

# SEALS

A Double-blind, Randomized, Placebo-controlled, Multicentric, Phase II Study in Adult Patients With Amyotrophic Lateral Sclerosis (ALS) to Assess Efficacy, Safety, Tolerability and Pharmacokinetics of Multiple Intravenous Infusions of NX210c

## Preliminary Results

Coordinating Investigator : **Dr Emilien BERNARD**  
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**Sponsor: Axoltis Pharma, Lyon, France**

**Coordinating Investigator : Dr Emilien BERNARD**

Hospices Civils de Lyon, Lyon, France



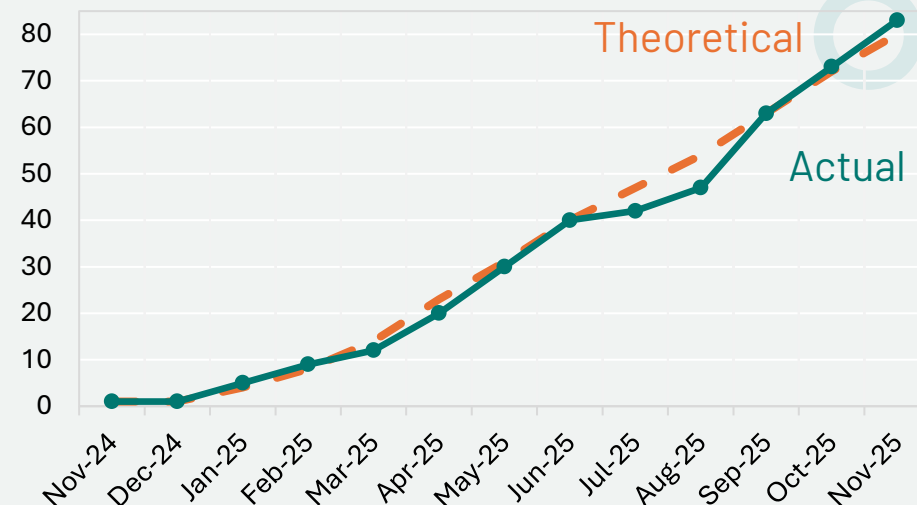
### Principal Investigators

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- **Pr Shahram ATTARIAN** - Hôpital de La Timone, Marseille, France



**16 Investigation sites**

**82 patients randomized in 12 months**



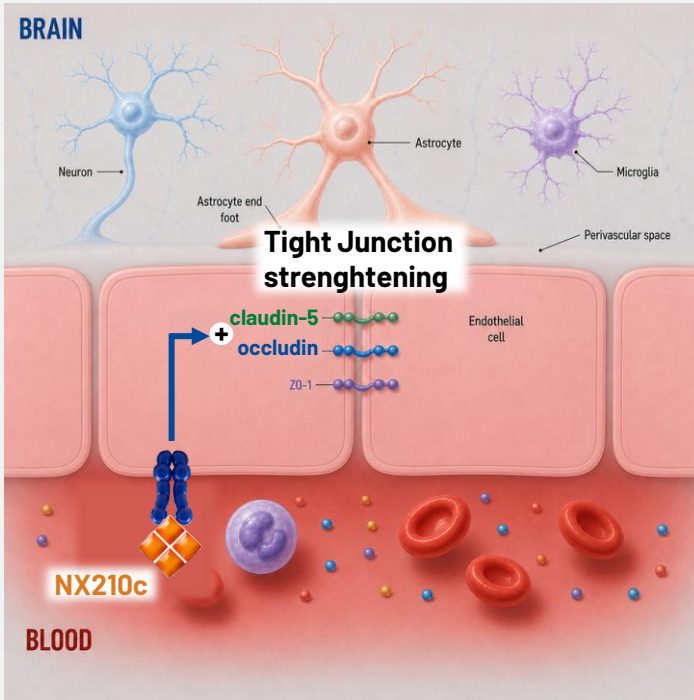
✓ **100% of the 82 randomized patients completed their treatment (3x/week/4weeks)**

