SHATTUCK LABS

Corporate Overview

Shattuck Labs, Inc.
NASDAQ: STTK
March 5, 2026

Forward-Looking Statements

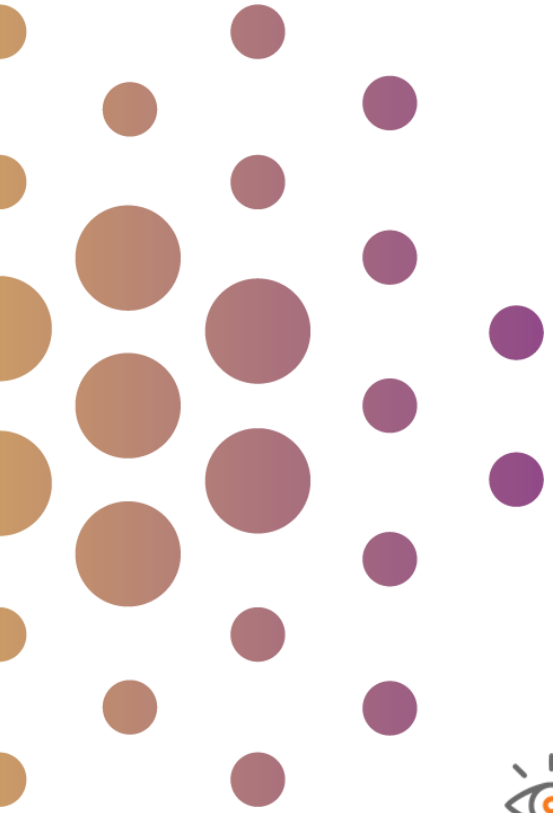
This presentation contains “forward-looking statements” within the meaning of the federal securities laws, which statements are subject to substantial risks and uncertainties and are based on our estimates and assumptions. All statements, other than statements of historical facts included in this presentation, 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 potential purity, potency, safety, and clinical benefits of our product candidates, including 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 for the fiscal year ended December 31, 2025 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

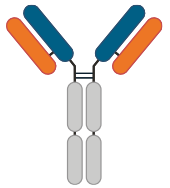
OUR MISSION

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 potentially first-in-class monoclonal and bispecific DR3 blocking antibodies for the treatment of patients with inflammatory and immune-mediated diseases**
Lead Program: SL-325	 • Potentially 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 Phase 2 clinical development planned in Crohn's disease • Enrollment nearly completed 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 • $78.1 million in cash and cash equivalents as of December 31, 2025 • $94.5 million in cash and cash equivalents as of February 28, 2026[1] • Cash runway expected to fund planned operations and clinical development into 2029[2]

DR3 = Death Receptor 3 (TNFRSF25)

1. This amount is preliminary, has not been audited or reviewed by the Company's independent registered public accounting firm, and is subject to change upon completion of the Company's financial closing procedures.
2. Based on cash and cash equivalents and short-term investments as of December 31, 2025, including the gross proceeds from the sale of common stock under the Company's at-the-market offering facility of $21.4 million in the first quarter of 2026, and assuming the receipt of $51.7 million upon the full exercise of the outstanding common stock warrants.

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 LABS

Note: *italicized* text denotes prior affiliation

Shattuck's Pipeline Targeting the TL1A/DR3 Pathway

Programs			Stage of Development		
Lead	Target(s)	Indications	IND-Enabling	Phase 1	Phase 2
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

SHATTUCK LABS

IBD = Inflammatory Bowel Disease

SHATTUCK LABS

TL1A / DR3 Biology

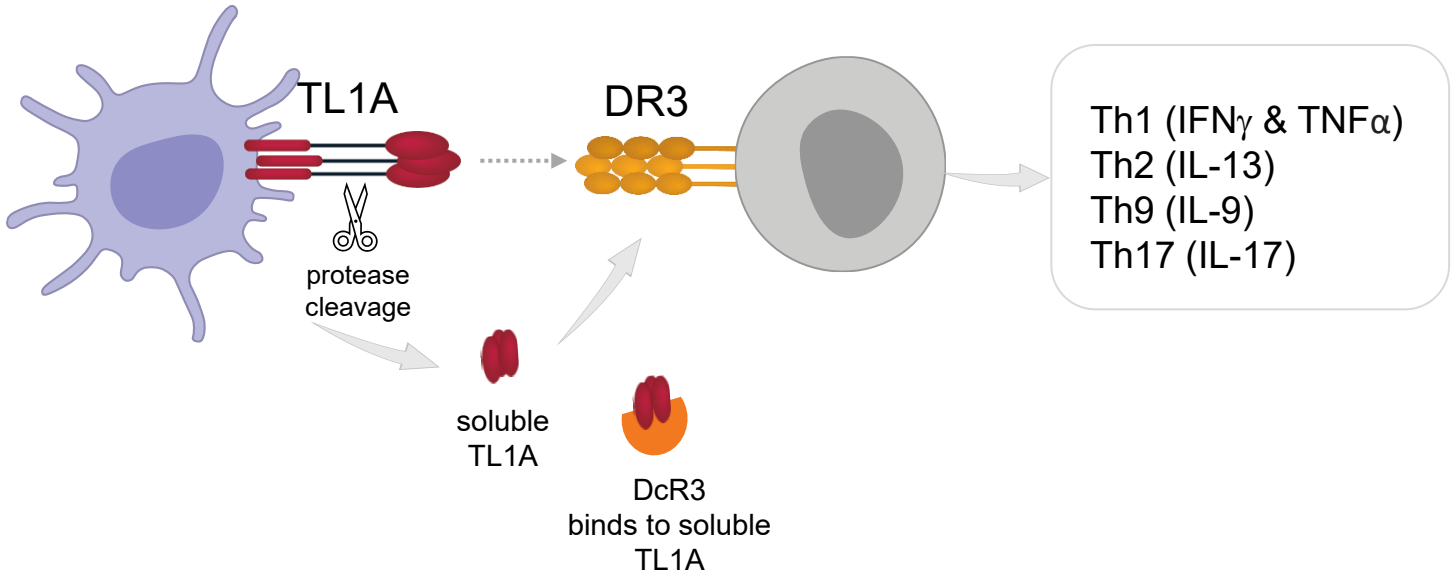
Rationale for Targeting the Receptor
In a Clinically-Validated Axis

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

Tissue Resident APCs

Lymphoid Cells In Blood and Tissue

Increased Inflammation Caused by T Helper (Th) Cell Driven Cytokine Production



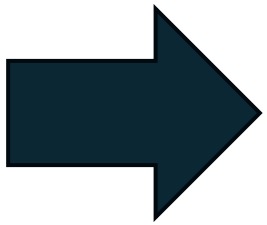
TL1A/DR3 Axis Biology

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

SHATTUCK LABS

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. ADA have been shown to reduce efficacy for TL1A blocking antibodies.



