacture of AMX0035 or any other current or future product candidates.

Although, to date, our business has not been materially impacted by the events described above, geopolitical tensions, or record inflation, it is impossible to predict the extent to which our operations will be impacted in the short and long term, or the ways in which such matters may impact our business. The extent and duration of the conflicts in Ukraine and Israel,

geopolitical tensions, record inflation and resulting market disruptions are impossible to predict but could be substantial. Any such disruptions may also magnify the impact of other risks we face.

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

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

We depend heavily on our executive officers, principal consultants and others, and the loss of their services would materially harm our business.

Our success depends, and will likely continue to depend, upon our ability to hire and retain the services of our current executive officers, principal consultants and others. We have entered into employment agreements with our current executive officers, but they may terminate their employment with us at any time. The loss of their services might impede the achievement of our research, development and commercialization objectives.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. For example, in February 2024, our then Chief Human Resource Officer, Debra Canner, was replaced by Linda Arsenault as our current Chief Human Resource Officer. In December 2023, our then Global Head of Clinical R&D and Chief Medical Officer, Patrick Yeramian, M.D., was replaced by Camille L. Bedrosian, MD as our current Chief Medical Officer. Additionally, in December, 2023, our then Chief Commercial Officer, Margaret Olinger, left the Company. Replacing executive officers or other 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 develop, gain regulatory approval of and commercialize products successfully.

Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees 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.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize AMX0035 or any other current or future product candidates will be limited.

We only have a limited number of employees to manage and operate our business.

As of December 31, 2023, we had 384 full-time employees. Our focus on the development and commercialization of AMX0035 requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. We cannot assure you that we will be able to hire and/or retain adequate staffing levels to develop and commercialize AMX0035 or to run our operations and/or to accomplish all of the objectives that we otherwise would seek to accomplish.

Our employees, independent contractors, consultants, collaborators and CROs may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and CROs may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates:

- FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities;
- manufacturing standards;
- federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities; and
- laws that require the reporting of financial information or data accurately.

Activities subject to these laws also involve the improper marketing, use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product materials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, disgorgement, integrity oversight and reporting obligations, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We currently expect to continue to significantly increase the number of our employees and the scope of our operations, particularly in the areas of regulatory affairs and sales, marketing and distribution, as well as to support our public company operations. To manage these growth activities, 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. Our management may need to devote a significant amount of its attention to managing these growth activities. Moreover, our expected growth could require us to relocate to a different geographic area of the country. 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 or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of AMX0035 or any other current or future product candidates.

A pandemic, epidemic, or outbreak of an infectious disease may materially and adversely affect our business, including our preclinical studies, clinical trials, third parties on whom we rely, our supply chain, our ability to raise capital, our ability to conduct regular business and our financial results.

We are subject to risks related to public health crises. For instance, from 2020 through 2022, we experienced certain impacts from the COVID-19 pandemic, including alterations to our preclinical and clinical trial activities, such as scheduling certain work off-site and performing off-site assessments. There can be no guarantee we will not experience other impacts in the future, such as being forced to further delay or pause enrollment, experiencing potential interruptions to our supply chain,

facing difficulties or additional costs in enrolling patients in future clinical trials or being able to achieve full enrollment of our studies within the timeframes we anticipate, or at all.

Any negative impact any future pandemic or similar disruption has on patient enrollment or treatment, or the development of AMX0035 and any other current or future product candidates, could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize AMX0035 and any other current or future product candidates, if approved, increase our operating expenses, which could have a material adverse effect on our financial results. The COVID-19 pandemic and other global macroeconomic factors have also caused significant volatility in public equity markets and disruptions to the U.S. and global economies and any future pandemic or similar disruption could lead to further market dislocation. Any such increased volatility and economic dislocation may make it more difficult for us to raise capital on favorable terms, or at all. If we or any of the third parties with whom we engage were to experience business disruptions, our ability to conduct our business in the manner and on the timelines presently planned could be materially and negatively affected, which could have a material adverse impact on our business and our results of operations and financial conditions. To the extent any future pandemic or similar disruption adversely affects our business and financial results, it may also heighten many of the other risks described in this ‘‘Risk Factors’’ section, such as those relating to the timing and completion of our clinical trials and our ability to obtain future financing.

Risks Related to Our Common Stock

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

The trading price of our common stock may be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. From example, from January 7, 2022, the first day that our stock traded on the Nasdaq Global Select Market, through December 31, 2023, our stock has traded within a range of a high price of $41.93 and a low price of $6.51 per share. In addition to the factors discussed in this “Risk Factors” section and elsewhere in Annual Report, these factors include:

- product revenues;
- the commencement, enrollment or results of our ongoing and future preclinical studies and clinical trials, or any future preclinical studies or clinical trials, we may conduct of AMX0035 and any other current or future product candidates, or changes in the development status of our current and any future product candidates;
- any additional regulatory submissions for AMX0035 or any other current or future product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority’s review of such submissions, including without limitation the FDA’s issuance of a “refusal to file” letter or a request for additional information;
- adverse results or delays in our preclinical studies and clinical trials, including PHOENIX, our global Phase 3 clinical trial of AMX0035 for the treatment of ALS;
- our decision to initiate a clinical trial, not to initiate a clinical trial, or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approvals for AMX0035 and any other current or future product candidates;
- changes in laws or regulations applicable to AMX0035 and any other current or future product candidates, including but not limited to clinical trial requirements for approvals;
- the failure to obtain coverage and adequate reimbursement of AMX0035 and any other current or future product candidates, if approved;
- changes on the structure of healthcare payment systems;
- any changes to our relationship with any manufacturers, suppliers, licensors, future collaborators or other strategic partners;
- our inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- our failure to successfully commercialize AMX0035 and any other current or future product candidates;

- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to the use of AMX0035 and any other current or future product candidates;
- introduction of new products or services offered by us or our competitors, or the release or publication of clinical trial results from competing product candidates;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position and rate of expenditures;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- overall performance of the equity markets;
- issuances of debt or equity securities;
- sales of our common stock by us or our stockholders in the future or the perception that such sales may occur;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- 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;
- general political, geographical, and economic conditions, including the impact of global health crises such as the COVID-19 pandemic, historically high inflation, rising interest rates and the ongoing conflicts in Ukraine and Israel; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and pharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

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

As widely reported, global credit and financial markets have experienced extreme volatility and disruptions in the past several years, including severely diminished liquidity and credit availability, declines in consumer confidence, increases in the rate of inflation and interest rates and uncertainty about economic stability, including most recently in connection with the conflict in Ukraine and Israel. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. Our business could also be impacted by volatility caused by geopolitical events such as the conflicts in Ukraine and Israel. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Furthermore, our stock price may decline due in part to the volatility of the stock market and the general economic downturn.

Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay, scale back or discontinue the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

We are no longer an emerging growth company and the reduced compliance requirements applicable to emerging growth companies no longer apply to us.

We no longer qualify as an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and as such we no longer are entitled to rely on exemptions from certain compliance requirements that are applicable to companies that are emerging growth companies. As a result, subject to certain grace periods, we are now required to:

- engage an independent registered public accounting firm to provide an attestation report on our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002;
- submit certain executive compensation matters to stockholder advisory votes; and
- disclose a compensation discussion and analysis, including disclosure regarding certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of the chief executive officer's compensation to median employee compensation.

We are no longer able to take advantage of cost savings associated with the JOBS Act. Furthermore, if the additional requirements applicable to non-emerging growth companies divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. Furthermore, if we are unable to satisfy our obligations as a non-emerging growth company, we could be subject to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation.

A significant portion of our total outstanding shares may be sold into the market, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. As of February 12, 2024, we had outstanding 67,782,139 shares of common stock, which may be resold in the public market immediately without restriction, unless held by our affiliates. Moreover, holders of approximately 11.8 million shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. In addition, the terms of any future debt or credit 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.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock, own a significant portion of our common stock. As a result, these stockholders acting together, could be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these stockholders, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that our stockholders may feel are in their best interest.

Delaware law and provisions in our amended and restated certificate of incorporation, or our certificate of incorporation, and amended and restated bylaws, or our bylaws, could make a merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock.

Provisions of our certificate of incorporation and bylaws may delay or discourage transactions involving an actual or potential change in our control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our certificate of incorporation and bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in our control);
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that our board of directors or any individual director may only be removed with cause and the affirmative vote of the holders of at least 66-2/3% of the voting power of all of our then-outstanding common stock;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose);
- provide that special meetings of our stockholders may be called only by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors; and
- provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for the following types of actions or proceedings under state, statutory and common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action or proceeding asserting a claim of breach of a fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders; (iii) any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees, arising out of or pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws; (iv) any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws; (v) any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and (vi) any action asserting a claim against us or any of our directors, officers or other employees governed by the internal affairs doctrine, in all cases to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants; provided these provisions of our certificate of incorporation and bylaws will not apply to suits brought to enforce a duty or liability created by the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction; and provided that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the U.S. shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act of 1933, as amended, or the Securities Act.

The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require approval by the holders of at least 66-2/3% of our then-outstanding common stock.

In addition, as a Delaware corporation, we are subject to Section 203 of the Delaware General Corporation Law. These provisions may prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a certain period of time. A Delaware corporation may opt out of this provision by express

provision in its original certificate of incorporation or by amendment to its certificate of incorporation or bylaws approved by its stockholders. However, we have not opted out of this provision.

These and other provisions in our certificate of incorporation, bylaws and Delaware law could make it more difficult for stockholders or potential acquirors to obtain control of our board of directors or initiate actions that are opposed by our then-current board of directors, including delay or impede a merger, tender offer or proxy contest involving our company. The existence of these provisions could negatively affect the price of our common stock and limit opportunities for you to realize value in a corporate transaction.

If we fail to maintain proper and effective internal control over financial reporting, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, our management is required to assess and report annually on the effectiveness of our internal control over financial reporting and to identify any material weaknesses in our internal control over financial reporting. As a result of no longer qualifying as an emerging growth company as defined in the JOBS Act and becoming a large accelerated filer, we are also required to comply with, among other requirements, the auditor attestation requirements of Section 404(b). Preparing such attestation report and the cost of compliance with reporting requirements that we had not previously implemented has and will continue to increase our expenses and require significant management time. Investors may find our common stock less attractive because of the additional compliance costs. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

The rules governing the standards that must be met for management and our independent registered public accounting firm to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. In connection with our and our independent registered public accounting firm's evaluations of our internal control over financial reporting, we may need to upgrade systems, including information technology, implement additional financial and management controls, reporting systems, and procedures, and hire additional accounting and finance staff.

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 addition, any testing by us or our independent registered public accounting firm conducted in connection with Section 404 may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior 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. Internal control deficiencies could also result in a restatement of our financial results in the future. We could become subject to stockholder or other third-party litigation, as well as investigations by the SEC, the Nasdaq Global Select Market, or other regulatory authorities, which could require additional financial and management resources and could result in fines, trading suspensions, payment of damages or other remedies. Further, any delay in compliance with the auditor attestation provisions of Section 404 could subject us to a variety of administrative sanctions, including ineligibility for short-form resale registration, action by the SEC and the suspension or delisting of our common stock, which could reduce the trading price of our common stock and could harm our business.

Our bylaws provide that the Court of Chancery of the State of Delaware and the federal district courts of the U.S. will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our bylaws provide that, to the fullest extent permitted by law and subject to the court's having personal jurisdiction over the indispensable parties named as defendants, the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action or proceeding asserting a breach of fiduciary duty owed by any of our current or former directors, officers or other employees to us or our stockholders;
- any action or proceeding asserting a claim against us or any of our current or former directors, officers or other employees arising out of or pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or bylaws;
- any action or proceeding to interpret, apply, enforce or determine the validity of our certificate of incorporation or our bylaws;

- any action or proceeding as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and
- any action asserting a claim against us or any of our directors, officers or other employees that is governed by the internal affairs doctrine.

This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our certificate of incorporation further provides that the federal district courts of the U.S. will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

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 either exclusive forum provision in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that we will need significant additional capital in the future to continue our planned operations, including conducting clinical trials, commercialization efforts if we are able to obtain marketing approval of any of AMX0035 or any other current or future product candidates, research and development activities, and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock, including shares of common stock sold in our public offerings.

Pursuant to our 2022 Stock Option and Incentive Plan, or the 2022 Plan, our management is authorized to grant stock options to our employees, directors and consultants. Additionally, the number of shares of our common stock reserved for issuance under our 2022 Plan will automatically increase on January 1 of each year, beginning on January 1, 2023 and continuing through and including January 1, 2032, by 5.0% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by our board of directors. In addition, pursuant to our ESPP, the number of shares of our common stock reserved for issuance will automatically increase on January 1 of each calendar year, beginning on January 1, 2023 (through January 1, 2032), by the lesser of (i) 1.0% of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of the automatic increase, and (ii) 1,210,000 shares; provided that before the date of any such increase, our board of directors may determine that such increase will be less than the amount set forth in clauses (i) and (ii). Unless our board of directors elects not to increase the number of shares available for future grant each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

General Risk Factors

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

As a public company, we incur significant and ongoing legal, accounting, and other expenses, particularly now that we are no longer an emerging growth company. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the SEC annual, quarterly, and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and the Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was

enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

Moreover, since we ceased to be an emerging growth company, we may no longer take advantage of certain exemptions from various reporting requirements that are applicable to public companies. This increase in reporting requirements will further increase our compliance burden. We expect to continue to incur substantial costs to comply with the rules and regulations applicable to public companies. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition, and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

Cyber-attacks or other failures in our telecommunications or IT systems, or those of our collaborators, CROs, third-party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations.

We, our collaborators, our CROs, third-party logistics providers, distributors and other contractors and consultants utilize IT systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including third parties gaining access to employee accounts using stolen or inferred credentials, computer malware, viruses, social engineering, spamming or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have generally been increasing in frequency and sophistication. Cyber-attacks also could include phishing attempts or e-mail fraud to, for example, cause payments or information to be transmitted to an unintended recipient. These threats pose a risk to the security of our, our collaborators', our CROs', third-party logistics providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems or to which they have access. Any cyber-attack, data breach, security incident or destruction, misuse, or loss of data could result in a violation of applicable U.S. and international privacy, data protection and other laws, and subject us to litigation and governmental investigations and proceedings by federal, state and local regulatory entities in the U.S. and by international regulatory entities, resulting in exposure to material civil and/or criminal liability. Further, our general liability insurance and corporate risk program may not cover all potential claims to which we are exposed and may not be adequate to indemnify us for all liability that maybe imposed and could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed, ongoing or future clinical trials for AMX0035 or any of our future product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches or incidents and may incur reputational harm and significant additional expense, including to implement further data protection or remedial measures, from fines and penalties or other liability, and from loss of existing and future business.

Our ability to use net operating losses and research and development credits to offset future taxable income may be subject to certain limitations.

As of December 31, 2023, we had U.S. federal net operating loss, or NOL, carryforwards of $69.8 million that carry forward indefinitely. The amount of annual utilization of these NOL carryforwards may be limited based on provisions of the Tax Cuts and Jobs Act of 2017, or TCJA. As of December 31, 2023, we also had U.S. federal research and development tax credit carryforwards of $6.8 million and we have additionally recorded deferred tax assets for U.S. state NOL and research and development tax credit carryforwards of $9.8 million. These U.S. federal research and development tax credit and U.S. state carryforwards could begin to expire if unused in 2042 and 2035, respectively. Utilization of all NOL and research and development tax credit carryforwards is conditioned upon us generating U.S. federal and state taxable income.

Ownership changes occurred in the years ended December 31, 2016 and 2023. In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the IRC, and corresponding provisions of state law, a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change NOL or tax credit carryforwards to offset future taxable income. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least five percent of a corporation's

stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the IRC. Our existing federal and state NOL and research and development tax credit carryforwards may be subject to limitations arising from these future ownership changes. Accordingly, we may not be able to utilize a material portion of these carryforwards. As described below, we maintain a full valuation allowance against all of our U.S. deferred tax assets. We may release all or a portion of the valuation allowance in the near-term; however, the release of the valuation allowance, as well as the exact timing and the amount of such release, continue to be subject to, among other things, our level of profitability, revenue growth, clinical program progression and expectations regarding future profitability.

We have been subject to securities class action litigation and could be subject to additional securities class action litigation in the future.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. Such litigation could result in substantial costs and a diversion of management's attention and resources, which could harm our business. For further information, see "Item 3. - Legal Proceedings."

Our failure to meet Nasdaq's continued listing requirements could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of the Nasdaq Global Select Market, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the minimum bid price requirement or prevent future non-compliance with the listing requirements of the Nasdaq Global Select Market.

If securities analysts publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock depends in part on the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who may cover us issues an adverse opinion about our company, our stock price would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Risk Management and Strategy

We recognize that cybersecurity threats have been increasing in number and severity in the general marketplace and in our industry. In an effort to address these threats, we maintain a cybersecurity risk management strategy that is designed to identify, assess, and manage cybersecurity risks to our business. Our cybersecurity risk management strategy includes various policies and components, including cybersecurity assessments, an incident response plan, evaluation of the security practices of our key vendors, and cybersecurity awareness training for our staff. We also leverage third-party technology and security tools and solutions, including alerting and monitoring tools, to support our cybersecurity program.

We engage a third-party to conduct a cybersecurity risk assessment on an annual basis, which is informed by the National Institute of Standards and Technology (NIST) Cybersecurity Framework. We have established a process for our IT security team to track and quantify known IT security risks and our remediation efforts through a cybersecurity risk register. The IT security team meets periodically to review and update the cybersecurity risk register based on feedback across the organization and the findings contained in our NIST-informed annual cybersecurity risk assessment. The IT security team reports on findings on at least an annual basis to the executive leadership team and the board of directors.