✓ **97% received ≥ 11 doses /12**  
3% 10 doses/12

# SEALS

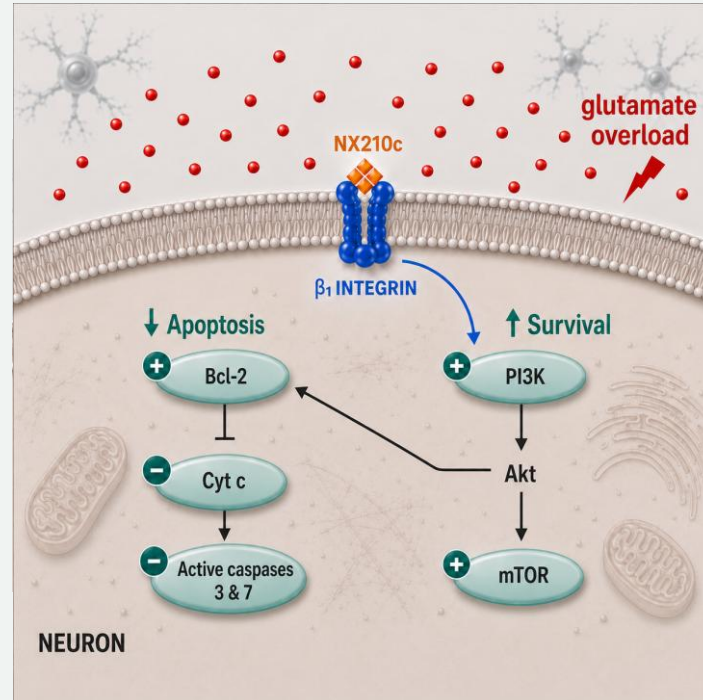
## NX210c, a peptide with combined properties

### BBB integrity restoration



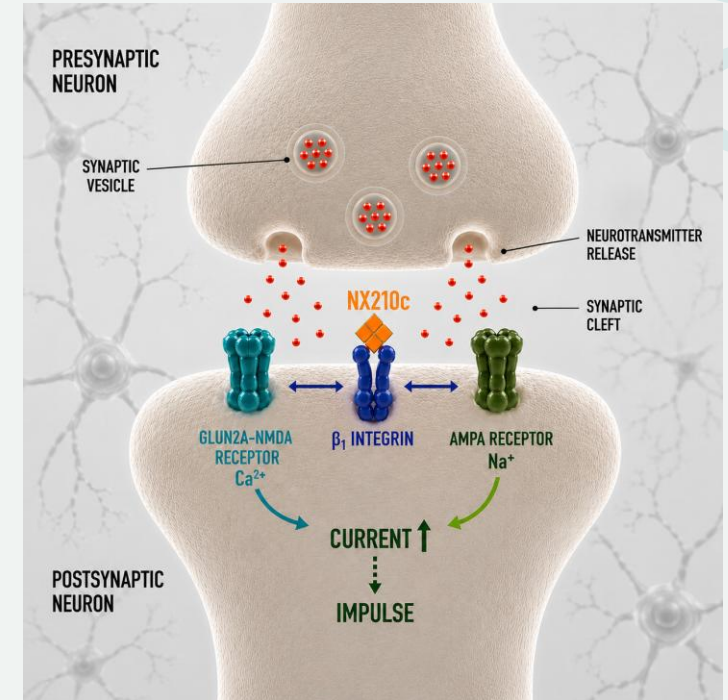
Green C. et al, *Fluids and Barriers of the CNS*, 2024

### Neuroprotection



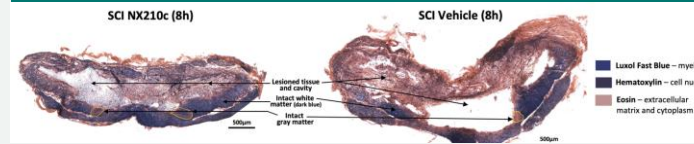
Deletage N. et al, *Neuroscience*, 2021

### neurotransmission enhancer

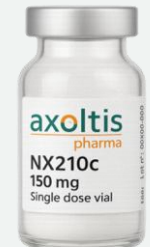
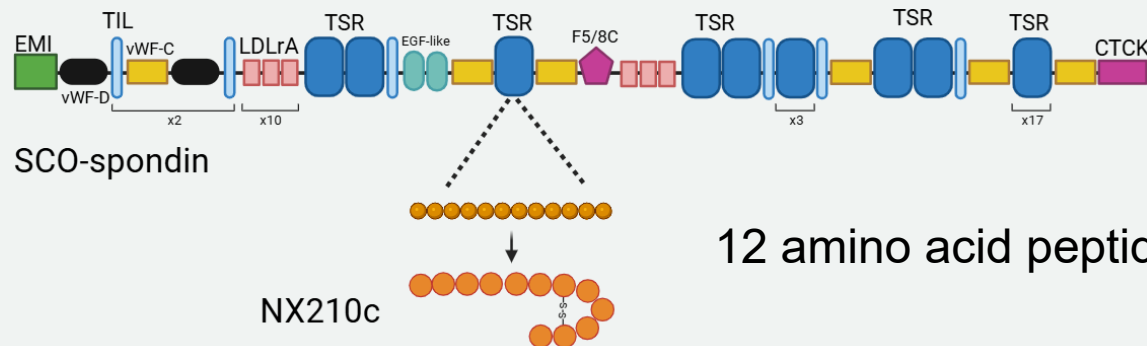