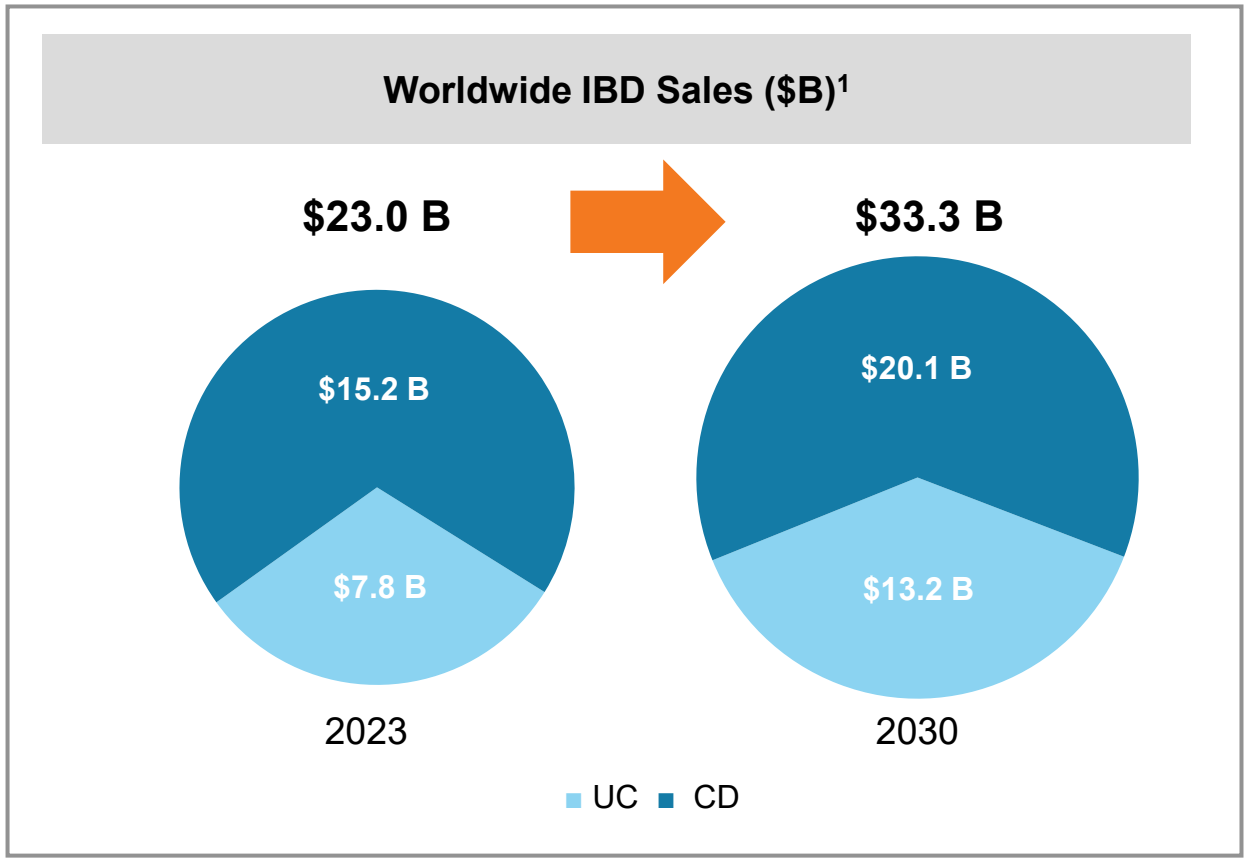
Potential First-in-Class DR3 Antibody: SL-325
Potential for Greater Efficacy: Blocking DR3 receptor may provide more potent and durable blockade of the TL1A/DR3 axis, due to the stable expression of DR3. This may allow SL-325 to be more efficacious than TL1A blocking antibodies.
Safety and Tolerability: 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 Significantly 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

SHATTUCK LABS

Sands B. et al. NEJM 2024
Roche. TUSCANY-2: A Dose-Ranging Phase IIb Study Evaluating Efficacy and Safety of RO7790121, an Antibody Against Tumor Necrosis Factor-like Ligand 1A (Anti-TL1A) in Adults with Moderately to Severely Active Ulcerative Colitis. https://medically.roche.com/global/en/inflammatory-disease/acg-2024/medical-material/ACG-2024-presentation-danese-TUSCANY-2-a-dose-ranging-phase-pdf.html
Teva. Teva and Sanofi Present New Positive Phase 2b Study Results at ECCO 2025 Reinforcing Best-in-Class Potential of Duvakitug (Anti-TL1A) in Ulcerative Colitis and Crohn's Disease. https://ir.tevapharm.com/news-and-events/press-releases/press-release-details/2025/Teva-and-Sanofi-Present-New-Positive-Phase-2b-Study-Results-at-ECCO-2025-ReinforcingBest-in-Class-Potential-of-Duvakitug-Anti-TL1A-in-Ulcerative-Colitis-and-Crohns-Disease/default.aspx

Inflammatory Bowel Disease Is a Large and Growing Market



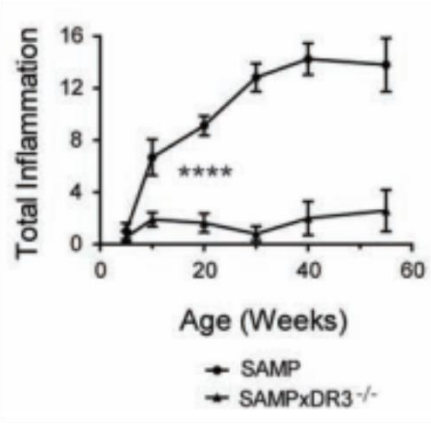
➔ Worldwide inflammatory bowel disease sales and prevalence expected to grow steadily to 2030

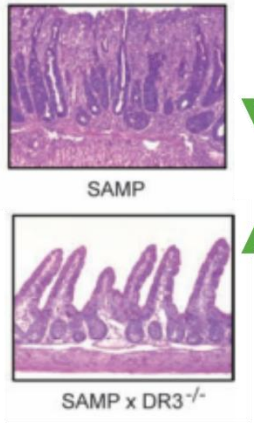
UC = Ulcerative Colitis; CD= Crohn's Disease

1. Evaluate Pharma

DR3 Inhibition Is Potentially More Potent Than TL1A Inhibition

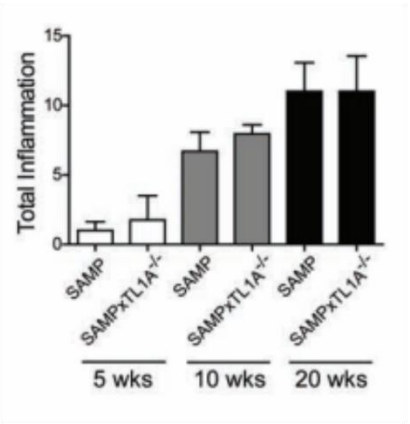
DR3 knockout in SAMP mouse

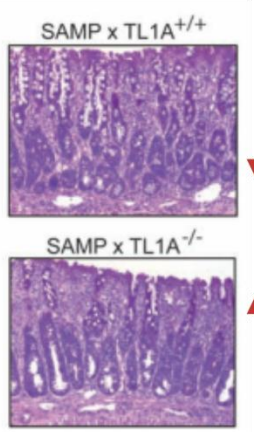




Fully prevents the onset of CD-like Ileitis

TL1A knockout in SAMP mouse

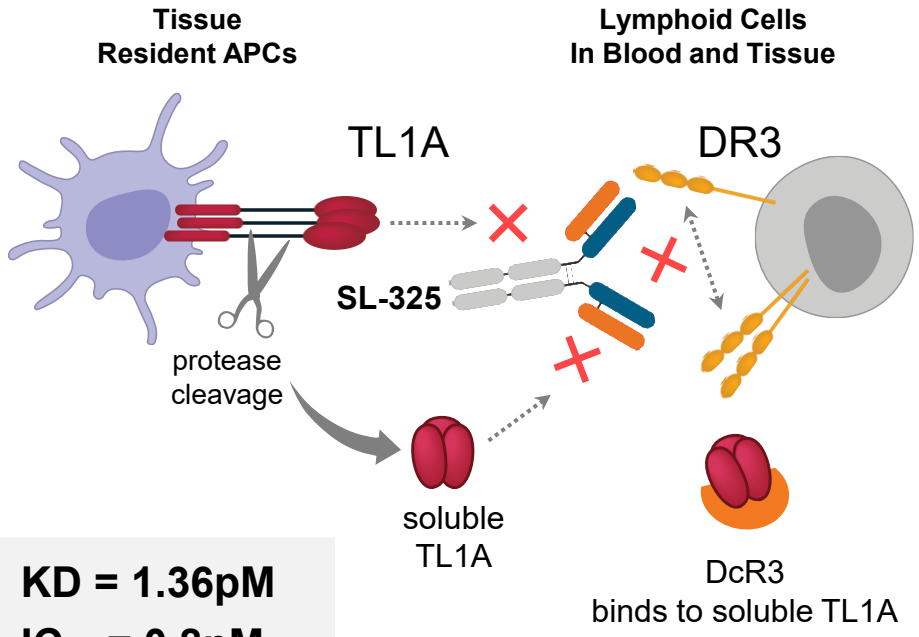




Only partially prevents the onset of CD-like Ileitis

Butto L. Inflamm Bowel Dis. 2019 Jan; 25(1): 14–26

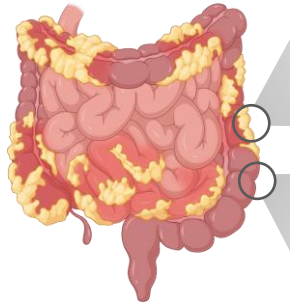
SL-325 Is a High-Affinity DR3-Specific Blocking Antibody

