CLT-14

A Phase 1, Multicenter, Randomized, Placebo-Controlled Multiple Ascending Dose Study to Evaluate the Safety and Tolerability of AMX0114 in Amyotrophic Lateral Sclerosis (LUMINA)

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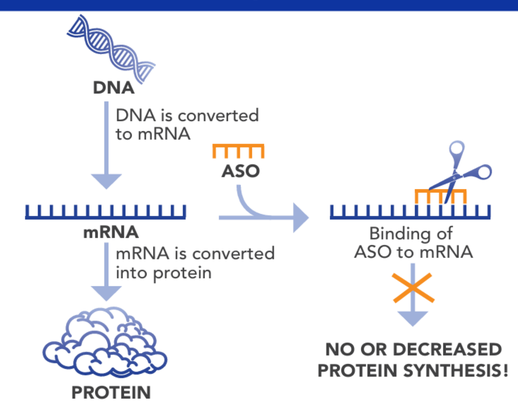
Calpain-2 is a Unique Target in ALS

- Calpain-2 is a calcium-activated cysteine protease that is a critical effector of axonal degeneration[1-3]
- Calpain-2 is implicated in the pathogenesis of ALS based on[3,6-8]:
  - Elevated levels of *CAPN2* mRNA in muscle and calpain-specific cleavage products in spinal cord and brain from people with ALS[9,11]
  - Linkage to NfL and TDP-43 pathology[8-10]
  - Therapeutic benefit of calpain-2 activity modulation in animal models of ALS[12]

AMX0114 is an ASO Inhibitor of Calpain-2



AMX0114 has been shown to achieve potent, dose-dependent, and durable knockdown of *CAPN2* mRNA and calpain-2 protein in human motor neurons[2]

Neuroprotective Effects Observed in in vitro ALS Models

- Reduced extracellular neurofilament light chain (NfL)[3]
- Reduced levels of a calpain-specific alpha-II spectrin breakdown product (SBDP-145)[4]
- Improved neuron survival and demonstrated neuroprotective effects[5]

LUMINA Multiple Ascending Dose Study Design

OBJECTIVE: Assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of AMX0114 in people living with ALS

Study Duration: ~25 weeks

Dosing and Administration
Intrathecal bolus every 4 weeks
for a total of up to 4 doses per cohort

Dose Escalation → Dose Escalation → Dose Escalation

Cohort 1	Cohort 2	Cohort 3	Cohort 4
(12.5 mg)	(X mg– planned)	(X mg – planned)	(X mg - planned)
AMX0114 (n=9)	AMX0114 (n=9)	AMX0114 (n=9)	AMX0114 (n=9)
Placebo (n=3)	Placebo (n=3)	Placebo (n=3)	Placebo (n=3)

Fully enrolled

Open-Label Extension

An open-label extension ***may*** be implemented if safety and efficacy data support a positive benefit-risk profile

Screening Period (up to 4 wk) → **Treatment Period** (~ 13 wk) → **Safety Follow-Up Period** (~ 8 wk)

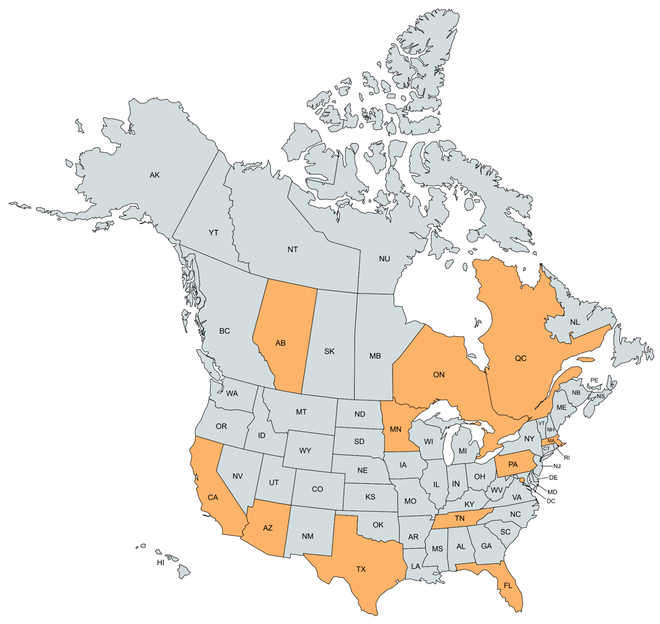
Key Trial Entry Criteria

- ✓ Age ≥18 years
- ✓ Diagnosis of clinically definite or clinically probable ALS, based on El Escorial criteria
- ✓ <24 month since onset of first ALS symptom
- ✓ Slow vital capacity (SVC) ≥ 65%
- ✓ Approved treatments for ALS are allowed if participant is on a stable dose for at least 30 days prior to baseline visit

Cohort 1 Safety Results

As of 11NOV2025, all participants in Cohort 1 have received at least 2 doses of AMX0114 or placebo. AMX0114 (12.5mg) is generally well-tolerated with no treatment-related SAEs or serious neurological adverse events[13] as of the data cut-off.

LUMINA will be conducted at ~15 sites in Canada and the United States, enrolling ~48 adult participants with ALS



Endpoints

Primary Endpoints

- Incidence of adverse events (AEs), serious adverse events (SAEs), and dose-limiting toxicities (DLTs)
- Incidence of abnormalities in clinical laboratory assessments, vital signs, physical and neurological examinations, and electrocardiograms

Secondary Endpoints

- PK concentrations, including plasma and cerebrospinal fluid (CSF) levels of AMX0114

Tertiary Endpoints

- Change from baseline of plasma and CSF pharmacodynamic measures of ALS and markers of target engagement (e.g., calpain-2, NfL, SBDP-145)
- Change from baseline of ALS Functional Rating Scale – Revised (ALSFRS-R) and slow vital capacity (SVC)

Conclusions

- AMX0114 is an ASO inhibitor of calpain-2, a critical effector of axonal degeneration
- AMX0114 has demonstrated target engagement, reduction of neurofilament light chain, and benefit on neuronal survival across multiple disease-relevant cell types and pre-clinical models
- LUMINA is a first-in-human, multiple ascending dose study evaluating the safety, tolerability, PK, and PD of AMX0114 in adults with ALS
- Sites are activated in Canada and the U.S., and the first cohort has been fully enrolled. AMX0114 has been generally well-tolerated, with no treatment-related SAEs as of the data cut-off on 11NOV2025.

Scan to Learn More about the LUMINA Trial

AMX0114 has not been approved for use by any health authorities (including the EMA, FDA, PMDA, and Health Canada).

References

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Disclosures

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