SHATTUCK LABS

Engineering Biologics for TNF Receptor Modulation

Corporate Overview

NASDAQ: STTK

October 1, 2024

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; the potential purity, potency and clinical benefits of our product candidates, including SL-325; the anticipated timing of an IND filing for SL-325; the anticipated timing and design of our planned and ongoing preclinical studies and clinical trials; 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, 2023 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.

SHATTUCK LABS

Shattuck Labs

Focused on Improving the Lives of Patients

OUR PURPOSE

Develop novel biologics for autoimmune, inflammatory, and other 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

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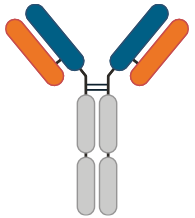
Shattuck Labs Overview

Shattuck Labs (NASDAQ: STTK)	**Biotechnology company specializing in the development of TNF receptor modulators and multifunctional fusion proteins for the treatment of autoimmune, inflammatory, and other indications**
Lead Program: SL-325	 • Potential first-in-class antagonist 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)
Preclinical Pipeline	• Bispecific variants of the DR3 targeted antibody for IBD and other autoimmune diseases • Bifunctional fusion proteins formulated as mRNA/LNP • TRIM7 inhibitors for oncology
Experienced Team and Strong Cash Position	• Highly experienced management team, board of directors, and scientific advisory board • $105.3 million in cash and cash equivalents and investments as of June 30, 2024 • Expected to fund planned operations into 2027

DR3 = Death Receptor 3 (TNFRSF25)

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Highly Experienced Management and Board

Established Track Record of Drug Discovery and Development

Management Team

Taylor Schreiber, MD, PhD
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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

George Fromm, PhD
Co-Chief Scientific Officer

Suresh de Silva, PhD
Co-Chief Scientific Officer

Stephen Stout, PhD
General Counsel, Corporate Secretary and Chief Ethics and Compliance Officer

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

Michael Lee
Redmile Group

Kate Sasser, PhD,
Chief Scientific Officer of Tempus

Taylor Schreiber MD, PhD
Chief Executive Officer, Shattuck

Clay Siegall, PhD
President, CEO and Chairman of the Board of Immunome; *CEO of Seattle Genetics*

Note: italicized text denotes prior affiliation

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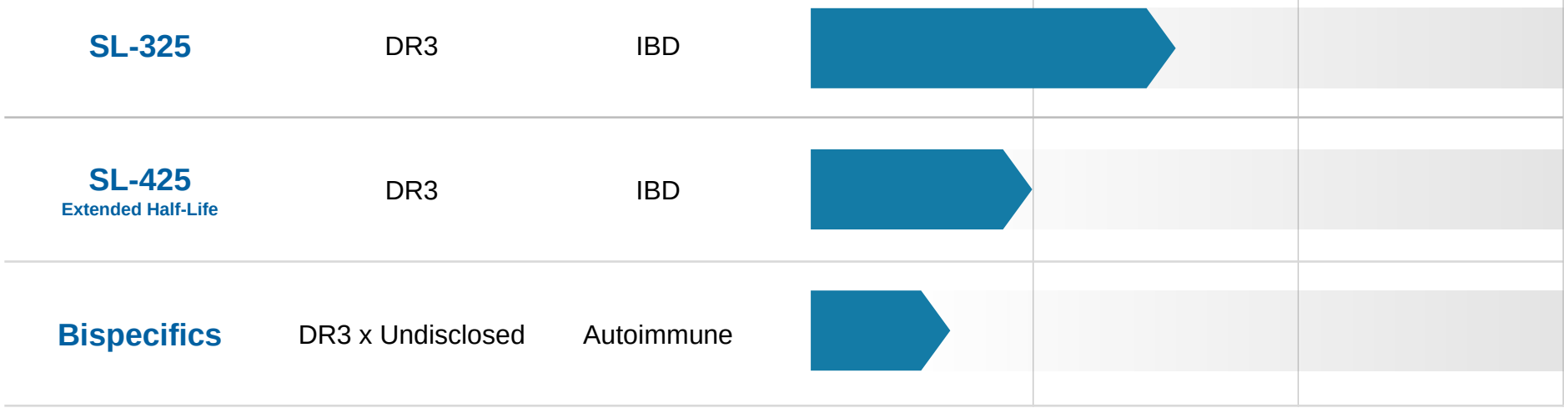
Shattuck's Pipeline

