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Corporate Overview

Shattuck Labs, Inc.

NASDAQ: STTK

November 6, 2025

Forward-Looking Statements

This presentation contains “forward-looking statements” within the meaning of the federal securities laws, which statements are subject to substantial risks and uncertainties and are based on our estimates and assumptions. All statements, other than statements of historical facts included in this presentation, are forward-looking statements, including statements concerning: our plans, objectives, goals, strategies or intentions relating to products and markets; whether the common stock warrants will be exercised and provide us with additional capital; the closing of the private placement and associated satisfaction of closing conditions, including with respect to clearance of our IND; the use of proceeds from the private placement; the potential purity, potency, safety, and clinical benefits of our product candidates, including SL-325; clearance of our IND filing for SL-325; the anticipated timing and design of our planned and ongoing preclinical studies and clinical trials, including timing of enrollment; the anticipated timing for data and the association of preclinical data with potential clinical benefit; the timing of anticipated milestones, plans and objectives of management for future operations; the anticipated development of additional preclinical pipeline programs; potential addressable market size; and our expectations regarding the time period over which our capital resources will be sufficient to fund our anticipated operations. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “design,” “estimate,” “predict,” “potential,” “plan,” or the negative of these terms, and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that could cause our actual results to differ materially from the forward-looking statements expressed or implied in this presentation, in addition to those risks and uncertainties, such as global macroeconomic conditions and related volatility; expectations regarding the initiation, progress, and expected results of our preclinical studies, clinical trials and research and development programs; expectations regarding the timing, completion and outcome of our clinical trials; the unpredictable relationship between preclinical study results and clinical study results; the timing or likelihood of regulatory filings and approvals; our expectations regarding the overall benefit of the strategic prioritization of our pipeline; liquidity and capital resources; and other risks and uncertainties described in “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K (File No. 001-39593) for the fiscal year ended December 31, 2024 and elsewhere in such filing and in our other periodic reports and subsequent disclosure documents filed with the U.S. Securities and Exchange Commission.

We cannot assure you that we will realize the results, benefits or developments that we expect or anticipate or, even if substantially realized, that they will result in the consequences or affect us or our business in the way expected. Forward-looking statements are not historical facts, and reflect our current views with respect to future events. Given the significant uncertainties, you should evaluate all forward-looking statements made in this presentation in the context of these risks and uncertainties and not place undue reliance on these forward-looking statements as predictions of future events. All forward-looking statements in this presentation apply only as of the date made and are expressly qualified in their entirety by the cautionary statements included in this presentation. We have no intention to publicly update or revise any forward-looking statements to reflect subsequent events or circumstances, except as required by law.

We obtained the data used throughout this presentation from our own internal estimates and research, as well as from research, surveys and studies conducted by third parties. Internal estimates are derived from publicly available information released and our own internal research and experience, and are based on assumptions made by us based on such data and our knowledge, which we believe to be reasonable. In addition, while we believe the data included in this presentation is reliable and based on reasonable assumptions, we have not independently verified any third-party information, and all such data involve risks and uncertainties and are subject to change based on various factors.

This presentation concerns a discussion of investigational drugs that are under preclinical and/or clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. They are currently limited by Federal law to investigational use, and no representations are made as to their safety or effectiveness for the purposes for which they are being investigated.

We Are Focused on Improving the Lives of Patients



OUR PURPOSE

Develop novel biologics for inflammatory and immune-mediated diseases



OUR VALUES

Bold, respectful, honest, balanced, grateful



OUR MISSION

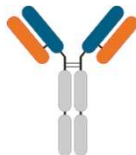
Work with a sense of urgency, focused on scientific excellence and thoughtful stewardship of resources, to translate innovative ideas into medicines that improve the lives of patients with serious diseases



OUR VISION

Build incredible therapeutics off the beaten path by challenging ourselves to think differently

Shattuck Labs Overview

Shattuck Labs (NASDAQ: STTK)	Clinical-stage biotechnology company pioneering the development of novel therapeutics targeting tumor necrosis factor (TNF) superfamily receptors for the treatment of patients with inflammatory and immune-mediated diseases
Lead Program: SL-325	 • Potential first-in-class blocking antibody targeting DR3, the receptor for TL1A • Picomolar binding affinity to DR3 and overlapping epitope with TL1A • Potential for superior efficacy in comparison to TL1A blocking antibodies • Initial clinical development in inflammatory bowel disease (IBD) • Enrollment ongoing in Phase 1 clinical trial in healthy volunteers
Preclinical Pipeline	• SL-425, a half-life extended DR3 blocking antibody • Bispecific antibodies targeting DR3 and other clinically validated targets in IBD
Experienced Team and Strong Cash Position	• Highly experienced management team, board of directors, and scientific advisory board • \$86.1 million in cash and cash equivalents as of September 30, 2025 • Cash runway expected to fund planned operations and clinical development into 2029¹

Highly Experienced Management and Board

Management Team



Taylor Schreiber, MD, PhD

Chief Executive Officer



Lini Pandite, MD, MBA

Chief Medical Officer



Casi DeYoung, MBA

Chief Business Officer



Andrew R. Neill, MBA

Chief Financial Officer



Abhinav Shukla, PhD

Chief Technical Officer



Suresh de Silva, PhD

Chief Scientific Officer



Stephen Stout, PhD

General Counsel,
Corporate Secretary and
Chief Ethics and
Compliance Officer

Board of Directors

Mona Ashiya, PhD

Member, OrbiMed Advisors

Dan Baker, MD

CEO of KiRa Biotech, Interim
CDO of Cue Biopharma, VP,
*Immunology, R&D at
Johnson & Johnson
(Janssen/Centocor)*

Helen M. Boudreau

*CFO of Proteostasis,
FORMA, Novartis US*

Neil Gibson, PhD

*Chief Scientific Officer, COI
Pharma; Chief Scientific
Officer, Pfizer Oncology*

George Golumbeski, PhD

Chairman of the Board; *EVP
of Business Development,
Celgene*

**Taylor Schreiber MD,
PhD**

Chief Executive Officer,
Shattuck

Clay Siegall, PhD

President, CEO and Chairman
of the Board of Immunome;
CEO & Founder of Seagen

Shattuck's Pipeline Targeting the TL1A/DR3 Pathway

Programs			Stage of Development		
Lead	Target(s)	Indications	Preclinical	IND-Enabling	Phase 1
SL-325	DR3	IBD			
SL-425 Extended Half-Life	DR3	IBD			
Bispecifics	DR3 x Undisclosed	Autoimmune			

- Developing potential first-in-class DR3 monospecific and bispecific antibodies
- Blocking DR3 may provide more potent inhibition of the TL1A/DR3 axis than TL1A blockade
- Blocking DR3 may prove to be less immunogenic than TL1A blockade



