Amylyx Pharmaceuticals Reports Second Quarter 2024 Financial Results

August 8, 2024

- *Expanded pipeline with avexitide, a Phase 3-ready GLP-1 receptor antagonist with FDA Breakthrough Therapy and Orphan Drug Designations; Phase 3 program initiation in post-bariatric hypoglycemia (PBH) on track for Q1 2025*
- *Company expects to present updated data from its Phase 2 HELIOS trial of AMX0035 in Wolfram syndrome at ISPAD 2024, including data from all 12 participants at Week 24 and any participant who completed their Week 36 or 48 assessment prior to the data cutoff*
- *Multiple ascending dose clinical trial of AMX0114 in people living with ALS planned to initiate in the second half of 2024*
- *Cash, cash equivalents and short-term investments of $309.8 million at June 30, 2024; cash runway expected into 2026*
- *Management to host conference call and webcast today at 8:00 a.m. Eastern Time*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 8, 2024-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) ("Amylyx" or the "Company") today reported financial results for the second quarter ended June 30, 2024.

"We recently expanded our late-stage pipeline with our acquisition of avexitide and now have three assets targeting orphan indications. Avexitide is Phase 3-ready with FDA Breakthrough Therapy Designation in post-bariatric hypoglycemia (PBH) and congenital hyperinsulinism, highly statistically significant data from two Phase 2 studies, and an FDA-agreed upon primary outcome for the pivotal study in PBH," said Joshua Cohen, Co-CEO of Amylyx. "PBH represents a major unmet need with an estimated 160,000 individuals in the U.S. impacted by symptomatic PBH, which can cause brain glucose starvation, known as neuroglycopenia. We are focused on progressing avexitide into Phase 3 development, which is on track to occur in Q1 2025, with topline data anticipated in 2026."

"Our recent restructuring and our focus on efficient and targeted clinical development is expected to help advance all four programs efficiently to potentially bring new treatments to communities with high unmet needs. We continue to make important progress in neurodegenerative diseases and are excited to share updated data from our Wolfram syndrome program in the months ahead," added Justin Klee, Co-CEO of Amylyx. "We also look forward to initiating a multiple ascending dose clinical trial of AMX0114 in ALS before the end of the year and reporting interim data from our AMX0035 progressive supranuclear palsy program in mid-2025."

Second Quarter and Recent Corporate Updates:

- **Acquired avexitide, a Phase 3-ready GLP-1 receptor antagonist with U.S. Food and Drug Administration (FDA) Breakthrough Therapy Designation and Orphan Drug Designation in hyperinsulinemic hypoglycemia.** Avexitide has been evaluated in five clinical trials for post-bariatric hypoglycemia (PBH) and has also been studied in three clinical trials for congenital hyperinsulinism (HI), two indications characterized by hyperinsulinemic hypoglycemia. In previous Phase 2 and Phase 2b studies in PBH, avexitide showed statistically significant reductions in hypoglycemic events. FDA guidance for industry combined with initial FDA feedback specific to the pivotal Phase 3 program of avexitide for PBH suggest that reduction in hypoglycemic events could be an endpoint to support approval following positive results from a pivotal Phase 3 clinical trial.
- **Announced interim data from the ongoing Phase 2 HELIOS clinical trial of AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO, also known as ursodoxicoltaurine]) in eight adults living with Wolfram syndrome which demonstrated encouraging improvement in glycemic control, pancreatic beta cell function, and vision.** Wolfram syndrome is a prototypical disease of endoplasmic reticulum stress that is rare, progressive, and monogenic and is characterized by childhood-onset diabetes mellitus, optic nerve atrophy, deafness, diabetes insipidus, and neurodegeneration. In April, the Company hosted a virtual webcast to discuss these data with Dr. Fumihiko Urano, a leading expert in Wolfram syndrome, the Principal Investigator of the Phase 2 HELIOS clinical trial in Wolfram syndrome, and the Samuel E. Schechter Professor of Medicine in the Division of Endocrinology, Metabolism & Lipid Research at Washington University School of Medicine in St. Louis. A replay is available here.
- **Received Orphan Drug Designation from the European Commission (EC) for AMX0035 for the treatment of Wolfram syndrome.** The designation was based on a positive opinion issued by the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA). The FDA previously granted AMX0035 Orphan Drug Designation for the treatment of Wolfram syndrome in 2020.