We have established a process to review and assess major software vendors' security practices prior to onboarding, which includes review of the vendors' responses to cybersecurity questionnaires and security audit reports and certifications, as applicable. Our process also includes contractual requirements for major vendors that process data on our behalf to maintain data protection safeguards.

We maintain a security awareness training program for employees, which is provided during onboarding. We also provide additional mandatory trainings, including phishing training, throughout the year.

We face a number of cybersecurity risks in connection with our business. Although such risks have not materially affected, and we do not believe they are reasonably likely to materially affect, our business strategy, results of operations or financial condition, to date, we have, from time to time, experienced threats to and security incidents related to our and our third-party vendors' information systems. For more information about the cybersecurity risks we face, see the risk factor entitled "Cyber-attacks or other failures in our telecommunications or IT systems, or those of our collaborators, CROs, third-party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations" in Item 1A- Risk Factors.

Governance of Cybersecurity Risks

Our board of directors is responsible for the general oversight of cybersecurity risks and is informed of key updates to our cybersecurity processes by our audit committee and relevant members of our executive leadership team on at least an annual basis.

Our audit committee and members of our executive leadership team meet with our Head of Global Information Technology on a quarterly basis, along with other members of our IT security team from time to time, to discuss cybersecurity matters, such as the emerging cybersecurity threat landscape, significant developments to our cybersecurity processes, and our cybersecurity risk assessments.

Our IT security team, led by the Head of Global Information Security, Governance and Architecture ("Head of Global ISGA"), is responsible for managing and directing the day-to-day information security strategy of the organization, including oversight of our cybersecurity tools, controls and strategies to protect organization assets, networks and data. The Head of Global ISGA reports to our Head of Global Information Technology. The Head of Global ISGA routinely reports on cybersecurity risks, projects, and initiatives to the Head of Global Information Technology, who regularly reports to executive management and the audit committee on these matters as described above.

The Head of Global ISGA maintains a Certified Information Systems Security Professionals, or CISSP, certification and has approximately two decades of IT security management experience. The IT security team is supported by external

vendors that provide managed services for network support, security operations and other IT areas as needed. Our IT security team also meets regularly with our Global Privacy Committee, which oversees our Enterprise Data Protection Program, to coordinate on cybersecurity initiatives and strategy related to protection of personal data.

Item 2. Properties.

Details of our principal properties as of December 31, 2023, are provided below:

Property Description	Location	Square Footage	Property Interest	Initial Lease Term End Date
Office space	Cambridge, Massachusetts	8,850	Leased	October 2026
Office space	Cambridge, Massachusetts	24,400	Leased	July 2025

We believe that our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

Item 3. Legal Proceedings.

On February 9, 2024, a putative class action lawsuit was filed in the U.S. District Court for the Southern District of New York against our Company and certain of our current and former officers (*Shih v. Amylyx Pharmaceuticals, Inc., et al.*, Case Number 1:24-CV-00988 (the "Shih Complaint")). The Shih Complaint asserts a claim against all defendants for alleged violations of Section 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder and a claim under Section 20(a) against certain current and former officers as alleged controlling persons. The Shih Complaint alleges that defendants made materially false and misleading statements related to the commercial results and prospects for RELYVRIO. The Shih Complaint seeks unspecified damages, interest, costs and attorneys' fees, and other unspecified relief that the court deems appropriate. The Company intends to defend against the Shih Complaint vigorously.

Item 4. Mine Safety Disclosures.

Not Applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock began trading on The Nasdaq Global Select Market on January 7, 2022, under the symbol "AMLX." Prior to that time, there was no public market for our common stock.

Holders of Record

As of February 12, 2024, we had approximately 21 holders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid a dividend on our common stock, and we do not anticipate declaring or paying dividends on our common stock in the foreseeable future. We currently intend to retain our future earnings, if any, to fund the development and growth of our business.

Securities Authorized for Issuance under Equity Compensation Plans

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

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

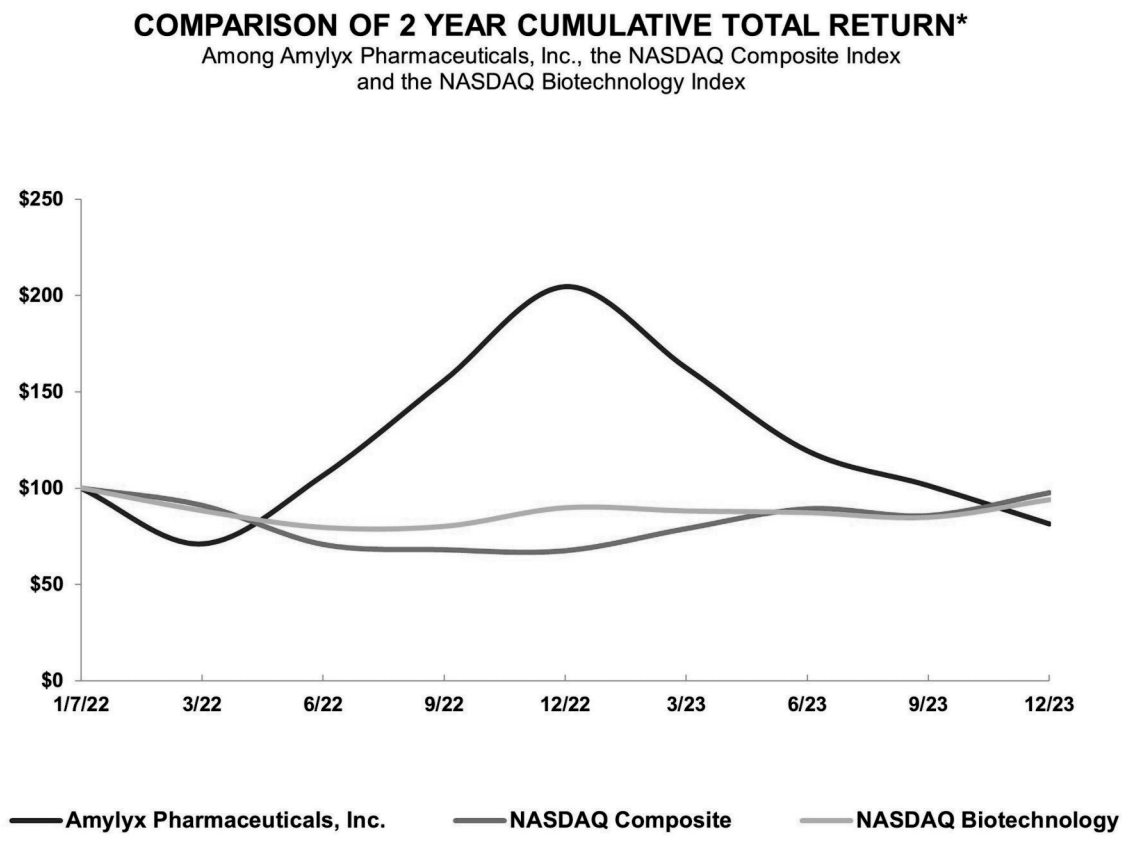
We did not purchase any of our registered equity during the period covered by this Annual Report.

Unregistered Sales of Securities

During the year ended December 31, 2023, we did not issue or sell any unregistered securities.

Stock Performance Graph

The following graph compares the performance of our Common Stock for the periods indicated with the performance of the Nasdaq Composite Index and the Nasdaq Biotechnology Index. This graph assumes an investment of $100 after the market closed on January 7, 2022 in our common stock and the Nasdaq Composite Index and the Nasdaq Biotechnology Index, and assumes reinvestment of dividends, if any. The stock price performance shown on the graph below is not necessarily indicative of future stock price performance. This graph is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any of our filings under the Securities Act, or the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



*$100 invested on 1/7/22 in stock or 12/31/21 in index, including reinvestment of dividends.
Fiscal year ending December 31.

Item 6. [Reserved]

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

The following information should be read in conjunction with the consolidated financial information and the notes thereto appearing elsewhere in this Annual Report.

This discussion and other parts of this Annual Report contain forward-looking statements that involve risks and uncertainties, such as statements of our plans, objectives, expectations and intentions. 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 the forward-looking statements contained in the following discussion and analysis.

Overview

Amylyx Pharmaceuticals, Inc. is a commercial-stage biotechnology company with a mission to end the suffering caused by neurodegenerative diseases. We have been working in ALS and neurodegenerative diseases for over a decade and have been making significant progress in transforming the treatment of these diseases.

Since our founding in 2013, we have transformed from a research-stage company focused on addressing the needs of patients suffering from neurodegenerative diseases to a commercial enterprise with development programs across several indications.

Our first commercial product, AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO], also known as RELYVRIO in the U.S. and ALBRIOZA in Canada) is the first and only ALS therapy of which we are aware that has been shown to slow disease progression, help maintain functional independence, and extend overall survival in the same clinical trial, with a generally well-tolerated side effect profile and oral administration. AMX0035 was commercially launched as RELYVRIO in the U.S. in October 2022 and commercially launched as ALBRIOZA in Canada in July 2022. Since the launch of RELYVRIO and ALBRIOZA through December 31, 2023, we have generated net product revenue of $403.0 million. We believe AMX0035 has the potential to become a widely-used ALS medication and provides an opportunity to transform ALS from a disease for which symptom management is the standard of care to a disease with meaningful interventions. In addition, we believe AMX0035 has the potential to be a foundational therapy for neurodegenerative diseases, meaning that it could be used alone or in conjunction with other therapies to change the treatment paradigm across a broad range of neurodegenerative diseases.

We are committed to bringing the benefits of AMX0035 to the more than 200,000 people living with ALS worldwide. We are building a global infrastructure to commercialize AMX0035 in additional jurisdictions where it may be approved and engaging with key stakeholders around the world to explore opportunities for access including the EU and Japan.

We continue to focus on the global PHOENIX Phase 3 clinical trial of AMX0035 for the treatment of ALS, a 48-week, randomized, double-blind, placebo-controlled trial at clinical sites in the U.S. and Europe, and expect to report topline results during or before the second quarter of 2024. If the data from PHOENIX are supportive, it will be the first time that two clinical trials have demonstrated a benefit in ALS. We believe that supportive PHOENIX data will further accelerate the commercial launch of AMX0035 and the transformation of the treatment of ALS.

In addition to ALS, we believe there is strong scientific rationale to use AMX0035 to treat other neurodegenerative diseases. AMX0035 was designed to slow or mitigate neurodegeneration by targeting ER stress and mitochondrial dysfunction, two connected central pathways that lead to neurodegeneration. We believe that our proprietary combination of PB and TURSO and their respective mechanisms of action will allow us to synergistically target abnormal cell death to better prevent neurodegeneration than treatment targeted at either mechanism of action alone. We are actively advancing clinical trials to evaluate AMX0035 in PSP and WS.

Since inception, we have devoted substantially all of our efforts to research and development, pre-commercialization and commercialization activities, including recruiting management and technical staff, raising capital, producing materials for preclinical studies and clinical trials, and building infrastructure to support such activities. As of December 31, 2023, we have funded our operations primarily through public offerings of our common stock, private sales of preferred stock, convertible notes, and more recently through revenue from sales of RELYVRIO and ALBRIOZA in the U.S. and Canada, respectively.

Prior to 2023, we had incurred operating losses and as of December 31, 2023, we had an accumulated deficit of $304.9 million. These losses resulted primarily from costs incurred in connection with research and development activities

and selling, general and administrative costs associated with our operations. We expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution of our approved products. We may incur significant losses and our financial results will be highly dependent upon our successful commercialization of RELYVRIO in the U.S. We will continue to incur significant expenses as we advance AMX0035 and any other current or future product candidates through preclinical and clinical development, set up and initiate additional trials, hire additional clinical, scientific, management and administrative personnel, seek regulatory approval and pursue commercialization of any approved product candidates. To date, we have primarily developed AMX0035 and AMX0114 internally, with assistance from our network of CROs and other advisors. This has resulted in increased research and development spending but has enabled us to manage AMX0035 and AMX0114 efficiently through the development and manufacturing process.

We also expect to continue to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses. As a result, we may need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate sufficient revenue from product sales to sustain profitability, we expect to finance our operations through the sale of equity, debt financings or other capital sources, including potential collaborations with other companies, royalty financings, or other strategic transactions. Our inability to raise capital as and when needed could have a negative impact on our financial condition and ability to pursue our business strategies. There can be no assurances that our current operating plan will be achieved or that additional funding, if required, will be available on terms acceptable to us, or at all.

As of December 31, 2023, we had cash, cash equivalents and short-term investments of $371.4 million. We believe that the revenue we generate from commercial sales of AMX0035 in the U.S. and Canada and our existing cash, cash equivalents and short-term investments as of December 31, 2023, will be sufficient to meet our anticipated operating and capital expenditure requirements for at least one year from the date of this Annual Report. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

Impact of Macroeconomic Factors

The development of AMX0035 and any future product candidates could be disrupted and materially adversely affected in the future by any pandemic or calamity. In addition, economic uncertainty in various global markets, including in the U.S., Europe and the Middle East, caused by political instability and conflict, such as the ongoing conflicts in Ukraine and Israel, and economic challenges caused by global pandemics or other public health events, have led to market disruptions, including significant volatility in commodity prices, credit and capital market instability and supply chain interruptions, which have caused record inflation globally. Our business, financial condition and results of operations could be materially and adversely affected by further negative impact on the global economy and capital markets resulting from these global economic conditions, particularly if such conditions are prolonged or worsen.

Although, to date, our business has not been materially impacted by these global economic and geopolitical conditions, it is impossible to predict the extent to which our operations will be impacted in the short and long term, or the ways in which such instability could impact our business and results of operations. The extent and duration of these market disruptions, whether as a result of the military conflict between Russia and Ukraine and effects of the Russian sanctions, the conflict in Israel, geopolitical tensions, record inflation or otherwise, are impossible to predict, but could be substantial. Any such disruptions may also magnify the impact of other risks described in this report.

For additional information on the various risks posed by the global economic uncertainty, please read the section entitled “Risk Factors” in this Annual Report.

Components of Our Results of Operations

Product Revenue, Net

In June 2022, AMX0035 received marketing authorization with conditions as ALBRIOZA by Health Canada for the treatment of ALS, and we began commercially selling ALBRIOZA within Canada in July 2022. In September 2022, AMX0035 received regulatory approval as RELYVRIO by the FDA for the treatment of ALS, and we launched RELYVRIO in the U.S. in October 2022. Product revenue, net recognized during the period relates primarily to units of ALBRIOZA and RELYVRIO sold in Canada and the U.S., respectively.

Operating Expenses

Cost of Sales

Cost of sales consists primarily of costs associated with the manufacturing of RELYVRIO, ALBRIOZA and certain period costs, which include:

- Direct materials costs;
- Drug product manufacturing costs;
- Packaging services;
- Transportation costs;
- Manufacturing overhead costs; and
- Royalties related to grants provided to us for the purpose of furthering the research and development of AMX0035 as a therapeutic benefit for ALS and AD. For additional information refer to Note 18 to our consolidated financial statements appearing at the end of this Annual Report.

As a result of global macroeconomic conditions, we may experience some disruption and volatility in our global supply chain network, and we may in the future experience disruptions in availability and delays in shipments of raw materials and packaging, as well as related cost inflation.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred in connection with the research and development of AMX0035. We expense research and development costs as incurred. These expenses include:

- expenses incurred under agreements with CROs, contract manufacturing organizations, or CMOs, as well as investigative sites and consultants that conduct our clinical trials, preclinical studies and other scientific development services;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing drug product for our preclinical studies and clinical trials, including manufacturing registration and validation batches, as well as pre-commercial manufacturing activities;
- expenses to acquire technologies to be used in research and development;
- employee-related expenses, including salaries, payroll taxes, related benefits and stock-based compensation expense for employees engaged in research and development functions; and
- costs related to compliance with quality and regulatory requirements.

Advance payments that we make for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered.

Certain of our indirect research and development expenses are not tracked on an indication-by-indication basis for AMX0035. We do not allocate employee costs and facilities, including depreciation or other indirect costs, to specific indications because these costs are deployed across multiple indications and, as such, are not separately classified. We use internal resources to oversee the research and discovery as well as to manage our preclinical development, process development, manufacturing and clinical development activities. These employees work across multiple indications and, therefore, we do not track their costs by indication.

Research and development activities are central to our business model. Product candidates such as AMX0035 in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, such as AMX0114, primarily due to the increased size and duration of later-stage clinical trials and related product manufacturing expenses. We expect that our research and development expenses will continue to increase in connection with our planned clinical development activities in the near term and in the future and to fund commercialization activities in the U.S., Canada and any other jurisdictions in which AMX0035 is approved. At this time, we cannot accurately

estimate or know the nature, timing and costs of the efforts that will be necessary to complete the clinical development of AMX0035 and any future product candidates. Our clinical development costs may vary significantly based on factors such as:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses that patients receive;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up periods;
- the cost and timing of manufacturing our current or future product candidates;
- the phase of development of our current or future product candidates;
- the efficacy and safety profile from clinical trials and preclinical studies of our current or future product candidates; and
- the number of product candidates we are developing.

The successful development and commercialization of AMX0035 and any other current or future product candidates is highly uncertain, due to the numerous risks and uncertainties associated with product development and commercialization, including the following:

- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical trials for separate indications we decide to pursue;
- raising additional funds, if necessary;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current development activities and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to Health Canada, the FDA or the EMA, or any other comparable foreign regulatory authority;
- the successful implementation and compliance with the terms of regulatory approvals from applicable regulatory authorities, including our marketing authorization with conditions from Health Canada for ALBRIOZA and the post-marketing requirements from the FDA for RELYVRIO;
- the successful receipt and related terms of regulatory approval for AMX0035 for the treatment of ALS, if approved in the future by the European Commission;
- the availability of drug substance and drug product for use in production of AMX0035;
- establishing and maintaining agreements with third-party manufacturers for clinical supply for our clinical trials and commercial manufacturing;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the U.S. and internationally;
- our ability to protect our rights in our intellectual property portfolio;

- the successful commercialization of ALBRIOZA in Canada and RELYVRIO in the U.S. of AMX0035 in other potential jurisdictions, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of our products and product candidates, if approved, by patients, the medical community and third-party payors;
- competition with other product; and
- a continued acceptable safety profile of our therapies in pre-approval market access programs or in commercial access following approval.