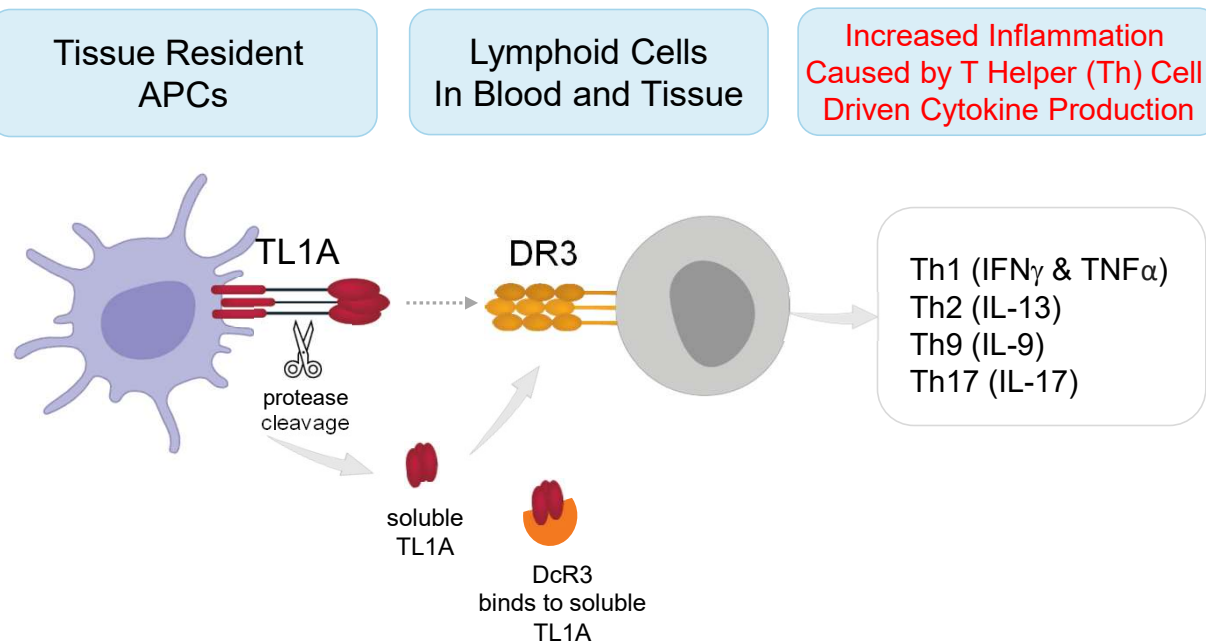
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TL1A / DR3 Biology

Rationale for Targeting the Receptor
In a Clinically-Validated Axis



TL1A Is the Sole Activating Ligand for DR3 and DR3 Activation Leads to Inflammation



TL1A/DR3 Axis Biology

- 1 TL1A is expressed primarily on tissue-resident antigen presenting cells (APCs), signals solely via DR3, and is neutralized by the soluble decoy receptor (DcR3)
- 2 DR3 is expressed by circulating and tissue-resident lymphoid cells and binds only to TL1A
- 3 Aberrant TL1A/DR3 pathway activation leads to inflammation, contributing to IBD and other autoimmune and inflammatory diseases

Clinical Validation of Blocking TL1A/DR3 Axis and Rationale for DR3 Targeting

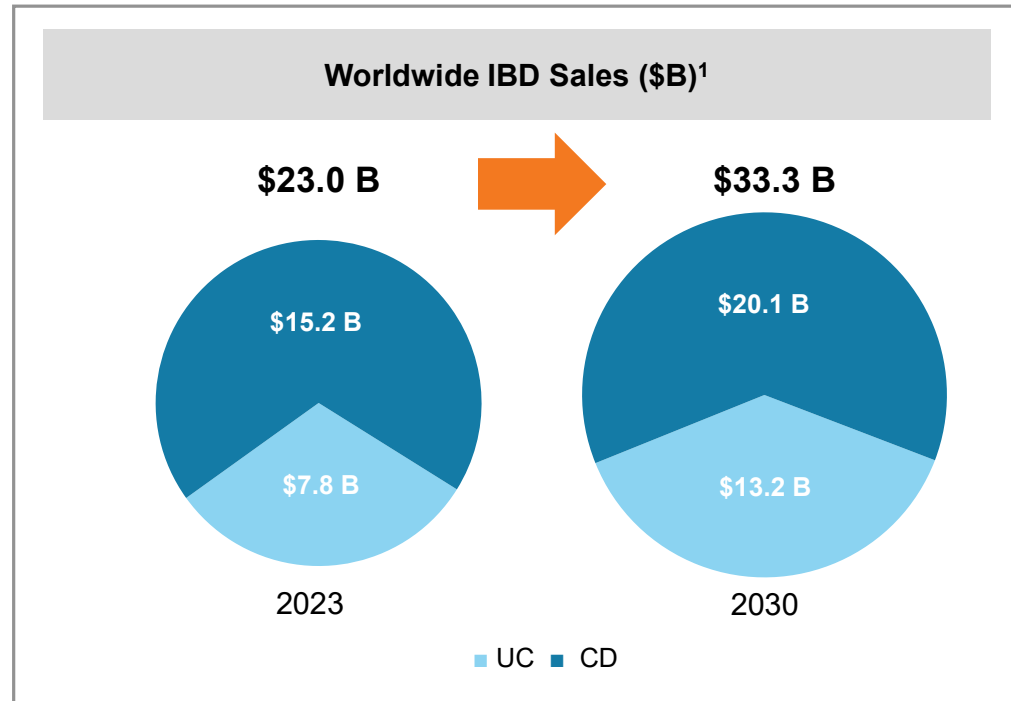
Anti-TL1A Antibodies
Validated Biology: Multiple third-party anti-TL1A antibodies have demonstrated clinical activity in Phase 2 trials in IBD; Phase 3 trials ongoing in IBD
Clinical Efficacy: Encouraging clinical remission rates vs. other IBD drug classes
Safety and Tolerability: Anti-TL1A therapies have been generally well tolerated
Immunogenicity: High rates of immunogenicity (ADA) due to formation of immune complexes, as anti-TL1A antibodies bind to free, circulating TL1A



Potential First-in-Class DR3 Antibody: SL-325
Potential for Greater Efficacy: Blocking DR3 receptor may provide more potent and durable blockade of the TL1A/DR3 axis, due to the stable expression of DR3. This may allow SL-325 to be more efficacious than TL1A blocking antibodies.
Safety and Tolerability: SL-325 is expected to have similar safety and tolerability as the TL1A blocking antibodies; SL-325 was well tolerated in acute toxicology study in non-human primates
Potential for Improved Immunogenicity Profile: SL-325 is expected to be less immunogenic than the anti-TL1A antibodies, because DR3 remains bound to the cell membrane and therefore immune complex formation is not expected. This may lead to greater and more durable efficacy and better use in combination strategies.

