

SITC 2021 Investor Conference Call & Webcast

NASDAQ: STTK

November 12, 2021

SHATTUCK LABS

PIONEERING NOVEL BI-FUNCTIONAL FUSION PROTEINS
EXPANDING THE BOUNDARIES OF BIOLOGIC MEDICINES

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, including statements concerning our plans, objectives, goals, strategies, future events, plans or intentions relating to products and markets, the safety, efficacy and clinical benefits of our product candidates, the anticipated timing of our planned clinical trials, including initiation of additional cohorts, the anticipated timing for data, the association of preclinical data with potential clinical benefit, the timing of anticipated milestones, plans and objectives of management for future operations and future results of anticipated product development efforts, the timing of expected announcements, and our liquidity and capital resources and business trends are all forward-looking statements. 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 the effects from the COVID-19 pandemic on our clinical trial activities, the uncertainties inherent in the clinical drug development process, such as the regulatory approval process, the timing of our regulatory filings, the potential for substantial delays, and the risk that earlier study results may not be predictive of future study results, manufacturing risks, and competition from other therapies or products, 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, 2020 and elsewhere in such filing and in our other periodic reports and subsequent disclosure documents filed with the U.S. Securities and Exchange Commission.

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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.

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Agenda

Introduction	Conor Richardson – Sr. Director, Finance & Investor Relations
ARC Platform Overview	Taylor Schreiber, M.D., Ph.D. – Chief Executive Officer
Review of SL-172154 Clinical Data	Lini Pandite, MBChB, M.B.A. – Chief Medical Officer
Review of SL-279252 Clinical Data	Lini Pandite, MBChB, M.B.A. – Chief Medical Officer
Corporate and Strategic Priorities	Andrew Neill, M.B.A. – Chief Financial Officer
ARC Platform Learnings	Taylor Schreiber, M.D., Ph.D. – Chief Executive Officer
Q&A	Shattuck Management

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Taylor Schreiber, M.D., Ph.D.
Chief Executive Officer

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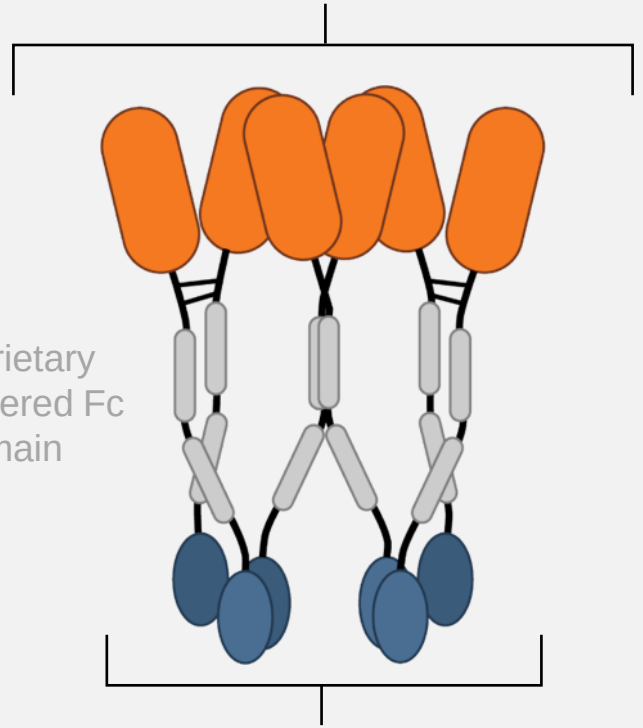
ARC Platform Technology

Designed to Simultaneously Block Immune Checkpoints and Activate TNF Receptors

6 Checkpoint Binding Domains



6 TNF Receptor Binding Domains
(two sets of TNF ligand trimers)

ARC Platform Structure and Advantages
✓ **Checkpoint Inhibition** Removes the “brakes" from the immune system
✓ **TNF Superfamily Agonism** Trimerized ligands activate trimeric TNF receptors
✓ **Colocalization of Multiple Mechanisms** Within a single therapeutic

