2022 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, 2022

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, 2022, was $788.1 million.

The number of shares of Registrant's Common Stock outstanding as of March 8, 2023 was 66,716,388.

DOCUMENTS INCORPORATED BY REFERENCE

The registrant intends to file a definitive proxy statement pursuant to Regulation 14A relating to the 2023 Annual Meeting of Stockholders within 120 days of the end of the registrant's fiscal year ended December 31, 2022. Portions of such definitive proxy statement for the 2023 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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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 and obtain additional regulatory approvals of AMX0035 and any future product candidates;
- our ability to successfully commercialize and market AMX0035 and any 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 potential market size, opportunity, demand and growth potential for AMX0035 and any 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 future product candidates, if approved;
- our ability to obtain funding for our operations;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, including our Phase 3 clinical trial of AMX0035 for the treatment of amyotrophic lateral sclerosis, or ALS, known as the PHOENIX trial, and our research and development activities;
- our ability to retain the continued service of our key professionals and to identify, hire and retain additional qualified professionals;
- our ability to continue to advance AMX0035 and advance any future product candidates into, and successfully complete, 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 decision by the European Medicines Agency, or EMA, regarding whether to approve AMX0035 for the treatment of adults with ALS;
- 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 product candidates, if approved;
- the rate and degree of market acceptance of AMX0035 and any future product candidates by physicians, patients, third-party payors and others in the medical community;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our 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 and needs for additional financing;
- our financial performance;
- the effects of rising inflation rates and the impact on operating costs, liquidity and access to credit on any of the foregoing or other aspects of our business operations;

- the effects of global economic uncertainty and financial market volatility caused by economic effects of rising inflation and interest rates, the COVID-19 pandemic, geopolitical instability, changes in international trade relationships and conflicts, such as the ongoing conflict between Russia and Ukraine, 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.

Introduction

Our mission is to one day end the suffering caused by neurodegenerative diseases. We are committed to supporting and creating more moments for the neurodegenerative disease community through the discovery and development of innovative new treatments. Our first product, RELYVRIO® (sodium phenylbutyrate and taurursodiol), previously known as AMX0035 in the U.S., is approved in the U.S. for the treatment of ALS in adults. AMX0035 is also approved with conditions by Health Canada and marketed as ALBRIOZA for the treatment of ALS in Canada.

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. We believe AMX0035 is the first drug candidate to show both a functional and survival benefit in a large-scale clinical trial of patients with ALS. The results of our Phase 2 clinical trial of AMX0035, known as the CENTAUR trial, were published in the *New England Journal of Medicine*, in two publications in *Muscle & Nerve*, and in the *Journal of Neurology*, *Neurosurgery*, and *Psychiatry*.

AMX0035 is a dual UPR-Bax apoptosis inhibitor composed of PB and TURSO (also known as TUDCA). 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, endoplasmic reticulum, or ER, stress, mitochondrial dysfunction, oxidative stress and disease-specific models of a variety of other conditions, as well as in vivo models of ALS, Alzheimer's disease, or AD, and multiple sclerosis, or MS. We believe AMX0035 has the potential to be a foundational therapy, 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 pursuing ALS as our first indication as it is a disease of rapid and profound neurodegeneration, and we are focused on the development and potential commercialization of AMX0035 for ALS globally.

We have received marketing authorization with conditions by Health Canada for ALBRIOZA for the treatment of ALS. We announced commercial availability of the product in July 2022. We have submitted to and received from the national reimbursement authorities, known as the Canadian Agency for Drugs and Technologies in Health, or CADTH, and l'Institut national d'excellence en santé et en services sociaux, or INESSS, recommendations regarding reimbursement for ALBRIOZA by the Canadian provincial governments, and are negotiating with both public and private payers to obtain reimbursement coverage.

We received approval by the FDA for RELYVRIO in September 2022, and commercial product was first available in October 2022. This decision represented Amylyx' first regulatory approval of AMX0035 in the U.S. and its second worldwide.

We are also actively pursuing regulatory approval of AMX0035 for the treatment of ALS in Europe. Our MAA remains under review by the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA. We submitted a Marketing Authorization Application, or MAA, to the EMA in Europe in the first quarter of 2022, which was validated in the same quarter. We completed the Scientific Advisory Group meeting. Certain major objections remain, and the CHMP has adopted another round of questions as part of the regulatory process. We are now in possession of those questions. In order to respond in accordance with the updated timelines, we now expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest.

In November 2021, we initiated a Phase 3 clinical trial of AMX0035 for the treatment of ALS, known as PHOENIX trial, at clinical trial sites in the U.S. and Europe. On February 2, 2023, we announced completion of enrollment in PHOENIX, which enrolled 664 participants. We anticipate topline results from the PHOENIX trial in mid-2024. This trial is designed to provide further data evaluating the safety and efficacy of AMX0035 over 48 weeks for the treatment of ALS to further support our global regulatory efforts. European participants completing the 48-week trial have the option to enroll in an open label extension (OLE) phase. During this phase, all participants receive AMX0035, and continued safety and efficacy measures will be assessed.

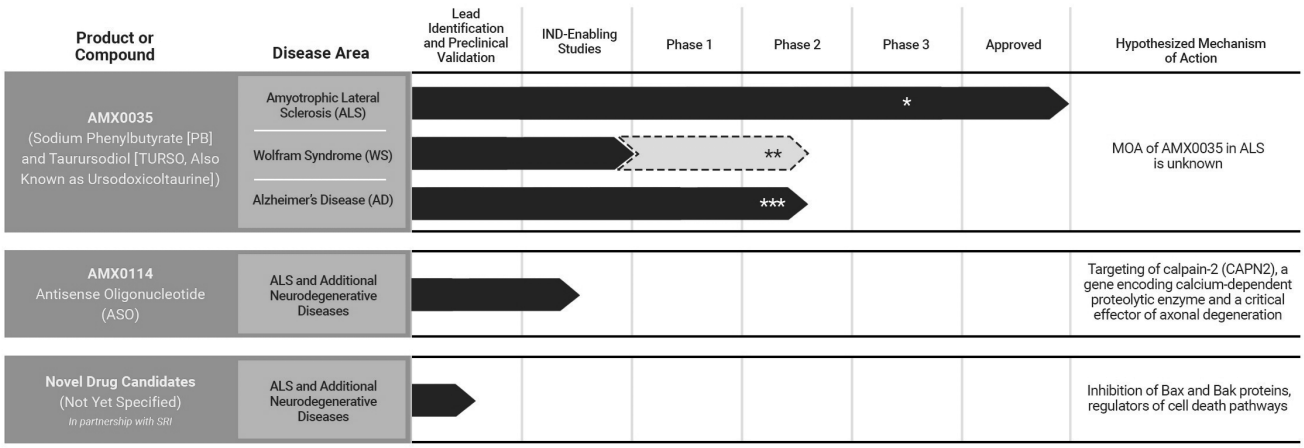
We are also developing AMX0035 for other neurodegenerative diseases by leveraging our deep knowledge of and relationships in the neurodegenerative space. We believe the approach of a dual UPR-Bax apoptosis inhibitor designed to help keep neurons alive could be clinically meaningful for the treatment of other neurodegenerative disease indications in

addition to ALS. Many common and rare neurodegenerative diseases are characterized by substantial neuronal cellular loss, including AD and Wolfram syndrome, as well as Parkinson's Disease, Huntington's Disease, Progressive Supranuclear Palsy, Multi-System Atrophy, and others. We conducted a Phase 2 clinical trial in AD, known as the PEGASUS trial, to obtain safety data along with initial efficacy and biomarker data which could help us prioritize additional indications to pursue with AMX0035. We believe the topline results from the PEGASUS trial, reported in November 2021, provide further biological knowledge about AMX0035 which will help inform future clinical development of AMX0035 for the treatment of AD and in other potential indications. Based on these topline results, AMX0035 met the PEGASUS trial's primary endpoint of safety and tolerability. The 6-month trial was not powered to evaluate differences between groups in efficacy outcomes and no differences were seen in a newly developed composite outcome of cognitive, functional, and imaging measures, or secondary efficacy endpoints of cognition, function, and imaging. In this trial, AMX0035 showed significant effects on biomarkers including neurogranin, YKL-40 or Chitinase 3-like 1 (CHI3L1), and fatty acid binding protein 3 (FABP3). These results build on previously reported findings that AMX0035 exhibited significant effects on the tau protein, tau phosphorylated at threonine 181, and the amyloid beta 42 to 40 (amyloid-ß1-42, amyloid-ß1-40) ratio in cerebrospinal fluid. We will continue to evaluate these data and discuss 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. In March 2023, we completed site activation for a Phase 2 clinical trial of AMX0035 for the treatment of Wolfram syndrome, and expect to enroll the first participant in the near term.

We also intend to prioritize our development efforts around neurodegenerative diseases that result in substantial disability, and ultimately death, and where unmet medical needs are greatest. For example, we recently presented initial *in vitro* data from our new, internally developed compound, AMX0114, targeting Calpain-2, a critical effector of axonal degeneration.

Since our founding in 2013, our goal has been to improve the quality of, and extend, life for patients suffering from neurodegenerative diseases. One of our key strategies towards achieving this goal has been to form direct relationships with patients, their families, advocacy groups, and healthcare professionals to bring much needed innovation to patients. Throughout the development of AMX0035, we have partnered with members of the disease communities we serve, including the ALS Association, the Northeast ALS Consortium, or NEALS, ALS Finding a Cure, the Healey Center at Massachusetts General Hospital, the Cure Alzheimer's Fund, the Alzheimer's Association and the Alzheimer's Drug Discovery Foundation, to ensure our goals are aligned with patient needs. In addition, many of the key opinion leaders in the ALS community were and are investigators in our recent and ongoing trials. These relationships are a cornerstone of our culture and corporate strategy.

Our current pipeline, including the stage of development and approvals of AMX0035 in our target indications, is represented in the table below.



*Therapy approved by the U.S. FDA for the treatment of ALS and approved with conditions by Health Canada. AMX0035 is an investigational drug not approved for use by EMA. MAA validated for review by EMA's CHMP in February 2022. Results from the Phase 3 PHOENIX trial in ALS are anticipated in 2024.

**In March 2023, we completed site activation for a Phase 2 clinical trial of AMX0035 for the treatment of Wolfram syndrome and expect to enroll the first participant in the near term.

***We are currently evaluating 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.

AMX0035 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, (also known as tauroursodeoxycholic acid, or TUDCA), which is a Bax inhibitor that reduces cell death through apoptosis. 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. We believe that our proprietary combination of these two mechanisms of action will allow us to target abnormal cell death to better prevent neurodegeneration than treatment with either mechanism of action alone.

The results of our CENTAUR trial were published in September 2020 in the *New England Journal of Medicine* and in October 2020 in the *Journal of Muscle and Nerve*. Trial results showed that patients receiving AMX0035 experienced statistically significant benefit in retention of function, as measured by the Revised ALS Functional Rating Scale, or ALSFRS-R, as well as nominally significant improvement in overall survival, or OS, when analyzing the full randomized population through the OLE trial in a post hoc analysis (July 20, 2020 and March 1, 2021 data cutoffs). Results of long-term effect of AMX0035 on tracheostomy/ventilation-free survival and hospitalization were published in May 2022 in the *Journal of Neurology Neurosurgery Psychiatry*. AMX0035 was shown to be generally well-tolerated with the prevalence of adverse events comparable across placebo and treatment groups. We believe AMX0035 is the first drug candidate in ALS to demonstrate a statistically significant benefit in function as measured by a prespecified mean rate change in ALSFRS-R and a nominally significant benefit in a longer-term post hoc analysis of OS, which are both important outcomes for people with ALS.

Our Company and Team

Amylyx was founded with the ambitious goal of improving the quality and length of life for patients suffering from neurodegenerative diseases. From a dorm room at Brown University in 2013, our Co-CEOs and Co-Founders, Josh Cohen and Justin Klee set out to determine why neurons die, and have ever since been working to develop AMX0035, which we believe is the first drug candidate to show function and survival benefits in patients with ALS, and other novel therapies. To help realize our goal, we have assembled a team with deep scientific, clinical, business and leadership experience, bolstered by expertise in biotechnology. Our Chief Financial Officer, James Frates, brings over 20 years of experience as the Chief Financial Officer of Alkermes. Our Chief Commercial Officer, Margaret Olinger, brings three decades of expertise in commercial launches and operations, most recently at Alexion. 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 Head of Regulatory Affairs, Tammy Sarnelli, brings more than 30 years of experience from Biogen and other companies in early and late-stage neurology and rare disease development. Our Global Head of Human Resources, Debra Canner, brings over 20 years of experience, having served as the Chief of Human Resources Officer at Akamai and as part of Genzyme. 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 Global Head of Clinical Research & Development and Chief Medical Officer, Patrick D. Yeramian, brings over 30 years of medical and pharmaceutical industry experience. This team brings a diverse set of skills uniquely suited to drive successful commercialization of AMX0035 in ALS while continuing to advance AMX0035 in other indications.

Effective December 1, 2022, Dr. Yeramian shifted to a part-time role and we expect he will ultimately transition out of his role into retirement, although no definitive date has been set for such transition. We have engaged in a search to identify a full-time successor as part of our management succession process.

We recently appointed Karen Firestone to our Board of Directors, effective as of March 16, 2023. Prior to founding her current fund, Aureus, Karen spent 22 years with Fidelity where, among other responsibilities, she managed the Biotechnology sector fund. She has a demonstrated track record of applying her strategic acumen and commercial mindset to drive progress in the space and look forward to her counsel as we continue working toward our mission.

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.*** We received FDA approval in the U.S. for AMX0035 as RELYVRIO for the treatment of ALS in adults in September 2022 and launched RELYVRIO commercially in the U.S. in October 2022. We received marketing authorization with conditions in Canada for ALBRIOZA for the treatment of ALS in June 2022 and

launched ALBRIOZA commercially in Canada in July 2022. We believe our commercial capabilities, coupled with our understanding of the ALS patient and medical community, will enable us to successfully commercialize RELYVRIO for ALS in the U.S. and ALBRIOZA for ALS in Canada and to launch AMX0035 for the treatment of ALS successfully in other key territories, if approved.

- ***Obtaining additional regulatory approvals of AMX0035 for ALS, with an initial focus on Europe.*** In June 2022, AMX0035 received marketing authorization with conditions as ALBRIOZA in Canada for the treatment of ALS and in September 2022, AMX0035 received approval in the U.S. as RELYVRIO for the treatment of ALS in adults. Based on the results from our CENTAUR trial, we have been exploring pathways towards regulatory approval in several additional territories, including Europe. We believe that the CENTAUR trial may also be able to support marketing authorization in Europe and other jurisdictions. We submitted an MAA in Europe in the first quarter of 2022, and we now expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest.
- ***Effectively and efficiently commercializing AMX0035 in other key territories, if approved.*** We are continuing to build our sales team, internal capabilities and outside vendor network to support commercialization in the U.S. and Canada. We will continue to build our capabilities in Europe and other jurisdictions to support commercialization of AMX0035, if approved. For example, in January 2023, we entered into a distribution agreement with Neopharm to commercialize AMX0035 in Israel, Gaza, West Bank and Palestinian Authority, subject to regulatory review and approval. We anticipate that our commercial infrastructure will be scalable for subsequent launches in other key markets if we receive marketing approval in these territories as well.
- ***Maximizing the therapeutic potential of AMX0035 by expanding into additional neurodegenerative diseases.*** We believe the 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 disease pathways, we believe AMX0035 may provide benefit across multiple diseases characterized by neurodegeneration. As we select the next indications for AMX0035 we will prioritize those indications which we believe, if successful, will most rapidly lead to marketed products and to patient benefit. We conducted our Phase 2 PEGASUS clinical trial in AD to obtain safety data along with initial efficacy and biomarker data, which will help us evaluate the development of AMX0035 for the treatment of AD within our clinical development strategy. In March 2023, we completed site activation for a Phase 2 clinical trial of AMX0035 for the treatment of Wolfram syndrome, and expect to enroll the first participant in the near term.
- ***Continuing to cultivate a network of patient advocacy groups, key opinion leaders, research institutions, and healthcare professionals to inform our patient-centric approach.*** We have cultivated a network of key constituents, which we believe will continue to help us to develop therapies in an efficient and impactful manner. Integrating the experiences and insights from these parties, which include patients, their families, and organizations such as the ALS Association, NEALS, ALS Finding a Cure, the Healey Center at Massachusetts General Hospital, the Cure Alzheimer's Fund, the Alzheimer's Association and the Alzheimer's Drug Discovery Foundation, continues to inform our approach to developing therapies that can potentially transform the lives of patients and their families. We intend to continue to engage with each of these constituents through conferences, clinical trials and informal communications as we further develop and pursue commercialization of AMX0035.
- ***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.

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 presented 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. Currently approved therapies for many neurodegenerative diseases are generally only symptom modifying and have demonstrated limited efficacy. There remains an urgent need for novel approaches to address most neurodegenerative diseases, especially for progressive and severe conditions such as ALS.

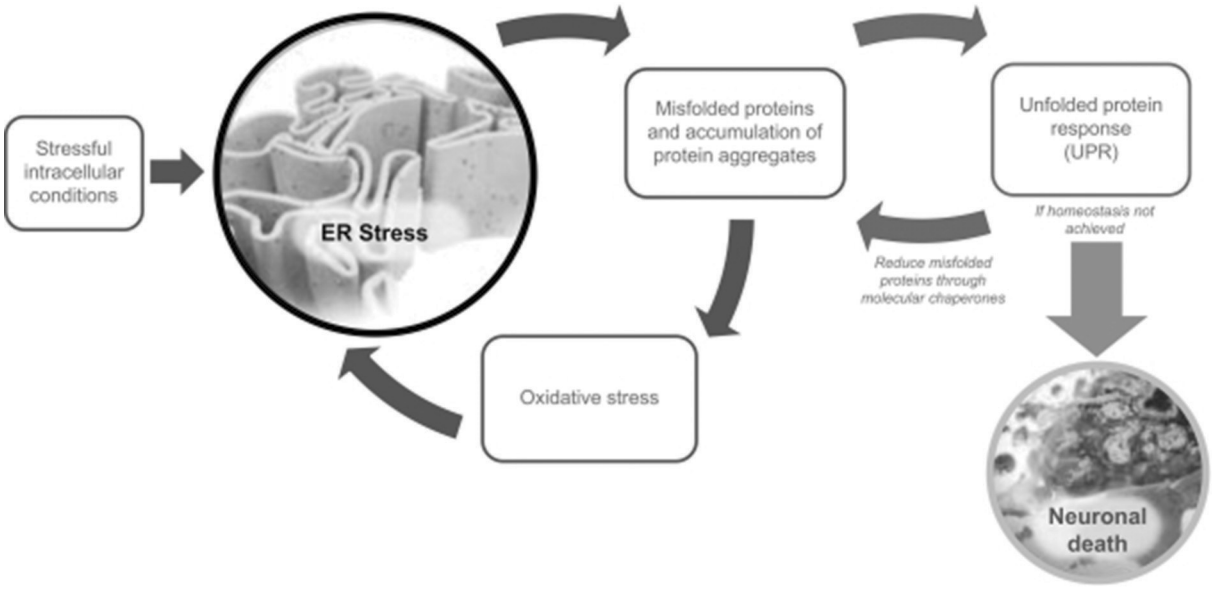
The Role of the Endoplasmic Reticulum and Mitochondria in Neurodegenerative Disease

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 our focus, which is to rescue ER and mitochondrial function, and to protect and preserve neurons.