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

IBD = Inflammatory Bowel Disease

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TL1A / DR3 Biology

Rationale for Targeting the Receptor
in a Clinically-Validated Axis

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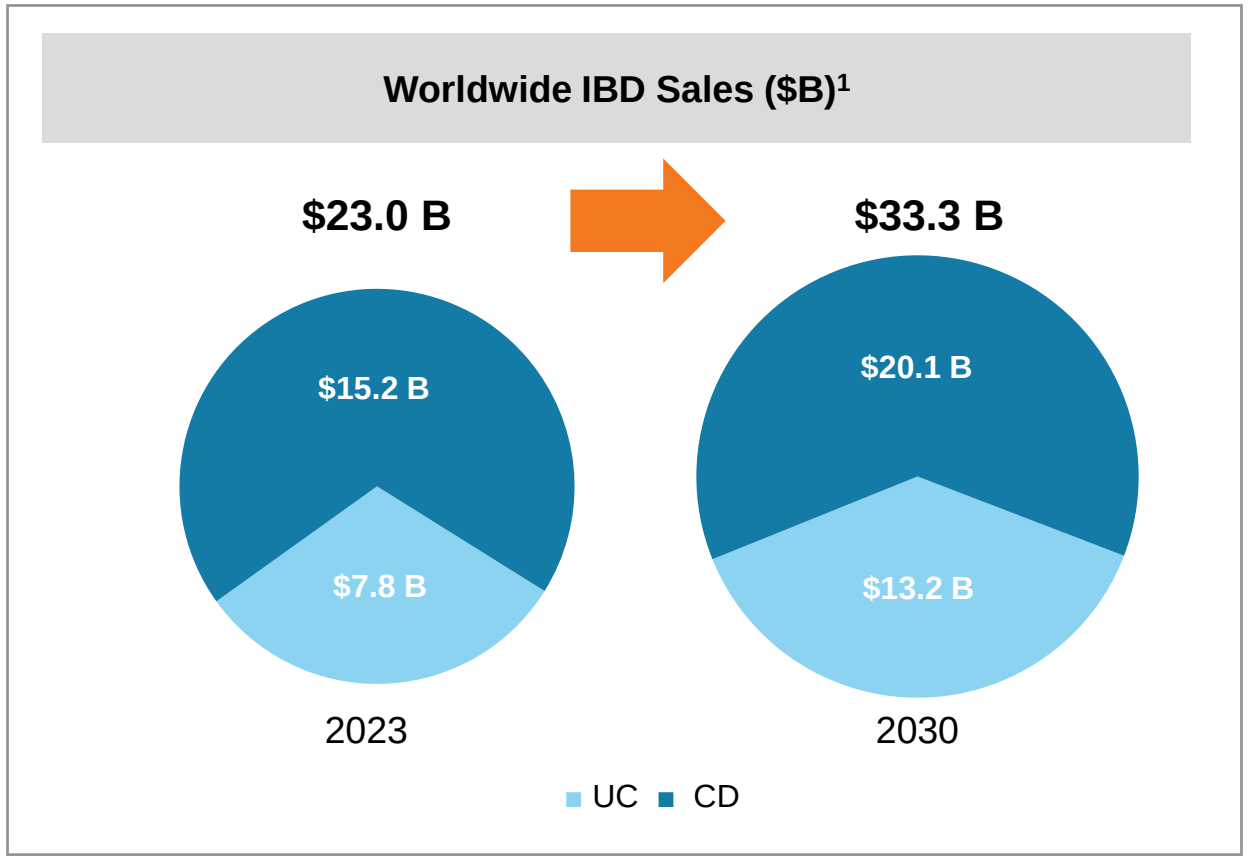
Inflammatory Bowel Disease Is a Large and Growing Market

New Approaches Are Driving Innovation and Improving Patient Outcomes



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

UC = Ulcerative Colitis; CD= Crohn's Disease

1. Evaluate Pharma

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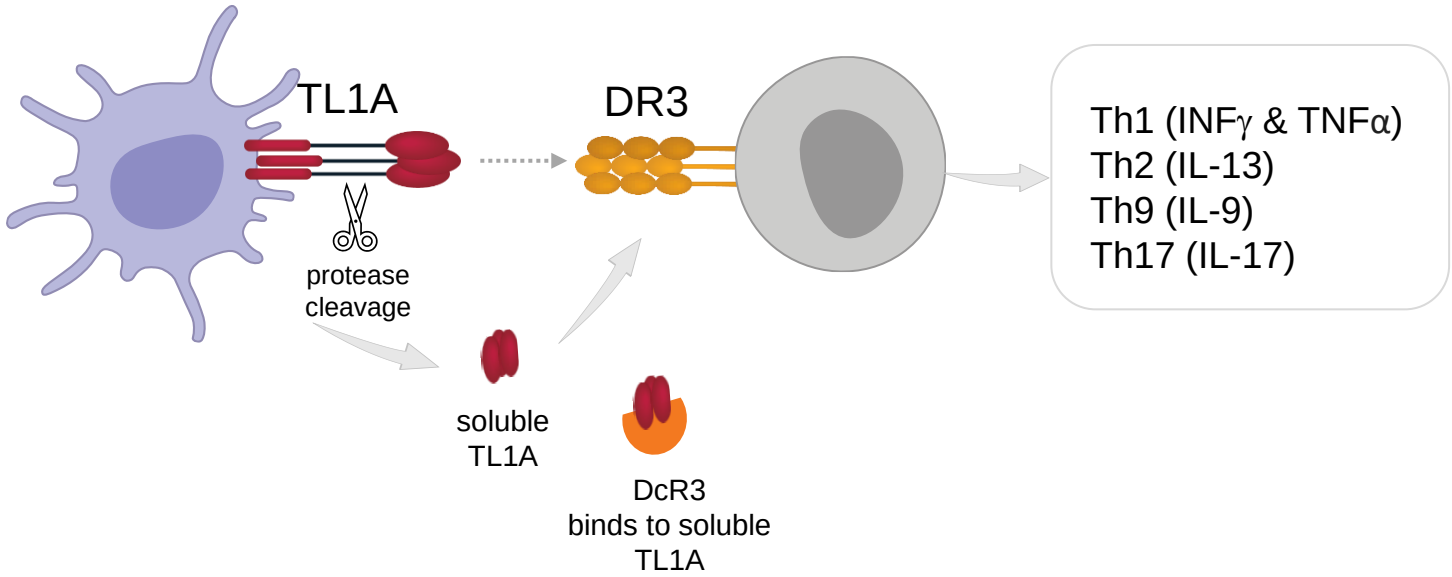
TL1A Is the Sole Activating Ligand for DR3

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), and binds to the DR3 receptor and 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