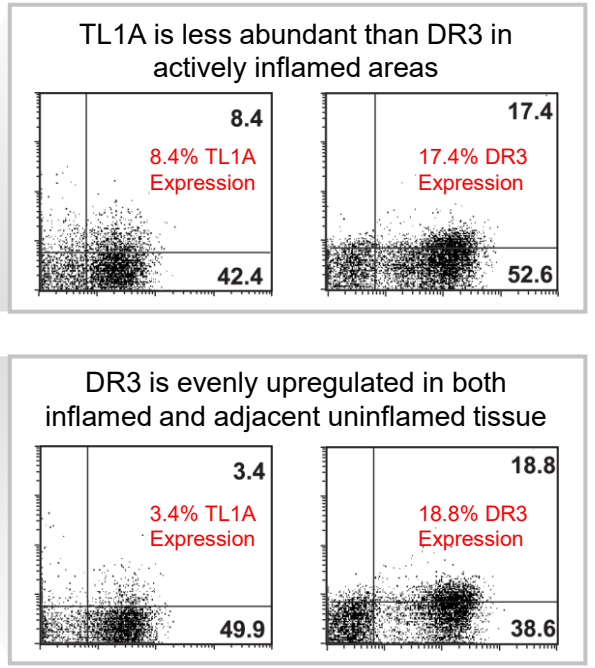


KD = 1.36pM

IC_{50} = 0.8nM

Crohn's Disease is characterized by discontinuous and migratory inflammation



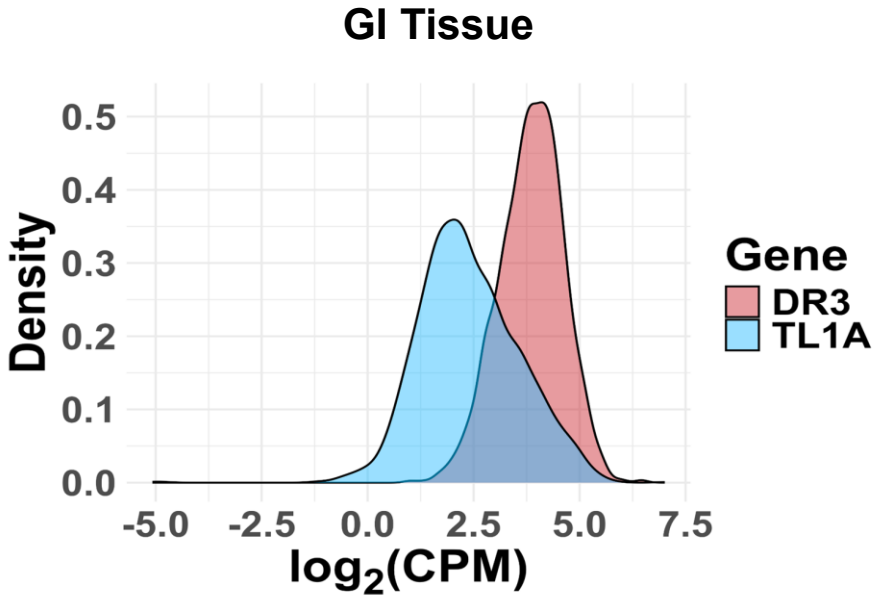


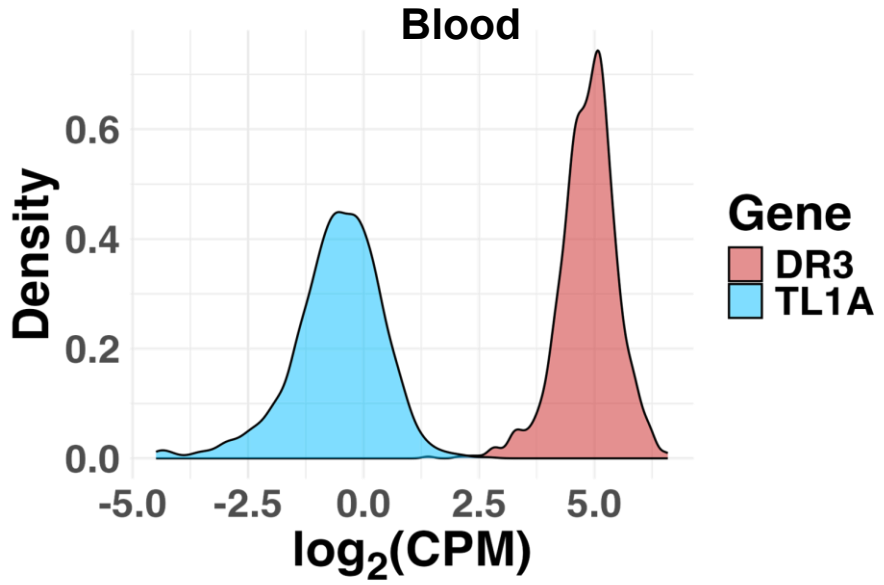
DR3 is constitutively expressed by lymphocytes both at involved and uninvolved areas of the gut

➔ 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

Prehn J. J Clinical Immunol 2004

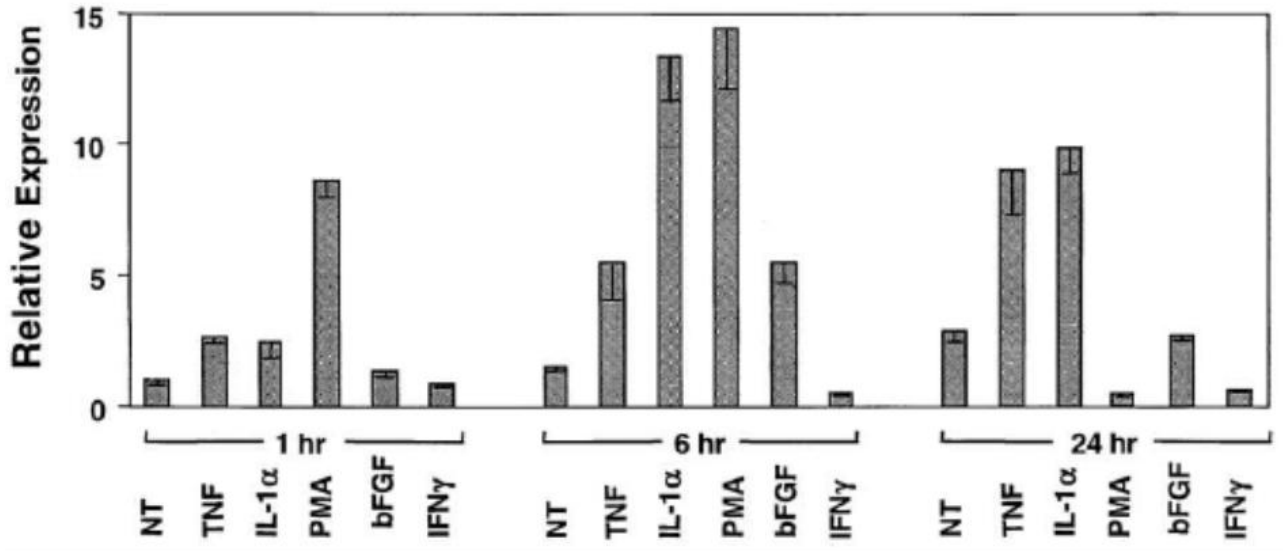
RNA Sequencing Data From UC and CD Patient Biopsies Confirm Constitutive and Higher Expression of DR3