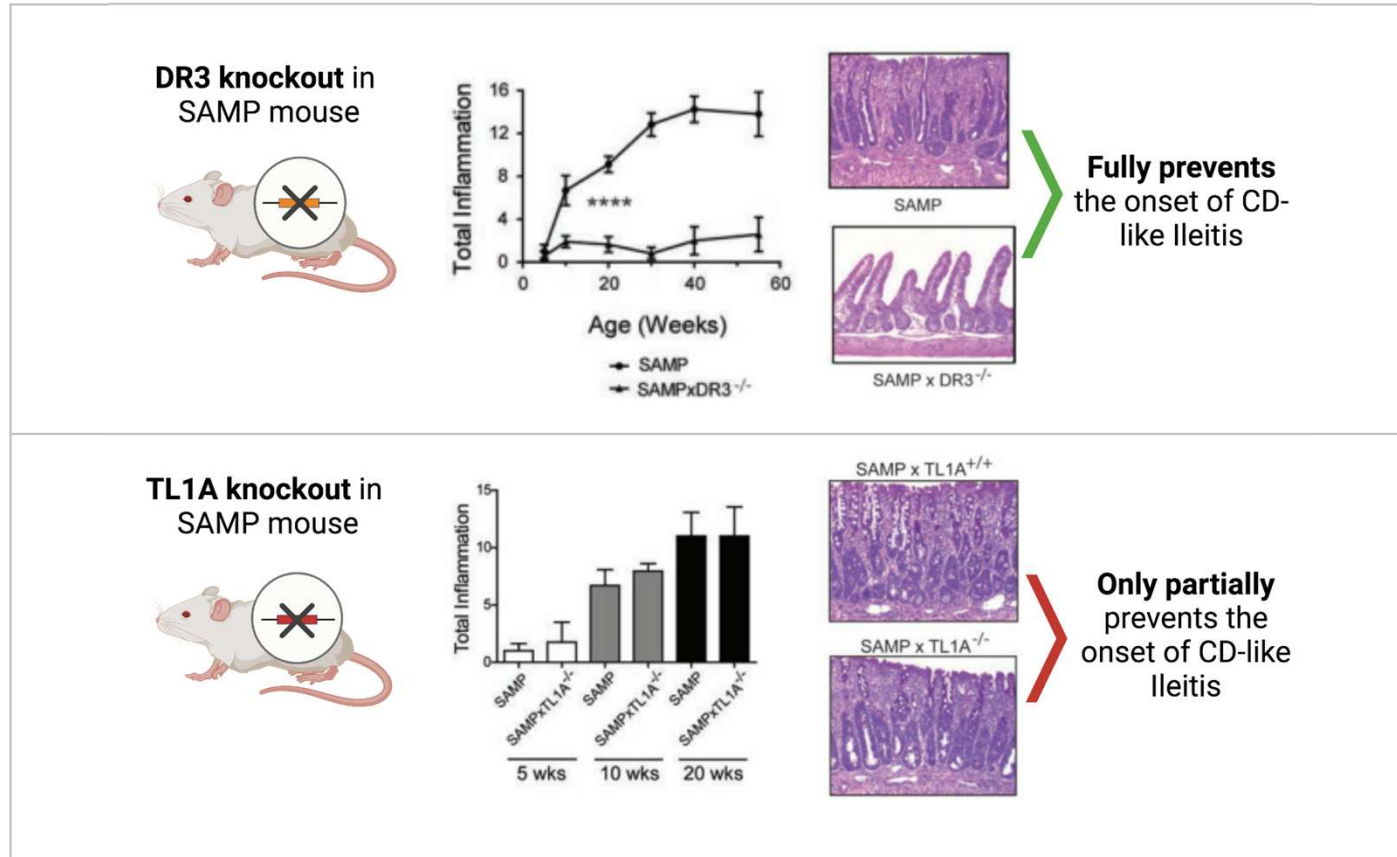
➔ SL-325 is a potential first-in-class DR3 blocking antibody targeting a clinically-validated axis

Inflammatory Bowel Disease Is a Large and Growing Market

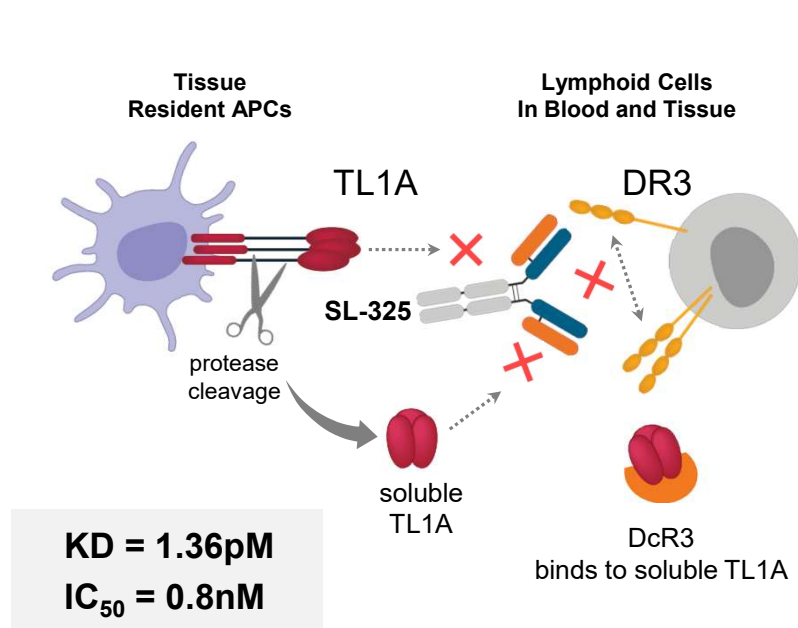


→ Worldwide inflammatory bowel disease sales and prevalence expected to grow steadily to 2030

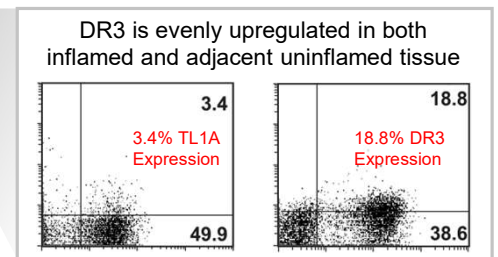
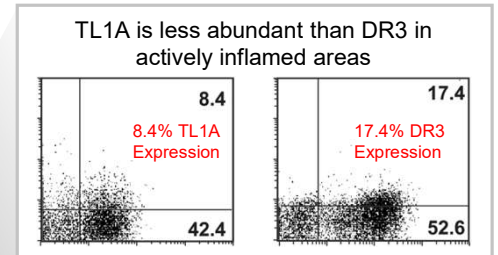
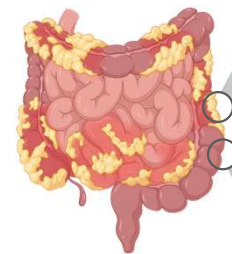
DR3 Inhibition Is Potentially More Potent Than TL1A Inhibition



