Amylyx Pharmaceuticals Reports Third Quarter 2024 Financial Results

November 7, 2024 at 7:00 AM EST

- *On track to initiate a Phase 3 program for Company's lead asset avexitide, a GLP-1 receptor antagonist with FDA Breakthrough Therapy and Orphan Drug Designations, in post-bariatric hypoglycemia (PBH) in the first quarter of 2025*
- *Reported positive topline data from Phase 2 HELIOS clinical trial of AMX0035 in Wolfram syndrome demonstrating improvement or stabilization across all disease measures at Week 24 and sustained improvement at Weeks 36 and 48*
- *Cash, cash equivalents and marketable securities of $234.4 million as of September 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)--Nov. 7, 2024-- Amylyx Pharmaceuticals, Inc. (Nasdaq: AMLX) ("Amylyx" or the "Company") today reported financial results for the third quarter ended September 30, 2024.

"This quarter, we continued to advance our late-stage pipeline as part of our goal to bring new potential treatments to communities with high unmet needs. We recently reported positive topline data from our Phase 2 HELIOS clinical trial in people living with Wolfram syndrome that show AMX0035 resulted in meaningful improvements across multiple measures of disease progression as well as sustained improvement over time. We plan to engage with the FDA and other stakeholders to inform our Phase 3 program in Wolfram," said Joshua Cohen and Justin Klee, Co-CEOs of Amylyx. "Additionally, we are on track to initiate a Phase 3 program for our lead asset avexitide in post-bariatric hypoglycemia in the first quarter of next year and remain on track to report interim data from our Phase 2b/3 ORION clinical trial of AMX0035 in progressive supranuclear palsy in mid-2025. With cash runway into 2026, we believe we are well positioned to deliver on these milestones as we continue our critical work in neurodegenerative diseases and endocrine conditions."

Third Quarter and Recent Updates:

- **Announced positive topline data for all 12 participants in the Phase 2 HELIOS clinical trial, a single-site, single-arm, open-label trial of AMX0035 (sodium phenylbutyrate [PB] and taurursodiol [TURSO, also known as ursodoxicoltaurine]) in adults living with Wolfram syndrome.** Wolfram syndrome is a rare, progressive, monogenic disease impacting approximately 3,000 people in the U.S. HELIOS showed improvement in pancreatic function, as measured by C-peptide response after 24 weeks of treatment with AMX0035, the trial's primary efficacy endpoint, in contrast to the expected decrease in pancreatic function with disease progression. Similar overall improvements or stabilization were observed across all secondary endpoints, including hemoglobin A1c (HbA1c), time in target glucose range assessed by continuous glucose monitoring (CGM), and visual acuity. The safety profile of AMX0035 in HELIOS was consistent with prior safety data. The Company is engaging with stakeholders and plans to meet with the U.S. Food and Drug Administration (FDA) to inform a Phase 3 program and expects to provide an update in 2025.
- **Acquired avexitide, a Phase 3-ready glucagon-like peptide-1 (GLP-1) receptor antagonist with 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 hypoglycemia events. FDA guidance for industry combined with initial FDA feedback specific to the planned pivotal Phase 3 program of avexitide for PBH suggest that reduction in hypoglycemia events could be an endpoint to support approval following positive results from a pivotal Phase 3 clinical trial.
- **Announced publication of data showing encouraging effects of AMX0035 on cerebrospinal fluid (CSF) biomarkers of core Alzheimer's disease (AD) pathology and neurodegeneration in the peer-reviewed medical journal *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, a journal of the Alzheimer's Association.** The exploratory analyses on CSF biomarkers from participants with AD from the Phase 2 PEGASUS clinical trial suggest that treatment with AMX0035 resulted in consistent changes in AD and neurodegeneration CSF biomarkers in participants with a broad range of disease severity. Findings from the exploratory analysis provide preliminary evidence that AMX0035 engages multiple pathological pathways related to neurodegeneration, including tau.
- **Presented the planned Phase 1 study design of AMX0114 in people living with amyotrophic lateral sclerosis (ALS) at the 2024 Northeast ALS Consortium Annual Meeting.** The Phase 1 LUMINA clinical trial, a multicenter, randomized,

placebo-controlled, multiple ascending dose trial, will evaluate the safety and biological activity of AMX0114 in approximately 48 people living with ALS. Four dose levels of AMX0114 or placebo are planned to be examined sequentially starting with 12.5 mg.

