

Prospectus supplement
(To prospectus dated March 3, 2026)**14,090,000 Shares of common stock**

We are offering 14,090,000 shares of our common stock, par value \$0.0001 per share.

Our common stock is listed on the Nasdaq Global Select Market, or Nasdaq, under the symbol "AMLX." On August 18, 2026, the closing price of our common stock, as reported on Nasdaq, was \$35.11 per share.

Investing in our securities involves significant risks that are described in the "[RISK FACTORS](#)" section beginning on page S-7 of this prospectus supplement and page 8 of the accompanying prospectus, and in the other documents that are incorporated by reference herein. You should read the entire prospectus supplement and the accompanying prospectus, including any information incorporated by reference herein or therein, carefully, before you make your investment decision.

We are a smaller reporting company as defined under Rule 405 of the Securities Act of 1933, as amended, or the Securities Act, and, as such, are subject to certain reduced public company reporting requirements. See "*Prospectus Supplement Summary—Implications of Being a Smaller Reporting Company*" on page S-4 of this prospectus supplement.

	Per share	Total
Public offering price	\$ 35.500	\$ 500,195,000
Underwriting discounts and commissions ⁽¹⁾	\$ 1.988	\$ 28,010,920
Proceeds, before expenses, to us	\$ 33.512	\$ 472,184,080

- (1) We have agreed to reimburse the underwriters for certain expenses. See "*Underwriting*" beginning on page S-20 of this prospectus supplement for additional information regarding the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to an additional 2,113,500 shares of our common stock at the public offering price less the underwriting discounts and commissions.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock against payment on or about August 21, 2026.

Leerink Partners**Morgan Stanley****Guggenheim Securities****LifeSci Capital****Prospectus Supplement dated August 19, 2026**

Table of Contents
Prospectus Supplement

ABOUT THIS PROSPECTUS SUPPLEMENT	Page S-ii
PROSPECTUS SUPPLEMENT SUMMARY	S-1
THE OFFERING	S-5
RISK FACTORS	S-7
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-9
USE OF PROCEEDS	S-11
DIVIDEND POLICY	S-12
DILUTION	S-13
CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS	S-15
UNDERWRITING	S-20
LEGAL MATTERS	S-24
EXPERTS	S-25
WHERE YOU CAN FIND MORE INFORMATION	S-26
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	S-27

Prospectus

About this Prospectus	<u>Page</u> ii
Special Note Regarding Forward-Looking Statements	1
The Company	4
Where You Can Find More Information	6
Incorporation By Reference	7
Risk Factors	8
Use of Proceeds	9
Description of Capital Stock	11
Description of Debt Securities	16
Description of Warrants	18
Description of Units	19
Plan of Distribution	20
Legal Matters	24
Experts	24

ABOUT THIS PROSPECTUS SUPPLEMENT

This document has two parts. The first part is this prospectus supplement, which describes the specific terms of this offering of common stock. The second part is the accompanying prospectus which provides more general information, some of which may not apply to this offering. The information included or incorporated by reference in this prospectus supplement also adds to, updates and changes information contained or incorporated by reference in the accompanying prospectus. If information included or incorporated by reference in this prospectus supplement is inconsistent with the accompanying prospectus or the information incorporated by reference therein, then this prospectus supplement or the information incorporated by reference in this prospectus supplement will apply and will supersede the information in the accompanying prospectus and the documents incorporated by reference therein.

This prospectus supplement is part of our shelf registration statement on Form S-3 (File No. 333-293956) that we filed with the Securities and Exchange Commission, or the SEC, on March 3, 2026, using a “shelf” registration process as a “well-known seasoned issuer” as defined in Rule 405 of the Securities Act of 1933, as amended, or the Securities Act, which became automatically effective upon filing. Under this shelf registration process, we may from time to time offer and sell any combination of the securities described in the accompanying prospectus, of which this offering is a part.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf. We have not, and the underwriters have not, authorized any other person to provide you with information different from that contained in this prospectus supplement and the accompanying prospectus or incorporated by reference in this prospectus supplement and the accompanying prospectus. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell or soliciting an offer to buy these securities under any circumstance in any jurisdiction where the offer or solicitation is not permitted. You should assume that the information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus prepared by us or on our behalf is accurate only as of the date of the respective document in which the information appears, and that any information in documents that we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus supplement, the accompanying prospectus and the information incorporated herein or therein by reference contains market data, industry statistics and other data that have been obtained or compiled from information made available by independent third parties. We have not independently verified the accuracy and completeness of such data.

It is important for you to read and consider all of the information contained in this prospectus supplement and the accompanying prospectus before making your investment decision. We include cross-references in this prospectus supplement and the accompanying prospectus to captions in these materials where you can find additional related discussions. The table of contents in this prospectus supplement provides the pages on which these captions are located. You should read both this prospectus supplement and the accompanying prospectus, together with the additional information described in the sections entitled “*Where you can find more information*” and “*Incorporation of certain information by reference*” of this prospectus supplement, before investing in our common stock.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such

representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

All references in this prospectus supplement and the accompanying prospectus to our consolidated financial statements include the related notes thereto.

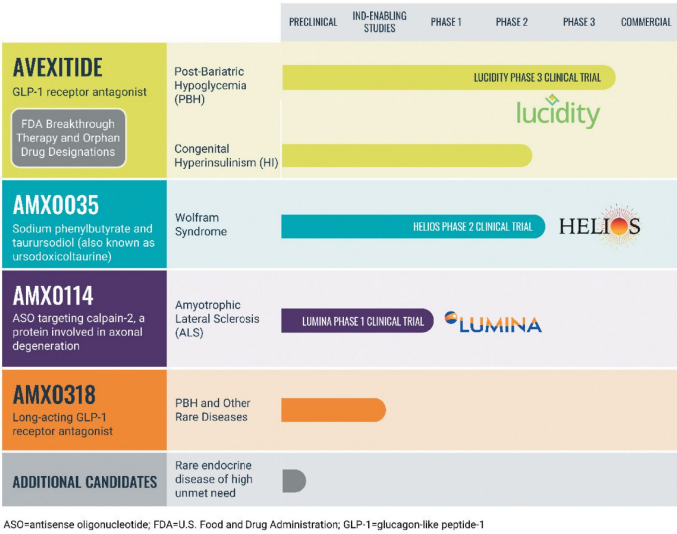
Unless otherwise indicated, the terms “Amylyx,” “the Company,” “we,” “us,” and “our” refer to Amylyx Pharmaceuticals, Inc. and its consolidated subsidiaries, unless the context otherwise requires. Amylyx and other trademarks or service marks of Amylyx appearing in this prospectus supplement are the property of Amylyx. The other trademarks, trade names and service marks appearing in this prospectus supplement are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

PROSPECTUS SUPPLEMENT SUMMARY

The following summary of our business highlights some of the information contained elsewhere in, or incorporated by reference into, this prospectus supplement. Because this is only a summary; however, it does not contain all of the information that may be important to you. You should carefully read this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference, which are described under “Incorporation of certain information by reference” in this prospectus supplement. You should also carefully consider the matters discussed in the section of this prospectus supplement entitled “Risk Factors” on page S-7 of this prospectus supplement and in the section entitled “Risk Factors” of our Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, and any subsequent reports we file with the SEC, which are incorporated by reference in this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement, before making an investment decision.

Company Overview

We are a pre-commercial pharmaceutical company with a mission to develop and advance novel therapies for communities with high unmet medical needs. We have preclinical and clinical development programs underway in endocrine conditions and neurodegenerative diseases. We are advancing a pipeline in which we have matched investigational therapies with diseases for which we believe these therapies can make the greatest impact, based on well-defined mechanistic rationales, clear clinical outcomes and biomarkers, and rigorous preclinical data, agnostic of modality. We are currently developing four investigational therapies for potential impact across several diseases: avexitide in post-bariatric hypoglycemia, or PBH, AMX0035 in Wolfram syndrome, AMX0114 in amyotrophic lateral sclerosis, or ALS, and AMX0318 in PBH and other rare diseases. Our current pipeline is represented in the table below.



Our lead investigational asset is avexitide, a first-in-class glucagon-like peptide-1, or GLP-1, receptor antagonist. Avexitide has been evaluated as a treatment for PBH and congenital hyperinsulinism, or congenital HI, two indications characterized by hyperinsulinemic hypoglycemia. The U.S. Food and Drug Administration, or the FDA, has granted avexitide Breakthrough Therapy Designation for both PBH and congenital HI, Rare Pediatric Disease Designation for congenital HI, and Orphan Drug Designation for the treatment of hyperinsulinemic hypoglycemia. PBH is a chronic metabolic condition that is estimated to affect approximately 8% of people in the U.S. who have undergone the two most common types of bariatric surgery, sleeve gastrectomy and Roux-en-Y gastric bypass, or RYGB, (approximately 160,000 people in the U.S.). PBH can be associated with substantial disability, compromising safety, disrupting independent living, and affecting nutritional status and overall quality of life. Despite the substantial burden, there are currently no FDA-approved therapies for PBH. Avexitide is a GLP-1 receptor antagonist designed to competitively bind to the GLP-1 receptor on pancreatic islet beta cells and inhibit the exaggerated GLP-1-driven insulin response characteristic of PBH, reducing inappropriate insulin secretion and stabilizing blood glucose levels.

LUCIDITY (NCT06747468) was a 78-participant, multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial which evaluated the efficacy and safety of avexitide in participants with PBH following RYGB surgery. The primary efficacy objective of LUCIDITY was to evaluate the FDA-agreed-upon primary outcome of reduction in the composite of Level 2 and Level 3 hypoglycemic events through Week 16. Safety and tolerability were also evaluated. In August 2026, we announced topline data from the LUCIDITY trial. See “Recent Developments” for additional information.

