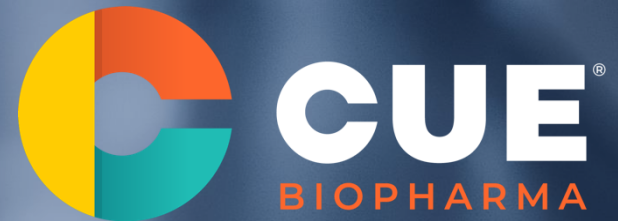




Transforming Patients' Lives Through Precision Immunoengineering in Autoimmune Disease

April 7, 2026



Cautionary Note Regarding Forward Looking Statements

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This presentation contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, that are intended to be covered by the “safe harbor” created by those sections. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as “believe,” “expect,” “may,” “will,” “should,” “would,” “could,” “seek,” “intend,” “plan,” “goal,” “project,” “estimate,” “anticipate,” “strategy,” “future,” “vision,” “likely” or other comparable terms, although not all forward-looking statements contain these identifying words. All statements other than statements of historical facts included in this presentation regarding our strategies, prospects, financial condition, operations, costs, plans and objectives are forward-looking statements. Examples of forward-looking statements include, among others, statements we make regarding our belief regarding the potential benefits and applications, novelty and market potential of our drug candidates and programs, our development plans with respect to our CUE-100, CUE-400, and CUE-500 series, the potential benefits of our collaborations, our expectations regarding the timing of milestone events, regulatory developments and expected future operating results. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, our

limited operating history, limited cash and a history of losses; our ability to obtain adequate financing to fund our business operations in the near term and successfully remediate our current “going concern” determination that we do not have sufficient capital on hand to continue operations beyond the next twelve months; our ability to achieve profitability; potential setbacks in our research and development efforts including negative or inconclusive results from our preclinical studies, or clinical trials or our ability to replicate in later clinical trials positive results found in preclinical studies and early-stage clinical trials of our product candidates; serious and unexpected drug-related side effects or other safety issues experienced by participants in clinical trials; our ability to secure required U.S. Food and Drug Administration (“FDA”) or other governmental approvals for our product candidates and the breadth of any approved indication; delays and changes in regulatory requirements, policy and guidelines including potential delays in submitting required regulatory applications to the FDA; our reliance on licensors, collaborators, contract research organizations, suppliers and other business partners; our ability to obtain adequate financing to fund our business operations in the future; our ability to maintain and enforce necessary patent and other intellectual property protection; competitive factors; general economic and market conditions; and the other risks and uncertainties described in the Risk Factors and in Management’s Discussion and Analysis of Financial Condition and Results of Operations sections of our most recently filed Annual Report on Form 10-K and any subsequently filed Quarterly Report(s) on Form 10-Q. Any forward-looking statement made by us in this presentation is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

This presentation contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.



Agenda and Speakers

Welcome to CUE's R&D Day Event to Discuss CUE-401, the Company's Lead Asset for the Treatment of Autoimmune & Inflammatory Diseases

| | |
|---|--|
| Welcome | Lucinda Warren, Interim President and CEO |
| CUE-401 | Dan Baker, MD, Interim Chief Development Officer |
| KOL Perspective – Tregs and Cytokines in Context | Dr. Richard DiPaolo Dr. Jonathan Kay |
| Discussion & Q&A | Cue Management & KOLs |
| Closing Remarks | Lucinda Warren, Interim President and CEO |



Lucinda Warren
*Interim President and
Chief Executive Officer*



Dan Baker, MD
*Interim Chief
Development Officer*



Richard DiPaolo, PhD
*Professor and Chair,
Department of Molecular
Microbiology &
Immunology, Saint Louis
University*



Jonathan Kay, MD, MACR
*Timothy S. & Elaine L. Peterson
Chair in Rheumatology at
UMass Chan Medical School.
Professor of Medicine &
Population & Quantitative
Health Sciences*



Pipeline to Maximize Value Creation

Focus on CUE-401 and Autoimmunity Enhances Near-Term Value with Disruptive Potential

CUE-401 Drive to Clinic

Manufacture and IND enabling activities completed

- IND to be filed 2Q 2026

CUE-501 Precision Approach to B Cell Depletion

Licensed to Boehringer Ingelheim

- Potential of up to ~\$345M in milestones plus royalties

CUE-100 Series Selective Targeting

Licensed to ImmunoScape

- Milestone payments, and high-single digit royalties
- 40% equity stake in ImmunoScape



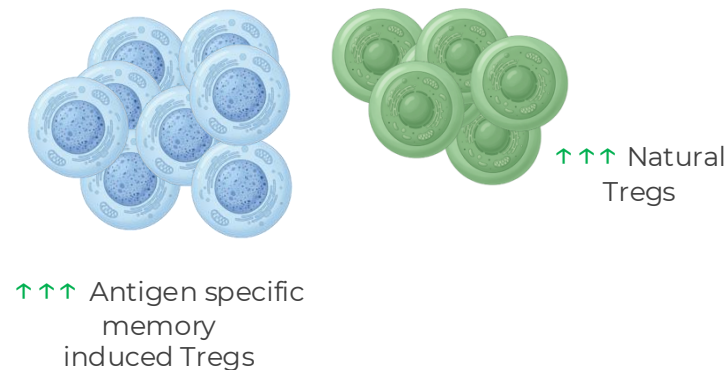
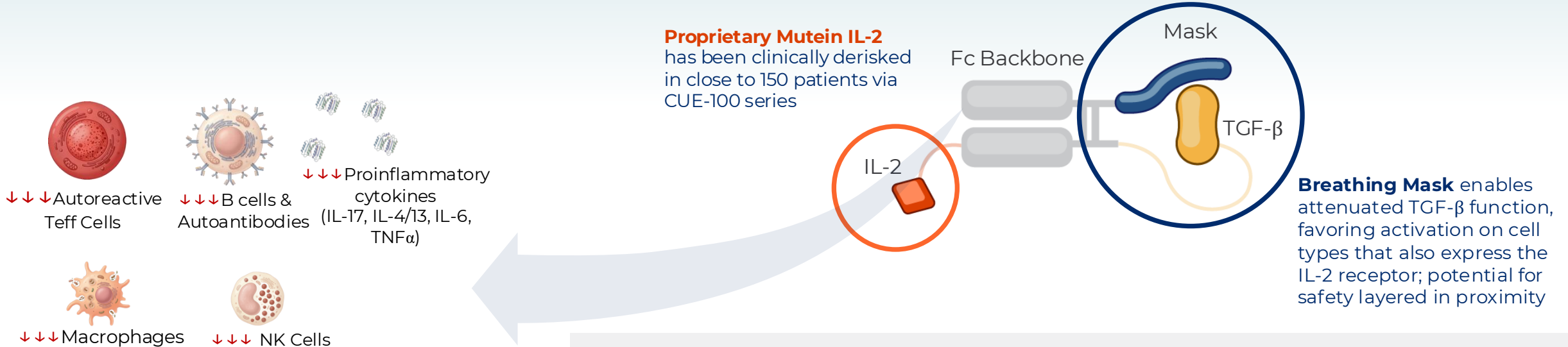
The Problem: Autoimmunity Arises When the Regulatory Function of T cells Becomes Deficient

The Resulting Inflammation Further Compromises Regulatory T cell Function



CUE-401: A Highly Differentiated Bifunctional Cytokine Therapeutic

Delivering via the Unique Pleiotropic Combination of IL-2 and TGF- β



- **CUE 401 is a first-in-class, bifunctional tolerogenic mechanism that harnesses attenuated components of TGF- β and IL-2**
 - Attenuating cytokine affinities retains key biologic functions & reduces potential for effects on non-immune cells
- **A novel approach utilizing the additive benefits of TGF- β in autoimmune disease versus IL-2 alone**
 - Targeted immune system suppression
 - Reduction of inflammation
 - Suppression of autoantibodies
 - Induction of tolerance via iTregs and nTregs
 - Conversion of CD4+ memory effector Tcells to antigen specific iTregs

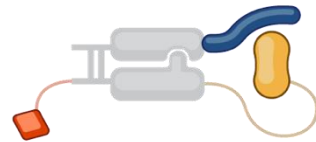


CUE-401: Potential Breakthrough Protein Design Solves Classic TGF- β Challenges of Safety and Manufacturability

- Attenuating Cytokine Affinities Retain Key Biologic Functions and Reduce Potential for Effects on Non-Immune Cells
- Mask Prevents Producer Cell Toxicity and Allows High Yields

IL-2 Variant

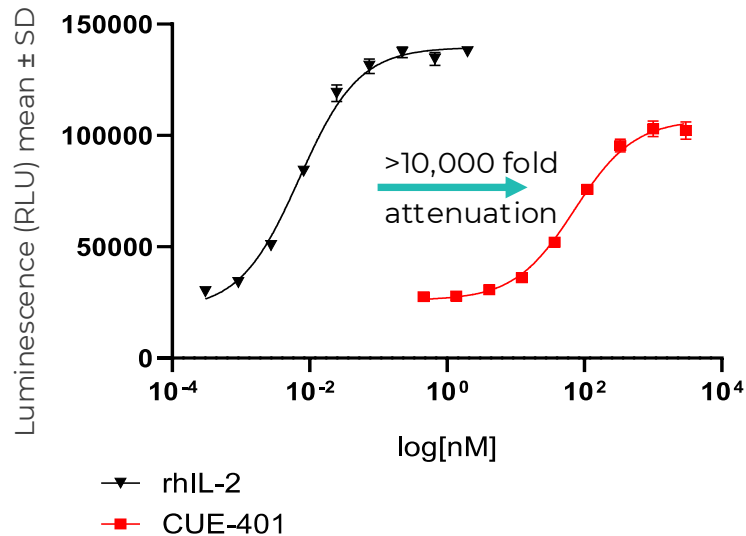
Affinity attenuated;
same as in CUE-100 series