A change in the outcome of any of these variables with respect to the development of AMX0035 or any future product candidates could have a significant impact on the cost and timing associated with the development of our product candidates. We may never succeed in obtaining or maintaining, as applicable, regulatory approval for AMX0035 or any future product candidates.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of salaries and related costs for personnel in executive, finance, sales, marketing, as well as administrative functions. Selling, general and administrative expenses also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax and administrative consulting services; corporate insurance costs; administrative travel expenses; sales and marketing expenses; information technology; charitable donations to independent charitable foundations; facility-related and other operating costs. We anticipate that our selling, general and administrative expenses will continue to increase in the future as we further increase our headcount to support our continued research activities and development of AMX0035 and as we commercialize AMX0035. We also anticipate that we will continue to incur increased accounting, audit, legal, regulatory, compliance, and director and officer insurance costs as well as investor and public relations expenses associated with being a public company. We have received marketing authorization with conditions for ALBRIOZA for the treatment of ALS in Canada and marketing authorization for RELYVRIO for the treatment of ALS in adults in the U.S.

Other Income, Net

Interest Income

Interest income consists primarily of the amortization of premiums and accretion of discounts on our short-term investments, and interest income earned on our cash, cash equivalents and short-term investments.

Other Expense, Net

Other expense, net consists primarily of net realized and unrealized losses on foreign exchange transactions.

Income Taxes

Income taxes are determined using the asset and liability approach. Deferred tax assets and liabilities represent future tax consequences of temporary differences between the financial statement carrying amounts and the tax basis of assets and liabilities and for tax attribute carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. Realization of our deferred tax assets is dependent upon the generation of future taxable income, the amount and timing of which are uncertain. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. During 2023, a portion of our valuation allowance has been reversed with respect to amounts we realized through current year U.S. federal and state taxable income. We continue to maintain a full valuation allowance against all of our U.S. deferred tax assets as of December 31, 2023 based on management's evaluation of all available evidence, including our history of incurring significant losses from operations. Our evaluation of all available evidence also includes consideration of regulatory approvals of and developments related to ALBRIOZA and RELYVRIO, including actual and forecasted revenues generated from the sale of these products. Given the early stage of our product commercialization, we are uncertain about the timing and amount of future sales. We may release all or a portion of the remaining valuation allowance in the near-term; however, the release of the valuation allowance, as well as the exact timing and the amount of such release, continue to be subject to,

among other things, our level of profitability, revenue growth, clinical program progression and expectations regarding future profitability.

As of December 31, 2023 and 2022, we had NOL carryforwards of approximately $69.8 million and $203.2 million, respectively, and state NOL carryforwards of approximately $124.6 million and $164.1 million, respectively, which are available to reduce future taxable income. All U.S. federal NOL carryforwards as of December 31, 2023 carry forward indefinitely. Of the $124.6 million state net operating loss carryforwards, $82.8 million relate to Massachusetts and begin to expire in 2035. As of December 31, 2023 and 2022, we also had federal tax credits of $6.8 million and $4.6 million, respectively, and state tax credits of $1.6 million and $1.2 million, respectively. The tax credit carryforwards will expire at various dates beginning in 2035.

Results of Operations

Comparison of the Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations for the years ended December 31, 2023 and 2022:

	Year Ended December 31,			
	2023	2022	$ Change	% Change
		(in thousands)		
Product revenue, net	$ 380,786	$ 22,230	$ 358,556	1613%
Operating expenses:				
Cost of sales	25,441	2,993	22,448	750%
Research and development	128,187	93,450	34,737	37%
Selling, general and administrative	188,356	127,128	61,228	48%
Total operating expenses	341,984	223,571	118,413	53%
Income (loss) from operations	38,802	(201,341)	240,143	(119)%
Other income, net:				
Interest income	16,155	4,291	11,864	276%
Other expense, net	(660)	(551)	(109)	20%
Total other income, net	15,495	3,740	11,755	314%
Income (loss) before income taxes	54,297	(197,601)	251,898	-127%
Provision for income taxes	5,026	774	4,252	549%
Net income (loss)	$ 49,271	$ (198,375)	$ 247,646	(125)%

* NM - not meaningful

Product revenue, net

We began commercially selling ALBRIOZA within Canada in July 2022 and RELYVRIO within the U.S. in October 2022. For the years ended December 31, 2023 and 2022, we recorded approximately $380.8 million and $22.2 million of product revenue, net, respectively. The increase is primarily related to RELYVRIO and ALBRIOZA being sold for the entirety of 2023 compared to the majority being sold in the fourth quarter in 2022. For further discussion regarding our revenue recognition policy, see Note 2, Summary of Significant Accounting Policies, in the Notes to the consolidated financial statements included this Annual Report.

Cost of sales

Cost of sales were $25.4 million for the year ended December 31, 2023, compared to $3.0 million for the year ended December 31, 2022. During these periods, cost of sales consisted of costs to procure, manufacture and distribute our marketed products, RELYVRIO and ALBRIOZA. In addition, included in cost of sales are costs to manufacture our marketed products, which have been provided to certain patients at no cost to them through either our interim access or patient assistance programs. Drug product given to patients at no cost to them is not included in product revenue, net. Based on our policy to expense costs associated with the manufacture of our products prior to regulatory approval, certain of the costs of units recognized as revenue during the years ended December 31, 2023 and 2022, or approximately $11.2 million and $3.4 million, respectively, were expensed prior to obtaining regulatory approvals and, therefore, are not included in cost of sales during these periods. We expect cost of sales to increase and gross margin to decrease as we deplete these inventories. We expect to use the remaining pre-commercialization inventory for product sales in the second quarter of 2024.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2023 and 2022:

	Year Ended December 31,			
	2023	2022	$ Change	% Change
	(in thousands)			
AMX0035 – ALS	$ 64,987	$ 60,649	$ 4,338	7%
AMX0035 – PSP	5,495	93	5,402	5,809%
Payroll and personnel-related	44,734	28,501	16,233	57%
Other	12,971	4,207	8,764	208%
	$ 128,187	$ 93,450	$ 34,737	37%

Research and development expenses were $128.2 million for the year ended December 31, 2023, compared to $93.5 million for the year ended December 31, 2022. During these periods, most of our research and development expenses were related to the development and clinical trials of AMX0035. The increase of $34.7 million was primarily due to a $16.2 million increase in payroll and personnel-related costs, which includes a $4.2 million increase in stock-based compensation, a $5.4 million increase in spending on AMX0035 for the treatment of PSP, a $4.3 million increase in spending on AMX0035 for the treatment of ALS and a $8.8 million increase in all other costs. The increase in payroll and personnel-related costs was primarily due to an increase in the number of employees supporting research and development efforts. The increase in spending on AMX0035 for the treatment of PSP was primarily related to costs to support the initiation of the ORION Phase 3 trial. The increase in spending on AMX0035 for ALS was primarily related to costs associated with our global Phase 3 PHOENIX trial, including its open label extension phase and the increase in other costs were primarily due to an increase in preclinical development activities. We expect to increase research and development for AMX0035 in other indications in future periods.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $188.4 million for the year ended December 31, 2023 compared to $127.1 million for the year ended December 31, 2022. The increase of $61.2 million was primarily due to increases of $30.2 million in payroll and personnel-related costs, which includes an $11.2 million increase in stock-based compensation, $16.1 million in consulting and professional services and $14.9 million in other expenses. The increase in payroll and personnel-related costs was primarily due to hiring additional personnel in commercial and general and administrative functions to support our growth, as well as commercialization preparation initiatives in the EU. The increases in consulting and professional services and other expenses were primarily due to an increase in spending for commercial activities, operations as a public company, and other expenses.

Other Income, Net

Interest Income

Interest income for the year ended December 31, 2023 was $16.2 million compared to $4.3 million for the year ended December 31, 2022. The increase was primarily attributable to favorable interest rates and higher short-term investment and cash equivalent balances driven by the proceeds received from our 2022 follow-on offering and cash receipts from sales of AMX0035.

Provision for Income Taxes

We recorded an income tax provision of $5.0 million and $0.8 million for the years ended December 31, 2023 and 2022, respectively. The income tax provision for the year ending December 31, 2023 includes the release of a portion of our valuation allowance with respect to amounts expected to be realized through current year U.S. federal and state taxable income. Current year U.S. federal and state taxable income is significantly impacted by a TCJA tax law change in effect from January 1, 2022 that requires capitalization and amortization of all research and experimentation costs under Section 174 of the IRC.

Liquidity and Capital Resources

Sources of Liquidity

In the second half of 2022, we began generating revenue from the sale of our approved drug product RELYVRIO, known as ALBRIOZA in Canada. To date, we have financed our operations primarily through revenue from the sale of our approved products, the sale and issuance of common stock, convertible preferred stock and convertible notes. As of December 31, 2023, we had cash, cash equivalents and short-term investments of $371.4 million.

From inception through December 31, 2023, we have raised $669.3 million in aggregate proceeds, net of issuance costs, primarily from the issuance of common stock, convertible preferred stock, convertible notes and grant agreements. Based on our current operational plans and assumptions, we believe that the revenue we generate from commercial sales of AMX0035 in the U.S. and Canada and our existing cash, cash equivalents, and short-term investments, will be sufficient to meet our anticipated operating and capital expenditure requirements for at least twelve months after the date of the filing of this Annual Report. We have based these estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect.

Capital Resources

We expect our expenses to increase in connection with our ongoing activities, particularly as we advance the preclinical activities, manufacturing and clinical trials of AMX0035 and any other current or future product candidates, execute on our commercialization plans for ALBRIOZA in Canada and RELYVRIO in the U.S., and prepare for the commercial launch of AMX0035 in other jurisdictions, if approved. In addition, we expect to incur additional costs associated with operating as a public company, including significant legal, accounting, investor relations and other expenses. Because we no longer qualify as an emerging growth company as defined in the JOBS Act and we are now considered a large accelerated filer, we are no longer entitled to rely on exemptions from certain compliance requirements that are applicable to companies that are emerging growth companies including, among other requirements, the auditor attestation requirements of Section 404(b) and reduced reporting requirements. Our expenses will also increase as we:

- continue our research and development efforts, including our ongoing Phase 3 trial of AMX0035 in PSP and our ongoing Phase 2 trial of AMX0035 for the treatment of WS;
- continue to develop AMX0114, antisense oligonucleotide, for the treatment of people living ALS;
- continue to commercialize AMX0035 (also known as ALBRIOZA in Canada and RELYVRIO in the U.S.) for the treatment of ALS in Canada and the U.S., and pursue launch of AMX0035 in other jurisdictions, if approved;
- pursue INDs of AMX0035 for additional indications;
- conduct preclinical studies and clinical trials for AMX0035 for additional indications and for potential future product candidates;
- seek to identify and develop, acquire or in-license additional product candidates;
- experience any delays or encounter any issues with any of the above, including but not limited to failed studies, complex results, safety issues, or other regulatory challenges;
- develop the necessary processes, controls and manufacturing data to obtain additional marketing approval for AMX0035 or approval for any future product candidates and to support manufacturing on a commercial scale;
- seek additional regulatory approvals for AMX0035 or approvals for any future product candidates that successfully complete clinical trials, if any;
- hire and retain additional personnel, such as preclinical, clinical, quality assurance, regulatory affairs, manufacturing, distribution, legal, compliance, finance, general and administrative, commercial and scientific personnel; and
- develop, maintain, expand and protect our intellectual property portfolio.

Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates and programs, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on and could increase significantly as a result of many factors, including:

- the scope, progress, results and costs of drug discovery, laboratory testing, preclinical and clinical development for AMX0035 and any future product candidates;
- the costs, timing and outcome of commercialization activities, including manufacturing, marketing, sales and distribution for AMX0035 in the U.S. and Canada, and, if approved, in the EU and other territories or for any future product candidates for which we receive regulatory approval;
- the costs, timing and outcome of regulatory review of AMX0035 and any future product candidates;
- our ability to establish and maintain collaborations, marketing, distribution and license agreements on favorable terms, if at all;
- our ability to enroll clinical trials in a timely manner and to quickly resolve any delays or clinical holds that may be imposed on our development activities;
- timing delays with respect to preclinical and clinical development of AMX0035 and any future product candidates, including as result of any future outbreak of any highly infectious or contagious diseases;
- the costs of expanding our facilities to accommodate our expected growth in personnel, and the costs of such additional personnel;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- the extent to which we acquire technologies or other assets;
- the sales price and availability of adequate third-party coverage and reimbursement for AMX0035 and any future product candidates, if and when approved; and
- the costs of operating as a public company.

Until such time, if ever, that we can generate product revenue sufficient to sustain profitability, we may finance our cash needs through equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, current ownership interests will be diluted. If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. In addition, debt financing, if available, may result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Cash Flows

Comparison of the Years Ended December 31, 2023 and 2022

The following table summarizes our sources and uses of cash for the years ended December 31, 2023 and 2022:

	Year Ended December 31,			
	2023	2022	$ Change	% Change
		(in thousands)		
Net cash provided by (used in) operating activities	$ 11,919	$ (179,871)	$ 191,790	(107)%
Net cash provided by (used in) investing activities	92,053	(238,988)	331,041	(139)%
Net cash provided by financing activities	3,543	431,789	(428,246)	(99)%
Effect of exchange rate changes on cash, cash equivalents and restricted cash equivalents	160	(65)	225	(346)%
Net increase in cash, cash equivalents and restricted cash equivalents	$ 107,675	$ 12,865	$ 94,810	737%

Operating Activities

During the year ended December 31, 2023, operating activities provided $11.9 million of cash, primarily resulting from our net income of $49.3 million, non-cash stock-based compensation expense of $37.2 million and $1.1 million of depreciation expense, offset by an increase of $65.7 million in net cash used in our operating assets and liabilities and net amortization of premiums and discounts on investments of $9.9 million.

Net cash used in our operating assets and liabilities primarily consisted of a $21.6 million increase in accrued expenses, a $15.9 million increase in accounts payable and a $1.8 million decrease in operating lease right-of-use assets. This was offset by a $73.1 million increase in inventories, a $24.7 million increase in accounts receivable, a $4.8 million increase in prepaid expenses and other current assets and a $2.0 million decrease in operating lease liabilities.

During the year ended December 31, 2022, operating activities used $179.9 million of cash, primarily resulting from our net loss of $198.4 million and net amortization of premiums and discounts on investments of $2.1 million, offset by $21.7 million of non-cash stock-based compensation expense, $0.5 million of depreciation expense and a $1.6 million increase in net cash used in our operating assets and liabilities.

Net cash used in our operating assets and liabilities primarily consisted of a $26.1 million increase in accrued expenses and deferred rent due to increased spending for external research and development to support our growth, a $1.9 million increase in accounts payable and a $0.5 million decrease in interest receivable from short-term investments. This was offset by a $15.3 million increase in accounts receivable, a $9.8 million increase in inventories, a $0.5 million increase in other assets and a $5.2 million increase in prepaid expenses and other current assets.

Investing Activities

During the year ended December 31, 2023, net cash provided by investing activities was $92.1 million resulting from $394.1 million of investments matured during the period offset by $300.8 million in purchases of short-term investments and $1.2 million in purchases of property and equipment.

During the year ended December 31, 2022, net cash used in investing activities was $239.0 million, resulting from $2.5 million in purchases of property and equipment and $415.9 million in purchases of short-term investments, offset by $179.4 million of investments matured during the period.

Financing Activities

During the year ended December 31, 2023, net cash provided by financing activities was $3.5 million. This amount consisted of $7.0 million of proceeds from exercises of stock options, offset by $3.3 million of withholding taxes paid on stock-based awards and $0.1 million in payments of deferred offering costs.

During the year ended December 31, 2022, net cash provided by financing activities was $431.8 million. This amount consisted of $200.9 million of proceeds from our initial public offering, or IPO, net of underwriter's discounts and commissions, $231.6 million of proceeds from our 2022 follow-on offering, net of underwriter's discounts and commissions, and $2.2 million of proceeds from exercises of stock options, offset by $2.8 million in payments of deferred offering costs.

*Purchase Commitment*s

We enter into agreements in the normal course of business with contract manufacturing organizations for raw material purchases and manufacturing services. As of December 31, 2023, we had committed approximately $195.0 million under these agreements related to raw material purchases and manufacturing services, which are expected to be paid through 2028.

Critical Accounting Policies and Significant Judgments and Estimates

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

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

Revenue Recognition

Our accounting policy for revenue recognition has a substantial impact on reported results and relies on certain estimates. Revenue is recognized following a five-step model under ASC Topic 606 - *Revenue from Contracts with Customers*, or Topic 606. Revenue is also reduced by variable consideration related to certain gross-to-net, or GTN, adjustments discussed below. These GTN adjustments involve significant estimates and judgment after considering historical experience, payer channel mix (e.g., Medicare or Medicaid), current contract prices under applicable programs, unbilled claims and processing time lags and inventory levels in the distribution channel. Estimates are assessed each period and adjusted as required to revise information or actual experience. In accordance with Topic 606, we recognize revenue on product sales when the customer obtains control of our product, which occurs at a point in time (upon delivery). Product revenues are recorded net of applicable GTN adjustments, including discounts and allowances. Payment from customers is typically due within 30 calendar days of the invoice date.

We will adjust our GTN estimates based on new information, including information regarding actual activity, as it becomes available. To date, actual GTN activity has not differed materially from our estimates. The following categories of GTN adjustments involve significant estimates, judgments and information obtained from external sources.