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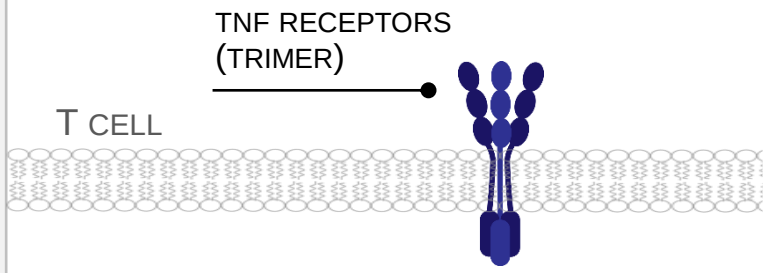
Current Antibody Therapy Approaches Have Limitations

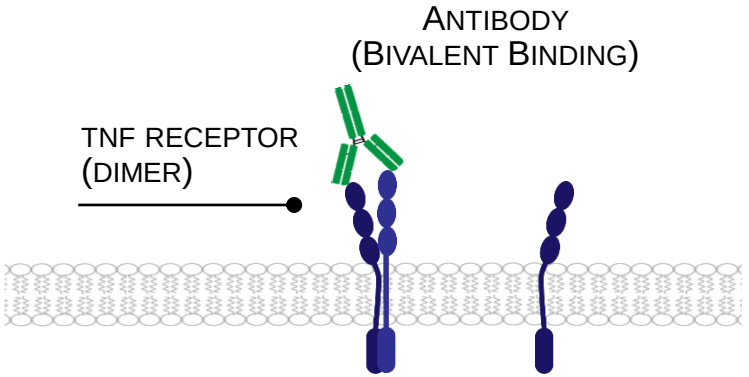
Bivalent Antibodies Cannot Efficiently Activate Trimeric Receptors

A.



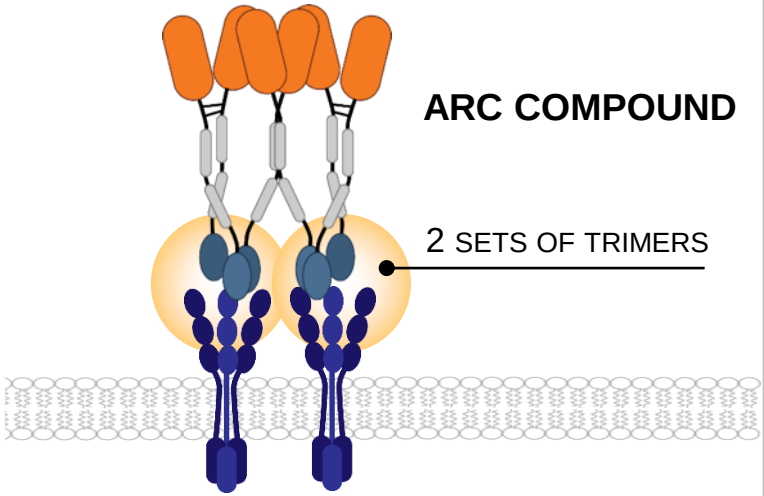
TNF receptors require trimerization for effective activation, and hexamers signal even more effectively than trimers†

B.



Bivalent antibodies cannot bring together TNF receptors to form a trimer due to a **structural mismatch**

C.



ARCs contain two preformed TNF ligand trimers, which match the requisite structure to efficiently **activate TNF receptor signaling**