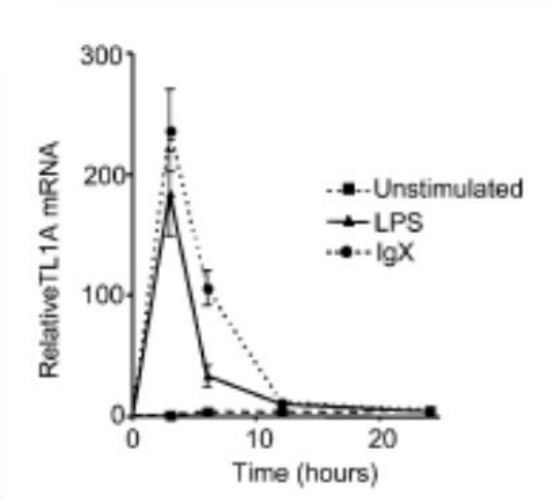




- Aggregated transcriptomic data (>2000 patients) confirms higher expression of DR3 than TL1A in the GI tract of UC and CD patients
- DR3 is also highly expressed in peripheral blood cells, TL1A is not

TL1A Is Transiently Expressed, Primarily in Tissues

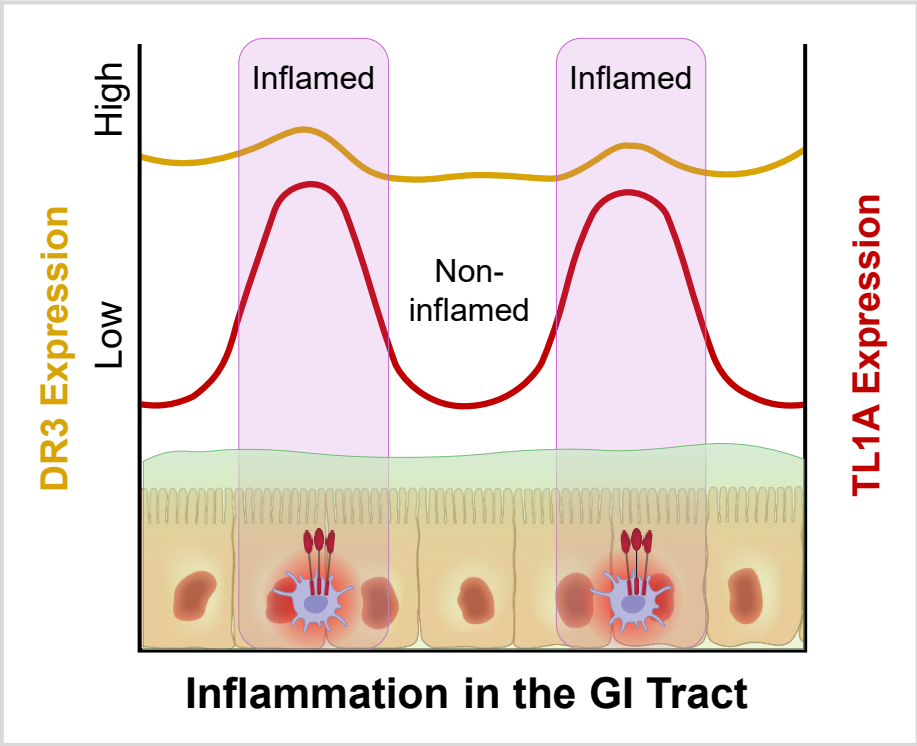




- TL1A is the monogamous ligand to DR3/TNFRSF25
- TL1A is rapidly inducible in dendritic cells, macrophages and certain non-hematopoietic cells by TLR or FcγR ligation
- TL1A is turned on and off quickly

Migone et al. *Immunity.* 2002;**16**:479-92
Meylan et al. Immunity 2008; **29**:79-89
Schreiber et al. *J Immunol* 2012;189(7);3311-8

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 tissue[1]
- 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

SHATTUCK LABS

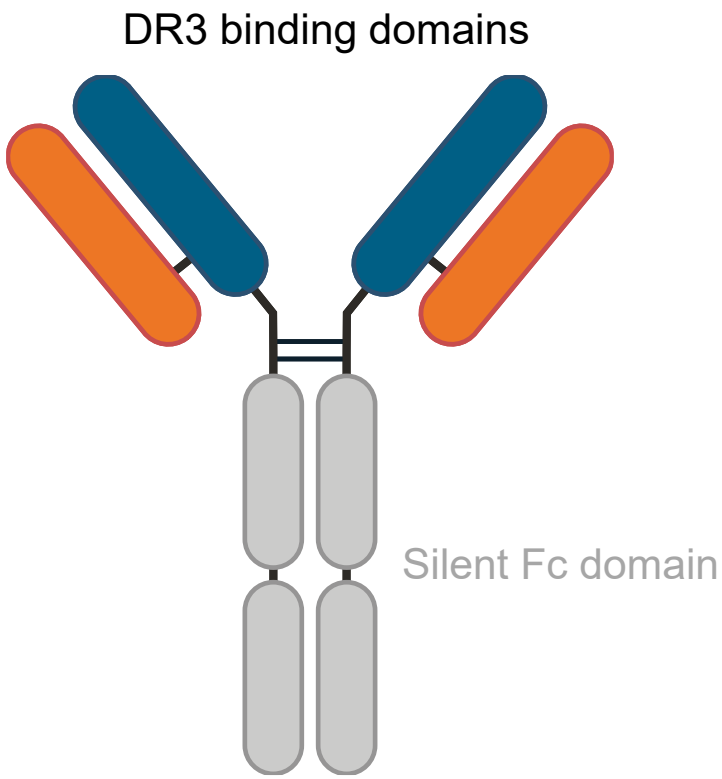
1. Prehn J et al. J Clin Immunol 2004; Bamias G et al. Gut 2024