Provider Chargebacks and Discounts

We participate in programs with government entities such as the U.S. Department of Veterans Affairs, and other parties, including covered entities under the 340B Drug Pricing Program, whereby pricing on products is extended below wholesaler list price to participating entities. These entities purchase products through wholesalers at the lower program price and the wholesalers then charge us the difference between their acquisition cost and the lower program price. Product revenue and accounts receivable is reduced for the estimated amount of unprocessed charge-back claims attributable to a sale.

Customers are offered cash discounts as an incentive for prompt payment. Product revenue and accounts receivable is reduced for the estimated amount of cash discount at the time of sale and the discount is typically taken by the customer

within one month.

Payor rebates

We participate in state government Medicaid programs and other qualifying Federal and state government programs requiring discounts and rebates to participating state and local government entities. All discounts and rebates provided through these programs are included in our Medicaid rebate accrual. Our rebate accrual calculations require us to estimate the magnitude of our revenue that will be subject to these rebates. Our rebate accruals are recorded in the same period in which the related revenue is recognized, resulting in a reduction of product revenue. The estimated amount of unpaid or unbilled rebates is presented as a liability.

Rebates and discounts are offered to managed healthcare organizations in the U.S. managing prescription drug programs and Medicare Advantage prescription drug plans covering the Medicare Part D drug benefit. The estimated amount of unpaid or unbilled rebates and discounts is presented as a liability.

Other incentives, returns, discounts and adjustments

Other GTN adjustments include incentives which we offer and includes voluntary patient assistance programs, such as our co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with the product that has been recognized as revenue for each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

Estimated product returns for established products are determined using quantitative and qualitative information including, but not limited to, expected experience with returns, projected demand, levels of inventory in the distribution channel, product dating and expiration period, and whether products have been discontinued, among others. The Company has received an immaterial amount of returns to date and believe that returns of product in future periods will be minimal.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make estimates of our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments if necessary.

The estimate of accrued research and development expense is dependent, in part, upon the receipt of timely and accurate reporting from CROs, CMOs and other third-party service providers. Examples of estimated accrued research and development expenses include fees paid to:

- vendors in connection with preclinical development activities;
- CROs and investigative sites in connection with preclinical studies and clinical trials; and
- CMOs in connection with drug substance and drug product formulation of preclinical study and clinical trial materials.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CMOs and CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. 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.

Income Taxes

We account for income taxes using the asset and liability approach. Deferred tax assets and liabilities represent future tax consequences of temporary differences between the financial statement carrying amounts and the tax basis of assets and liabilities and for tax attribute carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. Realization of our deferred tax assets is dependent upon the generation of future taxable income, the amount and timing of which are uncertain. Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. As of December 31, 2023, we continued to maintain a full valuation allowance against all of our U.S. federal and state deferred tax assets based on management's evaluation of all available evidence, including our history of incurring significant losses from operations. Our evaluation of all available evidence also includes consideration of revenue generated from the sale of ALBRIOZA and RELYVRIO in 2023. Given the early stage of our product launch, we are uncertain about the timing and amount of future sales that would result in sustained profitability that provides sufficient positive objective evidence of the recoverability of our deferred tax assets. We may release all or a portion of the valuation allowance in the near-term; however, the release of the valuation allowance, as well as the exact timing and the amount of such release, continue to be subject to, among other things, our level of profitability, revenue growth, clinical program progression and expectations regarding future profitability. We may become subject to income tax audits and adjustments by local tax authorities. The nature of uncertain tax positions is subject to significant judgment by management and subject to change, which may be substantial. We develop our assessment of uncertain tax positions, and the associated cumulative probabilities, using internal expertise and assistance from third-party experts. As additional information becomes available, estimates are revised and refined. Differences between estimates and final settlement may occur resulting in additional tax expense.

Inventory Valuation

We value our inventories at the lower of cost or estimated net realizable value. We determine the cost of our inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. We classify inventory as long-term when consumption or sale of the inventory is expected beyond twelve months. We perform an assessment of the recoverability of capitalized inventory during each reporting period, and we write down any excess and obsolete inventories to their estimated net realizable value in the period in which impairment is first identified. Such impairment charges, should they occur, are recorded within cost of sales. The determination of whether inventory costs will be realizable requires estimates by management such as the future demand of our products, estimated future sales, the remaining shelf life of goods on hand, and our current and future strategic plans.

If actual demand for our product declines, or if actual market conditions are less favorable than those projected by management, additional write-downs of inventory may be required which would be recorded as cost of sales in the consolidated statements of operations. Additionally, our product is subject to strict quality control and monitoring that we perform throughout the manufacturing process. In the event that certain batches or units of product do not meet quality specifications, we will record a charge to cost of sales, to write down any unmarketable inventory to its estimated net realizable value.

Although we believe that the assumptions we use in estimating inventory write-downs are reasonable, no assurance can be given that significant future changes in these assumptions or changes in future events and market conditions could result in different estimates.

Recently Issued Accounting Pronouncements

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

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

Market risk is the potential loss that may result from market changes associated with our business or with an existing or forecasted financial transactions. We are exposed to various market risks in the ordinary course of our business which are discussed below.

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2023, we had cash, cash equivalents and short-term investments of $371.4 million. Our cash equivalents are invested primarily in bank deposits and money market mutual funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Our investments are subject to interest rate risk and could fall in value if market interest rates increase. Due to the duration of our investment portfolio and the low risk profile of our investments, we do not believe an immediate 100 basis point change in interest rates would have a material effect on the fair market value of our portfolio. We have the ability to hold our investments until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

Foreign Currency and Currency Translation Risk

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with vendors that are located outside of the U.S. As a result, our operations may be subject to fluctuations in foreign currency exchange rates in the future. In addition, we translate the assets and liabilities of our foreign subsidiaries from their respective functional currencies to U.S. dollars at the appropriate rates as of the balance sheet date. Changes in the carrying value of these assets and liabilities attributable to fluctuations in rates are included in accumulated other comprehensive income (loss) on our consolidated balance sheets. Income statement accounts are translated using the monthly average exchange rates during the year.

Inflation Risk

We do not believe that inflation had a material effect on our business, financial condition, or results of operations during the twelve months ended December 31, 2023 and 2022. However, inflation has had, and may continue to have, an impact on the labor costs we incur to attract and retain qualified personnel.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the reports of our independent registered public accounting firms, appear beginning on page F-1 of this Annual Report.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, are designed to ensure that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure.

Our management, with the participation of our principal executive officers and our principal financial officer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2023. Based on the evaluation of

our disclosure controls and procedures as of December 31, 2023, our Chief Executive Officers and Chief Financial Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

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) under the Exchange Act. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting include policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect transactions relating to our business and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. GAAP, and that receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on the financial statements.

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

Under the supervision and with the participation of the Company's Chief Executive Officers and the Company's Chief Financial Officer, we assessed the effectiveness of our internal control over financial reporting based on the criteria for effective internal control over financial reporting under the 2013 "Internal Control—Integrated Framework", issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO. Based on such assessment, our management concluded that we maintained effective internal control over financial reporting as of December 31, 2023.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the year ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Amylyx Pharmaceuticals, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of Amylyx Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2023, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2023, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2023, of the Company and our report dated February 22, 2024, expressed an unqualified opinion on those financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

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

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

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 22, 2024

Item 9B. Other Information.

During the three months ended December 31, 2023, the following officers or directors of the Company (as defined in Rule 16a-1(f)) adopted the following trading plans for the sale of our common stock pursuant to the terms of the applicable plan; such plans are intended to satisfy the affirmative defense conditions of Rule 10b5–1(c)(1) of the Exchange Act:

- Joshua Cohen, our Co-Chief Executive Officer and a member of our board of directors, adopted a new Rule 10b5-1 trading plan on December 15, 2023, which is scheduled to expire on November 30, 2024. The aggregate number of shares of our common stock authorized to be sold under this new arrangement is 60,000;
- Justin Klee, our Co-Chief Executive Officer and a member of our board of directors, adopted a new Rule 10b5-1 trading plan on December 15, 2023, which is scheduled to expire on November 30, 2024. The aggregate number of shares of our common stock authorized to be sold under this new arrangement is 60,000.
- James Frates, our Chief Financial Officer, adopted a new Rule 10b5-1 trading plan on December 14, 2023, which is scheduled to expire on December 1, 2024. The aggregate number of shares of our common stock authorized to be sold under this new arrangement is 90,000.
- Gina M. Mazzariello, our Chief Legal Officer and General Counsel, adopted a new Rule 10b5-1 trading plan on December 14, 2023, which is scheduled to expire on March 8, 2025. The aggregate number of shares of our common stock authorized to be sold under this new arrangement is 76,290, which includes shares that may be withheld or sold to cover withholding taxes at the time of vesting.

No other director or officer has adopted or terminated any non-Rule 10b5-1 trading arrangements during the quarter ended December 31, 2023.

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included in the Proposal No. 1, Corporate Governance and Executive Officers section of our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in the Executive Compensation and Director Compensation sections (excluding the information under the heading "Pay Versus Performance") of our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in the Security Ownership of Certain Beneficial Owners and Management sections of our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in the Certain Relationships and Related Party Transactions and Corporate Governance sections of our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services.

Our independent public accounting firm is Deloitte & Touche LLP, Boston, Massachusetts, PCAOB Auditor ID: 34.

The information required by this Item 14 will be included in the Proposal No. 2 section of our definitive proxy statement to be filed with the SEC with respect to our 2024 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

a) Financial Statements

For a list of the consolidated financial statements included herein, see Index to the Consolidated Financial Statements on page F-1 of this Annual Report, which is incorporated into this Item by reference.

b) Exhibits

Exhibit Number	Description
3.1	Fourth Amended and Restated Certificate of Incorporation of Amylyx Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on January 11, 2022).
3.2	Second Amended and Restated Bylaws of Amylyx Pharmaceuticals, Inc. (Incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on January 11, 2022).
4.1	Specimen Common Stock Certificate (Incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
4.2	Second Amended and Restated Investors' Rights Agreement, dated as of July 1, 2021, among the Registrant and the parties thereto (Incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 (File No. 333-261703) filed with the Securities and Exchange Commission on December 16, 2021).
4.3	Description of Securities (Incorporated by reference to Exhibit 4.3 to the Registrant's Form 10-K filed with the Securities and Exchange Commission on March 31, 2022).
10.1#	2015 Stock Option and Incentive Plan, and form of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.2#	2022 Stock Option and Incentive Plan, and form of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.3#	Non-Employee Director Compensation Policy (Incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on March 21, 2023).
10.4#	Executive Cash Incentive Bonus Plan (Incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.5#	2022 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.3 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.6#	Lease Agreement, dated as of October 23, 2018, as amended, by and between the Registrant and Bullfinch Square Limited Partnership (Incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-1 (File No. 333-261703) filed with the Securities and Exchange Commission on December 16, 2021).
10.7#	Form of Employment Agreement, between the Registrant and Josh Cohen (Incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.8#	Form of Employment Agreement, between the Registrant and Justin Klee (Incorporated by reference to Exhibit 10.8 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.9#	Form of Employment Agreement, between the Registrant and James Frates (Incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).

10.10#	Form of Employment Agreement, between the Registrant and Margaret Olinger (Incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.11#	Form of Employment Agreement, between the Registrant and Patrick D. Yeramian, M.D. (Incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1/A (File No. 333-261703) filed with the Securities and Exchange Commission on January 3, 2022).
10.12#	Amendment to Employment Agreement, effective as of December 1, 2022, by and between the Company and Patrick Yeramian (Incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed with the Securities and Exchange Commission on December 6, 2022).
10.13#*	Amendment to Employment Agreement, effective as of November 27, 2023, by and between the Company and Patrick Yeramian.
10.14#	Form of Employment Agreement, between the Registrant and Gina Mazzariello (Incorporated by reference to Exhibit 10.18 to the Registrant's Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 13, 2023).
10.15#*	Form of Employment Agreement, between the Registrant and Camille Bedrosian.
10.16#	Form of Officer Indemnification Agreement (Incorporated by reference to Exhibit 10.13 to the Registrant's Registration Statement on Form S-1 (File No. 333-261703) filed with the Securities and Exchange Commission on December 16, 2021).
10.17#*	Separation Agreement between Registrant and Margaret Olinger dated December 31, 2023.
10.18†	Master Manufacturing Services Agreement, dated as of November 12, 2019, by and between the Registrant and Patheon Inc. (Incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1 (File No. 333-261703) filed with the Securities and Exchange Commission on December 16, 2021).
10.19†	First Amendment, dated as of January 18, 2021, to Product Agreement, dated as of November 12, 2019, pursuant to the Master Manufacturing Services Agreement, dated as of November 12, 2019, by and between the Registrant and Patheon Inc. (Incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 11, 2023).
10.20†	Second Amendment, dated as of March 20, 2023, to Product Agreement, dated as of November 12, 2019, as amended by Amendment No. 1, dated as of January 18, 2021, pursuant to the Master Manufacturing Services Agreement, dated as of November 12, 2019, by and between the Registrant and Patheon Inc. (Incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 11, 2023).
10.21†	Supply Agreement, dated as of October 29, 2019, by and between the Registrant and CU Chemie Uetikon GmbH (Incorporated by reference to Exhibit 10.15 to the Registrant's Registration Statement on Form S-1 (File No. 333-261703) filed with the Securities and Exchange Commission on December 16, 2021).
10.22†	First Amendment, effective as of January 1, 2023, to the Supply Agreement, dated as of October 29, 2019, by and between the Registrant and CU Chemie Uetikon GmbH (Incorporated by reference to Exhibit 10.4 to the Registrant's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on May 11, 2023).
10.23†	Research, Development and Supply Agreement, dated as of December 9, 2019, and Deed of Amendment, dated as of July 26, 2021, by and between the Registrant and ICE S.p.A. (formerly Prodotti Chimici e Alimentari S.p.A.), as amended (Incorporated by reference to Exhibit 10.16 to the Registrant's Registration Statement on Form S-1 (File No. 333-261703) filed with the Securities and Exchange Commission on December 16, 2021).
10.24†	Commercial Supply Agreement, dated as of August 8, 2023, by and between the Registrant and ICE S.p.A. (formerly Prodotti Chimici e Alimentari S.p.A.) (Incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on form 10-Q filed with the Securities and Exchange Commission on August 10, 2023).
21.1*	List of Subsidiaries of Registrant.
23.1*	Consent of Deloitte & Touche LLP, independent registered public accounting firm.
31.1*	Certification of Co-Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Co-Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.3*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

32.1+	Certification of Co-Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2+	Certification of Co-Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.3+	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.
97.1*	Compensation Recovery Policy
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.
+ Furnished herewith. This certification will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, except to the extent specifically incorporated by reference into such filing.
# Indicates a management contract or any compensatory plan, contract or arrangement.
† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with Item 601(b)(10) of Regulation S-K.

c) Financial Statement Schedules

No financial statements have been submitted because they are not required or are not applicable or because the information required is included in the consolidated financial statements or the notes thereto.

Item 16. Form 10-K Summary

None.

SIGNATURES

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

AMYLYX PHARMACEUTICALS, INC.

Date: February 22, 2024 By: /s/ Joshua B. Cohen
Joshua B. Cohen
Co-Chief Executive Officer

Date: February 22, 2024 By: /s/ Justin B. Klee
Justin B. Klee
Co-Chief Executive Officer

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

Name	Title	Date
/s/ Joshua B. Cohen **Joshua B. Cohen**	Co-Chief Executive Officer and Director (Principal Executive Officer)	February 22, 2024
/s/ Justin B. Klee **Justin B. Klee**	Co-Chief Executive Officer and Director (Principal Executive Officer)	February 22, 2024
/s/ James M. Frates **James M. Frates**	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 22, 2024
/s/ George Mclean Milne Jr. **George Mclean Milne Jr. Ph.D.**	Director	February 22, 2024
/s/ Paul Fonteyne **Paul Fonteyne, M.S., M.B.A.**	Director	February 22, 2024
/s/ Daphne Quimi **Daphne Quimi**	Director	February 22, 2024
/s/ Karen Firestone **Karen Firestone**	Director	February 22, 2024

Amylyx Pharmaceuticals, Inc.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the stockholders and the Board of Directors of Amylyx Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Amylyx Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2023 and 2022, the related consolidated statements of operations, comprehensive income (loss), redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the three years in the period ended December 31, 2023, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2023, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2023, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 22, 2024, expressed an unqualified opinion on the Company's internal control over financial reporting.

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 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. 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 was 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 critical audit matters 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 accounts or disclosures to which it relates.

Variable consideration related to gross-to-net ("GTN") adjustments - Refer to Notes 2 and 3 to the financial statements

Critical Audit Matter Description

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration related to certain GTN adjustments. Components of GTN adjustments include trade discounts and allowances, product returns, third-party payor rebates, and other allowances that are offered within contracts between the Company, its customers and payors relating to the sale of products. These GTN adjustments are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). Trade discounts and allowances, provider chargebacks and returns are recorded as reductions of accounts receivables, net on the consolidated balance sheets. Government and other rebates are recorded as a component of accrued expenses on the consolidated balance sheets.

Certain of the GTN adjustments involve the use of significant management assumptions and judgments. These significant assumptions and judgments include consideration of historical experience, payer channel mix (e.g., Medicare or Medicaid), current contract prices under applicable programs, unbilled claims and processing time lags and inventory levels in the distribution channel.