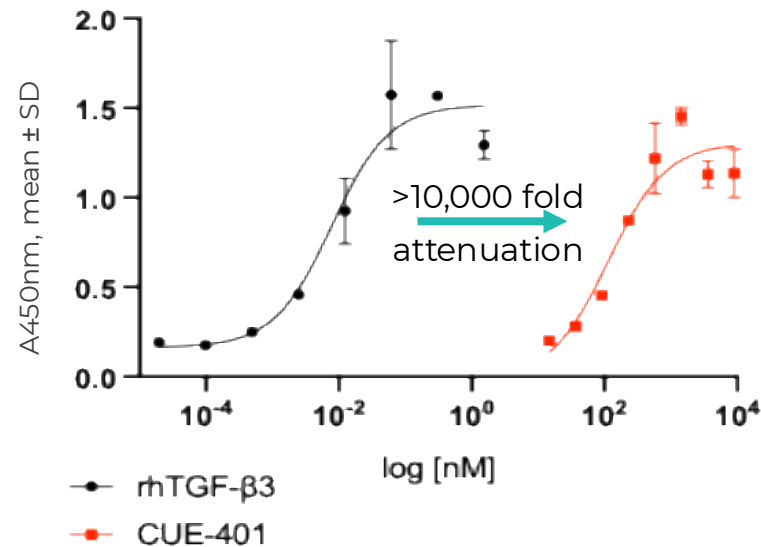
TGF- β Variant

Affinity attenuated;
improved safety and
manufacturability

IL-2 Induced Reporter



TGF- β -Induced Signaling



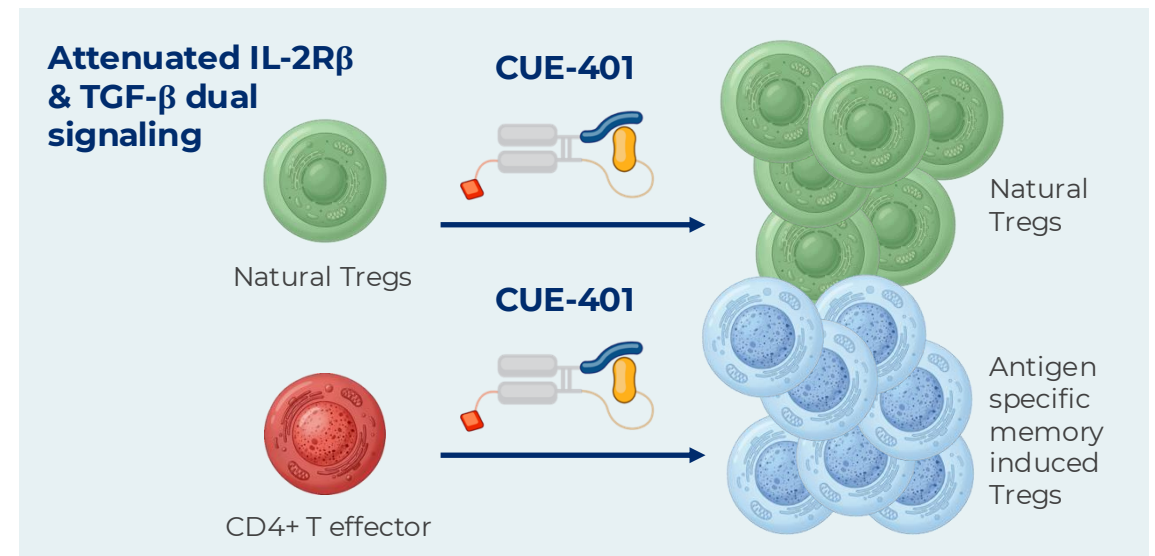
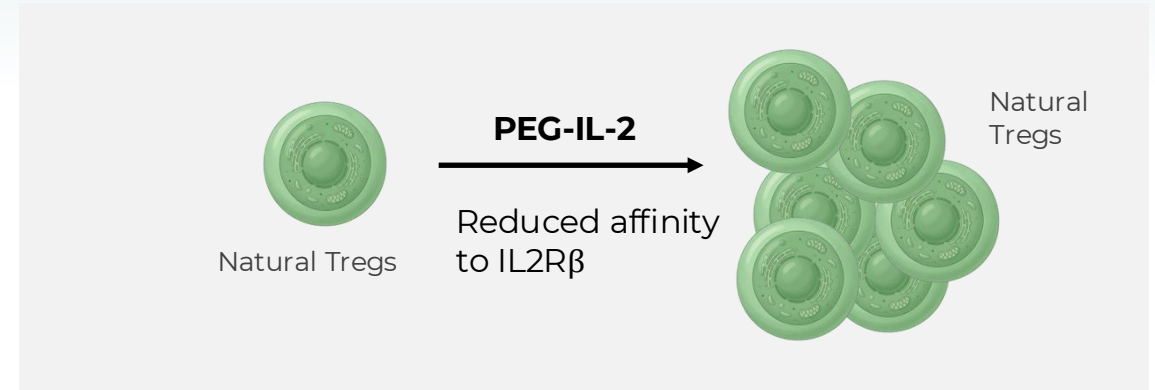
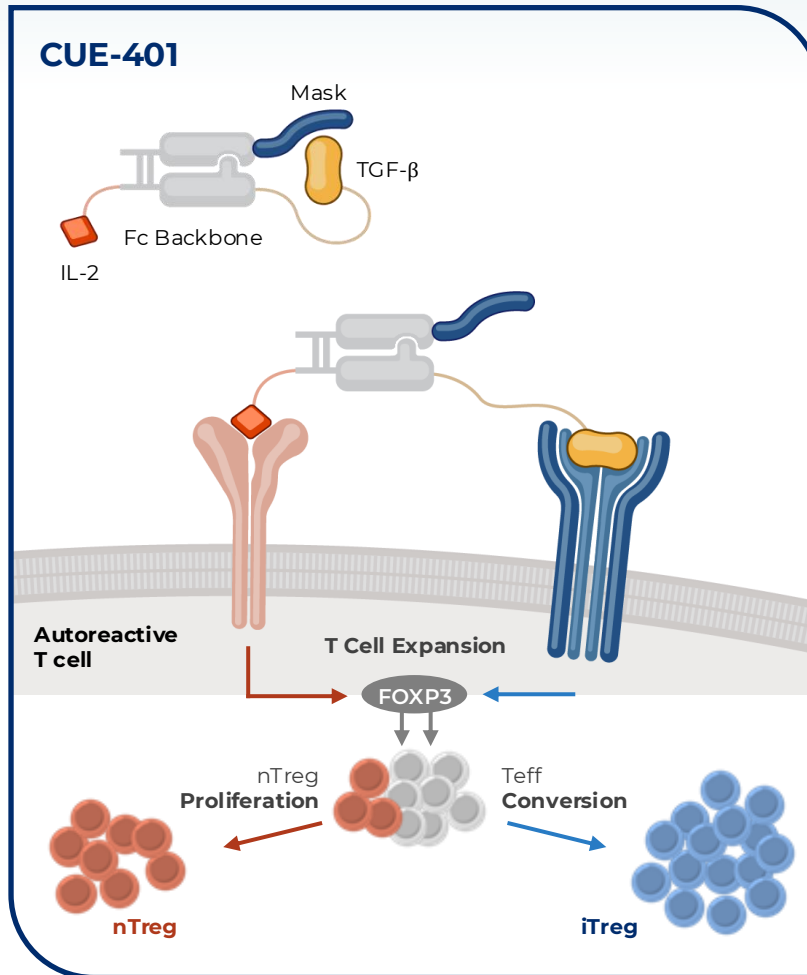
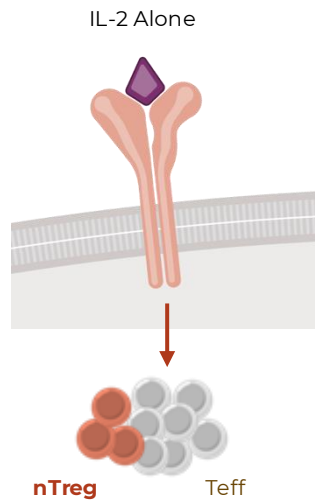
Potential for Elegant Protein Engineering to Enhance Safety and Enable Manufacturing

- Safety and efficacy observed in multiple animal models and toxicology program
- Production is established with successful production of 2000L batch. Master Cell Bank with cGMP production titer of ~ 8 g/L created
- Half-life in non-human primates around 3 days



CUE-401: Highly Differentiated and Potentially Best-in-Class Expanding Tregs and T cells to Promote Tolerance

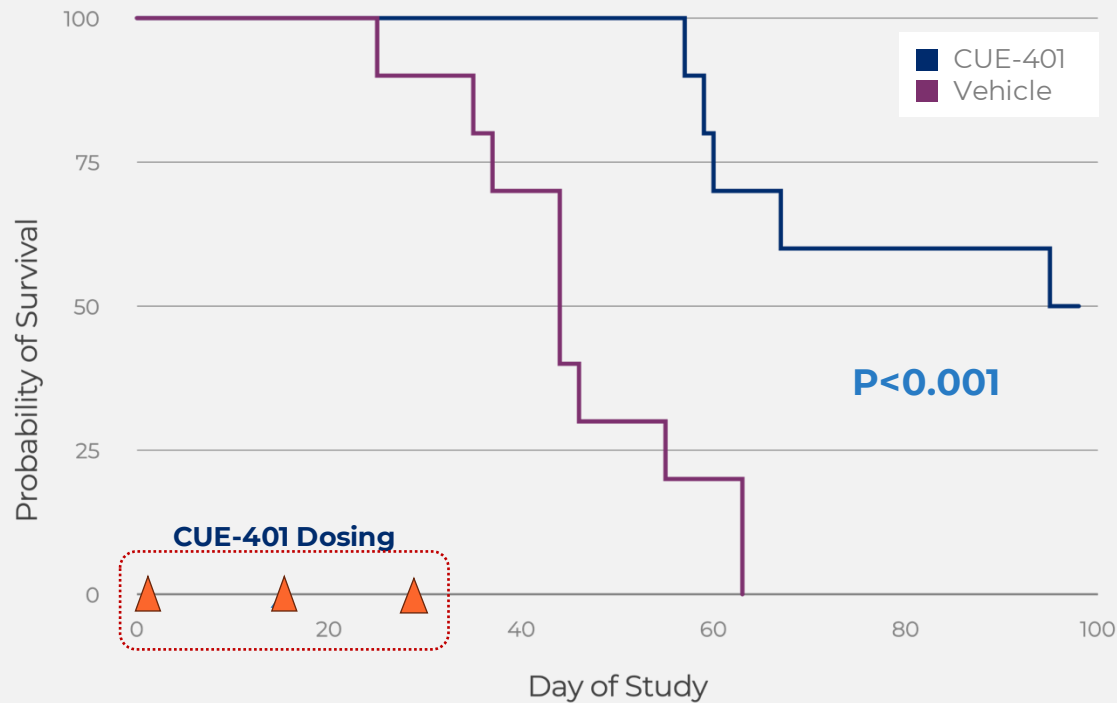
Mechanism confirmed by recent article from Stanford University*



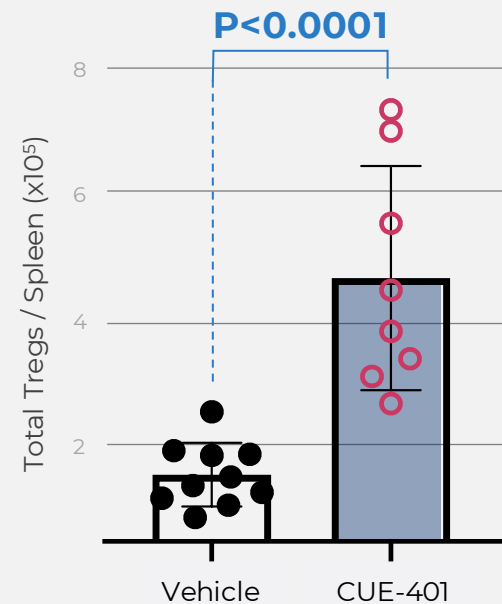
CUE-401: Durable Benefit in Model of Acute GVHD

