Eledon Pharmaceuticals

Targeted Immunology CD40/CD40L Therapeutics

Transplantation | Autoimmunity | ALS

September 2021

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, 2020, 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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Single Focus: Developing Best-in-Class Immune-Modulating Therapeutics with Validated Biology

Optimized & Differentiated Lead Asset: AT-1501

- Targeting CD40/CD40L pathway validated by extensive historical proof-of-concept data
- Engineered to increase potency, half-life and manufacturability vs. other anti-CD40 approaches
- Targeting both potential first-in-class and potential best-in-class indications

4 Shots on Goal in Conditions with Few or No Approved Medicines and High Morbidity

- Financed to support up to four clinical trials in: Solid Organ Transplantation (Kidney), Islet Cell Transplantation for Type 1 Diabetes, IgA Nephropathy, and Amyotrophic Lateral Sclerosis (ALS)
- Next generation antibody in pre-clinical development and future combination therapies possible

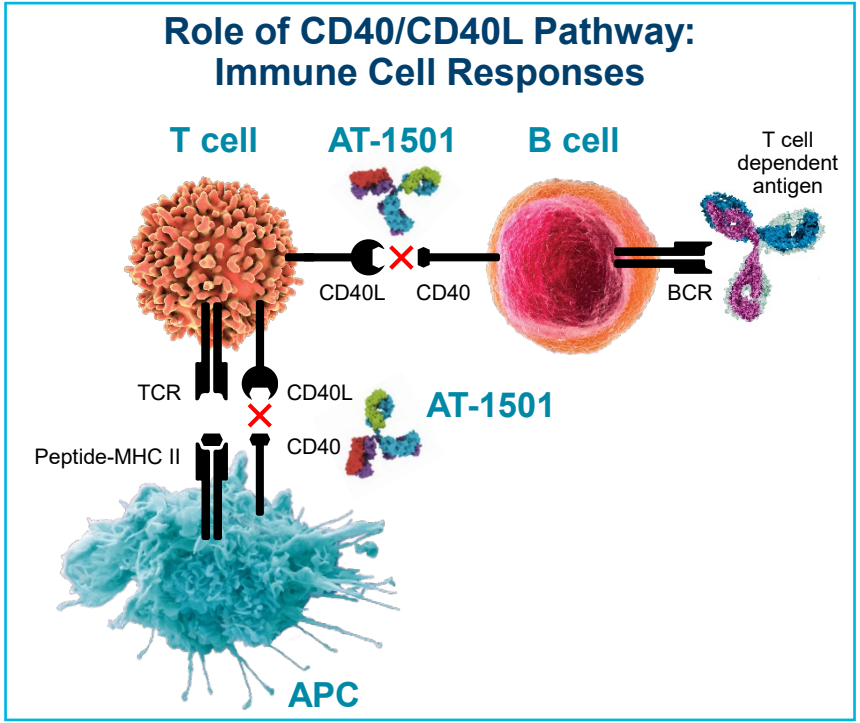
Near-Term Milestones and Strong Financial Profile

- Multiple interim and top-line data readouts expected beginning in 1H 2022
- $101M in cash and cash equivalents (as of June 30, 2021) expected sufficient to fund operations well into 2023

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

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

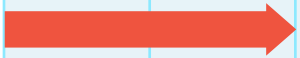
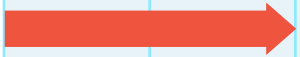


AT-1501: Potential Best-in-Class Anti-CD40/CD40L Antibody

Targeting CD40 Ligand vs. CD40 Receptor		IgG1 vs. fusion protein, pegylated FAB or IgG4
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.