Given the complexity involved, we identified management's estimation of significant assumptions as a critical audit matter. Auditing these significant assumptions involved especially subjective judgment and audit effort.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the GTN adjustments included the following, among others:

- We tested the effectiveness of internal controls over the development of the Company's significant assumptions utilized within the Company's GTN model.
- We evaluated the appropriateness and consistency of the Company's methods and significant assumptions used to calculate the GTN adjustments.
- We tested significant assumptions used to calculate the GTN adjustments by:
    - Performing sensitivity analyses addressing significant assumptions and subjective inputs utilized in the calculation.
    - Reviewing customer and third-party payor contracts and modifications.
    - Reviewing the terms of the discounts and rebates associated with the governmental programs the Company participates in.
    - Developing a range of independent expectations of the significant assumptions, including a comparison of contract prices under applicable programs to those used in management's calculations.
    - Performing lookback analyses by comparing amounts actually invoiced to and paid by the Company to the corresponding GTN adjustment recorded by the Company.
- We tested the mathematical accuracy of the GTN model.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 22, 2024

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

AMYLYX PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2023	**2022**
Assets		
Current assets:		
Cash and cash equivalents	$ 170,201	$ 62,526
Short-term investments	201,161	284,419
Accounts receivable, net	40,050	15,306
Inventories	38,323	9,769
Prepaid expenses and other current assets	14,931	10,113
Total current assets	464,666	382,133
Property and equipment, net	2,686	2,611
Restricted cash equivalents	719	719
Operating lease right-of-use assets	3,725	5,524
Long-term inventories	44,957	—
Other assets	701	466
Total assets	$ 517,454	$ 391,453
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 22,061	$ 6,257
Accrued expenses	57,724	38,312
Operating lease liabilities, current portion	2,257	2,040
Total current liabilities	82,042	46,609
Operating lease liabilities, net of current portion	1,980	4,237
Total liabilities	84,022	50,846
Commitments and contingencies (Note 18)		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized	—	—
Common stock, $0.0001 par value; 300,000,000 shares authorized; 67,707,432 and 66,512,011 shares issued and outstanding as of December 31, 2023 and 2022, respectively	7	7
Additional paid-in capital	738,177	694,906
Accumulated deficit	(304,949)	(354,220)
Accumulated other comprehensive income (loss)	197	(86)
Total stockholders' equity	433,432	340,607
Total liabilities, redeemable convertible preferred stock and stockholders' equity	$ 517,454	$ 391,453

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

AMYLYX PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)

	Year Ended December 31,		
	2023	2022	2021
Revenues:			
Product revenue, net	$ 380,786	$ 22,230	$ —
Grant revenue	—	—	285
Total revenues	380,786	22,230	285
Operating expenses:			
Cost of sales	25,441	2,993	—
Research and development	128,187	93,450	44,040
Selling, general and administrative	188,356	127,128	38,933
Total operating expenses	341,984	223,571	82,973
Income (loss) from operations	38,802	(201,341)	(82,688)
Other income (expense), net:			
Interest income	16,155	4,291	36
Change in fair value of convertible notes	—	—	(5,228)
Other expense, net	(660)	(551)	(51)
Total other income (expense), net	15,495	3,740	(5,243)
Income (loss) before income taxes	54,297	(197,601)	(87,931)
Provision for income taxes	5,026	774	—
Net income (loss)	$ 49,271	$ (198,375)	$ (87,931)
Net income (loss) per share			
Basic	$ 0.73	$ (3.39)	$ (13.35)
Diluted	$ 0.70	$ (3.39)	$ (13.35)
Weighted-average shares used in computing net income (loss) per share			
Basic	67,234,465	58,495,587	6,586,349
Diluted	69,991,340	58,495,587	6,586,349

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

AMYLYX PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(in thousands)

	Year Ended December 31,		
	2023	2022	2021
Net income (loss)	$ 49,271	$ (198,375)	$ (87,931)
Other comprehensive income (loss):			
Foreign currency translation gain (loss)	188	(69)	14
Net unrealized gain (loss) on investments held	95	(26)	(5)
Other comprehensive income (loss)	283	(95)	9
Comprehensive income (loss)	$ 49,554	$ (198,470)	$ (87,922)

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

AMYLYX PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance as of January 1, 2021	20,786,444	$ 72,062	6,137,206	$ 1	$ 1,188	$ —	$ (67,914)	$ (66,725)
Issuance of Series C-1 redeemable convertible preferred stock, net of issuance costs of $209	13,150,430	134,791	—	—	—	—	—	—
Conversion of convertible notes and accrued interest into Series C-2 redeemable convertible preferred stock, net of issuance cost of $50	3,170,585	32,498	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	883,281	—	343	—	—	343
Stock-based compensation expense	—	—	—	—	3,136	—	—	3,136
Other comprehensive loss	—	—	—	—	—	9	—	9
Net loss	—	—	—	—	—	—	(87,931)	(87,931)
Balance as of December 31, 2021	37,107,459	$ 239,351	7,020,487	$ 1	$ 4,667	$ 9	$ (155,845)	$ (151,168)
Conversion of preferred stock into common stock upon initial public offering	(37,107,459)	(239,351)	39,474,330	4	239,347	—	—	239,351
Issuance of common stock upon initial public offering, net of issuance costs of $19,639	—	—	11,369,369	1	196,378	—	—	196,379
Issuance of common stock upon follow-on offering, net of issuance costs of $15,719	—	—	7,697,812	1	230,611	—	—	230,612
Issuance of common stock upon exercise of stock options	—	—	950,013	—	2,189	—	—	2,189
Stock-based compensation expense	—	—	—	—	21,714	—	—	21,714
Other comprehensive loss	—	—	—	—	—	(95)	—	(95)
Net loss	—	—	—	—	—	—	(198,375)	(198,375)
Balance as of December 31, 2022	—	$ —	66,512,011	$ 7	$ 694,906	$ (86)	$ (354,220)	$ 340,607
Issuance of common stock upon exercise of stock options	—	—	1,010,376	—	5,725	—	—	5,725
Issuance of common stock upon vesting of RSUs	—	—	185,045	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	37,546	—	—	37,546
Other comprehensive income	—	—	—	—	—	283	—	283
Net income	—	—	—	—	—	—	49,271	49,271
Balance as of December 31, 2023	—	$ —	67,707,432	$ 7	$ 738,177	$ 197	$ (304,949)	$ 433,432

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

AMYLYX PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2023	**2022**	**2021**
Cash flows provided by (used in) operating activities:			
Net income (loss)	$ 49,271	$ (198,375)	$ (87,931)
Adjustments to reconcile net income (loss) to net cash used in operating activities:			
Stock-based compensation expense	37,161	21,714	3,136
Depreciation expense	1,088	487	52
(Accretion) amortization of investment (discounts) premiums	(9,940)	(2,056)	121
Change in fair value of convertible notes	—	—	5,228
Changes in operating assets and liabilities:			
Accounts receivable, net	(24,744)	(15,306)	—
Inventories	(73,129)	(9,769)	—
Interest receivable	23	487	(144)
Prepaid expenses and other current assets	(4,817)	(5,221)	(4,486)
Operating lease right-of-use assets	1,799	1,635	—
Other assets	(231)	(456)	125
Accounts payable	15,882	1,854	670
Accrued expenses and deferred rent	21,597	26,052	8,432
Operating lease liabilities	(2,041)	(917)	—
Accrued interest and accrued interest—related parties	—	—	(2)
Net cash provided by (used in) operating activities	11,919	(179,871)	(74,799)
Cash flows provided by (used in) investing activities:			
Purchases of property and equipment	(1,241)	(2,526)	(353)
Purchases of short-term investments	(300,826)	(415,873)	(49,053)
Proceeds from maturities of short-term investments	394,120	179,411	3,000
Net cash provided by (used in) investing activities	92,053	(238,988)	(46,406)
Cash flows provided by financing activities:			
Repayment and proceeds from PPP loan	—	—	(263)
Proceeds from initial public offering	—	200,897	—
Proceeds from follow-on offering	—	231,550	—
Initial public offering costs paid	—	(2,044)	—
Follow-on offering costs paid	(136)	(803)	—
Proceeds from issuance of convertible notes—related parties	—	—	14,272
Proceeds from issuance of convertible notes, net of issuance costs	—	—	11,887
Issuance costs related to conversion of convertible notes	—	—	(50)
Proceeds from issuance of Series C-1 redeemable convertible preferred stock	—	—	135,000
Issuance costs related to issuance of Series C-1 redeemable convertible preferred stock	—	—	(209)
Proceeds from exercise of stock options	6,994	2,189	343
Withholding taxes paid on stock-based awards	(3,315)	—	—
Payment of deferred offering costs	—	—	(2,474)
Net cash provided by financing activities	3,543	431,789	158,506
Effect of exchange rate changes on cash, cash equivalents and restricted cash equivalents	160	(65)	13
Net increase in cash, cash equivalents and restricted cash equivalents	107,675	12,865	37,314
Cash, cash equivalents and restricted cash equivalents, beginning of period	63,245	50,380	13,066
Cash, cash equivalents and restricted cash equivalents, end of period	$ 170,920	$ 63,245	$ 50,380
Supplemental disclosure of cash flow information:			
Conversion of convertible notes and accrued interest into Series C-2 redeemable convertible preferred stock	$ —	$ —	$ 32,548
Unrealized gain (loss) on short-term investments	$ 95	$ (26)	$ (5)
Taxes withheld on stock-based awards included in accrued expenses	$ 23	$ —	$ —
Purchases of property and equipment included in accounts payable	$ 20	$ 98	$ 22
Deferred offering costs included in accounts payable and accrued expenses	$ —	$ —	$ 967
Right-of-use assets and liabilities upon ASC 842 adoption	$ —	$ 2,201	$ —
Right-of-use assets obtained in exchange for lease liabilities	$ —	$ 4,958	$ —
Movement of deferred offering costs to equity	$ —	$ 5,457	$ —
Follow-on offering costs included in accounts payable and accrued expenses	$ —	$ 136	$ —
Conversion of preferred stock to common stock upon initial public offering	$ —	$ 239,351	$ —
Income taxes paid	$ 6,389	$ 27	$ —

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

1. NATURE OF BUSINESS

Amylyx Pharmaceuticals, Inc., together with its wholly owned subsidiaries, known as Amylyx or the Company, is a commercial-stage biotechnology company with a mission to end the suffering caused by neurodegenerative diseases. The Company is pursuing amyotrophic lateral sclerosis, or ALS, as its first indication and is focused on the development and potential commercialization of AMX0035 for ALS globally. AMX0035 is approved by the U.S. Food and Drug Administration, or the FDA, and marketed as RELYVRIO® (sodium phenylbutyrate and taurursodiol, also known as ursodoxicoltaurine) for the treatment of ALS in adults in the U.S. AMX0035 is also approved with conditions by Health Canada and marketed as ALBRIOZA™ for the treatment of ALS in Canada. The Company continues to focus on the completion of its global PHOENIX Phase 3 clinical trial, which will provide additional data on the efficacy and safety profile of AMX0035 in people living with ALS, and is also developing AMX0035 in other neurodegenerative diseases. AMX0035 was designed to target endoplasmic reticulum, or ER, stress and mitochondrial dysfunction, two connected central pathways that can lead to neurodegeneration. The Company is further investigating AMX0035 in diseases where ER and mitochondrial stress are implicated, including progressive supranuclear palsy, or PSP, and Wolfram syndrome, or WS. The Company dosed the first participant in the HELIOS trial, a Phase 2 trial of AMX0035 for the treatment of WS, in April 2023. The Company dosed the first participant in the ORION trial, a global, pivotal Phase 3 trial of AMX0035 for the treatment of PSP, in December 2023. The Company is also advancing additional drug candidates for neurodegenerative diseases including AMX0114, an antisense oligonucleotide, targeting Calpain-2, a key protein in axonal degeneration, among others.

Risks and Uncertainties

The Company is subject to risks and uncertainties common to companies in the biotechnology industry, including, but not limited to, the outcome of preclinical studies and clinical trials, market acceptance and the successful commercialization of its approved products ALBRIOZA, which received marketing authorization with conditions in Canada in June 2022, and RELYVRIO, which was approved by the FDA in the U.S. in September 2022, potential difficulties with or delays in timing with respect to regulatory approval processes, development by competitors of new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations, ability to secure additional capital to fund operations, and risks associated with the economic challenges caused by global health crises such as the COVID-19 pandemic and economic uncertainty in various global markets caused by geopolitical instability and conflict. The Company and its contractors may experience disruptions in supply of items that are essential for its research and development and commercial activities, including, for example, raw materials and bulk drug substances that the Company imports from Europe and Canada used in the manufacturing of AMX0035, and any additional or future product candidates.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

***Basis of Presentation and Consolidation*—**The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the U.S., or GAAP, and include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation. Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification, or ASC, and Accounting Standards Updates, or ASU, of the Financial Accounting Standards Board, or FASB.

***Use of Estimates*—**The preparation of the consolidated financial statements in conformity with GAAP requires the Company's management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the financial statements and the reported amount of expenses during the reporting period. Actual results could differ from those estimates. Management considers many factors in selecting appropriate financial accounting policies in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. Estimates are used in the following areas, among others: gross-to-net, or GTN, adjustments; recoverability of inventories, including those produced in preparation for product launches; accrued expenses; stock option valuations; valuation allowance for deferred tax assets and research and development expenses.

Revenue recognition—In June 2022, AMX0035 received marketing authorization with conditions as ALBRIOZA by Health Canada for the treatment of ALS, and the Company launched ALBRIOZA in Canada in July 2022. In September 2022, AMX0035 received approval as RELYVRIO by the FDA for the treatment of ALS in adults, and the Company launched RELYVRIO in the U.S. in October 2022.

The Company enters into arrangements with wholesalers, specialty pharmacies and specialty distributors, or Customers, to distribute ALBRIOZA, RELYVRIO and future approved products. In accordance with ASC Topic 606 - *Revenue from Contracts with Customers*, or Topic 606, revenue is recognized when the customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services.

To determine revenue recognition for arrangements that the Company determines are within the scope of Topic 606, the Company performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to arrangements that meet the definition of a contract under Topic 606, including when it is probable that the Company will collect the consideration the Company expects to be entitled to in exchange for the goods or services the Company transfers to its customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Revenue, Net

The Company sells its approved products to its Customers. These Customers subsequently resell our products to specialty pharmacy providers, specialty distributors, health care providers, certain medical centers or hospitals, and patients. In addition to agreements with the Customers, the Company enters into arrangements with specialty pharmacies, health care providers and payors that provide for government mandated and/or privately negotiated rebates with respect to the purchase of our products. The Company's customer identification process considers a number of factors, including contractual and legal factors, and who controls the Company's product and bears inventory risk. The Company evaluates these factors on a customer-by-customer basis to determine the appropriate customer for revenue recognition purposes. In some cases, the Company may use a third-party logistics providers to deliver the Company's product to its customers, but the Company recognizes revenue upon delivery to the customer, as its determined that the third-party logistics provider is acting as our agent. Changes in these factors or our assumptions regarding these factors could impact our revenue recognition

The Company recognizes revenue on product sales when the Customer obtains control of our product, which occurs at a point in time (upon delivery). Product revenues are recorded net of applicable GTN adjustments, which are described below.

If taxes should be collected from Customers relating to product sales and remitted to governmental authorities, they will be excluded from revenue. The Company expenses incremental costs of obtaining a contract when incurred, if the expected amortization period of the asset that the Company would have recognized is one year or less. However, no such costs were incurred during the years ended December 31, 2023, 2022 and 2021.

GTN Adjustments

Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration related to certain GTN adjustments. Components of GTN adjustments include trade discounts and allowances, product returns, third-party payor rebates, and other allowances that are offered within contracts between the Company, its Customers and payors relating to the sale of our products. These GTN adjustments, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable (if the amount is payable to the Customer) or a current liability (if the amount is payable to a party other than a Customer). These estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in Topic 606 for relevant factors such as historical experience, payer channel mix (e.g., Medicare or Medicaid), current contract prices under applicable programs, unbilled claims and processing time lags and inventory levels in the distribution channel. In certain circumstances, the Company applies the most likely method in Topic 606. The

determination to use the expected value method or the most likely method is based on the type of GTN adjustment and what method better predicts the amount of consideration we expect to be entitled to. Overall, these GTN adjustments reflect in the transaction price the amount of consideration to which the Company expects to be entitled to in exchange for transferring promised goods or services to its Customers.

The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our estimates, the Company will adjust these estimates, which would affect product revenue, net and earnings in the period such variances become known.

Trade Discounts and Allowances

The Company generally provides Customers with prompt payment discounts and pay fees for distribution services and for certain data that distributors provide to us that are explicitly stated in our contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. Payment from Customers is typically due within 30 calendar days of the invoice date, without consideration to the prompt payment discounts.

Product Returns

Consistent with industry practice, the Company generally offers Customers a limited right of return for product that has been purchased from the Company based on the product's expiration date, which is set to lapse within a specified period stated in the contract. Additionally, our limited right of return policy allows for eligible returns from Customers in circumstances where product was shipped in error or was damaged in shipping, or product was returned pursuant to an official drug recall.

The Company estimates the amount of product sales that may be returned by our Customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as reductions to accounts receivable, net on the consolidated balance sheets. The Company currently estimates returns using quantitative and qualitative information including, but not limited to, historical experience with returns, projected demand, levels of inventory in the distribution channel, product dating and expiration period, and whether products have been discontinued, among others. The Company has received an immaterial amount of returns to date and believes that returns of product in future periods will be minimal.

Provider Chargebacks and Discounts

Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from the Company. Customers charge the Company for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These GTN adjustments are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable, net. GTN adjustments for chargebacks consist of credits that Customers have not claimed, but for which we expect to issue for units that remain in the distribution channel inventories at each reporting period-end that we expect will be sold to qualified healthcare providers, and chargebacks that Customers have claimed, but for which we have not yet issued a credit.

Payor Rebates

The Company contracts with certain government and private payor organizations, primarily government and commercial health insurance companies, for the payment of rebates with respect to utilization of our products. The Company is subject to discount obligations under state Medicaid programs and Medicare. These GTN adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom it will owe an additional liability under the Medicare Part D program. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for

the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Other Incentives

Other incentives which the Company offers include voluntary patient assistance programs, such as its co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payors. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue for each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

***Comprehensive Loss*—**Comprehensive loss includes net loss, as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. Comprehensive loss is composed of net loss and other comprehensive (loss) income. Other comprehensive (loss) income consists of unrealized gains and losses on marketable securities and foreign currency translation.