Avexitide was generally well-tolerated, with a favorable safety profile replicated across the five previous clinical trials in people with PBH. In addition, avexitide demonstrated a clear GLP-1 antagonist pharmacodynamic effect, including lowering insulin and raising the glucose nadir, in healthy volunteers.

In May 2026, we announced the initiation of an Expanded Access Program (EAP) for the use of avexitide to treat U.S. adults with PBH following RYGB surgery. Initial eligible patients include individuals who have completed the pivotal Phase 3 LUCIDITY clinical trial and participants in a prior trial of avexitide in PBH following RYGB surgery.

AMX0035 is designed to slow or mitigate neurodegeneration by targeting endoplasmic reticulum, or ER stress, and mitochondrial dysfunction, two connected central pathways that lead to cell death and neurodegeneration. We are investigating AMX0035 in Wolfram syndrome, a neurodegenerative disease where ER stress and mitochondrial dysfunction are implicated. In June 2026, we presented longer-term Week 96 (n=9) data from HELIOS. At Week 96, measures of pancreatic function and glycemic control were stable or improved relative to baseline in most participants. Visual acuity and patient- and clinician-reported outcomes showed patterns consistent with disease stabilization with interpretation limited by the open-label, single-arm design and small sample size. The safety profile of AMX0035 in HELIOS data at Week 96 were generally consistent with prior safety data from prior studies of AMX0035. Nearly all adverse events, or AEs, were mild or moderate, and there were no serious adverse events, or SAEs, related to AMX0035 treatment. We continue to work with the FDA on a Phase 3 trial in Wolfram syndrome.

AMX0114 is an investigational antisense oligonucleotide targeting calpain-2, or *CAPN2*, with FDA Fast Track Designation for the potential treatment of ALS. The Phase 1 LUMINA clinical trial (NCT06665165) is a multinational, randomized, double-blind, placebo-controlled, multiple ascending dose trial evaluating the safety, tolerability, pharmacokinetics, and pharmacodynamics of AMX0114 in people living with ALS. LUMINA will also assess change from baseline in *CAPN2* levels, neurofilament light, or NfL, levels, and other pharmacodynamic biomarkers of ALS. LUMINA is anticipated to enroll approximately 48 adult participants. In June 2026, we presented Cohort 1 biomarker data at the Annual Meeting of the European Network to Cure ALS. AMX0114 showed no drug-related SAEs and no serious nervous system disorder AEs in Cohort 1 (lowest dose).

level 12.5 mg). These safety findings support continued evaluation of AMX0114 at higher dose levels in this multiple ascending dose trial. Biomarker levels, including spectrin breakdown product 145, NfL, and phosphorylated neurofilament heavy remained near baseline at Day 145. Cohorts 1 and Cohort 2 (25 mg) are fully enrolled, and Cohort 3 (50 mg) is fully enrolled.

AMX0318 is a novel GLP-1 receptor antagonist for long-acting administration selected as a development candidate for PBH and other rare diseases in January 2026. AMX0318 was selected as a development candidate after demonstrating robust preclinical and chemical properties, including a favorable pharmacokinetic profile that may support long-acting administration, a robust chemical stability profile, strong *in vitro* potency, evidence of *in vivo* activity and tolerability, and high solubility. AMX0318 was identified through a research collaboration with Gubra, a company specializing in peptide-based drug discovery and preclinical contract research services. Investigational new drug, or IND, enabling studies for AMX0318 are underway, with an IND submission targeted for 2027.

Recent Developments

LUCIDITY Topline Results

On August 18, 2026, we announced positive topline results from LUCIDITY, a 78-participant, multicenter, randomized, double-blind, placebo-controlled Phase 3 clinical trial evaluating the efficacy and safety of avexitide, an investigational, first-in-class GLP-1 receptor antagonist, in participants with PBH following RYGB surgery. Participants were randomized 3:2 to receive either 90 mg avexitide subcutaneously once daily or placebo. LUCIDITY met FDA-agreed-upon primary endpoint demonstrating a 55% reduction in the composite rate of Level 2 and Level 3 hypoglycemic events compared to placebo (p=0.000003). In addition, LUCIDITY met all secondary endpoints demonstrating consistent, highly statistically significant, and clinically meaningful reductions in Level 2 hypoglycemic events by self-monitoring of blood glucose, or SMBG, Level 2 hypoglycemic events by continuous glucose monitoring, or CGM, and Level 3 hypoglycemic events.

Avexitide was generally well-tolerated through the double-blind study period with a consistent and favorable safety profile replicated across all PBH clinical trials completed to date. The majority of adverse events in LUCIDITY were mild to moderate, and there were no serious adverse events related to avexitide treatment. The most common adverse events were diarrhea, injection site erythema, and injection site bruising. There were no changes in body weight observed in either the avexitide or placebo groups over the 16-week, double-blind period of the LUCIDITY trial.

We plan to submit a New Drug Application, or NDA, to the FDA by the end of 2026. The FDA previously granted avexitide Breakthrough Therapy Designation for PBH. LUCIDITY’s 32-week open label extension remains ongoing. The avexitide expanded access program also remains ongoing. We plan to present the data from LUCIDITY at an upcoming medical meeting.

Commercial Supply of Avexitide

We are currently in discussions with contract manufacturing organizations, or CMOs, to secure commercial supply of avexitide, if approved. We intend to enter into preliminary and/or definitive commercial supply agreements with such CMOs in the near term. There can be no assurance with respect to the timing of any such agreements, or that we will be able to negotiate such definitive agreements on terms acceptable to us, or at all. Any definitive agreements we enter into will supersede any preliminary agreements.

Company Information

We are incorporated in the State of Delaware. Our principal executive offices are located at 55 Cambridge Parkway, Suite 6W, Cambridge, Massachusetts 02142, and our telephone number is (617) 682-0917. We

maintain a website at www.amylyx.com where general information about us is available. The information contained on our website or social media accounts, or that can be accessed through our website or social media accounts, is not a part of this prospectus supplement and is not incorporated by reference into this prospectus supplement. You should not rely on any such information in deciding whether to purchase our securities.

Implications of Being a Smaller Reporting Company

We are a “smaller reporting company” as defined in Item 10(f)(1) of Regulation S-K. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements and reduced disclosure obligations regarding executive compensation. To the extent we take advantage of any reduced disclosure obligations, it may make the comparison of our financial statements with other public companies difficult or impossible. Because the market value of our common stock held by our non-affiliates was greater than \$700.0 million as of June 30, 2026, we will no longer qualify as a smaller reporting company as of January 1, 2027, although we will continue to use the scaled disclosures permitted for a smaller reporting company through our annual report on Form 10-K for the fiscal year ending December 31, 2026 and plan to begin providing non-scaled larger company disclosure in our Form 10-Q for the period ending March 31, 2027.

THE OFFERING	
Common stock offered by us	14,090,000 shares of our common stock.
Option to purchase additional shares	We have granted the underwriters an option to purchase up to an additional 2,113,500 shares of our common stock from us at the public offering price, less underwriting discounts and commissions, for a period of 30 days after the date of this prospectus supplement.
Common stock to be outstanding immediately after this offering	125,458,283 shares, (or 127,571,783 shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	We estimate that our net proceeds from this offering will be approximately \$471.7 million, or \$542.5 million if the underwriters exercise their option to purchase additional shares in full, after deducting underwriting discounts, commissions and estimated offering expenses payable by us. We intend to use the net proceeds we receive from this offering, together with our existing cash, cash equivalents and marketable securities, to fund the potential commercial launch of avexitide in the United States, if approved, including securing additional manufacturing capacity to meet commercial supply requirements, and for research and development, working capital and other general corporate purposes. See “<i>Use of Proceeds</i>” for additional information.
Risk factors	Your investment involves a high degree of risk. You should read the “ <i>Risk Factors</i> ” section of this prospectus supplement beginning on page S-7 and in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, as well as the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors to consider carefully before deciding to invest in our securities.
Nasdaq Global Select Market symbol and trading	“AMLX”
The number of shares of our common stock that will be outstanding immediately after this offering as shown above is based on 111,368,283 shares outstanding as of June 30, 2026. The number of shares outstanding as of June 30, 2026 as used throughout this prospectus supplement, unless otherwise indicated, excludes: • 11,067,306 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2026 under our 2022 Stock Option and Incentive Plan, or the 2022 Plan, at a weighted-average exercise price of \$12.75 per share; • 3,798,139 shares of common stock issuable upon the vesting and settlement of restricted stock units as of June 30, 2026 issued under our 2022 Plan; • 2,014,019 shares of common stock issuable upon the vesting and settlement of performance-based restricted stock units, or PSUs, as of June 30, 2026 issued under our 2022 Plan, including	

431,769 shares of common stock underlying PSUs that vested subsequent to June 30, 2026 through the date hereof upon achievement of performance conditions;

- 5,842,195 shares of our common stock that are available for future issuance as of June 30, 2026 under our 2022 Plan, as well as any future increases, including annual automatic evergreen increases, in the number of shares of common stock reserved for issuance thereunder in accordance with the terms of such plan;
- 263,900 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2026 under our 2023 Inducement Plan, or the Inducement Plan, at a weighted-average exercise price of \$13.69 per share;
- 62,967 shares of common stock issuable upon the vesting and settlement of restricted stock units as of June 30, 2026 issued under our Inducement Plan;
- 360,167 shares of our common stock that are available for future issuance under our Inducement Plan, as of June 30, 2026; and
- 3,732,336 shares of our common stock that are available for future issuance under our 2022 Employee Stock Purchase Plan, or the ESPP, as of June 30, 2026.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding stock options or settlement of unvested restricted stock units described above and no exercise by the underwriters of their option to purchase additional shares of our common stock.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus supplement or incorporated by reference in this prospectus supplement, including the risks and uncertainties discussed under “Risk Factors” in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2026, which are incorporated by reference herein in their entirety. If any of the risks incorporated by reference herein or set forth below occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks related to this offering

If you purchase securities in this offering, you will incur immediate and substantial dilution in the book value of your shares.