† Vanamee E et al., *Science Signaling,* Jan 2018

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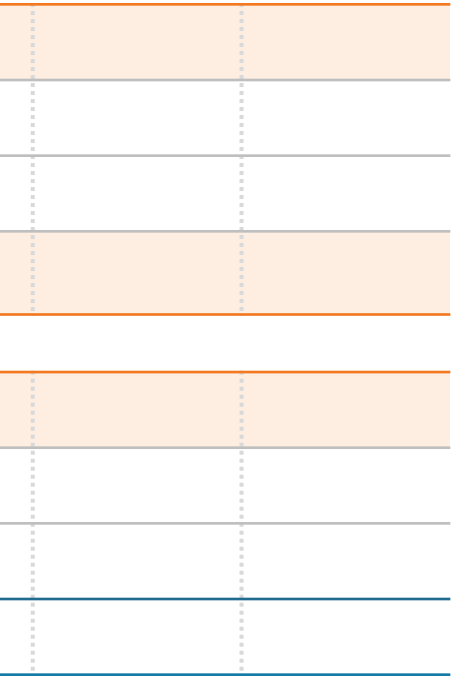
Shattuck's Development Pipeline

Deep Pipeline of Scientifically Validated and Novel Targets

PLATFORM	PROGRAM	DOMAINS: DOMAIN 1	DOMAINS: DOMAIN 2	INDICATIONS	STAGE OF DEVELOPMENT
CLINICAL-STAGE PIPELINE					
ARC	SL-172154	SIRPα	CD40L	Ovarian Cancer (1)	
				CSCC and HNSCC	
				AML and HR-MDS	
	SL-279252	PD-1	OX40L	Advanced Solid Tumors (2) and Lymphoma	
SELECT PRECLINICAL-STAGE PIPELINE					
ARC	SL-9258	TIGIT	LIGHT	Oncology (3)	
	SL-279137	PD-1	4-1BBL	Oncology	
	Multiple	Undisclosed		Oncology and Autoimmune	
GADLEN	Multiple	γδ TCR	Tumor Antigen	Oncology	



SITC Abstract Titles:

(1) Phase 1 Dose Escalation Study of the Agonist Redirected Checkpoint SL-172154 (SIRPα-Fc-CD40L) in Subjects with Platinum-Resistant Ovarian Cancer (Abstract #459)

(2) Phase 1 Dose Escalation and Dose Expansion Study of an Agonist Redirected Checkpoint (ARC) Fusion Protein, SL-279252 (PD1-Fc-OX40L), in Subjects with Advanced Solid Tumors or Lymphomas (Abstract #494)

(3) LIGHT (TNFSF14) Co-stimulation Enhances Myeloid Cell Activation and Anti-tumor Immunity in the Setting of PD-1 and TIGIT Checkpoint Blockade (Abstract #585)

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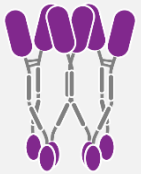
SITC Clinical Data Overview

Key Highlights

SL-172154 (SIRPα-Fc-CD40L)

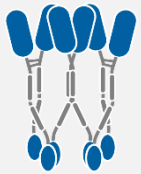


High Target Engagement
High CD47 target occupancy and CD40 target engagement

Potent Immune Activation
Dose-dependent CD40 activation

Favorable Safety Profile
No MTD reached to date, continuing dose escalation to 10 mg/kg

SL-279252 (PD1-Fc-OX40L)



Anti-Tumor Activity
Response rate consistent with PD1 experienced patient population †

On-Target TNF Activation
Dose-dependent OX40 activation

Favorable Safety Profile
No MTD reached to date, continuing dose escalation to 12 mg/kg

ARC Platform Validation



Active Clinical Compounds
Initial anti-tumor activity and unique pharmacodynamic effects

Unlocking TNF Receptor Biology
No DLTs to date at doses which achieve high target binding to both CD40 and OX40, with no evidence of bell-shaped dose-response curve

Intratumoral Immune Effects
Intravenous dosing of ARCs has led to activation of local immune response within tumor microenvironment

† Katayama et al., *Journal of Clinical Medicine,* 2018

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Lini Pandite, MBChB, M.B.A.
Chief Medical Officer

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ABSTRACT #459

SL-172154 (SIRPα-Fc-CD40L)

Phase 1 Dose Escalation Study of the Agonist Redirected Checkpoint SL-172154 (SIRPα-Fc-CD40L) in Subjects with Platinum-Resistant Ovarian Cancer

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SL-172154: Novel CD47 Inhibitor + CD40 Agonist