Upcoming Expected Milestones:

- **The Company plans to initiate a multiple ascending dose clinical trial of AMX0114 in people living with ALS in the second half of 2024**. Amylyx has completed IND-enabling studies of AMX0114, a potent antisense oligonucleotide targeting inhibition of calpain-2, a well-established target in a number of neurological diseases and a protease known to cleave many substrates including neurofilament, tau, and TDP43 proteins. Amylyx has observed rescue of cellular degeneration and neurofilament biology in multiple cellular experiments with AMX0114.

- **Amylyx plans to present updated Phase 2 HELIOS topline data at the International Society for Pediatric and Adolescent Diabetes (ISPAD) Conference in Lisbon, Portugal, October 16-19, 2024, including data for all 12 participants at Week 24 and additional longer-term data for any participant that completed their Week 36 or 48 visit prior to the data cutoff.** The Company is engaging with stakeholders, including the FDA, and planning for a single Phase 3 clinical trial. Amylyx will share additional details on the clinical trial design once finalized.

- **Amylyx expects to initiate its Phase 3 program for avexitide in PBH in Q1 2025.** Topline data are anticipated in 2026.

- **Data from an interim analysis of the ORION study of AMX0035 in progressive supranuclear palsy (PSP) continue to be expected in mid-2025.** The Company introduced an operationally seamless Phase 2b/3 study design into ORION. The first part will include approximately 100 people living with PSP. Amylyx plans to conduct an interim analysis in these participants and evaluate topline outcomes through Week 24. PSP is considered a tauopathy based on the strong genetic linkage of tau variants to the disease and presence of tau pathology in post-mortem brain samples. AMX0035 has been shown to significantly reduce tau in cerebrospinal fluid (CSF) in a Phase 2, randomized, placebo-controlled trial in Alzheimer's disease.

Financial Results for the Second Quarter Ended June 30, 2024

Net product revenue: Net product revenue was $(1.0) million for the three months ended June 30, 2024, as a result of adjustments to gross-to-net revenue reserve estimates. This is compared to net product revenue of $98.2 million for the same period in 2023. On April 4, 2024, the Company announced that it had started a process with the FDA and Health Canada to voluntarily discontinue the marketing authorizations for RELYVRIO® and ALBRIOZA™ and remove the product from the market based on topline results from the global Phase 3 PHOENIX trial, which failed to meet its prespecified primary and secondary endpoints. For the three months ended June 30, 2023, net product revenue was primarily related to units of RELYVRIO and ALBRIOZA sold in the U.S. and Canada.

Cost of Sales: Cost of sales were $7.4 million in the three months ended June 30, 2024, compared to cost of sales of $5.6 million for the same period in 2023. Cost of sales in the three months ended June 30, 2024 primarily relate to losses on firm purchase commitments under Amylyx' commercial manufacturing supply agreements for AMX0035 that were established prior to the results from the Phase 3 PHOENIX trial.

R&D Expenses: Research and development expenses were $23.3 million for the three months ended June 30, 2024, compared to $29.0 million for the same period in 2023. The decrease was primarily due to a decrease in payroll and personnel-related costs and a decrease in clinical expenses. The decrease in payroll and personnel-related costs was primarily related to a decrease in the number of employees as a result of the restructuring plan announced on April 4, 2024. The decrease in clinical expenses is primarily due to a decrease in spending on AMX0035 for the treatment of ALS due to the completion of the Phase 3 PHOENIX trial.

SG&A Expenses: Selling, general and administrative expenses were $21.6 million for the three months ended June 30, 2024, compared to $43.4 million for the same period in 2023. The decrease was primarily due to a decrease in payroll and personnel-related costs and a decrease in consulting and professional services. The decrease in payroll and personnel-related costs was primarily related to a decrease in the number of employees as a result of the restructuring plan announced on April 4, 2024. The decrease in consulting and professional services is primarily due to a decrease in commercial sales and marketing activity as a result of removing RELYVRIO/ALBRIOZA from the market in the U.S. and Canada based on topline results from the Phase 3 PHOENIX trial.

Restructuring Expenses: Restructuring expenses were $22.9 million for the three months ended June 30, 2024, compared to zero for the same period in 2023. Restructuring expenses included employee severance and termination benefits of approximately $21.8 million, contract termination costs, impairment of long-lived assets and other costs. The Company substantially completed its restructuring plan during the second quarter of 2024.

Net Loss: Net loss for the three months ended June 30, 2024 was $72.7 million, or $1.07 per share, compared to net income of $22.1 million, or $0.31 per diluted share for the same period in 2023.