Schreiber et al. Immunol Rev. 2013

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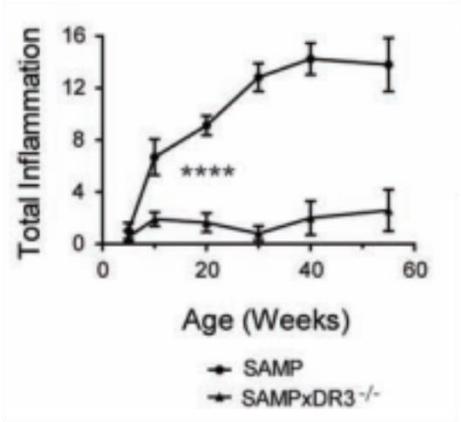
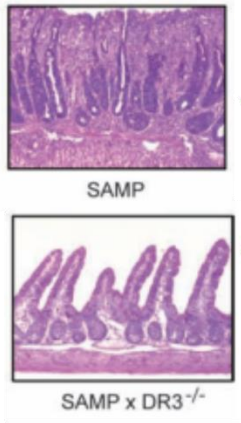
DR3 Inhibition is Potentially More Potent Than TL1A Inhibition

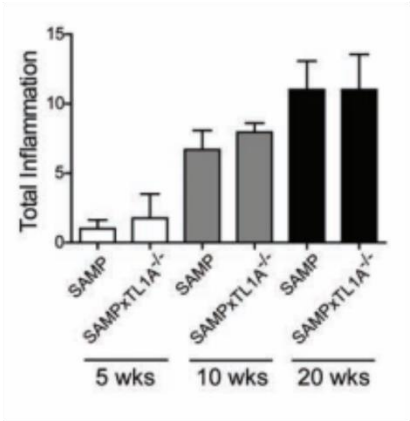
DR3 knockout in SAMP mouse

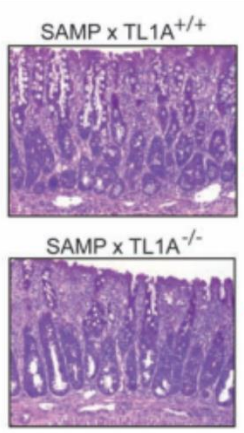




Fully prevents the onset of CD-like Ileitis

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

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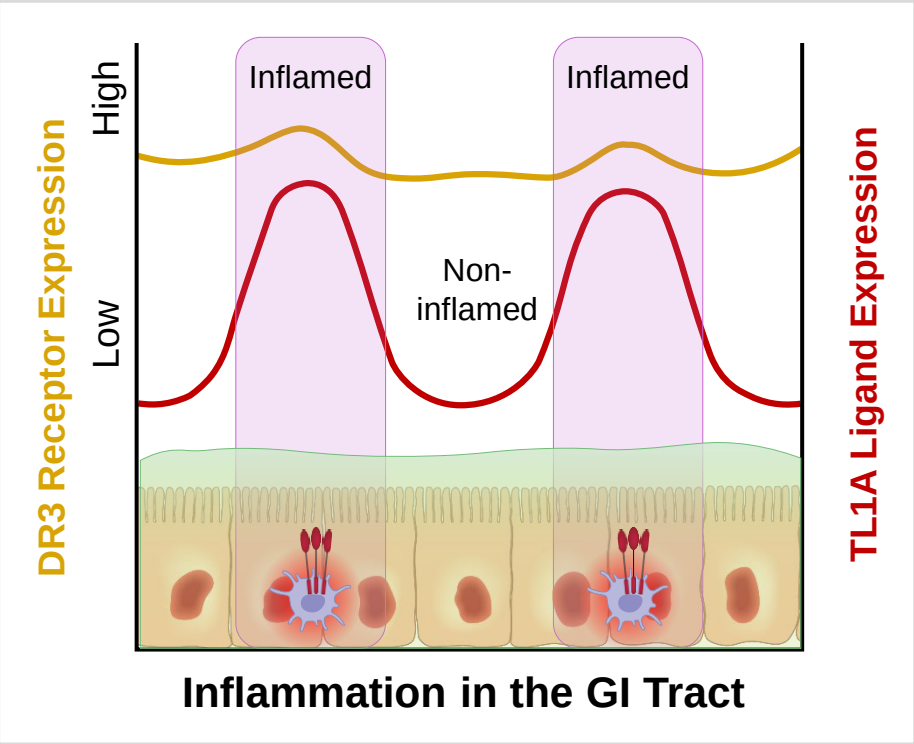
Targeting DR3 May Enable More Effective Treatment of Inflammation

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

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

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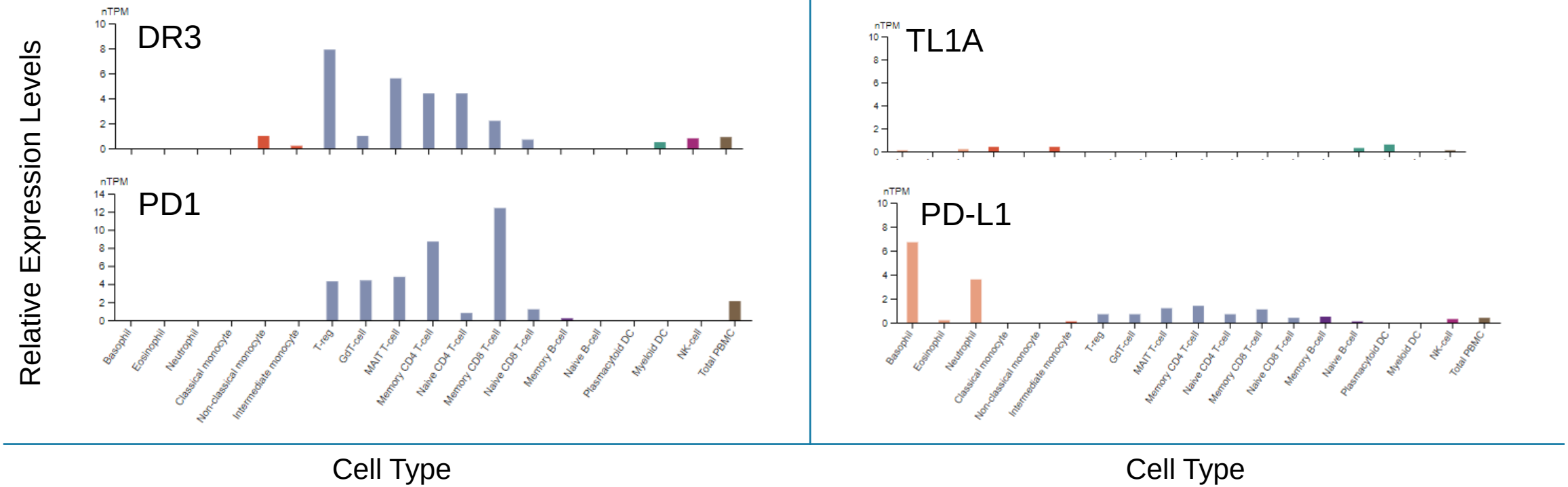
DR3/TL1A Expression Parallels PD1/PD-L1 Expression