SL-325 Is a High-Affinity DR3-Specific Blocking Antibody



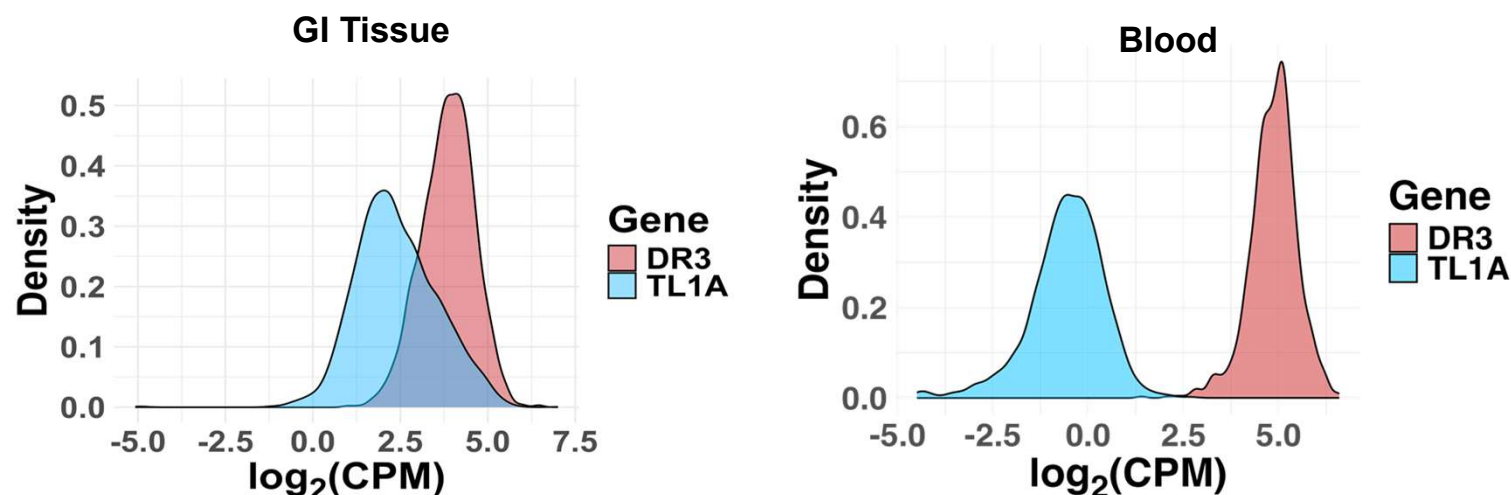
Crohn's Disease is characterized by discontinuous and migratory inflammation



DR3 is constitutively expressed by lymphocytes both at involved and uninvolved areas of the gut

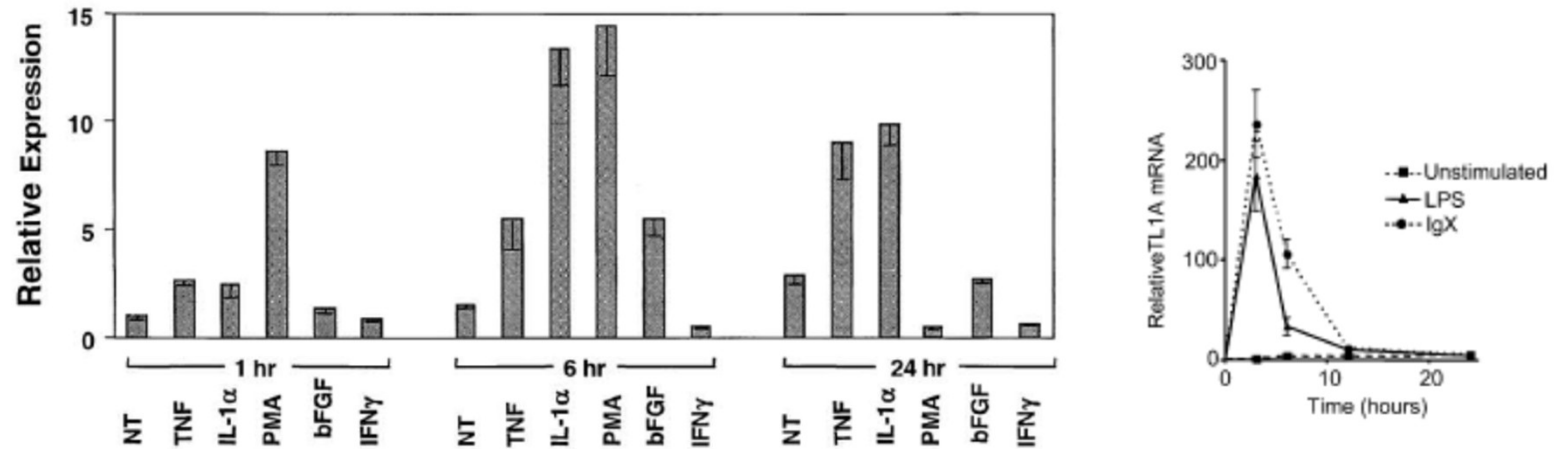
→ DR3 is more abundant, constitutively expressed. and evenly upregulated in involved and adjacent uninvolved GI tissue in UC and Crohn's Disease than TL1A, providing rationale as a better target for TL1A inhibition

RNA Sequencing Data From UC and CD Patient Biopsies Confirm Constitutive and Higher Expression of DR3



- Aggregated transcriptomic data (>2000 patients) confirms higher expression of DR3 than TL1A in the GI tract of UC and CD patients
- DR3 is also highly expressed in peripheral blood cells, TL1A is not

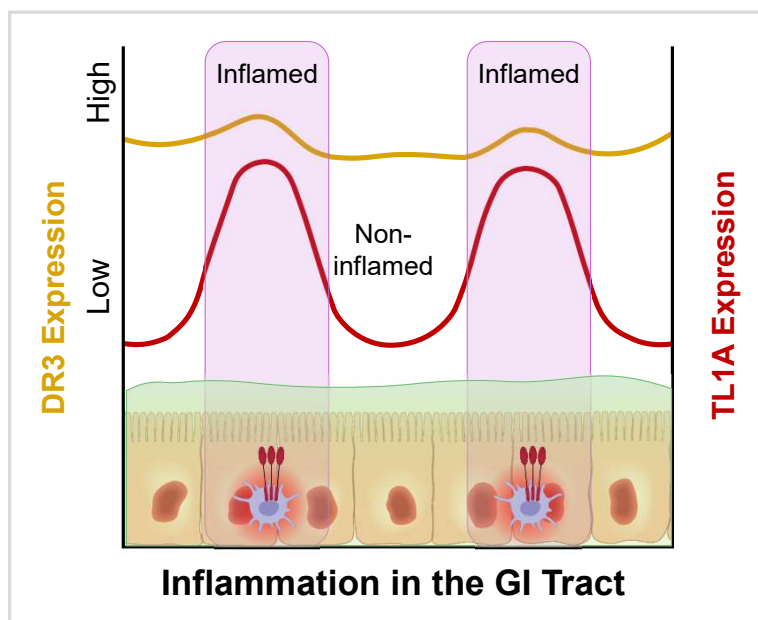
TL1A Is Transiently Expressed, Primarily in Tissues



- TL1A is the monogamous ligand to DR3/TNFRSF25
- TL1A is rapidly inducible in dendritic cells, macrophages and certain non-hematopoietic cells by TLR or Fc γ R ligation
- TL1A is turned on and off quickly

Targeting DR3 May Enable More Effective Treatment of Inflammation

DR3 Is Constitutively Expressed - TL1A Is Not



- TL1A is expressed transiently at sites of inflammation in the gut but not by adjacent non-inflamed tissue¹
- DR3 is expressed constitutively both at sites of inflammation and adjacent non-inflamed tissue
- Inflammation in Crohn's disease and Ulcerative Colitis is not static, and can wax and wane at distinct areas of the gut over time
- Constitutive expression of DR3 may enable durable receptor blockade to dampen the migration of inflammation from inflamed to adjacent non-inflamed areas of the bowel, contributing to endoscopic remission