Cash Position: Cash, cash equivalents, and short-term investments were $309.8 million at June 30, 2024, compared to $373.3 million at March 31, 2024. The Company expects cash runway into 2026.

Investor Conference Call Information

Amylyx' management team will host a conference call and webcast today, August 8, 2024, at 8:00 a.m. ET to discuss financial results and provide an update on the business. To access the conference call, please dial +1 (800)-836-8184 (U.S. & Canada) or +1 (646)-357-8785 (international) at least 10 minutes prior to the start time and ask to be joined into the Amylyx Pharmaceuticals

call. A live audio webcast of the call will be available under “Events and Presentations” in the Investor section of the Company’s website, https://investors.amylyx.com/news-events/events. The webcast will be archived and available for replay for 90 days following the event.

Available Information

We periodically provide other information for investors on our corporate website, https://amylyx.com, and our investor relations website, https://investors.amylyx.com. This includes press releases and other information about financial performance, information on corporate governance, and details related to our annual meeting of stockholders. We intend to use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD. Accordingly, investors should monitor our website, in addition to following the Company’s press releases, SEC filings, and public conference calls and webcasts.

About Avexitide

Avexitide is an investigational, first-in-class glucagon-like peptide-1 (GLP-1) receptor antagonist with the potential to treat hyperinsulinemic hypoglycemia that has been evaluated in five Phase 2 clinical studies for post-bariatric hypoglycemia (PBH) and has also been studied in congenital hyperinsulinism (HI). The U.S. Food and Drug Administration (FDA) has granted avexitide Breakthrough Therapy Designation for both indications, Rare Pediatric Disease Designation in congenital HI, and Orphan Drug Designation for the treatment of hyperinsulinemic hypoglycemia (which includes PBH and congenital HI). Avexitide is designed to bind to the GLP-1 receptor on pancreatic islet beta cells and block the effect of excessive GLP-1 to mitigate hypoglycemia by decreasing insulin secretion and stabilizing glucose levels. In PBH, excessive GLP-1 can lead to the hypersecretion of insulin and subsequent serious hypoglycemic events. In two Phase 2 PBH trials, avexitide demonstrated highly statistically significant reductions in hypoglycemic events. These events can lead to autonomic and neuroglycopenic symptoms that can have a devastating impact on daily living.

About AMX0035

AMX0035 is an investigational, oral, fixed-dose combination of sodium phenylbutyrate (PB) and taurursodiol (TURSO; also known as ursodoxicoltaurine outside of the U.S.). AMX0035 is designed to slow or mitigate neurodegeneration by targeting endoplasmic reticulum (ER) stress and mitochondrial dysfunction, two connected central pathways that lead to cell death and neurodegeneration. Preclinical studies have provided evidence that AMX0035 may reduce cell death and improve cellular function, also supporting the synergistic effect of AMX0035 compared to individual compounds. AMX0035 is being studied as a potential treatment in neurodegenerative diseases, including Wolfram syndrome and progressive supranuclear palsy (PSP).

About AMX0114

AMX0114 is an investigational, antisense oligonucleotide designed to target the gene encoding calpain-2, a key contributor to the axonal (Wallerian) degeneration pathway. Axonal degeneration has been recognized as an important early contributor to the clinical presentation and pathogenesis of ALS and other neurodegenerative diseases. Calpain-2 has been implicated in the pathogenesis of ALS based on findings of elevated levels of calpain-2 and its cleavage products in postmortem ALS tissue, therapeutic benefit of calpain-2 modulation in animal models of ALS, and the role of calpain-2 in cleaving neurofilament, a broadly researched biomarker in ALS. Preclinical studies completed to date have shown that AMX0114 achieves potent, dose-dependent, and durable knockdown of *CAPN2* mRNA expression and calpain-2 protein levels in human motor neurons. Moreover, in preclinical efficacy studies, treatment with AMX0114 reduced extracellular neurofilament light chain levels following neurotoxic insult in induced pluripotent stem cell (iPSC)-derived human motor neurons, and improved survival of iPSC-derived human motor neurons harboring ALS-linked, pathogenic TDP-43 mutations.