Increased Tissue Tregs & Maintenance of Graft 9+ Weeks Post-Treatment

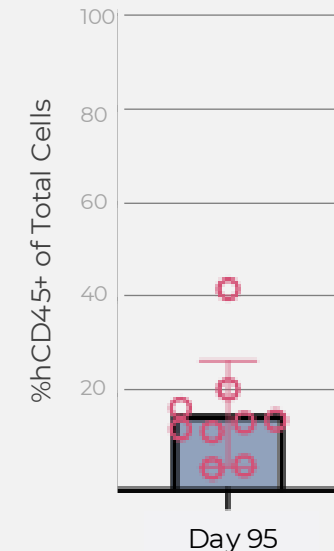
Delayed GVHD & Increased Overall Survival



Increased Treg Numbers in GVHD Target Tissue



Persistence of Human T Cell Graft Provides Evidence of Tolerance

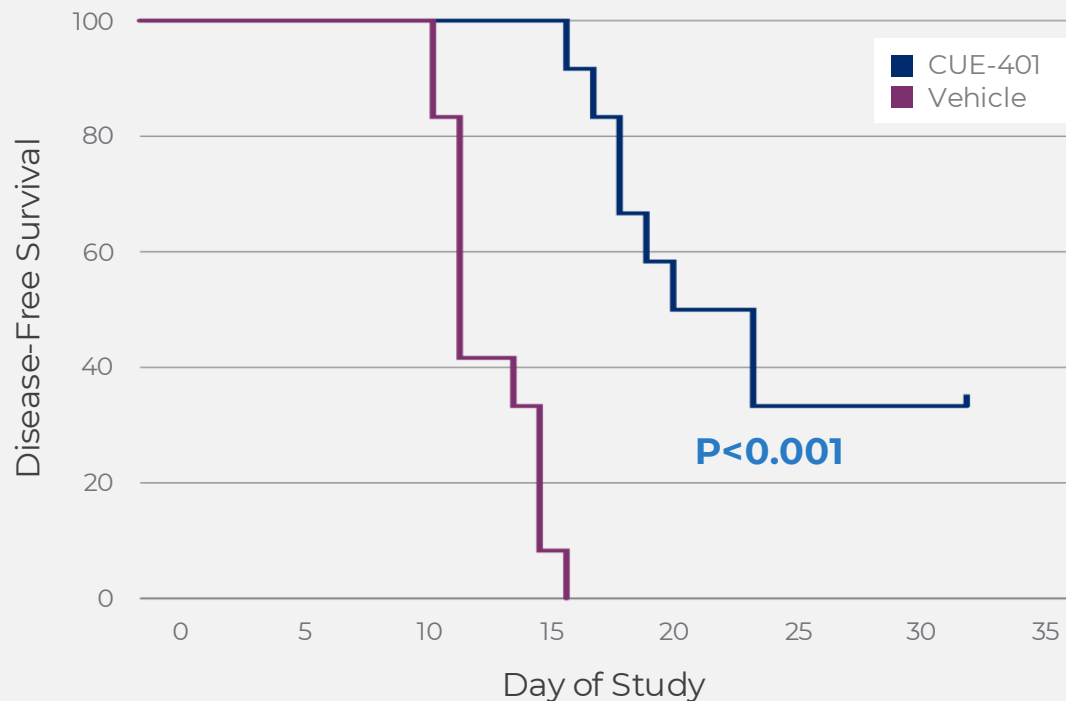


CUE-401: Efficacy in Diverse Models of Disease

Functional Suppression of Inflammation in Multiple Disease Models Supports Broad Applicability in the Clinic

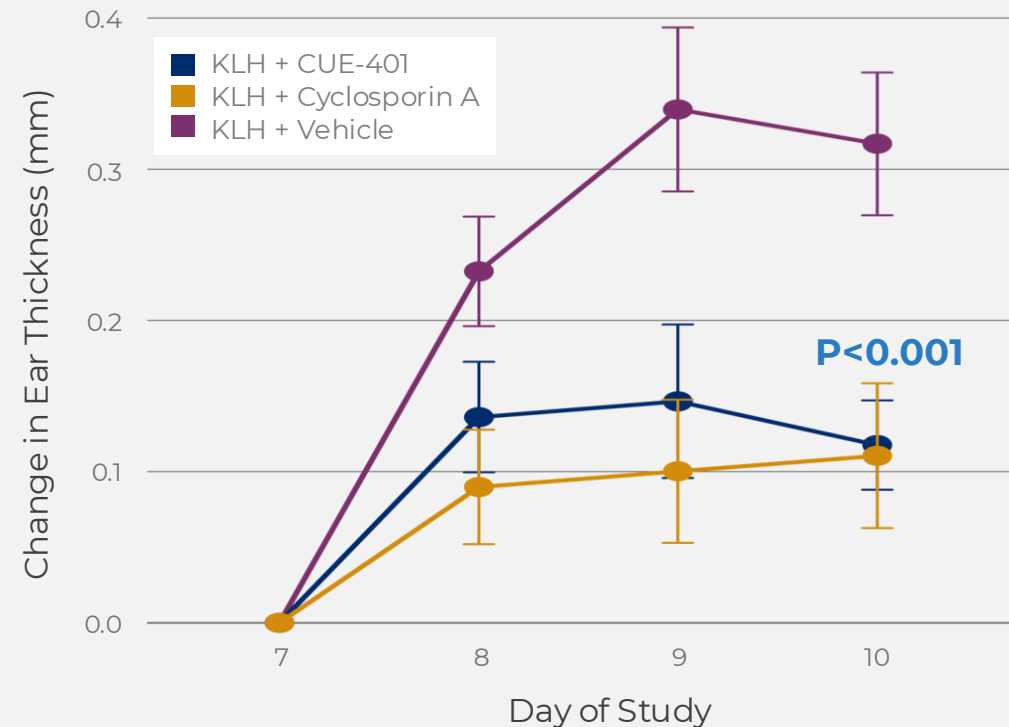
EAE Model of Multiple Sclerosis

Significant inhibition and delay of disease onset



Delayed Type Hypersensitivity – T Cell Mediated

Significant inhibition of cutaneous inflammation





Dr. Richard DiPaolo

Coordinated Delivery of IL-2 and TGF- β

Professor and Chair, Department of Molecular Microbiology & Immunology, Saint Louis University



SAINT LOUIS UNIVERSITY

SCHOOL OF MEDICINE

Rich DiPaolo, Ph.D.
Professor and Chair
Department of Molecular Microbiology & Immunology
Saint Louis University School of Medicine



The Challenge: Achieving Immune Tolerance to Treat Autoimmunity

Autoimmune diseases arise when peripheral tolerance breaks down.

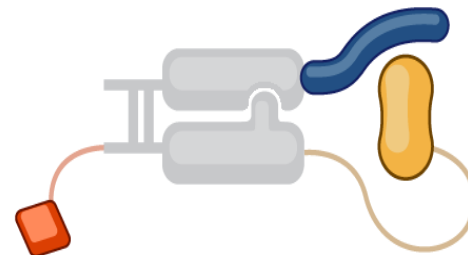
Regulatory T cells are essential for preventing this but selectively activating them in vivo is challenging.

IL-2 and TGF- β are both required for Treg biology, yet coordinating these signals pharmacologically has been challenging.

CUE-401 was designed to provide coordinated **IL-2 and TGF- β signals** in vivo to induce/expand/activate Tregs.

CUE-401

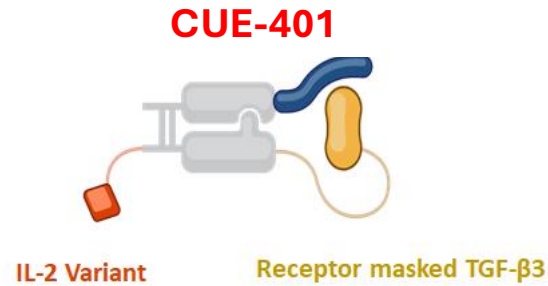
Fc Backbone



IL-2 Variant

Receptor masked TGF- β 3

In Vitro: Three Key Outcomes

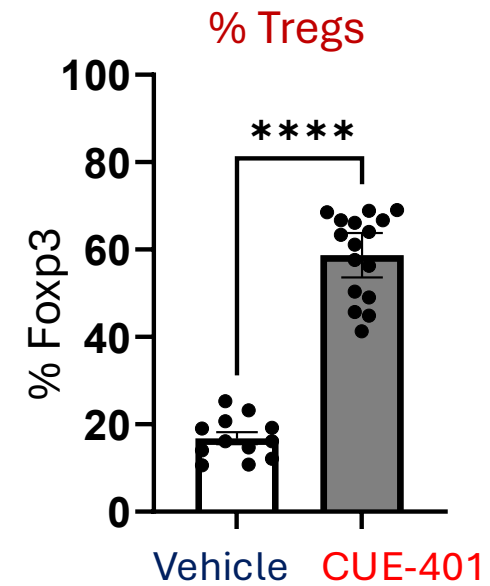
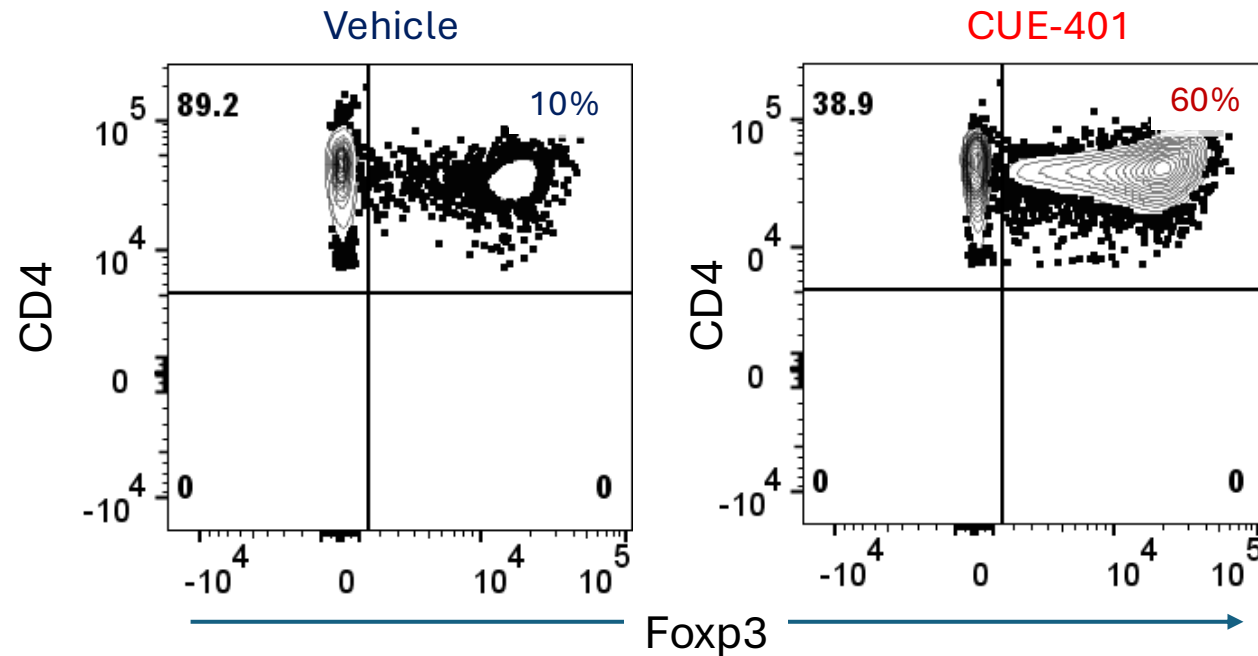


First, CUE-401 **induces** **Foxp3⁺ iTregs** from naïve CD4⁺Foxp3⁻ T cells at very high efficiency.

