# "SEALS": A Randomized, Double-Blind, Placebo-Controlled **Phase 2** Study Evaluating Efficacy And Safety Of **NX210c In Amyotrophic Lateral Sclerosis** (ALS) Patients

ENCALS MADRID2026

**# PO108**


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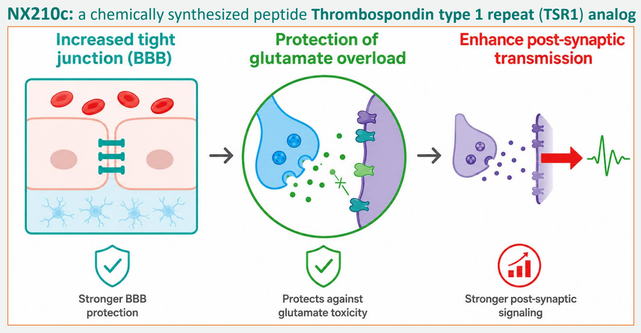
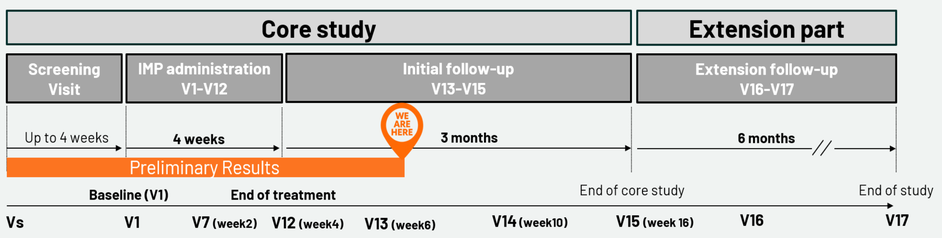
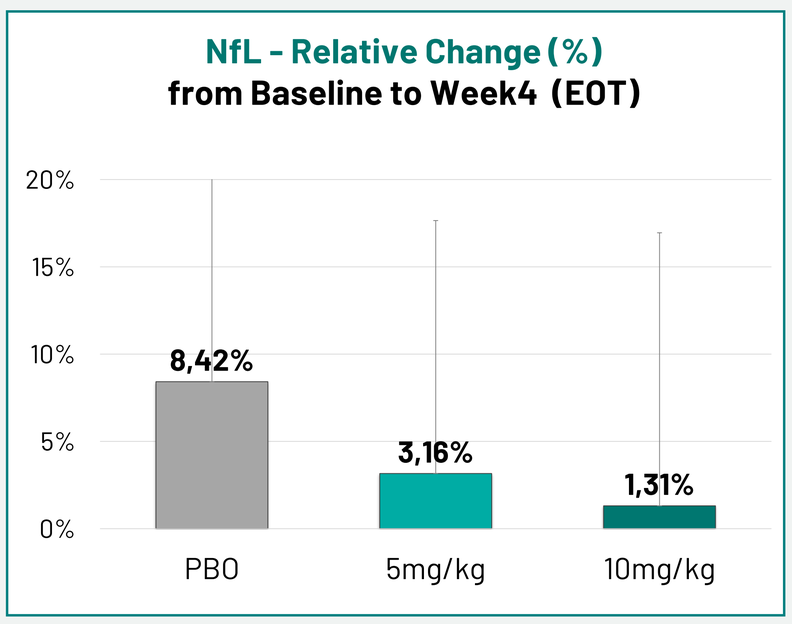
**Objective(s)**: To present **early results** of **biomarkers** & featured findings of **ALS patients treated with NX210c,** a therapeutic with properties targeting the **blood brain barrier (BBB), neuroprotection** and **neurotransmission.**