***Cash and Cash Equivalents*—**The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. Cash equivalents represent funds invested in readily available checking and money market funds.

***Restricted Cash Equivalents*—** Restricted cash equivalents consist of $0.2 million of cash serving as collateral for a letter of credit issued for the Company's office space, and $0.5 million as collateral for a corporate credit card program. As of December 31, 2023 and 2022, the Company's restricted cash equivalents balance was $0.7 million and $0.7 million, respectively.

***Accounts receivable, net*—** The Company's accounts receivable consists of amounts due from Customers related to product sales and have standard payment terms. The Company analyzes accounts that are past due for collectability and provides reserves against accounts receivable for expected credit losses that may result from a customer's inability to pay. Amounts determined to be uncollectible are written-off against the established reserve. As of December 31, 2023 and 2022, the credit profiles for the Company's customers were deemed to be in good standing and expected credit losses were not material.

***Short-Term Investments*—**Short-term investments are composed of U.S. treasury notes and bills, corporate debt securities, commercial paper and agency bonds with maturities of less than one year from the balance sheet date. The Company classifies all of its short-term investments as available-for-sale. Accordingly, these investments are recorded at fair value, which is determined based on quoted market prices. Unrealized gains and losses on available-for-sale securities are included as a separate component of other accumulated comprehensive loss. The cost of short-term investments is adjusted for amortization of premiums and accretion of discounts until maturity. Such amortization and accretion are included in interest income. Realized gains and losses are included in other expense, net. The Company evaluates short-term investments for other-than-temporary impairment at the balance sheet date. Declines in fair value, if any, determined to be other than temporary-than-temporary are also included in other income, net.

When assessing short-term investments for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, and the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. As of December 31, 2023 and 2022, there were no impairment charges on short-term investments.

***Concentrations of Credit Risk*—**Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash and cash equivalents, short-term investments and accounts receivable, net. The Company maintains its cash in financial institutions that it believes have high credit quality. The Company has not experienced any losses on such accounts, and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company's accounts receivable, net represents amounts due to the Company from customers. Amylyx performs ongoing credit evaluations of its customers and generally does not require collateral. The Company monitors its exposure and

records a reserve against uncollectible amounts as necessary. Three and four customers individually accounted for approximately 81% and 97% of total gross product revenue in 2023 and 2022, respectively. No revenue was recognized in 2021. Three and three customers individually accounted for approximately 81% and 98% of total accounts receivable, net as of December 31, 2023 and 2022, respectively.

***Fair Value Measurements*—**Assets and liabilities recorded at fair value on a recurring basis on the consolidated balance sheet are categorized based upon the level of judgment associated with the inputs used to measure their fair values. 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. The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

- ***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 that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The Company's financial instruments consist of cash, cash equivalents, restricted cash equivalents, short-term investments, accounts receivable, net, accounts payable and accrued expenses. The Company's short-term investments are carried at fair value, determined according to Level 1 and Level 2 inputs to the fair value hierarchy described above. The Company's 2021 Notes (as defined in Note 8) were carried at fair value, determined according to Level 3 inputs in the fair value hierarchy described above. The remaining financial instruments are stated at their respective carrying amounts, which approximate fair value due to the short-term nature of these assets and liabilities.

***Inventories*—**The Company values its inventories at the lower of cost or estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company classifies inventory as long-term when consumption or sale of the inventory is expected beyond its normal operating cycle of twelve months. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of sales. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required which would be recorded as cost of sales in the consolidated statements of operations.

The Company capitalizes inventory costs associated with the Company's products after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory acquired prior to receipt of regulatory approval of a product candidate is expensed as research and development expense as incurred. Inventory that can be used in either the production of clinical or commercial product is initially capitalized and subsequently expensed as research and development expense when identified for use in the manufacture of drugs still in development.

***Property and Equipment, net*—**Property and equipment are stated at cost, net of accumulated depreciation. Depreciation of property and equipment is calculated using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repairs that do not improve or extend the life of the assets are expensed when incurred. Upon sale or retirement of assets, the cost and accumulated depreciation are removed from the consolidated balance sheets

and any resulting gain or loss is reflected in the consolidated statements of operations in the period realized. The range of useful lives of property and equipment is as follows:

	Estimated Useful Life
Leasehold improvements	Lesser of the estimated life or remaining lease term
Furniture and fixtures	4 years
Computer hardware and software	3 years
Construction in progress	Not depreciated

Impairment of Long-Lived Assets—The Company evaluates assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses in the years ended December 31, 2023 and 2022.

Research and Development—Research and development expenses include costs directly attributable to the conduct of research and development activities. Expenditures relating to research and development are expensed in the period incurred. Nonrefundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made. In addition, research and development-related salaries and benefits, facility, and overhead costs, supplies and other related costs are included in research and development expense.

Sales and Marketing Costs—Sales and marketing expenses consist primarily of wages and benefits for sales and marketing personnel, professional and consulting fees, administrative travel expenses, and marketing and advertising costs such as marketing literature, promotional activities, conferences and seminars and branding. Sales and marketing, and advertising costs are expensed as incurred and included in selling, general and administrative expenses in the accompanying consolidated statements of operations. The Company considers advertising costs as expenses related to the promotion of the Company's commercial products. For the years ended December 31, 2023 and 2022, advertising costs were $9.5 million and $4.4 million, respectively. The Company did not have commercial products in 2021.

Patent-Related Costs—Patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as selling, general and administrative expenses in the accompanying consolidated statements of operations.

Stock-Based Compensation Expense—Stock-based compensation is recognized in the consolidated statements of operations based on their fair values on the date of grant over the requisite service period, which is generally equal to the vesting period of the respective award. Forfeitures are accounted for as they occur. Generally, the Company issues stock option awards with only service-based vesting conditions and records the expense for these awards using the straight-line method. The Company classifies stock-based compensation expense in the same manner in which the awards recipient's payroll or service provider's costs are classified.

The fair value of each restricted common stock award is estimated on the date of grant based on the fair value of the Company's common stock on that same date.

The fair value of each option grant is estimated on the date of grant using the Black-Scholes option pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the award, the risk-free interest rate, and expected dividends. The Company estimates its expected stock price volatility based on the historical volatility of publicly traded peer companies. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain vanilla" options. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. There is no expected dividend yield since the Company has never paid cash dividends on common stock and does not expect to pay any cash dividends in the foreseeable future. The stock price of the Company is based on the closing price on the date of grant. Prior to the IPO, as there was no public market for the Company's common stock, the estimated fair value of common stock was determined by the Company's Board of Directors as of the date of each option grant, with input from management, considering third-party valuations of its common stock as well as the Company's Board of Directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent third-party valuation through the date of the

grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately Held Company Equity Securities Issued as Compensation*.

***Contingencies*—**From time to time, the Company may have certain contingent liabilities that arise in the ordinary course of business activities. The Company accrues for loss contingencies when losses become probable and are reasonably estimable. If the reasonable estimate of the loss is a range and no amount within the range is a better estimate, the minimum amount of the range is recorded as a liability on the Company's consolidated balance sheets. The Company does not accrue for contingent losses that, in its judgement, are considered to be reasonably possible, but not probable; however, it discloses the range of reasonably possible losses. There were no loss or gain contingencies recorded in the Company's consolidated financial statements as of and during the years ended December 31, 2023 and 2022.

***Leases*—**The Company adopted the FASB, ASC 842, *Leases,* or ASC 842, on January 1, 2022. ASC 842 allows the Company to elect a package of practical expedients, which include: (i) an entity need not reassess whether any expired or existing contracts are or contain leases; (ii) an entity need not reassess the lease classification for any expired or existing leases; and (iii) an entity need not reassess any initial direct costs for any existing leases. Another practical expedient allows the Company to use hindsight in determining the lease term when considering lessee options to extend or terminate the lease and to purchase the underlying asset. The Company has elected to utilize this package of practical expedients and has not elected the hindsight methodology in its implementation of ASC 842.

The Company leases its offices, and may from time to time, enter into other lease agreements in conducting its business. The Company determines if an arrangement includes a lease at the inception of the agreement. For each of the Company's lease arrangements, the Company records a right-of-use asset representing the Company's right to use an underlying asset for the lease term and a lease liability representing the Company's obligation to make lease payments. Operating lease right-of-use assets and operating lease liabilities are recognized at the lease commencement date based on the net present value of the remaining future minimum lease payments over the lease term. If the interest rate implicit in the Company's leases is not readily determinable, in determining the weighted-average discount rate used to calculate the net present value of lease payments, the Company utilizes an estimate of its incremental borrowing rate based on market sources including interest rates for companies with similar credit quality for agreements of similar duration, determined by class of underlying asset, to discount the lease payments. Lease expense for the Company's operating leases is recognized on a straight-line basis over the lease term and variable lease costs are expensed as incurred. The Company did not have financing leases as of December 31, 2023 and 2022.

The Company elected the practical expedient not to apply the recognition and measurement requirements to short-term leases, which is any lease with a term of one year or less as of the lease commencement date. The lease may require the Company to pay additional amounts for maintenance and other expenses, which are generally referred to as non-lease components. The Company has elected the practical expedient to combine lease and non-lease components. If a lease includes options to extend the lease term, the Company does not assume the option will be exercised in its initial lease term assessment unless there is reasonable certainty that the Company will renew based on an assessment of economic factors present as of the lease commencement date.

Prior to the adoption of ASC 842, at the inception of each lease, the Company evaluated the lease agreement to determine whether the lease was an operating or capital lease in accordance with *ASC 840, Leases (ASC 840)*. When any one of the four test criteria in ASC 840 was met, the lease then qualified as a capital lease. If the lease agreements contained renewal options, tenant improvement allowances, rent holidays or rent escalation clauses, the Company recorded a deferred rent asset or liability equal to the difference between the rent expense and future minimum lease payments due. The rent expense related to operating leases was recognized on a straight-line basis in the statements of operations over the term of each lease.

***Income Taxes*—**The Company accounts for income taxes using the asset and liability approach. Deferred tax assets and liabilities represent future tax consequences of temporary differences between the financial statement carrying amounts and the tax basis of assets and liabilities and for loss carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. A valuation allowance is established to reduce deferred tax assets to the amounts expected to be realized. The Company also recognizes a tax benefit from uncertain tax positions only if it is "more likely than not" that the position is sustainable based on its technical merits. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes. To date, the Company has not incurred material interest and penalties related to income tax positions.

Valuation allowances are provided, if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. As of December 31, 2023, we continued to maintain a full valuation allowance against all of our U.S. federal and state deferred tax assets based on management's evaluation of all available evidence, including our history of incurring significant losses from operations. Our evaluation of all available evidence also includes consideration of regulatory approvals of ALBRIOZA and RELYVRIO, including revenue generated from the sale these products in 2023. Given the early stage of our product launch, we are uncertain about the timing and amount of future sales. We may release all or a portion of the valuation allowance in the near-term; however, the release of the valuation allowance, as well as the exact timing and the amount of such release, continue to be subject to, among other things, our level of profitability, revenue growth, clinical program progression and expectations regarding future profitability.

Segment Information—An operating segment is defined as a component of a business that engages in business activities for which it may earn revenues and incur expenses and for which discrete financial information is available that is evaluated regularly by the chief operating decision maker or makers in order to make decisions about resources to be allocated to the segment and assess its performance. The Company has determined that its CO-Chief Executive Officers are the chief operating decision makers, or CODM. The CODM reviews consolidated operating results to make decisions about allocating resources or capital to specific compounds or projects in line with the Company's overall strategies and goals. The Company's entire business is managed by a single management team, which reports to the CO-Chief Executive Officers. The Company has one operating segment which is the business of researching and developing therapeutics for neurodegenerative disorders. For the years ended December 31, 2023 and 2022, all of the Company's long-lived assets were held within the U.S.

Net income (loss) per share—The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net income (loss) per share is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period. Diluted net income (loss) is computed by adjusting net income (loss) attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares. For purpose of this calculation, stock options, convertible notes, and redeemable convertible preferred stock are considered potential dilutive common shares.

The Company's redeemable convertible preferred stock contractually entitles the holders of such shares to participate in dividends but does not contractually require the holders of such shares to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, such losses are not allocated to such participating securities. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recent Accounting Pronouncements

New Accounting Pronouncements Not Yet Adopted

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvement to Income Tax Disclosures*, or ASU 2023-09, to enhance the transparency and decision usefulness of income tax disclosures. ASU 2023-09 is effective for annual periods beginning after December 15, 2024 on a prospective basis. Early adoption and retrospective application is permitted. The Company is currently evaluating the impact of this ASU on its consolidated financial statements and related disclosures.

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*, or ASU 2023-09, which requires public entities to disclose information about their reportable segments' significant expenses on an interim and annual basis. ASU 2023-07 is effective for the Company beginning the year ended May 31, 2025. The Company is currently evaluating the impact of this ASU on its consolidated financial statements and related disclosures.

Recently Adopted Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326) Measurement of Credit Losses on Financial Instruments*, or ASU 2016-13. The provisions of ASU 2016-13 modify the impairment model to utilize an expected loss methodology in place of the currently used incurred loss methodology and require a consideration of a broader range of reasonable and supportable information to inform credit loss estimates. Credit losses relating to available-for-sale debt securities will be recorded through an allowance for credit losses rather than as a direct write-down to the security. The Company adopted ASU 2016-13 effective January 1, 2023, with no material impact on its consolidated financial statements and related disclosures.

Effective January 1, 2022, the Company adopted the requirements under the ASC 842 using the modified retrospective transition approach. Comparative periods have not been restated. This standard requires entities that lease assets to recognize the assets and liabilities for the rights and obligations created by those leases on the balance sheet. The Company elected the available package of practical expedients which allows it to not reassess previous accounting conclusions around whether arrangements are or contain leases, the classification of its leases, and the treatment of initial direct costs. The Company has made an accounting policy election to keep leases with an initial term of 12 months or less off of the balance sheet. ASC 842 was issued in order to increase transparency and comparability of financial reporting related to leasing arrangements. The main difference between previous GAAP, or ASC 840, and ASC 842 is the recognition of right-of-use lease assets and lease liabilities by lessees for those leases that were classified as operating leases under ASC 840. At January 1, 2022, the Company recorded right-of-use assets of $2.2 million and operating lease liabilities of $2.2 million. Adoption of the standard did not have a material impact on the consolidated statements of operations. For additional information regarding how the Company is accounting for leases under ASC 842, refer to Note 10.

3. PRODUCT REVENUE, NET

To date, the Company's only source of product revenue has been from the sales of RELYVRIO, known as ALBRIOZA in Canada. Significant judgment is required in estimating GTN adjustments considering historical experience, payer channel mix (e.g., Medicare or Medicaid), current contract prices under applicable programs, unbilled claims and processing time lags and inventory levels in the distribution channel. The following table reconciles gross product revenue to net product revenue:

	Year Ended December 31,		
	2023	2022	2021
	(in thousands)		
Product revenue, gross	$ 431,433	$ 27,104	$ —
GTN adjustments	(50,647)	(4,874)	—
Product revenue, net	$ 380,786	$ 22,230	$ —

The activity and ending reserve balance for GTN adjustments were as follows for the periods indicated:

	Chargebacks and Cash Discounts	Medicaid and Medicare Rebates	Other Rebates, Returns, Discounts and Adjustments	Total
	(in thousands)			
Ending balance at December 31, 2021	$ —	$ —	$ —	$ —
Provision related to sales in the current year	851	1,992	2,031	4,874
Adjustments related to prior period sales	—	—	—	—
Credits and payments made	(203)	—	(367)	(570)
Ending balance at December 31, 2022	$ 648	$ 1,992	$ 1,664	$ 4,304
Provision related to sales in the current year	17,898	10,887	22,378	51,163
Adjustments related to prior period sales	(280)	(236)	—	(516)
Credits and payments made	(15,123)	(7,697)	(12,969)	(35,789)
Ending balance at December 31, 2023	$ 3,143	$ 4,946	$ 11,073	$ 19,162

Included in the ending reserve balance for GTN adjustments are chargebacks resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from the Company, discounts to customers for prompt payment and estimates for product returns. Chargebacks, discounts and returns are recorded as reductions of accounts receivable, net on the consolidated balance sheets. In addition, included in the ending reserve balance for GTN adjustments are Medicaid and Medicare rebates, other

rebates for obligations under voluntary patient assistance programs, and accrued fees payable to customers. Medicaid and Medicare rebates, other rebates and fees are recorded as a component of accrued expenses on the consolidated balance sheets.

4. SHORT-TERM INVESTMENTS

The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation at each balance sheet date. The Company has classified all of its marketable securities at December 31, 2023 and 2022 as "available-for-sale" pursuant to ASC 320, *Investments – Debt and Equity Securities*. The Company records available-for-sale securities at fair value, with the unrealized gains and losses included as a separate component of other accumulated comprehensive income (loss). There were no realized gains or losses recognized during the years ended December 31, 2023 and 2022.

The Company adjusts the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. The cost of securities sold is based on the specific identification method. The Company includes interest and dividends on securities classified as available-for-sale in interest income. Accrued interest receivable relating to the Company's available-for-sale securities is presented within prepaid expenses and other current assets in the accompanying condensed consolidated balance sheets, and amounted to $0.5 million and $0.5 million at December 31, 2023 and 2022, respectively.

The following is a summary of available-for-sale securities with unrealized losses for less than 12 months as of December 31, 2023 and 2022 (in thousands):

	December 31, 2023		December 31, 2022	
	Fair Value	Unrealized Losses	Fair Value	Unrealized Losses
Treasury notes	$ —	$ —	$ 27,159	$ (14)
Treasury bills	—	—	9,839	(2)
Corporate debt securities	—	—	33,486	(55)
Agency bonds	4,996	(3)	—	—
Total available-for-sale securities in an unrealized loss position	$ 4,996	$ (3)	$ 70,484	$ (71)

At December 31, 2023, the Company's security portfolio consisted of 11 securities related to investments in debt securities available-for-sale, of which 1 security was in an unrealized loss position. There were no securities in an unrealized loss position for greater than 12 months as of December 31, 2023. The contractual terms of these investments do not permit the issuer to settle the securities at a price less than the amortized cost bases of the investments. The Company does not intend to sell the investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost bases. The Company did not record an allowance for credit losses as of December 31, 2023.

