Eledon Pharmaceuticals

ALS Phase 2a Clinical Trial Update

May 31, 2022

Forward-Looking Statements

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Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the ability to develop commercially viable product formulations; the sufficiency of the company's cash resources; the ability to obtain necessary regulatory and ethics approvals to commence additional clinical trials; whether data from early clinical trials will be indicative of the data that will be obtained from future clinical trials; whether the results of clinical trials will warrant submission for regulatory approval of any investigational product; whether any such submission will receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies and, if we are able to obtain such approval for an investigational product, whether it will be successfully distributed and marketed. These risks and uncertainties, as well as other risks and uncertainties that could cause the company's actual results to differ significantly from the forward-looking statements contained herein, are discussed in our annual report on Form 10-K for the year ended December 31, 2021, and other filings with the SEC which can be found at www.sec.gov. Any forward-looking statements contained in this presentation speak only as of the date hereof and not of any future date, and the company expressly disclaims any intent to update any forward-looking statements, whether as a result of new information, future events or otherwise.

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Tegoprubart: Pipeline in a Product Opportunity

Product Candidate	Indication	Development Stage				Anticipated Milestones
		Pre-clinical	Phase 1	Phase 2	Phase 3	
Tegoprubart (AT-1501)	Amyotrophic Lateral Sclerosis (ALS)					✓ Phase 2 top-line data in 2Q2022
	Kidney Transplantation					Enroll first Phase 1b patient Interim data readout late 2022
	Islet Cell Transplantation for Type 1 Diabetes					Enroll first Phase 2 patient Interim data readout late 2022
	IgA Nephropathy					On-going enrollment Interim data readout late 2022
AT-2001	Autoimmune Indications					Pre-clinical animal studies

Note: Development plans and timelines may change, including based on US and global regulatory interactions.

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ALS Overview & Market Opportunity

Characterized by **gradual, progressive muscle weakness**

Affects **~30,000 Americans**

~5,000 new cases diagnosed annually in the US and **~600,000** cases globally

Average age of **55** at time of diagnosis

Only **10%** of ALS cases are **hereditary**

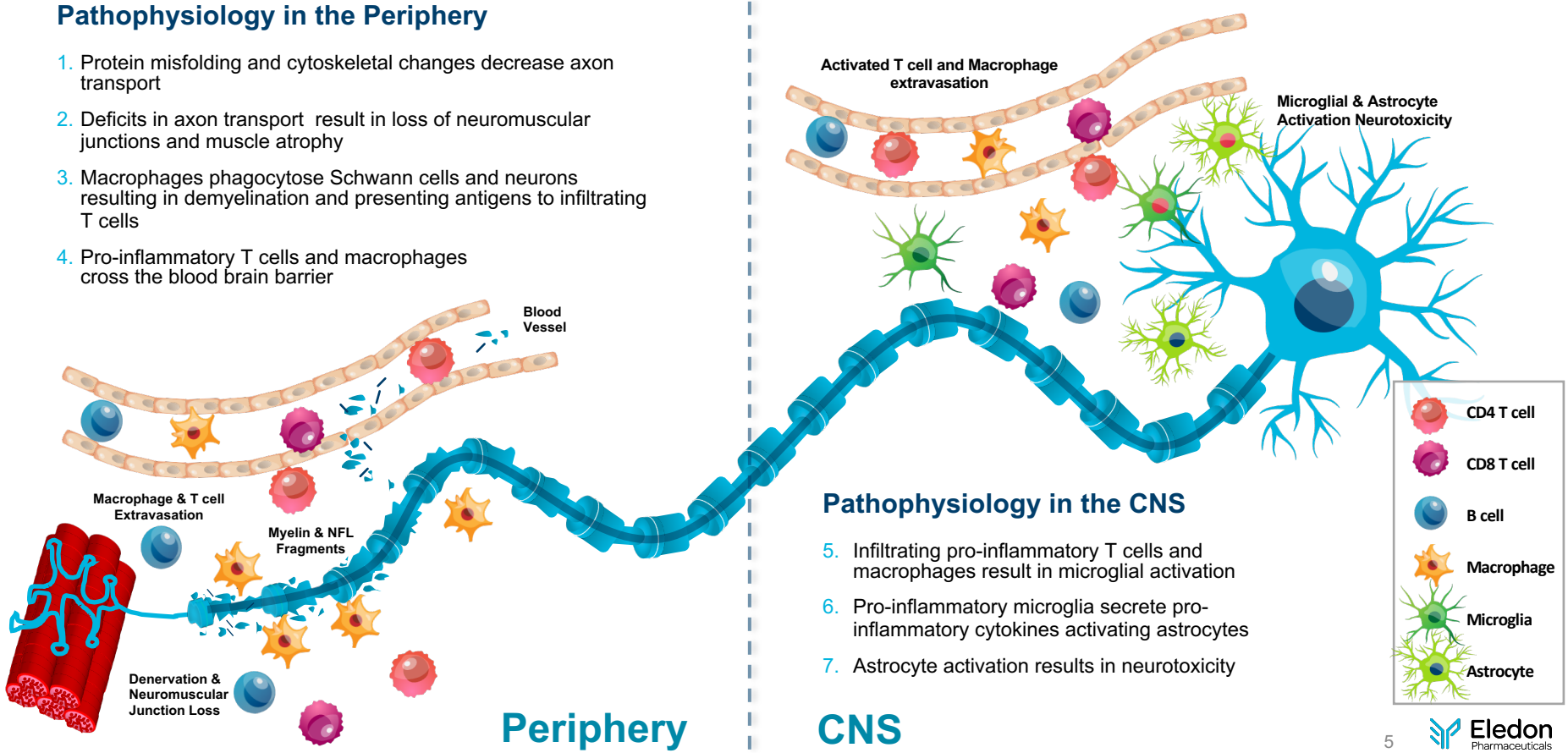
- People with ALS ultimately lose the ability to ambulate, move their arms, talk, swallow, and breath independently
- On average, death occurs between 3 to 5 years from diagnosis, most often from respiratory failure or cachexia