The public offering price will be substantially higher than the pro forma net tangible book value per share of our common stock after this offering. Based on the public offering price of \$35.50 per share of our common stock, purchasers of common stock in this offering will experience immediate dilution of \$29.83 per share in net tangible book value of the common stock. In addition, you will experience additional dilution upon exercise of any of the outstanding options, or vesting and settlement of the restricted stock units, and other equity awards that may be granted under our equity incentive plans, and when we otherwise issue additional shares of our common stock. For a further description of the dilution that you will experience immediately after this offering, see the section of this prospectus supplement entitled “Dilution.”

We have broad discretion in the use of our existing cash, cash equivalents and marketable securities and the net proceeds from this offering and may not use them effectively.

Although we currently intend to use the net proceeds from this offering in the manner described in the section titled “Use of Proceeds” in this prospectus supplement, our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. You will not have the opportunity to influence our decisions on how to use the net proceeds from this offering. The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to those of existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

Sales of a substantial number of shares of our common stock in the public market after this offering could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise

capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock. In addition, the sale of substantial amounts of our common stock could adversely impact the price of our common stock. As of June 30, 2026, 111,368,283 shares of our common stock were outstanding. The sale, or the availability for sale, of a large number of shares of our common stock in the public market could cause the price of our common stock to decline.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Since our common stock began trading on the Nasdaq Global Select Market, or Nasdaq, on January 7, 2022, our stock has traded at prices as low as \$1.58 per share and as high as \$41.93 per share. This volatility may affect the price at which you could sell the shares of our common stock, and the sale of substantial amounts of our common stock could adversely affect the price of our common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including those described in the sections captioned “*Risk Factors*” in this prospectus supplement, the accompanying prospectus, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2026 and the other documents incorporated by reference herein and therein.

As a result, you may not be able to sell your shares of common stock at or above the price at which you purchase them. In addition, the stock market in general, Nasdaq and the stock of biotechnology 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.

The sale of our common stock in this offering, and any future sales of our common stock, or the perception that such sales could occur, may depress our stock price and our ability to raise funds in new stock offerings.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. Sales of shares of our common stock in this offering, or the perception that such sales could occur, may lower the market price of our common stock and may make it more difficult for us to sell equity securities or equity-related securities in the future at a time and price that our management deems acceptable, or at all.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, contain forward-looking statements which are made pursuant to the safe harbor provisions of Section 27A of 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 prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein and therein, 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. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement and the accompanying prospectus, and in particular those factors referenced in the section “*Risk Factors*.”

The forward-looking statements are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- our ability to obtain regulatory approvals of avexitide in PBH, or any other indications, or AMX0035 in Wolfram syndrome, or any other indications, or any other current or future product candidates;
- the timing, progress and results of our research and development activities, preclinical studies and clinical trials, including the Phase 3 clinical program for avexitide in PBH, known as the LUCIDITY trial, our Phase 1 clinical trial of AMX0114 for the treatment of ALS, known as the LUMINA trial, our preclinical research for AMX0318 in PBH and other rare diseases, as well as any other development efforts, preclinical studies and clinical trials for our current and any future product candidates;
- our ability to successfully commercialize and market our 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, if needed, commercial supplies;
- the market size, opportunity, demand and growth potential for our current 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 our current and any future product candidates, if approved;
- our ability to obtain funding for our operations;
- our ability to retain the continued service of our key executives and to identify, hire and retain additional qualified professionals;
- our ability to successfully complete our ongoing or planned clinical trials of avexitide, AMX0035 and AMX0114, successfully complete our ongoing or planned IND-enabling studies of AMX0318, and to advance any other current or future product candidates into, and successfully complete, preclinical studies and clinical trials;
- our ability to successfully recruit and enroll suitable patients in our clinical trials;

- the timing or likelihood of the accomplishment of various scientific, clinical, regulatory filings and approvals and other product development objectives;
- the rate and degree of market acceptance of avexitide, AMX0035, AMX0114, AMX0318 and any other current or future product candidates, if approved, by physicians, patients, third-party payors and others in the medical community;
- the implementation of our business model and strategic plans for our business, products, product candidates and technology;
- our ability to identify, evaluate, in-license and develop additional products or product candidates to complement our existing pipeline and our ability to successfully incorporate acquired assets into our existing pipeline;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products, product candidates and technology;
- developments relating to our competitors and our industry, including any regulatory developments;
- our estimates regarding expenses, potential future revenue, capital requirements, cash runway and future needs for additional financing;
- fluctuations of our quarterly and annual operating results and the related effects on our stock price;
- the effect of unfavorable macroeconomic conditions or market volatility resulting from global economic conditions or geopolitical developments, including fluctuating interest rates, inflation, changes in governmental agencies, government shutdowns, international tariffs, trade protection measures, economic sanctions and potential economic slowdowns or recessions, or similar events, on our business;
- our expectations regarding the period during which we qualify as a “smaller reporting company” as defined by Rule 12b-2 of the Exchange Act;
- our expectations related to our use of proceeds from this offering and our existing cash, cash equivalents and marketable securities; and
- other statements about future events, including those listed under the section titled “*Risk Factors*” in this prospectus supplement and those listed in the documents incorporated by reference in this prospectus supplement.

We have included important factors in the cautionary statements included in this prospectus supplement and the accompanying prospectus and the documents we incorporate by reference herein and therein, particularly in the “*Risk Factors*” sections of these documents, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

You should read this prospectus supplement, the accompanying prospectus and the documents that we incorporate by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements in this prospectus supplement and the accompanying prospectus and the documents we incorporate by reference herein and therein represent our views as of the date of this prospectus supplement. We anticipate that subsequent events and developments will cause our views to change. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus supplement. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus supplement, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

USE OF PROCEEDS

We estimate that the net proceeds from this offering will be approximately \$471.7 million, or approximately \$542.5 million if the option to purchase additional shares is exercised in full by the underwriters, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds we receive from this offering, together with our existing cash, cash equivalents and marketable securities, to fund the potential commercial launch of avexitide in the United States, if approved, including securing additional manufacturing capacity to meet commercial supply requirements, and for research and development, working capital and other general corporate purposes.

We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes.

The amounts and timing of our actual expenditures will depend on numerous factors, including the progress of our clinical trials and other development efforts and other factors described under “*Risk Factors*” in this prospectus supplement and the documents incorporated by reference herein, as well as the amount of cash used in our operations. As a result, our management will have broad discretion over the uses of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the proceeds. Because the number and variability of factors that will determine our use of our existing cash, cash equivalents and marketable securities and the new proceeds from this offering, their ultimate use may vary from their currently intended use.

DIVIDEND POLICY

We have never declared nor paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share you will pay in this offering and the as adjusted net tangible book value per share of our common stock after this offering.

Our net tangible book value as of June 30, 2026 was approximately \$239.2 million, or approximately \$2.15 per share of common stock. Net tangible book value per share represents the amount of total tangible assets (total assets less intangible assets) less total liabilities, divided by the number of shares of our common stock outstanding as of June 30, 2026.

Net tangible book value dilution per share to investors participating in this offering represents the difference between the public offering price per share paid by purchasers of securities in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering. After giving effect to the sale of shares of our common stock in this offering at a public offering price of \$35.50 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2026 would have been approximately \$710.8 million, or \$5.67 per share. This represents an immediate increase in net tangible book value of \$3.52 per share to existing stockholders and immediate dilution of \$29.83 per share to investors purchasing our common stock in this offering. Dilution per share to investors purchasing shares of our common stock in this offering is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share paid by investors purchasing shares of our common stock in this offering. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$35.50
Historical net tangible book value per share as of June 30, 2026	\$2.15
Increase in net tangible book value per share attributable to this offering	<u>3.52</u>
As adjusted net tangible book value per share after giving effect to this offering	5.67
Dilution per share to investors participating in this offering	<u>\$29.83</u>

If the underwriters exercise their option to purchase 2,113,500 shares of common stock in full, the as adjusted net tangible book value after this offering would be \$6.12 per share, representing an immediate increase in as adjusted net tangible book value of \$3.97 per share to existing stockholders and immediate dilution in as adjusted net tangible book value of \$29.38 per share to investors purchasing common stock in this offering.

The information above and in the foregoing table is based on 111,368,283 shares outstanding as of June 30, 2026. The information above and in the foregoing table excludes as of June 30, 2026:

- 11,067,306 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2026 under our 2022 Plan, at a weighted-average exercise price of \$12.75 per share;
- 3,798,139 shares of common stock issuable upon the vesting and settlement of restricted stock units as of June 30, 2026 issued under our 2022 Plan;
- 2,014,019 shares of common stock issuable upon the vesting and settlement of the PSUs as of June 30, 2026 issued under our 2022 Plan, including 431,769 shares of common stock underlying PSUs that vested subsequent to June 30, 2026 through the date hereof upon achievement of performance conditions;
- 5,842,195 shares of our common stock that are available for future issuance as of June 30, 2026 under our 2022 Plan, as well as any future increases, including annual automatic evergreen increases, in the

number of shares of common stock reserved for issuance thereunder in accordance with the terms of such plan;

- 263,900 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2026 under our Inducement Plan, at a weighted-average exercise price of \$13.69 per share;
- 62,967 shares of common stock issuable upon the vesting and settlement of restricted stock units as of June 30, 2026 issued under our Inducement Plan;
- 360,167 shares of our common stock that are available for future issuance under our Inducement Plan, as of June 30, 2026; and
- 3,732,336 shares of our common stock that are available for future issuance under our ESPP as of June 30, 2026.

