Eledon Pharmaceuticals

Targeted Immunology CD40/CD40L Therapeutics

Transplantation | Autoimmunity | ALS

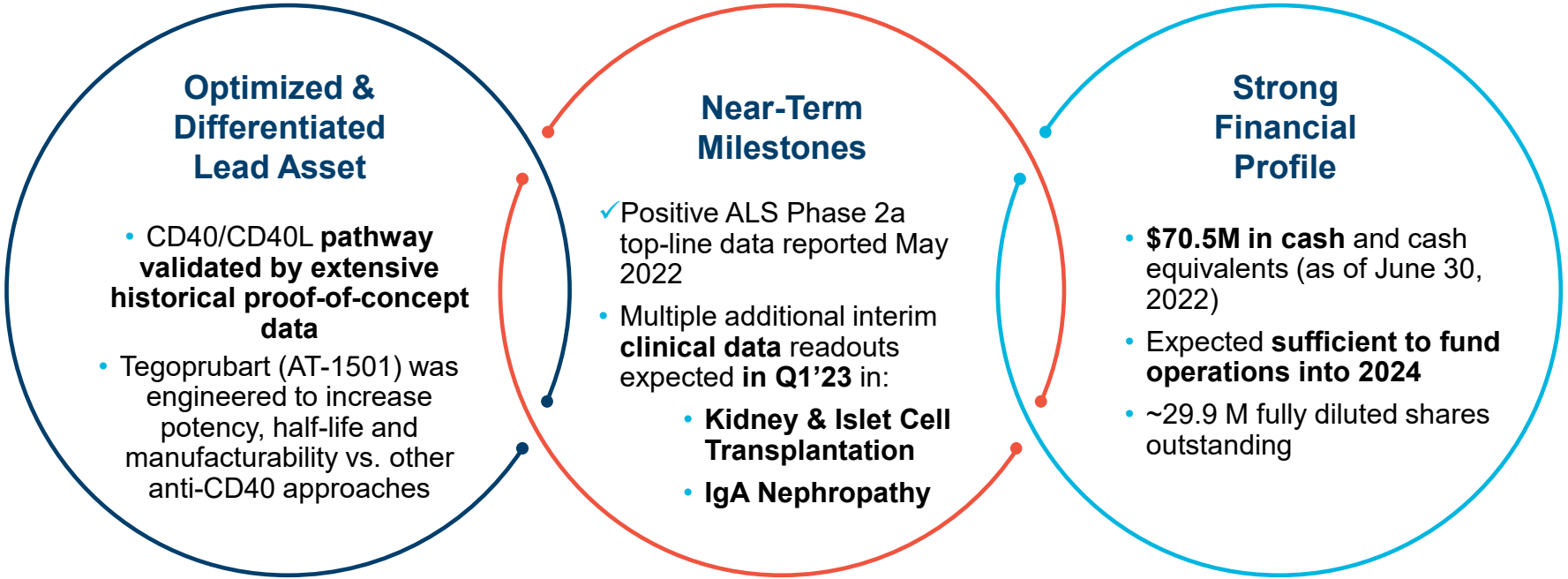
August 2022

Forward-Looking Statements

This presentation contains forward-looking statements that involves substantial risks and uncertainties. Any statements about the company's future expectations, plans and prospects, including statements about its strategy, future operations, development of its product candidates, and other statements containing the words "believes," "anticipates," "plans," "expects," "estimates," "intends," "predicts," "projects," "targets," "could," "may," and similar expressions, constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, although not all forward-looking statements include such identifying words. Forward-looking statements include, but are not limited to statements regarding: expectations regarding the timing for the commencement and completion of product development or clinical trials; the rate and degree of market acceptance and clinical utility of the company's products; the company's commercialization, marketing and manufacturing capabilities and strategy; the company's intellectual property position and strategy; the company's ability to identify additional products or product candidates with significant commercial potential; the company's estimates regarding expenses, future revenue, capital requirements and needs for additional financing; developments relating to the company's competitors and industry; and the impact of government laws and regulations.

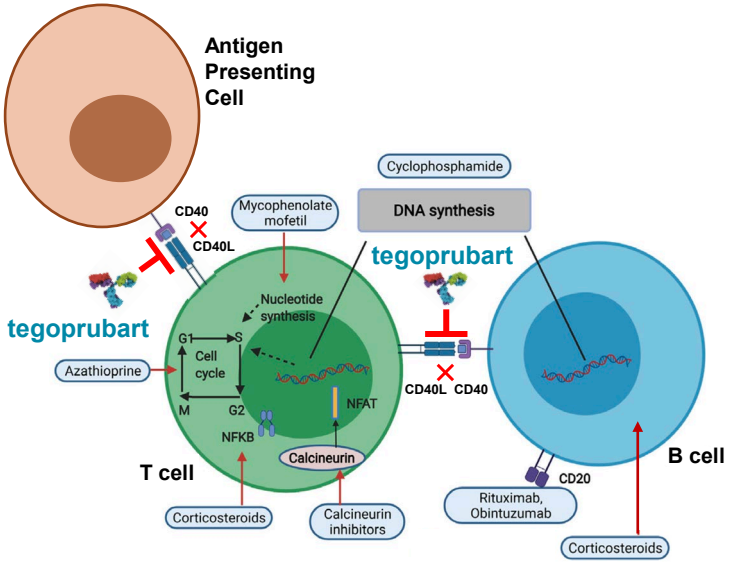
Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the ability to develop commercially viable product formulations; the sufficiency of the company's cash resources; the ability to obtain necessary regulatory 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.