ER Stress

The ER is responsible for protein and lipid synthesis, folding and quality control of proteins, and storing calcium for cellular energy production by the mitochondria. The ER is also a primary sensor of stressful intracellular conditions, activating a wide number of molecular pathways that belong to a specific process, referred to as the ER stress response, that controls protein homeostasis. ER stress, or dysfunction associated with protein misfolding and aggregation, has been implicated in the pathogenesis of neurodegenerative disease. In neurodegenerative disorders, misfolded proteins and accumulations of protein aggregates can cause oxidative stress and a feedback loop resulting in ER stress. When the ER stress response is activated due to misfolded and aggregated proteins, the UPR, is engaged as a regulatory mechanism to reduce the load of misfolded proteins and restore a healthy cellular state. Molecular chaperones are the critical regulators of protein homeostasis under ER stress. Pathological conditions such as neurodegenerative diseases that disturb protein folding and maturation can trigger ER stress and engage the UPR. When the natural protein homeostasis in the cell cannot be achieved, the UPR triggers cellular death, or apoptosis.

The Role of the ER in Neurodegenerative Disease



Mitochondrial Dysfunction

The mitochondria are a central regulatory point for the control of cell death. When mitochondria detect sufficient cell damage, they signal for the cell to initiate a cell death cascade. Among other steps, this cascade includes the recruitment of a series of apoptotic proteins including Bcl-2-associated X protein, or BAX, the release of cytochrome c from a pore in the mitochondrial membrane called the mitochondrial permeability transition pore, and finally the activation of caspase 3, an executioner protein for apoptosis.

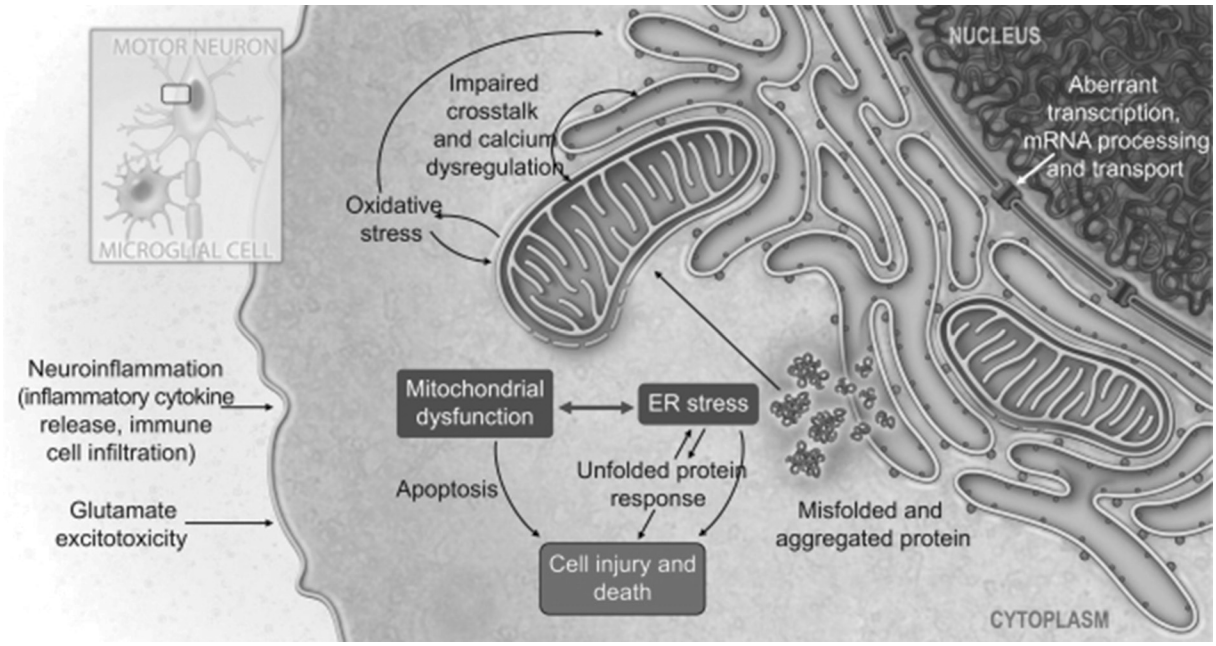
In neurodegenerative diseases, triggers such as altered calcium homeostasis, glutamate excitation of the cell, damage to the mitochondria or mitochondrial DNA and detection of aberrant double-stranded DNA and accumulation of unfolded proteins at the mitochondria all lead to mitochondrially mediated cell death. Inhibition of proteins such as BAX could result in a greater threshold for cell death and longer survival of key neurons implicated in the progression of neurodegenerative disease.

Linkage Between Mitochondria and ER

The mitochondria and the ER are often physically linked by a membrane called the mitochondrial associated ER membrane, or MAM. Through this linkage, calcium and molecules are shuttled between the two organelles. It is our belief that this connection, or crosstalk, allows the cell to integrate responses between the two organelles and that activation of mitochondrial damage pathways will activate the UPR and *vice versa*.

Both the mitochondria and the UPR in the ER can trigger cell death. As such, we believe both pathways are crucial to the pathogenesis of neurodegenerative diseases and both need to be addressed simultaneously to effect a substantial change in survival of neurons undergoing neurodegenerative processes.

The Role of the ER and Mitochondria in Neuron Death

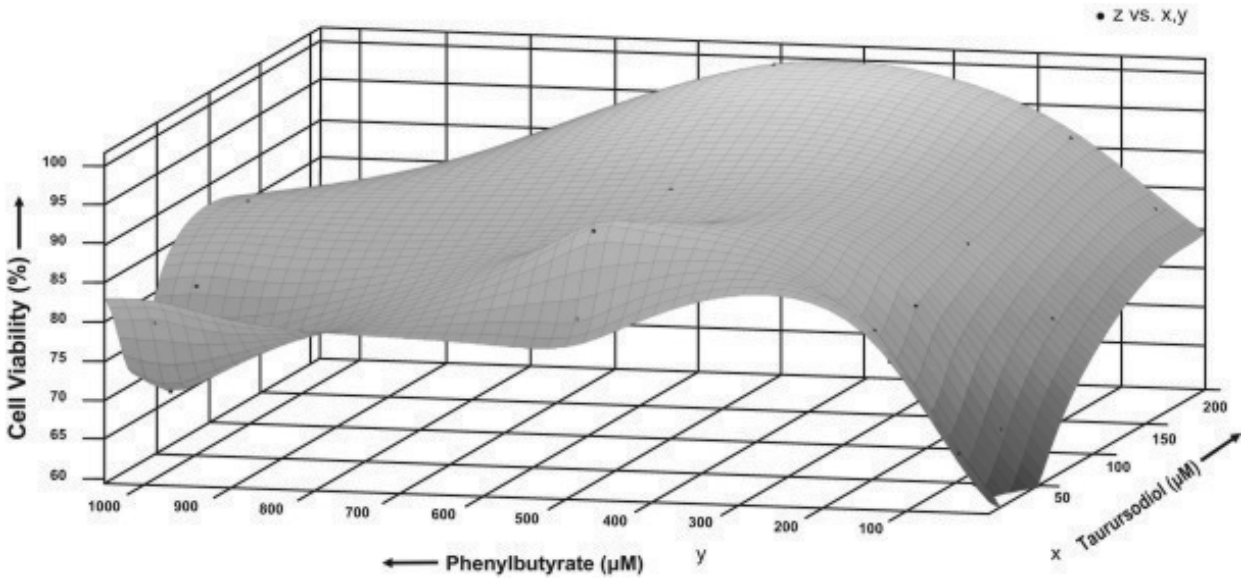


Background and Rationale for AMX0035

We have designed AMX0035 to reduce neuron death through simultaneous mitigation of ER stress and mitochondrial dysfunction. AMX0035 is a coformulation of two small molecules, PB and TURSO. 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*. 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, Progressive Supranuclear Palsy, 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 our proprietary drug candidate, AMX0035.

AMX0035 for the Treatment of ALS

Overview of ALS

We are initially developing AMX0035 for the treatment of ALS, an adult-onset, progressive, and fatal neurodegenerative disorder of the neuromuscular system resulting in muscle weakness and paralysis leading to death. ALS involves the progressive degeneration of motor neurons in the spinal cord and brain that are responsible for controlling voluntary muscle movement. This progressive loss of motor neurons leads to muscle weakness, loss of muscle mass, and inability to control movement. ALS remains universally fatal with a median survival of less than three years from symptom onset and less than two years from diagnosis. Despite being classified as a rare disease by the FDA and the EMA, ALS is considered one of the more common adult-onset neuromuscular diseases worldwide. We estimate based on public sources that there are approximately 29,000 ALS patients in the U.S. More than 30,000 ALS patients are estimated to be located in the EU and the United Kingdom, or UK, and about 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. Due to the two-year median survival of patients diagnosed with ALS, a high proportion of the patient population has been recently diagnosed and a therapy that is able to improve the survival of patients with ALS has the potential to increase the number of patients who are able to continue living with their disease.

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.

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. Only two 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 at once, like AMX0035, aligns with the emerging ALS treatment paradigm.

Clinical Development of AMX0035 for ALS

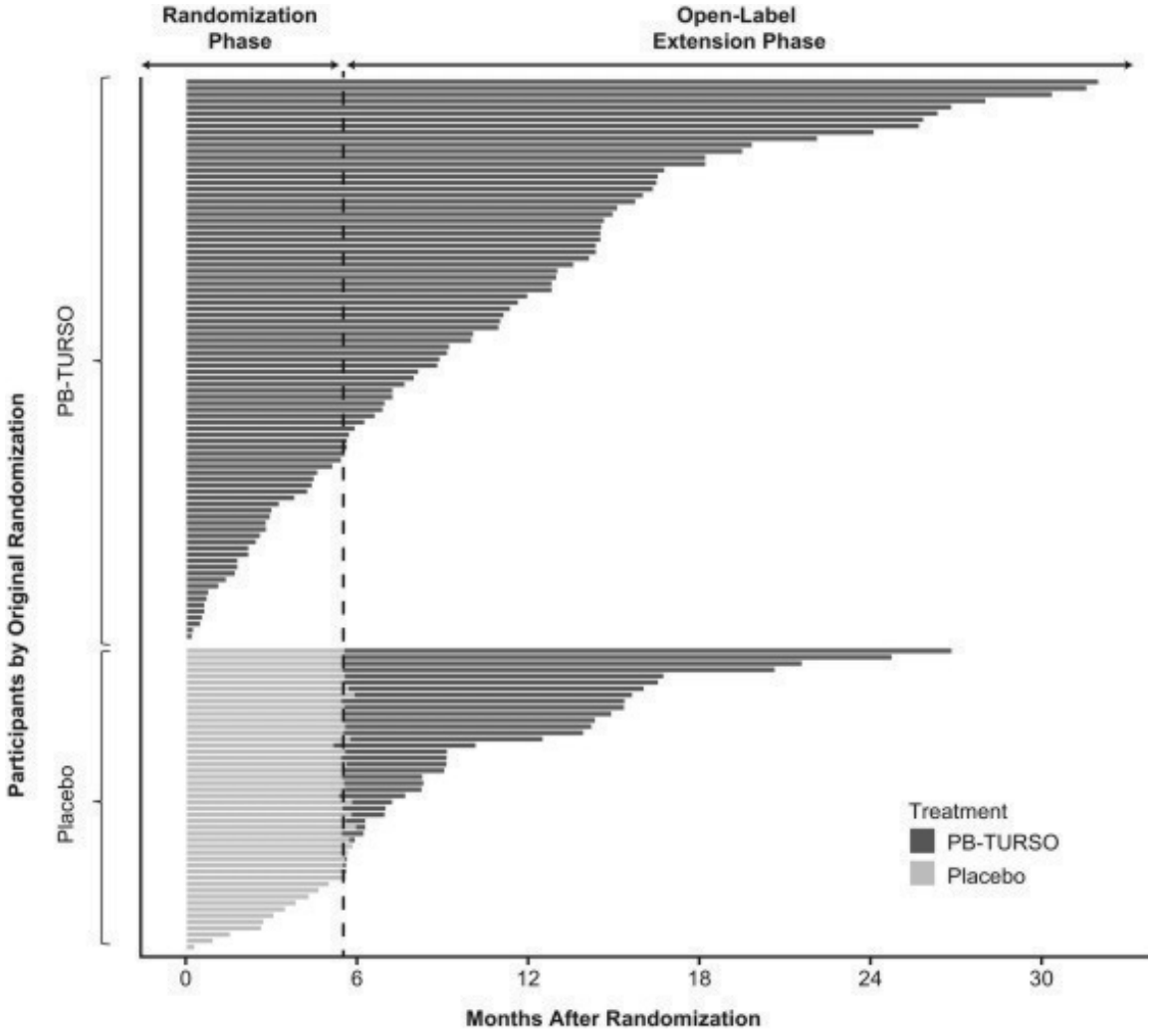
We designed our Phase 2 CENTAUR trial with input from leading ALS experts from NEALS to detect a significant difference between AMX0035 and placebo. The study also provided the option for participants to continue with available approved therapies, riluzole and edaravone, for the duration of the trial. The FDA granted orphan drug designation for AMX0035 for the treatment of patients with ALS in September 2017. The EMA granted orphan designation to AMX0035 for the treatment of patients with ALS in April 2020. 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. We submitted a New Drug Submission, or NDS, in Canada in the second quarter of 2021, an NDA in the U.S. in the fourth quarter of 2021 and an 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 following the second virtual meeting of the FDA's Peripheral and Central Nervous System Drugs Advisory Committee, or the Advisory Committee, held on September 7, 2022. As a result of the FDA's approval of AMX0035, we launched RELYVRIO commercially in the U.S. in October 2022. In Europe, our MAA also remains under review by CHMP. We completed the Scientific Advisory Group meeting. Certain major objections remain, and the CHMP has adopted another round of questions as part of the regulatory process. We are now in possession of those questions. In order to respond in accordance with the updated timelines, we now expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest.

CENTAUR, Our Phase 2 Trial of AMX0035 in ALS

In September 2020, we published detailed results from the Phase 2, randomized, double-blind, placebo-controlled CENTAUR trial. The CENTAUR trial was conducted at 25 centers of the NEALS, 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 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:

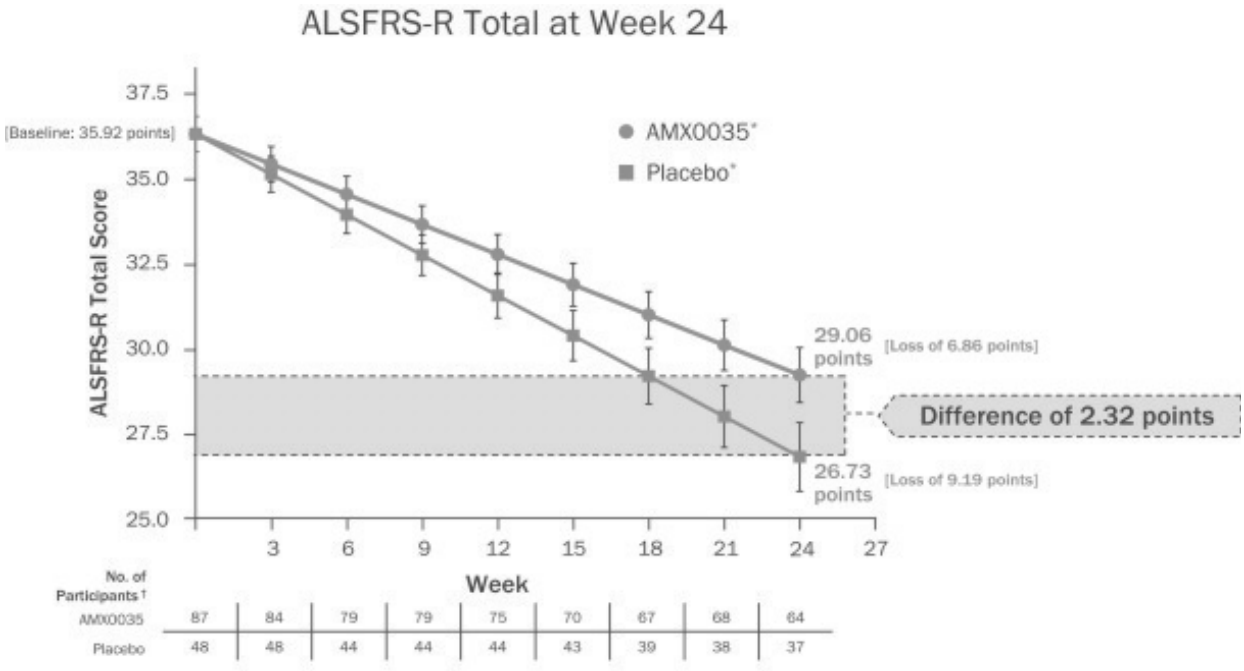


The primary efficacy outcome measure for the CENTAUR trial was the rate of decline in the ALSFRS-R total score. The ALSFRS-R scale is the most widely used ALS rating scale in ALS clinical practice and in ALS clinical trials. It measures patient's functional ability and is broken down into four domains: 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

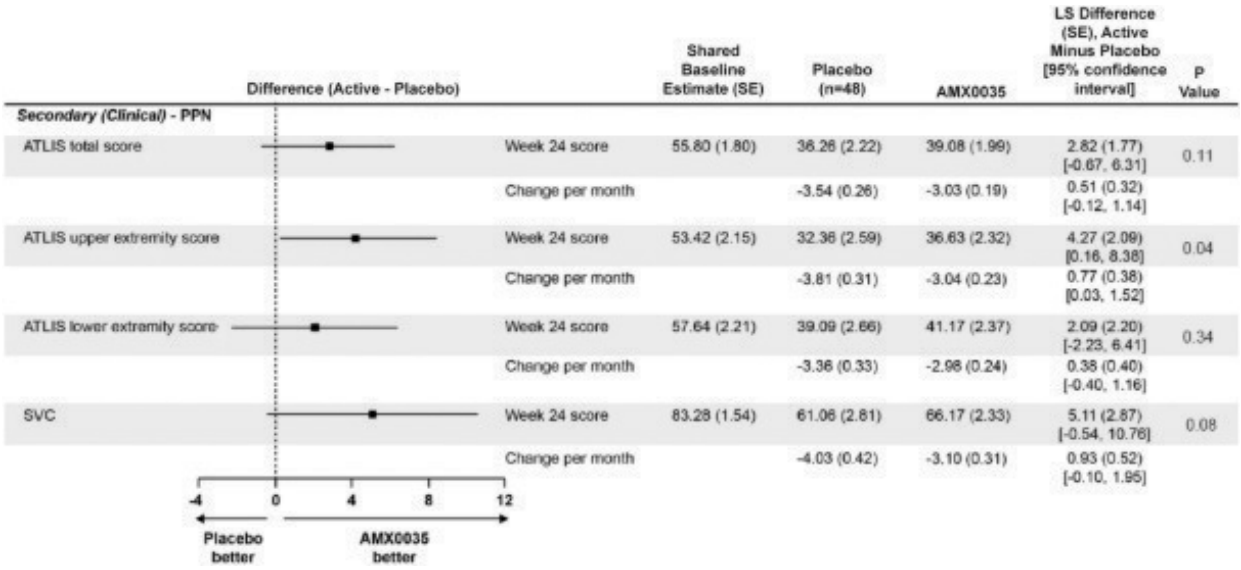
would be considered clinically meaningful, a difference of greater than or equal to 20% in ALSFRS-R total score was considered clinically meaningful by a majority of clinicians and researchers surveyed.



*77% of participants were on riluzole or edaravone at or prior to study entry.
†mITT population (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 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.