To the extent that outstanding options as of June 30, 2026 have been or may be exercised, unvested restricted stock units have settled or other shares issued, investors purchasing our securities in this offering may experience dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

CERTAIN U.S. FEDERAL INCOME TAX CONSIDERATIONS

Subject to the limitations, assumptions and qualifications described herein, the following is a summary of certain U.S. federal income tax considerations of the purchase, ownership and disposition of shares of our common stock, referred to in this section as the “Shares.” All prospective holders should consult their tax advisors with respect to the U.S. federal, state, and local and non-U.S. tax consequences of the purchase, ownership and disposition of the Shares.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, existing Treasury regulations promulgated thereunder, published administrative pronouncements and rulings of the U.S. Internal Revenue Service, or the IRS, and judicial decisions, all as in effect as of the date of this prospectus supplement. These authorities are subject to change and to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to holders described in this discussion. There can be no assurance that a court or the IRS will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling with respect to the U.S. federal income tax consequences to a holder of the purchase, ownership or disposition of the Shares.

This discussion addresses only Shares that are held as capital assets within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all the U.S. federal income tax consequences that may be relevant to particular holders in light of their individual circumstances, nor does it address any alternative minimum, Medicare contribution, estate or gift tax consequences, the special tax accounting rules under Section 451(b) of the Code, or any aspects of U.S. state or local or non-U.S. taxes. It does not address holders that are subject to special rules, such as:

- banks, insurance companies or other financial institutions;
- tax-exempt organizations or governmental organizations;
- brokers or dealers in securities;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons who hold any of the Shares as a position in a hedging transaction, “straddle,” “conversion transaction,” or other risk reduction transaction;
- persons deemed to sell any of the Shares under the constructive sale provisions of the Code;
- entities or arrangements classified as partnerships for U.S. federal income tax purposes or other pass-through entities such as subchapter S corporations (or investors in such entities or arrangements);
- regulated investment companies or real estate investment trusts;
- controlled foreign corporations, passive foreign investment companies or corporations that accumulate earnings to avoid U.S. federal income tax;
- U.S. Holders (as defined below) whose functional currency is not the U.S. dollar;
- “qualified foreign pension funds” as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds;
- persons that own, actually or constructively, more than 5% of our common stock;
- U.S. expatriates and former citizens or former long-term residents of the United States; or
- holders that acquire the Shares through the exercise of an employee stock option or otherwise as compensation or through a tax-qualified retirement plan.

If a holder is a partnership or other pass-through entity (including an entity or arrangement treated as a partnership or other pass-through entity for U.S. federal income tax purposes), the U.S. federal income tax treatment of a partner or beneficial owner will generally depend on the status of such partner or beneficial owner and the entity's activities. Partnerships, partners and beneficial owners in partnerships or other pass-through entities that own the Shares should consult their tax advisors as to the particular U.S. federal income tax considerations applicable to the acquisition, ownership and disposition of the Shares.

For purposes of this discussion, a "U.S. Holder" is a beneficial owner of the Shares, that, for U.S. federal income tax purposes, is:

- an individual that is a citizen or resident of the United States;
- a corporation, or an entity treated as a corporation, created or organized in or under the laws of the United States, any state thereof or the District of Columbia;
- a trust that (1) is subject to (A) the primary supervision of a court within the United States and (B) the authority of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code) to control all substantial decisions of the trust or (2) has a valid election in effect under applicable Treasury regulations to be treated as a United States person; or
- an estate that is subject to U.S. federal income tax on its income regardless of its source.

As used herein, the term "Non-U.S. Holder" means a beneficial owner, other than an entity treated as a partnership or other pass-through entity for U.S. federal income tax purposes, of the Shares that is for U.S. federal income tax purposes not a U.S. Holder. U.S. Holders and Non-U.S. Holders are collectively referred to herein as "holders."

PROSPECTIVE INVESTORS ARE URGED TO CONSULT THEIR TAX ADVISORS REGARDING THE PARTICULAR U.S. FEDERAL, STATE, AND LOCAL AND NON-U.S. TAX CONSEQUENCES TO THEM OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF THE SHARES.

Tax considerations applicable to U.S. Holders

Distributions on the Shares

We do not anticipate declaring or paying any cash dividends to holders of our common stock in the foreseeable future. If we make distributions of cash or other property on the Shares (other than certain distributions of stock), as described below, such distributions will constitute dividends to the extent paid out of our current or accumulated earnings and profits, as determined for U.S. federal income tax purposes. Dividends received by a corporate U.S. Holder may be eligible for a dividends received deduction, subject to applicable limitations. Dividends received by certain non-corporate U.S. Holders, including individuals, are generally taxed at the lower applicable capital gains rate provided certain holding period and other requirements are satisfied. Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital and first be applied against and reduce a U.S. Holder's adjusted tax basis in its Shares, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "*Sale or other taxable disposition of the Shares.*"

Sale or other taxable disposition of the Shares

Upon the sale, exchange or other taxable disposition of the Shares, a U.S. Holder will generally recognize capital gain or loss equal to the difference between the amount of cash and the fair market value of any other property received upon the sale, exchange or other taxable disposition and such U.S. Holder's adjusted tax basis in the Shares. This capital gain or loss will be long-term capital gain or loss if the U.S. Holder's holding period in such Shares is more than one year at the time of the sale, exchange or other taxable disposition. Long-term capital gains recognized by certain non-corporate U.S. Holders, including individuals, generally will be subject to reduced rates of U.S. federal income tax. The deductibility of capital losses is subject to certain limitations.

Backup withholding and information reporting

In general, backup withholding and information reporting requirements may apply to distributions on the Shares and to the receipt of proceeds on the sale, exchange or other taxable disposition of the Shares. Backup withholding (currently at a rate of 24 percent) may apply if a U.S. Holder fails to furnish its taxpayer identification number, a U.S. Holder fails to certify under penalties of perjury that such taxpayer identification number is correct and that such U.S. Holder is not subject to backup withholding (generally on a properly completed and duly executed IRS Form W-9), the applicable withholding agent is notified by the IRS that the U.S. Holder previously failed to properly report payments of interest or dividends, or such U.S. Holder otherwise fails to comply with the applicable requirements of the backup withholding rules.

Certain U.S. Holders generally are not subject to backup withholding and information reporting requirements, provided that their exemptions from backup withholding and information reporting are properly established. Backup withholding is not an additional tax. Any amounts withheld from a payment to a U.S. Holder under the backup withholding rules generally will be allowed as a credit against such U.S. Holder's U.S. federal income tax liability and may entitle such U.S. Holder to a refund, provided the required information is furnished to the IRS in a timely manner. U.S. Holders should consult their tax advisors regarding the application of backup withholding, the availability of an exemption from backup withholding, and the procedure for obtaining such an exemption, if available.

Tax considerations applicable to Non-U.S. Holders

Distributions on the Shares

As mentioned above, we do not anticipate declaring or paying any cash dividends to holders of our common stock in the foreseeable future. However, distributions of cash or other property (other than certain distributions of stock) on the Shares, as described above under "*Tax considerations applicable to U.S. Holders—Distributions on the Shares*" will constitute dividends to the extent paid out of our current or accumulated earnings and profits, as determined for U.S. federal income tax purposes. Distributions in excess of our current and accumulated earnings and profits will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its Shares, but not below zero. Any excess will be subject to the treatment as described below under "*Sale or other taxable disposition of the Shares*."

Dividends paid to a Non-U.S. Holder that are not effectively connected with the Non-U.S. Holder's conduct of a trade or business in the United States generally will be subject to withholding tax at a 30-percent rate or a reduced rate specified by an applicable income tax treaty. In order to obtain a reduced rate of withholding, the Non-U.S. Holder will be required to provide us or our paying agent with a properly executed applicable IRS Form W-8BEN or IRS Form W-8BEN-E (or appropriate successor form), as applicable, certifying under penalties of perjury that the Non-U.S. Holder is not a United States person and is eligible for the benefits under the applicable income tax treaty. These forms may need to be periodically updated. If a Non-U.S. Holder holds the Shares through a financial institution or other intermediary, the Non-U.S. Holder generally will be required to provide the appropriate documentation to the financial institution or other intermediary. A Non-U.S. Holder eligible for a reduced rate of U.S. withholding tax pursuant to an applicable income tax treaty who fails to timely provide an IRS Form W-8BEN or W-8BEN-E (or appropriate successor form), as applicable, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim with the IRS.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business in the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base maintained by the Non-U.S. Holder in the United States), the Non-U.S. Holder will generally be taxed on the dividends in the same manner as a U.S. Holder. In this case, the Non-U.S. Holder will be exempt from the withholding tax discussed in the preceding paragraph, although the Non-U.S. Holder will be required to provide a properly executed IRS Form W-8ECI (or appropriate successor form) in order to claim an exemption from withholding. Such effectively connected dividends, although not subject to

U.S. federal withholding tax, are subject to U.S. federal income tax on a net income basis at the regular U.S. federal income tax rates generally applicable to a United States person. Dividends received by a corporate Non-U.S. Holder that are effectively connected with such Non-U.S. Holder's conduct of a trade or business in the United States (and, if required by an applicable income tax treaty, attributable to a permanent establishment or fixed base maintained by the Non-U.S. Holder in the United States) may be subject to an additional branch profits tax at a 30-percent rate (or such lower rate as may be specified by an applicable income tax treaty). Non-U.S. Holders should consult their tax advisors with respect to other U.S. tax consequences of the acquisition, ownership and disposition of the Shares, including the possible imposition of the branch profits tax.

Sale or other taxable disposition of the Shares

Subject to the discussions below under “—*Information reporting and backup withholding*” and “—*FATCA*,” a Non-U.S. Holder generally will not be subject to U.S. federal income or withholding tax on gain realized on a sale, exchange or other taxable disposition of the Shares unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment or fixed base maintained by the Non-U.S. Holder in the United States),
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- we are or have been a “United States real property holding corporation,” as defined in the Code, at any time within the five-year period ending on the date of disposition or the Non-U.S. Holder's holding period, whichever period is shorter, and the Non-U.S. Holder is not eligible for an exemption under an applicable income tax treaty.