Single Company Focus: Leveraging Validated Biology to Develop Best-in-Class Immune-Modulating Therapeutics



Mechanism Overview of CD40L Inflammatory Signaling

CD40/CD40L Pathway and Tegoprubart Site of Action



- 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 away 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

Source: Adapted from Kant, 2022.

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Tegoprubart: Potential Best-in-Class Anti-CD40/CD40L Antibody

Targeting CD40 Ligand vs. CD40 Receptor		IgG1 vs. fusion protein or pegylated FAB
CD40L and CD40	**CD40L only**	
Targeting both anti-CD40L and anti-CD40 inhibits B cell polarization and class switching, as well as inhibits the pro-inflammatory polarization of $CD4^+$ Helper T cells	✓ Blocking anti-CD40L also inhibits CD11 costimulatory receptors on antigen presenting cells, thus blocking the pro-inflammatory polarization of $CD8^+$ Cytotoxic T cells	✓ Up to over 2x times longer half-life
	✓ Blocking CD40L also polarizes $CD4^+$ lymphocytes to $FoxP3^+$ Regulatory T cells (Tregs), thus creating a potentially more tolerogenic environment	✓ Manufacturing advantages
	✓ CD40L is more selectively expressed, providing the potential for additional safety and PK/PD/dosing advantages	✓ Less anti-drug antibodies

Note: Potential advantages versus selected other CD40/CD40L clinical programs; not based on head-to-head studies. Differences versus any individual competitive program may vary.

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 reported May 2022
	Kidney Transplantation					Enrolled first Phase 1b participant Interim data readout Q1 2023
	Islet Cell Transplantation for Type 1 Diabetes					Enroll first Phase 2 participant Interim data readout Q1 2023
	IgA Nephropathy					Enrolled first Phase 2 participant Interim data readout Q1 2023
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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Transplantation: Kidney & Islet Cell

Kidney Transplant Market Opportunity: Potential to Replace CNIs to become Standard of Care in Transplant

- **~23,000 U.S. kidney transplants per year** and ~227,000 Americans living with a functioning kidney graft

- CNIs are associated with an over **20% incidence of new onset diabetes in first 6 months post-transplant,** as well as **hypertension, kidney- and neuro-toxicity**
- **Fewer than 50% of transplanted kidneys** from deceased donors **function more than 10 years**

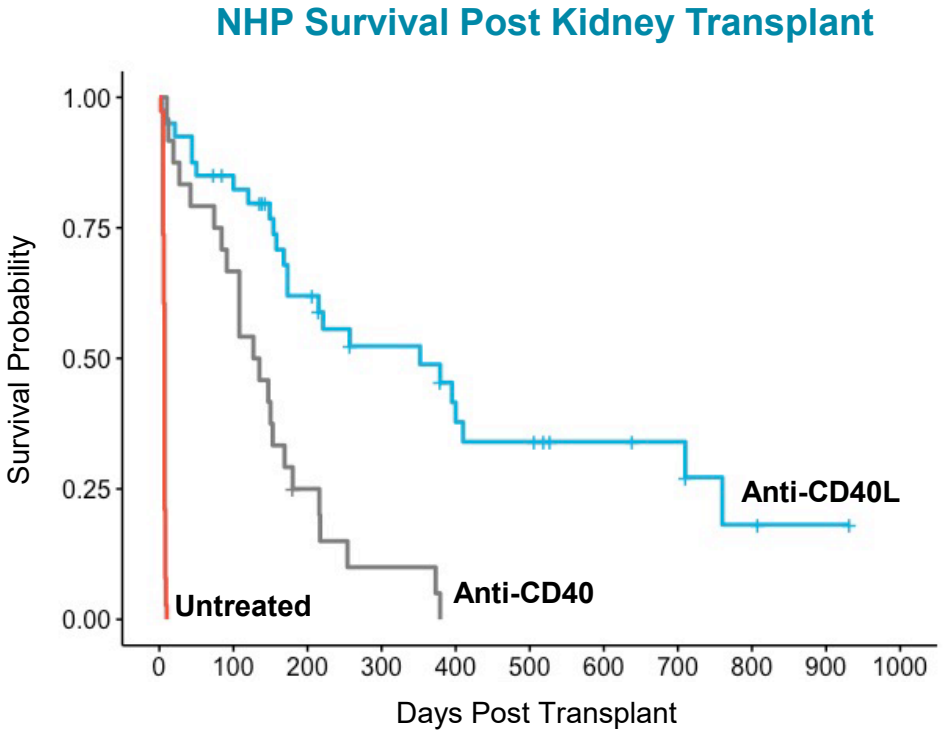
- ~90,000 Americans face a **3-5 year wait for a kidney BUT** up to **15% of transplants per year are re-transplants** further limiting organ availability for new patients

- **Pre-transplant: ~$90,000 per year cost for dialysis**
- **~450% increase in annual medical cost** to treat transplant patients who experience renal graft failure

Tegoprubart has **potential to reduce drug-associated morbidity and improve graft survival** associated with standard of care regimens, such as those including calcineurin inhibitors (CNIs)

Source: Donate Life America; NIDDK & Shapiro 2017; USRDS 2019; DHHS OPTN 2014; Ghisdal 2012; Kidney.org; Donate Life America.