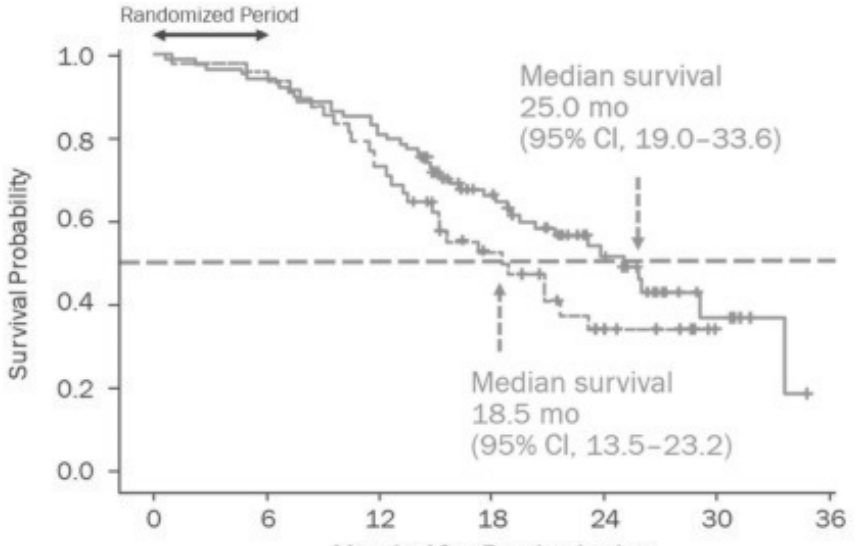
			Shared Baseline Estimate (SE)	Placebo (n=48)	AMX0035	LS Difference (SE), Active Minus Placebo [95% confidence interval]	p Value
Secondary (Clinical) - PPN							
ATLIS total score		Week 24 score	55.80 (1.80)	36.26 (2.22)	39.08 (1.99)	2.82 (1.77) [-0.67, 6.31]	0.11
		Change per month		-3.54 (0.26)	-3.03 (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).

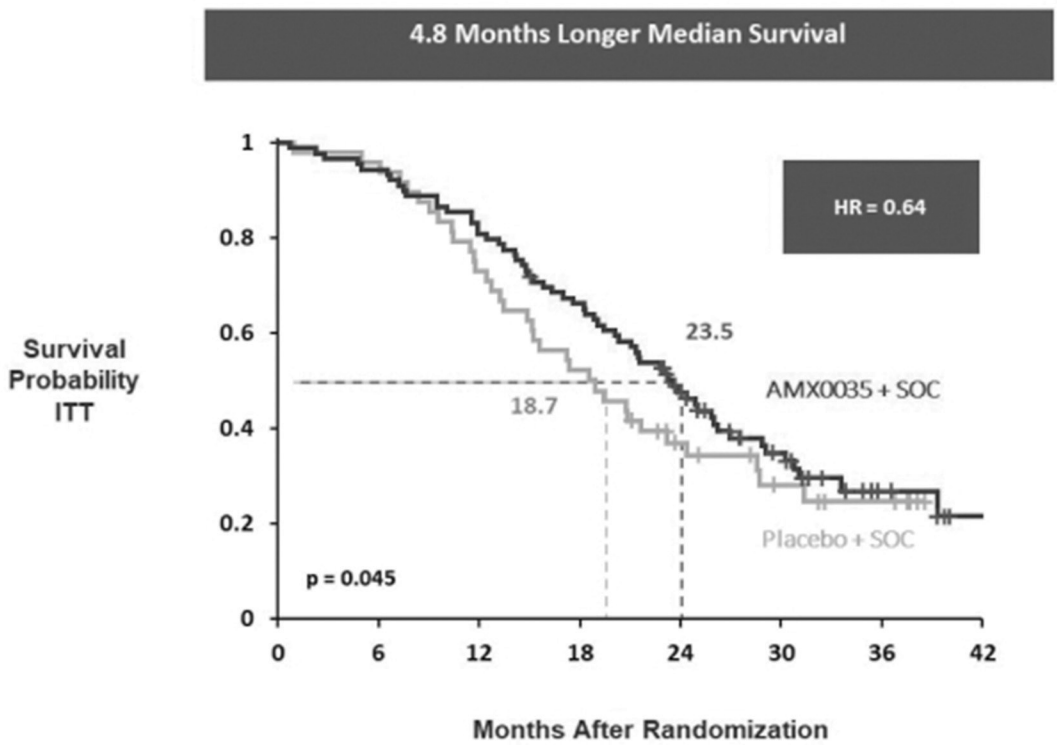
OS was analyzed for all subjects randomized in the CENTAUR trial (ITT analysis) and compared patients originally randomized to AMX0035 (n=89) with those randomized to placebo (n=48). In this post hoc analysis, the vital status of each participant was measured by a participant locating service which used sources such as the U.S. social security death index up to July 20, 2020 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 44% lower among those originally randomized to AMX0035 compared with those originally randomized to placebo (hazard ratio, or HR, of 0.56; a 95% confidence interval, or CI, ranging from 0.34 to 0.92; and a p-value of 0.023). Median survival duration was 25.0 months (95% CI of 19.0 to 33.6 months) in the group previously randomized to AMX0035 and 18.5 months (95% CI of 13.5 to 23.2 months) in the group previously randomized to placebo as seen in the graph below. As reflected in the data tables below, participants originally randomized to AMX0035 showed a longer median survival of 6.5 months (data cutoff July 20, 2020) and 4.8 months (data cutoff March 1, 2021) than those originally randomized to placebo. The FDA considers that the survival data available for RELYVRIO are exploratory and should be interpreted cautiously given the limitations of data collected outside of a controlled study.

Post Hoc Survival Analysis (July 20, 2020 Data Cutoff)



Originally Randomized to:							
AMX0035	No. at Risk	89	84	72	45	21	6	0
Placebo		48	46	35	19	9	0	0
	No. Censored	0	0	0	15	31	42	47
		0	0	0	7	11	20	20
	No. of Events	0	5	17	29	37	41	42
		0	2	13	22	28	28	28

Post Hoc Survival Analysis (March 1, 2021 Data Cutoff)



We also conducted three additional post hoc analyses of AMX0035 survival data which we provided as confirmatory evidence of our findings in the CENTAUR trial and which were provided to the FDA in support of our marketing application for AMX0035. These analyses consisted of the following: a new analysis utilizing a statistical method

to adjust for the effect of treatment crossover; a new 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; and a new analysis comparing observed survival from the CENTAUR treatment group to survival of matched treatment naïve participants from historical clinical trials of ALS.

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.

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

We submitted an NDA to the FDA in the fourth quarter of 2021 and, in September 2022, the FDA approved AMX0035 as RELYVRIO for the treatment of ALS in adults. We submitted an NDS for AMX0035 for the treatment of ALS to Health Canada in the second quarter of 2021, and in June 2022, AMX0035 received marketing authorization with conditions as ALBRIOZA in Canada. We also submitted an MAA for approval of AMX0035 for the treatment of ALS to the EMA CHMP in the first quarter of 2022, and we expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest.

In November 2021, we initiated our global 48-week PHOENIX, randomized, double-blind, placebo-controlled trial at clinical sites in the U.S. and Europe. The PHOENIX trial is designed to provide further data evaluating the safety and efficacy of AMX0035 for the treatment of ALS to further support our global regulatory efforts. Enrollment in this trial was completed in March 2022 in the U.S. and in February 2023 in Europe. We anticipate topline results from the PHOENIX trial in mid-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.

In July 2022, we announced a planned OLE for the PHOENIX trial and in March 2022, we announced the launch of a U.S. expanded access program, or EAP, that the FDA authorized for people with ALS who meet certain eligibility criteria for participation. The EAP will be wound down alongside the commercial launch of RELYVRIO in the U.S., with a target

close of the EAP in the first half of 2023. On February 2, 2023, we announced the completion of enrollment in the PHOENIX trial, which enrolled 664 participants. Because marketing approvals we have obtained may be limited, subject to restrictions or post-approval requirements, we may need to provide post-marketing support in those 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 (ALBRIOZA) for the treatment of ALS 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 anticipate topline results in mid-2024.

Any additional regulatory approvals we may receive may be limited or subject to restrictions or post-approval commitments.

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, Wolfram syndrome, Parkinson's Disease, Huntington's Disease, Progressive Supranuclear Palsy, 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, including the data from our recently completed PEGASUS trial; 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.

In March 2023, we completed site activation for a Phase 2 clinical trial of AMX0035 for the treatment of Wolfram syndrome, and expect to enroll the first participant in the near term.

Clinical Development of AMX0035 for AD

We designed our multicenter, randomized, double-blind, placebo-controlled Phase 2 PEGASUS trial with AD experts to evaluate the safety, tolerability and activity of AMX0035 in patients with late mild cognitive impairment, or MCI, or early-to-moderate dementia. The PEGASUS trial was designed to have broad entry criteria to include participants at different stages of AD to allow us to assess the biological effect of AMX0035 across the spectrum of disease and determine if there are any patients who might see a greater benefit from therapy. Eligible participants (n=95), adults ages 55 to 89 years old, 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.

	PB/TURSO (n=51)	Placebo (n=44)	Overall (N=95)
TEAEs, No. (%)	34 (67)	26 (59)	60 (63)
GI disorders	20 (39.2)	6 (13.6)	26 (27.3)
Drug withdrawn due to AE, No. (%)	4 (8)	1 (2)	5 (5)
Serious TEAEs	3 (6)	1 (2)	4 (4)
Treatment-related serious	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 primary endpoint of the trial was to compare the safety and tolerability of a fixed-dose combination of AMX0035 versus placebo in subjects with MCI (high or intermediate likelihood due to AD) or dementia due to AD over a 24-week treatment period.

The secondary endpoints of the trial were to:

- determine the effects of AMX0035 treatment on whole brain and regional brain atrophy, as assessed by volumetric MRI;
- assess the impact of AMX0035 treatment on clinical symptoms as measured by the Alzheimer's Disease Assessment Scale-Cognitive Subscale, or ADAS-Cog, the Dementia Severity Rating Scale, or DSRS, and the FAQ;
- assess the effect of AMX0035 treatment on measures of neuropsychiatric symptoms, as assessed by the Neuropsychiatric Inventory Questionnaire; and
- measure the effects of AMX0035 treatment on functional MRI measures including connectivity with resting state Blood Oxygenation Level Dependent imaging.

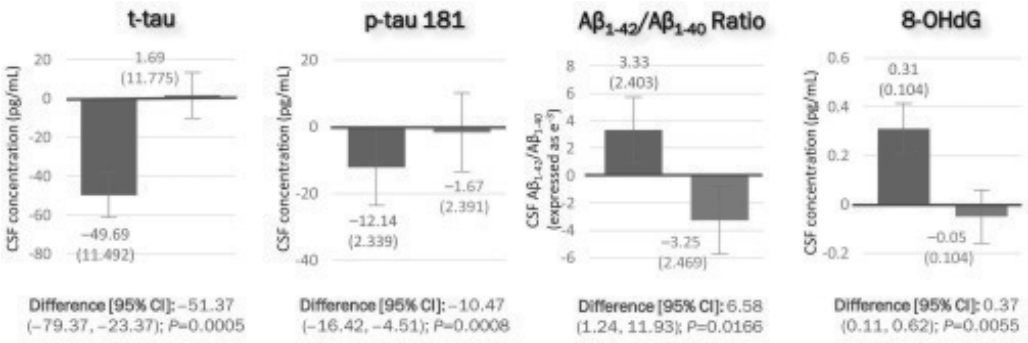
Additionally, the trial evaluated differences between the AMX0035 and placebo arms as measured by GST, a newly developed composite outcome of cognitive, functional, and imaging measures named the Global Statistical Test, or GST, over the 24-week treatment period. The GST is a combination of three change-from-baseline to end-of-study endpoints: Cognition (Modified Alzheimer's Disease Composite Score, or MADCOMS), Function (Functional Activities Questionnaire, or FAQ) and Total Hippocampal Brain Volume (Magnetic Resonance Imaging, or MRI). The GST is calculated for each subject as a mean score across the above three component endpoints for each subject in the trial. This mean score was then analyzed as an efficacy variable.

Finally, 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:

Outcome, LS mean (SE)	Week 24 change from baseline		Difference	Difference 95% Confidence index
	PB/TURSO	Placebo		
GST	0.24 (0.06)	0.17 (0.06)	0.07 (0.08)	(−0.09, 0.23)
MADCOMS	0.91 (0.29)	1.03 (0.30)	−0.12 (0.41)	(−0.93, 0.69)
FAQ	3.22 (0.73)	1.71 (0.79)	1.50 (0.98)	(−0.44, 3.45)
Hippocampal volume[a], mm	-59.6 (23.6)	-53.5 (24.6)	-6.17 (34.5)	(-74.8, 62.4)

[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, which have been and will be informative as we continue clinical development of AMX0035 in AD and other potential indications. We believe these insights will help us to examine any effects of AMX0035 on AD's progression, which could inform future work in AD as well as clinical trial design for other indications. We will continue to evaluate these data and discuss 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 AMX0035 for Wolfram Syndrome

In March 2023, we completed site activation for a Phase 2 clinical trial of AMX0035 for the treatment of Wolfram syndrome, and expect to enroll the first participant in the near term. 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. Amylyx anticipates topline results from the trial in 2024.

Researchers from the Washington University School of Medicine in St. Louis, in collaboration with Amylyx, recently published preclinical data exploring the potential of AMX0035 as a novel therapeutic approach for Wolfram syndrome. 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 Wolfram syndrome. The study

demonstrated that iPSC-derived Wolfram syndrome 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 Wolfram syndrome.

Wolfram syndrome is a rare, pediatric, life-threatening disease thought to be caused by variants in the Wolfram syndrome 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. Wolfram syndrome results in deafness, blindness, ataxia, neurodegeneration and ultimately death. There are currently no drugs approved for Wolfram syndrome.

Wolfram syndrome 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 MAM.

AMX0035 targets pathways central to Wolfram syndrome, including the UPR, and has shown beneficial effects in a variety of models of Wolfram syndrome, 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 Wolfram syndrome, 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 equal to 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 Wolfram Syndrome. 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 Wolfram syndrome 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 Wolfram syndrome, 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 Wolfram syndrome.

Patient Advocacy

The patient advocacy landscapes for ALS and other neurodegenerative diseases are large, and encompass groups at the international, multiregional and country-specific level. We have built strong medical and commercial relationships at the international level, with our current emphasis being on ALS advocacy groups in the U.S., Canada and Europe. We plan to engage country-specific groups in Europe based on clinical trial results, as well as our medical and commercial priorities.

Working with key advocacy groups is critical to our mission, as patients 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 and able to answer questions from their members about PB, TURSO and AMX0035.

We engaged with patient advocacy groups in the U.S. and Europe for feedback on the design of our ongoing global Phase 3 PHOENIX trial of AMX0035 for the treatment of ALS, which is emblematic of the partnerships we are building with the community. In addition, we treat patient advocacy groups as important stakeholders as we address access to AMX0035 outside ongoing clinical trials, such as expanded access and compassionate use programs. We have sought and will continue to seek guidance and insights from as many patient advocacy groups as possible and have plans in place to engage groups on an ongoing basis. These groups have also reviewed messaging and press releases from the company to ensure they take into account the patient voice.

Commercialization

Since obtaining regulatory approval, we have seen strong interest in AMX0035, and we are encouraged by the early success of our commercial launch. We believe the global commercial opportunity for AMX0035 in ALS is driven by its being the first and only treatment for ALS of which we are aware that potentially provides a combination of longer retention of function, improved survival, a generally well-tolerated 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. AMX0035 is also being considered for other neurodegenerative disorders.

ALS is a rare disease, but public sources estimate that ALS affects at least 200,000 people worldwide, and we estimate that there are approximately 29,000 ALS patients in the U.S. More than 30,000 ALS patients are estimated to be living with ALS in the EU and the UK and about 3,000 ALS patients are estimated to be living with ALS in Canada. In the U.S., ALS is treated by neurologists at certified ALS Centers or by other neurologists. In Canada and in Europe, most ALS patients are treated at ALS Centers. The vast majority of people with ALS (over 90%) have sporadic disease, showing no clear family history. 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. People with ALS spend approximately one-third of their disease course searching for a diagnosis and, once diagnosed, there are few approved therapies available. ALS is a relentlessly progressive and highly heterogenous disease that arises from multiple mechanistic underpinnings, leading patients to experience variable onset, persistent progression, and shortened survival. The disease remains universally fatal with median survival of less than three years from symptom onset and less than two years from diagnosis.

We have conducted market research with physicians, patients, caregivers, nurses, and payors in the U.S., Western Europe and Canada to understand the unmet need and potential of AMX0035 in ALS. Clinicians universally report dissatisfaction with currently approved therapies and state the need for additional options for their ALS patients. When shown a target product profile for AMX0035, the majority of ALS specialists and neurologists with whom we spoke are open to utilizing it in early-to-mid-stage patients, with some also stating the potential for use in late-stage patients.

We submitted an NDA to the FDA in the fourth quarter of 2021 and, in September 2022, the FDA approved AMX0035 as RELYVRIO for the treatment of ALS in adults. We submitted an NDS for AMX0035 in ALS with Health Canada in the second quarter of 2021, which received marketing authorization with conditions as ALBRIOZA by Health Canada in June 2022. We also submitted an MAA in Europe in the first quarter of 2022, and we expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest. We also plan to discuss AMX0035 with other health authorities around the world to determine the most appropriate path forward in their respective territories. We also initiated our ongoing Phase 3 PHOENIX trial in the fourth quarter of 2021 to further support the safety and efficacy of AMX0035 for the treatment of ALS and our global regulatory efforts, and in February 2023 we announced completion of enrollment in that trial.

Our pre-launch activities in other key jurisdictions include building awareness of and education regarding the disease severity and pathophysiology of ALS, increasing understanding of the clinical impact of a change in a patient's ALSFRS-R score, and building general awareness of our company through active participation in key neurology conferences, patient meetings, partnerships with patient advocacy groups, targeted omnichannel initiatives and payor education in each of the key territories. In addition, we intend to continue to pursue an active public relations strategy. For example, the double-blind results of our CENTAUR trial have already been published in the *New England Journal of Medicine*, while the long-term survival study results appeared in the *Journal of Muscle & Nerve*.

Our initial plans are to continue to build out our commercial operations in the U.S. and Canada and to build commercial operations in Europe to be prepared for potential approval of AMX0035 in the EU. There are approximately 186 ALS Association certified, recognized, or affiliated centers in the U.S., 17 Canadian ALS Research Network Clinics in Canada, and an established network of ALS Centers of Excellence per country in each of the major EU countries, which we plan to target with a specialty key account management team. We will continue to evaluate market entry opportunities beyond these geographies either on our own or with a partner.

Competition

Overview

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.

AMX0035 for the Treatment of ALS

Prior to AMX0035, in the past 30 years, only two product candidates had been approved for the treatment of ALS in the U.S. and Canada, and only one product candidate had been approved for the treatment of ALS in Europe. These two previously approved drugs, riluzole (marketed under the name Rilutek) and edaravone (marketed under name Radicava in the U.S. and Radicut in Japan), are often used in combination. We expect that further therapies and drugs which may be approved in the future will also be used in combination with existing drugs, absent incompatibility or other barriers to combination. For example, in May 2022, Mitsubishi Tanabe Pharma America, Inc. announced that the FDA approved an oral formulation of intravenous, or IV, administered alternative to Radicava for the treatment of ALS.

We believe there are currently no other approved treatments for ALS which show both a functional and survival benefit for ALS patients. Patients with ALS in North America are commonly treated with riluzole and edaravone, which are palliative in nature. However, we are aware of several product candidates in clinical development that may compete with AMX0035 for the treatment of ALS, including product candidates being developed by Biogen, Seelos Therapeutics and Prilenia Therapeutics. To date, we believe none of the above product candidates has shown statistically significant clinical results on prespecified outcomes in any prior trials. We anticipate that ALS will continue to be an area of research in the healthcare sector and that drug candidates will continue to be developed and studied for treatment of the disease.

While we anticipate the general practice in ALS will continue to be the use of approved agents as single drug therapy or combination, our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or tolerable or are less expensive than AMX0035 or products that we may develop. In addition, we are aware of one ongoing clinical study in Europe which is evaluating the effects on ALS of TURSO, one of the two components in AMX0035. The outcome of this study could have an impact on the commercial potential of AMX0035.