SHATTUCK LABS

SL-325 Program

Potential First-In-Class DR3 Blocking Antibody

SL-325 Designed for Potent DR3 Blockade

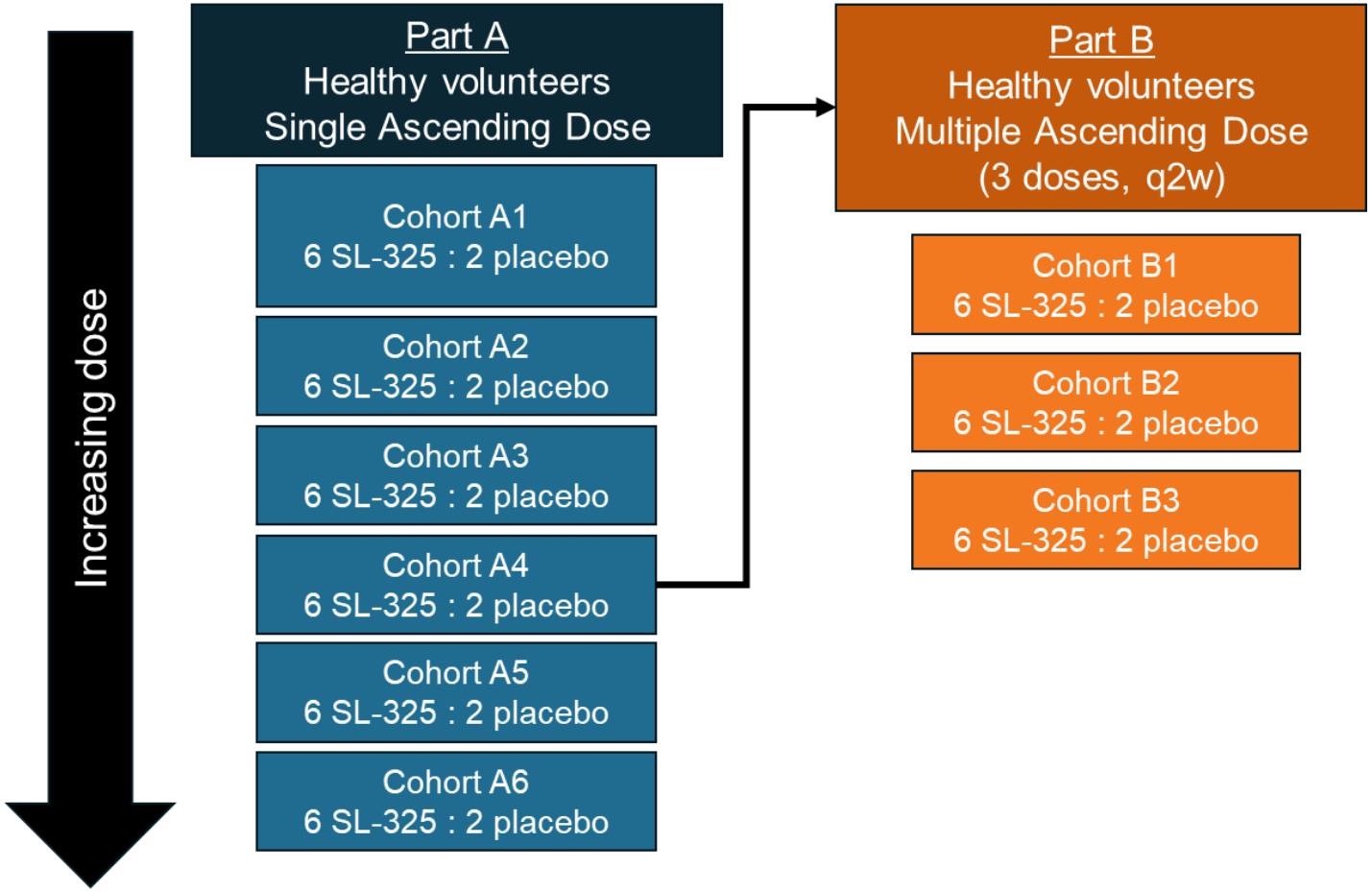


SL-325

- **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; Enrollment is Nearly Complete

- **Phase 1 Clinical Trial Design**
  - Single ascending dose (SAD) and multiple ascending dose (MAD) study in healthy volunteers
  - Planned enrollment of ~70 participants
- **Enrollment in the SAD portion of the trial, and two of three MAD cohorts, now complete**
- **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



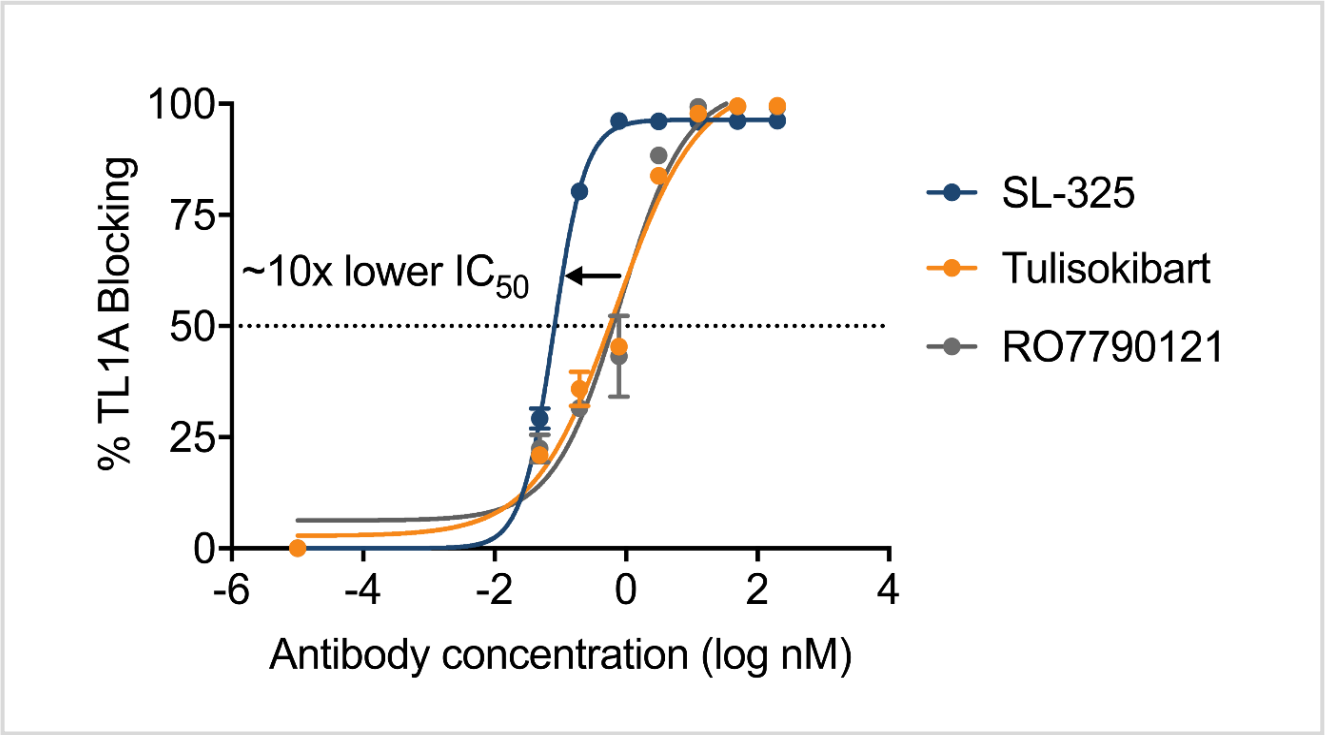
SHATTUCK LABS

SHATTUCK LABS

SL-325 Preclinical Data

In vitro and GLP NHP Data

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



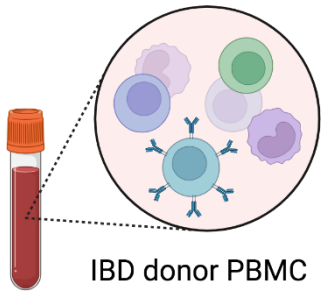
➔ SL-325 potently blocks TL1A binding to DR3 in vitro

➔ ~10-fold greater potency than benchmark anti-TL1A antibodies

SHATTUCK LABS

No head-to-head clinical trials of SL-325 and Tulisokibart or RO7790121 have been conducted.
Note: Studies were performed using a sequence equivalent of Tulisokibart or RO7790121.