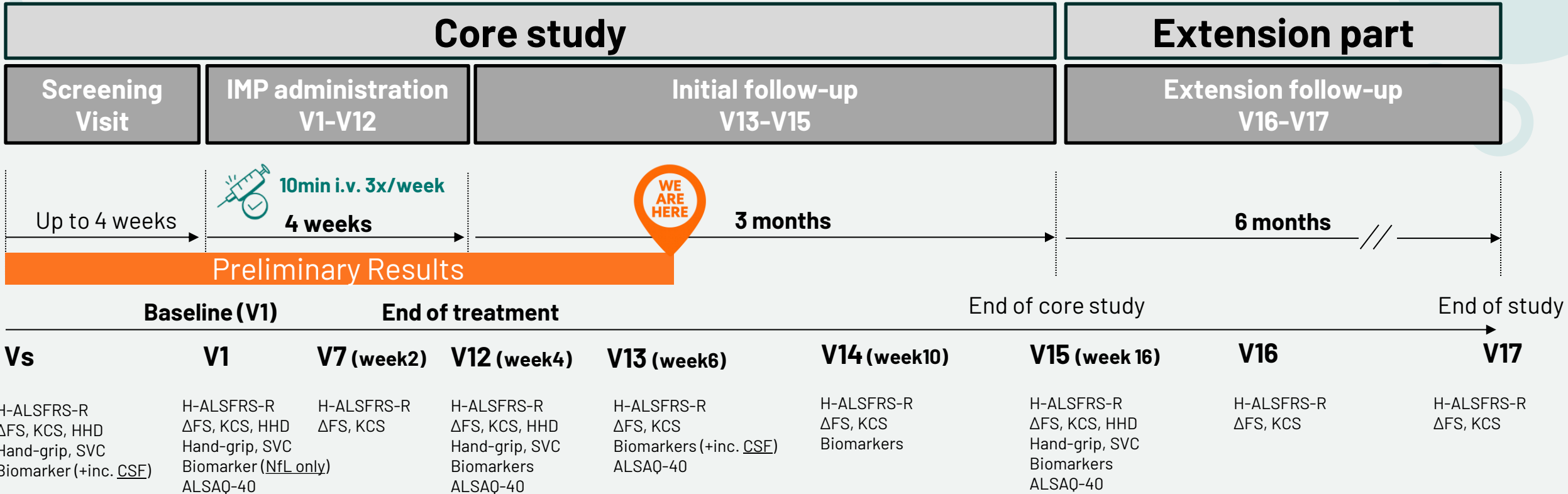
Lemarchant S. et al, *Int J Mol Sci.*, 2022

### neurite outgrowth and re-myelination in a Spinal Cord Injury model



Punjani N. et al, *J Neurotrauma.*, 2026





### Key inclusion criteria:

- Adults with El Escorial Revised criteria diagnosis
- ALS symptoms ≤36 months
- King's Clinical Staging Stage ≤3
- Slow vital capacity (SVC) ≥55% of predicted value
- Serum NfL >10 pg/mL
- Stable background treatment (riluzole)
  - For extension part only: >50% of IMP doses received