AT-1501: Pipeline in a Product Opportunity

Product Candidate	Indication	Development Stage				Anticipated Milestones
		Pre-clinical	Phase 1	Phase 2	Phase 3	
AT-1501	**Amyotrophic Lateral Sclerosis (ALS)**					Complete enrollment Phase 2 results expected in 1H 2022
	Kidney Transplantation					Initiate ex-US Clinical study 4Q 2021 NHP study readout expected mid 2022
	Islet Cell Transplantation for Type 1 Diabetes					Enroll first Phase 2 patient in Canada Interim data readout expected in 1H 2022
	IgA Nephropathy					Initiate Phase 2 trial in late 2021
AT-2001	**Autoimmune Indications**					Lead optimization

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

AT-1501 Phase 1a/1b Single Ascending Dose Trial Completed in Healthy Subjects and ALS Patients

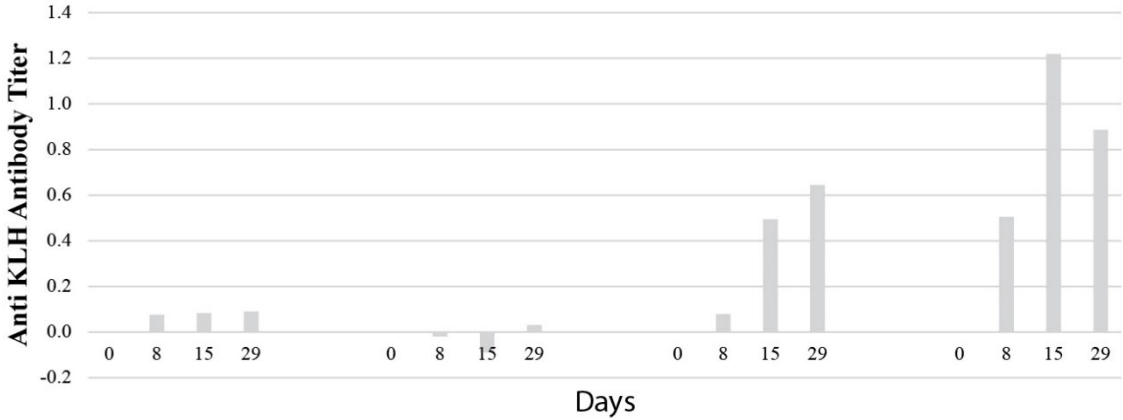
Healthy Volunteers or ALS Patients Receiving Either AT-1501 (mg/kg, IV) or Placebo

Subjects	Healthy	Healthy	ALS	Healthy	Healthy	Healthy	1501	Placebo
Dose (mg/kg)	0.5	1	**1**	2	4	8	NA	NA
n=	6	3	**3**	3	3	6	24	8
Number of Subjects (%) Experiencing TEAEs by Maximum Toxicity Grade								
Grade 1 (% Subjects Experiencing Events)	3 (50.0%)	2 (66.7%)	2 (66.7%)	2 (66.7%)	1 (33.3%)	1 (16.7%)	11 (45.8%)	5 (62.5%)
Grade 2 (% Subjects Experiencing Events)	–	–	1 (33.3%)	–	–	1 (16.7%)	2 (8.3%)	–
Grade 3	–	–	–	–	–	–	–	–
Grade 4	–	–	–	–	–	–	–	–
Grade 5	–	–	–	–	–	–	–	–