Inhibition of CD40L Improved Survival vs. CD40 Inhibition in Non-Human Primate (NHP) Kidney Transplantation Monotherapy Studies



In aggregated data from published studies, **NHPs receiving anti-CD40L** (e.g., 5c8, AI794, IDEC-131) immunomodulation monotherapy post kidney transplantation **had longer average survival** than both those receiving anti-CD40 monotherapy (e.g., 4D11, cH5D12, Chi220, ASKP1240) and untreated controls

Source: Perrin, 2022.
Note: **Meta-analysis not based on head-to-head studies.** Differences between any individual programs may vary.

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CNIs Have Been Associated with a Range of Short-Term Toxicities when used in Kidney Transplantation

Adverse Event (6 months post transplant)	Cyclosporin (n=336)	Tacrolimus (n=346)
NODAT / Impaired Fasting Glucose	26.0%	33.6%
Any renal impairment	23.1%	23.7%
Tremor	14.8%	21.7%
Any serious infection	24.4%	19.4%
Hypertension	13.9%	15.0%
Hirsutism / Hypertrichosis	8.9%	0.6%
Alopecia	1.2%	3.2%

Source: Vincenti, 2007.
Note: NODAT = New Onset Diabetes Mellitus After Transplantation.

Incidence of CNI Related Adverse Events Such as Nephrotoxicity May Increase with Time Post Transplant

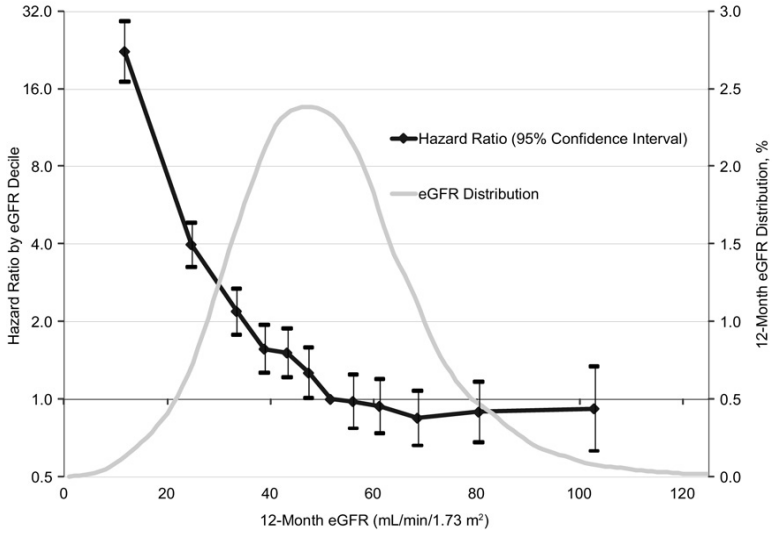
Organ Transplant	Duration of CNI Exposure (Years)	CNI Nephrotoxicity (defined as decreased kidney function / histology)
Kidney-Pancreas	1 5 10	30% 55% 100%
Liver	4 5	16% 18%
Bone Marrow	8	67%
Heart	5 10	9% 9% ESRD
Lung	5	14%
Intestine	5	21%

CNI related nephrotoxicity risks adversely impacting the functional lifespan of transplanted kidneys

Source: Kemper, 2014.

Kidney Allograft Function is an Early Predictor of Future Graft Failure

eGFR at 12 months is associated with subsequent death-censored graft failure



- Graft function measured using eGFR at 12 months post transplant is associated independently with subsequent graft failure
- Of multiple covariates, **12-month eGFR is the strongest predictor of graft failure**

Source: Am J Kidney Dis. 2011 Mar; 57(3):466-75.

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Phase 2 Kidney Transplantation Study Design

DESIGN

- 52-week, head-to-head, superiority trial, open label, 2-arm, active comparator safety, PK and efficacy study
- Approximately 120 participants (60/arm) undergoing kidney transplantation at multiple sites in the United States and other countries
- Participants will receive tegoprubart or the active comparator, tacrolimus, as part of an immunosuppressive regimen including corticosteroids and mycophenolate mofetil (MMF) or mycophenolate sodium (MPS)

PLANNED DATA GENERATION

- **Safety & tolerability**
- **Graft function (eGFR)**
- **Rates of graft functional impairment**
- **Biopsy proven acute rejection (BPAR)**
- **Rate of new onset diabetes mellitus (NODAT)**
- **Rate of participant and graft survival**
- **PK and immunogenicity**

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

Phase 1b Kidney Transplantation Study Design

DESIGN

- 52-week, open label, single dose level study
- Up to 12 participants undergoing kidney transplantation at multiple sites in Canada, the United Kingdom and Australia
- Kidney transplant using standard induction therapy plus maintenance therapy with tegoprubart as a replacement for CNIs (tacrolimus)