SL-325 Blocks TL1A-Induced IFNγ Secretion From IBD Patient PBMCs



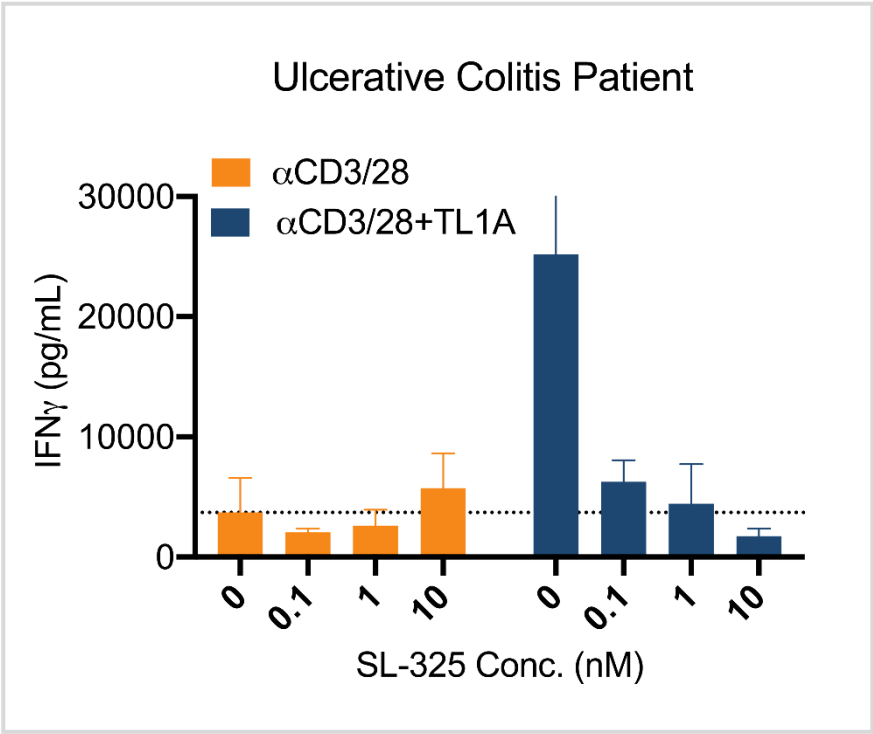
IBD donor PBMC

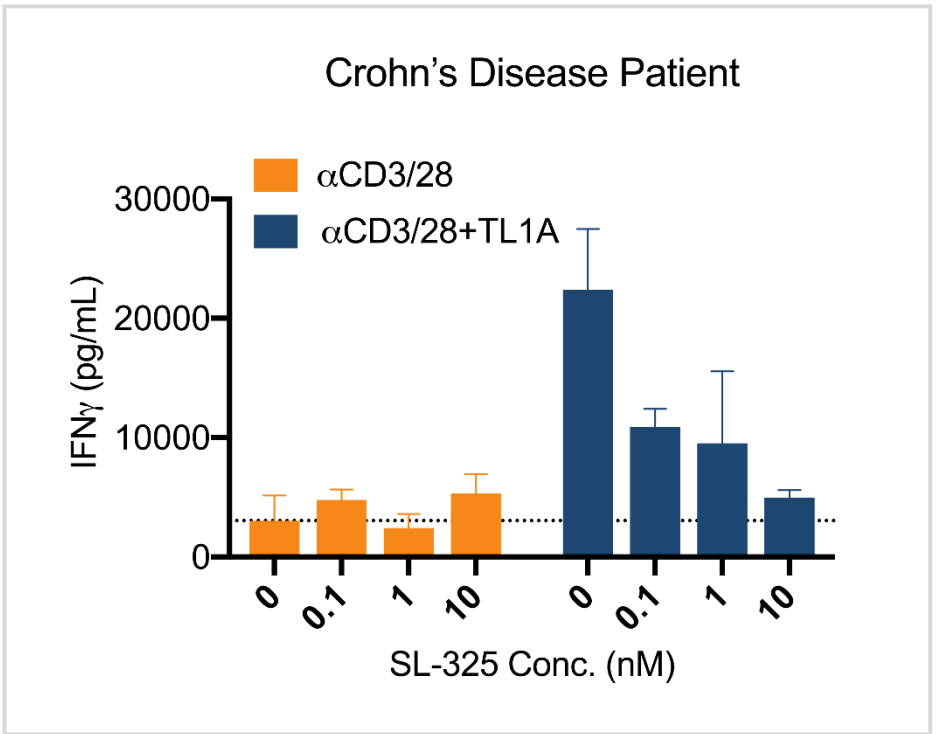
↓

Activate with αCD3/28
+/- soluble TL1A recombinant protein
+/- DR3 Blocking Antibody

↓

Measure IFNγ secretion



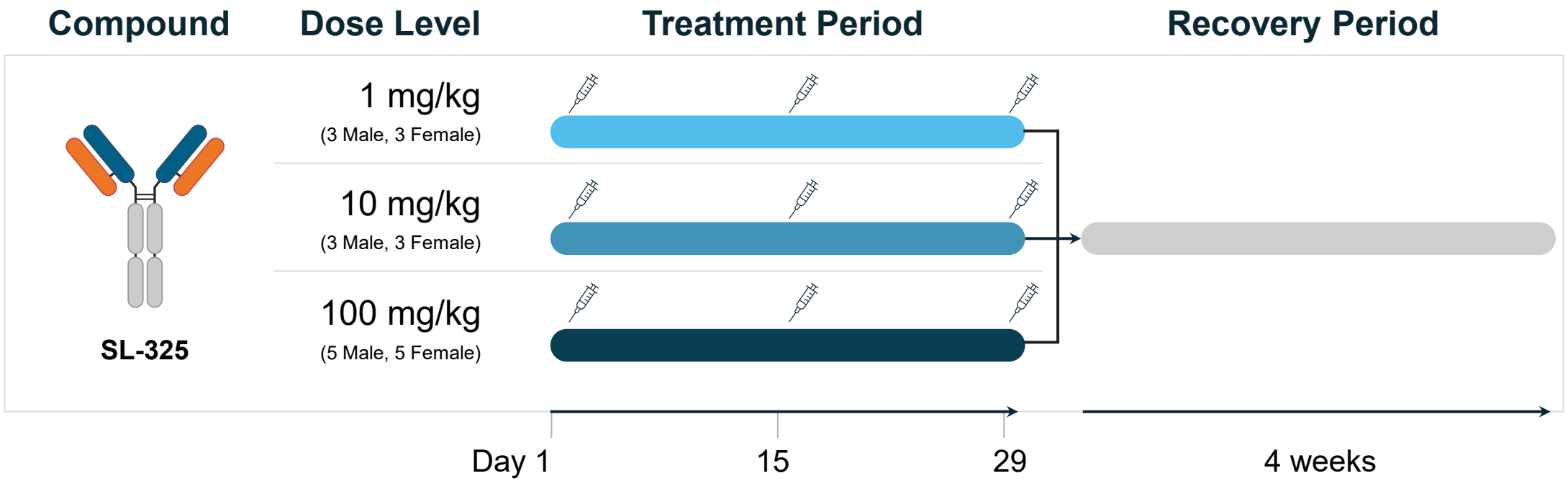


➔ SL-325 efficiently blocked IFNγ across all tested IBD patient samples

SHATTUCK LABS

PBMCs = Peripheral blood mononuclear cells

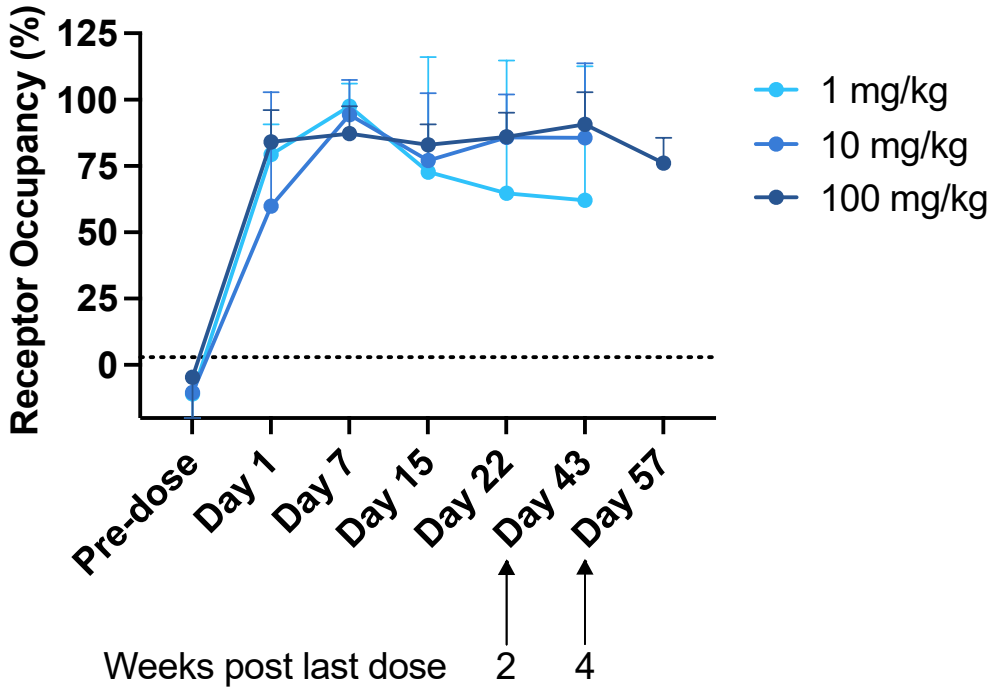
SL-325 NHP Study Design and Safety Overview