A large number of trials and studies are ongoing in the many additional neurodegenerative diseases which we are evaluating for future clinical work for AMX0035 including AD, Wolfram syndrome, Parkinson's Disease, Huntington's Disease, Progressive Supranuclear Palsy, Multi-System Atrophy, primary lateral sclerosis, ischemic stroke, MS, Friedreich's ataxia, Leigh's syndrome and Leber's hereditary optic neuropathy. Some of these diseases also have therapies approved which impact disease progression. The competitive landscape in these diseases will affect the potential opportunity for AMX0035.

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 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, 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 December 2019, we entered into a supply agreement with Prodotti Chimici e Alimentari S.p.A. (now ICE S.p.A., or ICE), as amended in July 2021, pursuant to which ICE agreed to supply to us, on a non-exclusive basis, bulk drug substance of TURSO, which we use in the manufacture of AMX0035. The agreement has an initial term of five years and will automatically renew for successive terms of five years, unless earlier terminated. ICE may terminate the agreement upon three months written notice. Additionally, 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

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. Our current patent portfolio as of the date of this prospectus includes three patent families. In those three families, we currently own a total of 100 issued patents and pending patent applications directed to our technologies, including AMX0035. Currently, our patent portfolio includes six issued U.S. patents, 52 issued foreign patents, 11 pending U.S. patent applications and 31 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 52 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, China, the EU, Hong Kong, 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.

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 opponents contended that the patent should be revoked in its entirety on various grounds, including for allegedly having an insufficient disclosure and for lack of inventive step. The EPO issued a preliminary opinion dated October 13, 2021, and a summons to attend oral proceedings (also dated October 13, 2021) that set a date of June 2, 2022 for the oral proceedings. At the oral proceedings on June 2, 2022, the Opposition Division maintained European Patent, EP2978419 as granted. The scope of the issued claims was not limited. On June 17, 2022, the Opposition Division handed down the written decision providing detailed legal reasoning for the outcome of the oral proceedings. On August 4, 2022, Bruschettini S.r.l. filed a notice of appeal. The other opponent did not file a notice of appeal. On September 29, 2022, Bruschettini S.r.l filed a request to withdraw the appeal. As the sole appellant has withdrawn their appeal, the Board of Appeal has closed the appeal proceedings and terminated the opposition proceedings with communication dated October 14, 2022. The decision of the Opposition Division has become final and EP2978419 is maintained as granted.

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.

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 Investigational New Drug application, or 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.

Combination Rule for Fixed-Dose Combination Products

Under the 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. To satisfy these requirements, the FDA typically requires a clinical factorial study, designed to assess the effects attributable to each drug in the combination product. This is particularly true when the ingredients are directed at the same sign or symptom of the disease or condition.

The FDA has accepted a variety of approaches to satisfy the combination rule. In December 2015, the FDA proposed regulations that would allow the agency to waive the requirements of the combination rule for certain drug products under particular circumstances. The FDA has not, to date, finalized these regulations, but the FDA has stated that factorial studies may be unethical (e.g., omitting a drug known to improve survival) or impractical (there may be too many components to conduct a factorial study, meaning the trial cannot be conducted). The FDA has also stated that it may be possible to use other types of clinical and nonclinical data and mechanistic information available to demonstrate the contributions of the individual active ingredients to the effect of the combination.

Similar requirements may be imposed on us by the EMA in the EU and comparable regulatory authorities in other jurisdictions. While no similar combination rule formally exists in Canada, Health Canada may consider the contributions of each component in a combination product in connection with review of the NDS.

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, or PSP, within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs. 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 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 or listed patents. 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.

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. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the U.S. Changes to the manufacturing process are strictly

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

Once an approval of a drug is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market, 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. 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; 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; addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created 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. On June 17, 2021, the Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court's decision, President Biden issued an Executive Order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The Executive Order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. In addition, in February 2023, HHS issued a proposal in response to an October 2022 executive order from President Biden that includes a proposed prescription drug pricing model that will test whether targeted Medicare payment adjustments will sufficiently incentivize manufacturers to complete confirmatory trials for drugs approved through FDA's

accelerated approval pathway. It is unclear how these or other healthcare reform measures of the executive branch or other efforts, if any, will impact our business.

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 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 rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it may not qualify for the orphan drug exemption. 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).

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 European Union, 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 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 2003/94/EC, 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.

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.

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 studies 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.

Rest of the World Regulation

For other countries outside of Canada, the EU and the U.S., such as countries in Eastern Europe, 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 studies 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, 2022, we had 262 full-time employees. Of our workforce, 83 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. Our human capital resources objectives 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.

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 incurred significant losses since our inception. Until we are able to generate sufficient revenue from approved products, we anticipate that we will continue to incur significant losses.
- We have only recently obtained regulatory approval for and launched RELYVRIO in the U.S. and ALBRIOZA in Canada and, prior to their launch, we have never generated revenue from product sales. If the commercial launches of RELYVRIO in the U.S. and ALBRIOZA in Canada are unsuccessful, and AMX0035 is not approved in other jurisdictions or for other indications, we may never be profitable.
- We have a limited operating history and our only product, AMX0035, has only recently been approved by the FDA in the U.S. and only recently received marketing authorization with conditions 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 experience as a commercial company and we may not be successful in commercializing AMX0035 or any future product candidates in the U.S., Canada or anywhere else, if and when approved, and we may be unable to generate meaningful product revenue.
- AMX0035 may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.
- If the FDA, Health Canada, the EMA or other comparable foreign regulatory authorities approve generic versions of AMX0035 or any 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.
- Healthcare insurance coverage and reimbursement, both from public drug plans and private health care insurers, may be limited or unavailable for RELYVRIO in the U.S. and ALBRIOZA in Canada, and for AMX0035 and any future product candidates, if approved anywhere else, which could make it difficult for us to sell any product candidates or therapies 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 mean that we need to delay or even cease operations, and a delay in obtaining or inability to maintain such approval would delay commercialization of AMX0035 and adversely impact our ability to generate revenue, our business and our results of 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 obtain or maintain regulatory approval for AMX0035 or any 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.
- 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 future product candidates, and our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.
- Our use of third parties to manufacture AMX0035 and approved products in compliance with cGMP may increase the risk that we will not have sufficient cGMP, compliant quantities of AMX0035, products, 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

- A pandemic, epidemic, or outbreak of an infectious disease, such as the ongoing COVID-19 pandemic, 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 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 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.

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 incurred significant losses since our inception. Until we are able to generate sufficient revenue from approved products, we anticipate that we will continue to incur significant losses.

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 recently approved by the FDA, and ALBRIOZA, which has received marketing authorization with conditions from Health Canada, but we have only recently begun generating revenue from product sales to date in the U.S., Canada or elsewhere. We will also continue to incur significant research and development and other expenses related to clinical development, commercialization, approvals in additional jurisdictions and ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. 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, more recently, commercialization activities. Our financial condition and operating results, including our revenues, expenses and net losses, 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 will continue to have, an adverse effect on our stockholders' equity and working capital. Our net losses were $198.4 million and $87.9 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $354.2 million. We may continue to incur significant losses and our financial results will be highly dependent upon the successful launch and commercial sales of RELYVRIO in the U.S. We will continue to incur expenses related to our research and development activities and pre-commercialization activities in Europe, among other things.

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

- further build out our sales, marketing, pharmacovigilance and distribution infrastructure and scale-up manufacturing capabilities to commercialize AMX0035 and any product candidate for which we may obtain approval;
- continue to develop and conduct clinical trials for AMX0035 for the treatment of ALS, AD, Wolfram and potential other additional indications, including our PHOENIX trial;
- initiate and continue research, preclinical and clinical development efforts for any future product candidates;
- seek to identify additional product candidates;
- seek to maintain regulatory approvals in the U.S. and Canada and obtain regulatory approvals in the European Union, or the EU, and other geographies for AMX0035 for the treatment of ALS, AD and 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 the EMA or other 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;
- establish sales, marketing, pharmacovigilance, distribution, manufacturing, supply chain and other commercial infrastructure to commercialize any products for which we may in the future obtain regulatory approval;
- add operational, financial and management information systems and personnel, including personnel to support our product candidate development and 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, for commercialization of AMX0035 in the U.S. and Canada. As of December 31, 2022, we had 262 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 future product candidates we may develop.

We have only recently obtained regulatory approval for and launched RELYVRIO in the U.S. and ALBRIOZA in Canada and, prior to their launch, we have never generated revenue from product sales. If the commercial launches of RELYVRIO in the U.S. and ALBRIOZA in Canada are unsuccessful, and AMX0035 is not approved in other jurisdictions or for other indications, we may never be profitable.

Our ability to become and remain profitable depends on our ability to generate revenue from our approved products, RELYVRIO in the U.S. and ALBRIOZA in Canada. Other than RELYVRIO in the U.S. and ALBRIOZA in Canada, we have not yet launched any other approved products for commercial sale and have only recently begun generating revenue from product sales. Successful commercialization will require achievement of many key milestones, which vary by jurisdiction and may include demonstrating safety and efficacy in clinical trials, obtaining and maintaining regulatory, including marketing, approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain regulatory approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Even if we successfully launch and commercialize RELYVRIO in the U.S. and ALBRIOZA in Canada, we may be unable to achieve or maintain profitability, unless AMX0035 is approved in other jurisdictions or for additional indications. 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 further losses or if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Our failure to become and remain profitable 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 continue to 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 our only product, AMX0035, has only recently been approved by the FDA in the U.S. and only recently received marketing authorization with conditions in Canada, which may make it difficult to evaluate the prospects for our future viability.

We have only recently commenced our transition from a clinical-stage to a commercial-stage company. 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 preparing for and commencing commercialization of AMX0035. We have not yet demonstrated an ability to generate significant revenues, or clearly conduct sales and marketing activities necessary for successful product commercialization. In June 2022, AMX0035 received marketing authorization with conditions from Health Canada for the treatment of ALS. One of the conditions of the marketing authorization in Canada is the provision of data from our ongoing 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. We also have a pending MAA before the EMA, and we expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest. 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.

At a second meeting of the FDA's 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. The outcomes of the PHOENIX trial and any potential withdrawal could have a material adverse effect on our business.

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 prospectus for profitability. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We are transitioning from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We may require substantial additional funding 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 commercialize AMX0035 in jurisdictions in which it has received regulatory approval and to continue the clinical development of AMX0035 and the preclinical and clinical development of any future product candidates. If we are unable to obtain and maintain marketing approvals for AMX0035 or any future product candidates that we develop, including any indication for which we are developing or may develop AMX0035, we will require significant additional amounts of cash in order to continue to develop AMX0035 and any 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, developing and commercializing AMX0035 for the treatment of ALS, AD and potential additional indications, as well as any future product candidates we may develop;
- the timing of, and the costs involved in, obtaining and maintaining marketing approvals for AMX0035 for the treatment of ALS, AD and potential additional indications, and any future product candidates we may develop and pursue;
- the number of future 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 of regulatory approval on a jurisdiction-by-jurisdiction basis, revenue, if any, received from commercial sales of AMX0035 for any approved indications or any 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, 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 economic challenges caused by the COVID-19 pandemic and economic uncertainty in various global markets due to geopolitical instability and conflict, including the ongoing conflict in Ukraine, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, high rates of inflation and rising interest rates, declines in economic growth, increases in unemployment 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 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 future product candidates or other research and development initiatives. We may need to seek collaborators for AMX0035 and any 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 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 have begun to generate with 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. 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 from AMX0035 or any future product candidates, we expect 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. In addition, securing financing could 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 its financial condition and results of operations.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank, or SVB, was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation, or the FDIC, as receiver. Similarly, on March 12, 2023, Signature Bank and Silvergate Capital Corp. were each swept into receivership. Although a statement by the Department of the Treasury, the Federal Reserve and the FDIC stated that all depositors of SVB would have access to all of their money after only one business day of closure, including funds held in uninsured deposit accounts, borrowers under credit agreements, letters of credit and certain other financial instruments with SVB, Signature Bank or any other financial institution that is placed into receivership by the FDIC may be unable to access undrawn amounts thereunder. If any of our counterparties to any such instruments 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 such 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. In this regard, counterparties to SVB credit agreements and arrangements, and third parties such as beneficiaries of letters of credit (among others), may experience direct impacts from the closure of SVB and uncertainty remains over liquidity concerns in the broader financial services industry. Similar impacts have occurred in the past, such as during the 2008-2010 financial crisis. As of March 10, 2023, we had less than $1 million of our cash and cash equivalent and short-term investment balances on deposit with SVB, and also held securities in a sweep account and asset management account purchased through SVB but managed in segregated custodial accounts by third party asset managers.

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

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

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

- Delayed access to deposits or other financial assets or the uninsured loss of deposits or other financial assets;
- Loss of access to revolving existing credit facilities or other working capital sources and/or the inability to refund, roll over or extend the maturity of, or enter into new credit facilities or other working capital resources;
- Potential or actual breach of contractual obligations that require us to maintain letters or credit or other credit support arrangements; or
- Termination of cash management arrangements and/or delays in accessing or actual loss of funds subject to cash management arrangements.

In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our

financial and/or contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our current and/or projected business operations and financial condition and results of operations.

In addition, any further deterioration in the macroeconomic economy or financial services industry could lead to losses or defaults by parties with whom we conduct business, which in turn, could have a material adverse effect on our current and/or projected business operations and results of operations and financial condition. For example, a party with whom we conduct business may fail to make payments when due, default under their agreements with us, become insolvent or declare bankruptcy. Any bankruptcy or insolvency, or the failure to make payments when due, of any counterparty of ours, or the loss of any significant relationships, could result in material losses to us and may material adverse impacts on our business.

Risks Related to Commercialization of AMX0035 or Future Product Candidates

We have limited experience as a commercial company and we may not be successful in commercializing AMX0035 or any future product candidates in the U.S., Canada or anywhere else, if and when approved, and we may be unable to generate meaningful product revenue.

We recently launched ALBRIOZA in Canada and RELYVRIO in the U.S. and, if approved, we also intend to commercialize AMX0035 in the EU with specialized teams, given the relative rarity of ALS and certain of the other indications we are targeting. We are currently 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 successfully commercialize AMX0035 for the treatment of ALS, AD and other indications, or any of our 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 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 future product that we may develop;
- 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 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 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 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 any of AMX0035 or future product candidates for which we obtain marketing approval, we will be unable to generate any 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 is, and will continue to be, expensive and time-consuming and could delay any further product launch. Moreover, we cannot be certain that we will be able 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 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 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, AD, Wolfram syndrome and other neurodegenerative diseases and for any future product candidates we may 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 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. For example, as we begin to commercialize RELYVRIO in the U.S., ALBRIOZA in Canada and 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 now initially focused primarily on the annual incidence of ALS. This means the initial market opportunity for AMX0035 and any future product candidates may be smaller than the total addressable market opportunity that could be achieved over time. If we are unable to successfully commercialize AMX0035 or any 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, 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 achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

Even if AMX0035 for the treatment of any indication, or any 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 to their patients' treatment regimen, or may cease to add AMX0035 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, they may be unable to add AMX0035 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 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 become profitable. The degree of market acceptance of AMX0035 and any 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;
- 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 potential 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 of PB, which is available as a generic drug, along with the potential sale in some jurisdictions of TURSO, which preparations are of unknown identity and may not be legally sold for the treatment of ALS, 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 of unknown identity and 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 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 the U.S. and Europe may reach different conclusions from 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 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 is entitled to 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 (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 marketing 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.

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 or any future product candidates for which we, or any future collaborators, obtain regulatory approval will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. AMX0035 and any 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.

AMX0035 received approval by the FDA for the treatment of ALS in adults (known as RELYVRIO) in September 2022 and marketing authorization with conditions by Health Canada for the treatment of ALS (known as ALBRIOZA) in June 2022. We have a pending MAA before the EMA for AMX0035 for the treatment of ALS and we may seek approval of AMX0035 in additional jurisdictions and in additional indications. AMX0035 or any 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 for notifying 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 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, 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.

Healthcare insurance coverage and reimbursement, both from public drug plans and private health care insurers, may be limited or unavailable for RELYVRIO in the U.S. and ALBRIOZA in Canada, and for AMX0035 and any future product candidates, if approved anywhere else, which could make it difficult for us to sell any product candidates or therapies profitably.

The success of AMX0035 and any future product candidates, if approved, depends on the availability of adequate coverage and reimbursement from third-party payors. Because AMX0035 and any 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 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 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 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 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 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 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 achieve 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 future product candidates.

Moreover, increasing efforts by governmental and other third-party payors in Canada, the EU, the U.S. 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 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 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.

In the U.S., there have been and continue to be a number of legislative initiatives to contain healthcare costs.

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 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, attain 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 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 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 may implement programs to assist them, 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 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.

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 and UK, including personal health data, is subject to 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. 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), 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. 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. 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 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. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties.

Similar actions are either in place or underway 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—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. Many other states are considering similar legislation. A broad range of legislative measures also has been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding the privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

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.

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.

We currently only have one advanced product candidate, AMX0035, and our current business and future success depends entirely on our ability to develop, maintain, or obtain additional, regulatory approvals for, and then successfully commercialize, AMX0035, which we are developing for patients with ALS, Wolfram syndrome, 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 and intend to conduct additional clinical trials for other indications in the future. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development that may be able to better sustain failure of a lead product candidate.

We recently 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 and we have a MAA pending before the EMA for AMX0035. Accordingly, we are investing the majority of our efforts and financial resources in the further development and commercialization of our product candidate, 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, AD and other indications. The future regulatory and commercial success of AMX0035 or any 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 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 future product candidates;
- making arrangements with third-party manufacturers, or establishing manufacturing capabilities, for both clinical and commercial supplies of AMX0035 or any future product candidates;
- entry into collaborations to further the development of AMX0035 or any 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 launching and 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;
- 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, any such approval may be subject to limitations on the indications or uses or the patient populations for which we may market the product. 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 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 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 to satisfy other regulatory requirements could adversely affect our development efforts for AMX0035 in other indications.

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 mean that we need to delay or even cease operations, and a delay in obtaining or inability to maintain such approval would delay commercialization of AMX0035 and adversely impact our ability to generate revenue, our business and our results of operations.

If we are not successful in commercializing AMX0035, or are significantly delayed in doing so, our business will be materially harmed, and we may need to curtail or cease operations. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution 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. We are not permitted to market AMX0035 until we receive approval or marketing authorization from the relevant regulatory authority. 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 PHOENIX trial and additional planned or ongoing studies. We are also actively pursuing regulatory approval of AMX0035 for the treatment of ALS in Europe. Our MAA remains under review by the CHMP of the EMA. We completed the Scientific Advisory Group meeting. Certain major objections remain, and the CHMP has adopted another round of questions as part of the regulatory process. We are now in possession of those questions. In order to respond in accordance with the updated timelines, we now expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest. It is possible that we may be unable to successfully address the outstanding major objections to achieve EMA approval in this review cycle.

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;
- our ability to enroll an adequate number of patients in and successfully complete our ongoing global Phase 3 PHOENIX trial;
- 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. To satisfy these requirements, the FDA typically requires a clinical factorial study, designed to assess the effects attributable to each drug in the combination product. This is particularly true when the ingredients are directed at the same sign or symptom of the disease or condition.

The FDA has accepted a variety of approaches to satisfy the combination rule. In December 2015, the FDA proposed regulations that would allow the agency to waive the requirements of the combination rule for certain drug products under particular circumstances. The FDA has not, to date, finalized these regulations, but the FDA has stated that factorial studies may be unethical (e.g., omitting a drug known to improve survival) or impractical (there may be too many components to conduct a factorial study, meaning the trial cannot be conducted). The FDA has also stated that it may be possible to use other types of clinical and preclinical data and mechanistic information available to demonstrate the contributions of the individual active ingredients to the effect of the combination.