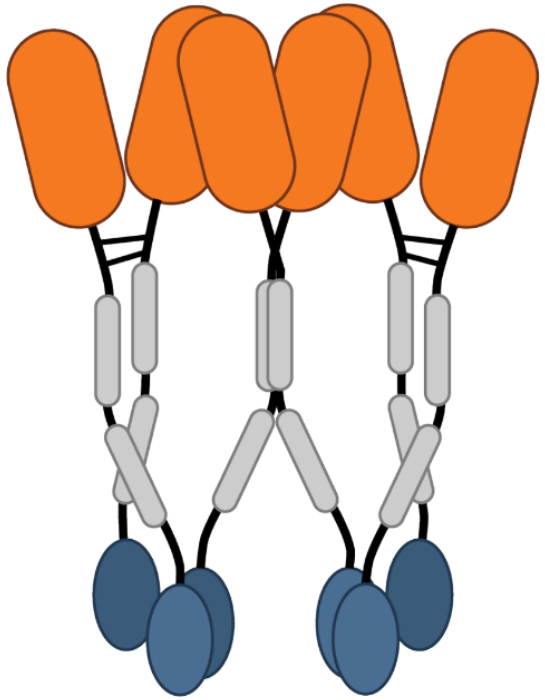
Rationally Designed to Maximize the Benefits of CD47 Blockade

Highly Differentiated
CD47 Inhibitor

Dual Mechanism
of Action

Unique Activator of
CD40 Pathway

SL-172154
(SIRPα-Fc-CD40L)



6 SIRPα Binding Domains
Blocks “Don’t Eat Me” CD47
Macrophage Checkpoint

Inert IgG4 Fc

2 CD40L Trimers
Provides CD40 Stimulation to
Antigen Presenting Cells

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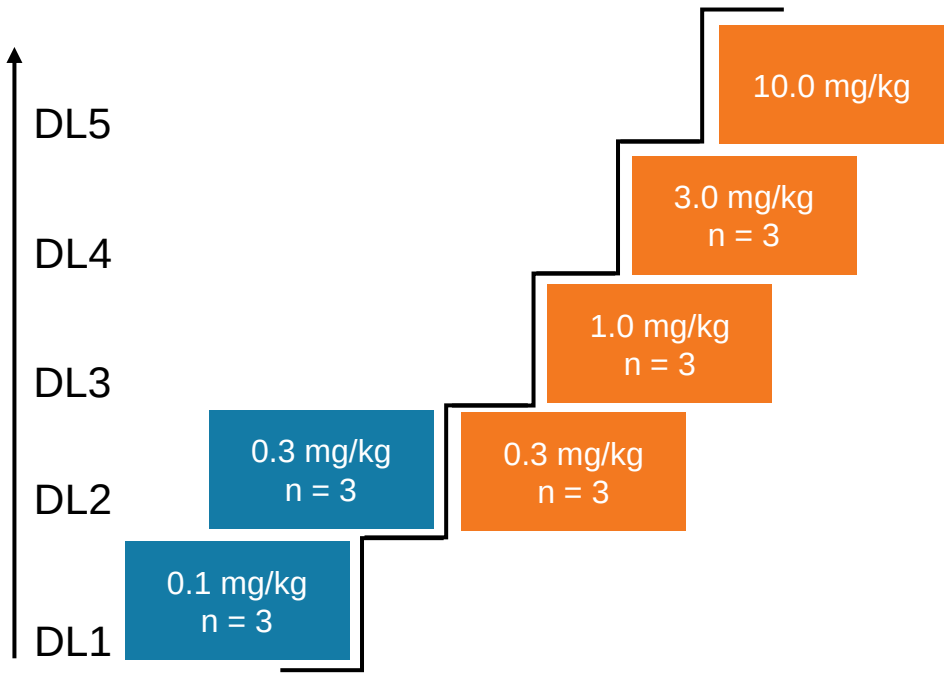
SL-172154: Phase 1A in Ovarian Cancer