PLANNED DATA GENERATION

- **Safety & tolerability**
- **PK/PD**
- **Graft survival & function**
- **Biopsy proven acute rejection**
- **Immune cell infiltrate of graft biopsy**
- **Biomarker measures of kidney injury and rejection risk**

This study will run in parallel to the Phase 2 clinical trial of tegoprubart in kidney transplantation

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

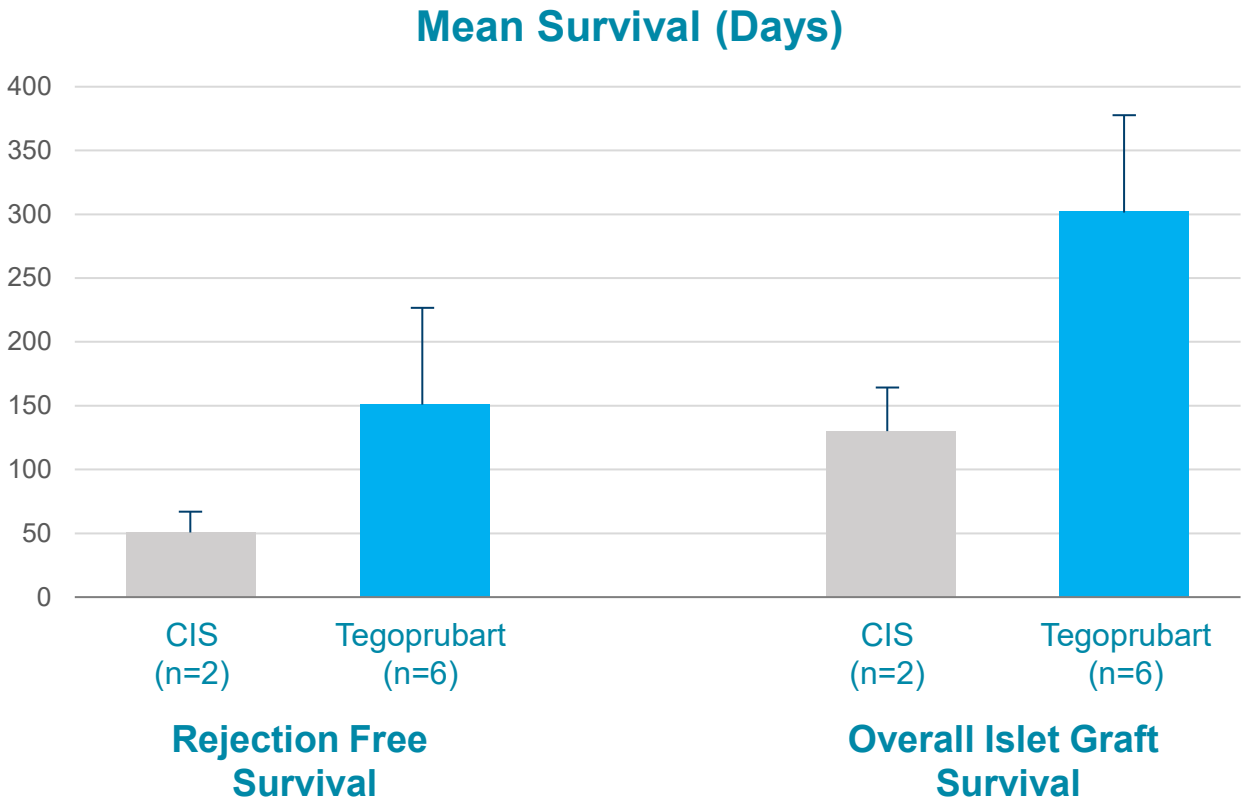
Islet Cell Transplant Opportunity: Potential to Unlock Islet Cell Transplant Market

- ~1.3M Americans live with Type 1 diabetes
- **~70,000 (5%) estimated to have "BT1D, " the Brittle form of Type 1 Diabetes**
- BT1D patients have difficult-to-manage glucose levels with **severe blood glucose fluctuations despite treatment** and **higher risk of diabetes related death**
- Minimally invasive islet cell transplantation underutilized in part because of **need for multiple transplant grafts** (usually within 90 days) due to immunosuppressive regimens with **CNIs, that may be toxic to transplanted insulin producing islet cells**

Tegoprubart has **potential to unlock islet cell transplant market by improving islet cell graft survival & reducing side effects** associated with standard of care regimens, such as those including calcineurin inhibitors (CNIs)

Source: Brittle Diabetes Foundation; NIDDK & Shapiro AM, Pokrywczynska M, Ricordi C. Clinical pancreatic islet transplantation. *Nature Reviews. Endocrinology.* 2017;13(5):268–277. Cartwright QJM 2011

Tegoprubart Prolonged Graft Survival vs. CNI Containing Regimen (CIS) in a Non-Human Primate Islet Cell Transplant Model…



Source: Kenyon, 2021.