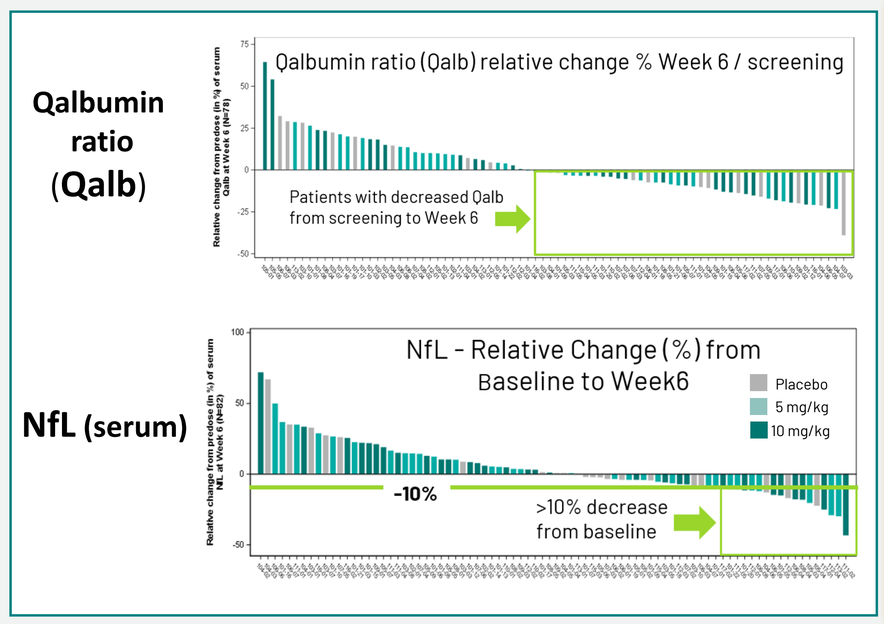



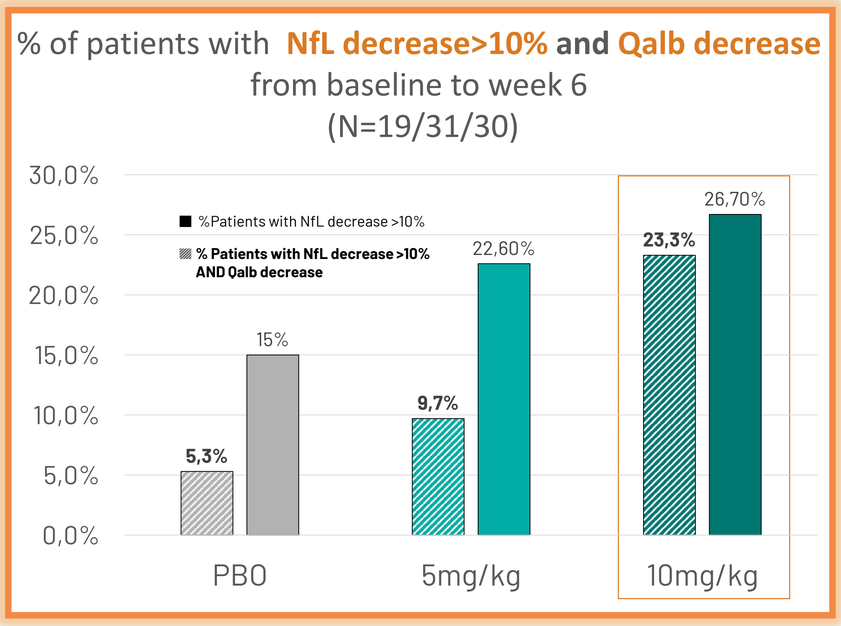




## Key SEALS Phase 2 Features

| | |
|---|---|
| **Study Design** | Biomarker study; **82 patients randomized**, **3:3:2** (5mg/kg, 10 mg/kg, placebo) |
| **Stratification** | Baseline NfL threshold = 95 pg/mL (blood/serum) |
| **Treatment** | **4-week IV dosing; 3 infusions per week** |
| **Sampling** | Blood (primary); lumbar punctures at screening and 2 weeks post-treatment; urine |
| **Follow-up** | **Core: biomarkers** + clinical endpoints; Extension: survival, time-to-event, clinical data |
| **Secondary Endpoints** | Function (ALSFRS-R, SVC); strength (dynamometry); biomarkers (blood/CSF/urine); safety & tolerability; progression & survival; QoL (ALSAQ-40); pharmacokinetics |
| **Digital Twins** | Synthetic placebo arm (of 62 patients); statistical enrichment |
| **Population** | ALS by El Escorial, **≤36 months** from symptoms, **SVC ≥55%**; **well-balanced**, representative of real-world ALS distributions |
| **Primary Endpoint** | Change in biomarkers: serum NfL or QAlb ratio from pre-dose to Week 6 |




Although the difference between groups was not significant, a **dose dependent trend in relative NfL level was identified at week 4 (End of Treatment).**

**NfL decreases and Qalb decreases were observed.**

At 10mg/kg, a notable proportion of **patients treated with NX210c** that showed **decreased NfL ALSO** showed **Qalb decrease.**

| **Parameters at baseline** | | **NX210c 5mg/kg n=31** | **NX210c 10mg/kg n=31** | **Active dose n=62** | **Placebo n=20** |
|---|---|---|---|---|---|
| **Serum NfL threshold 95pg/mL** | n High/Low | 9/22 | 10/21 | 19/43 | 6/14 |
| **Serum NfL (pg/ml) at screening** | Mean (SD) | 78.29 (36.63) | 86.74 (52.04) | 82.51 (44.83) | 89.24 (62.71) |
| **Qalbumin ratio % at screening** | Mean (SD) | 6.50 (1.84) | 8.31 (4.53) | 7.40 (3.55) | 7.19 (3.18) |
| **Abnormal Qalb** | n (%) | 6 (19.4%) | 15 (48.4%) | 21 (33.8%) | 6 (30.0%) |
| **H-ALSFRS-R global score (/48)** | Median [Min ; Max] | 40 [29 ; 45] | 37 [30 ; 46] | 38 [29 ; 46] | 37 [24 ; 47] |