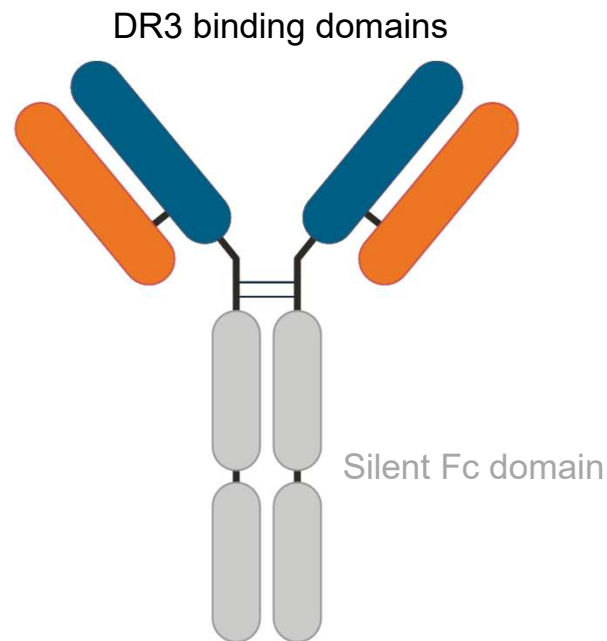
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SL-325 Program

Potential First-In-Class DR3 Blocking Antibody



SL-325 Designed for Potent DR3 Blockade



SL-325

- ✓ Picomolar binding affinity (1.3 pM) to DR3 and overlapping epitope with TL1A binding site
- ✓ Does not bind to DcR3 (decoy receptor)
- ✓ Potent blockade of monomeric and trimeric TL1A to DR3 in preclinical models
- ✓ Receptor blockade expected to provide more durable protection from inflammation than ligand blockade because DR3 is constitutively expressed

Phase 1 Clinical Trial of SL-325 is Currently Enrolling

- **Phase 1 Clinical Trial Design**

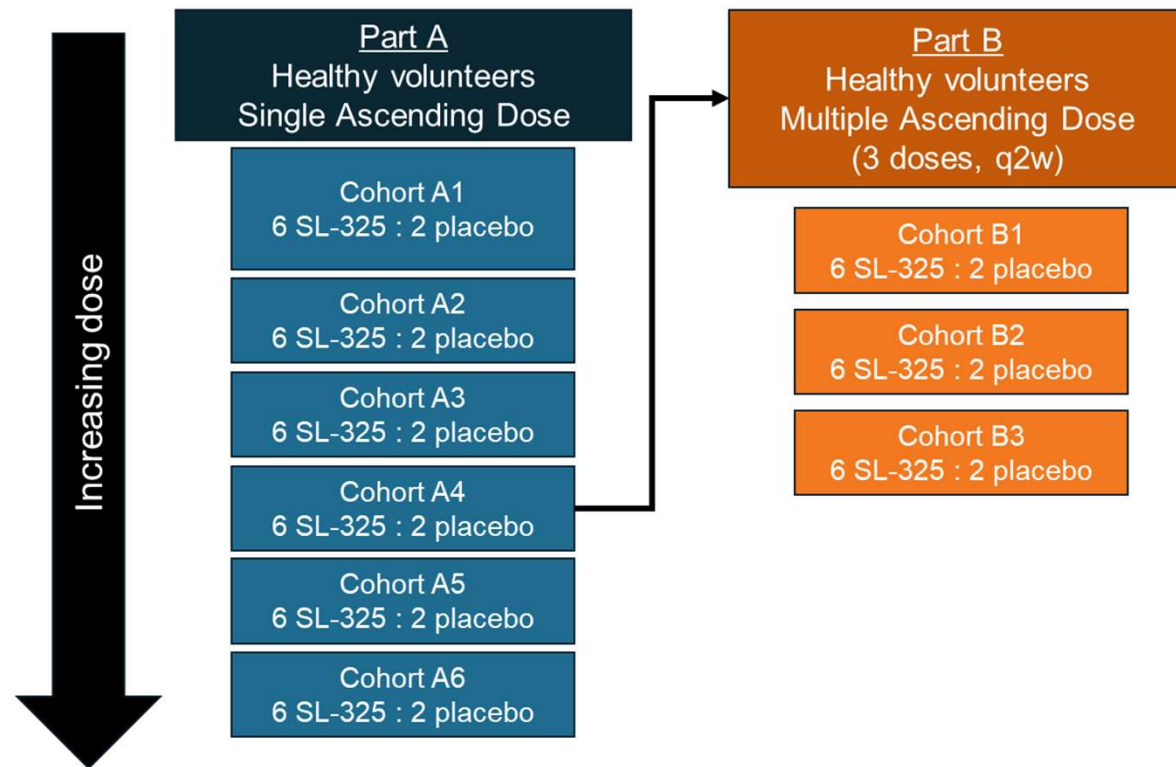
- Single ascending dose (SAD) and multiple ascending dose (MAD) study in healthy volunteers
- Planned enrollment of ~70 participants

- **Objectives of Phase 1 Study**

- Safety and Tolerability
- PK Profile
- Immunogenicity Profile
- Durability of DR3 Receptor Occupancy
- Confirmation of Lack of Agonism

- **Outcomes from Phase 1 Study**

- Recommended Phase 2 Dose and Schedule
- Acceptable profile for continued development





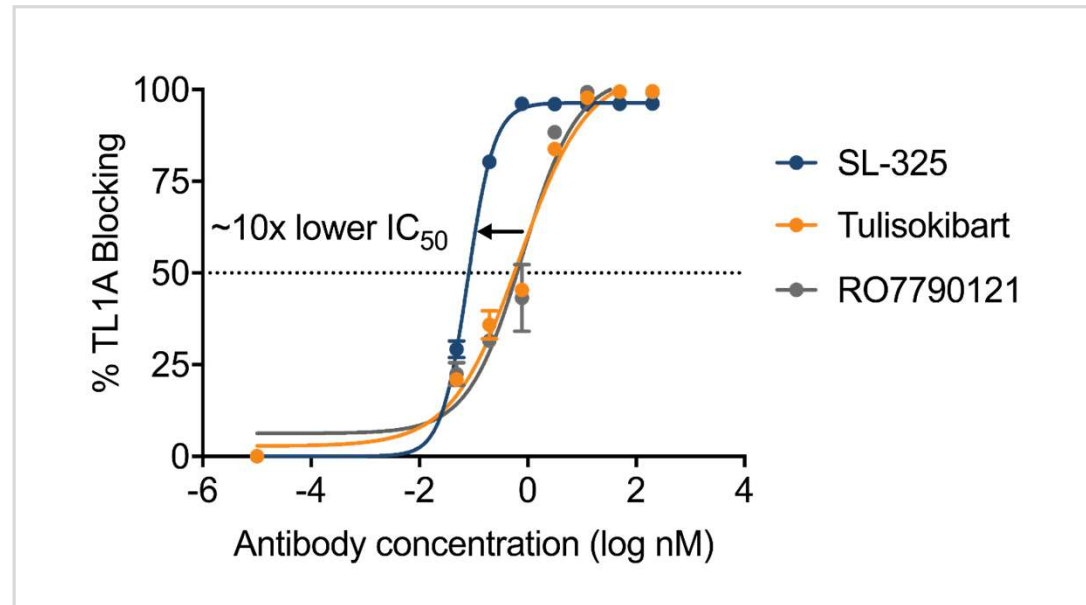
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SL-325 Preclinical Data