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. 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 MAA. There can be no assurance that the EMA will conclude 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 future product candidates for treating neurodegenerative and CNS disorders. Developing and commercializing AMX0035 and any 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 obtain or maintain regulatory approval for AMX0035 or any 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.

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. In June 2022, we obtained marketing authorization with conditions for AMX0035 (ALBRIOZA) in Canada and in September 2022, we received approval from the FDA for AMX0035 (RELYVRIO) in the U.S. While we have received approval from the FDA and marketing authorization with conditions from Health Canada, and have submitted an MAA to the EMA, to date, we have not submitted any other similar drug approval

submissions to comparable foreign regulatory authorities for AMX0035 or any other product candidate. Our MAA for AMX0035 is still under review by the EMA, and there can be no assurance that we will receive approval. We completed the Scientific Advisory Group meeting. Certain major objections remain, and the CHMP has adopted another round of questions as part of the regulatory process. We are now in possession of those questions. In order to respond in accordance with the updated timelines, we now expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest. It is possible that we may be unable to successfully address the outstanding major objections to achieve EMA approval in this review cycle.

One of the conditions of the marketing authorization in Canada is the provision of data from our ongoing 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. 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.

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. 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 PHOENIX trial and the seriousness of ALS. 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. For example, the Rapporteurs Day 190 Joint CHMP Response Assessment Report contains major objections relating to the sufficiency of the clinical data in CENTAUR to support approval. If we experience delays in obtaining and maintaining 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 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. It is possible that even if AMX0035 or any 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 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 future product candidate, or mistakenly believe that AMX0035 or any future product candidates are toxic or not well-tolerated when that is not in fact the case.

AMX0035 could fail to obtain additional 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 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 may require additional trials or studies to support marketing approval;
- the data collected from clinical trials of AMX0035 or any 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. 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 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 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 ongoing 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. Additionally, the EMA may also find that our CENTAUR trial, together with any data from our global Phase 3 PHOENIX trial that may be provided during or after the review period for these applications, is not sufficient to support our request for marketing authorization in the EU. 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. 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 become profitable.

In addition, disruptions caused by the COVID-19 pandemic 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 toward the COVID-19 pandemic. 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 COVID-19, 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 the ongoing COVID-19 pandemic. As a result of the COVID-19 pandemic, we may face delays in meeting our anticipated timelines for our ongoing and planned clinical trials.

Since March 2020, when foreign and domestic inspections were largely placed on hold due to the COVID-19 pandemic, the FDA has been working to resume pre-pandemic levels of inspection activities, including routine surveillance, bioresearch monitoring and pre-approval inspections. Should the FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be adequate, the agency has stated that it generally intends to issue, depending on the circumstances, a complete response letter or defer action on the application until an inspection can be completed. Further, if there is inadequate information to make a determination on the acceptability of a facility, the FDA may defer action on the application until an inspection can be completed. During the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities. For example, with respect to new sites or facilities in the EEA which have never had a cGMP inspection or authorization, the EMA has stated that a distant assessment may be conducted in order to evaluate if the site could be authorized without an on-site pre-approval inspection. If an approval is granted, it should be indicated that the certificate has been granted on the basis of a distant assessment and an on-site inspection should be conducted when circumstances permit. If a cGMP certificate cannot be granted as a result of the distant assessment, a clock-stop in the regulatory approval process will be imposed until an on-site inspection is possible. In addition, even if we were to obtain approval, regulatory authorities may approve AMX0035 or any 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 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 and commercialization of AMX0035 or any future product candidates.

To obtain regulatory approval to commercialize AMX0035 and any 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 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 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 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 future product candidate or other materials necessary to conduct clinical trials of AMX0035 or any 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, 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 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 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, in July 2022 we received marketing authorization with conditions of AMX0035 (ALBRIOZA) from Health Canada for the treatment of ALS. One of the conditions of the marketing authorization in Canada is the provision of data from our ongoing 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 obtain or 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 and maintaining approval or if we fail to obtain approval of any product candidates we may develop, the commercial prospects for those product candidates, including for AMX0035 in other indications, 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 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., and to continue development of AMX0035 for additional indications or of future product candidates. 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 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 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 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, AD and additional indications and any future product candidates, or could render further development impossible. For example, the impact of public health epidemics, such as the ongoing COVID-19 pandemic, may delay or prevent patients from enrolling or from receiving treatment in accordance with the protocol and the required timelines, which could delay our clinical trials, or prevent us or our partners from completing our clinical trials at all, and harm our ability to obtain and maintain approval for such product candidate. 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 the COVID-19 pandemic 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 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 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 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 ongoing 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 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 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 a 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, 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. On March 18, 2022, we launched an FDA-authorized EAP in the U.S. for AMX0035 for certain adults with ALS and this program will be wound down alongside the commercial launch of RELYVRIO in the U.S., with a target close of the EAP in the first half of 2023. We may launch additional EAPs of AMX0035 in the EU.

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 product candidates, we may be unable to grow our business and our ability to achieve our strategic objectives would be impaired.

Although the development and commercialization of AMX0035 for the treatment of ALS is our current primary focus, as part of our longer-term growth strategy, we plan 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 multiple clinical trials in patients with ALS 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, Wolfram syndrome and other indications, 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. 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 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., Orphazyme A/S, Biohaven Pharmaceutical Holding Co Ltd., UCB S.A., Alexion Pharmaceuticals, Inc. and Apellis Pharmaceuticals, Inc., specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. In the third quarter of 2022, the FDA accepted Biogen, Inc.'s NDA for toferson, an investigational drug for superoxide dismutase 1 (SOD1) ALS.

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.

We have received approval for AMX0035 (RELYVRIO) in the U.S. and marketing authorization with conditions for AMX0035 (ALBRIOZA) in Canada and have submitted a marketing application in the EU. 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 Wolfram syndrome 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, the EMA Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the EU. 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 drug in the EU would be sufficient to justify the necessary investment in developing the drug or biologic 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 is entitled to 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 drug 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 Wolfram syndrome 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 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 can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug 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 other similar medicinal products. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. Orphan drug 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 Wolfram syndrome, 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 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 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 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 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 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 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 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 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 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 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 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 future product candidates, and our prospects with respect to those 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 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 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 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 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 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 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 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 future product candidates. In such an event, our financial results and the commercial prospects for AMX0035 or any 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 the COVID-19 pandemic or other infectious diseases 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 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 and approved products in compliance with cGMP may increase the risk that we will not have sufficient cGMP-compliant quantities of AMX0035, products, 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 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. In addition, we typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements with any commercial manufacturer. Moreover, the extent to which the COVID-19 pandemic impacts our ability to procure sufficient supplies for the development of AMX0035, and any future products and product candidates will depend on whether the economic challenges caused by the COVID-19 pandemic 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 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 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 conflict in Ukraine 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 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 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 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 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 future product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of AMX0035 or any future product candidates. The facilities used by our contract manufacturers to manufacture AMX0035 or any 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 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 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 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 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 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 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.

Since the beginning of the COVID-19 pandemic, several vaccines for COVID-19 have received Emergency Use Authorization by the FDA and a number of those later received marketing approval. Additional vaccines may be authorized or approved in the future. The resultant demand for vaccines and potential for manufacturing facilities and materials to be commandeered under the Defense Production Act of 1950, or equivalent foreign legislation, is having rippling effects across the contract manufacturing industry, which may make it more difficult to obtain materials or manufacturing slots for the production needed for our clinical trials and, if approved, our future commercial supply, which could lead to delays in our trials and commercial distribution.

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 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 achieve 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 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 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 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 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 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 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 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 future product candidates. If any third-party patents or patent applications are found to cover AMX0035 or any 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 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 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 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 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 future product candidates. We also expect to collaborate with third parties on the development of AMX0035 and any 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

A pandemic, epidemic, or outbreak of an infectious disease, such as the ongoing COVID-19 pandemic, 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 such as the ongoing COVID-19 pandemic. For instance, from 2020 through 2022, we experienced certain impacts of 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, 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.

The economic challenges caused by the COVID-19 pandemic has been and may continue to be extensive in many aspects of society and could continue to result in significant disruptions to the global economy, as well as businesses and capital markets around the world. The full extent to which the COVID-19 pandemic could ultimately impact our business, preclinical studies, clinical trials and financial results will depend on future developments, which are highly uncertain and cannot be accurately predicted, including the emergence of new variants and subvariants of the virus that causes COVID-19, such as the Omicron variants and subvariants, for which current vaccinations may be less effective or ineffective, among others. Other global health concerns could also result in social, economic, and labor instability in the countries in which we or the third parties with whom we engage operate.

Any negative impact the COVID-19 pandemic or any future pandemic or similar disruption has on patient enrollment or treatment, or the development of AMX0035 and any 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 future product candidates, if approved, increase our operating expenses, which could have a material adverse effect on our financial results. The COVID-19 pandemic has 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 the COVID-19 pandemic or 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.

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 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 are experiencing volatility and disruption caused by the ongoing Russia-Ukraine conflict and the effects of sanctions imposed on Russia as a result of the conflict. 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 has contributed to record inflation globally. We are continuing to monitor inflation, the situation in Ukraine and global capital markets and assessing its potential impact on our business, including the impact on the supply chains we rely on for the manufacture of AMX0035 or other future product candidates.

Although, to date, our business has not been materially impacted by the ongoing military conflict between Russian and Ukraine, 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 conflict in Ukraine, 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, including Josh Cohen and Justin Klee, our Co-Chief Executive Officers, James Frates, our Chief Financial Officer, Margaret Olinger, our Global Head of Commercial and Chief Commercial Officer, and Patrick Yeramian, our Global Head of Clinical Research & Development and Chief Medical Officer. We have entered into employment agreements with Mr. Cohen, Mr. Klee, Mr. Frates, Ms. Olinger and Dr. Yeramian, 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. 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 future product candidates will be limited.

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

As of December 31, 2022, we had 262 full-time employees. Our focus on the development 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 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 future product candidates.

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. In addition to the factors discussed in this "Risk Factors" section and elsewhere in Annual Report, these factors include:

- 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 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 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;
- 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 future product candidates;
- changes in laws or regulations applicable to AMX0035 and any 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 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 future product candidates;
- additions or departures of key scientific or management personnel;

- unanticipated serious safety concerns related to the use of AMX0035 and any 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 the COVID-19 pandemic, historically high inflation, rising interest rates and the ongoing conflict in Ukraine; 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, declines in economic growth, increases in the rate of inflation and interest rates, increases in unemployment rates and uncertainty about economic stability, including most recently in connection with the ongoing COVID-19 pandemic and the conflict in Ukraine. 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 war in the Ukraine. 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 an emerging growth company and a smaller reporting company, and the reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2022, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company until December 31, 2027, although circumstances could cause us to lose that status earlier, including if we become a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, or if we have total annual gross revenue of $ 1.235 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three year period before that time, in which case we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company", which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. Investors may find our common stock less attractive because we may rely on these exemptions. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter. 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.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of accounting standards that have different effective dates for public and private companies until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards, and therefore we will not be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

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 March 8, 2023, we had outstanding 66,716,388 shares of common stock, which may be resold in the public market immediately without restriction, unless held by our affiliates. Moreover, holders of approximately 15.9 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.

We are obligated to develop and maintain proper and effective internal controls over financial reporting and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common shares.

We will be required, pursuant to Section 404 of the Sarbanes Oxley Act, or Section 404, to furnish a report by management on, among other things, the effectiveness of our internal controls over financial reporting for the fiscal year ending December 31, 2023. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal controls over financial reporting. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting until our first annual report required to be filed with the SEC following the date we are no longer an emerging growth company, as defined in the JOBS Act, and are not a smaller reporting company with less than $100 million in annual revenue. At such time as we are required to obtain auditor attestation, if we then have a material weakness, we would receive an adverse opinion regarding our internal control over financial reporting from our independent registered public accounting firm. We are required to disclose significant changes made in our internal controls procedures on a quarterly basis.

We continue the costly and challenging process of enhancing our financial reporting systems and processes as necessary to allow for the operation of effective internal controls over financial reporting to comply with the requirements of Section 404. We may not be able to complete our assessment, testing and any required remediation of internal controls over financial reporting in a timely fashion. Our compliance with Section 404 will require that we incur substantial legal, accounting and other compliance expense and expend significant management efforts. We currently do not have an internal audit group. We will need to hire additional accounting and finance personnel and consultants with appropriate public company experience and technical accounting knowledge to develop and maintain the internal controls over financial reporting necessary to comply with Section 404.

We have identified past material weaknesses in our internal controls over financial reporting. If during the evaluation and testing of our internal controls over financial reporting, we identify one or more additional material weaknesses in future periods, we will be unable to assert that our internal controls over financial reporting are effective. We cannot assure you that there will not be additional material weaknesses in our internal controls over financial reporting in the future. Any failure to maintain effective internal controls over financial reporting could severely inhibit our ability to accurately report our financial condition or results of operations. If we are unable to conclude that our internal controls over financial reporting are effective, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common shares could decline, and we could be subject to sanctions or investigations by the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal controls over financial reporting, or to implement or maintain other

effective control systems required of public companies, could also negatively impact our ability to access to the capital markets.

In addition, effective disclosure controls and procedures enable us to make timely and accurate disclosure of financial and non-financial information that we are required to disclose. As a public company, if our disclosure controls and procedures are ineffective, we may be unable to report our financial results or make other disclosures accurately and on a timely basis, which could cause our reported financial results or other disclosures to be materially misstated and result in the loss of investor confidence and cause the market price of our common shares to decline.

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 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 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 that we did not incur as a private 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 establishment and 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. Emerging growth companies and smaller reporting companies are exempted from certain of these requirements, but we may be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. 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 information technology 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, spamming or other means, and deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. Cyber-attacks also could include phishing attempts or e-mail fraud to 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. Any cyber-attack, data breach or destruction 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 and may incur significant additional expense to implement further data protection measures.

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, 2022, we had U.S. federal and state net operating loss carryforwards of $203.2 million and $164.1 million, respectively, some of which begin to expire in 2034. As of December 31, 2022 and 2021, we also had U.S. federal research and development tax credit carryforwards of $4.6 million and $2.7 million, respectively, which begin to expire in 2029. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future taxable income or tax liabilities, respectively. U.S. federal and certain state net operating losses generated in taxable years beginning after December 31, 2017 are not subject to expiration. Federal net operating losses generally may not be carried back to prior taxable years except that, under the Coronavirus Aid, Relief and Economic Security Act, federal net operating losses generated in 2018, 2019 and 2020 may be carried back to each of the five taxable years preceding the taxable year in which the loss arises. Additionally, for taxable years beginning after December 31, 2020, the deductibility of federal net operating losses generated in taxable years beginning after December 31, 2017 is limited to 80% of our taxable income in such taxable year.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, 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 net operating loss carryforwards or tax credits, or NOLs or credits, 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. Our existing federal and state NOLs and our existing research and development credits may be subject to limitations arising from previous ownership changes and, if we undergo an ownership change, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. We have not yet completed a Section 382 analysis. In addition, 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 Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating U.S. federal and state taxable income. As described above, we have incurred significant net losses since our inception and anticipate that we may incur significant losses in the future; and therefore, we do not know whether or when we will generate the U.S. federal or state taxable income necessary to utilize our NOLs or credits that are subject to limitation by Sections 382 and 383 of the Code.

We could be subject to securities class action litigation.

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. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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 2. Properties.

Details of our principal properties as of December 31, 2022, 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.

We are not currently subject to any material legal proceedings.

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 March 8, 2023, we had approximately 28 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 and Use of Proceeds

Recent Sales of Unregistered Securities

During the year ended December 31, 2022, we did not issue or sell any unregistered securities.

Use of Proceeds from Initial Public Offering

On January 6, 2022, our Registration Statements on Form S-1 (File Nos. 333-261703 and 333-262046) relating to our initial public offering, or IPO, were declared effective by the SEC. As of December 31, 2022, all proceeds from our IPO were fully utilized primarily to advance AMX0035 through clinical trials, manufacture drug supply, prepare for potential commercialization and for working capital and general corporate purposes.

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

Our mission is to one day end the suffering caused by neurodegenerative diseases. We are committed to supporting and creating more moments for the neurodegenerative disease community through the discovery and development of innovative new treatments. Our first product, RELYVRIO® (sodium phenylbutyrate and taurursodiol), previously known as AMX0035 in the U.S., is approved in the U.S. for the treatment of ALS in adults. AMX0035 is also approved with conditions by Health Canada and marketed as ALBRIOZA for the treatment of ALS in Canada.

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. We believe AMX0035 is the first drug candidate to show both a functional and survival benefit in a large-scale clinical trial of patients with amyotrophic lateral sclerosis, or ALS. The results of our Phase 2 clinical trial of AMX0035, known as the CENTAUR trial, were published in the *New England Journal of Medicine*, in two publications in *Muscle & Nerve*, and in the *Journal of Neurology*, *Neurosurgery*, and *Psychiatry*.

AMX0035 is a dual UPR-Bax apoptosis inhibitor composed of PB and TURSO (also known as TUDCA). 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, endoplasmic reticulum, or ER, stress, mitochondrial dysfunction, oxidative stress and disease-specific models of a variety of other conditions, as well as in vivo models of ALS, Alzheimer's disease, or AD, and multiple sclerosis, or MS. We believe AMX0035 has the potential to be a foundational therapy, 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 pursuing ALS as our first indication as it is a disease of rapid and profound neurodegeneration, and we are focused on the development and potential commercialization of AMX0035 for ALS globally.

We have received marketing authorization with conditions by Health Canada for ALBRIOZA for the treatment of ALS. We announced commercial availability of the product in July 2022. We have submitted to and received from the national reimbursement authorities, known as the Canadian Agency for Drugs and Technologies in Health, or CADTH, and l'Institut national d'excellence en santé et en services sociaux, or INESSS, recommendations regarding reimbursement for ALBRIOZA by the Canadian provincial governments, and are negotiating with both public and private payers to obtain reimbursement coverage.

We received approval by the FDA for RELYVRIO in September 2022, and commercial product was first available in October 2022. This decision represented Amylyx' first regulatory approval of AMX0035 in the U.S. and its second worldwide.

We are also actively pursuing regulatory approval of AMX0035 for the treatment of ALS in Europe. Our MAA remains under review by the Committee for Medicinal Products for Human Use, or CHMP, of the EMA. We submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, in Europe in the first quarter of 2022, which was validated in the same quarter. We completed the Scientific Advisory Group meeting. Certain major objections remain, and the CHMP has adopted another round of questions as part of the regulatory process. We are now in possession of those questions. In order to respond in accordance with the updated timelines, we now expect an opinion from CHMP mid-year and a decision in the third quarter of 2023 at the earliest.

In November 2021, we initiated a Phase 3 clinical trial of AMX0035 for the treatment of ALS, known as PHOENIX trial, at clinical trial sites in the U.S. and Europe. On February 2, 2023, we announced completion of enrollment in PHOENIX, which enrolled 664 participants. We anticipate topline results from the PHOENIX trial in mid-2024. This trial is designed to provide further data evaluating the safety and efficacy of AMX0035 over 48 weeks for the treatment of ALS to further support our global regulatory efforts. European participants completing the 48-week trial have the option to enroll in

an open label extension (OLE) phase. During this phase, all participants receive AMX0035, and continued safety and efficacy measures will be assessed.