- **Received clearance from Health Canada for the Company's Clinical Trial Application for AMX0114 in people living with ALS. Amylyx plans to begin the LUMINA trial with a starting dose of 12.5 mg in Canada by the end of 2024 or in early 2025.** The Company also submitted an Investigational New Drug application to the FDA for AMX0114. The FDA restricted dosing to an amount that is lower than the Company's proposed starting dose of 12.5 mg and has requested additional information, which resulted in a clinical hold. Toxicology data from studies showed a greater than 10X safety margin at the starting dose of 12.5 mg based on the no observed adverse effect level (NOAEL) determined by independent toxicology firms. Amylyx is working to address FDA comments and believes the trial can be completed outside of the U.S. if needed. The Company expects early cohort data from LUMINA in 2025.

Upcoming Expected Milestones:

- **The Company plans to initiate the Phase 1 LUMINA clinical trial of AMX0114 in people living with ALS by the end of 2024 or in the beginning of 2025 in Canada.** AMX0114 is an 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 expects early cohort data from LUMINA in 2025.
- **Amylyx continues to expect initiation of its Phase 3 program for avexitide in PBH in the first quarter of 2025.** Topline data are anticipated in 2026.
- **Data from an interim analysis of the Phase 2b/3 ORION clinical trial of AMX0035 in progressive supranuclear palsy (PSP) continue to be expected in mid-2025.** ORION is an operationally seamless Phase 2b/3 clinical trial. The Phase 2b portion will include approximately 100 people living with PSP. Amylyx plans to conduct an interim analysis in these participants through Week 24 and will use this data to inform a go/no-go decision on the Phase 3 portion of the trial in mid-2025.

Financial Results for the Third Quarter Ended September 30, 2024

Net product revenue: Net product revenue was $0.4 million for the three months ended September 30, 2024 and was related to adjustments to the Company's gross-to-net accrual estimates for prior period sales of RELYVRIO ® and ALBRIOZA™. As previously disclosed, 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 did not meet its prespecified primary and secondary endpoints.

Cost of Sales: Cost of sales were $0.8 million in the three months ended September 30, 2024, and were related to estimated losses on firm commitments under commercial manufacturing supply agreements for AMX0035 that were established prior to the results from the Phase 3 PHOENIX trial.

Acquired in-process research and development: Acquired in-process research and development expenses were $36.2 million for the three months ended September 30, 2024, compared to zero for the same period in 2023. The increase was due to the acquired in-process research and development assets of avexitide.

R&D Expenses: Research and development expenses were $21.2 million for the three months ended September 30, 2024, compared to $30.0 million for the same period in 2023. The decrease was primarily due to a decrease in clinical expenses and a decrease in payroll and personnel-related costs. The decrease in clinical expenses is primarily due to a decrease in spending on AMX0035 for the treatment of ALS following the topline data from the PHOENIX trial. The decrease in payroll and personnel-related costs was primarily related to a decrease in the number of employees following the restructuring plan announced on April 4, 2024.

SG&A Expenses: Selling, general and administrative expenses were $17.8 million for the three months ended September 30, 2024, compared to $48.7 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 was primarily due to a decrease in commercial sales and marketing activity as a result of removing RELYVRIO/ALBRIOZA from the markets in the U.S. and Canada based on topline results from the Phase 3 PHOENIX trial.

Net Loss: Net loss for the three months ended September 30, 2024, was $72.7 million, or $1.07 per share, compared to net income of $20.9 million, or $0.30 per diluted share for the same period in 2023.

Cash Position: Cash, cash equivalents, and marketable securities were $234.4 million as of September 30, 2024, compared to $309.8 million as of June 30, 2024. The Company expects cash runway into 2026.

Investor Conference Call Information

Amylyx' management team will host a conference call today, November 7, 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 that has been evaluated in five Phase 2 clinical studies for post-bariatric hypoglycemia (PBH) and has also been studied in congenital hyperinsulinism (HI), with U.S. Food and Drug Administration (FDA) Breakthrough Therapy Designation for both indications and FDA Rare Pediatric Disease Designation in 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 hypoglycemia events. In two Phase 2 PBH trials, avexitide demonstrated highly statistically significant reductions in hypoglycemia events. These events can lead to autonomic and neuroglycopenic symptoms that can have a devastating impact on daily living.

About AMX0035

AMX0035 is an oral, fixed-dose combination of sodium phenylbutyrate (PB) and taurursodiol (TURSO; also known as ursodoxicoltaurine outside of the U.S.). AMX0035 was 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. We believe that our proprietary combination of PB and TURSO and their complementary mechanisms of action will allow us to synergistically target abnormal cell death to better prevent neurodegeneration than treatment targeted at either mechanism of action alone. AMX0035 is being studied as a potential treatment for Wolfram syndrome and progressive supranuclear palsy, two neurodegenerative diseases.