### Groups:

- 3:3:2 randomization
- NX210c 5mg/kg
  - NX210c 10mg/kg
  - Placebo

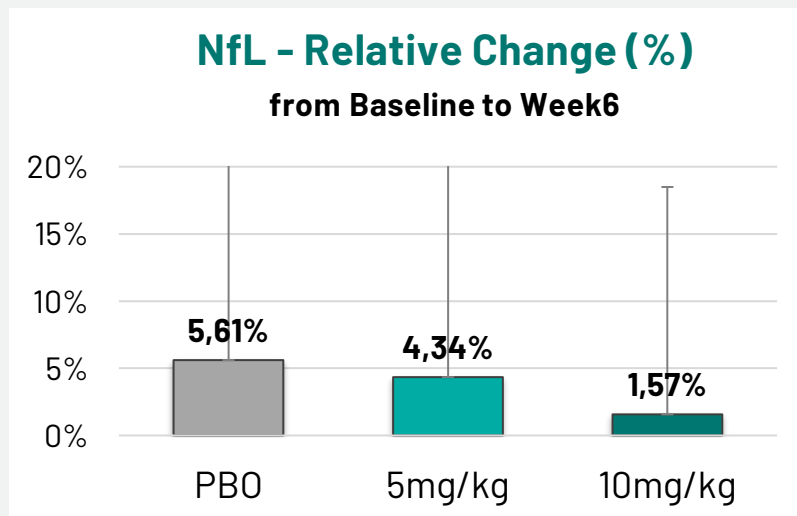
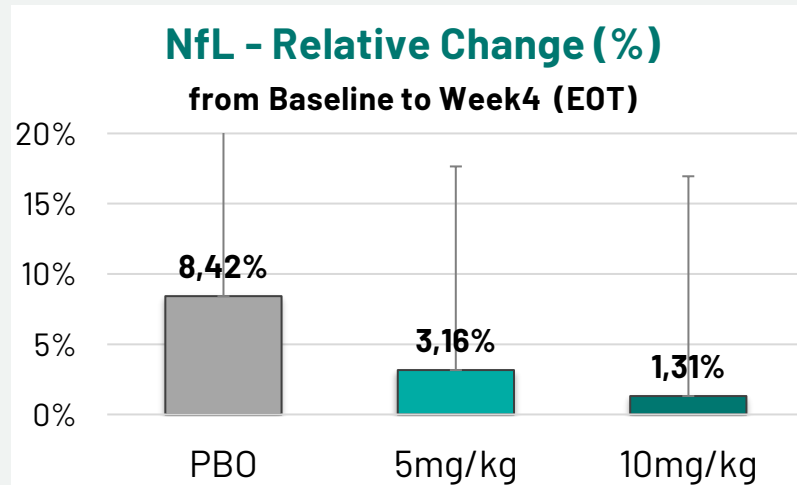
### Primary endpoint: Changes in serum NfL or Qalbumin from predose to 6-week

### Secondary endpoints:

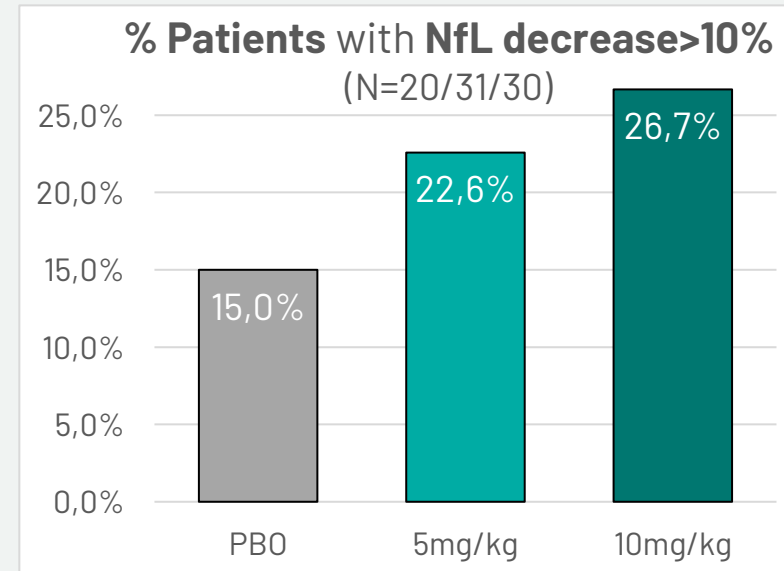