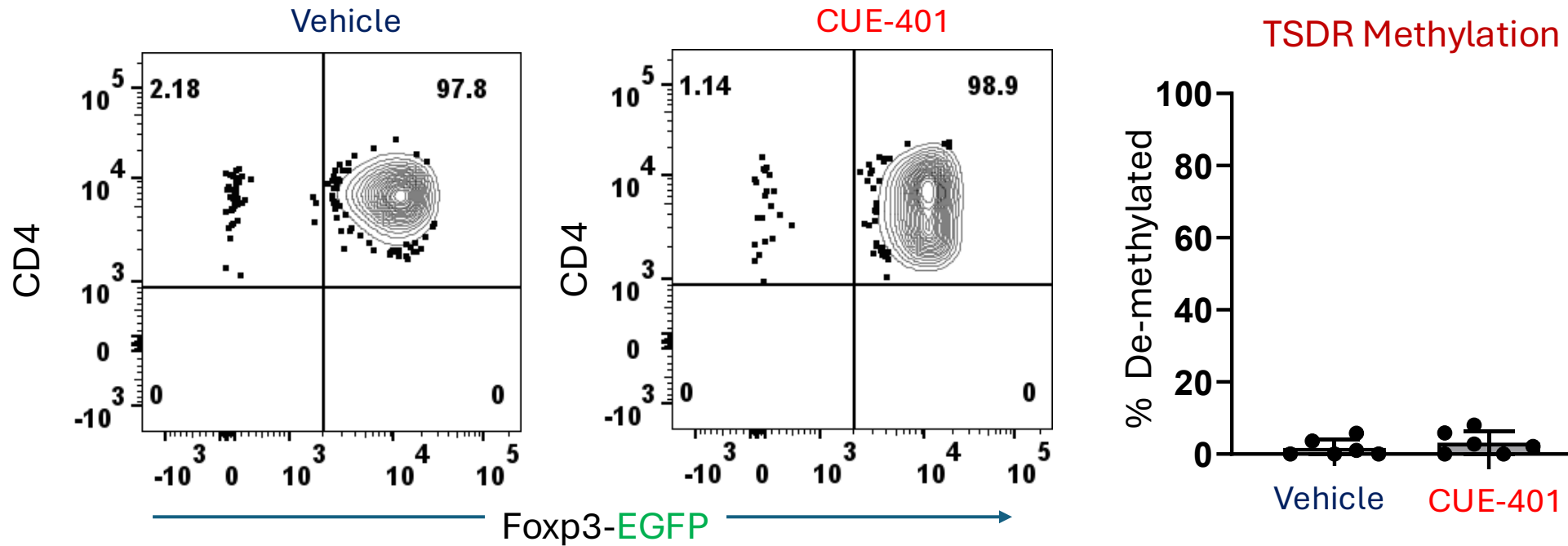
Second, it **expands** **endogenous CD4⁺Foxp3⁺ Tregs** while maintaining Foxp3 expression.

Third, it **reprograms** **CD4⁺CD44^{hi} effector/memory T cells** toward a less inflammatory state, reducing cytokine production.

Robust Treg Expansion after a Single Dose of CUE-401



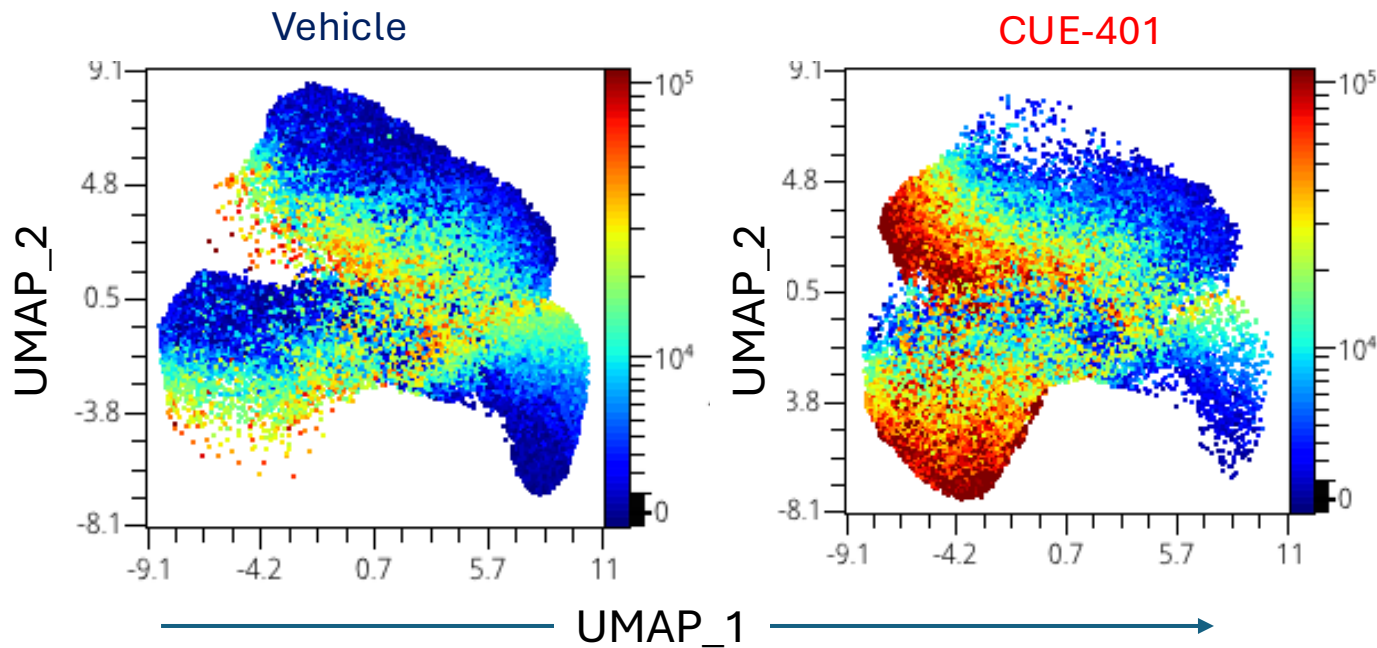
CUE-401 Expanded Tregs are Stable



CUE-401 Expanded Tregs are Activated



Flow Cytometry



GITR^{hi}
CD25^{hi}
CTLA-4^{hi}
CD103^{hi}
Ki67

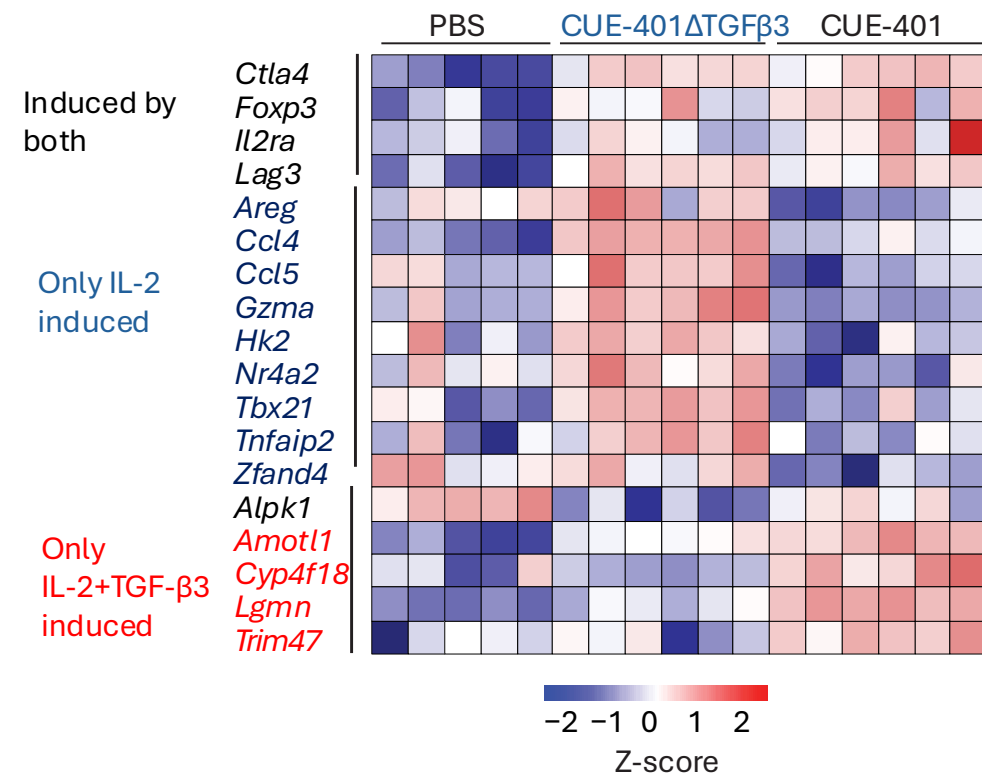
RNA Seq

Itgae (CD103),
Nrp1,
Il2ra,
Il2rb,
Lag3,
Tnfrsf18 (GITR),
Icosl,
Klrg1

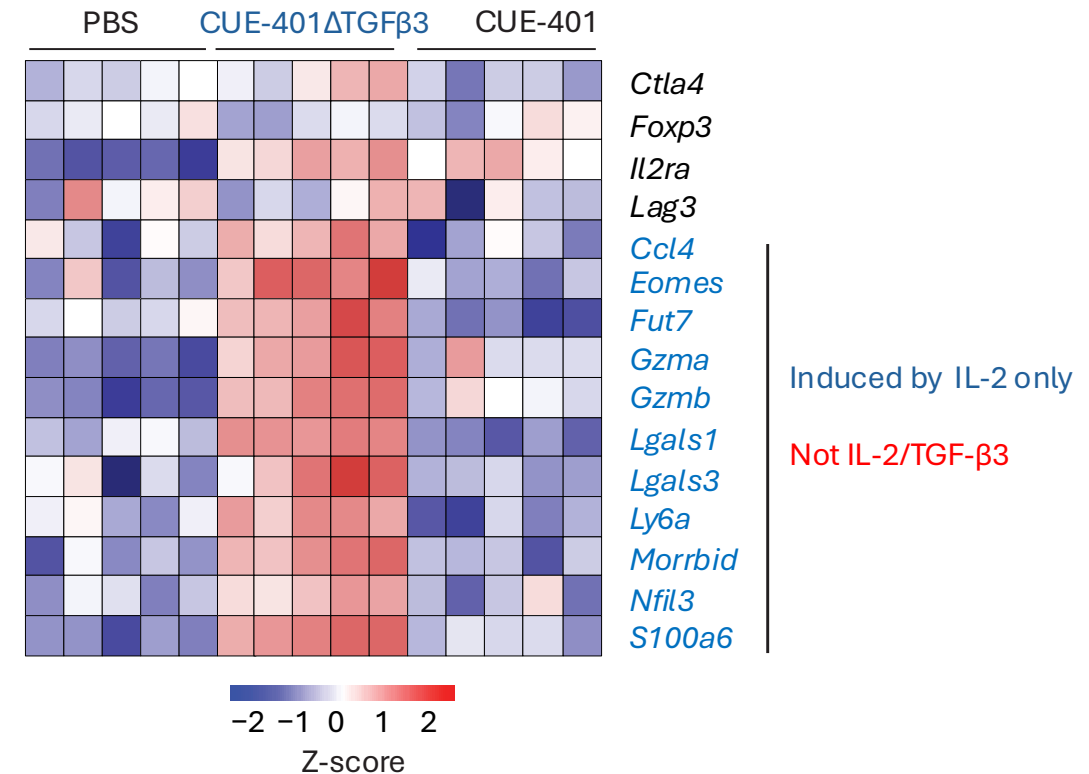
CUE-401 is Distinct from IL-2 and More Specific for Tregs