Prior to January 1, 2023, the Company evaluated short-term investments for other-than-temporary impairment at the balance sheet date. Declines in fair value, if any, determined to be other-than-temporary were also included in other income, net. When assessing short-term investments for other-than-temporary declines in value, the Company considered such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, and the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. The Company determined it did not hold any investments with any other-than-temporary impairment as of December 31, 2022.

Short-term investments, which are classified as available-for-sale, consisted of the following:

December 31, 2023	Amortized Cost Basis	Unrealized Gain	Unrealized Loss	Fair Values
		(in thousands)		
Treasury bills	$ 196,098	$ 67	$ —	$ 196,165
Agency bonds	4,999	—	(3)	4,996
Total short-term investments	$ 201,097	$ 67	$ (3)	$ 201,161

December 31, 2022	Amortized Cost Basis	Unrealized Gain	Unrealized Loss	Fair Values
		(in thousands)		
Treasury notes	$ 27,173	$ —	$ (14)	$ 27,159
Treasury bills	59,326	10	(2)	59,334
Commercial paper	134,375	—	—	134,375
Corporate debt securities	58,795	13	(55)	58,753
Agency bonds	4,781	17	0	4,798
Total short-term investments	$ 284,450	$ 40	$ (71)	$ 284,419

5. INVENTORIES

Inventories consisted of the following:

	December 31,	
	2023	2022
	(in thousands)	
Raw materials	$ 53,144	$ 7,151
Work in process	18,945	1,681
Finished goods	11,191	937
Total inventories	$ 83,280	$ 9,769

The Company capitalizes inventory costs associated with the Company's products after regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. As of December 31, 2023, the Company had $2.7 million of inventory on hand that was acquired prior to regulatory approvals. This inventory was expensed to research and development as the future economic benefit was not probable. The Company began to capitalize inventory costs upon receipt of regulatory approvals in 2022. Long-term inventory consists primarily of raw materials, which have a current usable period of approximately two to three years in its raw material form. Raw material has until its stated expiry date to be manufactured into finished goods, at which point the material has another twelve to eighteen months of useful life. The Company classifies inventory as long-term when consumption or sale of the inventory is expected beyond twelve months. Inventory amounts written down as a result of obsolescence or other reasons are charged to cost of sales. For the years ended December 31, 2023, 2022, and 2021 the Company recognized write-downs of $3.3 million, $0.4 million and zero, respectively.

6. PROPERTY AND EQUIPMENT, NET

Property and equipment, net consisted of the following:

	December 31,	
	2023	2022
	(in thousands)	
Furniture and fixtures	$ 382	$ 362
Computer hardware and software	3,167	1,810
Leasehold improvements	176	176
Construction in progress	589	803
Total property and equipment	4,314	3,151
Less: accumulated depreciation	(1,628)	(540)
Total property and equipment, net	$ 2,686	$ 2,611

7. ACCRUED EXPENSES

Accrued expenses consisted of the following:

	December 31,	
	2023	2022
	(in thousands)	
Accrued external research and development	$ 12,625	$ 8,424
Accrued benefits and incentive compensation	16,790	15,231
Accrued manufacturing	1,652	4,596
Accrued consulting and other professional fees	6,506	4,116
Accrued rebates and co-pay assistance	16,063	3,582
Accrued royalties	3,111	1,358
Other accrued expenses	977	1,005
Total accrued expenses	$ 57,724	$ 38,312

8. CONVERTIBLE NOTES

Issuance of the 2021 Notes

In January 2021, the Company issued, in aggregate, $27.3 million in convertible notes, or 2021 Notes, to certain investors, including related parties, of which proceeds of $1.2 million were received in advance of issuance of the 2021 Notes in December 2020 and the remaining proceeds of $26.1 million were received in January and February 2021. The 2021 Notes were to mature on June 30, 2022 and carried both automatic and optional conversion features. The 2021 Notes were secured and carried an interest rate of 3%. The Company recorded the $1.2 million of proceeds received in December 2020 as proceeds received in advance of issuance of 2021 Notes in the consolidated balance sheet as of December 31, 2020, as the subscription agreement and commitment to issue the 2021 Notes was not effective until January 2021.

The Company qualified for and elected to account for the 2021 Notes under the fair value option and, in doing so, bypassed the analysis of potential embedded derivative features. The Company believes that the fair value option better reflects the underlying economics of the 2021 Notes. As a result, the 2021 Notes were recorded at fair value upon issuance, which was determined to be equal to principal amounts of these notes of $27.3 million. At each financial reporting period, and immediately prior to conversion, the Company remeasured the fair value of the 2021 Notes. The change in fair value of the 2021 Notes from issuance date to the conversion date totaled $5.2 million, which is recorded as change in fair value of convertible notes in the consolidated statement of operations for the year ended December 31, 2021.

Conversion of the 2021 Notes

In July 2021, the Company consummated a financing transaction in which it issued shares of Series C-1 redeemable convertible preferred stock. The consummation of this financing transaction resulted in the automatic conversion of the 2021 Notes into shares of Series C-2 redeemable convertible preferred stock (together with the Series C-1 redeemable convertible preferred stock, the "Series C Preferred Stock") pursuant to their original terms. The Series C Preferred Stock was determined to have a fair value of $10.265809. Under the fair value option, the 2021 Notes were remeasured to fair value immediately prior to conversion at a price per share equal to the fair value of the Series C-1 redeemable convertible preferred stock. The Company recorded $5.2 million loss related to change in fair value of the 2021 Notes in its consolidated statement of operations for the year ended December 31, 2021. The 2021 Notes converted into 3,170,585 shares of Series C-2 redeemable convertible preferred stock at the effective conversion price of $8.725938.

Convertible Notes—Related Parties

There were no convertible notes issued to related parties that were outstanding as of December 31, 2023 and 2022. In connection with the issuance of the 2021 Notes, the Company issued, in aggregate, $14.3 million of convertible notes to certain related parties. These notes were issued under the same terms and conditions as the 2021 Notes.

9. FAIR VALUE MEASUREMENTS

The following tables present information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values:

	December 31, 2023			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Assets:				
Cash equivalents	$ 76,710	$ —	$ —	$ 76,710
Short-term investments:				
Treasury bills	196,165	—	—	196,165
Agency bonds	—	4,996	—	4,996
Total short-term investments	196,165	4,996	—	201,161
Restricted cash equivalents	719	—	—	719
Total financial assets	$ 273,594	$ 4,996	$ —	$ 278,590

	December 31, 2022			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Assets:				
Cash equivalents	$ 23,567	$ 9,989	$ —	$ 33,556
Short-term investments:				
Treasury notes	27,159	—	—	27,159
Treasury bills	59,334	—	—	59,334
Commercial paper	—	134,375	—	134,375
Corporate debt securities	—	58,753	—	58,753
Agency bonds	—	4,798	—	4,798
Total short-term investments	86,493	197,926	—	284,419
Restricted cash equivalents	719	—	—	719
Total financial assets	$ 110,779	$ 207,915	$ —	$ 318,694

Valuation of Short-Term Investments

The Company classifies its money market funds, treasury notes and treasury bills as Level 1 assets under the fair value hierarchy, as these assets have been valued using quoted market prices for identical assets in active markets without any valuation adjustment. The Company classifies its commercial paper, corporate debt securities, and agency bonds as Level 2 assets under the fair value hierarchy, as these assets have been valued using information obtained through a third-party pricing service at each balance sheet date, using observable market inputs that may include trade information, broker or dealer quotes, bids, offers, or a combination of these data sources.

The Company does not hold any short-term investments classified as Level 3, which are securities valued using unobservable inputs. The Company has not transferred any investment securities between the classification levels.

There were no other assets or liabilities that were measured at fair value on a recurring basis as of December 31, 2023 and 2022.

10. LEASES

The Company leases its office facilities under non-cancelable operating leases that expire at various dates through October 2026. The Company entered into an office space lease at 121 First Street in Cambridge, Massachusetts on January 10, 2022, for 36 months, with an option to extend the lease for 3 years. Because the Company was not reasonably certain to exercise the option to extend the lease at inception, the option to extend was not considered in determining the lease term. The Company initially recognized a right-of-use asset of $5.0 million and a lease liability of $5.0 million upon commencement of the lease.

Components of lease expense required by ASC 842 are presented below for the years ended December 31, 2023 and 2022:

	Year Ended December 31,	
	2023	2022
	(in thousands)	
Lease cost		
Operating lease cost	$ 2,175	$ 2,136
Total lease cost	$ 2,175	$ 2,136

Lease liabilities are measured by calculating the present value of remaining lease payments under the lease arrangement. Since the rates implicit in our leases are not readily determinable, the Company uses estimated incremental borrowing rates in determining the discount rate used to calculate the present value of remaining lease payments. The incremental borrowing rate is the rate of interest that the Company would have to pay to borrow, on a collateralized basis, an amount equal to the lease payments over a similar term equal to the lease term in a similar economic environment. The incremental borrowing rate is based on the information available at commencement date. As the Company has no recent external borrowings, the incremental borrowing is a hypothetical rate based on our understanding of what our credit rating would be and adjusted to reflect a collateralized borrowing.

The Company's leases contain renewal options that can extend the lease for additional years. Because the Company is not reasonably certain to exercise these renewal options, they are not considered in determining the lease terms, and associated potential additional payments are excluded from lease payments. The Company has elected to account for each lease component and its associated non-lease components as a single lease component and has allocated all of the contract consideration across lease components only. The Company has existing net leases in which the non-lease components (e.g., common area maintenance) are paid separately from rent based on actual costs incurred and therefore are not included in the operating lease right-of-use assets and lease liabilities and are reflected as an expense in the period incurred.

The following table summarizes the presentation in the Company's consolidated balance sheet of its operating leases:

	December 31,	
	2023	2022
	(in thousands)	
Assets		
Operating lease right-of-use assets	$ 3,725	$ 5,524
Liabilities		
Operating lease right-of-use liabilities, current	$ 2,257	$ 2,040
Operating lease right-of-use liabilities, net of current portion	1,980	4,237
Total operating lease liabilities	$ 4,237	$ 6,277

During the years ended December 31, 2023 and 2022, the Company made cash payments for operating leases of $2.4 million and $1.4 million, respectively. Future minimum lease payments under non-cancelable leases as of December 31, 2023, were as detailed below (in thousands):

	As of December 31, 2023
2024	$ 2,478
2025	1,586
2026	476
2027	—
2028	—
Total undiscounted lease payments	4,540
Less: imputed interest	(303)
Total operating lease liabilities	$ 4,237

As of December 31, 2023 and 2022, the weighted average remaining lease term was 2 years and 2.9 years, respectively. As of December 31, 2023 and 2022, the weighted average incremental borrowing rate used to determine the operating lease right-of-use assets was 7.3%.

11. REDEEMABLE CONVERTIBLE PREFERRED STOCK

On July 1, 2021, the Company amended its certificate of incorporation in which it authorized 13,150,430 shares of Series C-1 redeemable convertible preferred stock and 3,170,585 shares of Series C-2 redeemable convertible preferred stock.

In July 2021, the Company consummated a financing transaction in which it issued 13,150,430 shares of Series C-1 redeemable convertible preferred stock. In connection with the issuance of these shares, the principal including accrued interest of the 2021 Notes totaling $27.7 million automatically converted into 3,170,585 shares of Series C-2 redeemable convertible preferred stock.

The Company's redeemable convertible preferred stock consisted of the following:

	December 31, 2021 (dollars in thousands)				
	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A preferred stock	6,289,609	6,289,609	$ 7,675	$ 7,730	6,407,256
Series B preferred stock	15,100,000	14,496,835	$ 64,387	$ 246,070	16,746,059
Series C-1 preferred stock	13,150,430	13,150,430	$ 134,791	$ 135,000	13,150,430
Series C-2 preferred stock	3,170,585	3,170,585	$ 32,498	$ 27,666	3,170,585
	37,710,624	37,107,459	$ 239,351	$ 416,466	39,474,330

In January 2022, upon the completion of the Company's IPO, all of the Company's outstanding shares of preferred stock were converted into shares of its common stock. There were no redeemable convertible preferred stock outstanding as of December 31, 2023 or 2022.

12. STOCKHOLDERS' EQUITY (DEFICIT)

Common Stock—Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders provided, however, that, except as otherwise required by law, holders of common stock shall not be entitled to vote on any amendment to the Company's Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the Delaware General Corporation Law. Common stockholders are entitled to receive dividends, as may be declared by the Company's Board of Directors, if any, subject to the preferential dividend rights of the Preferred Stock. No dividends were declared or paid during the years ended December 31, 2023 and 2022.

The Company had reserved shares of common stock for issuance in connection with the following:

	December 31,	
	2023	2022
Common stock authorized	300,000,000	300,000,000
Common stock issued and outstanding	67,707,432	66,512,011
Common stock authorized and reserved for future issuances:		
Common stock reserved for the exercise of stock options	9,823,248	8,480,950
Common stock reserved for the unvested restricted stock units	1,112,542	740,297
Common stock reserved for future issuance of share-based awards	5,253,507	2,817,751
Total common stock authorized and reserved for future issuance	16,189,297	12,038,998
Unreserved common stock available for future issuance	216,103,271	221,448,991

In January 2022, the Company completed its IPO in which the Company issued and sold 11,369,369 shares of its common stock at a price of $19.00 per share. After deducting underwriting discounts and commissions and estimated offering expenses, the Company received net proceeds of approximately $196.4 million. Upon the completion of the IPO, all of the Company's outstanding shares of preferred stock were converted into shares of its common stock.

In October 2022, the Company completed a follow-on public offering in which the Company issued 7,697,812 shares of its common stock at a price of $32.00 per share. After deducting underwriting discounts and commissions and estimated offering expenses, the Company received net proceeds of approximately $230.6 million.

13. STOCK OPTION AND GRANT PLAN

***Stock Incentive Plan*—**In January 2022, the Company's board of directors adopted, and its stockholders approved the 2022 Stock Option and Incentive Plan, or 2022 Plan, which became effective on January 5, 2022, at which point no further grants would be made under the 2015 Stock Option and Restricted Stock Plan, or 2015 Plan. Under the 2022 Plan, the Company may grant incentive stock options, or ISOs, non-statutory stock options, stock appreciation rights, restricted stock units, restricted stock awards and other stock-based awards. As of December 31, 2023, there were 3,454,220 shares available for future issuance under the 2022 Plan. The options issued under the 2022 Plan expire 10 years following the date of grant. Stock options and restricted stock units typically vest over 4 years. We recognize the compensation cost of awards subject to service-based vesting conditions over the requisite service period, which is generally equal to the vesting period of the respective award.

Initially, subject to adjustment as provided in the 2022 Plan, the aggregate number of shares of the Company's common stock available for issuance under the 2022 Plan is 7,650,000. The number of shares of the Company's common stock reserved for issuance under the 2022 Plan will automatically increase on January 1 of each year commencing January 1, 2023, by 5% of the total number of shares of the Company's common stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by the Company's board of directors. The maximum current number of shares that may be issued pursuant to the exercise of ISOs under the 2022 Plan is 7,650,000.

The maximum number of shares of the Company's common stock subject to awards granted under the 2022 Plan or otherwise during a single calendar year to any individual nonemployee director, taken together with any cash fees paid by the Company to such nonemployee director during the calendar year for serving on the Company's board of directors, will not exceed $750,000 in total value, or, with respect to the calendar year in which a nonemployee director is first appointed or elected to the Company's board of directors, $1,000,000.

All options and awards granted under the 2015 Plan consisted of the Company's common stock. As of January 6, 2022, no additional stock awards have been or will be granted under the 2015 Plan. Although the 2015 Plan was terminated as to future awards in January 2022, it continues to govern the terms of options that remain outstanding under the 2015 Plan.

***Inducement Plan*—**In July 2023, the Company's board of directors adopted the Amylyx Pharmaceuticals, Inc. 2023 Inducement Plan, or the Inducement Plan, to grant equity awards to induce highly-qualified prospective officers and employees who are not currently employed by the Company to accept employment and provide them with a proprietary interest in the Company. The Company has reserved 750,000 shares of its common stock that may be issued under the Inducement Plan. As of December 31, 2023, there were 529,167 shares available for future issuance under the Inducement Plan.

***Employee Stock Purchase Plan*—**In January 2022, the Company's board of directors adopted the 2022 Employee Stock Purchase Plan, or ESPP, which was subsequently approved by the Company's stockholders. The ESPP initially reserves and authorizes the issuance of up to a total of 605,000 shares of common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase each January 1, beginning on January 1, 2023 and each January 1 thereafter through January 1, 2032, by the least of (i) 1% of the outstanding number of shares of our common stock on the immediately preceding December 31, (ii) 1,210,000 shares or (iii) such number of shares of common stock as determined by the ESPP administrator. The initial purchase period under the ESPP has not yet commenced. As of December 31, 2023, there were 1,270,120 shares available for future issuance under the ESPP.

General Option Information

The Company estimates the fair value of stock option awards on the grant date using the Black-Scholes option pricing model with the following weighted-average assumptions:

	Year Ended December 31,		
	2023	2022	2021
Grant price	$ 29.58	$ 20.29	$ 7.69
Risk-free interest rate	3.77%	1.97%	1.01%
Expected term (in years)	6.05	6.07	5.73
Expected volatility	70.35%	88.75%	81.61%
Dividend yield	0.00%	0.00%	0.00%

The per share weighted average grant date fair value of stock options granted during the year ended December 31, 2023, 2022 and 2021 was $19.56, $15.10 and $5.25, respectively.