Very high 5-year ALS morbidity and mortality despite two FDA approved treatments

Pathophysiology of Amyotrophic Lateral Sclerosis

Pathophysiology in the Periphery

1. Protein misfolding and cytoskeletal changes decrease axon transport
2. Deficits in axon transport result in loss of neuromuscular junctions and muscle atrophy
3. Macrophages phagocytose Schwann cells and neurons resulting in demyelination and presenting antigens to infiltrating T cells
4. Pro-inflammatory T cells and macrophages cross the blood brain barrier



Pathophysiology in the CNS

5. Infiltrating pro-inflammatory T cells and macrophages result in microglial activation
6. Pro-inflammatory microglia secrete pro-inflammatory cytokines activating astrocytes
7. Astrocyte activation results in neurotoxicity

Periphery **CNS**

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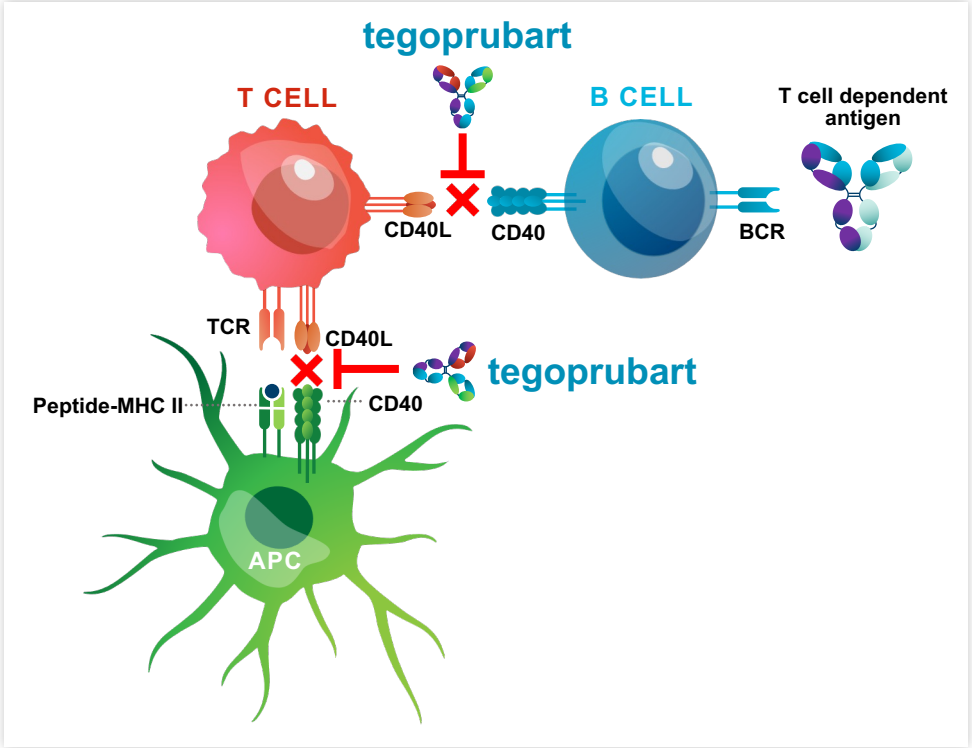
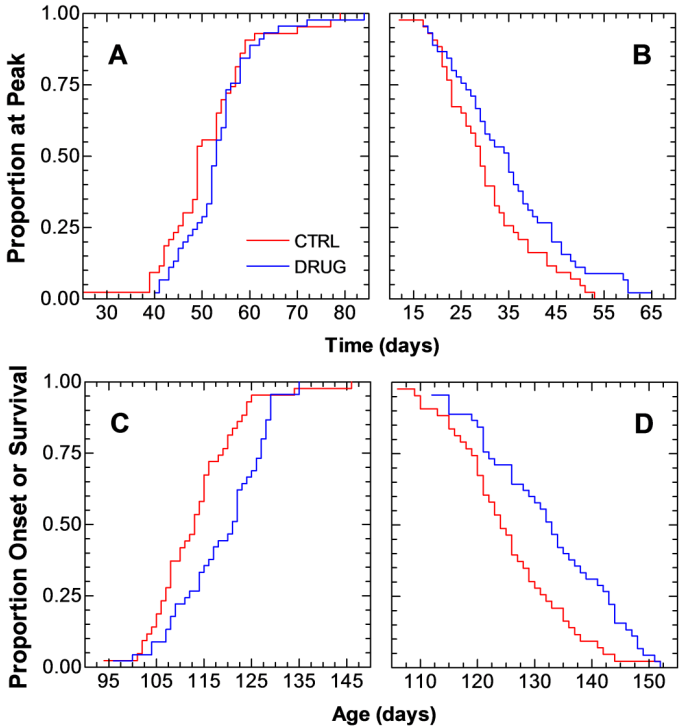
Mechanism Overview of CD40L Inflammatory Signaling

- Interaction of CD40 with CD40L on immune cells **mediates activation of the co-stimulatory immune pathway**, controlling "cross talk" between the adaptive and innate immune systems
- Maximal activation of inflammatory system is a 3-step process requiring co-stimulatory signaling
  - **Step 1:** Major histocompatibility complexes (MHC) and CD3/TCR engagement
  - **Step 2:** CD40 and CD40L binding resulting in cell division and clonal expansion
  - **Step 3:** Pro-inflammatory response by polarized T cells expressing inflammatory chemokines and cytokines
- Blocking CD40L shifts polarization from pro-inflammatory signaling to T cell anergy, apoptosis, and polarization to a Treg environment
  - Blocking CD40L thus **does not generally result in lymphopenia** often seen with immunosuppressive agents



Blocking CD40L Ameliorates Disease in SOD1 Mice



Blocking CD40L improves body-weight maintenance, delays disease onset and extends survival in SOD1 mice

A. Kaplan-Meier time-to-event analysis for time required to attain peak body weight. Time to peak was not significantly ($p = 0.35$) changed by anti-CD40L treatment
B. Body-weight maintenance was significantly ($p = 0.0413$) improved by anti-CD40L treatment
C. Time-to-event analysis for disease onset (neurological severity score of 2) was significantly ($p = 0.0038$) delayed by anti-CD40L treatment
D. Time-to-event analysis for age at which mice died was significantly ($p = 0.0043$) prolonged by anti-CD40L treatment

Source: Lincecum, 2010.