Sorted Tregs



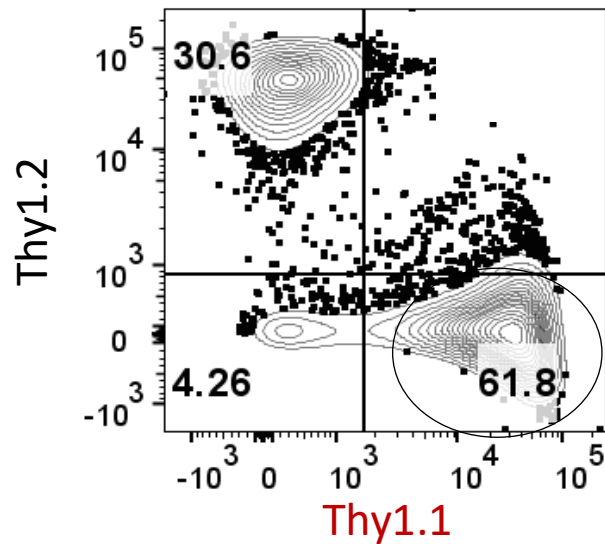
Sort Tconv



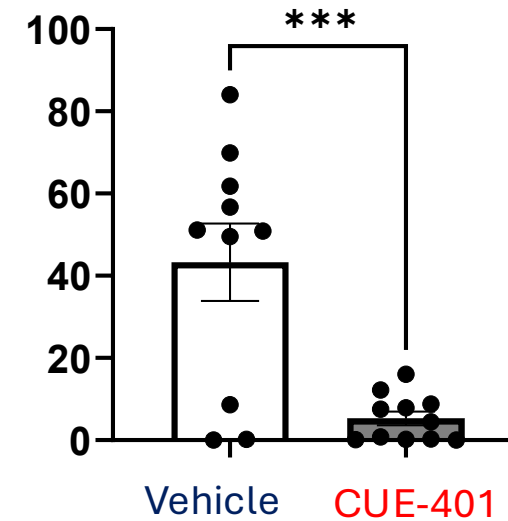
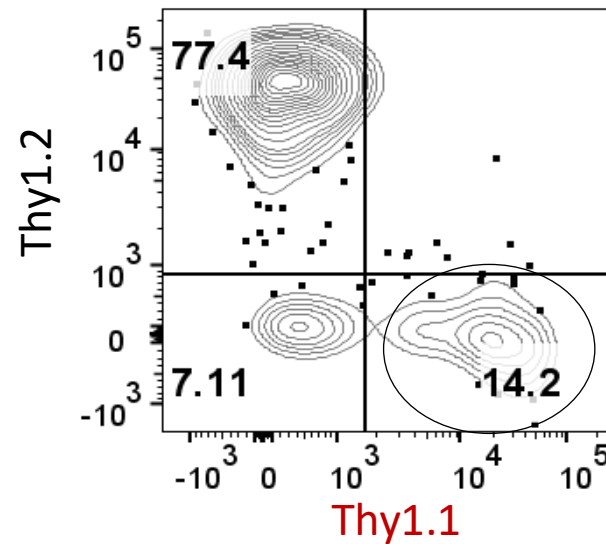
CUE-401 Suppresses Autoreactive T cells



Vehicle Treated



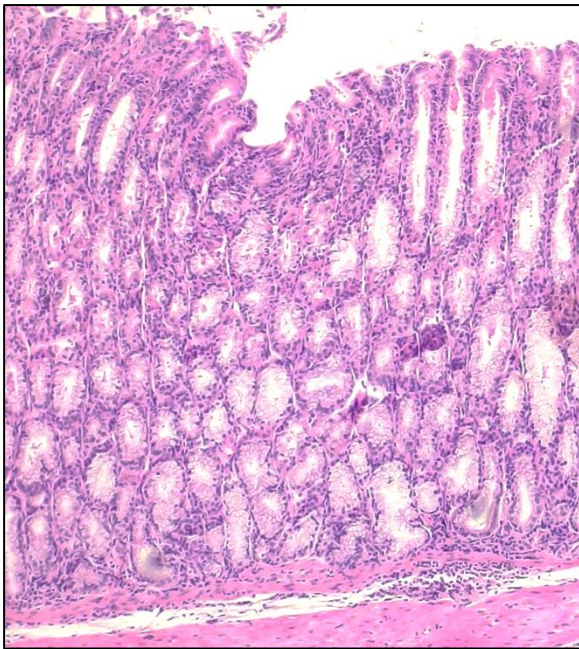
CUE-401 Treated



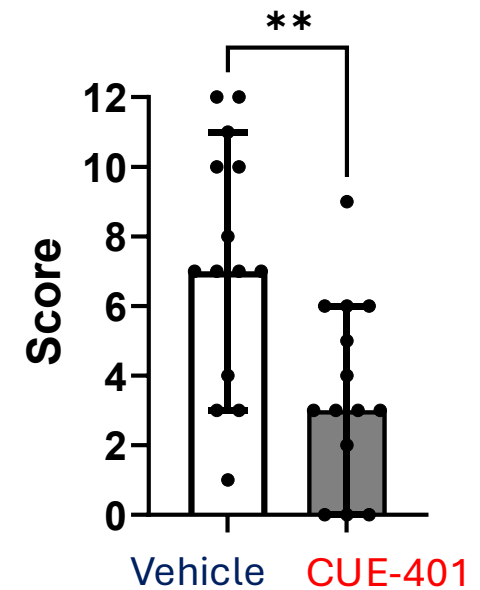
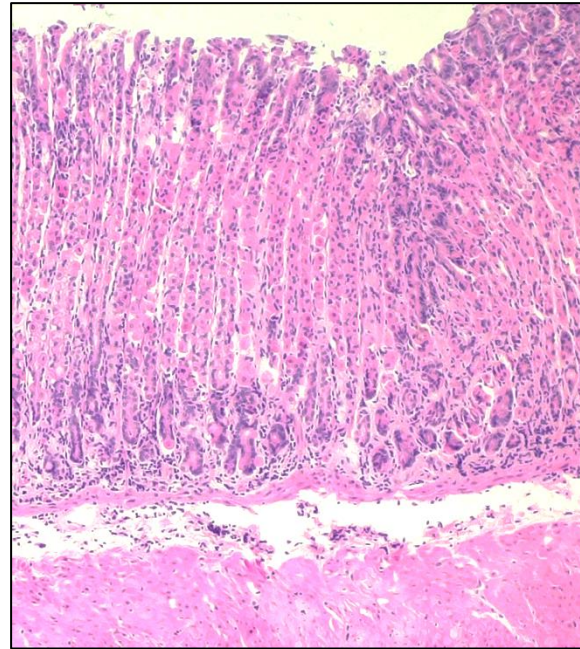
CUE-401 Provides Durable Protection from Autoimmunity



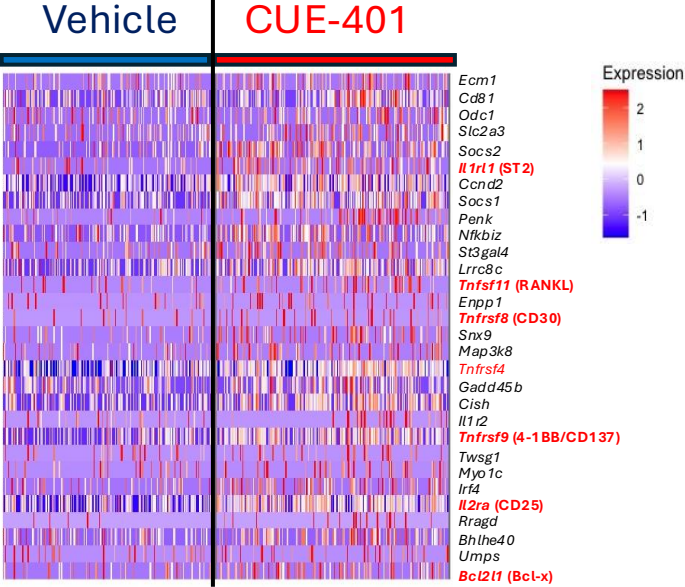
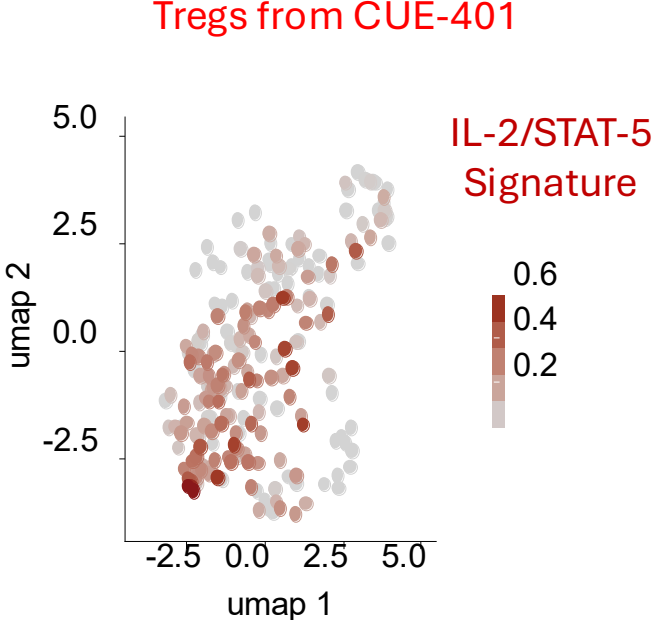
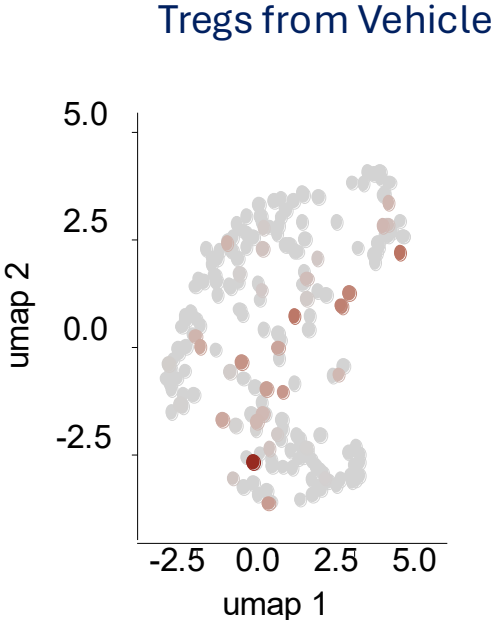
Vehicle Treated



CUE-401 Treated



CUE-401 Expands/Activates Tregs During Autoimmunity



- Il2ra* (CD25)**
- Tnfrsf11* (RANKL)**
- Tnfrsf8* (CD30)**
- Tnfrsf9* (4-1BB/CD137)**
- Bcl2l1* (Bcl-x)**

Key Takeaways

To Summarize:

Coordinated IL-2 and TGF- β 3 signaling delivered by CUE-401 induces, expands, and stabilizes Tregs; specifically targets Tregs and avoids effector activation; and produces durable immune tolerance. This represents a pharmacologic strategy for in vivo Treg programming in autoimmune settings.