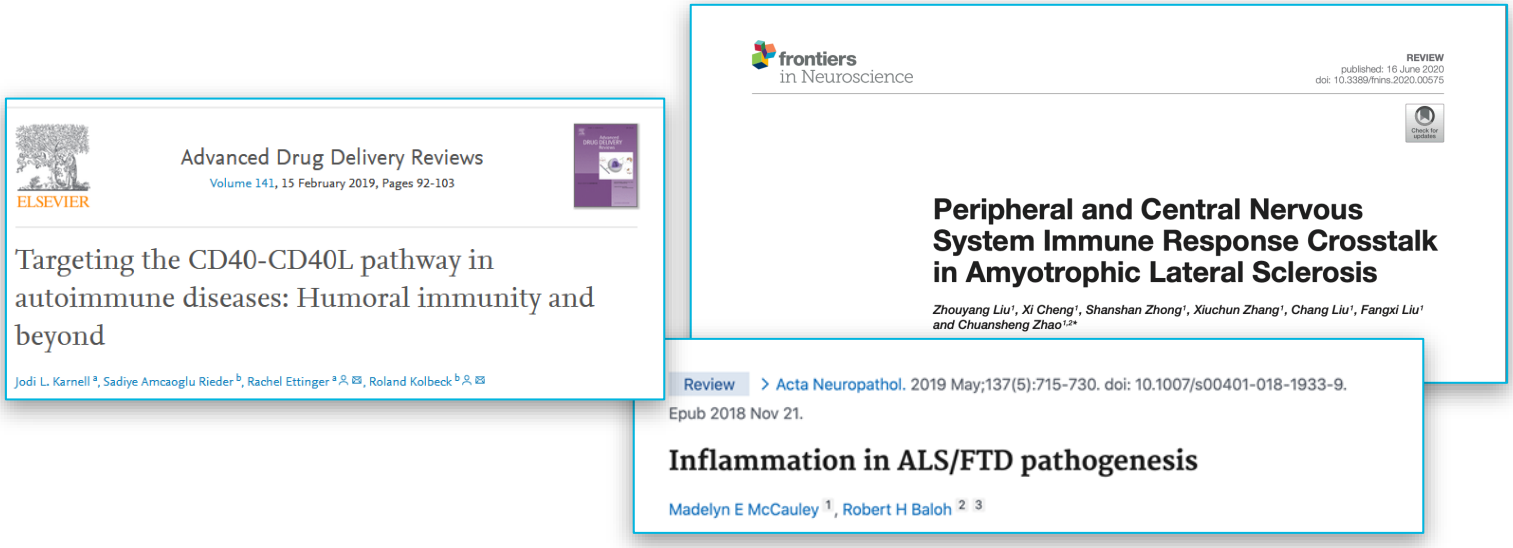
Phase 1 KLH Challenge Demonstrates Functional Activity

- 4 healthy volunteers received keyhole limpet hemocyanin (KLH), a potent immune challenge, via subcutaneous injection
- Subjects 1-3 also received simultaneous 8 mg/kg IV AT-1501
- More closely resembling potential clinical use, AT-1501 subjects were not pre-treated with the study drug in the days to weeks prior to receiving KLH

AT-1501 fully inhibited immune response to KLH in two subjects (subjects 1 and 2) and partially inhibited immune response to KLH in the third subject (subject 3)



Autoimmune Pathogenesis of ALS is Increasingly Recognized



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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**

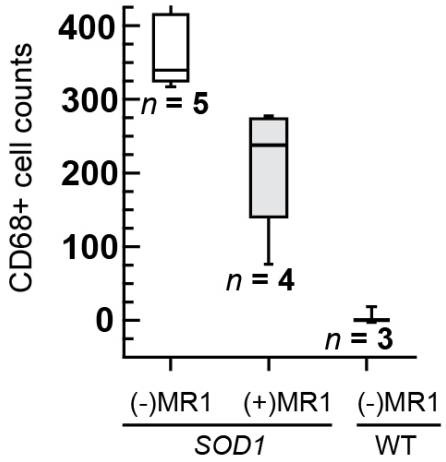
People with ALS ultimately **lose the ability to ambulate**, lose the ability to swallow, and when breathing muscles become affected, need permanent ventilatory support to assist with breathing

50% and 80% of ALS patients die within **3 and 5 years** from diagnosis, respectively. Most people die from respiratory failure or cachexia