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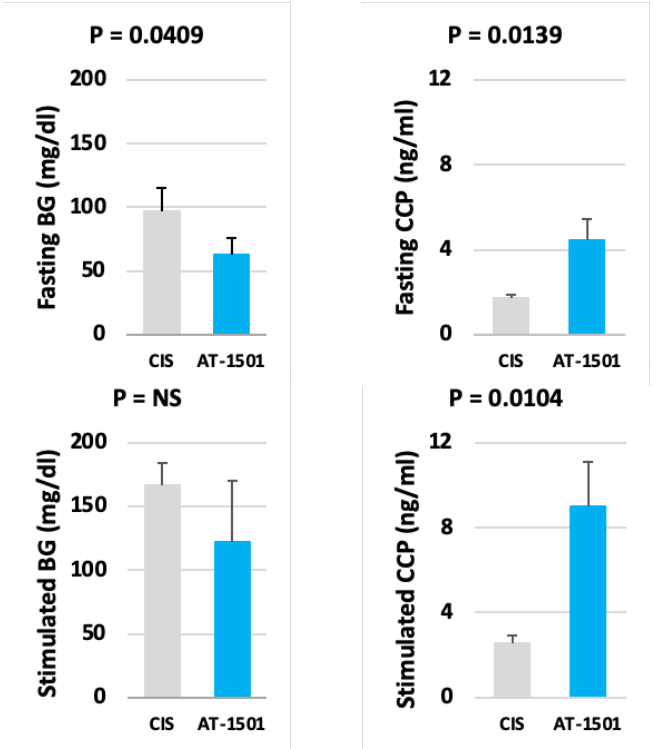
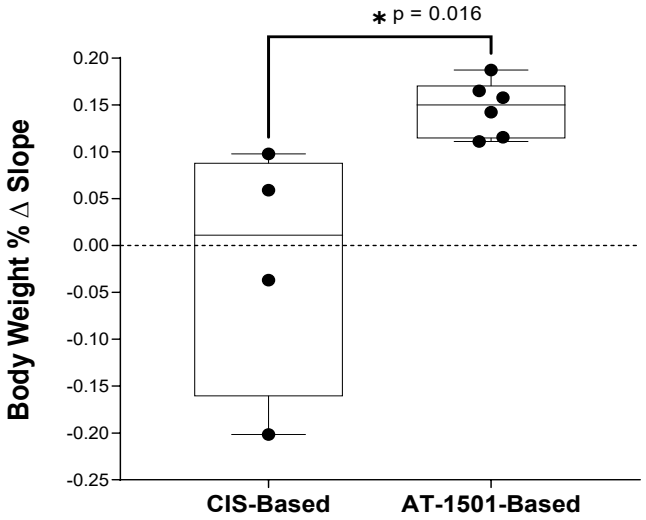
… And Tegoprubart was Associated With Better Metabolic Control as Well as Healthier Animals Overall as Demonstrated by Body Weight

Tegoprubart (AT-1501) vs. CNI Regimens (CIS) in NHP Islet Cell Transplantation Model





Source: Kenyon @ IPITA 2021.

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Phase 2 Islet Cell Transplantation for T1D Study Design

DESIGN

- 52-week, open label, single dose level study
- Initial group of up to 6 participants with Type 1 Diabetes (T1D) in the United States
- Islet cell transplant combined with induction therapy plus tegoprubart and mycophenolate mofetil (MMF) every third week by IV infusion

PLANNED DATA GENERATION

- **Safety & tolerability**
- **Graft function & insulin independence**
  - e.g., C-peptide, HbA1C
- **Number of hypoglycemic events**
- **Need for repeat islet cell transplant(s)**

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

Neurodegeneration: ALS

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

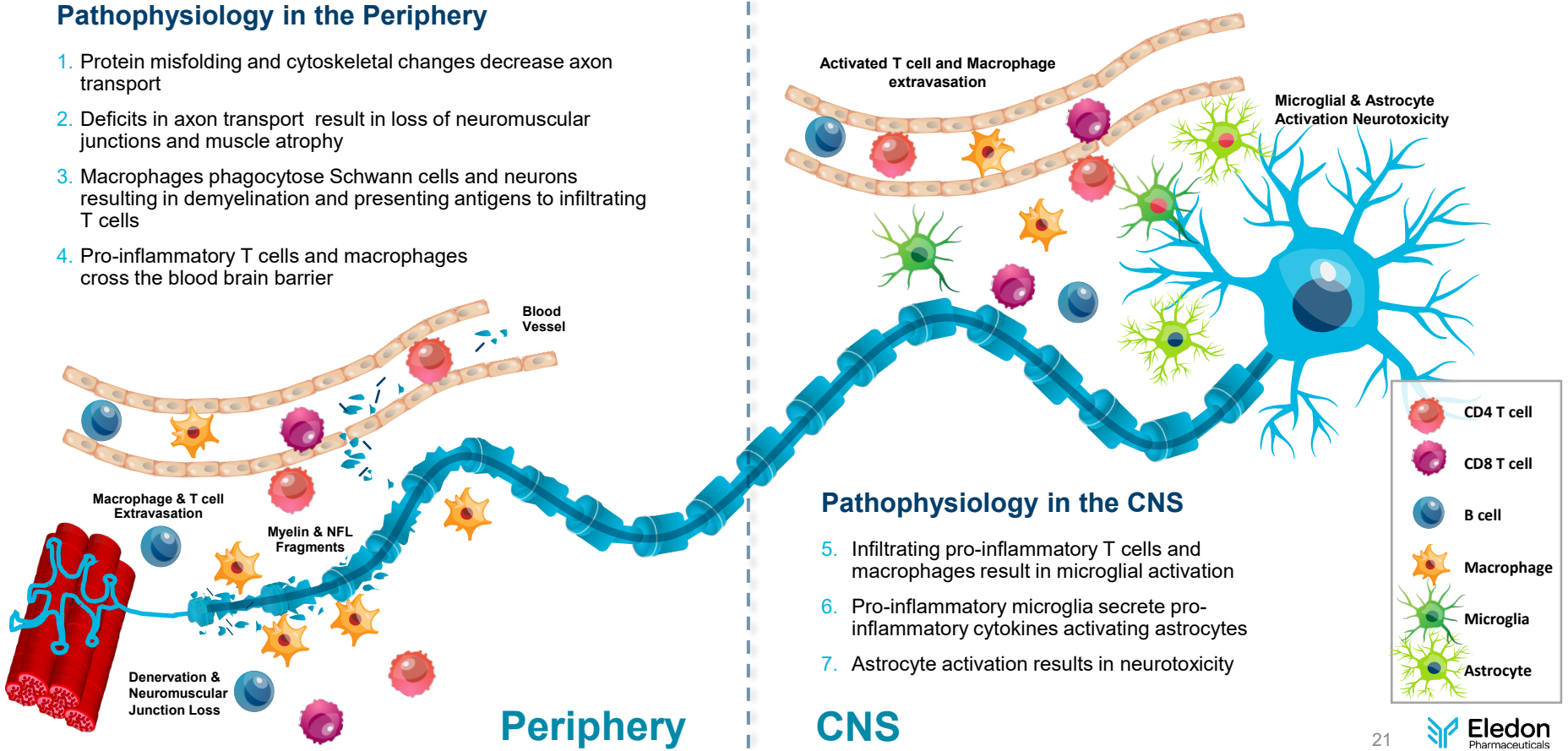
Only **10%** of ALS cases are **hereditary**