In vitro and GLP NHP Data

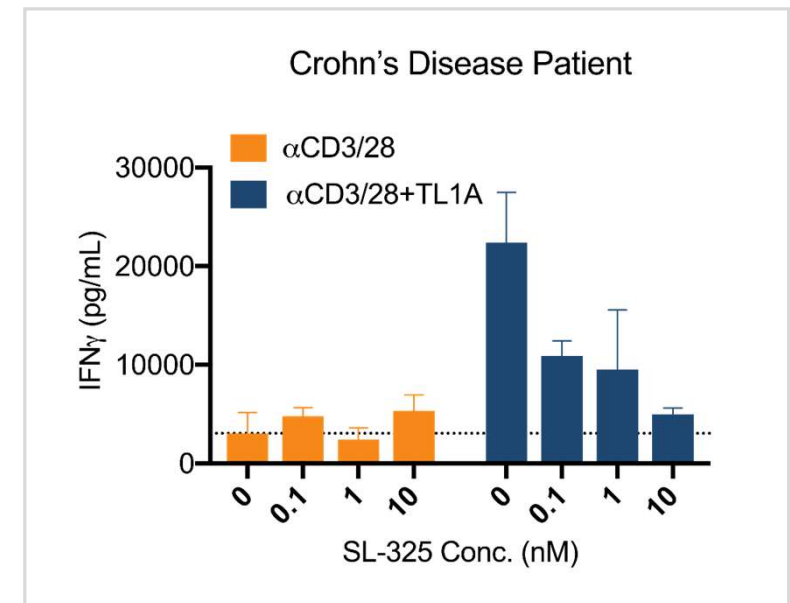
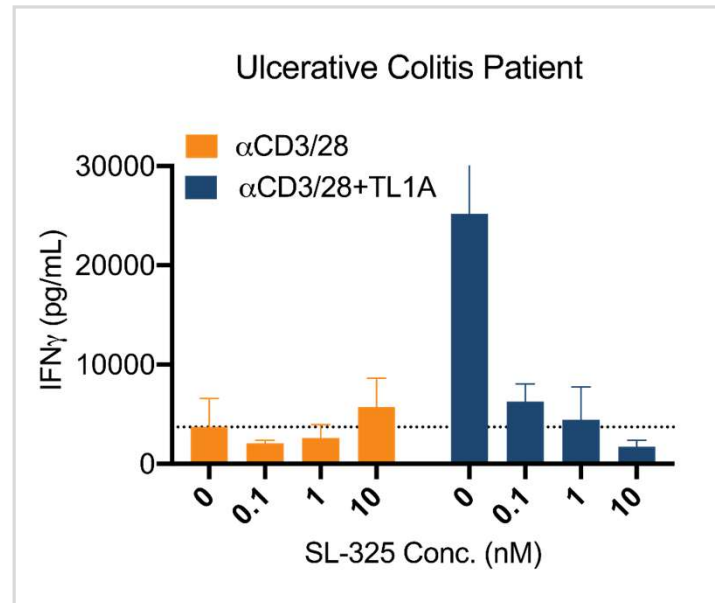
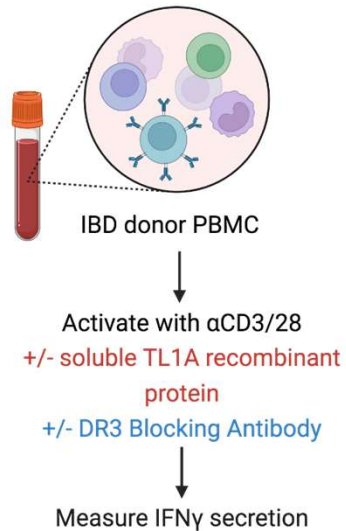


SL-325 Blocks TL1A Binding at Lower Concentrations Than Benchmark Anti-TL1As



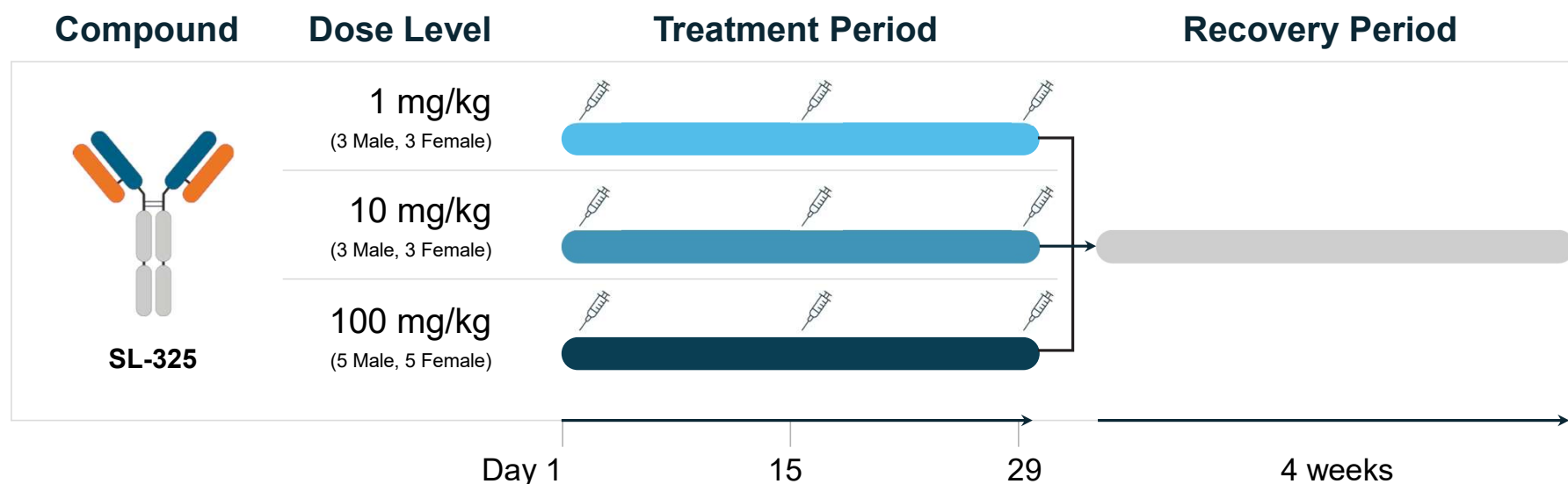
- ➔ SL-325 potently blocks TL1A binding to DR3 in vitro
- ➔ ~10-fold greater potency than benchmark anti-TL1A antibodies