Implications & Future Directions

We think this approach has broad potential applications in autoimmunity, transplantation, and chronic inflammatory diseases

Acknowledgments

I'd like to thank members of the DiPaolo Lab at Saint Louis University and our collaborators at Cue Biopharma.



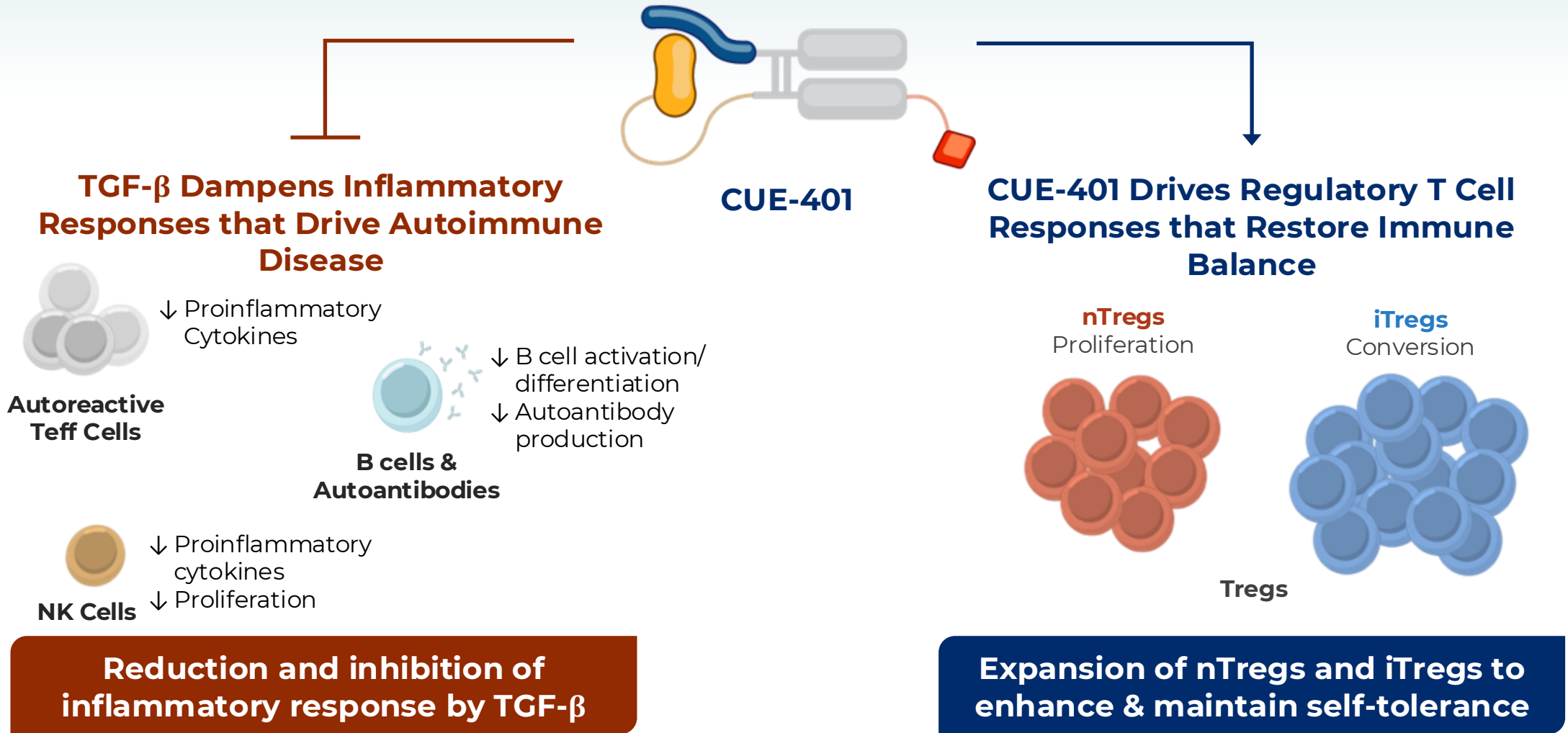
Dr. Jonathan Kay

Effective Immunomodulating Capabilities

Timothy S. & Elaine L. Peterson Chair in Rheumatology at UMass Chan Medical School, Professor of Medicine & Population & Quantitative Health Sciences



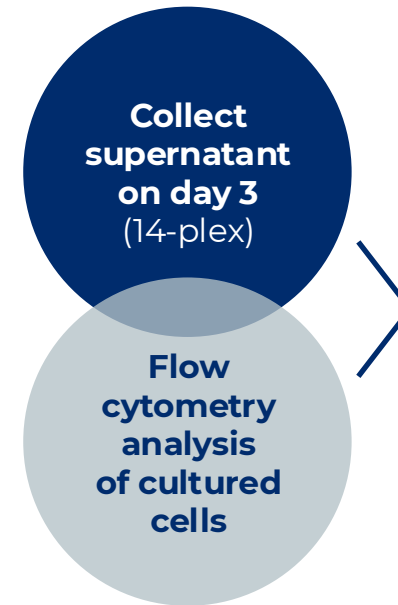
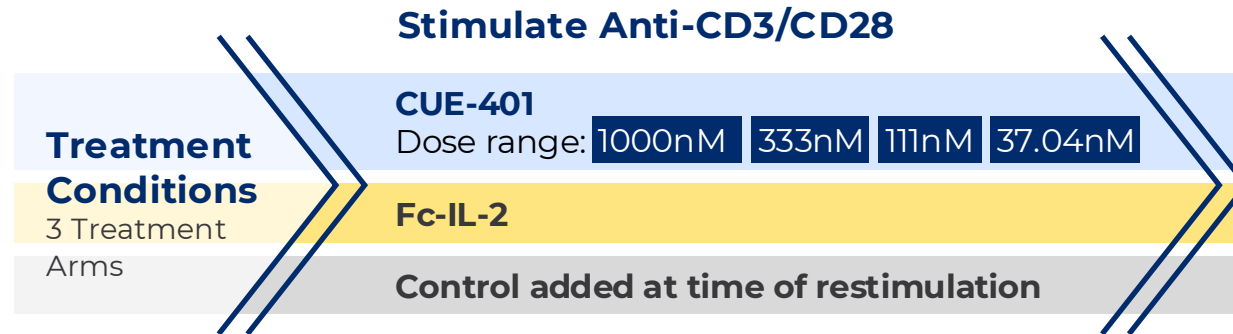
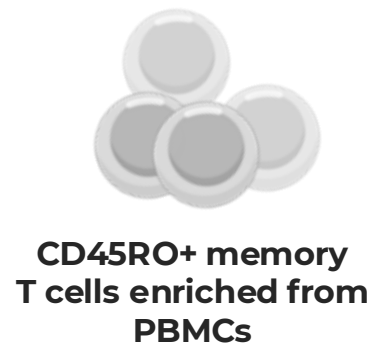
CUE-401 Harnesses Complementary Methods of Immunoregulation



Method to Measure Effects of CUE-401 on Effector T cell Cytokine Production

Hypothesis

CUE-401 suppresses production of proinflammatory cytokines by human CD4+ Teff/memory cells in a dose-dependent manner

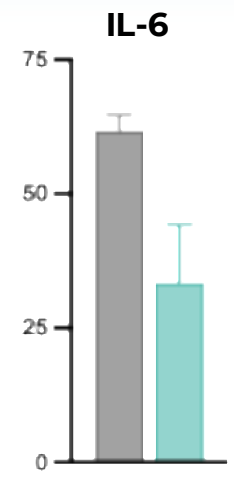
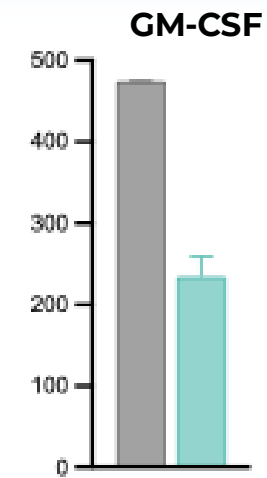
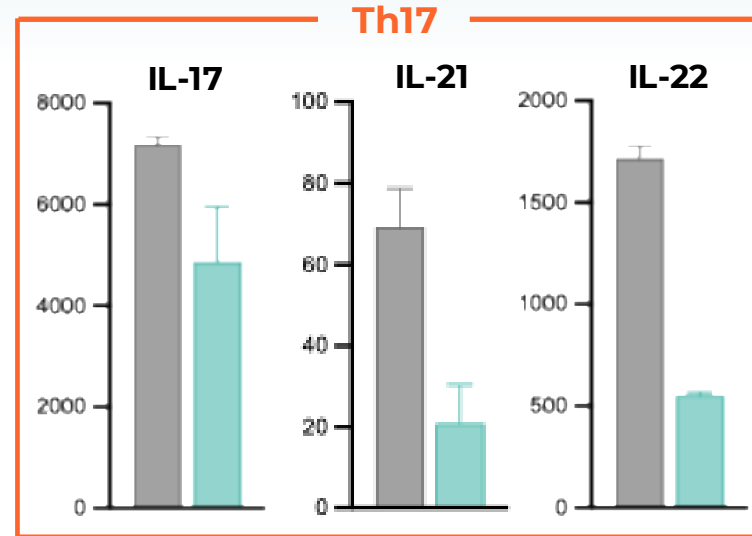
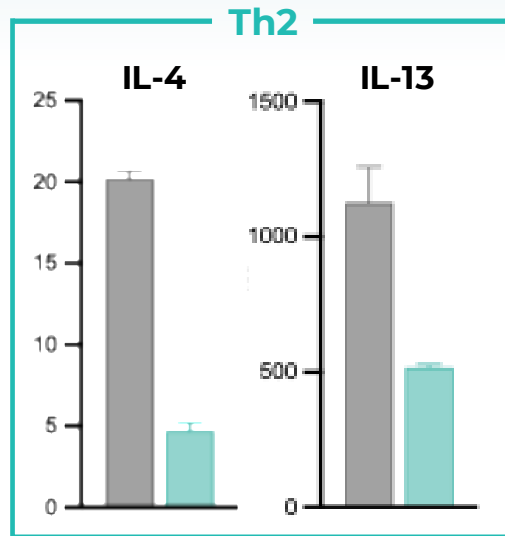
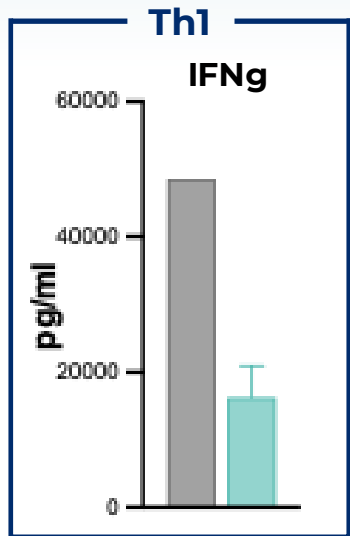