- 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, **despite 2 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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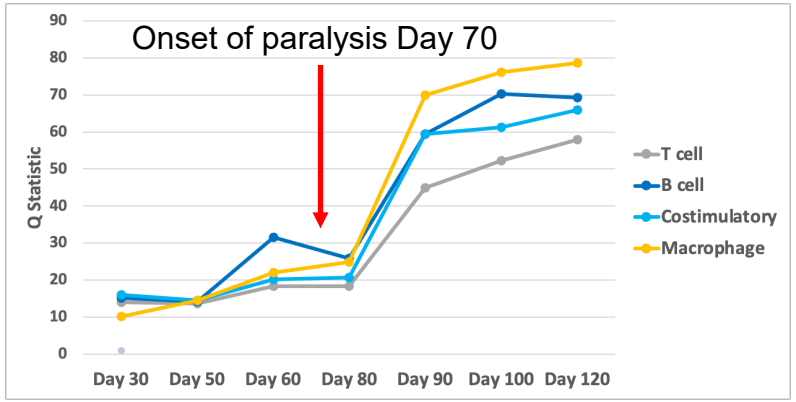
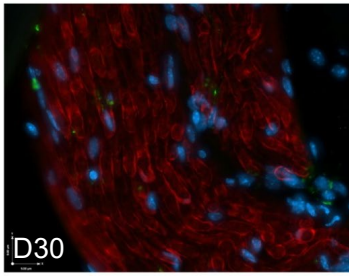
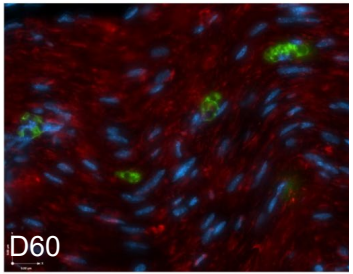
Inflammatory Pathways are Activated in the Periphery in ALS Animal Models

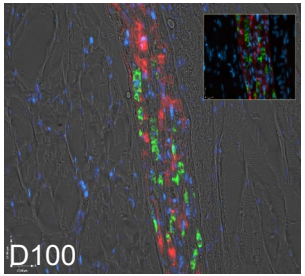
Activation of Inflammatory Pathway in ALS Rodent Skeletal Model

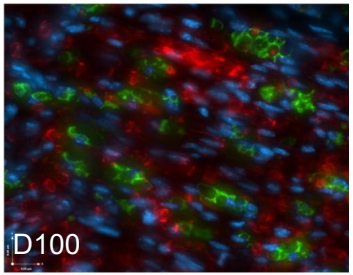


- Macrophages accumulate on peripheral nerves in skeletal muscle
- Staining shows Myelin (Red), Macrophages (Green), and Nuclei (Blue)









Source: Lincecum, 2010.