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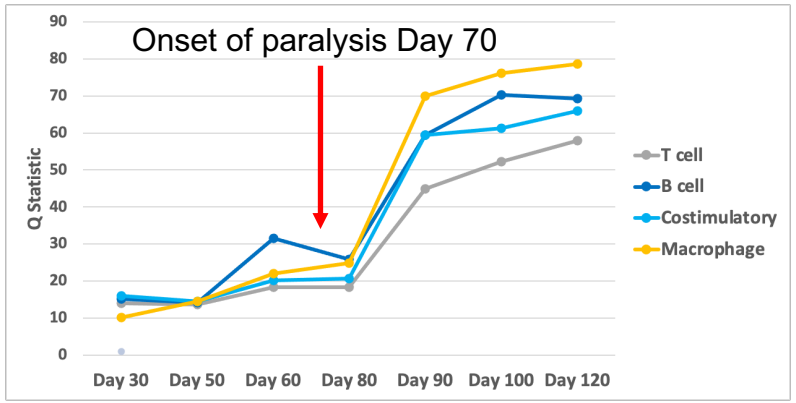
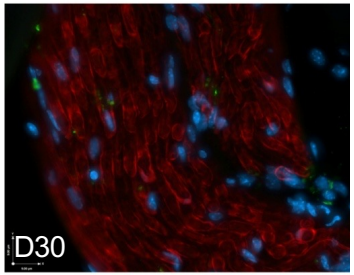
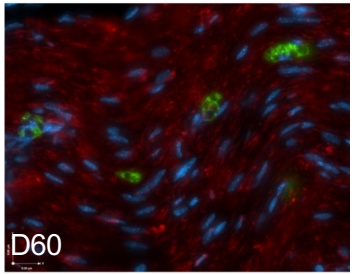
Inflammatory Pathways are Activated in the Periphery in ALS Animal Models

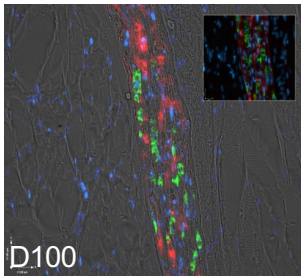
Activation of Inflammatory Pathway in ALS Rodent Skeletal Model

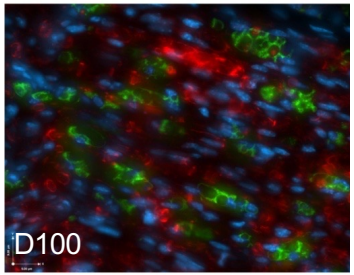


- Macrophages accumulate on peripheral nerves in skeletal muscle
- Staining shows Myelin (Red), Macrophages (Green), and Nuclei (Blue)









Source: Lincecum, 2010.

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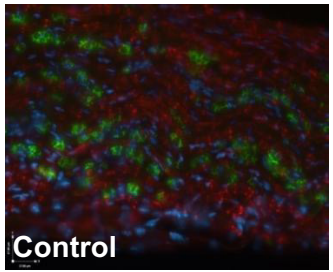
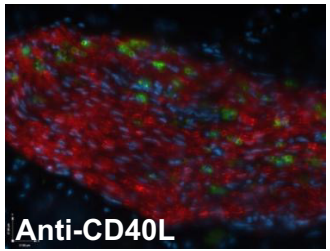
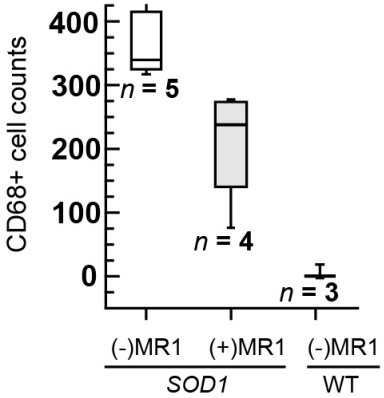
Blocking CD40L Reduces Neuroinflammation and Improves Motor Neuron Survival in SOD1 Mice

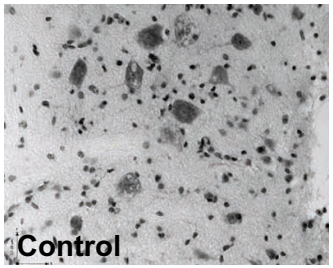
Anti-CD40L (MR1) treatment reduces macrophage infiltrate and "attack" of denervated peripheral nerves in skeletal muscle

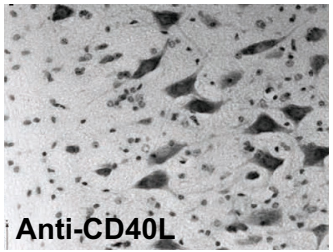


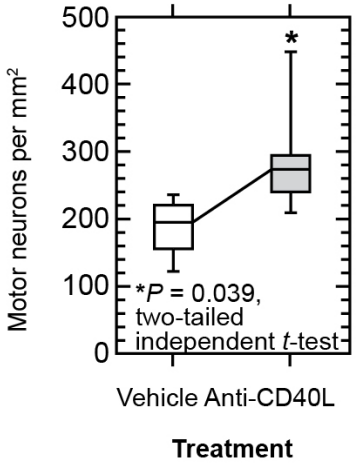




Anti-CD40L treatment reduces neuroinflammation in the spinal cord resulting in improved motor neuron survival







Source: Lincecum, 2010.