Analyte

- GM-CSF
- IFN- γ
- IL-4
- IL-5
- IL-6
- IL-9
- IL-10
- IL-13
- IL-17A
- IL-21
- IL-22
- IL-31
- MIP-1 α
- TNF- α

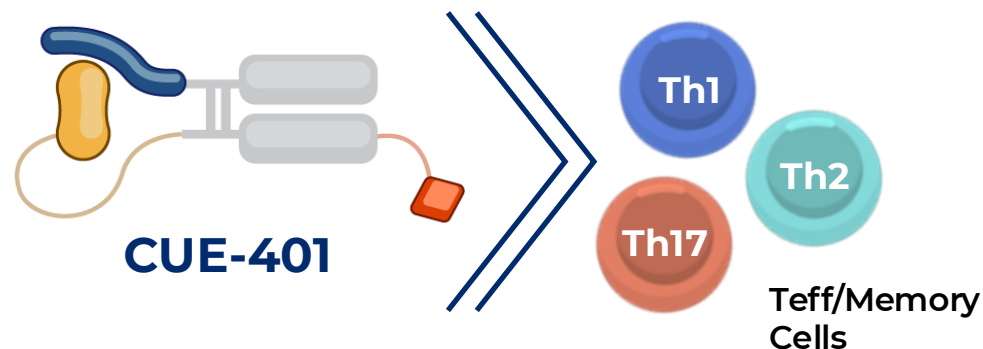


CUE-401 Inhibits Proinflammatory Cytokine Production by Teff/mem Cells



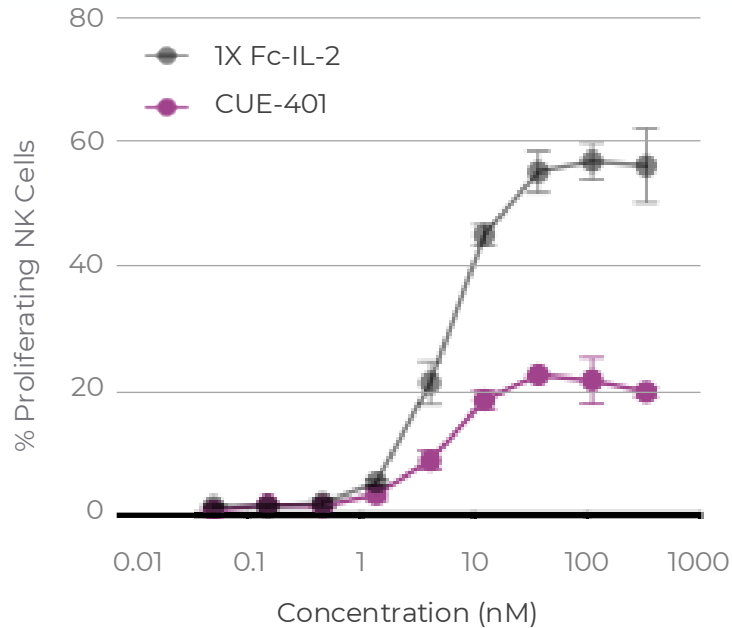
■ Fc-IL2
■ CUE-401

▼ Proinflammatory cytokines associated with Th1, Th2, and Th17 responses

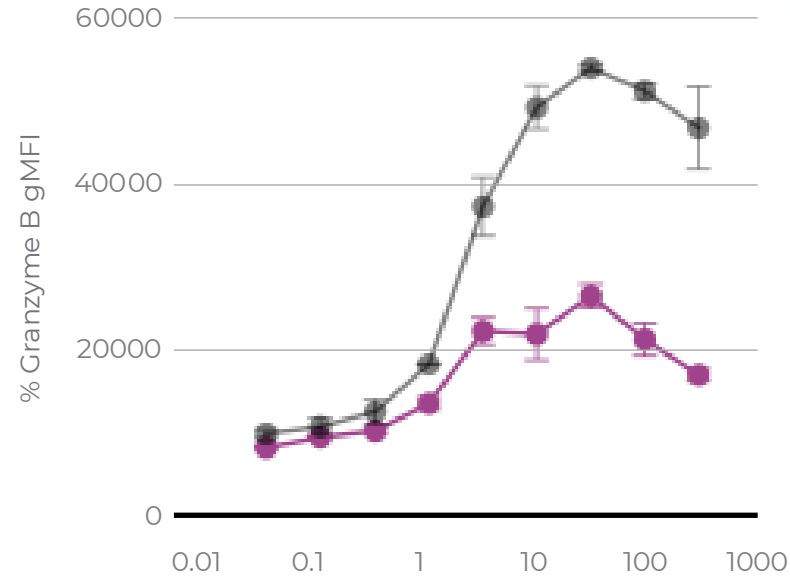


CUE-401 Restrains NK Cell Activity Induced by IL-2

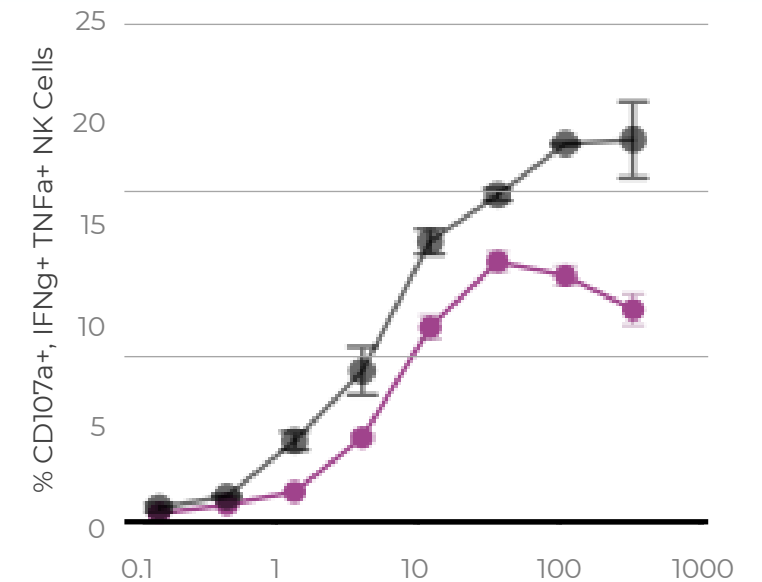
↓ IL-2 Induced NK Cell Proliferation



↓ NK Cell Granzyme B Expression



↓ Cytokine Producing NK Cells



↑ **Greater Treg selectivity**

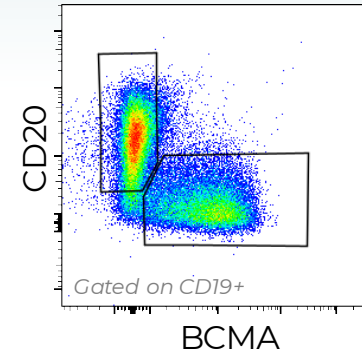
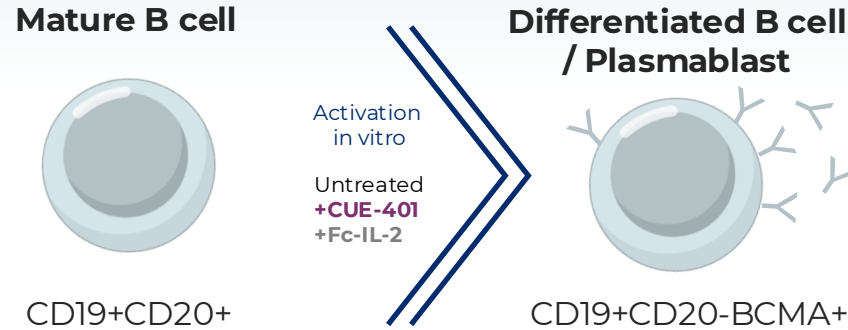
↓ Proliferation
↓ Cytokine and Granzyme B

↓ Potentially non-selective effects due to NK cell expansion

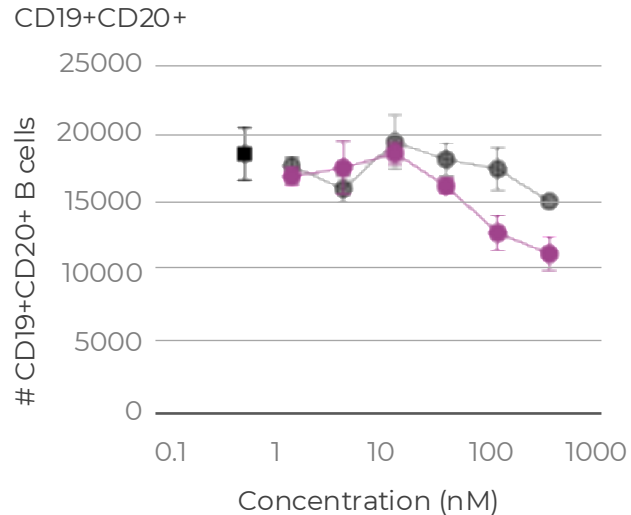


CUE-401 Suppresses Plasma Cell Differentiation and Antibody Production

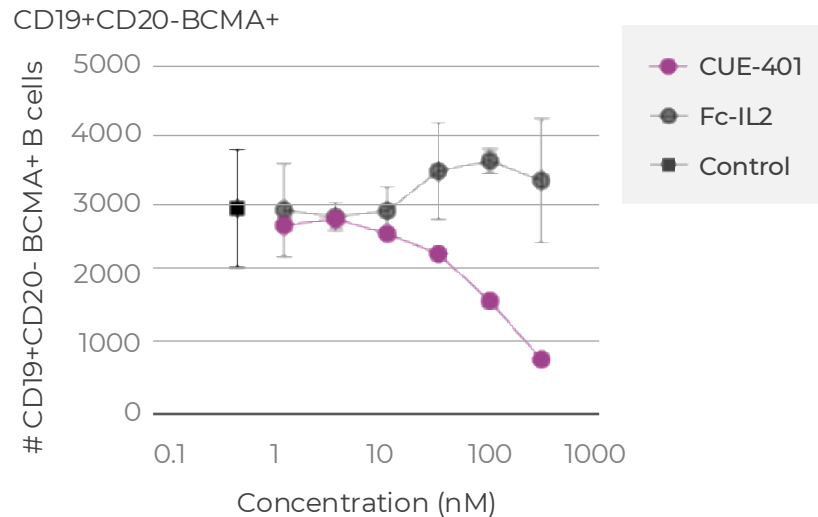
CUE-401 does not alter the mature B cell population, but suppresses differentiation of plasma cells and antibody production