Trial Design and Objectives

Dose Escalation per Modified Toxicity Probability Interval (mTPI-2) Design (N=15)



Schedule 1 (D1, D8, D15) then every two weeks (Q2W); cycle length = 28d

Schedule 2 once weekly (QW); cycle length = 28d

Study Objectives: Evaluate the safety, identify a dose and schedule, and characterize the PK, immunogenicity, PD, and anti-tumor activity of SL-172154

Key Inclusion Criteria

- Locally advanced or metastatic ovarian cancer, primary peritoneal cancer or fallopian tube cancer
- Refractory to existing therapy(ies) and ineligible for further platinum therapy; subjects with homologous recombination deficiency positive disease must have received prior PARPi with or without bevacizumab
- Age 18 years or older
- ECOG performance status of 0 or 1
- Measurable disease per RECIST v1.1

Lakhani et al., *SITC*, 2021
Data cut off: September 15, 2021

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SL-172154: Baseline Characteristics and Disposition

Heavily Pre-Treated Patient Population

- Age: 67 (median), 33-79 (range)
- Prior lines of systemic therapy: 5 (median), 2-7 (range)

Tumor Characteristics (All Treated)

Total number of subjects		**N = 15**
Tumor characteristics (all treated)		**n (%)**
Cancer type	Ovarian cancer	9 (60)
	Primary peritoneal cancer	4 (27)
	Fallopian tube cancer	2 (13)
FIGO stage	Stage III	6 (40)
	Stage IV	9 (60)
Grade	High grade	11 (73)
	Grade 3	1 (7)
	Unknown	3 (20)
Histologic classification	Serous carcinoma	11 (73)
	Adenocarcinoma	2 (13)
	Serous adenocarcinoma	2 (13)

FIGO = International Federation of Gynecology and Obstetrics

Lakhani et al., *SITC*, 2021
Data cut off: September 15, 2021

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SL-172154: Summary of Safety in All Treated Subjects

Favorable Safety Profile

Treatment-Related AEs in ≥ 2 Subjects

Total number of subjects	**N = 15**
Treatment-related AEs (any grade)	**n (%)**
Any	14 (93%)
IRR	8 (53%)
Fatigue	7 (47%)
Nausea	4 (27%)
Decreased appetite	3 (20%)
Chills	2 (13%)
Diarrhea	2 (13%)
Dyspnea	2 (13%)

- ➔ No dose-limiting toxicities
- ➔ No ≥ G3 treatment-related AEs

Infusion Related Reactions (IRR)

17 IRR events in 8 subjects (53%)

- 14 IRRs were G2 in severity and 2 IRRs were G1 in severity
- 1 IRR event was G3 and deemed secondary to iron infusion
- IRRs were manageable with pre-medications and did not prevent completion of infusion or lead to discontinuation of SL-172154