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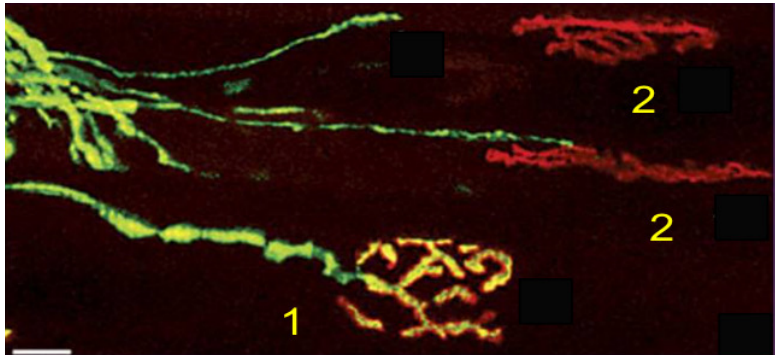
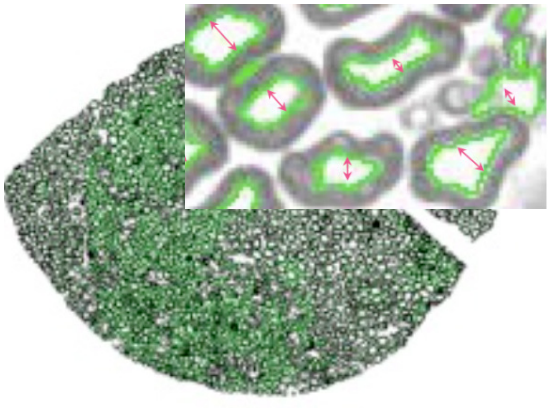
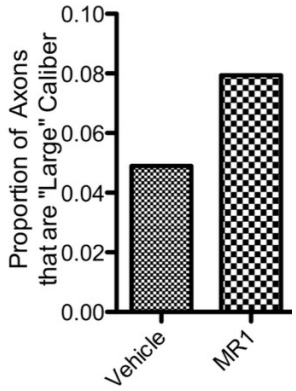
Blocking CD40L Improves Neuromuscular Junction Occupancy and Demyelination in SOD1 Mice



Staining: Myelin (green), alpha bungarotoxin acetylcholine receptors (red)

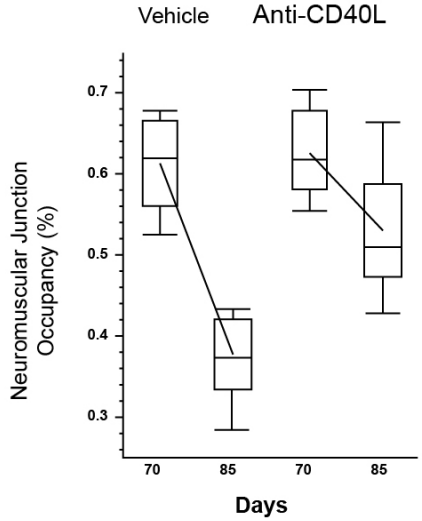
1: Innervated neuromuscular junction
2: Denervated neuromuscular junction





Anti-CD40L treatment (MR1) increases survival of large caliber axons

Anti-CD40L treatment reduces macrophage infiltrate resulting in increased neuromuscular junction occupancy



Source: Lincecum, 2010; ALS Therapy Development Institute, unpublished data.