Expression Differences in Peripheral Cells

Stably Expressed Receptors | **Transiently Expressed Ligands**



- Targeting of stably expressed receptors may be more efficacious than targeting transiently expressed ligands
- TL1A antibodies must penetrate tissues and remain present at high concentrations to inhibit TL1A when it is transiently expressed, like PD-L1 blocking antibodies

The Human Protein Atlas

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SL-325 Program

Potential First-In-Class DR3 Antagonist Antibody

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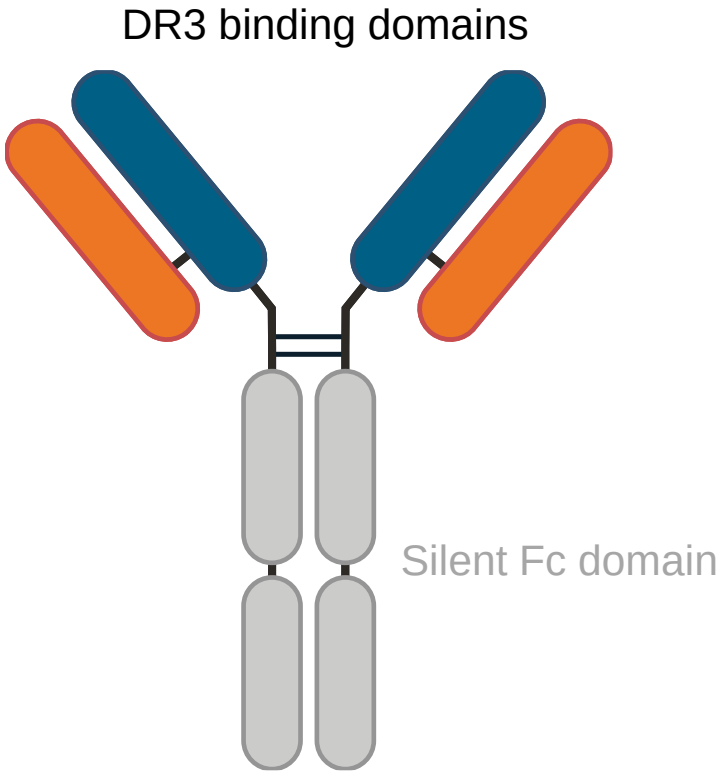
SL-325 Designed for Potent DR3 Blockade



SL-325

- **Picomolar binding affinity to DR3 and overlapping epitope with TL1A**
- **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**

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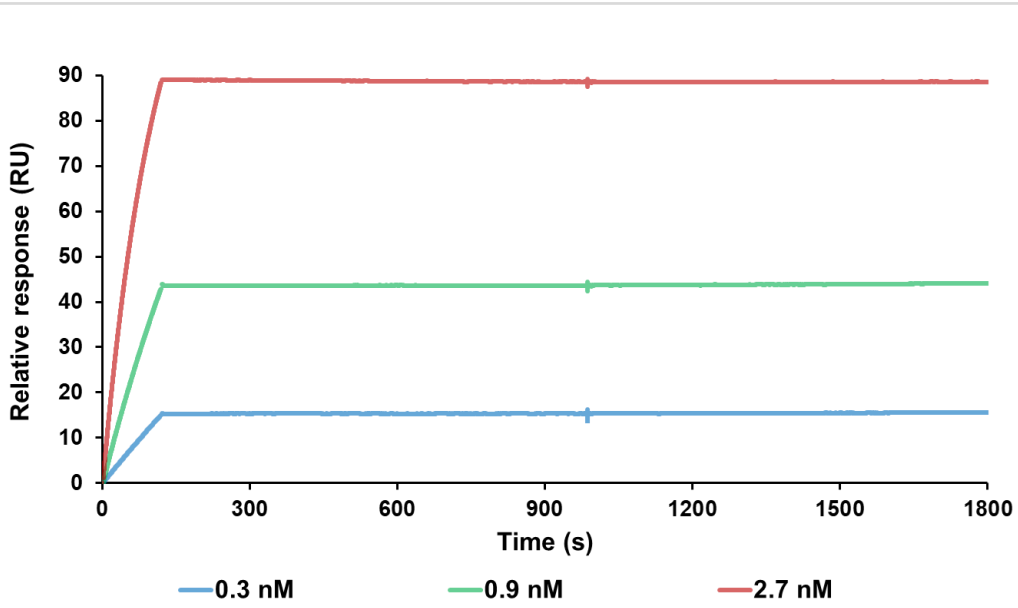
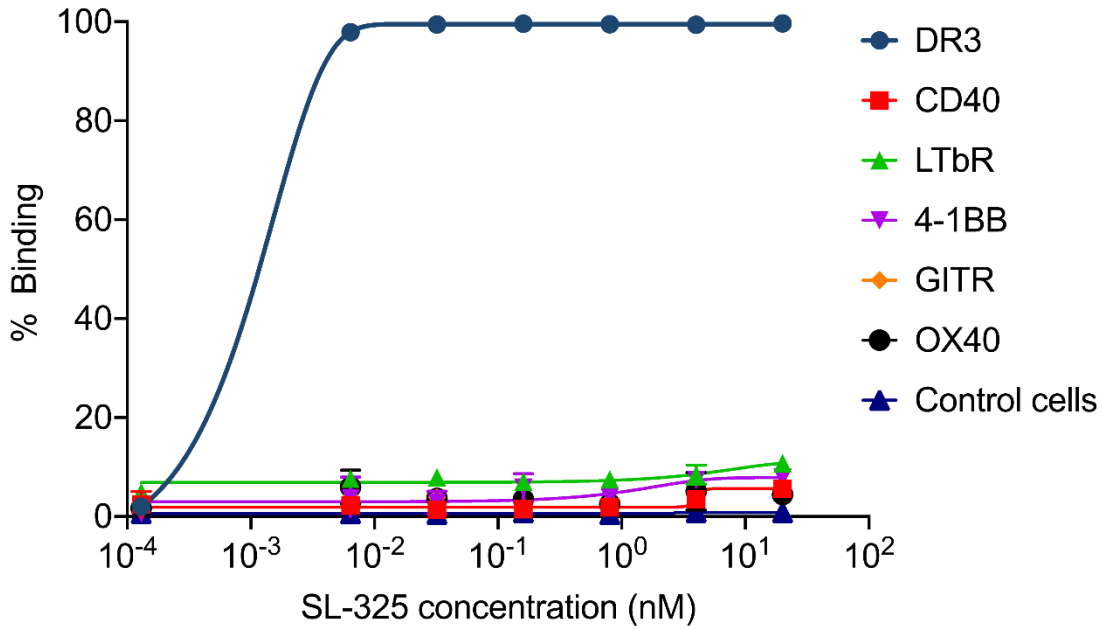
SL-325 Binds to Human DR3 with High Affinity and Specificity