About Post-Bariatric Hypoglycemia (PBH)

Symptomatic post-bariatric hypoglycemia (PBH) is a condition that affects approximately 8% of people who have undergone bariatric surgery. It is characterized by exaggerated secretion of glucagon-like peptide-1 (GLP-1), dysregulated secretion of insulin, and a rapid drop in blood sugar. PBH can cause serious hypoglycemic events associated with brain glucose starvation, known as neuroglycopenia, including impaired cognition, cardiac arrhythmias, loss of consciousness, and seizures. PBH is associated with a high degree of disability and can result in major disruptions to life, including falls, motor vehicle accidents, and job and income loss. It is estimated that ~160,000 people are currently living with symptomatic PBH in the U.S., classifying it as an orphan condition.

About Congenital Hyperinsulinism (HI)

Congenital hyperinsulinism (HI) is a rare disease characterized by hypersecretion of insulin leading to severe, persistent hypoglycemia in infants and young children with limited therapeutic options. Common symptoms of congenital HI include lack of energy, irritability, lethargy, and excessive hunger. Repeated episodes of low blood glucose increase the risk for serious complications such as breathing difficulties, seizures, intellectual disability, vision loss, brain damage, and coma.

About the HELIOS Trial

The HELIOS trial (NCT05676034) is a 12-participant, open-label Phase 2 trial designed to study the effect of AMX0035 on safety and tolerability, and various measures of endocrinological, neurological, and ophthalmologic function in adult participants living with

Wolfram syndrome.

About Wolfram Syndrome

Wolfram syndrome is a rare, progressive, monogenic disease characterized by childhood-onset diabetes, optic nerve atrophy, and neurodegeneration. Common manifestations of Wolfram syndrome include diabetes mellitus, optic nerve atrophy, central diabetes insipidus, sensorineural deafness, neurogenic bladder, and progressive neurologic difficulties. The prognosis of Wolfram syndrome is poor, and many people with the disease die prematurely with severe neurological disabilities. Literature suggests approximately 3,000 people are living with Wolfram syndrome in the U.S.

Wolfram syndrome is often characterized as a prototypical disease of endoplasmic reticulum (ER) stress. ER stress and mitochondrial dysfunction are believed to drive the underlying disease pathophysiology in Wolfram syndrome. Individuals with Wolfram syndrome generally have mutations in the *WFS1* gene, which encodes wolframin, a protein spanning the membrane of the ER. Wolframin is thought to play a role in protein folding and aid in the maintenance of ER function by regulating calcium levels. Loss of wolframin function leads to ER stress and impaired mitochondrial dynamics.

About the ORION Trial

The ORION trial (NCT06122662) is a global, randomized, double-blind, placebo-controlled Phase 2b/3 clinical trial designed to assess the efficacy, safety, and tolerability of AMX0035 compared to placebo in people living with progressive supranuclear palsy (PSP). ORION was designed and planned in collaboration with key global academic leaders, people living with PSP and their caregivers, and industry advocacy organizations.

About PSP

Progressive supranuclear palsy (PSP) is a sporadic, rare, and adult-onset neurodegenerative disorder that affects walking and balance, eye movement, swallowing, and speech. People living with PSP have a life expectancy of six to eight years after initial diagnosis, and its epidemiology is similar to that of amyotrophic lateral sclerosis (ALS). PSP typically begins in late-middle age and rapidly progresses over time. The disease affects approximately seven in 100,000 people worldwide, and there are currently no disease-modifying therapies approved for the treatment of PSP.

PSP is characterized by abnormal tau inclusions and is consequently also known as a tauopathy. Similar to other neurodegenerative diseases, pathophysiologic changes underlying PSP are multifactorial, with several genetic and environmental factors likely contributing to tau dysfunction and aggregation.

Multiple pathways, including genetic mutations, endoplasmic reticulum (ER) stress, and the activation of unfolded protein response, mitochondrial dysfunction, and neuroinflammation have been implicated as contributors to tau dysfunction and aggregation.

About ALS

Amyotrophic lateral sclerosis (ALS, also known as motor neuron disease) 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. More than 90% of people with ALS have sporadic disease, showing no clear family history. ALS affects around 30,000 people in the U.S., and more than 30,000 people are estimated to be living with ALS in Europe (European Union and the United Kingdom). People living with ALS have a median survival of approximately two years from diagnosis.

About Amylyx Pharmaceuticals

Amylyx is committed to the discovery and development of new treatment options for communities with high unmet needs, including people living with serious and fatal diseases. The Company has preclinical or clinical development programs underway in neurodegenerative, neuroendocrine, and endocrine diseases. Since its founding, Amylyx has been guided by science to address unanswered questions, keeping communities at the heart and center of all decisions. Amylyx is headquartered in Cambridge, Massachusetts. For more information, visit amylyx.com and follow us on LinkedIn and X. For investors, please visit investors.amylyx.com.