We were incorporated under the laws of the State of Delaware on January 10, 2014. Between 2020 and 2022 we created wholly owned subsidiaries, Amylyx Pharmaceuticals Canada, Inc., or Amylyx Canada, in Calgary, Canada, Amylyx Pharmaceuticals EMEA B.V., or Amylyx EMEA, in Amsterdam, Netherlands, Amylyx Pharmaceuticals Distribution Ltd., or Amylyx Ireland, in Dublin, Ireland, Amylyx Pharmaceuticals Germany GmbH, or Amylyx Germany, in Munich, Germany and Amylyx Pharmaceuticals France SAS, or Amylyx France, in Paris, France. Since inception, we have devoted substantially all of its efforts to research and development and pre-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. Other than RELYVRIO in the U.S. and ALBRIOZA in Canada, we do not have any products approved for sale and as of December 31, 2022. As of December 31, 2022, we have funded our operations primarily through the public offering of our common stock, private sales of preferred stock, and convertible notes. We have also generated grant revenues through five grants from ALS Association, ALS Finding a Cure Foundation, Cure Alzheimer's Fund, Alzheimer's Drug Discovery Foundation and Alzheimer's Association, or Grantors.

We have incurred operating losses since inception, including a net loss of $198.4 million and $87.9 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $354.2 million. These losses have resulted primarily from costs incurred in connection with research and development activities and 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 continue to 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 future product candidates through preclinical and clinical development, 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 internally, with assistance from our network of contract research organizations, or CROs, and other advisors. This has resulted in increased research and development spending but has enabled us to manage AMX0035 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 that we did not incur as a private company. 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, if ever, 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, however, 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, 2022, we had cash, cash equivalents and short-term investments of $346.9 million. On October 11, 2022, we completed the sale of 7,697,812 shares of our common stock in an underwritten public offering, or our 2022 follow-on offering, pursuant to which we received net proceeds of approximately $230.6 million, including exercise in full of the underwriters' option to purchase additional shares, and after deducting underwriting discounts and commissions and other offering costs. We believe that the revenue we have begun to generate with 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 this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "—Liquidity and Capital Resources—Funding Requirements" below.

Impact of COVID-19 and Other Macroeconomic Factors

The development of AMX0035 and any future product candidates could be disrupted and materially adversely affected in the future by the continuing COVID-19 pandemic or any future pandemic or calamity. The spread of COVID-19 and identification of new variants and subvariants of the virus has impacted the global economy and our operations, including requiring us to make certain alterations to our preclinical and clinical trial activities, such as scheduling certain work off-site and performing off-site assessments. The COVID-19 pandemic could also continue to affect our employees or the employees of research sites and service providers on whom we rely as well as those of companies with which we do business, including our suppliers, thereby disrupting our business operations. Moreover, the full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations, liquidity and financial condition will depend on future

developments, which are highly uncertain and cannot be accurately predicted, including new information that may develop concerning COVID-19, the emergence of new variants and subvariants and the actions taken to contain it or treat its impact and the economic impact on local, regional, national and international markets. We continue to monitor COVID-19 levels local to our research operations and adapt our employee working practices to ensure essential staffing levels in our operations remain in place, including maintaining key personnel in our laboratories.

In addition, economic uncertainty in various global markets, including the U.S. and Europe, caused by political instability and conflict, such as the ongoing conflict in Ukraine, and economic challenges caused by the COVID-19 pandemic, 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, 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 COVID-19 pandemic and 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. All product revenue net, recognized during the period relates 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;
- 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, 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 substantially 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 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 necessary additional funds;
- 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 receipt and related 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 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 commercialization in Canada and the U.S. of AMX0035 (known as ALBRIOZA in Canada and RELYVRIO in the U.S.) and in other potential jurisdictions, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of AMX0035, 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 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; insurance costs; administrative travel expenses; sales and marketing expenses; information technology; 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 continue to increase headcount and incur other significant costs related to our pre-commercialization activities as we prepare for potential near term regulatory approvals. 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. and are pursuing regulatory approval of AMX0035 for the treatment of ALS in Europe. As we implement our commercialization plans in Canada and the U.S. and prepare for a potential approval in Europe, we have been incurring a substantial increase, and anticipate further increases in, payroll and expense as a result of our preparation for commercial operations, especially as it relates to the sales and marketing of AMX0035.

Other Income (Expense), 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 realized and unrealized losses on foreign exchange transactions.

Change in Fair Value of Convertible Notes

Change in fair value of convertible notes is comprised of adjustments to the fair value of our 2021 Notes. As permitted under ASC Topic 825, *Financial Instruments* (ASC 825), we elected the fair value option to account for our 2021 Notes, and as a result, we measured our 2021 Notes at fair value at each financial reporting period and immediately before conversion in July 2021. All changes to the fair value of our 2021 Notes for the year ended December 31, 2021 resulted in a loss. Our 2021 Notes converted into shares of Series C-2 redeemable convertible preferred stock concurrently with the issuance of our Series C-1 redeemable convertible preferred stock. Immediately prior to the conversion, we determined the fair value of our 2021 Notes based on the fair value of the Series C-1 redeemable convertible preferred stock and the conversion price at which these notes converted, which was at 85% of the fair value of the Series C-1 redeemable convertible preferred stock.

Income Taxes

The provision for income taxes primarily consists of provisions for foreign taxes payable.

As of December 31, 2022 and 2021, we had federal net operating loss carryforwards of approximately $203.2 million and $115.7 million, respectively, and state net operating loss carryforwards of approximately $164.1 million and $102.9 million, respectively, which are available to reduce future taxable income. Of the $203.2 million federal net operating loss carryforwards, $1.3 million begin to expire in 2034 and the remaining $201.9 million net operating losses carryforward indefinitely. Of the $164.1 million state net operating loss carryforwards, $113.0 million of Massachusetts net operating loss carryforwards begin to expire in 2034. As of December 31, 2022 and 2021, we also had federal tax credits of $4.6 million and $2.7 million, respectively, and state tax credits of $1.2 million. The tax credit carryforwards will expire at various dates beginning in 2034.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

The following table summarizes our results of operations for the years ended December 31, 2022 and 2021:

	Year Ended December 31,			
	2022	2021	$ Change	% Change
		(in thousands)		
Revenues:				
Product revenue, net	$ 22,230	$ —	$ 22,230	*NM
Grant revenue	—	285	(285)	(100)%
Total revenues	22,230	285	21,945	7,700%
Operating expenses:				
Cost of sales	2,993	—	2,993	*NM
Research and development	93,450	44,040	49,410	112%
Selling, general and administrative	127,128	38,933	88,195	227%
Total operating expenses	223,571	82,973	140,598	169%
Loss from operations	(201,341)	(82,688)	(118,653)	143%
Other income (expense), net:				
Interest income	4,291	36	4,255	*NM
Change in fair value of convertible notes	—	(5,228)	5,228	(100)%
Other expense, net	(551)	(51)	(500)	980%
Total other income (expense), net	3,740	(5,243)	8,983	(171)%
Loss before income taxes	(197,601)	(87,931)	(109,670)	125%
Provision for income taxes	774	—	774	*NM
Net loss	$ (198,375)	$ (87,931)	$ (110,444)	126%

* 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 year ended December 31, 2022, we recorded approximately $22.2 million of product revenue, net. 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 of $3.0 million for the year ended December 31, 2022, consisted of costs to procure, manufacture and distribute our marketed product, RELYVRIO and ALBRIOZA. In addition, included in cost of sales are costs to manufacture our marketed product which has been provided to patients at no cost to them while insurance reimbursement is established. We expect these costs to continue into 2024, and to a lesser degree, indefinitely. 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 year ended December 31, 2022, or approximately $3.4 million, were expensed prior to obtaining regulatory approvals and, therefore, are not included in cost of sales during this period. 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 2024.

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2022 and 2021:

	Year Ended December 31,			
	2022	2021	$ Change	% Change
	(in thousands)			
AMX0035 - ALS	$ 60,742	$ 25,756	$ 34,986	136%
Payroll and personnel-related	28,501	8,972	19,529	218%
Other	4,207	9,312	(5,105)	(55)%
	$ 93,450	$ 44,040	$ 49,410	112%

Research and development expenses were $93.5 million for the year ended December 31, 2022, compared to $44.0 million for the year ended December 31, 2021. During these periods, most of our research and development expenses were related to the development of and clinical trials of AMX0035. The increase of $49.4 million was primarily due to a $35.0 million increase in spending on AMX0035 for the ALS indication, a $19.5 million increase in payroll and personnel-related costs, and a $5.1 million decrease in all other costs. The increases in spending on AMX0035 were primarily related to costs associated with our global Phase 3 PHOENIX trial of AMX0035 in ALS that was initiated in November 2021, including its open label extension phase, and consulting and manufacturing development expenses in anticipation of potential commercialization, which includes inventory raw material purchases made in anticipation of the lead time necessary to have it available to meet our clinical trial and potential commercialization needs. 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 decreases in other costs were primarily due to a decrease in costs associated with research and development spend for AMX0035 in other indications, as we focused our efforts on ALS leading up to our approvals. 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 $127.1 million for the year ended December 31, 2022 compared to $38.9 million for the year ended December 31, 2021. The increase of $88.2 million was primarily due to increases of $55.4 million in payroll and personnel-related costs, including stock-based compensation, $15.9 million in consulting and professional services and $17.1 million in insurance and 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 and launch preparation initiatives. The increases in consulting and professional services and insurance and other expenses were primarily due to an increase in spending for commercial readiness activities and operations as a public company.

Other Income (Expense), Net

Interest Income

Interest income for the year ended December 31, 2022 was $4.3 million compared to less than $0.1 million for the year ended December 31, 2021. The increase was primarily attributable to higher investment balances driven by our proceeds received from our IPO and our 2022 follow-on offering, resulting in higher interest earned.

Change in Fair Value of Convertible Notes

The change in fair value of convertible notes was zero for the year ended December 31, 2022, due to conversion to preferred stock in July 2021, compared to $5.2 million for the year ended December 31, 2021. The $5.2 million recorded for the year ended December 31, 2021 represented a loss in fair value related to our 2021 Notes.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant operating losses and generated revenues through five grants from the Grantors. In the second half of 2022 we commenced 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, convertible notes and grant agreements with the Grantors. As of December 31, 2022, we had cash, cash equivalents and short-term investments of $346.9 million.

From inception through December 31, 2022, we have raised $663.6 million in aggregate proceeds, net of issuance costs, primarily from the issuance of convertible preferred stock, convertible notes and grant agreements. In July 2021, we issued and sold shares of Series C-1 preferred stock for an aggregate purchase price of approximately $135.0 million. The 2021 Notes automatically converted into shares of Series C-2 preferred stock pursuant to their original terms in July 2021 in connection with our sale of Series C-1 preferred stock. In January 11, 2022, we completed the IPO of our common stock pursuant to which we received aggregate net proceeds of $196.4 million after deducting underwriting discounts and commissions and other offering costs. On October 11, 2022, we completed the sale of 7,697,812 shares of our common stock in an underwritten public offering, pursuant to which we received net proceeds of approximately $230.6 million, including exercise in full of the underwriters' option to purchase additional shares, and after deducting underwriting discounts and commissions and other offering costs. Based on our current operational plans and assumptions, We believe that the revenue we have begun to generate with 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.

Capital Resources

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we advance the preclinical activities, manufacturing and clinical trials of AMX0035 and any future product candidates, implement 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 that we did not incur as a private company. Our expenses will also increase as we:

- continue our research and development efforts, including our ongoing global Phase 3 PHOENIX trial of AMX0035 for the treatment of 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 Europe, 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;

- develop, maintain, expand and protect our intellectual property portfolio; and
- continue to transition our organization to being a public company.

We are now a publicly traded company and will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, as well as rules adopted by the SEC and the Nasdaq Global Select Market, require public companies to implement specified corporate governance practices that are currently not applicable to private companies. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting for the current year ending December 31, 2022. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we have engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and demands significant effort. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. We expect these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

Based on our current operational plans and assumptions, we believe that the revenue we have begun to generate with 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. As we progress with our development activities and the regulatory review process, we expect to incur significant commercialization expenses related to product manufacturing, pre-commercial activities and commercialization.

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 ALBRIOZA in Canada, RELYVRIO in the U.S. and for AMX0035, if approved, in 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 the ongoing COVID-19 pandemic or other pandemics or disruptions;
- 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 achieve profitability, we expect to 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, 2022 and 2021

The following table summarizes our sources and uses of cash for the years ended December 31, 2022 and 2021:

	Year Ended December 31,			
	2022	2021	$ Change	% Change
	(in thousands)			
Net cash used in operating activities	$ (179,871)	$ (74,799)	$ (105,072)	140%
Net cash used in investing activities	(238,988)	(46,406)	(192,582)	415%
Net cash provided by financing activities	431,789	158,506	273,283	172%
Effect of exchange rate changes on cash, cash equivalents and restricted cash equivalents	(65)	13	(78)	(600)%
Net increase in cash, cash equivalents and restricted cash equivalents	$ 12,865	$ 37,314	$ (24,449)	(66)%

Operating Activities

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.

During the year ended December 31, 2021, operating activities used $74.8 million of cash, primarily resulting from our net loss of $87.9 million, offset by a $5.2 million change in fair value of convertible notes, $3.1 million of non-cash stock-based compensation expense, $0.1 million of depreciation expense, $0.1 million net amortization of premiums and discounts on investments, and a $4.6 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 $8.4 million increase in accrued expenses and deferred rent due to increased spending for external research and development to support our growth, a $0.7 million increase in accounts payable and a $0.1 million decrease in other assets, offset by a $0.1 million increase in interest receivable from short-term investment and $4.5 million increase in prepaid expenses and other current assets due to increase in sign-on bonuses as a result of an increase in headcount and increase in other receivables related to milestones achieved under the grant agreements for which we were owed by the grantors.

Investing Activities

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.

During the year ended December 31, 2021, net cash used in investing activities was $46.4 million, resulting from $0.4 million in purchases of property and equipment and $49.1 million in purchases of short-term investments, offset by $3.0 million of investments matured during the period.

Financing Activities

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 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.

During the year ended December 31, 2021, net cash provided by financing was $158.5 million. This amount consisted of $134.8 million of net proceeds from the sale of our Series C-1 redeemable convertible preferred stock, $14.3 million of net proceeds from the issuance of convertible notes to related parties, $11.9 million of net proceeds from the issuance of the convertible notes and $0.3 million of proceeds from exercises of stock options, offset by a $2.5 million payment of deferred offering costs, $0.3 million repayment of PPP loan, and less than $0.1 million of issuance costs related to the conversion of the convertible notes, which was related to the 2021 Notes.

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: (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) we satisfy a performance obligation. 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.

We enter into arrangements with wholesalers, specialty pharmacies and specialty distributors, or Customers, to distribute ALBRIOZA, RELYVRIO and future approved products. 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.

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 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, 2022, we continued to maintain a full valuation allowance against all of our 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 2022. 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. 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.

Emerging Growth Company and Smaller Reporting Company Status

The Jumpstart Our Business Startups Act of 2012, or JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably

opt out of the extended transition period provided in the JOBS Act. As a result, we will not be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies, and our consolidated financial statements may not be comparable to other public companies that comply with new or revised accounting pronouncements as of public company effective dates. We may choose to early adopt any new or revised accounting standards whenever such early adoption is permitted for private companies.

We will cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1.235 billion or more, (ii) the last day of our fiscal year following the fifth anniversary of the date of the closing of our initial public offering, (iii) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years or (iv) the date on which we are deemed to be a large, accelerated filer under the rules of the Securities and Exchange Commission.

We are also a "smaller reporting company", and we will continue to be a smaller reporting company until the first quarter of the fiscal year following the determination that the market value of our stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenue are more than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure and have certain other reduced disclosure obligations, including, among other things, being required to provide only the two most recent fiscal years of audited financial statements.

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.

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

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 Securities Exchange Act of 1934, as amended (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, 2022. Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, 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.

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.

As of December 31, 2022, 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, 2022.

Changes in Internal Control over Financial Reporting

During the year ended December 31, 2022, we began generating revenue from the sale of ALBRIOZA in Canada and RELYVRIO in the U.S. We consider the accounting for our product revenue to be material to our results of operations in future periods, and believe that the additional internal controls and procedures relating to the accounting for product revenue, and related commercial inventory, have a material effect on our internal control over financial reporting. Other than described

above, there was no change in our internal control over financial reporting that occurred during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on the Effectiveness of Controls

The effectiveness of any system of internal control over financial reporting, including ours, is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Accordingly, in designing and evaluating the disclosure controls and procedures, management recognizes that any system of internal control over financial reporting, including ours, no matter how well designed and operated, can only provide reasonable, not absolute assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply its judgment in evaluating the benefits of possible controls and procedures relative to their costs. Moreover, 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. We intend to continue to monitor and upgrade our internal controls as necessary or appropriate for our business but cannot assure you that such improvements will be sufficient to provide us with effective internal control over financial reporting.

Item 9B. Other Information.

None.

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

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by 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 2023 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 of our definitive proxy statement to be filed with the SEC with respect to our 2023 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 2023 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 2023 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, LLC, 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 2023 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 10.3 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).
10.4#	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 10.5 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#	Form of Director Indemnification Agreement (Incorporated by reference to Exhibit 10.12 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).
10.13#	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).
10.14†	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).
10.15†	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).
10.16†	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).
10.17#	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).
10.18#*	Form of Employment Agreement, between the Registrant and Gina Mazzariello
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.
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Filed herewith.