DR3 Binding Kinetics



DR3 Binding Specificity



- SL-325 binds to recombinant human DR3 with a K_D of 1.3pM
- SL-325 does not bind DcR3 or other members of the TNF receptor superfamily

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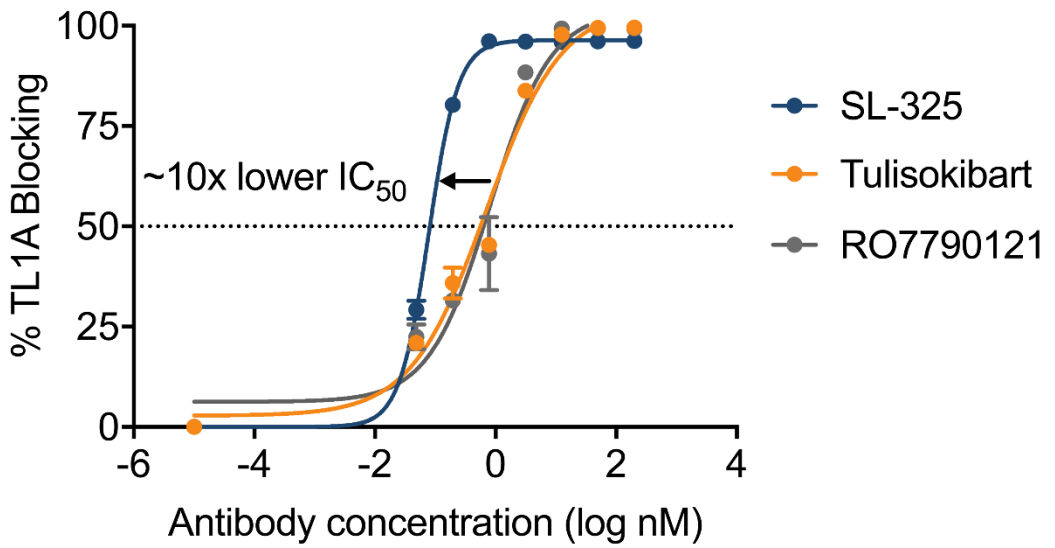
SL-325 Blocks TL1A Binding at Lower Concentrations than Benchmark Anti-TL1As



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

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

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.

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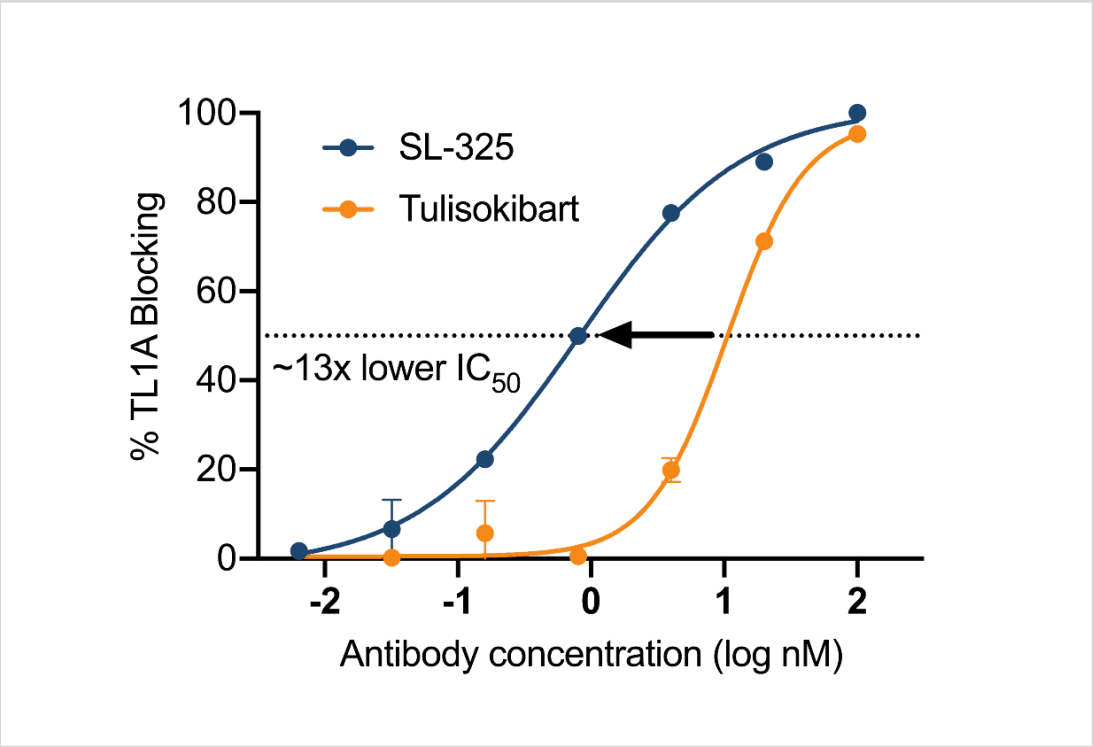
SL-325 Blocks TL1A Binding to Cell Expressed DR3 More Efficiently than Benchmark Anti-TL1A