We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are or have been a United States real property holding corporation during the specified testing period, as long as our common stock is regularly traded on an established securities market (such as the Nasdaq Global Market) at any time during the calendar year in which the disposition occurs, a Non-U.S. Holder will not be subject to U.S. federal income tax on the disposition of the Shares if the Non-U.S. Holder does not own or has not owned (actually or constructively) more than 5 percent of our common stock at any time during the shorter of the two periods mentioned above.

If a Non-U.S. Holder recognizes gain on a sale, exchange or other taxable disposition of the Shares that is effectively connected with the Non-U.S. Holder's conduct of a trade or business in the United States (and if required by an applicable income tax treaty, is attributable to a permanent establishment or fixed base maintained by the Non-U.S. Holder in the United States), the Non-U.S. Holder will generally be subject to U.S. federal income tax at the regular U.S. federal income tax rates generally applicable to a United States person. If the Non-U.S. Holder is a corporation, the Non-U.S. Holder may also be subject to the branch profits tax at a 30-percent rate or such lower rate as may be specified by an applicable income tax treaty. Non-U.S. Holders should consult their tax advisors with respect to other U.S. tax consequences of the acquisition, ownership and disposition of the Shares, including the possible imposition of the branch profits tax.

A Non-U.S. holder described in the second bullet point above will be subject to U.S. federal income tax at a 30-percent rate (unless otherwise provided pursuant to an applicable income tax treaty) on gain recognized on a sale, exchange or other taxable disposition of the Shares, but such gain may be offset by certain U.S.-source capital losses (even though the Non-U.S. Holder is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses.

Information reporting and backup withholding

Information returns will be filed with the IRS in connection with distributions on the Shares. Copies of the information returns reporting those distributions and withholding may also be made available to the tax authorities in the country in which a Non-U.S. Holder is a resident under the provisions of an applicable income tax treaty or agreement. Unless a Non-U.S. Holder complies with certification procedures to establish that the Non-U.S. Holder is not a United States person, information returns may also be filed with the IRS in connection with the proceeds from a sale, exchange or other disposition of the Shares to or through the U.S. office (and, in certain cases, the foreign office) of a broker.

A Non-U.S. Holder may be subject to backup withholding (currently at a rate of 24 percent) on payments on the Shares or on the proceeds from a sale, exchange or other disposition of the Shares unless the Non-U.S. Holder complies with certification procedures to establish that the Non-U.S. Holder is not a United States person or otherwise establishes an exemption. Compliance with the certification procedures required to claim a reduced rate of withholding under a treaty (including properly certifying non-U.S. status on an IRS Form W-8BEN, IRS Form W-8BEN-E or other appropriate version of IRS Form W-8 (or appropriate successor form)) generally will satisfy the certification requirements necessary to avoid backup withholding as well. Notwithstanding the foregoing, U.S. federal backup withholding may apply if the payor has actual knowledge, or reason to know, that a Non-U.S. Holder is a United States person.

Backup withholding is not an additional tax. Any amounts withheld from a payment to a Non-U.S. Holder under the backup withholding rules generally will be allowed as a credit against such Non-U.S. Holder's U.S. federal income tax liability and may entitle such Non-U.S. Holder to a refund, provided the required information is furnished to the IRS in a timely manner. Non-U.S. Holders are urged to consult their tax advisors regarding the application of backup withholding and the availability of and procedure for obtaining an exemption from backup withholding in their particular circumstances.

FATCA

Provisions of the Code commonly referred to as "FATCA" require withholding of 30 percent on distributions on the Shares, as well as payments of gross proceeds of dispositions of the Shares, to a "foreign financial institution" (which is broadly defined for this purpose and in general includes investment vehicles) and certain other non-U.S. entities unless various U.S. information reporting and due diligence requirements (generally relating to ownership by United States persons of interests in or accounts with those entities) have been satisfied or an exemption applies. However, the IRS has issued proposed Treasury regulations that eliminate FATCA withholding on payments of gross proceeds (but not on payments of dividends). Pursuant to the preamble to the proposed Treasury regulations, any applicable withholding agent may (but is not required to) rely on this proposed change to FATCA withholding until final Treasury regulations are issued or the proposed Treasury regulations are withdrawn. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. If FATCA withholding is imposed, a beneficial owner that is not a foreign financial institution generally may obtain a refund of any amounts withheld by filing a U.S. federal income tax return (which may entail significant administrative burden). Non-U.S. Holders should consult their tax advisors regarding the effects of FATCA on their investments in the Shares.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR TAX ADVISORS REGARDING THE PARTICULAR U.S. FEDERAL, STATE AND LOCAL AND NON-U.S. TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF THE SHARES, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.

UNDERWRITING

Leerink Partners LLC, Morgan Stanley & Co. LLC, Guggenheim Securities, LLC and LifeSci Capital LLC are acting as representatives of each of the underwriters named below and as joint bookrunning managers for this offering. Subject to the terms and conditions set forth in the underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

<u>Underwriter</u>	<u>Number of Shares</u>
Leerink Partners LLC	5,424,650
Morgan Stanley & Co. LLC	5,001,950
Guggenheim Securities, LLC	2,818,000
LifeSci Capital LLC	845,400
Total	14,090,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of the shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and subject to other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Discounts and Commissions

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the initial public offering price set forth on the cover page of this prospectus supplement and to dealers at that price less a concession not in excess of \$1.1928 per share. After the initial offering of the shares, the public offering price, concession or any other term of this offering may be changed by the representatives.

The following table shows the initial public offering price, underwriting discounts and commissions and proceeds, before expenses, to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	<u>Per Share</u>	<u>Total</u>	
		<u>Without Option</u>	<u>With Option</u>
Initial public offering price	\$ 35.500	\$ 500,195,000	\$ 575,224,250
Underwriting discounts and commissions	\$ 1.988	\$ 28,010,920	\$ 32,212,558
Proceeds, before expenses, to us	\$ 33.512	\$ 472,184,080	\$ 543,011,692

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$500,000. We also have agreed to reimburse the underwriters for up to \$25,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this

reimbursed fee is deemed underwriting compensation for this offering. The underwriters have also agreed to reimburse us for certain expenses in connection with the offering.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus supplement, to purchase up to 2,113,500 additional shares at the initial public offering price, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to the conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We and our officers and our directors have agreed with the underwriters, subject to certain exceptions, not to dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through the date 45 days after the date of this prospectus supplement, except with the prior written consent of Leerink Partners LLC, Morgan Stanley & Co. LLC and Guggenheim Securities, LLC.

Nasdaq Global Select Market Listing

Our common stock is listed on the Nasdaq Global Select Market under the symbol "AMLX."

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit the underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with this offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in this offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares granted to them under the underwriting agreement described above. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of this offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a

decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with this offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Some of the underwriters and certain of their affiliates may in the future engage in investment banking and other commercial dealings in the ordinary course of business with us and our affiliates, for which they may in the future receive customary fees, commissions and expenses.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling Restrictions

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area, each, a Relevant State, no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that shares may be offered to the public in that Relevant State at any time:

- A. to any legal entity which is a qualified investor as defined under Article 2 of the Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares shall require us or any of the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation. For the purposes of this provision, the expression an “offer to the public” in relation to

any shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation (EU) 2017/1129, as amended.

Notice to Prospective Investors in the United Kingdom

No shares of our common stock have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares of common stock which has been approved by the Financial Conduct Authority, except that the shares of our common stock may be offered to the public in the United Kingdom at any time:

- A. to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the representatives for any such offer; or
- C. in any other circumstances falling within Section 86 of the Financial Services and Markets Act 2000, or the FMSA,

provided that no such offer of the shares shall require us or any representative to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an “offer to the public” in relation to the shares in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares and the expression “UK Prospectus Regulation” means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.

Notice to Prospective Investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

LEGAL MATTERS

Certain legal matters, including the legality of the securities offered, will be passed upon for us by Goodwin Procter LLP, New York, New York. The underwriters are being represented in this offering by Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York.

EXPERTS

The financial statements of Amylyx Pharmaceuticals, Inc. incorporated by reference in this prospectus supplement and the effectiveness of Amylyx Pharmaceuticals, Inc.'s internal control over financial reporting have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their reports. Such financial statements are incorporated by reference in reliance upon the reports of such firm, given their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus supplement in accordance with the rules of the SEC. We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents also may be accessed through the SEC's electronic data gathering, analysis and retrieval system, via electronic means, including the SEC's home page on the Internet (www.sec.gov). You may also inspect the registration statement, this prospectus supplement and the accompanying prospectus on this website.

Our website is located at www.amylyx.com. Information contained on our website is not incorporated by reference into this prospectus supplement, and, except for the documents incorporated by reference as noted below, you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement or the accompanying prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference.

We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus supplement and prior to the termination of this offering:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2025, filed with the SEC on March 3, 2026;
- our [Definitive Proxy Statement on Schedule 14A](#) (other than information furnished rather than filed), filed with the SEC on April 23, 2026;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2026 and June 30, 2026, filed with the SEC on [May 7, 2026](#) and [August 6, 2026](#), respectively;
- our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on [January 8, 2026](#), [June 4, 2026](#), [August 18, 2026](#) and [August 18, 2026](#); and
- the description of our common stock contained in our registration statement on [Form 8-A](#) filed with the SEC on January 4, 2022, as the description therein has been updated and superseded by the description of our common stock contained in 3 to our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021, as filed with the SEC on March 31, 2022, including any amendments or reports filed for the purposes of updating this description.

Unless specifically stated to the contrary, information that we furnish (and that is not deemed “filed” with the SEC) under Items 2.02 and 7.01 of any Current Reports on Form 8-K, including the related exhibits under Item 9.01, is not incorporated by reference into this prospectus supplement or the registration statement of which this prospectus supplement is a part.