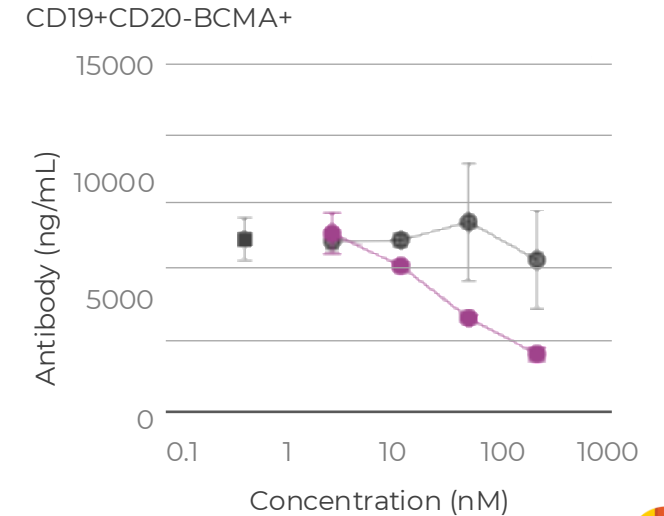
Mature B Cells



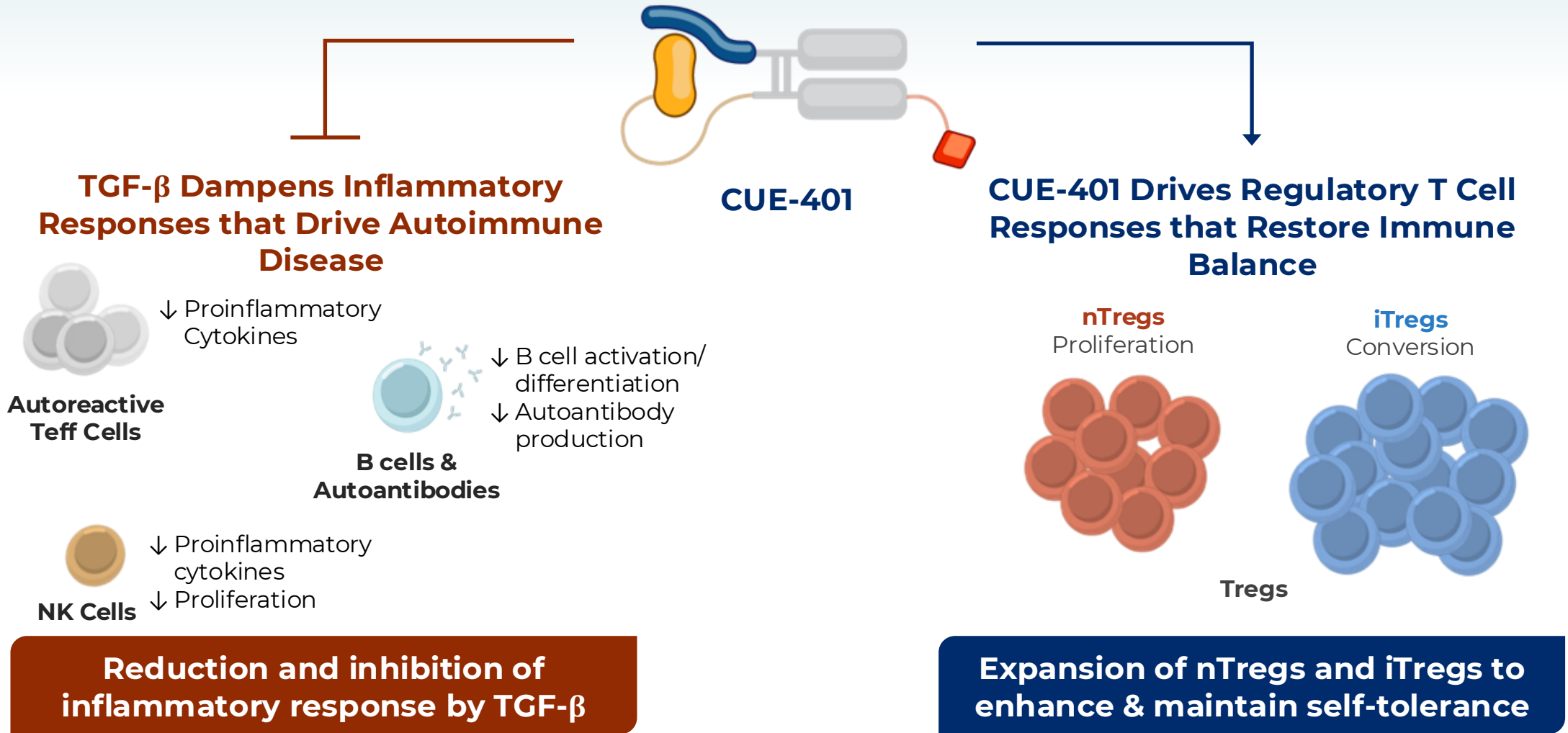
Differentiated B Cells



Antibody Production



CUE-401 Harnesses Complementary Methods of Immunoregulation



Phase 1 Single and Multiple Ascending Dose Study

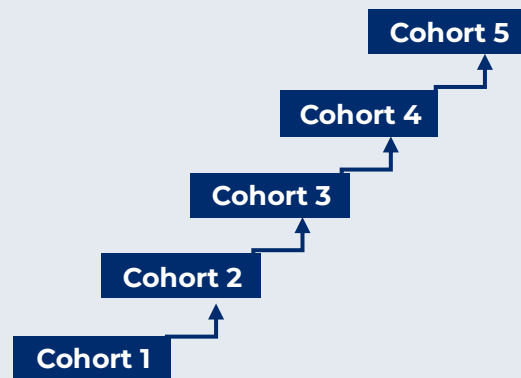
Study Initiation Planned Q3 2026 with SAD Readout by Q4 2026 and MAD Readout Complete Q2 2027

PART 1

Single Ascending Dose (SAD) in Healthy Volunteers

Phase 1 (Part 1) Study Design:

- Blinded, randomized, placebo controlled
- n=40 subjects over 5 dose levels

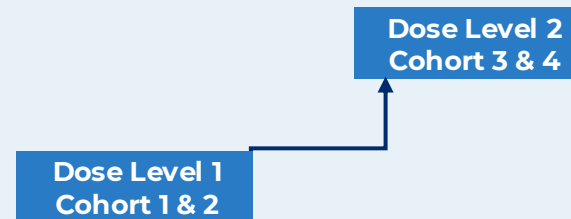


PART 2

Multiple Ascending Dose (MAD) in Healthy Volunteers

Phase 1 (Part 2) Study Design:

- Blinded, randomized, placebo controlled
- n=32 subjects over 2 dose levels



Total Study Period: 12 months with data readouts within 6 months

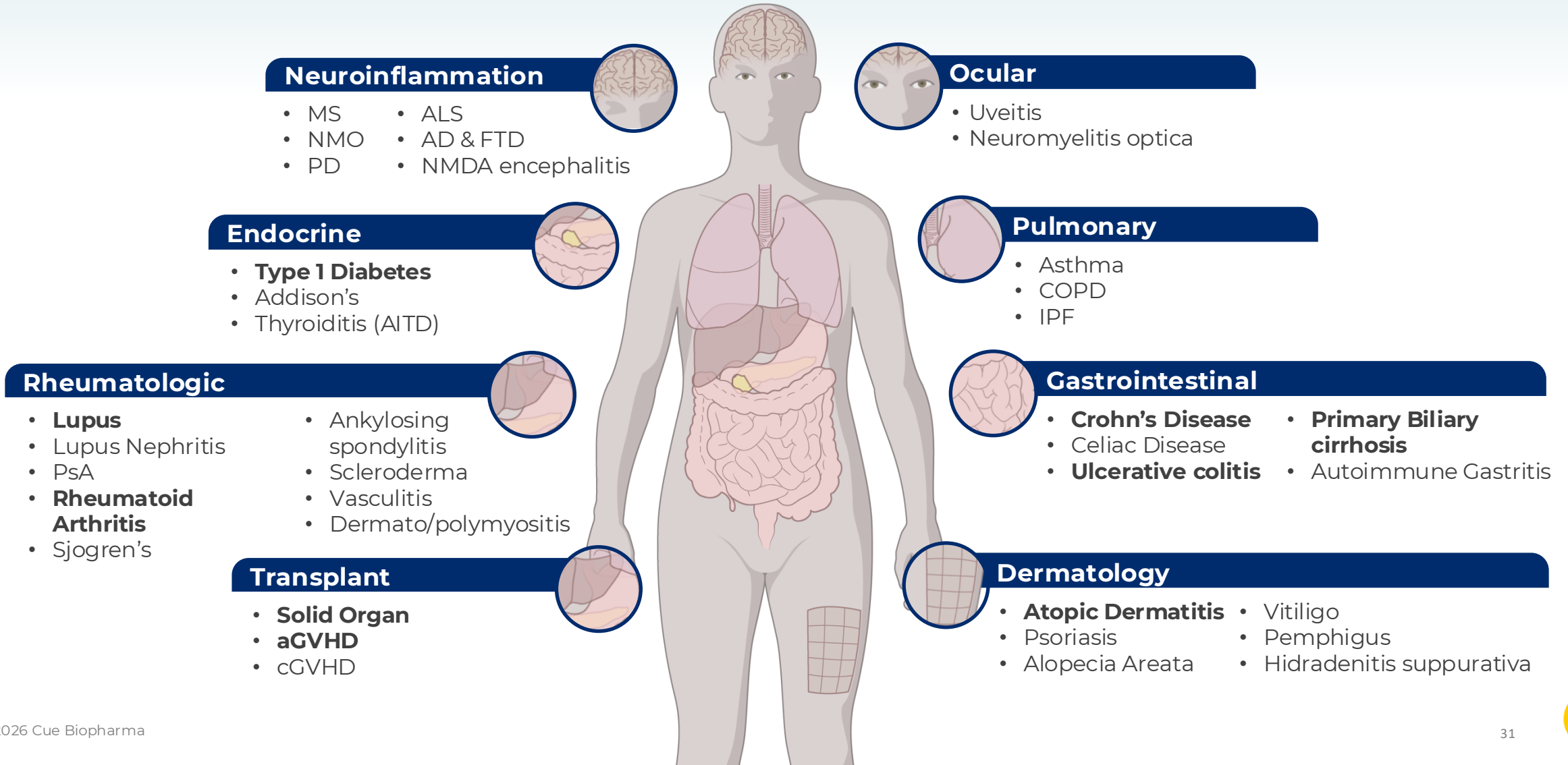
Endpoints:

- Safety and tolerability
- Biomarker driven PK/PD characterization
 - T cell phenotyping
 - Treg/Teff ratios
 - T cell, B cell, NK cell
 - Cytokines



Unique Mechanism of Action

Robust Restoration of Immune Regulatory Control is the Key to Accessing Expansive Treatment Opportunities



KOLs & Cue Management Discussion and Q&A Session





Thank you

About Cue Biopharma

The innate sophistication of the immune system inspires us to engineer precision immunotherapies that transform patients' lives.