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Inflammatory Biomarkers & CD40L Levels are Elevated in Serum of Patients with ALS

Serum Biomarker Levels: ALS Patients vs. Controls

Serum	Ctrl (n = 94)	ALS (n = 60)	*p* value
Nf-L (pg/ml)	30.20 ± 23.41	512.4 ± 417.4	**< 0.0001**
VCAM-1 (ng/ml)	647 ± 181	891 ± 366	**< 0.0001**
ICAM-1 (ng/ml)	485 ± 120	750 ± 297	**< 0.0001**
VEGF (pg/ml)	199.1 ± 232.5	150.0 ± 77.23	0.523
Eotaxin (pg/ml)	242.4 ± 143.3	284.5 ± 104.6	0.134
MCP-1 (pg/ml)	256.9 ± 96.94	373.8 ± 169.1	**< 0.0001**
IP-10 (pg/ml)	384.7 ± 289.5	640.2 ± 320.4	**< 0.0001**
IL-17a (pg/ml)	0.68 ± 0.53	1.38 ± 1.48	**< 0.0001**
TNF-α (pg/ml)	1.76 ± 0.72	4.99 ± 7.85	**< 0.0001**
IL-2 (pg/ml)	N.A	0.40 ± 0.41	
IL-10 (pg/ml)	0.29 ± 0.34	0.51 ± 0.19	**< 0.0001**
IL-8 (pg/ml)	106.1 ± 186.5	172.3 ± 354.9	0.395
IL-6 (pg/ml)	0.58 ± 0.58	2.0 ± 2.6	**< 0.0001**
IL-1β (pg/ml)	N.A	0.47 ± 0.73	
IFN-γ (pg/ml)	5.31 ± 5.22	2.96 ± 2.25	**< 0.0001**

- **Levels of inflammatory biomarkers have been found to be elevated in ALS patients and correlated with disease progression**
- **CD40-CD40L signaling** between antigen presenting cells and T-cells is **upregulated in** the blood of **56% of patients with ALS**
  - **sCD40L levels** have also demonstrated **correlation with rate of disease progression**

Source: Brodovitch, 2021; Ots, 2022.

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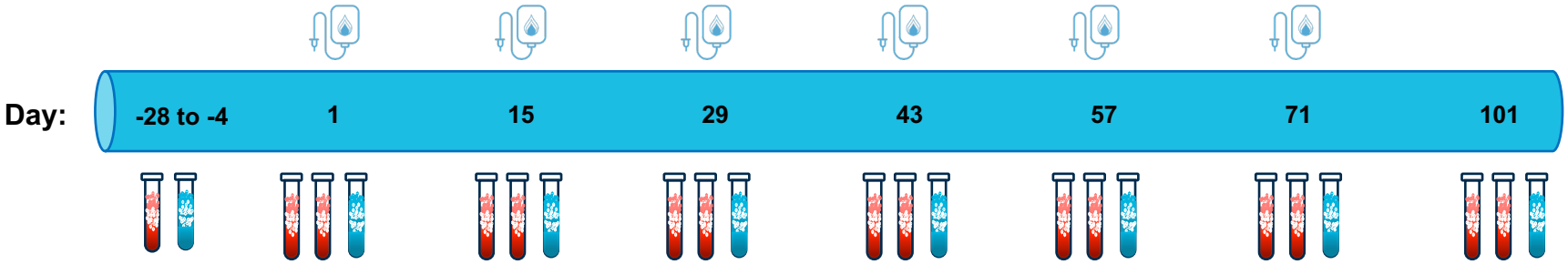
Phase 2a ALS: Study Design



- 12-week, open label, multiple ascending dose level study
- Four sequential dose cohorts of 9 patients (1 and 2 mg/Kg) and 18 patients (4 and 8 mg/Kg) each
- Each subject serves as own control by comparing changes from baseline assessment

Phase 2a ALS: Demographics

- 54 subjects recruited
- Average age - 59 years old
  - 72% male
  - 96% Caucasian
- Average baseline ALSFRS-R of 39.5
  - 7 subjects had ALSFRS–R < 35 or ALS Bulbar domain scores ≤ 4 at first infusion

- **Demographics and stage of disease confirm overall recruitment of target population**
- **Recruited population generally in line with demographics of ALS in the United States**
- **Some patients enrolled who at 1st infusion would not have met screening entry criteria**

Phase 2 ALS: Planned Data Generation

Safety & Tolerability

Biomarkers of CD40L target engagement

Pro-inflammatory Biomarkers

Exploratory Endpoints

- Key sub-analyses:
    1. Compare subjects who did or not achieve target engagement as defined by a change in CXCL-13
    2. Compare subjects who had target engagement but differed in changes in pro-inflammatory biomarkers (i.e., High vs. Low Responders)

Phase 2a ALS: Safety & Tolerability

- All adverse events were reviewed by an independent data safety monitoring board that recommended continued dosing