Upon written or oral request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, a copy of the documents incorporated by reference into this prospectus supplement but not delivered with the prospectus supplement. You may request, and we will provide you with, a copy of these filings, at no cost, by calling us at (617) 682-0917 or writing to us at Amylyx Pharmaceuticals, Inc., 55 Cambridge Parkway, Suite 6W, Cambridge, Massachusetts 02142. You may also access these documents, free of charge on the SEC’s website at www.sec.gov.

Any statement contained in this prospectus supplement, or in a document all or a portion of which is incorporated by reference, shall be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement or any document incorporated by reference modifies or supersedes such statement. Any such statement so modified or superseded shall not, except as so modified or superseded, constitute a part of this prospectus supplement.

PROSPECTUS



**COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
UNITS**

We may offer from time to time, in one or more offerings, any combination of the following securities: common stock, preferred stock, debt securities, warrants, and units, or collectively, the securities. We may offer and sell these securities at times, in amounts, at prices and on terms to be determined at or prior to the time of each offering.

This prospectus describes some of the general terms that may apply to these securities. The specific terms of these securities and information regarding the offering in which these securities will be offered will be provided in supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with each offering of the securities. The prospectus supplements may add, update or change the information contained in this prospectus. You should read this prospectus and any applicable prospectus supplement and any applicable free writing prospectus together with additional information described under the heading “*Where You Can Find More Information*” carefully before you invest.

We may offer and sell these securities to or through one or more underwriters, dealers or agents, or directly to one or more purchasers, on a continuous or delayed basis, on or off the Nasdaq Global Select Market, or Nasdaq. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission, or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the “*Plan of Distribution*” section of this prospectus for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

Our common stock is listed on Nasdaq under the symbol “AMLX.” On March 2, 2026, the closing sale price of our common stock on Nasdaq was \$15.30 per share.

As of the date of this prospectus, we are a smaller reporting company as defined under Rule 405 of the Securities Act of 1933, as amended, or the Securities Act, and, as such, are subject to certain reduced public company reporting requirements. See “*Prospectus Summary—Implications of Being a Smaller Reporting Company*” on page 4 of this prospectus.

Investing in our securities involves certain risks. See the “[Risk Factors](#)” section on page 8 of this prospectus, in any applicable prospectus supplement and any related free writing prospectus, and in our Securities and Exchange Commission, or the SEC, filings that are incorporated by reference herein. You should read the entire prospectus carefully before you make your investment decision.

Neither the SEC nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is March 3, 2026.

TABLE OF CONTENTS

	Page
About this Prospectus	ii
Special Note Regarding Forward-Looking Statements	1
The Company	4
Where You Can Find More Information	6
Incorporation By Reference	7
Risk Factors	8
Use of Proceeds	9
Description of Capital Stock	11
Description of Debt Securities	16
Description of Warrants	18
Description of Units	19
Plan of Distribution	20
Legal Matters	24
Experts	24

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement on Form S-3ASR that we have filed with the SEC as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act, utilizing a “shelf” registration process. Under this shelf registration process, we may sell the securities or any combination of the securities described in this prospectus in one or more offerings.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with additional information described under the heading “*Where You Can Find More Information*” and “*Incorporation by Reference*.”

Registration of the securities covered by this prospectus does not mean that these securities will necessarily be offered or sold. As of the date of filing this prospectus, we have no specific plans for selling the securities registered hereunder.

We have not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information contained in or incorporated by reference in this prospectus or any prospectus supplement or in any such free writing prospectus is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

This prospectus, any applicable prospectus supplement or free writing prospectus and the information incorporated herein or therein by reference contains market data, industry statistics and other data that have been obtained or compiled from information made available by independent third parties. We have not independently verified the accuracy and completeness of such data. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement, or any applicable free writing prospectus may involve estimates, assumptions, and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading “*Risk Factors*” contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, and under similar headings in other documents that are incorporated by reference into this prospectus. Accordingly, you should not place undue reliance on this information.

Amylyx and other trademarks or service marks of Amylyx appearing in this prospectus are the property of Amylyx. The other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference herein and therein, 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 prospectus, including the documents that we incorporate by reference herein, 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. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus and in particular those factors referenced in the section “Risk Factors.”

These forward-looking statements may be based on our management’s belief and assumptions and on information currently available to them. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- our ability to obtain regulatory approvals of avexitide in post-bariatric hypoglycemia, or PBH, or any other indications, or AMX0035 in Wolfram syndrome, or any other indications, or any other current or future product candidates;
- the timing, progress and results of our research and development activities, preclinical studies and clinical trials, including the Phase 3 clinical program for avexitide in PBH, known as the LUCIDITY trial, our Phase 1 clinical trial of AMX0114 for the treatment of amyotrophic lateral sclerosis, or ALS, known as the LUMINA trial, our preclinical research for AMX0318 in PBH, as well as any other development efforts, preclinical studies and clinical trials for our current and any future product candidates;
- our ability to successfully commercialize and market our 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, if needed, commercial supplies;
- the market size, opportunity, demand and growth potential for our current 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 our current and any future product candidates, if approved;
- our ability to obtain funding for our operations;
- our ability to retain the continued service of our key executives and to identify, hire and retain additional qualified professionals;
- our ability to successfully complete our ongoing or planned clinical trials of avexitide, AMX0035 and AMX0114, successfully complete our ongoing or planned investigational new drug, or IND, enabling studies of AMX0318, and to advance any other current or future product candidates into, and successfully complete, preclinical studies and clinical trials;

- our ability to successfully recruit and enroll suitable patients in our clinical trials;
- the timing or likelihood of the accomplishment of various scientific, clinical, regulatory filings and approvals and other product development objectives;
- the rate and degree of market acceptance of avexitide, AMX0035, AMX0114, AMX0318 and any other current or future product candidates, if approved, by physicians, patients, third-party payors and others in the medical community;
- the implementation of our business model and strategic plans for our business, products, product candidates and technology;
- our ability to identify, evaluate, in-license and develop additional products or product candidates to complement our existing pipeline and our ability to successfully incorporate acquired assets into our existing pipeline;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our products, product candidates and technology;
- developments relating to our competitors and our industry, including any regulatory developments;
- our estimates regarding expenses, potential future revenue, capital requirements, cash runway and future needs for additional financing;
- fluctuations of our quarterly and annual operating results and the related effects on our stock price;
- the effect of unfavorable macroeconomic conditions or market volatility resulting from global economic conditions or geopolitical developments, including fluctuating interest rates, inflation, changes in governmental agencies, government shutdowns, international tariffs, trade protection measures, economic sanctions and potential economic slowdowns or recessions, or similar events, on our business; and
- other statements about future events, including those listed under the section titled “Risk Factors” in this prospectus and those listed in the documents incorporated by reference in this prospectus.

Any forward-looking statements in this prospectus 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 section entitled “*Risk Factors*” and elsewhere in our filings with the SEC. 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 prospectus 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 prospectus or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to 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 prospectus, 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 that modify or impact any of the forward-looking statements contained in this prospectus will be deemed to modify or supersede such statements in this prospectus.

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 prospectus. 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.

THE COMPANY

Amylyx Pharmaceuticals, Inc. (also referred to as Amylyx, we, our or us) is a clinical-stage pharmaceutical company with a mission to develop and advance novel therapies for communities with high unmet medical needs. We have preclinical and clinical development programs underway in endocrine conditions and neurodegenerative diseases. We are advancing a pipeline in which we have matched investigational therapies with diseases for which we believe these therapies can make the greatest impact, based on well-defined mechanistic rationales, clear clinical outcomes and biomarkers, and rigorous preclinical data, agnostic of modality.

Our lead investigational asset is avexitide, a first-in-class inhibitor of glucagon-like peptide-1, or GLP-1, receptor activity. Avexitide has been evaluated as a treatment for PBH and congenital hyperinsulinism, or Congenital HI, two indications characterized by hyperinsulinemic hypoglycemia. The U.S. Food and Drug Administration has granted avexitide Breakthrough Therapy Designation for both PBH and Congenital HI, Rare Pediatric Disease Designation in Congenital HI, and Orphan Drug Designation for the treatment of hyperinsulinemic hypoglycemia.

AMX0035 is designed to mitigate neurodegeneration by targeting endoplasmic reticulum, or ER, stress and mitochondrial dysfunction, two cellular processes central to neuronal cell death and neurodegeneration. We are investigating AMX0035 in Wolfram syndrome, a neurodegenerative disease where ER stress and mitochondrial dysfunction are implicated.

AMX0114 is an investigational antisense oligonucleotide, targeting calpain-2, or CAPN2. Decades of scientific literature and published data demonstrate that CAPN2, a protein involved in neurofilament biology, plays an essential role in axonal degeneration, which is a critical effector in the progression of various neurodegenerative diseases including ALS. ALS is a relentlessly progressive and fatal neurodegenerative disorder caused by motor neuron death in the brain and spinal cord. Motor neuron loss in ALS leads to deteriorating muscle function, the inability to move and speak, respiratory paralysis, and, eventually, death. ALS is defined as a rare disease, but it affects as many as 30,000 adults in the U.S. and 3,000 in Canada. The most common form of the disease is sporadic ALS, with more than 90% of people with ALS showing no clear family history.

AMX0318 is a long-acting GLP-1 receptor antagonist identified through a research collaboration with Gubra A/S, a company specializing in peptide-based drug discovery and preclinical contract research services. In January 2026, we announced the selection of AMX0318 as a development candidate for PBH and other rare diseases. AMX0318 has completed extensive preclinical evaluation, including stability, solubility, potency, in vivo pharmacokinetics and pharmacodynamics, and in vivo tolerability studies. We expect the program to advance into investigational new drug, or IND, enabling studies in 2026, with an IND submission targeted for 2027, pending successful completion of IND-enabling studies.