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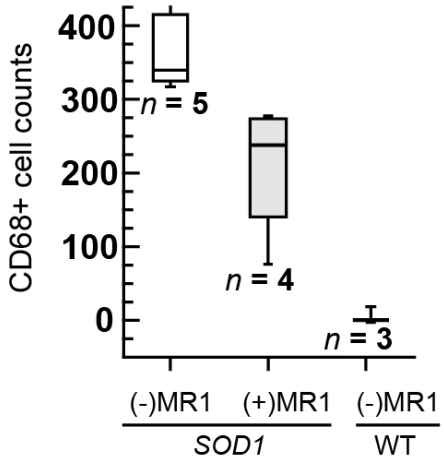
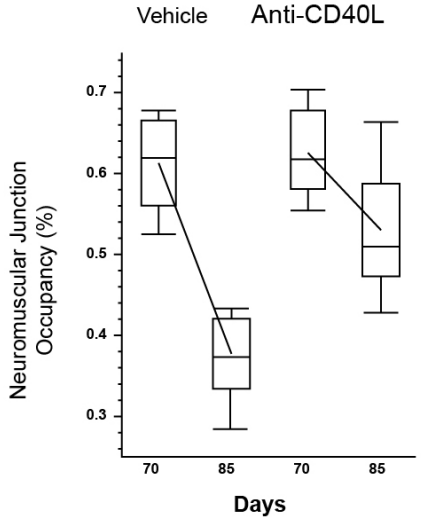
Anti-CD40L Historical Antibody Improves Motor Neuron Survival & Decreases Inflammation in Peripheral Nerves of ALS Mice

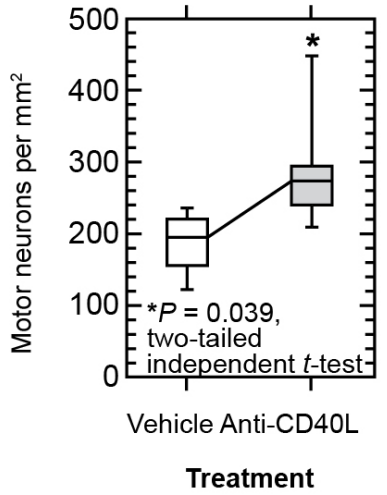
Anti-CD40L (MR1) treatment reduces macrophage infiltrate and "attack" of denervated peripheral nerves in skeletal muscle



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



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



Source: Lincecum, 2010.

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

Serum Biomarker Levels:

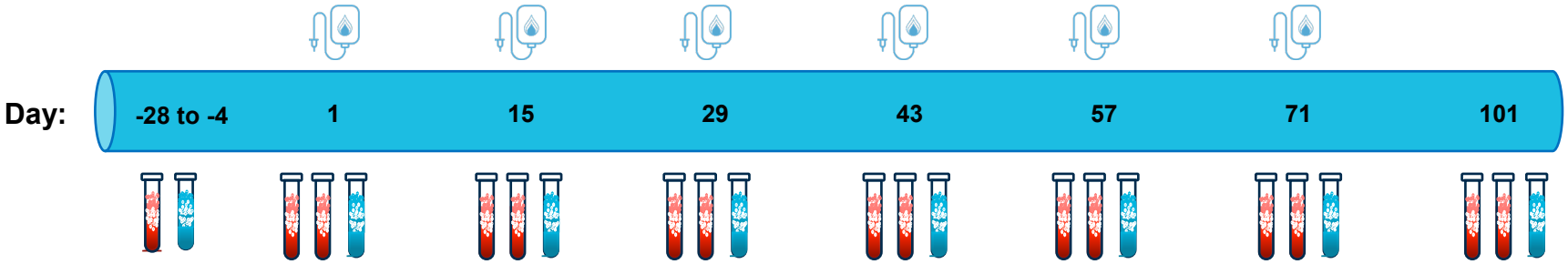
ALS Patients vs. Controls

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.

Phase 2a ALS: Study Design



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

Phase 2a ALS: Demographics

- 54 participants recruited
- Average age - 59 years old
  - 72% male
  - 96% Caucasian
- Average baseline ALSFRS-R of 39.5
  - 7 participants 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 participants 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-analysis:
    1. Compare participants who did or not achieve target engagement as defined by a change in CXCL-13

Phase 2a ALS: Safety & Tolerability

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

- 35.2% of participants 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 participants experienced adverse events leading to withdrawal
    - 1 participant withdrew because of worsening depression in the 1 mg/Kg cohort
    - 1 participant 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*
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)

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

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

Group	All Participants	Baseline Criteria	Positive Target Engagement
PRO-ACT *(Comparator)*	-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
Low Dose (1/2 mgs)	-0.89 **7.2%** n=18	-0.89 **7.2%** n=18	-0.68 **(18.1%)** n=11
High Dose (4/8 mgs)	-1.08 **30.1%** n=36	-0.66 **(20.5%)** n=29	-0.66 **(20.5%)** n=29

- **All Participants** includes 54 participants enrolled in the study
- **Baseline Criteria** excludes 7 participants in High Dose cohorts 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 participants with at least a 10% decrease in CXCL13
- **Participants without Target Engagement had a mean change of –1.14 or 37.3% compared to PRO-ACT**

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Phase 2 ALS: Data Summary

Safety & Tolerability

- 35.2% of participants 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

Autoimmunity: IgA Nephropathy

IgA Nephropathy Overview & Market Opportunity

Characterized by gradual, progressive **kidney function deterioration**

Most common primary glomerulo-nephritis effecting over **~150,000 Americans**

Up to **~40% of patients** may ultimately progress to **End Stage Kidney Disease**