- 35.2% of patients had 1 or more drug-related adverse events (AEs)
  - No drug-related serious or severe AEs
  - Occurrence of drug-related adverse events was balanced across dose cohorts
  - No thrombosis or signs of platelet activation
  - 2 subjects experienced adverse events leading to withdrawal
    - 1 subject withdrew because of worsening depression in the 1 mg/Kg cohort
    - 1 subject withdrew because of malaise in the 2 mg/Kg cohort

- Anti-Drug Antibodies detected in ~4.2% of samples
  - ADAs of low titer and did not effect tegoprubart levels

Phase 2a ALS: Key Observed Biomarker Decreases at Week 12

CD40L Target Engagement

Biomarker	Significance at 2mg/Kg	Significance at 4mg/Kg	Significance at 8mg/Kg
CXCL13	X	*p<0.01*	*p<0.0001*
CD40L	*p<0.0001*	*p<0.0001*	*p<0.0001*

Pro-Inflammatory

Biomarker	Significance at 1 or 2mg/Kg	Significance at 4mg/Kg	Significance at 8mg/Kg
TNF-α	X	*p<0.0001*	*p<0.0001*
MCP1	X	X	*p=0.0002*
IL-6	X	X	X
EN-RAGE	X	*p=0.05*	*p=0.02*
CRP	X	*p=0.03*	*p=0.003*

- Up to 23 of 32 inflammatory biomarkers detected were significantly reduced at 4 and 8 mg/Kg dose levels, including: IgA, IgE, IgM, C3, CXCL9 & CXCL10
- IL-1 was not significantly detected in the 54 subject cohort

Phase 2a ALS: Monthly Change in ALSFRS-R by Cohort, Baseline Criteria, Target Engagement, and Level of Response

Monthly Change in ALSFRS-R (% Improvement vs. PRO-ACT)

Group	All Subjects	Baseline Criteria	Positive Target Engagement	High Responders
PRO-ACT *(Comparator)*	-0.83	-0.83	-0.83	-0.83
All	-1.02 **22.9%** n=54	-0.75 **(9.6%)** n=47	-0.67 **(19.3%)** N=40	-0.60 **(27.7%)** n=37
Low Dose (1/2 mgs)	-0.89 **7.2%** n=18	-0.89 **7.2%** n=18	-0.68 **(18.1%)** n=11	-0.71 **(14.5%)** n=10
High Dose (4/8 mgs)	-1.08 **30.1%** n=36	-0.66 **(20.5%)** n=29	-0.66 **(20.5%)** n=29	-0.57 **(31.3%)** n=27

- **All Subjects** includes 54 subjects enrolled in the study
- **Baseline Criteria** excludes 7 subjects with an ALSFRS-R < 35 at time of first infusion and/or a total aggregate score ≤ 4 out of 12 in the bulbar domains of ALSFRS-R
- **Positive Target Engagement** defined as subjects with at least a 10% decrease in CXCL13
- **Low Dose Subjects without Target Engagement had a mean change of –1.14 or 37.3% vs. PRO-ACT**
- **High Responders** defined as subjects with a minimum 10% reduction in 75% or more of inflammatory biomarkers

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Phase 2 ALS: Data Summary

Safety & Tolerability

- 35.2% of patients had 1 or more drug-related adverse events (AEs)
- No drug-related serious or severe AEs
- Occurrence of drug-related adverse events was balanced across dose cohorts

Biomarkers of CD40L target engagement

- At 4 and 8 mg / kg dose levels, target engagement was demonstrated using CD40L and CXCL13 biomarkers related to T cell and B cell function, respectively

Pro-inflammatory Biomarkers

- Dose dependent, significant reductions were observed in up to 23 of 32 biomarkers, including TNF-α, MCP1, EN-RAGE, and C-Reactive Protein

Exploratory Endpoints

- Target engagement and level of reduction in pro-inflammatory biomarkers were associated with a trend in the slowing of disease progression as measured by ALSFRS slope when compared to a cohort from the ALS PRO-ACT database

2022 Execution Priorities

- ✓ Complete ALS Phase 2 study and release data
- Continue IgA Nephropathy clinical trial enrollment
- Begin Kidney Transplantation clinical trial enrollment
- Begin Islet Cell Transplantation for Type 1 Diabetes clinical trial enrollment
- Advance tegoprubart subcutaneous formulation

Interim clinical data readouts in up to 3 other open label studies expected by year-end

Note: Development plans and timelines subject to change based on several factors, including US and global regulatory agency interactions.

Q&A

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