We are incorporated in the State of Delaware. Our principal executive offices are located at 55 Cambridge Parkway, Suite 6W, Cambridge, Massachusetts, 02142, and our telephone number is (617) 682-0917. We maintain a website at www.amylyx.com where general information about us is available. The information contained on our website or social media accounts, or that can be accessed through our website or social media accounts, is not a part of this prospectus and is not incorporated by reference into this prospectus. You should not rely on any such information in deciding whether to purchase our securities.

Implications of Being a Smaller Reporting Company

We are a “smaller reporting company” as defined in Item 10(f)(1) of Regulation S-K. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements and reduced disclosure obligations regarding executive compensation. To the extent we take advantage of any reduced disclosure obligations, it may make the comparison of our financial statements with other public companies difficult or impossible.

SECURITIES WE MAY OFFER

We may offer from time to time, in one or more offerings, any combination of the following securities in amounts, at prices and on terms to be determined by market conditions at the time of offering: common stock, preferred stock, debt securities, warrants, and units. This prospectus may not be used to offer or sell securities unless accompanied by an applicable prospectus supplement. This prospectus provides you with a general description of the securities we may offer, and the particular terms of any security will be described in the applicable prospectus supplement. Each time we sell securities described herein, we will provide prospective investors with a supplement to this prospectus that will contain specific information about the terms of that offering, including the specific amounts, prices and terms of the securities offered. The applicable prospectus supplement may add, update or change information contained in this prospectus or in documents incorporated by reference in this prospectus. You should read the prospectus supplement related to any securities being offered. We may sell the securities to or through underwriters, dealers or agents, directly to purchasers or through a combination of any of these methods of sale or as otherwise set forth below under “*Plan of Distribution*.” We, as well as any agents acting on our behalf, reserve the sole right to accept and to reject in whole or in part any proposed purchase of securities. Any prospectus supplement will set forth the names of any underwriters, dealers, agents or other entities involved in the sale of securities described in that prospectus supplement and any applicable fee, commission or discount arrangements with them.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains periodic and current reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is www.sec.gov. Other information about us is also on our website at www.amylyx.com. However, except for the information specifically incorporated by reference herein as set forth below, the information on or accessible through the SEC's website and the information on or accessible through our website do not constitute a part of this prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to “incorporate by reference” the information we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and all documents subsequently filed with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act, prior to the termination of the offering under this prospectus:

- (a) our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2025, filed with the SEC on March 3, 2026;
- (b) our [Definitive Proxy Statement on Schedule 14A](#) (other than information furnished rather than filed), filed with the SEC on April 24, 2025;
- (c) our Current Report on [Form 8-K](#) (other than information furnished rather than filed) filed with the SEC on January 8, 2026; and
- (d) the description of our common stock contained in our registration statement on [Form 8-A](#) filed with the SEC under Section 12(b) of the Exchange Act on January 4, 2022, as the description therein has been updated and superseded by the description of our common stock contained in our Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2021, as filed with the SEC on March 31, 2022, including any amendments or reports filed for the purposes of updating this description.

Unless specifically stated to the contrary, none of the information that we disclose under Items 2.02 or 7.01 of any Current Report on Form 8-K that we may from time to time furnish to the SEC or any other document or information deemed to have been furnished and not filed with the SEC will be incorporated by reference into, or otherwise included in, this prospectus.

Any statement contained in this prospectus or in a document (or part thereof) incorporated or considered to be incorporated by reference in this prospectus shall be considered to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document (or part thereof) that is or is considered to be incorporated by reference in this prospectus modifies or supersedes that statement. The modifying or superseding statement need not state that it has modified or superseded a prior statement or include any other information set forth in the document that it modifies or supersedes. Any statement so modified or superseded shall not be considered, except as so modified or superseded, to constitute any part of this prospectus.

You may request, and we will provide you with a copy of these filings at no cost by calling us at (617) 682-0917 or writing to us at Amylyx Pharmaceuticals, Inc., 55 Cambridge Parkway, Suite 6W, Cambridge, Massachusetts 02142. You may also access these documents free of charge on the SEC’s website at www.sec.gov.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before making a decision to invest in our securities, you should carefully consider the risks described under “Risk Factors” in the applicable prospectus supplement and in our most recent Annual Report on Form 10-K, and any updates to those risk factors in our subsequent Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, together with all of the other information appearing or incorporated by reference herein, in light of your particular investment objectives and financial circumstances. Although we discuss key risks in our discussion of risk factors, new risks may emerge in the future, which may prove to be significant. We cannot predict future risks or estimate the extent to which they may affect our business, results of operations, financial condition and prospects. If any of these risks or uncertainties actually occurs, they could materially and adversely affect our business, financial condition, results of operations, cash flows or prospects, which in turn could materially and adversely affect the price of our securities and might cause you to lose all or part of your investment in the offered securities.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from any sale of our securities offered by us under this prospectus. Unless otherwise indicated in a prospectus supplement, the net proceeds from our sale of securities will be used for general corporate purposes, including working capital, expenses related to research, clinical development and commercial efforts and general and administrative expenses, acquisitions and other business opportunities.

Because we may issue securities from time to time in one or more offerings pursuant to this prospectus, the net proceeds from the sale of securities may be received and used by us at different times. Pending the use of such proceeds, we may invest the net proceeds in short term, interest-bearing securities or other investments in accordance with our investment policy, or hold such proceeds as cash.

TAXATION

The applicable prospectus supplement may also contain information about any material U.S. federal income tax considerations relating to the securities covered by such prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following summary of the terms of our capital stock is not meant to be complete and is qualified by reference to the relevant provisions of the Delaware General Corporation Law, or the DGCL, and our Fourth Amended and Restated Certificate of Incorporation, or our certificate of incorporation, and our Second Amended and Restated Bylaws, or our bylaws. For a complete description of the matters set forth in this section titled "Description of Capital Stock," you should refer to the provisions of our Certificate of Incorporation and Bylaws. See "Where You Can Find More Information" above.

General

Our authorized capital stock consists of 300,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share, all of which shares of preferred stock are undesignated.

Common Stock

Voting Rights. The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights.

Dividend Rights. Holders of our common stock are entitled to receive ratably any dividends declared by our board of directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock.

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

Other Rights. Holders of our common stock have no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action. No shares of preferred stock are outstanding, and we have no present plan to issue any shares of preferred stock.

When we offer to sell a particular series of preferred stock, we will describe the specific terms of the securities in a supplement to this prospectus. The preferred stock will be issued under a certificate of designations relating to each series of preferred stock and is also subject to our certificate of incorporation. The transfer agent for each series of preferred stock will be described in the prospectus supplement.

Registration Rights

Certain holders of our common stock are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of an amended and restated investors' rights

agreement, or the investors' rights agreement, between us and certain holders of our common stock. The investors' rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under the investors' rights agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

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

The demand registration rights and short form registration rights granted under the investors' rights agreement will terminate on the earlier of (i) a deemed liquidation event, as defined in our certificate of incorporation, (ii) January 11, 2027, the fifth anniversary of the completion of our initial public offering and (iii) such time as SEC Rule 144 under the Securities Act or another similar exemption under the Securities Act is available for the sale of all of such holder's shares without limitation during a three-month period without registration.

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

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

Board Composition and Filling Vacancies

Our certificate of incorporation provides for the division of our board of directors into three classes serving staggered three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 66-2/3% or more of the shares then entitled to vote at an election of directors. Further, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

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

Meetings of Stockholders

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

Advance Notice Requirements

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

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our bylaws and certificate of incorporation must be approved by not less than 66-2/3% of the outstanding shares entitled to vote on the amendment, and not less than 66-2/3% of the outstanding shares of each class entitled to vote thereon as a class. Our bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the bylaws; and may also be amended by the affirmative vote of at least 66-2/3% of the outstanding shares entitled to vote on the amendment, or, if our board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock

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

Exclusive Jurisdiction for Certain Actions

Our bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws, or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and

officers. The enforceability of similar exclusive forum provisions in other companies' bylaws has been challenged in legal proceedings, and it is possible that a court could rule that this provision in our bylaws is inapplicable or unenforceable.

Our bylaws also provide that the United States Federal District Courts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act or the Exchange Act, unless we consent in writing to an alternative forum, is intended to allow for the consolidation of multi-jurisdiction litigation, avoid state court forum shopping, provide efficiencies in managing the procedural aspects of securities litigation and reduce the risk that the outcome of cases in multiple jurisdictions could be inconsistent. Although our bylaws contain the choice of forum provisions described above, it is possible that a court could rule that such provisions are inapplicable for a particular claim or action or that such provisions are unenforceable. For example, under the Securities Act, federal courts have concurrent jurisdiction over all suits brought to enforce any duty or liability created by the Securities Act, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

Section 203 of the Delaware General Corporation Law

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

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

Section 203 defines a business combination to include:

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

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

Exchange Listing

Our common stock is listed on the Nasdaq Global Select Market under the trading symbol “AMLX.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information that we include in any applicable prospectus supplements, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities in more detail in the applicable prospectus supplement. The terms of any debt securities and related guarantees offered under a prospectus supplement may differ from the terms described below.

We may issue senior debt securities under an indenture, or the senior debt indenture, to be entered into between us and the trustee named in the senior debt indenture. We may issue subordinated debt securities under an indenture, or the subordinated debt indenture, and together with the senior debt indenture, the indentures, and each individually, an indenture, to be entered into between us and the trustee named in the subordinated debt indenture.

We have summarized certain terms and provisions of the indentures. The summary is not complete. Forms of the indentures have been filed as exhibits to the registration statement of which this prospectus forms a part, which we have filed with the SEC. You should read the indentures for the provisions that may be important to you. The indentures are subject to and governed by the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. The senior debt indenture and the subordinated debt indenture are substantially identical, except for the provisions relating to subordination and covenants. See “—*Subordinated Debt*.”