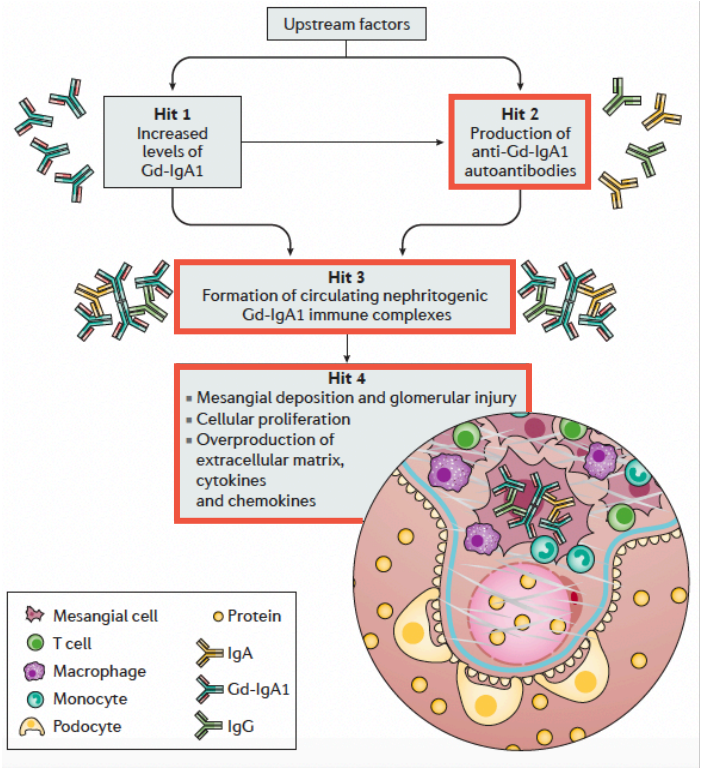
Average age at time of diagnosis **between 20 to 40 years of age**

Clear regulatory path starting with proteinuria

- **Up to ~50-60% of patients may require additional therapy to control proteinuria and slow disease progression**

Source: Glassrock, 2019; Schena, 2018.

IgA Nephropathy Overview & Market Opportunity



- Current Standard of Care and other drugs in development generally aim to either reduce production of antibodies or reduce the leakage of antibodies and subsequent tissue damage by decreasing local blood pressure (i.e., either Hits #2 or #4)
- **Tegoprubart has the potential to hit at the root of the pathophysiology by reducing production of IgA autoantibodies and thus the immune complex formation (i.e., Hits #2, #3 and #4)**

Source: Lai, 2016.

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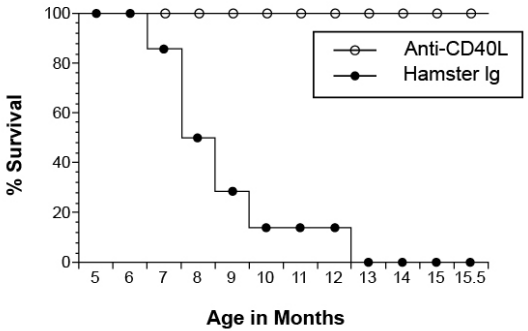
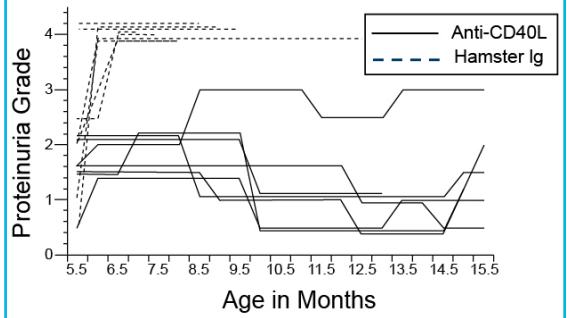
Blocking CD40L Ameliorates Glomerulosclerosis and Proteinuria in Historical Autoimmune Nephritis Rodent Models

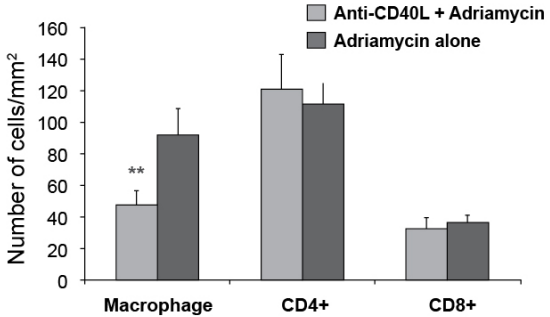
Blocking CD40L improved survival in a Lupus Nephritis mouse model



Blocking CD40L improved proteinuria in a Lupus Nephritis mouse model



Treatment with anti-CD40L reduced tissue damage and macrophage infiltration in Adriamycin induced glomerulosclerosis mouse model



Source: Kalled, 1999.

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Phase 2 IgAN Study Design

DESIGN

- 96 week open-label, dose-ranging trial
- Primary endpoint at week 24
- Up to 42 participants in total with IgAN in low dose and high dose cohorts
- Elevated proteinuria (>0.75g / 24 hours) despite optimized ACE / ARB therapy

PLANNED DATA GENERATION

- **Safety & Tolerability**
- **Change in protein / UPCR**
- **Change in eGFR**
- **Comparison of efficacy in low dose vs. high dose of tegoprubart**

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

Execution Priorities

2022 Execution Priorities

- ✓ Complete ALS Phase 2 study and release data
- Continue IgA Nephropathy clinical trial enrollment
- Continue 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 open label studies expected Q1’23

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

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