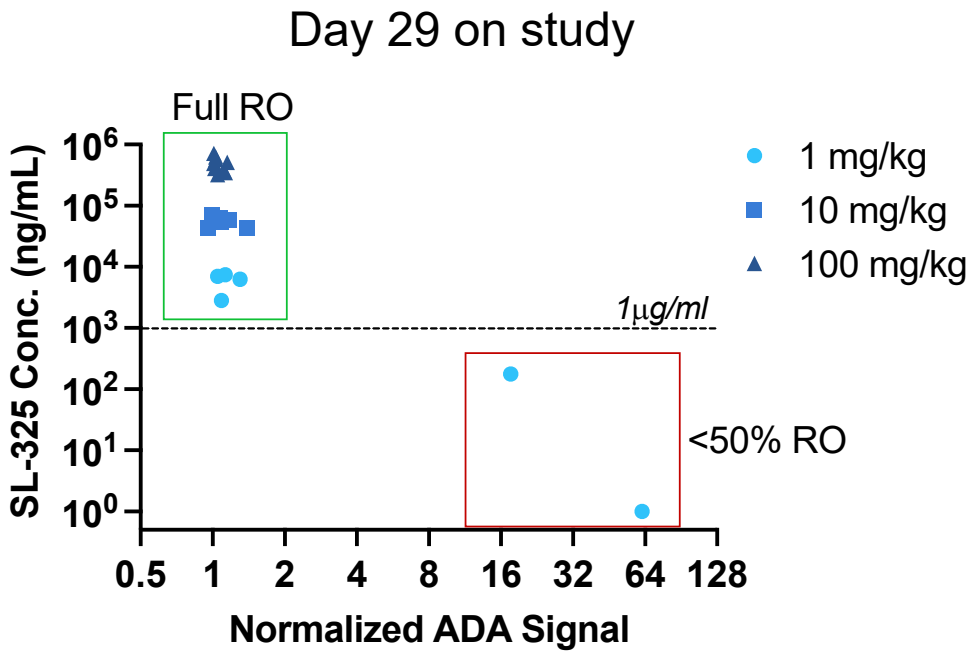


- No infusion-related reactions were observed in any group
- No-observed-adverse effect level (NOAEL) is the top dose of 100 mg/kg
- No changes in clinical pathology parameters, gross pathology, or histopathology analysis observed

Vehicle controlled group, n=10 in the NHP study
Study endpoints: Safety, PK analysis, DR3 RO, ADA analysis, peripheral immunophenotyping and terminal histopathology analysis
RO= Receptor Occupancy
This slide shows preliminary data and analysis available to Shattuck as of the February 6, 2025.

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

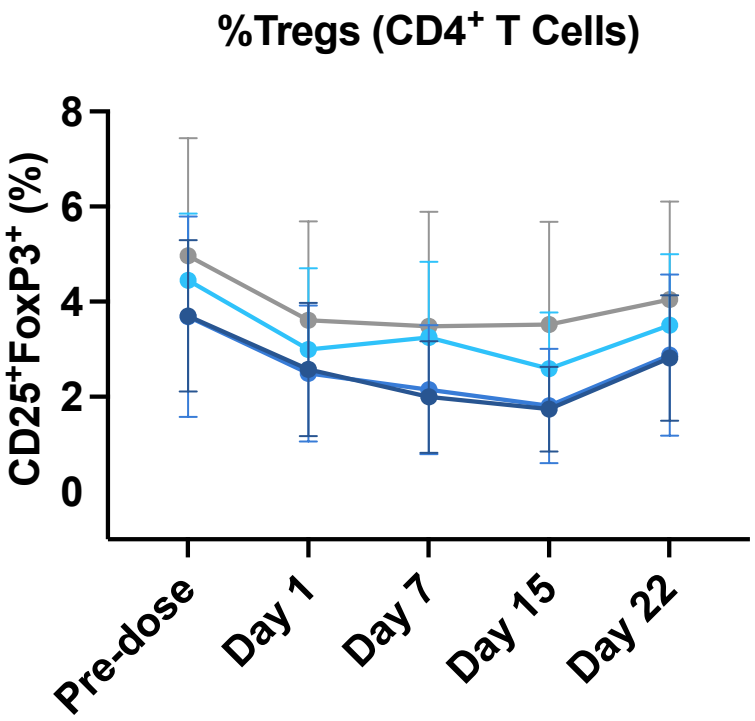


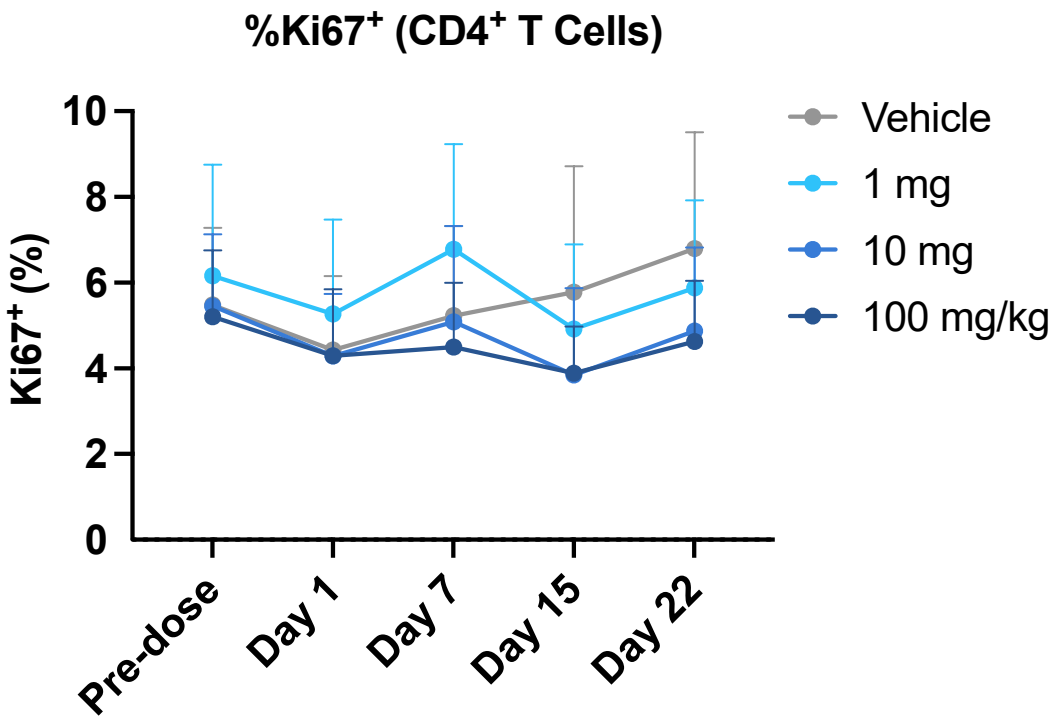


- Full DR3 RO was observed at all dose levels, and binding was durable for at least four weeks post-dose
- In two animals that developed ADA, a drop in DR3 RO was observed, suggesting trough concentrations ≥1 µg/mL maintain full RO

This slide shows preliminary data and analysis available to Shattuck as of the February 6, 2025.