➔ SL-325 outperformed the benchmark anti-TL1A antibody in blocking TL1A binding to DR3 on cells

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

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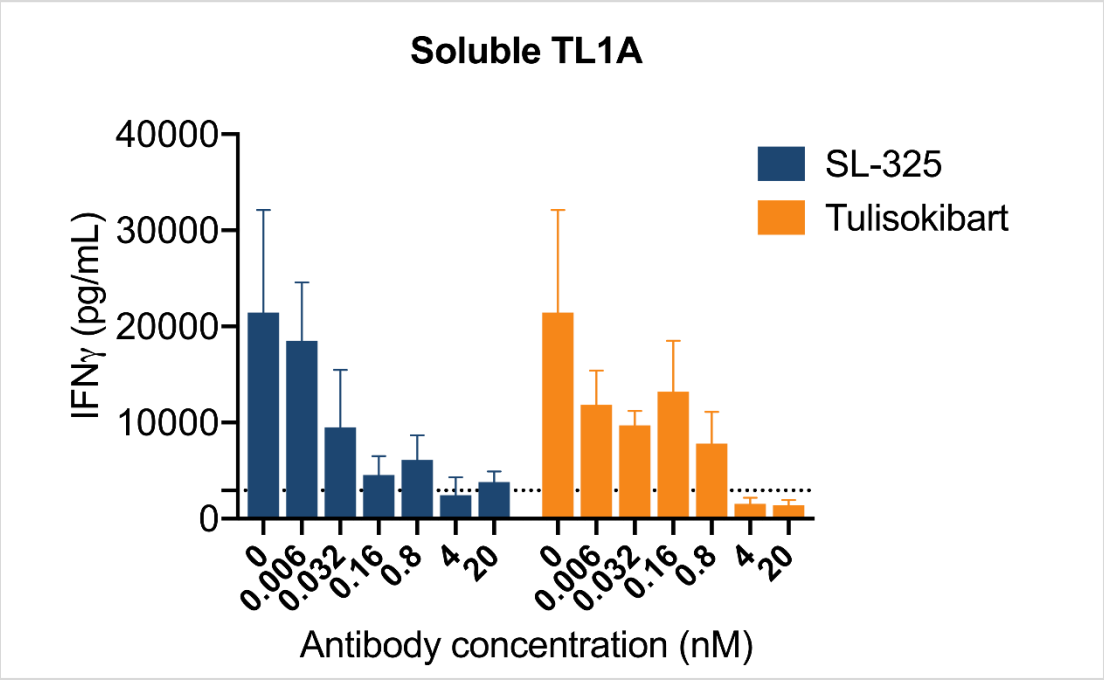
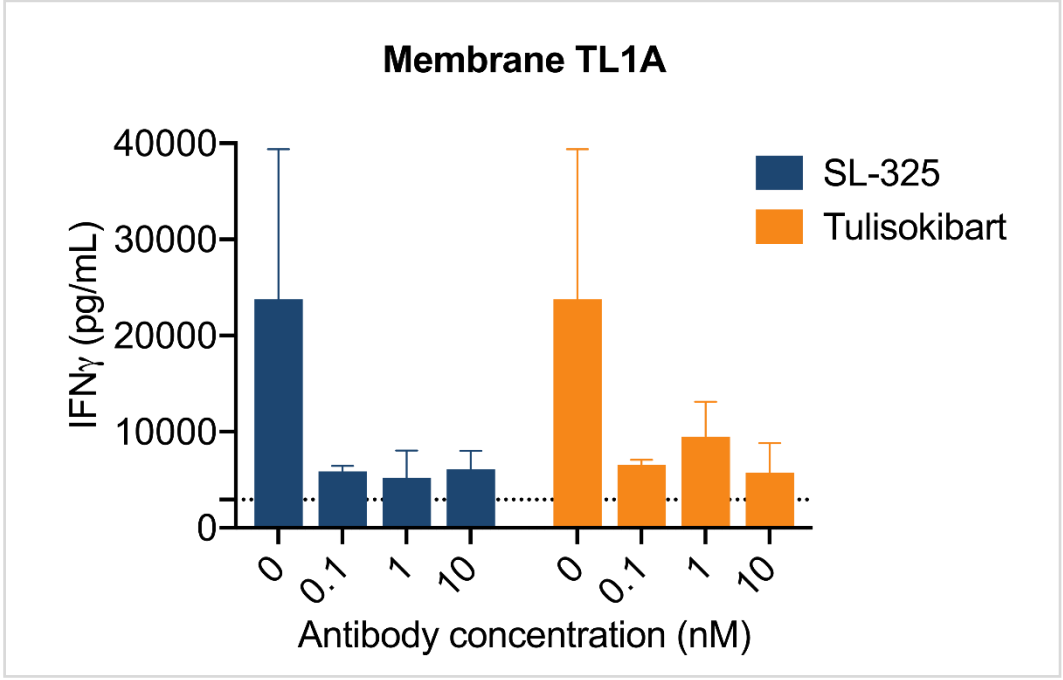
SL-325 Blocks Soluble and Membrane Bound TL1A Induced IFNγ Secretion from Healthy Donor PBMCs