Forward-Looking Statements

Statements contained in this press release and related comments in our earnings conference call regarding matters that are not historical facts are “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, the potential of AMX0035 (sodium phenylbutyrate and taurursodiol) as a treatment for Wolfram syndrome and PSP or other neurodegenerative diseases; expectations regarding the timing of the announcement of results from the Company’s Phase 3 ORION trial of AMX0035 for the treatment of PSP, and additional results from the Company’s Phase 2 HELIOS trial of AMX0035 for the treatment of Wolfram syndrome and plans to possibly initiate a phase 3 trial, including planned discussions with regulatory authorities related thereto; the potential for AMX0114 as a treatment for ALS and the planned initiation of a trial evaluating AMX0114 in ALS; expectations regarding the Company’s ability to develop, manufacture and commercialize avexitide, if approved; the potential for

avexitide as a treatment for PBH; expectations regarding the timing for initiation and readout of the Phase 3 avexitide program in PBH; and expectations regarding the Company's cash runway and longer-term strategy. Any forward-looking statements in this press release and related comments in the Company's earnings conference call are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements include: the success, cost, and timing of Amylyx' program development activities; Amylyx' ability to execute on its regulatory development plans and expectations regarding the timing of results from its planned data announcements and initiation of clinical studies; the risk that early-stage results may not reflect later-stage results; Amylyx' ability to fund operations, and the impact that global macroeconomic uncertainty, geopolitical instability, and public health events will have on Amylyx' operations, as well as the risks and uncertainties set forth in Amylyx' United States Securities and Exchange Commission (SEC) filings, including Amylyx' Annual Report on Form 10-K for the year ended December 31, 2023, and subsequent filings with the SEC. All forward-looking statements contained in this press release and related comments in our earnings conference call speak only as of the date on which they were made. Amylyx undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

AMYLYX PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
UNAUDITED
(in thousands)

	June 30, 2024	December 31, 2023
Assets		
Cash, cash equivalents and short-term investments	$ 309,812	$ 371,362
Accounts receivable, net	4,091	40,050
Inventories	—	83,280
Prepaid expenses and other current assets	12,819	14,931
Other assets	5,440	7,831
Total assets	$ 332,162	$ 517,454
Liabilities and Stockholders' Equity		
Accounts payable and accrued expenses	$ 67,712	$ 79,785
Other liabilities	3,141	4,237
Total liabilities	70,853	84,022
Stockholders' equity	261,309	433,432
Total liabilities and stockholders' equity	$ 332,162	$ 517,454

AMYLYX PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
UNAUDITED
(in thousands, except share and per share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2024	2023	2024	2023
Product revenue, net	$ (1,023)	$ 98,216	$ 87,620	$ 169,644
Operating expenses:				
Cost of sales	8	5,580	5,953	10,863
Cost of sales - inventory impairment and loss on firm purchase commitments	7,410	—	117,871	—
Research and development	23,347	29,044	59,955	53,236
Selling, general and administrative	21,647	43,391	79,406	87,397
Restructuring expenses	22,851	—	22,851	—
Total operating expenses	75,263	78,015	286,036	151,496
(Loss) income from operations	(76,286)	20,201	(198,416)	18,148
Other income, net	3,586	3,806	7,165	7,262
(Loss) income before income taxes	(72,700)	24,007	(191,251)	25,410
Provision for income taxes	—	1,933	242	1,763
Net (loss) income	$ (72,700)	$ 22,074	$ (191,493)	$ 23,647

Net (loss) income per share				
Basic	$ (1.07)	$ 0.33	$ (2.82)	$ 0.35
Diluted	$ (1.07)	$ 0.31	$ (2.82)	$ 0.34
Weighted-average shares used in computing net (loss) income per share				
Basic	68,024,929	67,233,617	67,939,642	66,976,871
Diluted	68,024,929	70,132,040	67,939,642	70,471,821

View source version on businesswire.com: https://www.businesswire.com/news/home/20240808415481/en/

Media
Amylyx Media Team
+1 (857) 799-7274
amylyxmediateam@amylyx.com

Investors
Lindsey Allen
Amylyx Pharmaceuticals, Inc.
+1 (857) 320-6244
Investors@amylyx.com

Source: Amylyx Pharmaceuticals, Inc.