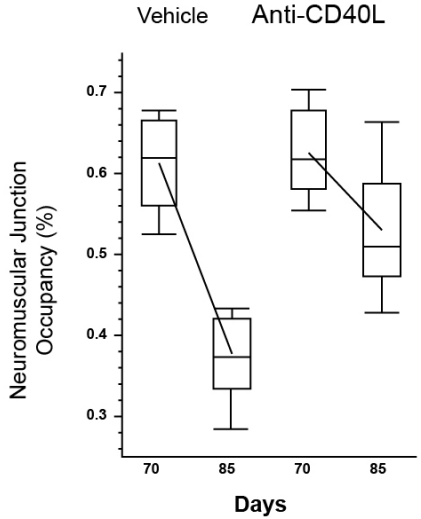
Very high 5-year ALS morbidity and mortality despite two FDA approved treatments

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

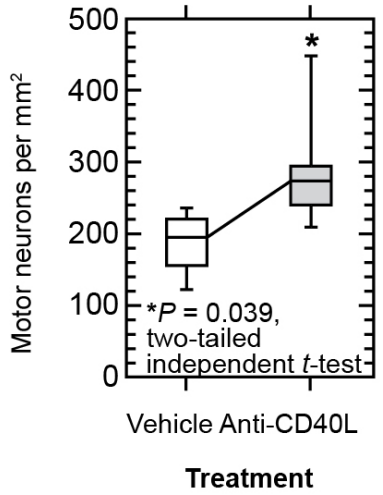
Anti-CD40L (MR1) treatment reduces macrophage infiltrate and "attack" of denervated peripheral nerves in skeletal muscle



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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Phase 2 ALS Study Design

DESIGN

- 12-week, open label, multiple ascending dose level study
- Four dose cohorts of up to ~18 patients each
- Each subject serves as own control by comparing changes from baseline

PLANNED DATA GENERATION

- **Safety & tolerability**
- **Biomarkers of CD40L target engagement**
  - e.g., CXCL13
- **Pro-inflammatory chemokines and cytokines upregulated in ALS**
  - e.g., TNF-α, MCP1, IL-6, Enraged
- **Exploratory endpoints**
  - e.g., ALS Functional Rating Scale, respiratory function, Neurofilament Light Chain

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

Kidney Transplant Market Opportunity

- Over **23,000 U.S. kidney transplants per year** and ~193,000 Americans have a functioning kidney transplant

- Over **20% incidence of new onset diabetes in first 6 months post-transplant** in CNI treated patients
- **CNIs** are also associated with **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**

- Up to **15% of transplants per year are re-transplants** further limiting organ availability for new patients

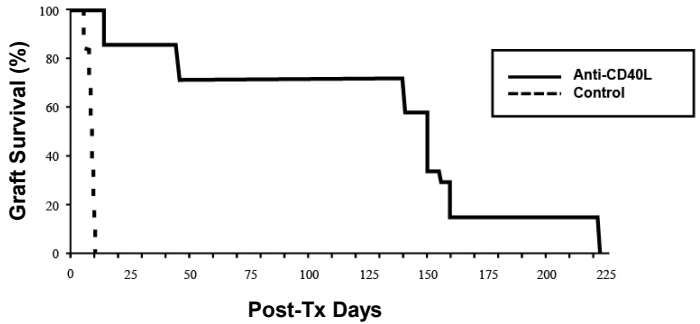
- **~450% increase in annual medical cost** to treat transplant patients who experience renal graft failure

AT-1501 has **potential to reduce drug-associated morbidity and improve graft survival** associated with standard of care regimens, such as those including calcineurin inhibitors (CNIs)

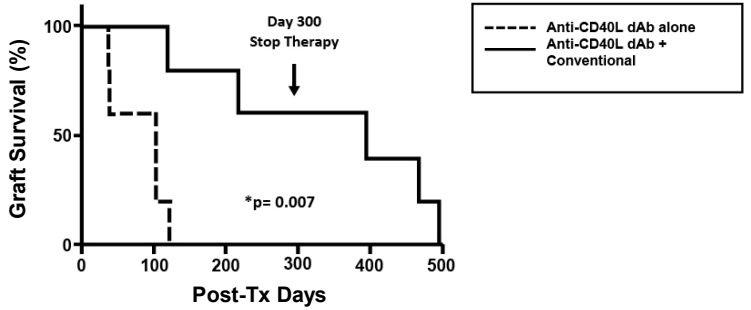
Source: Donate Life America; NIDDK & Shapiro AM, Pokrywczynska M, Ricordi C. Clinical pancreatic islet transplantation. *Nature Reviews. Endocrinology*. 2017;13(5):268–277; 2019 USRDS; DHHS OPTN 2014; Ghisdal 2012