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

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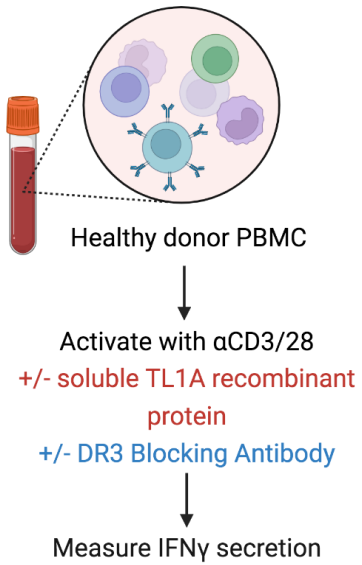
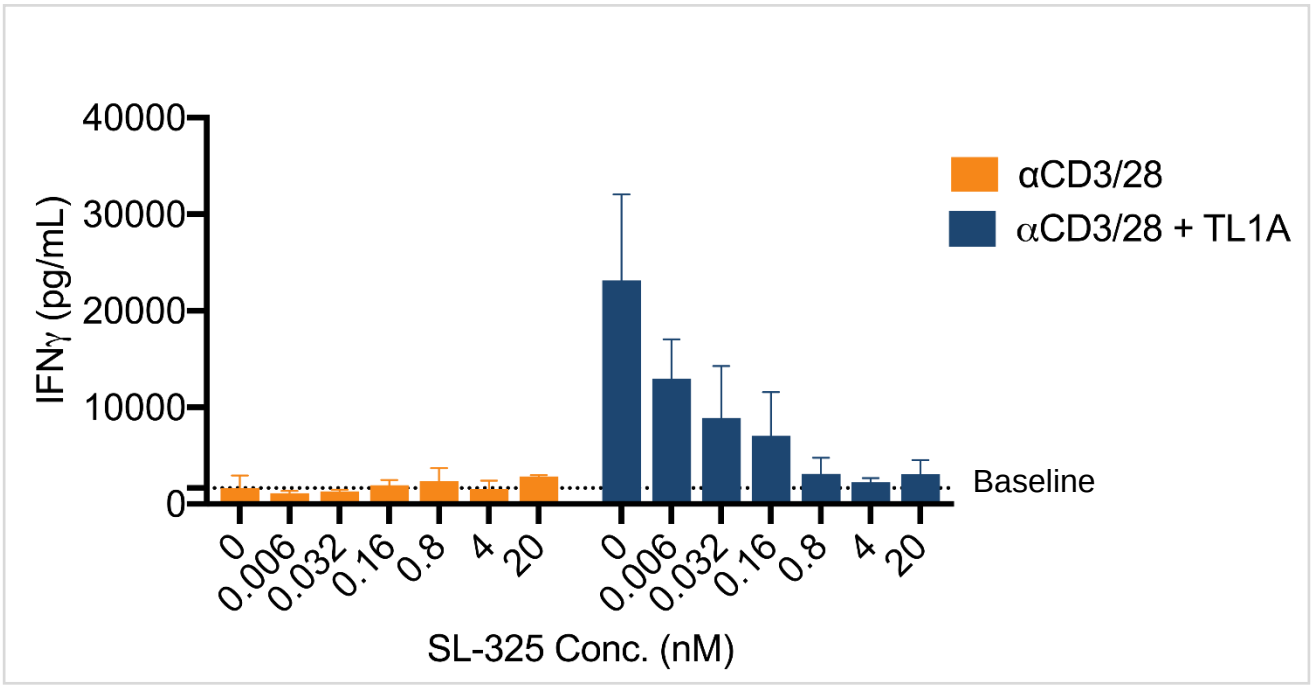
SL-325 Blocks TL1A-Induced IFNγ Release from Human Lymphocytes





➔ SL-325 efficiently prevented IFNγ secretion induced by TL1A binding to DR3

➔ SL-325 was engineered to remove Fc gamma receptor binding

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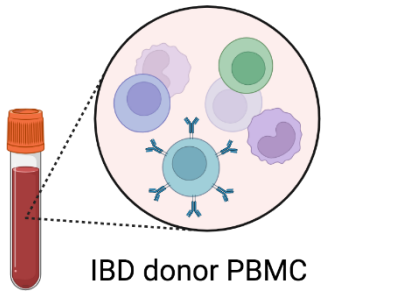
SL-325 Blocks TL1A-Induced IFNγ Secretion from IBD Patient PBMCs