A summary of option activity for the year ended December 31, 2023, is as follows:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2022	8,480,950	$ 13.19	8.2	$ 201,765
Granted	2,864,696	$ 29.55		
Exercised	(1,010,376)	$ 5.66		
Cancelled or forfeited	(512,022)	$ 19.86		
Outstanding at December 31, 2023	9,823,248	$ 18.39	7.9	$ 27,639
Exercisable at December 31, 2023	3,877,634	$ 12.58	7.0	$ 18,240
Unvested at December 31, 2023	5,945,614	$ 22.17	8.5	$ 9,399

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock. The aggregate intrinsic value of options exercised during the years ended December 31, 2023, 2022 and 2021 was $20.6 million, $14.2 million and $6.2 million respectively.

The total fair value of stock options vested during the years ended December 31, 2023, 2022 and 2021 was $31.2 million, $8.8 million and $1.3 million, respectively.

Restricted Stock Unit Activity

A summary of restricted stock unit activity for the year ended December 31, 2023, is as follows:

	Number of shares	Weighted Average Grant Date Fair Value
Nonvested as of December 31, 2022	740,297	$ 20.02
Granted	637,664	$ 29.04
Vested	(185,045)	$ 20.02
Forfeited	(80,374)	$ 25.41
Nonvested as of December 31, 2023	1,112,542	$ 24.80

***Stock-Based Compensation Expense*—**The Company recorded stock-based compensation expense in the following expense categories of its statements of operations:

	Year Ended December 31,		
	2023	2022	2021
		(in thousands)	
Research and development expenses	$ 9,843	$ 5,639	$ 888
Selling, general and administrative expenses	27,318	16,075	2,248
Total stock-based compensation	$ 37,161	$ 21,714	$ 3,136

The Company capitalized stock-based compensation expense of $0.4 million, less than $0.1 million, and zero for the years ended December 31, 2023, 2022 and 2021, respectively. Stock-based compensation recognized through cost of sales were $0.2 million, less than $0.1 million, and zero for years ended December 31, 2023, 2022 and 2021, respectively.

The following table summarizes stock-based compensation by type of award:

	Year Ended December 31,		
	2023	2022	2021
		(in thousands)	
Stock options	$ 30,500	$ 18,844	$ 3,136
Restricted stock units	6,661	2,870	—
Total stock-based compensation expense	$ 37,161	$ 21,714	$ 3,136

The following table summarizes unrecognized stock-based compensation expense as of December 31, 2023, by type of awards, and the weighted-average period over which that expense is expected to be recognized. The total unrecognized stock-based compensation expense will be adjusted for actual forfeitures as they occur.

	As of December 31, 2023	
	Unrecognized Expense	Weighted-average Recognition Period
	(in thousands)	(in years)
Stock options	$ 78,966	2.63
Restricted stock units	$ 21,693	2.91

14. INCOME TAXES

The components of net loss before the provision for income taxes are as follows:

	Year Ended December 31,		
	2023	2022	2021
		(in thousands)	
U.S.	$ 52,263	$ (198,704)	$ (87,904)
Non-U.S.	2,034	1,103	(27)
Income (loss) before income taxes	$ 54,297	$ (197,601)	$ (87,931)

The provision for income taxes is as follows:

	Year Ended December 31,		
	2023	2022	2021
		(in thousands)	
Current income tax provision			
U.S. - Federal	$ 1,219	$ —	$ —
U.S. - State	2,839	—	—
Non-U.S.	1,192	774	—
	$ 5,250	$ 774	$ —
Deferred income tax provision			
Non-U.S.	$ (224)	$ —	$ —
Provision for income taxes	$ 5,026	$ 774	$ —

A reconciliation of the Company's effective income tax rate to the U.S. statutory federal income tax rate of 21% for the years ended December 31, 2023, 2022 and 2021 is as follows:

	Year Ended December 31,		
	2023	2022	2021
Tax at U.S. statutory tax rate	21.0%	21.0%	21.0%
State income tax benefit	3.3%	3.9%	4.0%
Research and development tax credits	(12.6)%	1.4%	1.5%
Executive Compensation	6.2%	(0.5)%	—%
Uncertain Tax Positions	2.1%	(0.2)%	(0.2)%
Valuation allowances	(12.2)%	(25.5)%	(24.4)%
Other	1.5%	(0.5)%	(1.9)%
Effective income tax rate	9.3%	(0.4)%	0.0%

Deferred tax assets and liabilities were as follows:

	Year Ended December 31,	
	2023	2022
	(in thousands)	
Deferred tax assets:		
Federal net operating loss carryforwards	$ 14,667	$ 42,673
State net operating loss carryforwards	8,164	10,628
Capitalized research and development costs	39,297	18,079
Inventory	1,090	5,721
Tax credits	8,039	5,581
Stock Based Compensation	3,792	1,804
Accruals and other	10,425	7,480
Total deferred tax assets	$ 85,474	$ 91,966
Valuation allowance	(83,922)	(90,587)
Net total deferred tax assets	$ 1,552	$ 1,379
Deferred tax liabilities:		
Other	(1,328)	(1,379)
Total deferred tax liabilities	$ (1,328)	$ (1,379)
Net deferred tax assets	$ 224	$ —

On a periodic basis the Company reassess the valuation allowance that has been established, weighing all positive and negative evidence. In 2023, the Company reassessed the valuation allowance and considered negative evidence, including cumulative losses over the three years ended December 31, 2023, and positive evidence, including recent regulatory approvals of ALBRIOZA and RELYVRIO, 2023 profitability and positive cash flow, and realization of a portion of prior year U.S. federal and state NOL and research and development tax credit carryforwards. After assessing both the negative and positive evidence, the Company concluded that a full valuation should continue to be retained against the net deferred tax assets as of December 31, 2023. It is possible that all or a portion of the valuation allowance will be released in the near-term. The release of the valuation allowance, as well as the exact timing and the amount of such release, continue to be subject to, among other things, levels of profitability, revenue growth, clinical program progression and expectations regarding future profitability.

As of December 31, 2023 and 2022, the Company had federal NOL loss carryforwards of approximately $69.8 million and $203.2 million, respectively, and state NOL loss carryforwards of approximately $124.6 million and $164.1 million, respectively, which are available to reduce future taxable income. All U.S. federal NOL carryforwards as of December 31, 2023 carry forward indefinitely. Of the $124.6 million state NOL carryforwards, $82.8 million relate to Massachusetts and begin to expire in 2035. As of December 31, 2023 and 2022, the Company also had federal tax credits of $6.8 million and $4.6 million, respectively, and state tax credits of $1.6 million and $1.2 million, respectively. The tax credit carryforwards will expire at various dates beginning in 2035.

The utilization of NOL and research and development tax credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the IRC. Ownership changes occurred in the years ended December 31, 2016 and

2023. These ownership changes do not impact the Company's overall ability to utilize NOL carryforwards and research and development tax credit carryforwards but may limit the amount that can be utilized annually to offset future taxable income.

The following table reflects the roll-forward of the Company's valuation allowance for the years ended December 31, 2023, 2022 and 2021:

	Year Ended December 31,		
	2023	2022	2021
		(in thousands)	
Valuation allowance at beginning of year	$ 90,587	$ 40,346	$ 18,900
(Decreases) increases recorded to income tax provision	(6,665)	50,241	21,446
Valuation allowance at end of year	$ 83,922	$ 90,587	$ 40,346

The decrease in the valuation allowance recorded during the year primarily relates to taxable income resulting pre-tax profits earned in 2023 and increased as a result of required capitalization of research and development costs.

The Company accounts for uncertainty in income taxes under the provisions of ASC 740 which defines the thresholds for recognizing the benefits of tax return positions in the consolidated financial statements as "more likely than not" to be sustained by the taxing authority. The tax benefit is measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate settlement. A reconciliation of the beginning and ending amount of gross unrecognized tax benefits is as follows:

	Year Ended December 31,		
	2023	2022	2021
		(in thousands)	
Balance at beginning of the period	$ 1,013	$ 564	$ 349
Increases (decreases) related to tax positions taken during prior years	271	(32)	—
Increases related to tax positions taken during the current year	925	481	215
Balance at end of the period	$ 2,209	$ 1,013	$ 564

The Company has reviewed the tax positions taken, or to be taken, in its tax returns for all tax years currently open to examination by a taxing authority. All uncertain tax benefits, if recognized, would impact the effective tax rate if recognized, offset by changes to the Company's valuation allowance which also would impact the effective tax rate. The Company does not expect the amount of unrecognized tax benefits to materially change over next 12 months. The Company accrues interest and penalties related to unrecognized tax benefits as a component of its provision for income taxes. The Company did not recognize any interest or penalties related to uncertain tax positions during the years ended December 31, 2023, 2022 and 2021.

The Company files U.S. federal, foreign and state income tax returns in various jurisdictions. The status of limitations varies by jurisdiction. There are currently no federal or state audits or examinations in process.

15. EMPLOYEE BENEFIT PLANS

The Company maintains a tax-qualified retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax-advantaged basis. Plan participants are able to defer eligible compensation subject to applicable annual IRC limits. For the year ended December 31, 2022, the Company provided a safe-harbor contribution of 3% of employee compensation to employees who satisfy the minimum service requirements. Effective October 1, 2023, the safe-harbor contribution was increased to 5%. The Company made $2.3 million and $1.2 million of safe-harbor contributions for the years ended December 31, 2023 and 2022, respectively.

16. NET INCOME (LOSS) PER SHARE

Net Income (Loss) per Share

Basic earnings per share is computed by dividing net income (loss) by the weighted average number of common shares outstanding during the period. Diluted earnings per share is calculated based on the combined weighted average

number of common shares and potentially dilutive shares, which include the assumed exercise of employee stock options and unvested restricted stock units. In computing diluted earnings per share, the Company utilizes the treasury stock method.

A summary of the numerator and denominators used in the computation of earnings per share follows (in thousands, except share and per share data:

	December 31,		
	2023	2022	2021
Numerator:			
Net income (loss)	$ 49,271	$ (198,375)	$ (87,931)
Denominator:			
Weighted-average shares used to compute basic net income (loss) per share	67,234,465	58,495,587	6,586,349
Dilutive effect of employee stock options and restricted stock units	2,756,875	—	—
Weighted-average shares used to compute diluted net income (loss) per share	69,991,340	58,495,587	6,586,349
Net income (loss) per share			
Basic	$ 0.73	$ (3.39)	$ (13.35)
Diluted	$ 0.70	$ (3.39)	$ (13.35)

Because the Company reported a net loss for the twelve months ended December 31, 2022 and 2021, basic and diluted net loss per share were the same. All stock options and restricted stock units were excluded from the computation of diluted weighted-average shares outstanding because such securities would have an antidilutive impact for the twelve months ended December 31, 2022 and 2021. The following stock options and restricted stock units outstanding at each period end have been excluded from the calculation of diluted net income (loss) per share because their inclusion would have been antidilutive:

	December 31,		
	2023	2022	2021
Options to purchase common stock	5,775,303	8,480,950	5,339,011
Restricted stock units	543,233	740,297	—
Redeemable convertible preferred stock	—	—	39,474,330
Total excluded common stock equivalents	6,318,536	9,221,247	44,813,341

17. RELATED PARTY TRANSACTIONS

Convertible Notes

In connection with the issuance of the 2021 Notes, the Company issued, in aggregate, $14.3 million of convertible promissory notes to Morningside Ventures Investments Limited, and certain members of the board of directors of the Company. Morningside Ventures Investments Limited was a 5% significant stockholder of the Company at the time of the transaction. These notes were issued under the same terms and conditions as the 2021 Notes (see Note 8).

Supplier Agreements

In the ordinary course of business, the Company may purchase materials or supplies or services from entities that are associated with a party that meets the criteria of a related party of the Company. These transactions are reviewed quarterly and to date have not been material to the Company's consolidated financial statements.

18. COMMITMENTS AND CONTINGENCIES

***Legal Proceedings*—**As of December 31, 2023, the Company is not a party to any material legal proceedings. At each reporting date, the Company evaluates whether or not a potential loss amount or potential range of loss is probable and reasonably estimated under the provisions of the authoritative guidance that addresses accounting for contingencies. The Company recognizes expenses for its costs related to its legal proceedings, as incurred.

***Royalty Payments*—**Between August 2016 and February 2019, the Company entered into grant agreements with the ALS Association, ALS Finding a Cure Foundation, Alzheimer's Drug Discovery Foundation, Alzheimer's Association and

Cure Alzheimer's Fund, or Grantors. Under the terms of the agreements, the Company was granted, in aggregate, $4.3 million. These grants were provided to the Company for the purpose of furthering the research and development of AMX0035 as a therapeutic benefit for ALS and Alzheimer's disease. Under the terms of the arrangements, the Company would receive a tranche of funds as it completed certain milestones. Pursuant to the terms of the grant agreements, the Company has certain payment obligations that are contingent upon future events such as the achievement of commercialization or the receipt of proceeds from a revenue generating transaction resulting from the projects for which the grants are used for.

Pursuant to the terms of the respective grant agreements among the Company, ALS Association and ALS Finding a Cure, the Company will be required to make royalty payments to each Grantor in the total amount equal to 150% of the grant received. The royalty payments will be achieved through a combination of the following payment methods: (i) an annual installment payment of 3% of net sales of any products developed under the project for which the grant was used for and (ii) 3% of cash proceeds resulting from revenue generating transaction under the project for which the grants are used for. During the years ended December 31, 2023, 2022 and 2021, the Company recorded $3.1 million, $1.4 million and zero in royalty expense, respectively, which is included in cost of sales in the consolidated financial statements. As of December 31, 2023, no further royalties remain to be accrued under the grant agreements with the ALS Association and ALS Finding a Cure Foundation.

Under the terms of the respective grant agreements among the Company, Alzheimer's Drug Discovery Foundation, the Alzheimer's Association, and Cure Alzheimer's Fund, the Company will make royalty payments up to the maximum amount of $15.0 million to each Grantor (or $45.0 million in aggregate). The royalty payment will be made through a combination of the following payment methods: (i) 4% of annual net sales of any product commercialized from the project for which the grant was used for and directly related to the treatment of the Alzheimer's disease and (ii) 15% of all royalties and cash proceeds resulting from revenue generating transactions associated with the projects for which the grants were used for under the grant agreements. As the conditions that would trigger royalty payments under the agreements have not occurred, no amounts have been recorded in the consolidated financial statements for the years ended December 31, 2023 and 2022.

***Purchase Commitments*—**The Company enters into agreements in the normal course of business with contract manufacturing organizations for raw material purchases and manufacturing services. As of December 31, 2023, the Company had committed approximately $195.0 million under these agreements related to raw material purchases and manufacturing services, which are expected to be paid through 2028.

19. SUBSEQUENT EVENTS

On February 9, 2024, a putative class action lawsuit was filed in the U.S. District Court for the Southern District of New York against the Company and certain of its current and former officers (*Shih v. Amylyx Pharmaceuticals, Inc., et al.*, Case Number 1:24-CV-00988 (the "Shih Complaint"). The Shih Complaint asserts a claim against all defendants for alleged violations of Section 10(b) of the Exchange Act and Rule 10b-5 promulgated thereunder and a claim under Section 20(a) against certain current and former officers as alleged controlling persons. The Shih Complaint alleges that defendants made materially false and misleading statements related to the commercial results and prospects for RELYVRIO. The Shih Complaint seeks unspecified damages, interest, costs and attorneys' fees, and other unspecified relief that the court deems appropriate. The Company intends to defend against the Shih Complaint vigorously. At this time, an estimate of the impact, if any, of these claims cannot be made.

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BOARD OF DIRECTORS

Joshua Cohen
Co-Chief Executive Officer and Director

Justin Klee

Co-Chief Executive Officer and Director

Karen Firestone
Chairman, CEO, and Co-Founder of Aureus Asset Management

Paul Fonteyne
Former Chair and CEO of Boehringer-Ingelheim, USA

George Mclean Milne, Jr., Ph.D.
Former Executive Vice President of Global Research and Development and President, Worldwide Strategic and Operations Management of Pfizer Inc.

Daphne Quimi
Chief Financial Officer of Amicus Therapeutics

Bernhardt Zeiher, MD.
Director of Entrada Therapeutics and Former Chief Medical Officer of Astellas Pharma

EXECUTIVE OFFICERS

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Co-Chief Executive Officer and Director

Justin Klee

Co-Chief Executive Officer and Director

James Frates

Chief Financial Officer

Gina M. Mazzariello
Chief Legal Officer and General Counsel

Camille L. Bedrosian, M.D.
Chief Medical Officer

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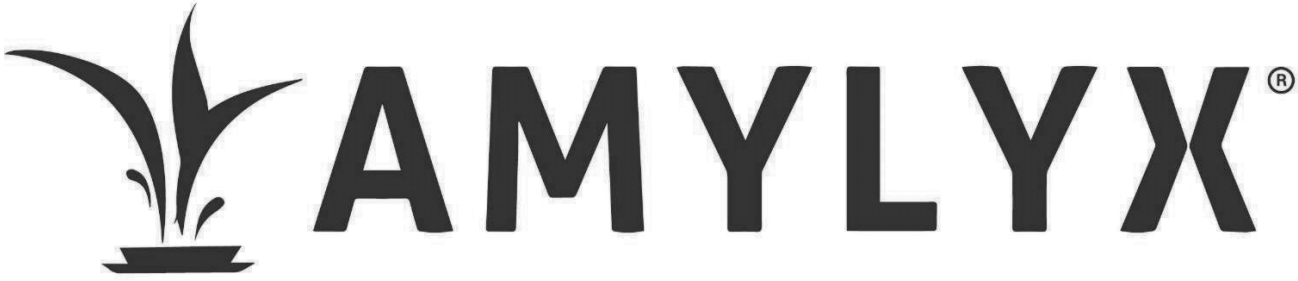
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