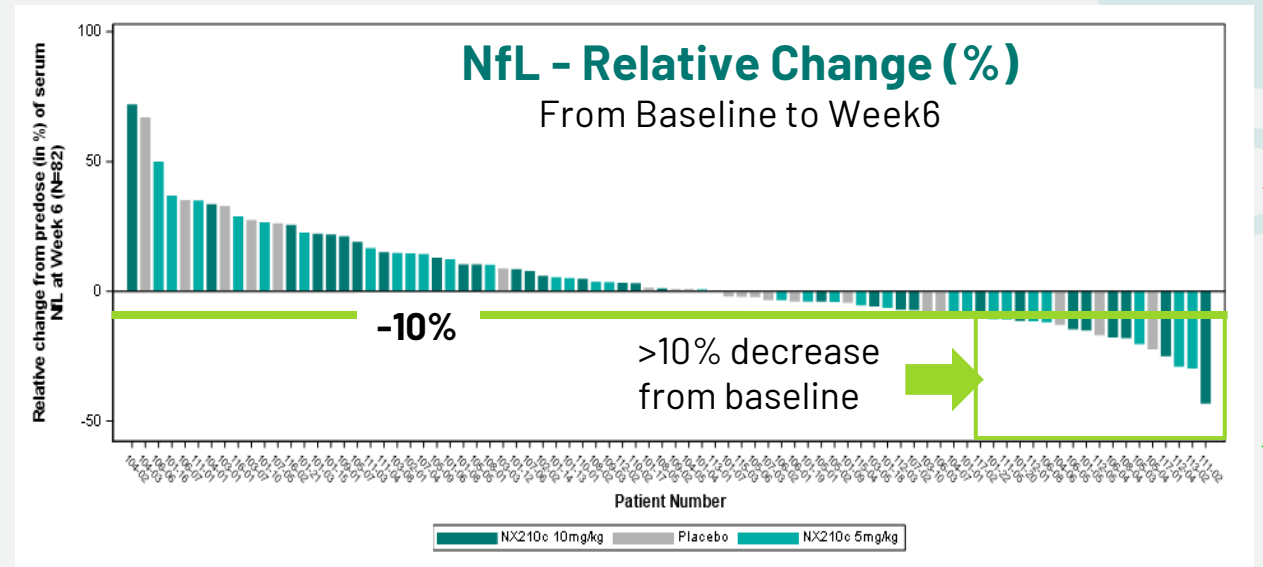
- Biomarkers: blood, CSF, urine
- Functional capacities and quantitative strength:
  - SVC, HHD, bilateral hand-grip
- ALSFRS-R (global, subscores), (ΔFS), time to event, survival, CAFS
- Quality of life (ALSAQ-40)
- Safety/tolerability and PK (20 patients subset)