IBD donor PBMC

↓

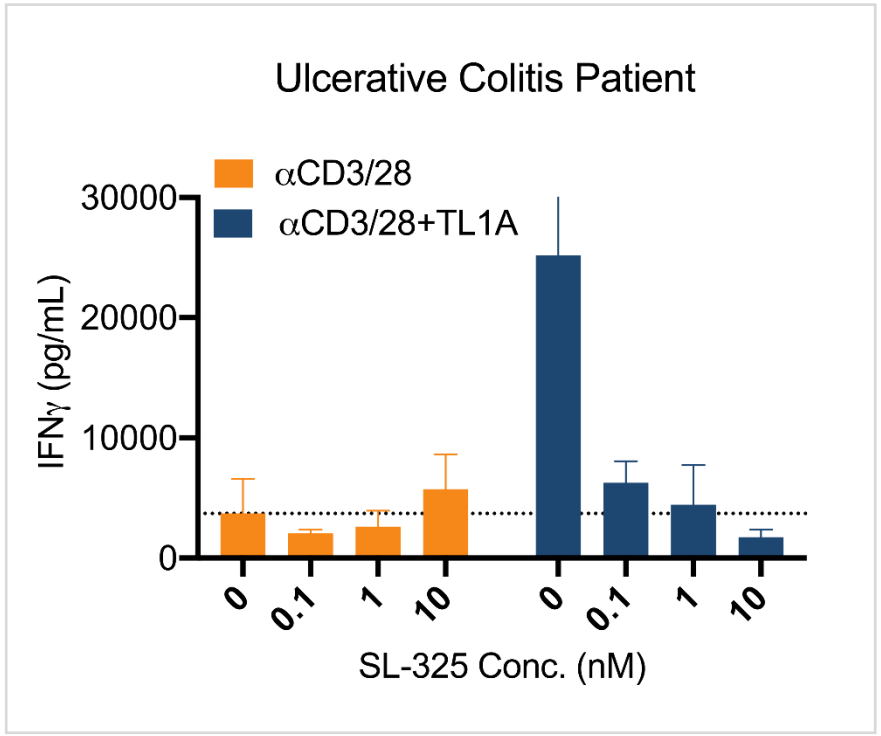
Activate with αCD3/28

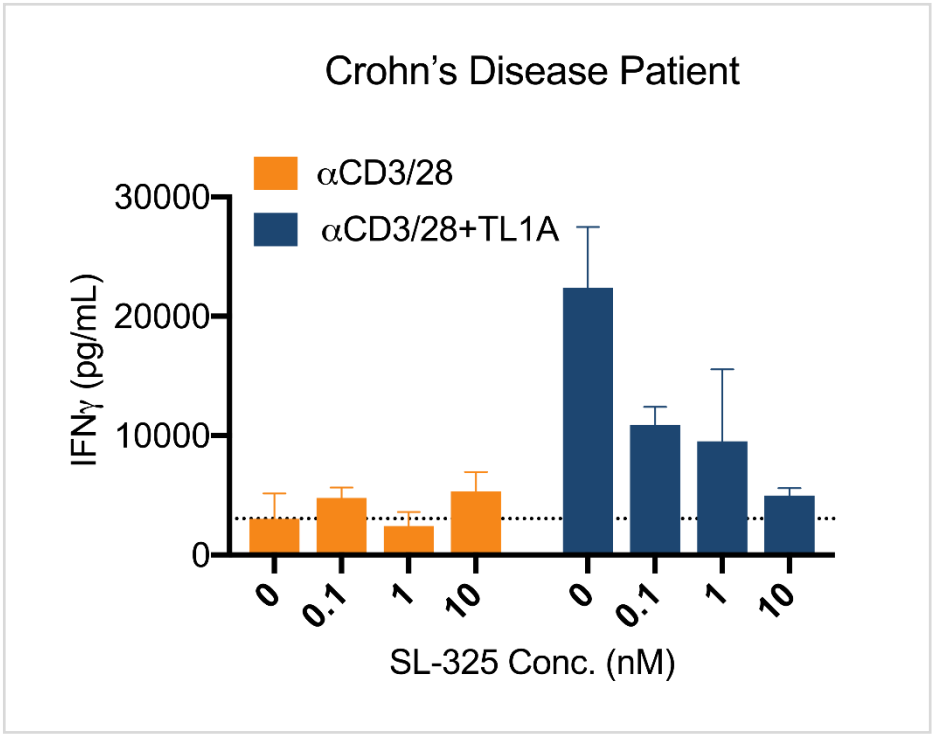
+/- soluble TL1A recombinant protein

+/- DR3 Blocking Antibody

↓

Measure IFNγ secretion





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

PBMCs = Peripheral blood mononuclear cells

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TL1A/DR3 Axis Development Landscape

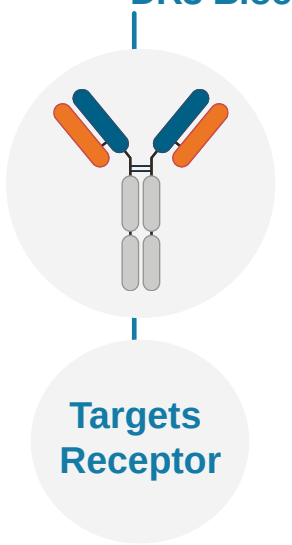
All Current Competitor Strategies Are TL1A Blocking mAbs

TL1A Blocking mAbs

MERCK	sanofi teva	Roche	SPYRE THERAPEUTICS
Humanized mAb	Human IgG1 mAb	Fully human mAb	Fully human IgG1 mAb
Tulisokibart	TEV-48574	RO7790121	SPY002

abbvie	xencor	absci
Fully human mAb	Human IgG1 mAb	AI platform-designed mAb
FG-M701	XmAb942	ABS-101

DR3 Blocking mAbs



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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
- ✓ No interference with prior TL1A mAb treatment
- ✓ 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

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Shattuck Labs Expected Milestones

Developing the Next Generation TNF Receptor Modulators

First-in-Class DR3 Antagonist Program

- ✓ SL-325 demonstrates superior TL1A/DR3 blockade in preclinical studies as compared to benchmark TL1A antibodies
- ✓ 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[1]
- ✓ High unmet need in IBD and other inflammatory autoimmune diseases

Executing on Upcoming Milestones

- ✓ IND-enabling work ongoing; expected IND filing in Q3 2025
- ✓ Initial clinical data expected in 2026
- ✓ Cash runway expected to fund operations and development into 2027

1. Sands B et al. NEJM 2024

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Thank You

Investor Relations

InvestorRelations@ShattuckLabs.com

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