Lakhani et al., *SITC*, 2021
Data cut off: September 15, 2021

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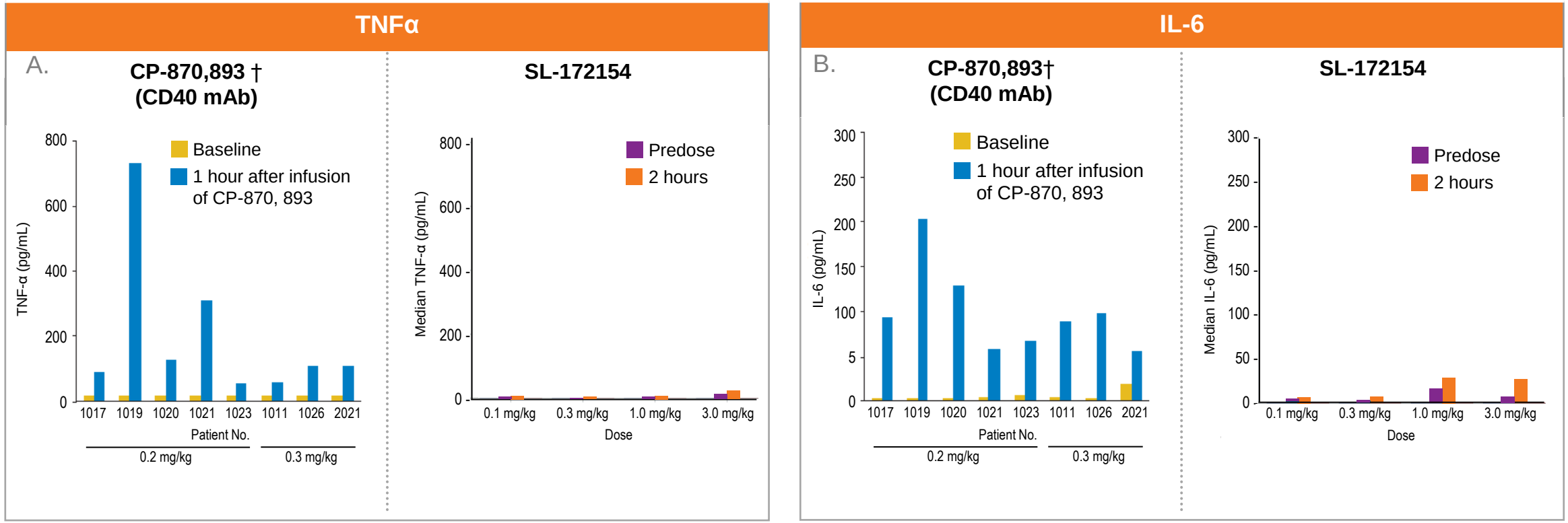
Distinct Profile of TNFα and Interleukin-6 (IL-6) Relative to CD40 mAbs



➔ DLTs attributed to CRS have limited dose escalation of CD40 agonist mAbs

➔ No notable increases in TNFα and IL-6 have been observed with SL-172154

➔ SL-172154 is currently dosing at 10X the dose of CP-870,893

† Vonderheide et al., *Journal of Oncology*, 2007

Data cut off: October 6, 2021

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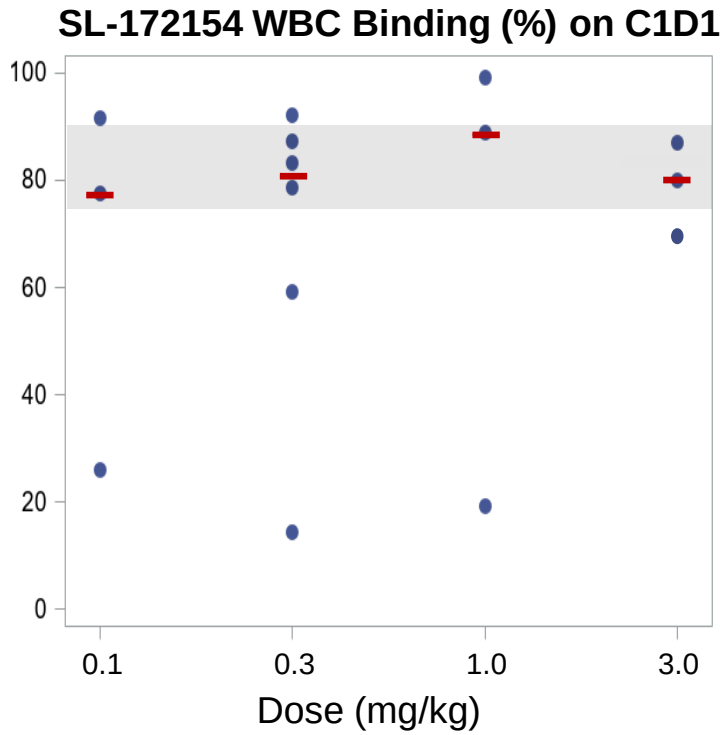
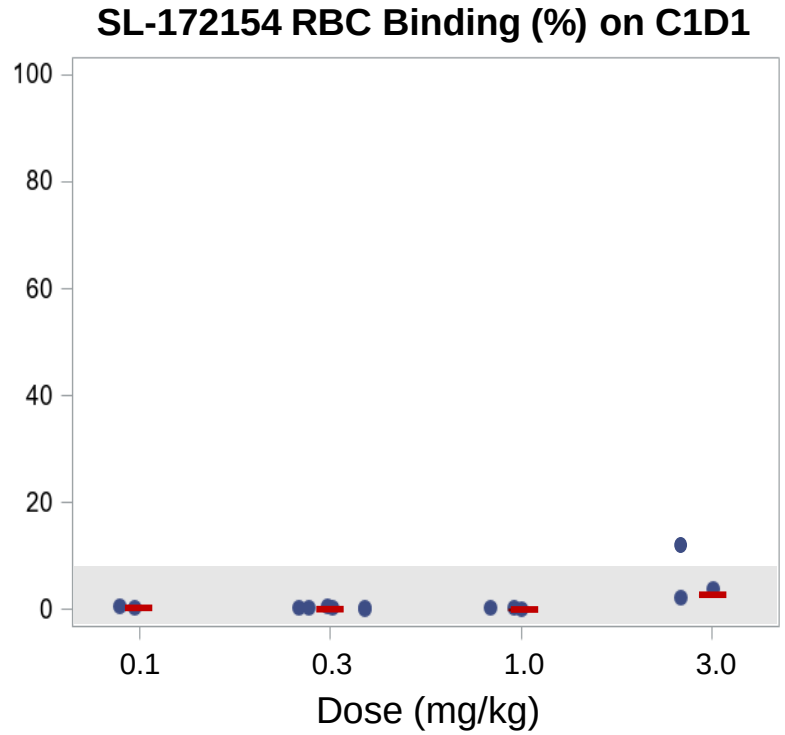
High CD47 Target Occupancy of SL-172154