Parameters at baseline			NX210c 5mg/kg n=31	NX210c 10mg/kg n=31	Active dose n=62	Placebo n=20
<b>Age</b>		Median [Min ; Max]	55.3 [37.8 ; 80.2]	51.6 [32.1 ; 73.3]	55.0 [32.1 ; 80.2]	59.2 [34.8 ; 68.6]
<b>Sex</b>	Female / Male	n/n	11/20	7/24	18/44	6/14
<b>Ethnicity</b>	Caucasian / others	n(%) / n	28 (90.3%) / 3	29 (93.5%) / 2	57 (91.9%) / 5	18 (90.0%) / 2
<b>Weight (Kg)</b>		Median [Min ; Max]	76 [45 ; 110]	73 [44 ; 102]	74 [44 ; 110]	79 [51 ; 95]
<b>Type of ALS</b>	Familial	n(%)	2 (6.5%)	3 (9.7%)	5 (8.1%)	2 (10.0%)
	Sporadic	n(%)	28 (90.3%)	27 (87.1%)	55 (88.7%)	16 (80.0%)
	Unknown	n(%)	1 (3.2%)	1 (3.2%)	2 (3.2%)	2 (10.0%)
<b>Site of ALS</b>	Bulbar	n(%)	6 (19.4%)	5 (16.1%)	11 (17.7%)	2 (10.0%)
	Spinal (all limb-onset)	n(%)	25 (80.6%)	26 (83.9%)	51 (82.3%)	18 (90.0%)
<b>H-ALSFRS-R global score (/48)</b>		Median [Min ; Max]	40 [29 ; 45]	37 [30 ; 46]	38 [29 ; 46]	37 [24 ; 47]
<b>ALS revised El Escorial classification</b>	Definite ALS	n(%)	19 (61.3%)	19 (61.3%)	38 (61.3%)	11 (55.0%)
	Probable ALS	n(%)	5 (16.1%)	8 (25.8%)	13 (21.0%)	5 (25.0%)
	Probable ALS, lab. results supported	n(%)	6 (19.4%)	4 (12.9%)	10 (16.1%)	0 (0.0%)
	Possible ALS	n(%)	1 (3.2%)	0 (0.0%)	1 (1.6%)	4 (20.0%)
<b>Patients still treated with Riluzole/Rilutek</b>		n(%)	29 (93.5%)	31 (100.0%)	60 (96.8%)	19 (95.0%)
<b>Serum NfL threshold 95pg/mL</b>		n High/Low	9/22	10/21	19/43	6/14
<b>Serum NfL (pg/ml) at screening</b>		Mean (SD)	78.29 (36.63)	86.74 (52.04)	82.51 (44.83)	89.24 (62.71)
<b>Qalbumin ratio % at screening</b>		Mean (SD)	6.50 (1.84)	8.31 (4.53)	7.40 (3.55)	7.19 (3.18)
<b>Abnormal Qalb</b>		n(%)	6 (19.4%)	15 (48.4%)	21 (33.8%)	6 (30.0%)