Anti-CD40L Antibodies Prevent Renal Allograft Transplant Rejection in Nonhuman Primate Models

Short term exposure to **anti-CD40L antibody inhibits acute renal allograft transplant rejection** in nonhuman primates



Inhibition of renal allograft transplant rejection in nonhuman primates after short term anti-CD40L antibody exposure in conjunction with induction immunotherapy, steroids, and mycophenolate mofetil, showed **persistent effect even after therapy was discontinued**



Source: Kim, 2017; Kanmaz, 2004.

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Phase 1b Kidney Transplantation Study Design

DESIGN

- 52-week, open label, single dose level study
- 6 – 12 subjects undergoing kidney transplantation at multiple sites in Canada, with potential for European expansion
- Kidney transplant using standard induction therapy plus maintenance therapy with AT-1501 as a replacement for 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**

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

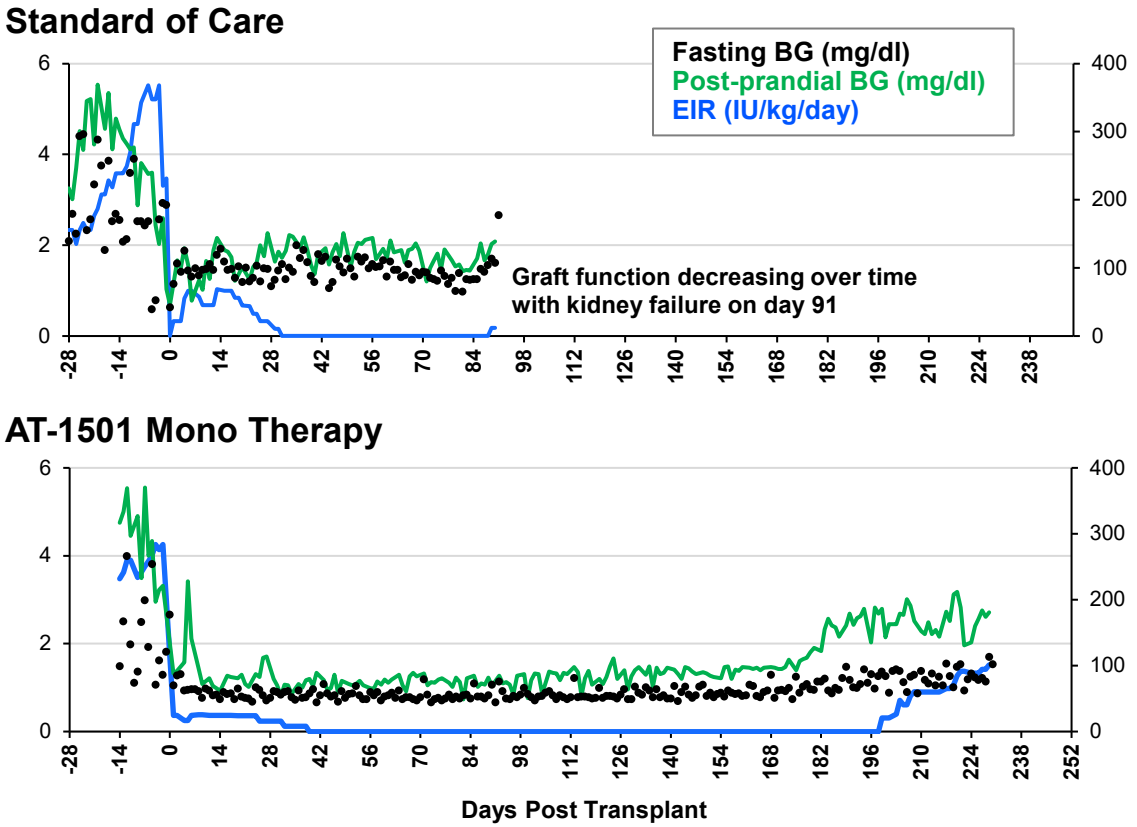
Islet Cell Transplant Market Opportunity