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 an excessive glucagon-like peptide-1 (GLP-1) response, dysregulated secretion of insulin, and a rapid drop in blood sugar. PBH can cause serious hypoglycemia events associated with brain glucose starvation, known as neuroglycopenia, including impaired cognition, cardiac arrythmias, 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

HELIOS (NCT05676034) is a 12-participant, single-site, single-arm, open-label, proof of biology, 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. Participants in HELIOS receive AMX0035 for up to 96 weeks followed by a four-week safety follow-up. Primary and secondary outcomes are assessed at Week 24 and at longer-term time points.

In September 2022, researchers from Washington University School of Medicine in St. Louis, including Dr. Urano, in collaboration with Amylyx, published preclinical data on AMX0035 in beta cell, neuronal cell, and mouse models of Wolfram syndrome in the peer-reviewed Journal of Clinical Investigation Insight. The FDA and the European Commission granted Orphan Drug Designation to AMX0035 for the treatment of Wolfram syndrome in November 2020 and August 2024, respectively.

About Wolfram Syndrome

Wolfram syndrome is a rare, monogenic neurodegenerative disease characterized by childhood-onset diabetes, optic nerve atrophy, and neurodegeneration. Common manifestations of Wolfram syndrome include diabetes mellitus and diabetes insipidus, gradual vision loss leading to blindness, hearing loss, neurogenic bladder, difficulties with balance and coordination, and difficulty breathing. Genetic and experimental evidence suggests that endoplasmic reticulum (ER) dysfunction is a critical pathogenic component of Wolfram syndrome. The prognosis of Wolfram syndrome is poor, and many people with the disease die prematurely with severe neurological disabilities.

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 fatal neurodegenerative disorder that affects movement, gait, balance, eye movements, swallowing, and speech. People living with PSP have a life expectancy of six to eight years after initial diagnosis. 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 neurodegenerative diseases and endocrine conditions. 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 avexitide as a treatment for PBH and HI; expectations regarding the timing of initiation of a Phase 3 trial of avexitide in PBH; 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; planned discussions with regulatory authorities related to AMX0035 for the treatment of Wolfram syndrome; the potential for AMX0114 as a treatment for ALS and the planned initiation of a trial evaluating AMX0114 in ALS, including potential expansion into the U.S.; the Company's expectations regarding its financial performance; 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.

AMYLYX PHARMACEUTICALS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

UNAUDITED

(in thousands)

	September 30, 2024	December 31, 2023

Assets

Cash, cash equivalents and short-term investments	$ 234,395	$ 371,362
Accounts receivable, net	1,731	40,050
Inventories	—	83,280
Prepaid expenses and other current assets	9,137	14,931
Other assets	5,450	7,831
Total assets	$ 250,713	$ 517,454
Liabilities and Stockholders' Equity		
Accounts payable and accrued expenses	$ 51,943	$ 79,785
Other liabilities	2,567	4,237
Total liabilities	54,510	84,022
Stockholders' equity	196,203	433,432
Total liabilities and stockholders' equity	$ 250,713	$ 517,454

AMYLYX PHARMACEUTICALS, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS

UNAUDITED

(in thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	**2023**	**2024**	**2023**
Product revenue, net	$ 416	$ 102,693	$ 88,036	$ 272,337
Operating expenses:				
Cost of sales	—	5,218	5,953	16,081
Cost of sales - inventory impairment and loss on firm purchase commitments	809	—	118,680	—
Acquired in-process research and development	36,203	—	36,203	—
Research and development	21,237	30,037	81,192	83,273

Selling, general and administrative	17,828	48,718	97,234	136,115
Restructuring expenses	—	—	22,851	—
Total operating expenses	76,077	83,973	362,113	235,469
(Loss) income from operations	(75,661)	18,720	(274,077)	36,868
Other income, net	2,957	3,691	10,122	10,953
(Loss) income before income taxes	(72,704)	22,411	(263,955)	47,821
Provision for income taxes	—	1,518	242	3,281
Net (loss) income	$ (72,704)	$ 20,893	$ (264,197)	$ 44,540
Net (loss) income per share				
Basic	$ (1.07)	$ 0.31	$ (3.89)	$ 0.66
Diluted	$ (1.07)	$ 0.30	$ (3.89)	$ 0.63
Weighted-average shares used in computing net (loss) income per share				
Basic	68,091,446	67,414,669	67,990,613	67,124,407
Diluted	68,091,446	69,748,547	67,990,613	70,143,659

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