SL-325 Blocks TL1A-Induced IFN γ Secretion From IBD Patient PBMCs



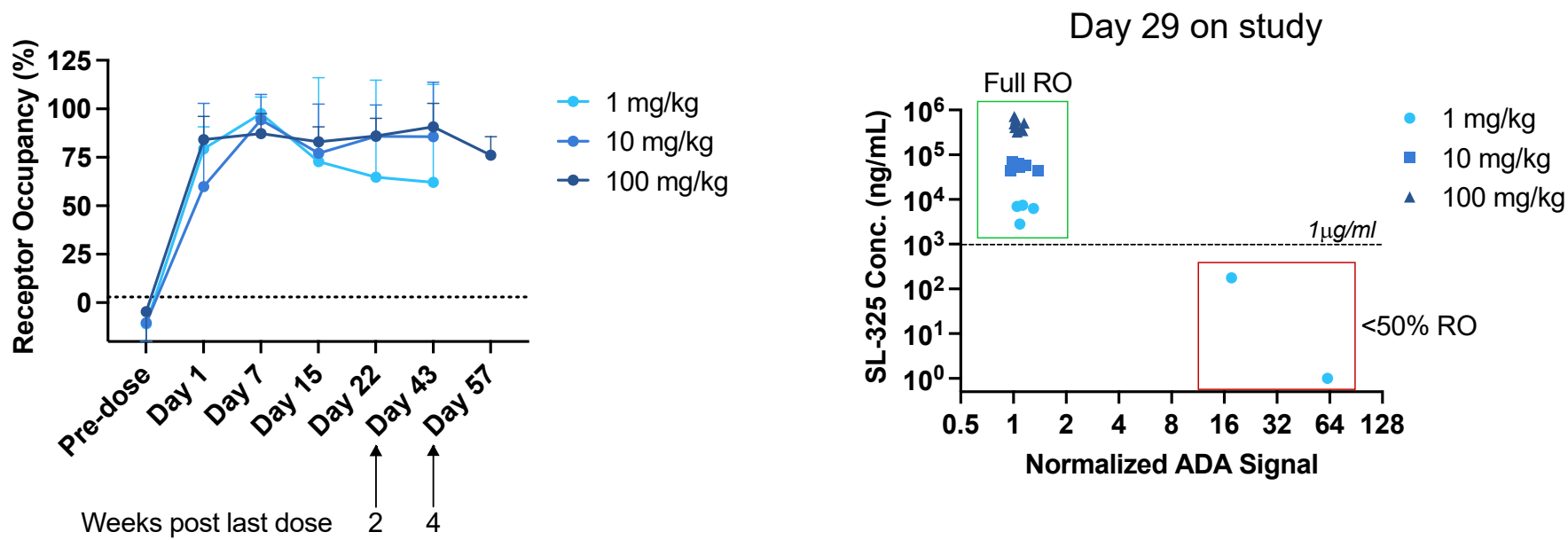
➔ SL-325 efficiently blocked IFN γ across all tested IBD patient samples

SL-325 NHP Study Design and Safety Overview



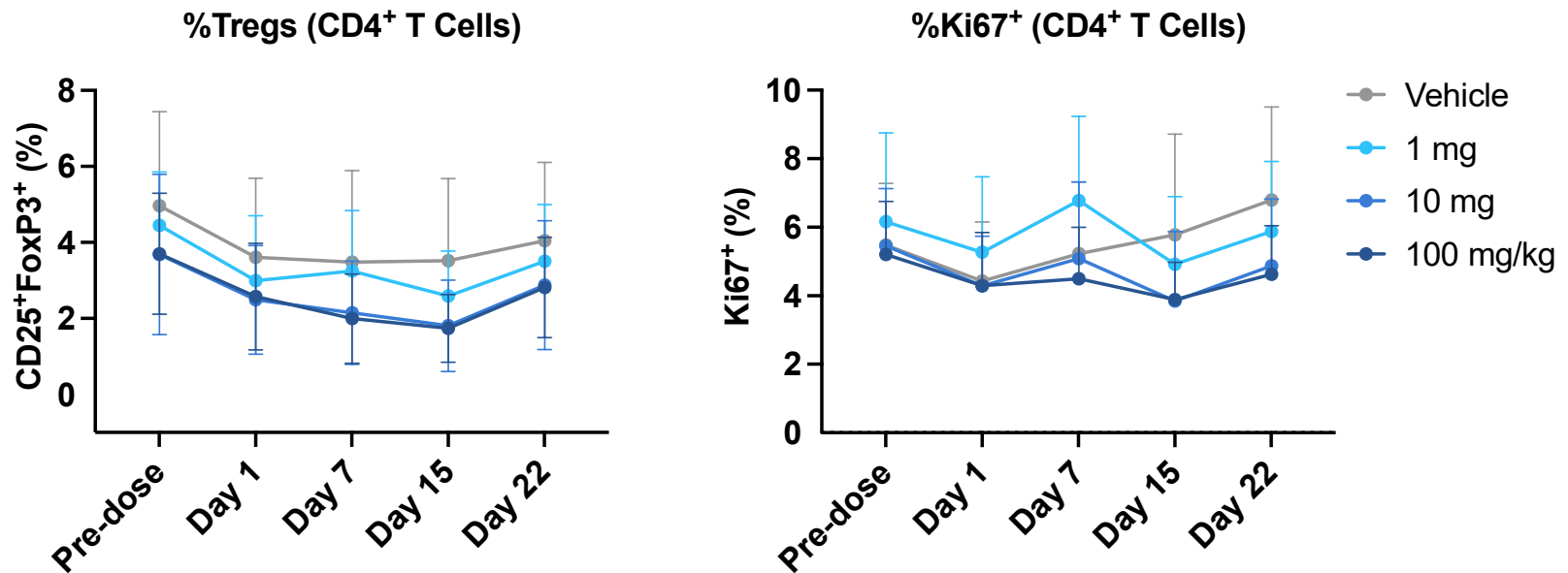
- ➔ No infusion-related reactions were observed in any group
- ➔ No-observed-adverse effect level (NOAEL) is the top dose of 100 mg/kg
- ➔ No changes in clinical pathology parameters, gross pathology, or histopathology analysis observed

SL-325 Achieved Full and Durable Receptor Occupancy (RO)



- ➔ Full DR3 RO was observed at all dose levels, and binding was durable for at least four weeks post-dose
- ➔ In two animals that developed ADA, a drop in DR3 RO was observed, suggesting trough concentrations ≥ 1 µg/mL maintain full RO