- ~1.3M Americans live with Type 1 diabetes (T1D)
- **~70,000 (5%) estimated to have Brittle form of T1D**
- 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) in part due to immunosuppressive regimens with **CNIs, that may be toxic to transplanted insulin producing islet cells**

AT-1501 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

Non-Human Primate Islet Cell Transplant Model: SOC Versus AT-1501 Blood Glucose Stabilization



In animals whose islet cells were ablated to induce T1D and who then underwent islet cell transplantation, **AT-1501 provided for better blood glucose level stabilization and less drug related animal morbidity and mortality** than standard of care

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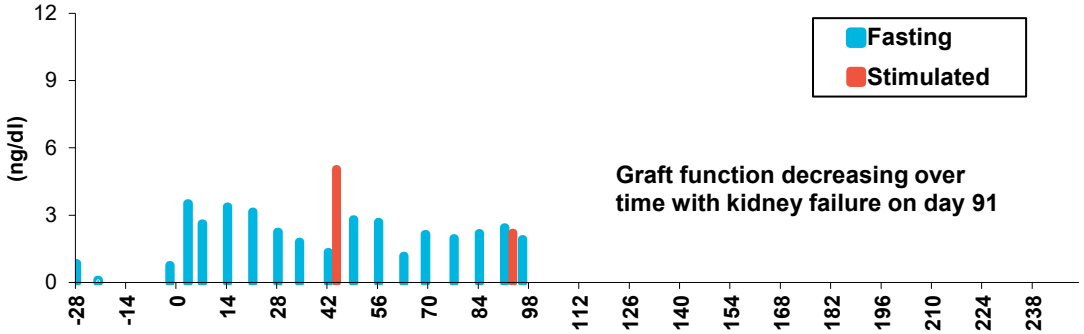
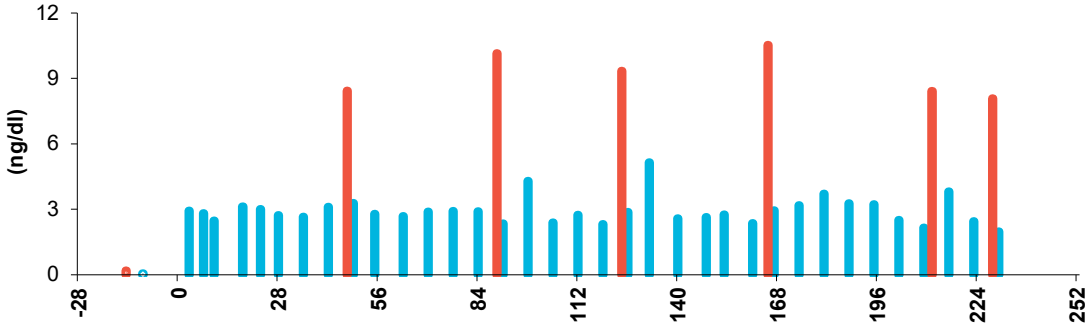
Non-Human Primate Islet Cell Transplant Model: SOC Versus AT-1501 C-peptide Levels

Standard of Care



AT-1501 Mono Therapy



- C-peptide levels are a surrogate biomarker of insulin production, islet cell viability and function
- In response to meal stimulation, functioning islets produce more insulin and thus C-peptide
- **Animals receiving AT-1501 showed better islet cell function than those receiving standard of care**

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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 subjects with Type 1 Diabetes (T1D) at a single Canadian site (up to 12 subjects overall)
- Islet cell transplant combined with induction therapy plus AT-1501 and mycophenolate mofetil 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.