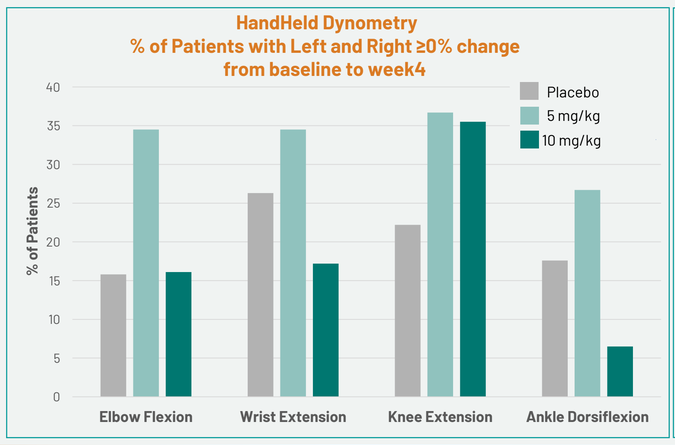
9 months after last patient in, 69 patients suffered from at least one adverse event (AE): **SAE: 11** (1 possibly related)

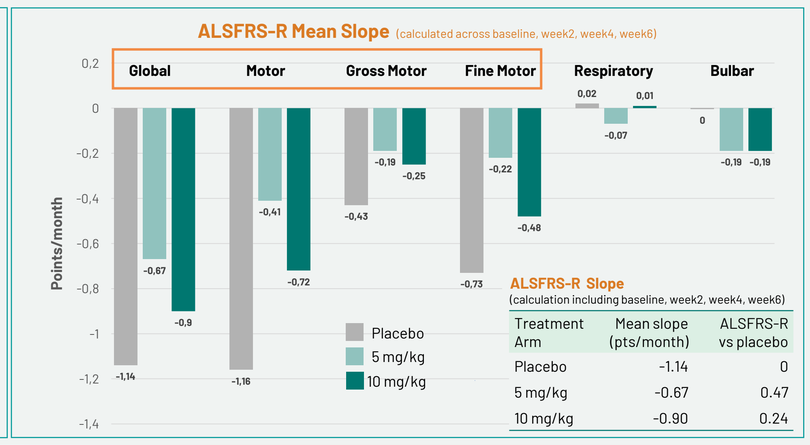
| **AE** | **Relation to IMP** | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Unrelated | | | | Unlikely | | | | Possible | | | | Probable | | | | Related | | | |
| **350** | 207 | | | | 50 | | | | 65 | | | | 6 | | | | 22 | | | |
| | **Severity** | | | | | | | | | | | | | | | | | | | |
| | Mild | Moderate | Severe | IRR | Mild | Moderate | Severe | IRR | Mild | Moderate | Severe | IRR | Mild | Moderate | Severe | IRR | Mild | Moderate | Severe | IRR |
| **350** | 144 | 38 | 25 | 0 | 37 | 9 | 3 | 1 | 37 | 2 | 1 | 25 | 5 | 1 | 0 | 0 | 20 | 0 | 0 | 2 |

**Conclusion**: Early results of **serum NfL and Qalb, strength and function** in **ALS patients treated with NX210c,** a therapeutic with properties targeting the **blood brain barrier (BBB), neuroprotection** and **neurotransmission,** show **good safety** and **early, promising indicators of potential efficacy.** Further analysis is under way.

Handheld Dynamometry performed in the upper and lower limb bilaterally:

End of Treatment **strength** suggests a **potential benefit** in a higher percentage of patients **treated with NX210c** (at 5mg/kg dose) compared to placebo.




ALSFRS-**global** and **motor** scores, **2 weeks after treatment course**:

Even early, a higher proportion of patients **treated with NX210c** tended to show **less decline** compared to placebo.

| Matrix | Key Biomarkers |
|---|---|
| Plasma / Serum | NfL, Claudin-5, albumin, IgG, GFAP, TNFα, SPARCL1, PDGFRβ, VCAM1, MMP-9 (activity), ICAM-1, S100β, TGFβ1, Homocysteine |
| CSF | NfL, albumin, IgG, GFAP, SPARCL1, PDGFRβ, S100β, YKL-40 |
| Urine | p75NTR/p75ECD |

The full dataset will continue to be harnessed

- ➢ *In silico* methods will include **Digital Twins**, endpoint **modeling, PKPD** analysis and **dose/regimen optimization for next clinical development**
- ➢ **Responder(s)** characterization through **precision profiling** of biomarkers & clinical outcomes

**Learn More**

**See also**

**POSTER #PO101**
**POSTER #PO127**

**We are grateful to patients, sites and partners for making this work possible!**

**Disclosures:**
AJ & SM are employed by Axoltis Pharma. AJ is consultant for Axoltis Pharma.


The Phase II clinical trial "SEALS" includes AURALS collaborative project which is granted by