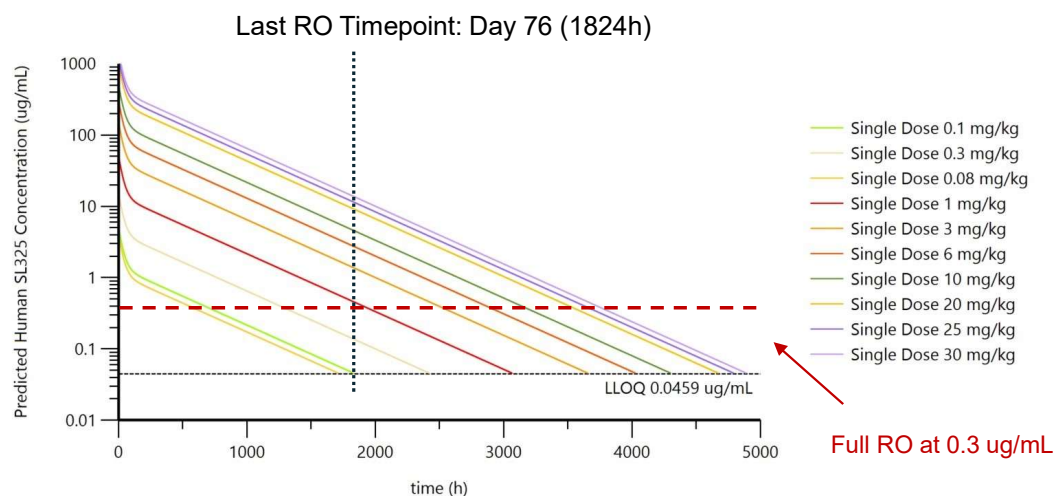
SL-325 Showed No Signs of DR3 Agonism



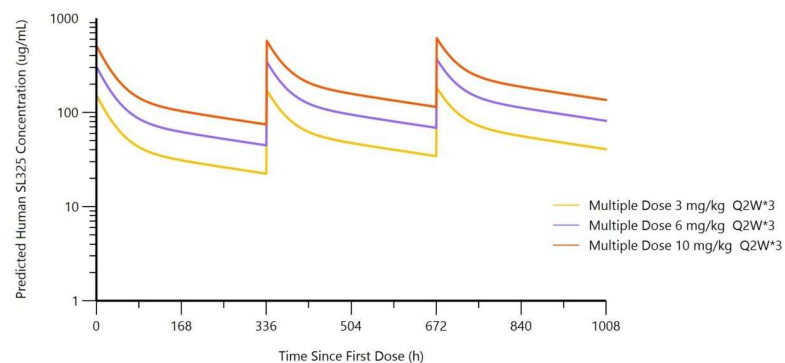
➔ Peripheral blood flow cytometry confirmed that there was no evidence of T cell proliferation in any treated animal

Predicted Human SL-325 PK Profiles Full RO at All Doses and High Trough Concentrations with Repeat Dosing

Predicted Human SL-325 PK Profiles in Serum Following Single IV Dose



Predicted Human SL-325 PK Profiles in Serum Following Q2W*3 IV Dose



- ➔ PK profile suggests that full RO may be maintained for >2 months at doses of ≥ 1 mg/kg
- ➔ Targeting Q4W induction dosing, with less frequent dosing in the maintenance phase



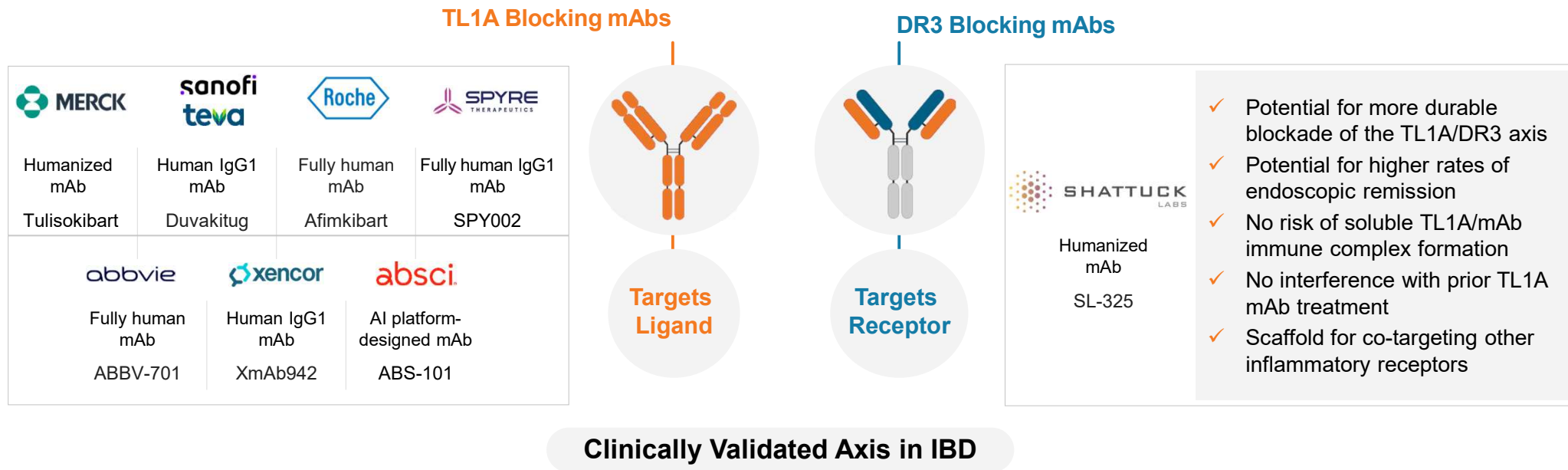
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Development Opportunities and Milestones



TL1A/DR3 Axis Development Landscape



➔ SL-325 offers a first-in-class approach in the clinically validated TL1A/DR3 axis by blocking DR3

Shattuck Labs Expected Milestones

First-in-Class DR3 Antagonist Program

- ✓ SL-325 demonstrated superior TL1A/DR3 blockade in head-to-head preclinical studies as compared to benchmark TL1A antibodies
- ✓ Completed GLP tox study; SL-325 RO and PK profile suggestive of extended dosing intervals
- ✓ Targeting DR3 enables bispecific strategies to other inflammatory receptors co-expressed by DR3+ immune cells

Pursuing Established Clinical Market

- ✓ SL-325 positioned in established clinically-validated IBD patient population
- ✓ Large and growing market with \$33.3 billion in worldwide sales by 2030¹
- ✓ Despite approved therapies, continued high unmet need in IBD and other inflammatory autoimmune diseases

Executing on Upcoming Milestones

- ✓ Enrollment ongoing in Phase 1 clinical trial evaluating SL-325 in healthy volunteers
- ✓ Complete enrollment in the Phase 1 SAD/MAD study expected in Q2 2026
- ✓ Cash runway expected to fund planned operations and clinical development into 2029²

Cash and Shares Outstanding

\$86.1 million cash as of September 30, 2025⁽¹⁾

Expected cash runway into 2029⁽²⁾

Shares Outstanding		Number of Shares (M)
Common Stock	Shares Outstanding	63.1
Common Stock Equivalents	Pre-Funded Warrants	40.5
Warrants Outstanding	Common Stock Warrants (\$1.0846 Exercise Price)	52.6
Total Outstanding ⁽³⁾		156.3

1. Includes cash and cash equivalents and short-term investments as of September 30, 2025

2. Based on cash and cash equivalents and short-term investments as of September 30, 2025, plus up to \$57 million to be received if outstanding common stock warrants are exercised in full

3. Excludes shares issuable pursuant to issued and outstanding employee stock options and unvested restricted stock units



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Thank You

Investor Relations

InvestorRelations@ShattuckLabs.com