+ 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: March 13, 2023 By: /s/ Joshua B. Cohen

Joshua B. Cohen
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)	March 13, 2023
/s/ Justin B. Klee **Justin B. Klee**	Co-Chief Executive Officer and Director (Principal Executive Officer)	March 13, 2023
/s/ James M. Frates **James M. Frates**	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	March 13, 2023
/s/ George Mclean Milne Jr. **George Mclean Milne Jr. Ph.D.**	Director	March 13, 2023
/s/ Paul Fonteyne **Paul Fonteyne, M.S., M.B.A.**	Director	March 13, 2023
/s/ Daphne Quimi **Daphne Quimi, M.B.A.**	Director	March 13, 2023

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, 2022 and 2021, the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows, for each of the two years in the period ended December 31, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

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

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

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

/s/ Deloitte & Touche LLP
Boston, Massachusetts

March 13, 2023
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,	
	2022	**2021**
Assets		
Current assets:		
Cash and cash equivalents	$ 62,526	$ 50,191
Short-term investments	284,419	45,927
Prepaid expenses and other current assets	10,113	5,392
Accounts receivable, net	15,306	—
Inventories	9,769	—
Deferred offering costs	—	3,441
Total current assets	382,133	104,951
Property and equipment, net	2,611	474
Restricted cash equivalents	719	189
Operating lease right-of-use assets	5,524	—
Other assets	466	—
Total assets	$ 391,453	$ 105,614
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 6,257	$ 4,372
Accrued expenses and other current liabilities	38,312	13,024
Operating lease liabilities, current portion	2,040	—
Total current liabilities	46,609	17,396
Operating lease liabilities, net of current portion	4,237	—
Deferred rent	—	35
Total liabilities	50,846	17,431
Commitments and contingencies (Note 18)		
Series A redeemable convertible preferred stock, $0.0001 par value; 0 and 6,289,609 shares authorized, issued and outstanding as of December 31, 2022 and 2021, respectively	—	7,675
Series B redeemable convertible preferred stock, $0.0001 par value; 0 and 15,100,000 shares authorized as of December 31, 2022 and 2021, respectively; 0 and 14,496,835 shares issued and outstanding as of December 31, 2022 and 2021, respectively	—	64,387
Series C-1 redeemable convertible preferred stock, $0.0001 par value; 0 and 13,150,430 shares authorized, issued and outstanding as of December 31, 2022 and 2021, respectively	—	134,791
Series C-2 redeemable convertible preferred stock, $0.0001 par value; 0 and 3,170,585 shares authorized, issued and outstanding as of December 31, 2022 and 2021, respectively	—	32,498
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value; 10,000,000 and 0 shares authorized as of December 31, 2022 and 2021, respectively; 0 shares issued or outstanding as of December 31, 2022 and 2021	—	—
Common stock, $0.0001 par value; 300,000,000 and 56,500,000 shares authorized as of December 31, 2022 and 2021, respectively; 66,512,011 and 7,020,487 shares issued and outstanding as of December 31, 2022 and 2021, respectively	7	1
Additional paid-in capital	694,906	4,667
Accumulated deficit	(354,220)	(155,845)
Accumulated other comprehensive (loss) income	(86)	9
Total stockholders' equity (deficit)	340,607	(151,168)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 391,453	$ 105,614

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,	
	2022	2021
Revenues:		
Product revenue, net	$ 22,230	$ —
Grant revenue	—	285
Total revenues	22,230	285
Operating expenses:		
Cost of sales	2,993	—
Research and development	93,450	44,040
Selling, general and administrative	127,128	38,933
Total operating expenses	223,571	82,973
Loss from operations	(201,341)	(82,688)
Other income (expense), net:		
Interest income	4,291	36
Change in fair value of convertible notes	—	(5,228)
Other expense, net	(551)	(51)
Total other income (expense), net	3,740	(5,243)
Loss before income taxes	(197,601)	(87,931)
Provision for income taxes	774	—
Net loss	$ (198,375)	$ (87,931)
Net loss per share attributable to common stockholders —basic and diluted	$ (3.39)	$ (13.35)
Weighted-average shares used in computing net loss per share attributable to common stockholders—basic and diluted	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 LOSS
(in thousands)

	Year Ended December 31,	
	2022	2021
Net loss	$ (198,375)	$ (87,931)
Other comprehensive (loss) income:		
Foreign Currency translation adjustment	(69)	14
Unrealized loss on short-term investments	(26)	(5)
Other comprehensive (loss) income	(95)	9
Comprehensive loss	$ (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)

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Series C-1 Redeemable Convertible Preferred Stock		Series C-2 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	Shares	Amount	Shares	Amount	Shares	Amount				
Balance as of December 31, 2020	6,289,609	$ 7,675	14,496,835	$ 64,387	—	$ —	—	$ —	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	6,289,609	$ 7,675	14,496,835	$ 64,387	13,150,430	$ 134,791	3,170,585	$ 32,498	7,020,487	$ 1	$ 4,667	$ 9	$ (155,845)	$ (151,168)
Conversion of preferred stock into common stock upon initial public offering	(6,289,609)	(7,675)	(14,496,835)	(64,387)	(13,150,430)	(134,791)	(3,170,585)	(32,498)	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

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,	
	2022	**2021**
Cash flows used in operating activities:		
Net loss	$ (198,375)	$ (87,931)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	21,714	3,136
Depreciation expense	487	52
Amortization (accretion) of investment premiums (discounts)	(2,056)	121
Change in fair value of convertible notes	—	5,228
Changes in operating assets and liabilities:		
Accounts receivable, net	(15,306)	—
Inventories	(9,769)	—
Interest receivable	487	(144)
Prepaid expenses and other current assets	(5,221)	(4,486)
Operating lease right-of-use assets	1,635	—
Other assets	(456)	125
Accounts payable	1,854	670
Accrued expenses and deferred rent	26,052	8,432
Operating lease liabilities	(917)	—
Accrued interest and accrued interest—related parties	—	(2)
Net cash used in operating activities	(179,871)	(74,799)
Cash flows used in investing activities:		
Purchases of property and equipment	(2,526)	(353)
Purchases of investments	(415,873)	(49,053)
Proceeds from maturities of short-term investments	179,411	3,000
Net cash used in investing activities	(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	(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	2,189	343
Payment of deferred offering costs	—	(2,474)
Net cash provided by financing activities	431,789	158,506
Effect of exchange rate changes on cash, cash equivalents and restricted cash equivalents	(65)	13
Net increase in cash, cash equivalents and restricted cash equivalents	12,865	37,314
Cash, cash equivalents and restricted cash equivalents, beginning of period	50,380	13,066
Cash, cash equivalents and restricted cash equivalents, end of period	$ 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 loss on short-term investments	$ 26	$ 5
Purchases of property and equipment included in accounts payable	$ 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	$ 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 one day end the suffering caused by neurodegenerative diseases. The Company is focused on the development and potential global commercialization of its product candidate, AMX0035 (sodium phenylbutyrate and taurursodiol, also known as ursodoxicoltaurine) for the treatment of amyotrophic lateral sclerosis, or ALS. Our first product, RELYVRIO® (sodium phenylbutyrate and taurursodiol), previously known as AMX0035 in the U.S., is approved in the U.S. for the treatment of ALS in adults. AMX0035 is also approved with conditions by Health Canada and marketed as ALBRIOZA for the treatment of ALS in Canada. The Company's Marketing Authorisation Application, or MAA, for AMX0035 for the treatment of ALS remains under review by the Committee for Medicinal Products for Human Use, or CHMP, of the European Medicines Agency, or EMA. The Company is developing AMX0035 for other neurodegenerative diseases by leveraging its unique knowledge and relationships in the neurodegenerative space.

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 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 the regulatory approval processes of the EMA and other comparable foreign authorities, 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 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 future product candidates.

Going Concern

In accordance with Accounting Standards Update, or ASU, 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern (Subtopic 205-40)*, the Company has evaluated whether there are conditions and events that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date the consolidated financial statements are issued.

Since its inception, the Company has devoted substantially all of its efforts to research and development and pre-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. Expenses have primarily been for research and development and related general and administrative costs, and 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 continue to increase headcount and incur other significant costs related to our commercialization activities. The Company has generated revenues through five grants from the ALS Association, ALS Finding a Cure Foundation, Cure Alzheimer's Fund, Alzheimer's Drug Discovery Foundation and Alzheimer's Association, or Grantors. In addition to money received from its grants, the Company has also financed its operations through the public offering of its common stock, private sales of preferred stock, and convertible notes, and more recently through revenue from sales of RELYVRIO and ALBRIOZA in the U.S. and Canada, respectively.

The accompanying consolidated financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and satisfaction of liabilities in the normal course of business. The Company has incurred recurring losses and negative cash flows from operations since inception. As of December 31, 2022, the Company

had an accumulated deficit of $354.2 million. The Company expects its operating losses and negative operating cash flows may continue into the future as it continues initial sales of ALBRIOZA in Canada and RELYVRIO in the U.S., and continues to build capabilities and develop AMX0035, and any future product candidates. The Company expects that its cash, cash equivalents and short-term investments as of December 31, 2022, and product revenue from RELYVRIO and ALBRIOZA sales, will enable the Company to fund its ongoing operating expenses and capital expenditure requirements for at least the twelve-month period following the issuance of these consolidated financial statements.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

***Basis of Presentation and Consolidation*—**The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the 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 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, inventory, determining the fair value of convertible notes, accrued expenses, stock-based compensation, operating lease right-of-use assets and lease liabilities, 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, other retail pharmacies, 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, 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 current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. 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, 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.

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.

Grant Revenue—Grant revenue consists of amounts earned from performing contracted research and development services. The grants between the Company and the Grantors generally provide for the Company to meet certain research milestones in order for funds to be provided. The Company accounts for grants received to perform research and development services in accordance with ASC 730-20, *Research and Development Arrangements*, which requires an assessment, at the inception of the grant, of whether the grant is a liability or a contract to perform research and development services for others. If the Company is obligated to repay the grant funds to the Grantor regardless of the outcome of the research and development activities, then the Company is required to estimate and recognize that liability. Alternatively, if the Company is not required to repay, or if it is required to repay the grant funds only if the research and development activities are successful, then the grant agreement is accounted for as a contract to perform research and development services for others, in which case, grant revenue is recognized as the related research and development expenses are incurred. The Company obtained funding from the Grantors of zero and $0.3 million during the years ended December 31, 2022 and 2021, respectively, which was recorded as grant revenue in the Company’s consolidated statements of operations. Under the terms of the grants, the Company will be required to pay royalties upon occurrence of contingent future events (see Note 18).

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, 2022 and 2021, the Company's restricted cash equivalents balance was $0.7 million and $0.2 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. Given the nature collectability of the Company's accounts receivable to-date, an allowance for doubtful accounts is not deemed necessary at December 31, 2022 and 2021.

***Short-Term Investments*—**Short-term investments are composed of 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, 2022 and 2021, 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 at December 31, 2022, 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. Four customers individually accounted for approximately 97% of total gross product revenue in 2022 and three customers individually accounted for approximately 98% of total accounts receivable, net as of December 31, 2022.

***Convertible Note—Derivative*—**The Company reviews the terms of the convertible note issued to determine whether there are features, including redemption and conversion features, which are required to be bifurcated and accounted for separately as derivative financial instruments. In circumstances where the host instrument contains more than one embedded derivative instrument that is required to be bifurcated, the bifurcated derivative instruments are accounted for as a single, compound derivative instrument.

Bifurcated embedded derivatives are initially recorded at fair value and are then revalued at the end of each reporting period and immediately prior to the conversion or the extinguishment of the convertible note. Changes in the fair value are reported in the consolidated statement of operations. When the convertible note contains embedded derivative instruments that are to be bifurcated and accounted for as liabilities, the total proceeds received are first allocated to the fair value of all the bifurcated derivative instruments. The remaining proceeds, if any, are then allocated to the host instruments themselves, usually resulting in those host instruments being recorded at a discount from their face value. The discount from the face value of the convertible note, together with the stated interest on the host instrument, is amortized over the life of the host instrument through periodic charges to interest expense. The Company's convertible notes, as further discussed in Note 8, had embedded derivatives that required bifurcation from the host instrument.

Convertible Note—Beneficial Conversion Feature—If the conversion feature is not treated as a derivative, the Company assesses whether it is a beneficial conversion feature, or BCF. A BCF exists if the conversion price of the convertible note is less than the price of the stock into which it is convertible to on the commitment date. This typically occurs when the conversion price is less than the fair value of the stock on the date the instrument was issued. The value of a BCF is equal to the intrinsic value of the feature, the difference between the effective conversion price and the fair value of the stock into which it is convertible to and is recorded as additional paid-in capital and as a debt discount in the consolidated balance sheets. The Company amortizes the debt discount as non-cash interest expense over the life of the underlying convertible note using the effective interest method. If the convertible note is retired early, the associated debt discount is then recognized immediately as non-cash interest expense in the consolidated statements of operations. If the conversion feature does not qualify for either the derivative treatment or as a BCF, the convertible note is treated as traditional debt.

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 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 materials are released to production for use in the manufacture of drugs still in development.

Deferred Offering Costs—The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings, including the initial public offering, or IPO, as deferred costs

until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of proceeds generated as a result of the offering. Should an in-process equity financing be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statements of operations. After consummation of equity financings, the Company recorded deferred offering costs in stockholders' equity (deficit) of $5.5 million and zero for the years ended December 31, 2022 and 2021, respectively. The Company recorded deferred offering costs of zero and $3.4 million, which are included in the consolidated balance sheet as of December 31, 2022 and 2021, respectively.

***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, 2022 and 2021.

***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 costs are expensed as incurred and included in selling, general and administrative expenses in the accompanying consolidated statements of operations.

***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 and comprehensive loss.

***Stock-Based Compensation Expense*—**The Company accounts for stock-based compensation under the provisions of ASC 718-10, *Compensation—Stock Compensation*, which requires all share-based payments to employees, non-employees and directors, including grants of stock options and restricted stock, to be 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, 2022 and 2021.

***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 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 taxes, insurance, 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. The Company did not have financing leases as of December 31, 2022 and 2021.

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 interest and penalties related to uncertain 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, 2022, we continued to maintain a full valuation allowance against all of our 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 2022. 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, 2022 and 2021, 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 attributable to common stockholders 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) attributable to common stockholders 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.

Emerging Growth Company Status—The Company is an emerging growth company, or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act, and may take advantage of certain exemptions

from various reporting requirements that are applicable to other public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act and has elected to use the extended transition period for complying with new or revised accounting standards. As a result of this election, the Company's consolidated financial statements may not be comparable to companies that comply with public company FASB standards' effective dates. The Company intends to take advantage of the reduced reporting requirements and exemptions up until the last day of the fiscal year following the fifth anniversary of an offering or such earlier time that it is no longer an EGC.

Recent Accounting Pronouncements

New Accounting Pronouncements Not Yet Adopted—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. ASU 2016-13 requires a cumulative effect adjustment to the consolidated balance sheet as of the beginning of the first reporting period in which the guidance is effective. In November 2019, the FASB issued ASU 2019-10, *Financial Instruments—Credit Losses (Topic 326), Derivatives and Hedging (Topic 815) and Leases (Topic 842): Effective Dates*, which defers the effective date of ASU 2016-13 to fiscal years beginning after December 15, 2022 for all entities except Securities and Exchange Commission filers that are not smaller reporting companies. ASU 2016-13 will be effective for the Company for the period beginning January 1, 2023. The Company intends to adopt the ASU when it becomes effective. The Company is currently evaluating the impact of this ASU and does not expect that adoption of this standard will have a material impact on its consolidated financial statements and related disclosures.

Recently Adopted Accounting Pronouncements

Effective January 1, 2022, the Company adopted the requirements under the ASC 842 using the cumulative effect adjustment transition option. 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, which it began shipping to Customers in Canada and the U.S. in July 2022 and October 2022, respectively. Significant judgment is required in estimating GTN adjustments considering historical experience, payer channel mix, current contract prices, unbilled claims, processing time lags, inventory levels in the distribution channel and estimated product returns. The following table reconciles gross product revenue to net product revenue:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Product revenue, gross	$ 27,104	$ —
GTN adjustments	(4,874)	—
Product revenue, net	$ 22,230	$ —

4. SHORT-TERM INVESTMENTS

Short-term investments, which are classified as available-for-sale, consisted of the following:

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

December 31, 2021	Amortized Cost Basis	Unrealized Loss	Fair Values
		(in thousands)	
Commercial paper	$ 33,979	$ (1)	$ 33,978
Corporate debt securities	11,953	(4)	11,949
Total short-term investments	45,932	(5)	45,927

As of December 31, 2022 and 2021, all investments had contractual maturities within one year. The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts until maturity. Such amortization and accretion are included in interest income. There were no realized gains and losses recognized during the years ended December 31, 2022 and 2021. 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 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. The Company has the ability to hold its investments until maturity and generally does not intend to sell any investments prior to recovery of their amortized cost basis for any investment in an unrealized loss position. As of December 31, 2022 and 2021, there were no impairment charges on short-term investments.

5. INVENTORIES

Inventories consisted of the following:

	December 31,	
	2022	2021
	(in thousands)	
Raw materials	$ 7,151	$ —
Work in process	1,681	—
Finished goods	937	—
Total inventories	$ 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. Inventory on hand determined to not have a future economic benefit and acquired prior to receipt of the marketing authorization for ALBRIOZA in Canada, totaling approximately $22.9 million, was expensed as research and development expense as incurred. The Company began to capitalize the costs determined to have a probable future economic benefit associated with the production of ALBRIOZA upon receipt of Health Canada approval in June 2022. Finished goods have a shelf life of 12-15 months from the date of manufacture.

Of the inventories reported on balance sheet at December 31, 2022, the Company had $3.2 million of long-term raw materials that are not expected to be realized in cash, sold or consumed during the next 12 months.

6. PROPERTY AND EQUIPMENT, NET

Property and equipment, net consisted of the following:

	December 31,	
	2022	2021
	(in thousands)	
Furniture and fixtures	$ 362	$ 88
Computer hardware and software	1,810	250
Leasehold improvements	176	50
Construction in progress	803	139
Total property and equipment	3,151	527
Less: accumulated depreciation	(540)	(53)
Total property and equipment, net	$ 2,611	$ 474

7. ACCRUED EXPENSES

Accrued expenses consisted of the following:

	December 31,	
	2022	2021
	(in thousands)	
External research and development	$ 8,424	$ 5,666
Payroll and employee related expenses	15,231	4,280
Manufacturing	4,596	—
Accrued consulting and other professional fees	4,116	2,820
Rebates and other GTN adjustments	3,582	—
Royalty payable	1,358	—
Other accrued expenses	1,005	258
Total accrued expenses	$ 38,312	$ 13,024

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 2021 Notes contained the following features:

Automatic Conversion Features—The 2021 Notes were to automatically convert into Conversion Shares upon (i) an IPO, (ii) any transaction in which the Company merges with, consolidates with or enters into other similar transaction with a Special Purpose acquisition Corp, or SPAC, resulting in some or all of its shares being registered for sale under applicable securities laws and listed for trading on a national or foreign exchange, or De-SPAC transaction, (iii) the acquisition of the Company by another person or entity by means of any transaction in which holders of the outstanding voting securities of the Company immediately before such transaction held less than 50% of the voting securities of the Company or the surviving corporation after such transaction or a sale of all or substantially all of the assets of the Company but excluding De-SPAC transaction, IPO, and the occurrence of equity financing in which the Company sold shares of its preferred stock for new money and which was neither an IPO or a Qualified Financing, or Change of Control, and (iv) the closing of a sale of an equity transaction in which the Company sold shares with an aggregate gross proceeds of at least $10.0 million, or Qualified Financing.

In the event of a Change of Control, De-SPAC transaction, or an IPO, the Conversion Shares would be common stock of the Company. In the event of a Qualified Financing, the Conversion Shares would be shares of preferred stock issued in such transaction.

Optional Conversion Feature—The holders of the 2021 Notes had the option to elect to convert their notes into Conversion Shares at the Conversion Price upon the occurrence of an equity financing in which the Company sold shares of its preferred stock for new money and which was neither an IPO or a Qualified Financing, or Non-Qualified Financing, and together with the IPO, De-SPAC transaction, Change of Control, and the Qualified Financing, collectively, the "Conversion Events"). In the event of a Non-Qualified Financing, the Conversion Shares would be the class of equity shares issued in such transaction. The 2021 Notes would be deemed to have converted into the Conversion Shares if no election was made by the holders of the 2021 Notes.

Conversion Price—Upon the occurrence of an IPO, the 2021 Notes would convert into shares of common stock at the conversion price equal to the lesser of (i) 85% of the price at which the Company offered each share of common stock in the IPO without deducting any amount for discounts, commissions, fees, or other costs and (ii) $600.0 million divided by the fully diluted capital.

Upon the occurrence of a De-SPAC transaction, the 2021 Notes would convert into shares of common stock at the conversion price equal to the lesser of (i) 85% of the common stock price in the De-SPAC transaction, which would be determined by dividing (x) the total consideration to be paid to common stockholders upon a De-SPAC transaction less the principal amount of the 2021 Notes including accrued and unpaid interest by (y) the common stock issued and outstanding immediately prior to the De-SPAC transaction and that would be exchanged as a result of the De-SPAC transaction including common stock that would be issued upon the exercise of stock options immediately before the Change of Control transaction but excluding the common stock issuable upon conversion of the 2021 Notes and (ii) $600.0 million divided by the fully diluted capital.

Upon the occurrence of a Change of Control, the 2021 Notes would convert into shares of common stock at the conversion price equal to the lesser of (i) 85% of the common stock price in the Change of Control, which would be determined by dividing (x) the total consideration to be paid to common stockholders upon a Change of Control less the principal amount of the 2021 Notes including accrued and unpaid interest by (y) the common stock issued and outstanding immediately prior to the Change of Control and that would be exchanged upon a Change of Control including common stock that would be issued upon the exercise of stock options before the Change of Control but excluding the common stock issuable upon conversion of the 2021 Notes and (ii) $600.0 million divided by the fully diluted capital.

Upon a Qualified Financing, the 2021 Notes would convert into shares of preferred stock issued in the Non-Qualified Financing at the conversion price equal to the lesser of (i) 85% of the lowest price at which the Company sold shares of its stock in the Qualified Financing and (ii) $600.0 million divided by the fully diluted capital.