IgA Nephropathy Overview & Market Opportunity

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

Most common primary glomerulo-nephritis effecting over **~100,000 Americans**

Up to **~50% of patients** progress to **End Stage Kidney Disease** within ~10-20 years

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

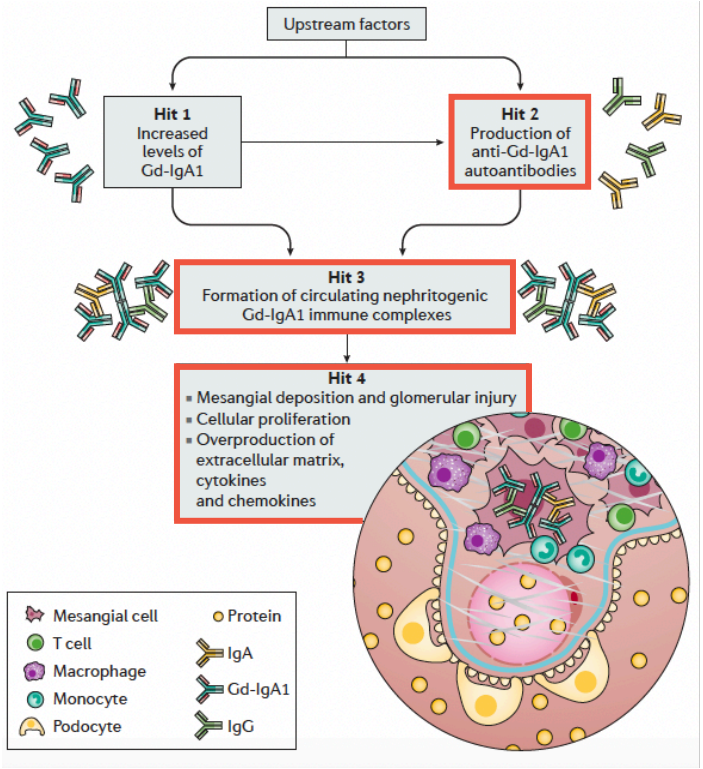
Clear regulatory path starting with proteinuria

~50-60% of patients require additional therapy to standard of care to control proteinuria and slow disease progression

No FDA approved treatments

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)
- **AT-1501 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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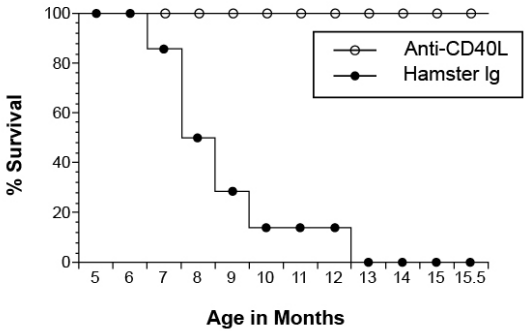
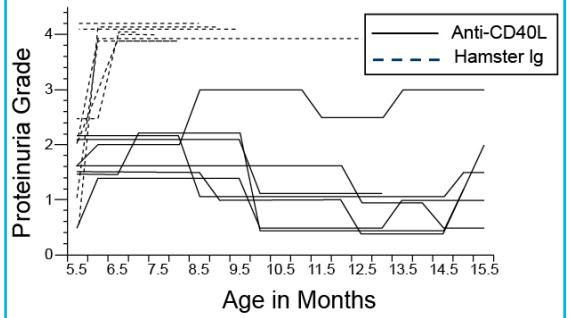
Blocking CD40L Ameliorates Glomerulosclerosis and Proteinuria in Historical Autoimmune Nephritis Rodent Models