SL-325 Showed No Signs of DR3 Agonism





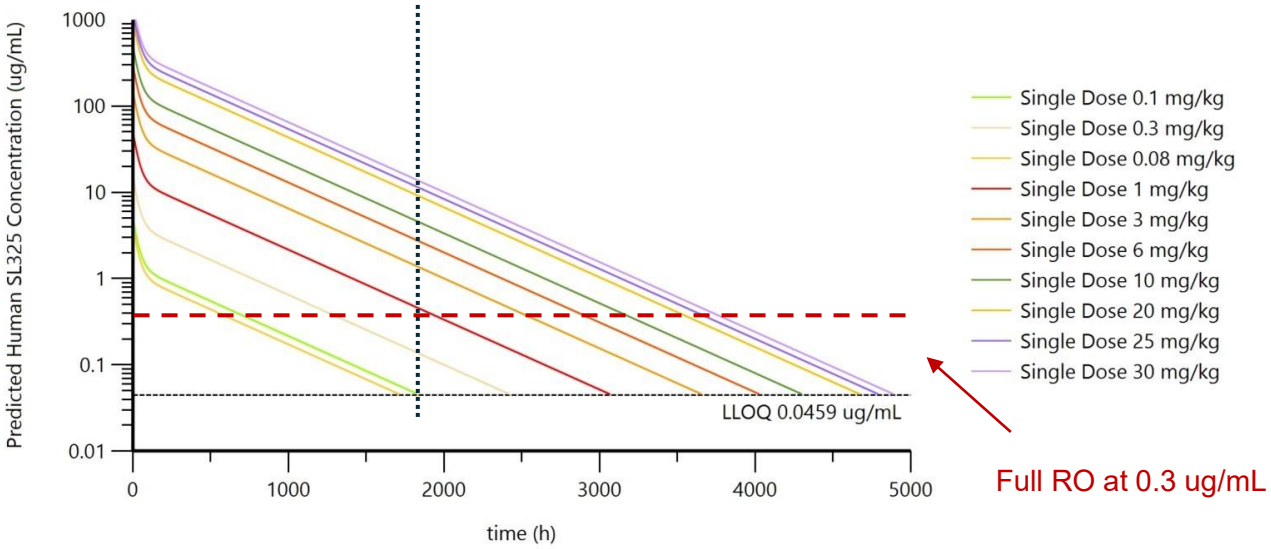
➔ Peripheral blood flow cytometry confirmed that there was no evidence of T cell proliferation in any treated animal

This slide shows preliminary data and analysis available to Shattuck as of the February 6, 2025.

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

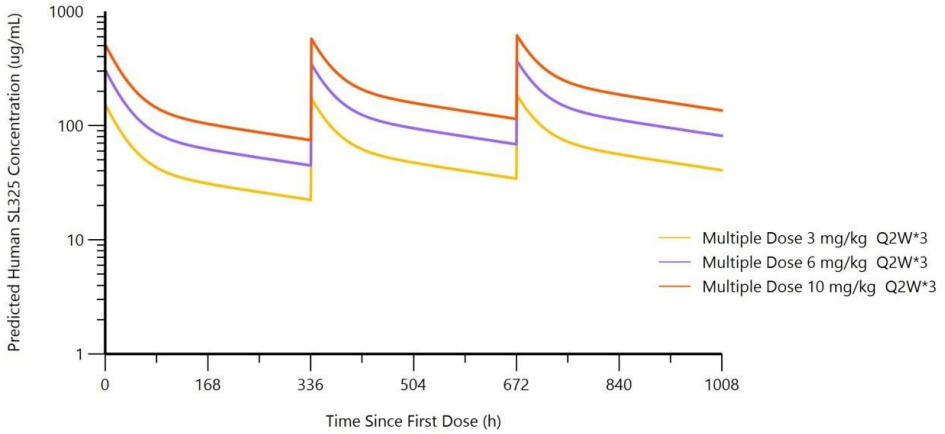
Predicted Human SL-325 PK Profiles in Serum Following Single IV Dose

Last RO Timepoint: Day 76 (1824h)



Full RO at 0.3 ug/mL

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

SHATTUCK LABS

SHATTUCK LABS

Corporate

Development Opportunities and Milestones

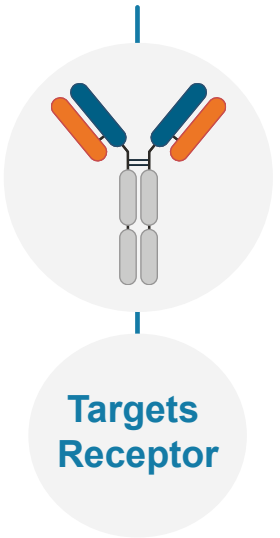
TL1A/DR3 Axis Development Landscape

TL1A Blocking mAbs

MERCK	sanofi teva	Roche	SPYRE THERAPEUTICS
Humanized mAb	Human IgG1 mAb	Fully human mAb	Fully human IgG1 mAb
Tulisokibart	Duvakitug	Afimkibart	SPY002

abbvie	xencor	absci
Fully human mAb	Human IgG1 mAb	AI platform-designed mAb
ABBV-701	XmAb942	ABS-101

DR3 Blocking mAbs



SHATTUCK LABS

Humanized mAb

SL-325

- ✓ Potential for more durable blockade of the TL1A/DR3 axis
- ✓ Potential for higher rates of endoscopic remission
- ✓ No risk of soluble TL1A/mAb immune complex formation
- ✓ Expected low ADA potentially improves combinability with other mAbs
- ✓ Scaffold for co-targeting other inflammatory receptors

Clinically Validated Axis in IBD

➔ 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 Blocking Ab Program

- ✓ SL-325 demonstrated superior TL1A/DR3 blockade in head-to-head preclinical studies as compared to benchmark TL1A antibodies
- ✓ Completed Acute and Chronic GLP tox studies; 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 in IBD with $33.3 billion in worldwide sales by 2030[1]
- ✓ Despite approved therapies, continued high unmet need in IBD and other inflammatory autoimmune diseases

Executing on Upcoming Milestones

- ✓ Enrollment nearly complete in Phase 1 clinical trial evaluating SL-325 in healthy volunteers
- ✓ Clinical data from the Phase 1 SAD/MAD clinical trial expected in Q2 2026
- ✓ Expect to initiate Phase 2b clinical trial in CD in Q3 2026
- ✓ Cash runway expected to fund planned operations and clinical development into 2029[2]

SHATTUCK LABS

1. Evaluate Pharma
2. Based on cash and cash equivalents and short-term investments as of December 31, 2025, including the gross proceeds from the sale of common stock under the Company's at-the-market offering facility of $21.4 million in the first quarter of 2026, and assuming the receipt of $51.7 million upon the full exercise of the outstanding common stock warrants.

Cash and Shares Outstanding

$78.1 million cash as of December 31, 2025[1]

$94.5 million cash as of February 28, 2026[2]

Expected cash runway into 2029[3]

Shares Outstanding[4]		Number of Shares (M)
Common Stock	Shares Outstanding	71.6
Common Stock Equivalents	Pre-Funded Warrants	42.3
Warrants Outstanding	Common Stock Warrants ($1.0846 Exercise Price)	47.6
	Total Outstanding[4]	**161.5**

1. Includes cash and cash equivalents and short-term investments as of December 31, 2025.
2. Includes cash and cash equivalents and short-term investments as of Feburary 28, 2026. This amount is preliminary, has not been audited or reviewed by the Company's independent registered public accounting firm, and is subject to change upon completion of the Company's financial closing procedures.
3. Based on cash and cash equivalents and short-term investments as of December 31, 2025, including the gross proceeds from the sale of common stock under the Company's at-the-market offering facility of $21.4 million in the first quarter of 2026, and assuming the receipt of $51.7 million upon the full exercise of the outstanding common stock warrants.
4. As of February 28, 2026. Excludes shares issuable pursuant to issued and outstanding employee stock options and unvested restricted stock units.

SHATTUCK LABS

SHATTUCK LABS

Thank You

Investor Relations
InvestorRelations@ShattuckLabs.com