We may issue debt securities up to an aggregate principal amount as we may authorize from time to time. The prospectus supplement will describe the terms of any debt securities being offered, including:

- classification as senior or subordinated debt securities;
- ranking of the specific series of debt securities relative to other outstanding indebtedness, including subsidiaries' debt;
- if the debt securities are subordinated, the aggregate amount of outstanding indebtedness, as of a recent date, that is senior to the subordinated securities, and any limitation on the issuance of additional senior indebtedness;
- the designation, aggregate principal amount and authorized denominations;
- the maturity date;
- the interest rate, if any, and the method for calculating the interest rate;
- the interest payment dates and the record dates for the interest payments;
- any mandatory or optional redemption terms or prepayment, conversion, sinking fund or exchangeability or convertibility provisions;
- the place where we will pay principal and interest;
- if other than denominations of \$1,000 or multiples of \$1,000, the denominations the debt securities will be issued in;
- whether the debt securities will be issued in the form of global securities or certificates;
- additional provisions, if any, relating to the defeasance of the debt securities;
- the currency or currencies, if other than the currency of the United States, in which principal and interest will be paid;
- any United States federal income tax consequences;
- the dates on which premium, if any, will be paid;

- our right, if any, to defer payment interest and the maximum length of this deferral period;
- any listing on a securities exchange;
- the initial public offering price; and
- other specific terms, including any additional events of default or covenants.

Senior Debt

We will issue under the senior debt indenture the debt securities that will constitute part of our senior debt. These senior debt securities will rank equally and *pari passu* with all of our other unsecured and unsubordinated debt.

Subordinated Debt

We will issue under the subordinated debt indenture the debt securities that will constitute part of our subordinated debt. Payment by us of the principal of, premium, if any, and interest on any series of subordinated debt securities issued under the subordinated debt indenture will be subordinated to the extent set forth in an indenture supplemental to the subordinated indenture relating to such series. The specific subordination terms will be set forth in a supplemental indenture to the subordinated debt indenture and described in the prospectus supplement for the relevant series of debt.

DESCRIPTION OF WARRANTS

The following description, together with the additional information that we include in any applicable prospectus supplements, summarizes the material terms and provisions of the warrants that we may offer under this prospectus. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any warrants in more detail in the applicable prospectus supplement. The terms of any warrants offered under a prospectus supplement may differ from the terms described below.

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. Warrants may be issued independently or together with any other securities and may be attached to, or separate from, such securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent. The terms of any warrants to be issued and a description of the material provisions of the applicable warrant agreement will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement will describe the following terms of any warrants in respect of which this prospectus is being delivered:

- the title of such warrants;
- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the currency or currencies in which the price of such warrants will be payable;
- the securities purchasable upon exercise of such warrants;
- the price at which and the currency or currencies in which the securities purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants shall commence and the date on which such right shall expire;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;
- information with respect to book-entry procedures, if any;
- if applicable, a discussion of any material United States federal income tax considerations; and
- any other terms of such warrants, including terms, procedures and limitations relating to the exchange and exercise of such warrants.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

As specified in the applicable prospectus supplement, we may issue units consisting of one or more warrants, debt securities, shares of preferred stock, shares of common stock or any combination of such securities. The applicable supplement will describe:

- the terms of the units and of the warrants, debt securities, preferred stock and common stock comprising the units, including whether and under what circumstances the securities comprising the units may be traded separately;
- a description of the terms of any unit agreement governing the units; and
- a description of the provisions for the payment, settlement, transfer or exchange of the units.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, “at the market offerings,” negotiated transactions, block trades or a combination of these methods or any other method permitted by law. We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers. The securities may be distributed at a fixed price or prices, which may be changed, market prices prevailing at the time of sale, prices related to the prevailing market prices, or negotiated prices, either:

- on or through the facilities of Nasdaq or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker otherwise than on Nasdaq or such other securities exchanges or quotation or trading services.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. In the prospectus supplement relating to such offering, we will name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay to any such agent. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent(s), dealer(s) or underwriter(s), if any;
- the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;
- any over-allotment or other options under which underwriters may purchase additional securities from us;
- any agency fees or discounts or commissions to be allowed or paid to the agent or underwriters;
- all other items constituting agents’ or underwriters’ compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are used in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement, sales agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

In connection with the offering of securities, we may grant to the underwriters an option to purchase additional securities with an additional underwriting commission, as may be set forth in the applicable prospectus supplement. If we grant any such option, the terms of such option will be set forth in the prospectus supplement for such securities.

If a dealer is used in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer, who may be deemed to be an “underwriter” as that term is defined in the Securities Act, may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Offered securities may also be offered and sold, if so indicated in the prospectus supplement, in connection with a remarketing upon their purchase, in accordance with a redemption or repayment pursuant to their terms, or otherwise, by one or more remarketing firms, acting as principals for their own accounts or as agents for us. Any remarketing firm will be identified and the terms of its agreement, if any, with us and its compensation will be described in the applicable prospectus supplement. Remarketing firms may be deemed to be underwriters in connection with their remarketing of offered securities.

Certain agents, underwriters and dealers, and their associates and affiliates, may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

If any securities are offered by us through underwriters, the underwriters will acquire the securities for their own account and may resell them from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Underwriters may offer and sell securities to the public either through underwriting syndicates represented by one or more managing underwriters or directly by one or more firms acting as underwriters. Unless otherwise provided in the applicable prospectus supplement, the obligations of the underwriters to purchase the securities will be subject to certain conditions, and the underwriters will be obligated to purchase all of the offered securities if they purchase any of them. In connection with the sale of securities, underwriters may be deemed to have received compensation from us in the form of underwriting discounts or commissions and dealers may receive compensation from the underwriters in the

form of discounts or concessions. The underwriters may change from time to time any initial public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over allot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

We may engage in “at the market offerings” into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. To the extent that we make sales through one or more underwriters or agents in at the market offerings, we will do so pursuant to the terms of a sales agency financing agreement or other at the market offering arrangement between us and the underwriters or agents. If we engage in at the market sales pursuant to any such agreement, we will issue and sell our securities through one or more underwriters or agents, which may act on an agency basis or a principal basis. During the term of any such agreement, we may sell securities on a daily basis in exchange transactions or otherwise as we agree with the underwriters or agents. Any such agreement will provide that any securities sold will be sold at prices related to the then prevailing market prices for our securities. Therefore, exact figures regarding proceeds that will be raised or commissions to be paid cannot be determined at this time. Pursuant to the terms of the agreement, we may agree to sell, and the relevant underwriters or agents may agree to solicit offers to purchase blocks of our securities. The terms of any such agreement will be set forth in more detail in the applicable prospectus supplement.

In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in one business day, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than one scheduled business day after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the first business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than one scheduled business day after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. Any underwriters to whom we sell securities for public offering and sale may make a market in those securities, but they will not be obligated to do so and they may discontinue any market making at any time without notice. The

securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading market for any of the securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

The anticipated date of delivery of offered securities will be set forth in the applicable prospectus supplement relating to each offering.

LEGAL MATTERS

The legality of any securities offered hereby will be passed upon for us by Goodwin Procter LLP, New York, NY, and for any underwriters or agents, by counsel named in the applicable prospectus supplement.

EXPERTS

The financial statements of Amylyx Pharmaceuticals, Inc. incorporated by reference in this prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report. Such financial statements are incorporated by reference in reliance upon the report of such firm, given their authority as experts in accounting and auditing.



14,090,000 Shares of common stock

Prospectus Supplement

Leerink Partners Morgan Stanley Guggenheim Securities LifeSci Capital

August 19, 2026

Calculation of Filing Fee Tables

S-3

Amylyx Pharmaceuticals, Inc.

Table 1: Newly Registered and Carry Forward Securities

☐ Not Applicable

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Fee Previously Paid in Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to be Paid	1 Equity	Common Stock, par value \$0.001 per share	457(r)	16,203,500	\$ 35.50	575,224,250.00	\$ 0.0001381	\$ 79,438.47				
Fees Previously Paid												
Carry Forward Securities												
Carry Forward Securities												
Total Offering Amounts:						\$ 575,224,250.00		\$ 79,438.47				
Total Fees Previously Paid:								\$ 0.00				
Total Fee Offsets:								\$ 0.00				
Net Fee Due:								\$ 79,438.47				

Offering Note

¹ The amount registered assumes the exercise in full of the underwriters' option to purchase up to 2,113,500 additional shares of common stock. The filing fee, calculated in accordance with Rule 457(r) under the Securities Act of 1933, as amended, has been transmitted to the Securities and Exchange Commission in connection with the securities offered by means of this prospectus supplement. This "Calculation of Filing Fee" table shall be deemed to update the "Calculation of Registration Fee" table in the Registrant's Registration Statement on Form S-3ASR filed with the Securities and Exchange Commission on March 3, 2026 (File No. 333-293956).

Table 2: Fee Offset Claims and Sources

☒ Not Applicable

	Registrant or Filer Name	Form or Filing Type	File Number	Initial Filing Date	Filing Date	Fee Offset Claimed	Security Type Associated with Fee Offset Claimed	Security Title Associated with Fee Offset Claimed	Unsold Securities Associated with Fee Offset Claimed	Unsold Aggregate Offering Amount Associated with Fee Offset Claimed	Fee Paid with Fee Offset Source
Rules 457(b) and 0-11(a)(2)											
Fee Offset Claims											
Fee Offset Sources											
Rule 457(p)											
Fee Offset Claims											
Fee Offset Sources											

Table 3: Combined Prospectuses

☒ Not Applicable

Security Type	Security Class Title	Amount of Securities Previously Registered	Maximum Aggregate Offering Price of Securities Previously Registered	Form Type	File Number	Initial Effective Date
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Narrative Disclosure

The maximum aggregate offering price of the securities to which the prospectus relates is \$575,224,250.00. The prospectus is a final prospectus for the related offering.