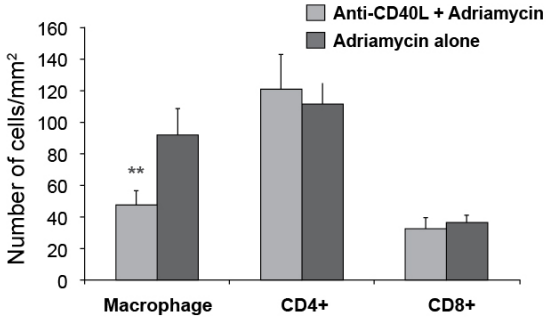
Blocking CD40L improved survival in a Lupus Nephritis mouse model



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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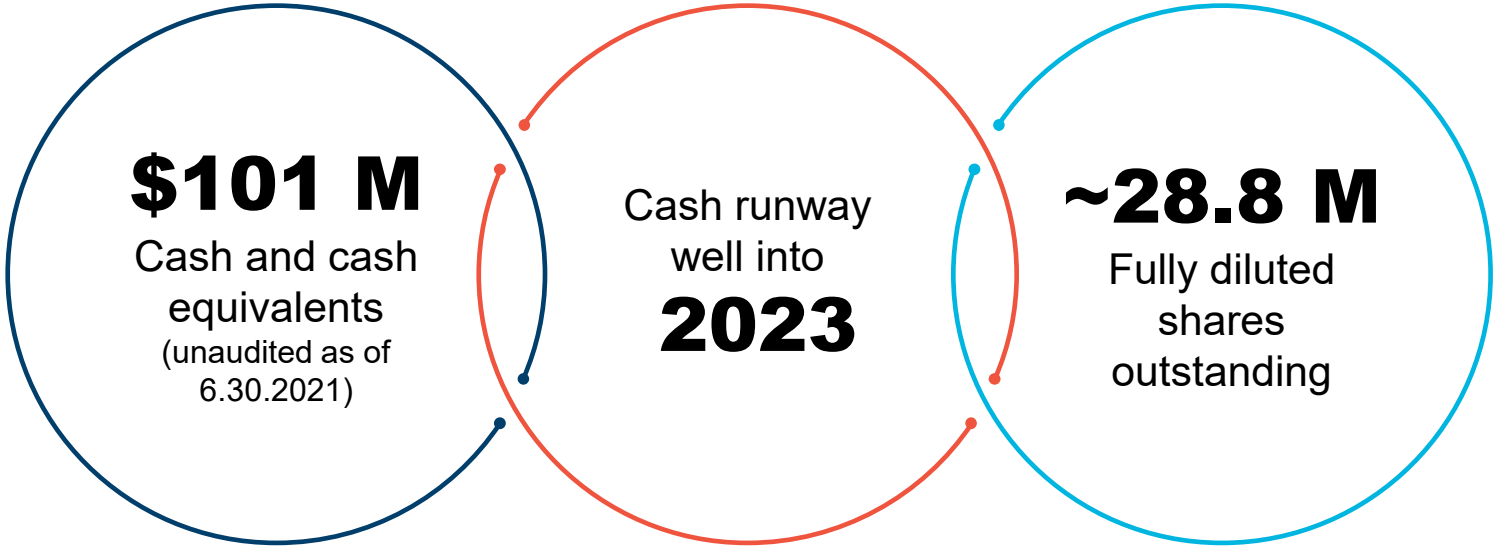
Strong Financial Profile



2021 Execution Priorities

- Complete ALS Phase 2 study enrollment
- Begin enrollment of Islet Cell Transplantation for Type 1 Diabetes trial
- Launching Kidney Transplantation clinical trial in Canada
- Initiate Kidney Transplantation non-human primate study
- Initiate IgA Nephropathy clinical trial
- Advance AT-1501 subcutaneous formulation

Targeting interim and top-line clinical data readouts in up to 4 indications in 2022, with the first data readouts expected beginning in 1H2022

Note: As of May 1, 2021. Development plans and timelines subject to change based on several factors, including US and global regulatory agency interactions.

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