### A dose dependent trend to NfL % Change



Non-significant change between groups

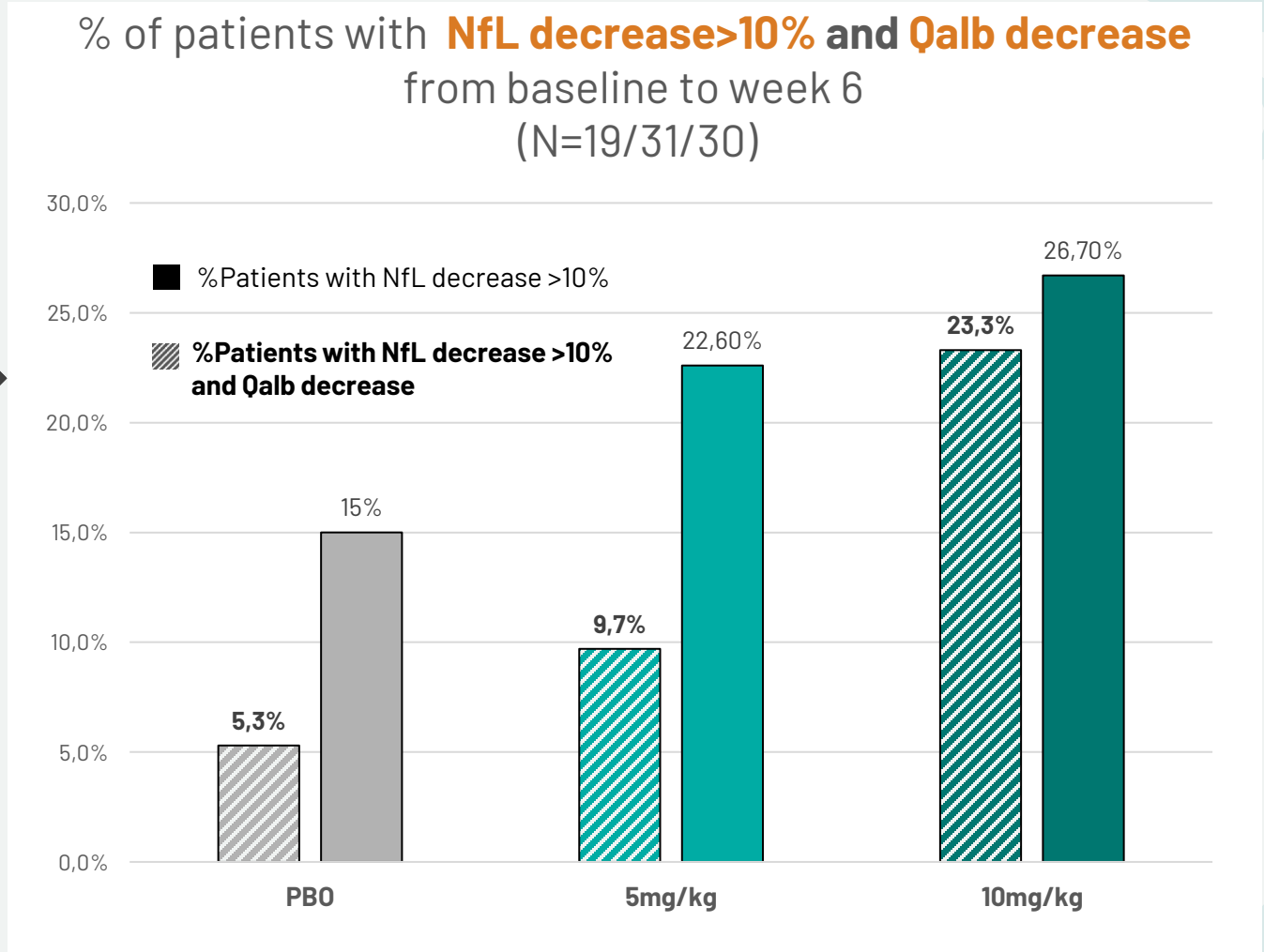
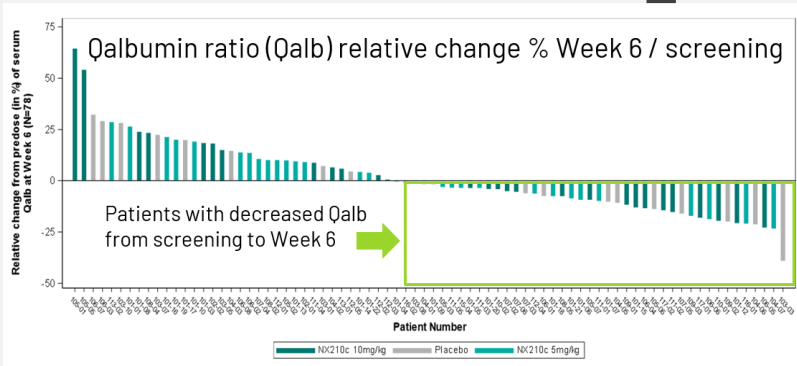
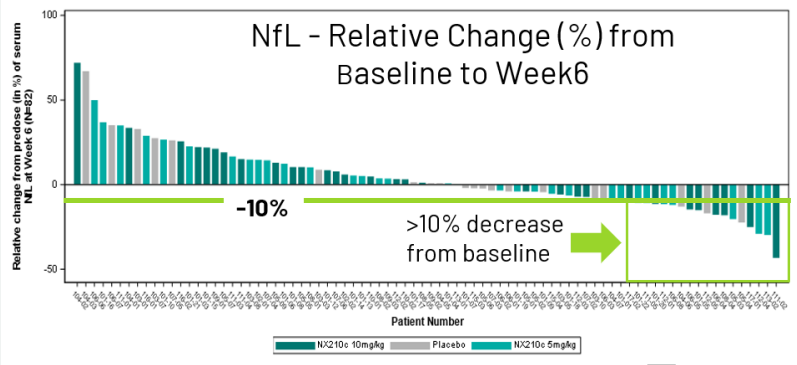