Repayment—Each holder of the 2021 Notes had the option to elect to receive a payment in the amount equal to the principal amount plus accrued and unpaid interests upon a Change of Control. If a Change of Control occurred and no election was made by the holder, the principal amount and accrued and unpaid interest would be deemed to have automatically be converted into shares of the Company's common stock of the Company immediately prior to the close of the Change of Control.

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.

There were no convertible notes outstanding as of December 31, 2022 and 2021.

Convertible Notes—Related Parties

There were no convertible notes issued to related parties that were outstanding as of December 31, 2022 and 2021. 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.

Valuation of the 2021 Notes

At the issuance date of the 2021 Notes, the Company determined that the fair value of the 2021 Notes approximated the principal amounts of the 2021 Notes as the transaction was deemed to be at arm's length. Subsequent measurement of fair value of the 2021 Notes at each reporting period was estimated based on significant inputs not observable in the market, which represents a Level 3 measurement within the fair value hierarchy. The Company used a scenario-based analysis to incorporate estimates and assumptions concerning the Company's prospects and market indications into a model to estimate the value of the 2021 Notes. The most significant estimates and assumptions used as inputs were those concerning timing, probability of possible scenarios for conversion or settlement of the 2021 Notes and discount rates. The fair value of the 2021 Notes upon settlement in July 2021 was determined based on the fair value of the Series C-1 redeemable convertible preferred stock issued. This method was selected as the Company concluded that the contemporaneous financing transaction was an arm's length transaction. The issuance of the Series C-1 redeemable convertible preferred stock was considered to be a Qualified Financing (see Note 11) pursuant to the original terms of the 2021 Notes. Accordingly, the fair value calculation for the 2021 Notes immediately before conversion considered both the fair value of the Series C-1 redeemable convertible preferred stock and the conversion price, which was 85% of the fair value of the Series C-1 redeemable convertible preferred stock. The fair value of the 2021 Notes as of June 30, 2021 was determined to be the same as that on the settlement date in July 2021 based on management's determination of no material changes to the assumptions underlying the determination of the fair value of the 2021 Notes.

9. FAIR VALUE MEASUREMENTS

The following table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values:

	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

	December 31, 2021			
	Level 1	Level 2	Level 3	Total
	(in thousands)			
Assets:				
Money market funds	$ 49,271	$ —	$ —	$ 49,271
Short-term investments:				
Commercial paper	—	33,978	—	33,978
Corporate debt securities	—	11,949	—	11,949
Total short-term investments	—	45,927	—	45,927
Restricted cash	189	—	—	189
Total financial assets	$ 49,460	$ 45,927	$ —	$ 95,387

Valuation of Short-Term Investments

The Company estimates the fair values of the short-term investments by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. The Company validates the prices provided by our third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

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, 2022 and 2021.

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 year ended December 31, 2022:

	Year ended December 31, 2022
	(in thousands)
Lease cost	
Operating lease cost	$ 2,136
Total lease cost	$ 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 (in thousands):

	As of December 31, 2022
Assets	
Operating lease right-of-use assets	$ 5,524
Liabilities	
Operating lease right-of-use liabilities, current	$ 2,040
Operating lease right-of-use liabilities, net of current portion	4,237
Total operating lease liabilities	$ 6,277

During the year ended December 31, 2022, the Company made cash payments of $1.4 million for operating leases. Future minimum lease payments under non-cancelable leases as of December 31, 2022, were as detailed below (in thousands):

	As of December 31, 2022
2023	$ 2,417
2024	2,478
2025	1,586
2026	476
2027	—
Total undiscounted lease payments	6,957
Less: imputed interest	(680)
Total operating lease liabilities	$ 6,277

As of December 31, 2022, the weighted average remaining lease term was 2.9 years and the weighted average incremental borrowing rate used to determine the operating lease right-of-use assets was 7.3%.

ASC 840 Disclosures

Future minimum lease payments under non-cancelable leases as of December 31, 2021, were as detailed below (in thousands):

	As of December 31, 2021
2022	$ 532
2023	541
2024	555
2025	563
2026	476
Total operating lease liabilities	$ 2,667

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

As of December 31, 2021, the holders of the Series C Preferred Stock, or together with the Series A redeemable convertible preferred stock and the Series B redeemable convertible preferred stock, collectively, the Preferred Stock, had the following rights and preferences:

Conversion— On June 18, 2020, in connection with the conversion of the 2017 Notes, the Company adjusted the conversion price for the Series A redeemable convertible preferred stock of $1.229073 per share to $1.2065. The adjustment was made in accordance with the anti-dilution provisions in the certificate of incorporation then in effect immediately prior to the conversion of the 2017 Notes. The adjustment to the conversion price resulted in neither modification nor extinguishment of the Series A redeemable convertible preferred stock as the terms of the Series A redeemable convertible preferred stock were not amended. The adjustment to the conversion price resulted in additional 117,650 shares of common stock to be issued to holders of the Series A redeemable convertible preferred stock upon conversion of such shares into common stock. As of December 31, 2020, these additional shares of common stock were not issued and outstanding.

In July 2021, in connection with the conversion of the 2021 Notes, the Company adjusted the conversion price for the Series B redeemable convertible preferred stock of $16.974077 per share to $14.6942. The adjustment was made in accordance with the anti-dilution provisions in the certificate of incorporation then in effect immediately prior to the conversion of the 2021 Notes. The adjustment to the conversion price resulted in additional 2,249,224 shares of common stock into which Series B redeemable convertible preferred stock would be convertible. As of December 31, 2021, these additional shares were not issued and outstanding. Each share of Preferred Stock is convertible into an equivalent number of common stock, at any time, at the option of the holder. The initial conversion price for the Series C-1 redeemable convertible preferred stock and Series C-2 redeemable convertible preferred stock is the respective original issue prices.

The conversion price for the Preferred Stock was subject to adjustments for stock splits, stock dividends, or similar recapitalization, and subject to adjustments in accordance with the anti-dilution provisions.

The shares of Preferred Stock were to automatically convert into common stock of the Company immediately upon either (a) the closing of the sale of shares of common stock to the public in a firm commitment underwritten public offering pursuant to an effective registration statement under the Securities Act, resulting in at least $75.0 million of proceeds, net of the underwriting discount and commissions, to the Company, or Qualified IPO, or (b) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of a majority of the then outstanding shares of Preferred Stock.

Dividends—Dividends may be paid to the holders of the Series A redeemable convertible preferred stock. The holders the Series A redeemable convertible preferred stock are entitled to receive non-cumulative dividends at a rate per annum of $0.073744 per share when and if declared by the Board of Directors. The holders of the Series B redeemable

convertible preferred stock were entitled to receive a non-cumulative dividend at the rate of 6% per annum of the Series B original issue price per share when and if declared by the Board of Directors. As of December 31, 2021, no cash dividends were declared or paid. From and after the date of issuance of the Series C Preferred Stock, the Company was not to set, declare, pay or set aside unless holders of the Series C Preferred Stock then outstanding shall first receive, or simultaneously receive, dividends on each outstanding share of Series C Preferred Stock in an amount equal to (i) in the case of dividends being distributed to common stock or any class or series of capital stock that is convertible into common stock, the equivalent dividend on an as-converted basis or (ii) in the case of dividends being distributed on a series or class not convertible into common stock, an additional dividend equal to a dividend rate calculated based on the respective original issue price of the Series C Preferred Stock. The original issue prices per share for the Series C-1 redeemable convertible preferred stock and Series C-2 redeemable convertible preferred stock were $10.265809 and $8.725938, respectively.

Voting Rights— The holders of the Preferred Stock were entitled to vote on any matter presented to stockholders of the Company for consideration. Each holder of the Preferred Stock was entitled to cast the number of votes equal to the number of shares of common stock into which the shares of the Preferred Stock held by such holder were convertible on such date.

Redemption—The Preferred Stock did not contain any mandatory redemption features. In accordance with FASB ASC Topic 480, *Distinguishing Liabilities from Equity*, preferred stock issued with redemption provisions that are outside of the control of the Company or that contain certain redemption rights in a deemed liquidation event is required to be presented outside of stockholders' equity (deficit) on the face of the consolidated balance sheets. The Company classified the Preferred Stock outside of the stockholders' equity (deficit) as mezzanine equity because in the event of certain deemed liquidation events, which included events such as a sale or merger, that were not solely within the control of the Company, the shares of the Preferred Stock would have become redeemable at the option of the holders. The Company did not adjust the carrying values of the Preferred Stock to the redemption values of such shares since a deemed liquidation event did not occur and the shares were not probable of becoming redeemable in the future as of the consolidated balance sheet dates.

Liquidation—In the event of a liquidation, deemed liquidation, dissolution or winding up of the Company, holders of the Preferred Stock would have been entitled to be paid out of the assets of the Company that were available for distribution before any payment is made to the holders of common stock. The amount to paid would have been the greater of (i) respective original issue prices plus any dividends declared but unpaid or (ii) the amount that would have been payable had all shares of Preferred Stock been converted into common stock immediately before such event. If upon any such liquidation, deemed liquidation, dissolution or winding up of the Company, the assets of the Company available for distribution to its stockholders would have been insufficient to pay the holders of Preferred Stock the full amount to which they would have been entitled, the holders of Preferred Stock would have shared ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

After the payment of all preferential amounts required to be paid to the holders of Preferred Stock, the remaining assets of the Company available for distribution to its stockholders would have been distributed among the holders of the shares of common stock on a pro rata basis based on the number of shares held by each such holder.

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, 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, 2022 and 2021.

The Company had reserved shares of common stock for issuance in connection with the following:

	December 31,	
	2022	2021
Common stock authorized	300,000,000	56,500,000
Common stock issued and outstanding	66,512,011	7,020,487
Common stock authorized and reserved for future issuances:		
Series A redeemable convertible preferred stock	—	6,407,256
Series B redeemable convertible preferred stock	—	16,746,059
Series C-1 redeemable convertible preferred stock	—	13,150,430
Series C-2 redeemable convertible preferred stock	—	3,170,585
Common stock reserved for the exercise of stock options	8,480,950	5,339,011
Common stock reserved for the unvested restricted stock units	740,297	—
Common stock reserved for future issuance of share-based awards	2,817,751	1,444,492
Total common stock authorized and reserved for future issuance	12,038,998	46,257,833
Unreserved common stock available for future issuance	221,448,991	3,221,680

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, 2022, there were 2,817,751 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.

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,	
	2022	2021
Grant price	$ 20.29	$ 7.69
Risk-free interest rate	1.97%	1.01%
Expected term (in years)	6.07	5.73
Expected volatility	88.75%	81.61%
Dividend yield	0.00%	0.00%

The per share weighted average grant date fair value of stock options granted during the year ended December 31, 2022 and 2021 was $15.10 and $5.25, respectively.

A summary of option activity for the year ended December 31, 2022, 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, 2021	5,339,011	$ 5.54	8.7	$ 15,627
Granted	4,237,720	$ 20.29		
Exercised	(950,013)	$ 2.33		
Cancelled or forfeited	(145,768)	$ 10.98		
Outstanding at December 31, 2022	8,480,950	$ 13.19	8.2	$ 201,765
Exercisable at December 31, 2022	2,055,416	$ 6.03	7.0	$ 63,408
Unvested at December 31, 2022	6,425,534	$ 15.47	8.6	$ 138,357

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, 2022 and 2021, was $14.2 million and $6.2 million, respectively.

The total fair value of stock options vested during the years ended December 31, 2022 and 2021 was $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, 2022, is as follows:

	Number of shares	Weighted Average Grant Date Fair Value
Nonvested as of December 31, 2021	—	$ —
Granted	752,613	$ 19.98
Vested	—	$ —
Forfeited	(12,316)	$ 17.82
Nonvested as of December 31, 2022	740,297	$ 20.02

***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,	
	2022	2021
	(in thousands)	
Research and development expenses	$ 5,639	$ 888
Selling, general and administrative expenses	16,075	2,248
Total stock-based compensation	$ 21,714	$ 3,136

The following table summarizes stock-based compensation by type of award:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Stock options	$ 18,844	$ 3,136
Restricted stock units	2,870	—
Total stock-based compensation expense	$ 21,714	$ 3,136

The following table summarizes unrecognized stock-based compensation expense as of December 31, 2022, 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, 2022	
	Unrecognized Expense	Weighted-average Recognition Period
	(in thousands)	(in years)
Stock options	$ 61,049	2.79
Restricted stock units	$ 11,950	3.25

14. INCOME TAXES

The components of net loss before the provision for income taxes are as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
U.S.	$ (198,704)	$ (87,904)
Non-U.S.	1,103	(27)
Loss before income taxes	$ (197,601)	$ (87,931)

The provision for income taxes for the years ended December 31, 2022 and 2021 is as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Current income tax provision		
U.S. - Federal	$ —	$ —
U.S. - State	—	—
Non-U.S.	774	—
Provision for income taxes	$ 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, 2022 and 2021 is as follows:

	Year Ended December 31,	
	2022	2021
Tax at U.S. statutory tax rate	21.0%	21.0%
State income tax benefit	3.9%	4.0%
Research and development tax credits	1.4%	1.5%
Valuation allowances	(25.5)%	(24.4)%
Other	(1.2)%	(2.1)%
Effective income tax rate	(0.4)%	0.0%

Deferred tax assets and liabilities reflect the net tax effects of net operating loss and tax credit carryforwards and temporary differences between the carrying amount of assets and liabilities for financial reporting and the amounts used for tax purposes. Significant components of the Company's deferred tax assets and liabilities were as follows for the years ended December 31, 2022 and 2021:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Deferred tax assets:		
Federal net operating loss carryforwards	$ 42,673	$ 24,303
State net operating loss carryforwards	10,628	5,474
Capitalized research and development costs	18,079	6,205
Inventory	5,721	—
Tax credits	5,581	2,808
Accruals and other	9,284	1,556
Total deferred tax assets	$ 91,966	$ 40,346
Valuation allowance	(90,587)	(40,346)
Net total deferred tax assets	$ 1,379	$ —
Deferred tax liabilities:		
Other	(1,379)	—
Total deferred tax liabilities	$ (1,379)	$ —
Net deferred tax assets	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. The Company has considered its history of cumulative losses, including significant losses incurred in every year since inception, including 2022, and has concluded that it is more likely than not that it will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2022 and 2021.

On a periodic basis the Company reassess the valuation allowance that has been established, weighing positive and negative evidence. In 2022, the Company reassessed the valuation allowance and considered negative evidence, including cumulative losses over the three years ended December 31, 2022, and positive evidence, including regulatory approvals of ALBRIOZA and RELYVRIO. After assessing both the negative and positive evidence, the Company concluded that a full valuation should be retained against the net deferred tax assets as of December 31, 2022. 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, 2022 and 2021, the Company had federal net operating loss carryforwards of approximately $203.2 million and $115.7 million, respectively, and state net operating loss carryforwards of approximately $164.1 million and $102.9 million, respectively, which are available to reduce future taxable income. Of the $203.2 million federal net operating loss carryforwards, $1.3 million begin to expire in 2034 and the remaining $201.9 million net operating losses carryforward indefinitely. Of the $164.1 million state net operating loss carryforwards, $113.0 million of Massachusetts net operating loss carryforwards begin to expire in 2034. As of December 31, 2022 and 2021, the Company also had federal tax

credits of $4.6 million and $2.7 million, respectively, and state tax credits of $1.2 million. The tax credit carryforwards will expire at various dates beginning in 2034.

The utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. The Company has not conducted a formal study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382 and 383 of the Code, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards may be subject to an annual limitation, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization.

The Company has not yet conducted a study of its research and development credit carryforward. Such a study, once undertaken by the Company, may result in an adjustment to the Company's research and development credit carryforward. A full valuation allowance has been provided against the Company's research and development credit and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance.

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets as of December 31, 2022 and 2021, because the Company's management has determined that it is more likely than not that these assets will not be fully realized. The increase in the valuation allowance recorded during the year primarily relates to the net operating loss incurred by the Company as well as the increase in research and development credits.

The following table reflects the roll-forward of the Company's valuation allowance:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Valuation allowance at beginning of year	$ 40,346	$ 18,900
Increases recorded to income tax provision	50,241	21,446
Valuation allowance at end of year	$ 90,587	$ 40,346

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 for the years ended December 31, 2022 and 2021 is as follows:

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Balance at beginning of the period	$ 564	$ 349
Increases (decreases) related to tax positions taken during prior years	(32)	—
Increases related to tax positions taken during the prior years	481	215
Balance at end of the period	$ 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. Unrecognized tax benefits represent the aggregate tax effect of differences between tax return positions and the benefits recognized in the consolidated financial statements. The Company does not expect the amount of unrecognized tax benefits to 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 two years ended December 31, 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 Internal Revenue Code limits. The Company provides a safe-harbor contribution of 3% of employee compensation to employees who satisfy the minimum service requirements. The Company made $1.2 million and $0.3 million of safe-harbor contributions for the years ended December 31, 2022 and 2021, respectively.

16. NET LOSS PER SHARE

***Net Loss per Share Attributable to Common Stockholders*—**Because the Company reports a net loss attributable to common stockholders, basic and diluted net loss per share attributable to common stockholders are the same for both periods presented. All preferred stock, stock options and restricted stock units have been excluded from the computation of diluted weighted-average shares outstanding because such securities would have an antidilutive impact. The following common stock equivalents outstanding at each period end have been excluded from the calculation of diluted net loss per share because their inclusion would have been antidilutive:

	December 31,	
	2022	2021
Options to purchase common stock	8,480,950	5,339,011
Restricted stock units	740,297	—
Redeemable convertible preferred stock	—	39,474,330
Total excluded common stock equivalents	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 is a 5% significant stockholder of the Company. 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

***Operating Leases*—**The Company leases its 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. As of January 1, 2022, the Company adopted ASC 842 which requires lessees to recognize assets and liabilities on the balance sheet for the rights and obligations created by leases. As a result of this adoption, the Company recorded a right-of-use asset and corresponding lease liability on the consolidated balance sheet. The Company continues to recognize rent expense, which is calculated as the remaining cost of the lease allocated over the remaining lease term on a straight-line basis. See Note 10 for additional information regarding the Company's operating leases.

***Letter of Credit*—**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, 2022 and 2021, the Company's restricted cash equivalents balance was $0.7 million and $0.2 million, respectively

Legal Proceedings—The Company is not currently 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 agreements with the 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 disease and Alzheimer's disease. Under the terms of the arrangements, the Company would receive a tranche of funds as it completes 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 year ended December 31, 2022, the Company recorded $1.4 million in royalty expense, which is included in cost of sales in the consolidated financial statements.

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 year ended December 31, 2022.

19. SUBSEQUENT EVENTS

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company has evaluated all subsequent events and determined that there are no material recognized or unrecognized subsequent events requiring disclosure, except as described below.

Silicon Valley Bank ("SVB") was closed on March 10, 2023 by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation ("FDIC") as receiver. At the time of closing, the Company maintained less than $1.0 million of its cash in deposit accounts with SVB and held sufficient liquid assets at Bank of America to manage its operational needs. The vast majority of the Company's cash, cash equivalents and short-term investments reside in custodial accounts held by U.S. Bank for which SVB Asset Management is the advisor. The Company's investment portfolio currently does not contain any securities of SVB. On March 12, 2023, the U.S. Treasury, Federal Reserve, and FDIC announced that SVB depositors will have access to all of their money starting March 13, 2023. The Company does not believe it will be impacted by the closure of SVB and will continue to monitor the situation as it evolves.

On March 13, 2023, the Company announced the appointment of Karen Firestone, Chairman, CEO, and co-founder of Aureus Asset Management and prior fund manager at Fidelity Investments, to the company's Board of Directors. Ms. Firestone's appointment to the Board of Directors is effective as of March 16, 2023.

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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

EXECUTIVE OFFICERS

Joshua Cohen
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

Margaret Olinger
Chief Commercial Officer

Patrick D. Yeramian, M.D.
Chief Medical Officer

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