A 10% decrease as soon as Week 6 is encouraging. This population should be profiled also regarding other biomarkers and clinical observations.

*Ref: 10% reduction of NfL (over 24-week period of treatment) are linked to lower mortality risk (Healey ALS platform trial – Clene inc.)*

# SEALS

## Patients proportion having a serum NfL decrease >10% and Qalb decrease from baseline to week 6

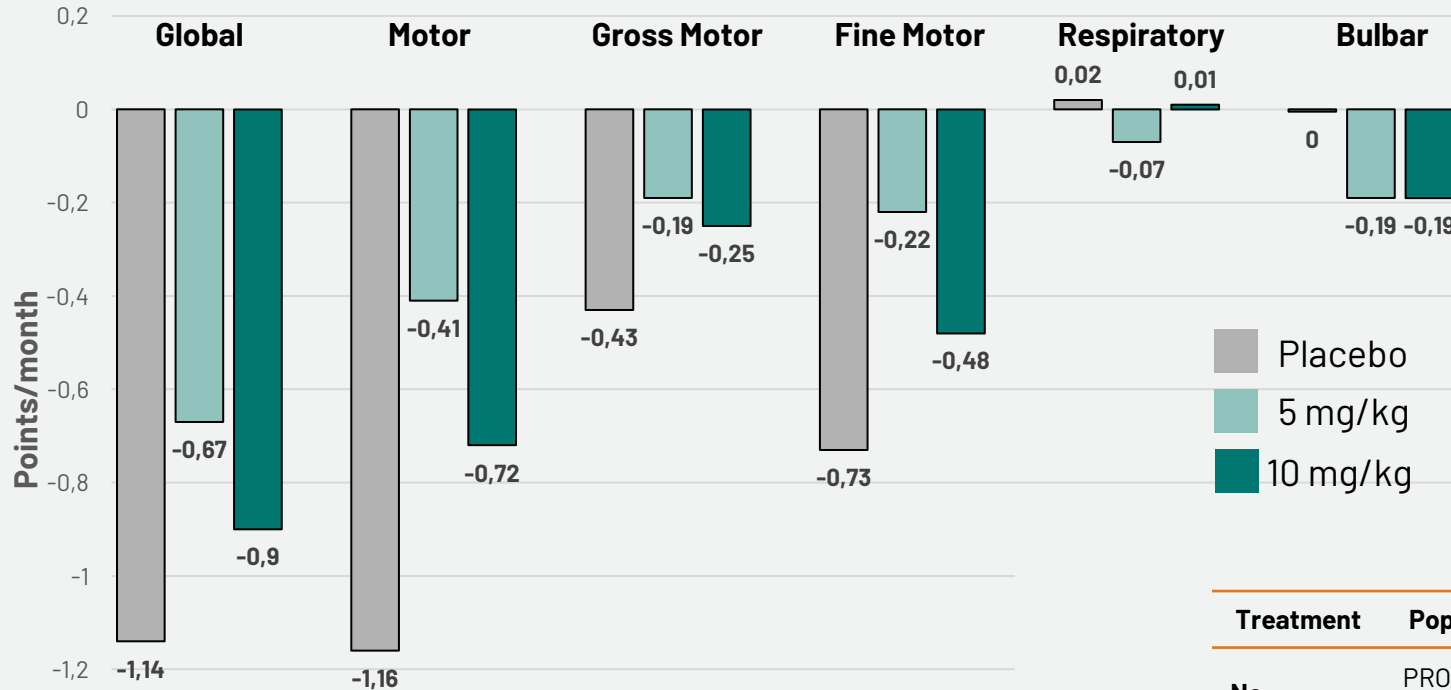


About 33% of ALS patients have Qalb above the normal range values

This has to be considered in the profiling of ALS patients

## Clinical Observations at week 6 after start of treatment ALSFRS-R

**ALSFRS-R Mean Slope** (baseline, week2, week4, week6)



A Good Safety and Tolerability Profile

A trend to reduce the rate of functional decline (ALSFRS-R slope reduction)

**ALSFRS-R Slope - Global Score**

(calculation including baseline, week2, week4, week6)

Treatment Arm	Mean slope (pts/month) (SD)	ALSFRS-R vs placebo
Placebo	<b>-1.14</b> (1.82)	0
5 mg/kg	<b>-0.67</b> (1.50)	0.47
10 mg/kg	<b>-0.90</b> (1.63)	0.24

Treatment	Population studied	Reported ALSFRS-R slope / decline	reference
<b>No treatment</b>	PRO-ACT cohort (>8,600 ALS patients)	<b>-1.02 ± 2.3</b> pts/month	Atassi et al., Neurology, 2014 (PRO-ACT)
<b>Edaravone</b>	Early, selected ALS population	-5.01 points over 24 weeks ≈ <b>-0.83</b> pts/month vs <b>placebo -7.50 ≈ -1.25</b> pts/month	MCI-186-19 trial, The Lancet Neurology, 2017
<b>AMX0035</b>	CENTAUR trial	<b>-1.24</b> pts/month vs <b>placebo ≈ -1.66</b> pts/month	Paganoni et al., NEJM, 2020
<b>Tofersen</b>	SOD1-ALS (VALOR + OLE)	-6.0 points at 52 weeks ≈ <b>-0.50</b> pts/month vs <b>placebo -9.5 ≈ -0.79</b> pts/month	Miller et al., NEJM, 2022

Supported by the good safety profile and the results at 6 weeks after the start of the treatment, the full dataset will be harnessed in the next months to:

- **Amplify the placebo group** with 62 **digital twins' generation**.
- Perform *in silico* **modeling for next clinical development steps**:
  - **Precision profiling / Responders' characterization**
  - **Dose and regimen optimization** (frequency of course of treatment)

**SEALS**



Thanks a lot to Patients, Caregivers, Investigators and their Clinical staffs, Axoltis team and CRO/Providers !

**Meet you soon to know more !**

**POSTER: #P0108 SEALS: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Study Evaluating Efficacy And Safety Of NX210c In Amyotrophic Lateral Sclerosis (ALS) Patients: Topline Results**

**POSTER : #P0101 NX210c, A Promising Drug Candidate For Neurodegenerative Diseases**

**POSTER : #P0127 Augmented Placebo Control Using Synthetic Profile in ALS Clinical Trials: A Methodological Framework**

**Day:** June 24

**Room:** Exhibition area

**Time:** 17:20h - 19:00h

**Session:** ENCALS RESEARCH FORUM