Preferentially Binds CD47 on Leukocytes Compared to RBCs

Median
Subject





➔ SL-172154 approaches near full occupancy on leukocytes with increasing dose

➔ Minimal binding to RBCs observed

Lakhani et al., *SITC*, 2021
Data cut off: October 6, 2021

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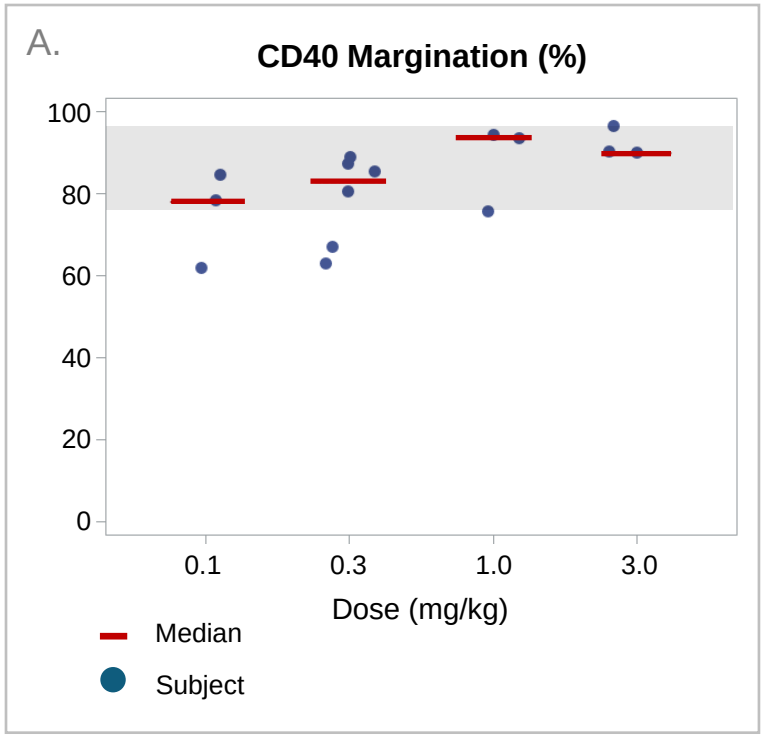
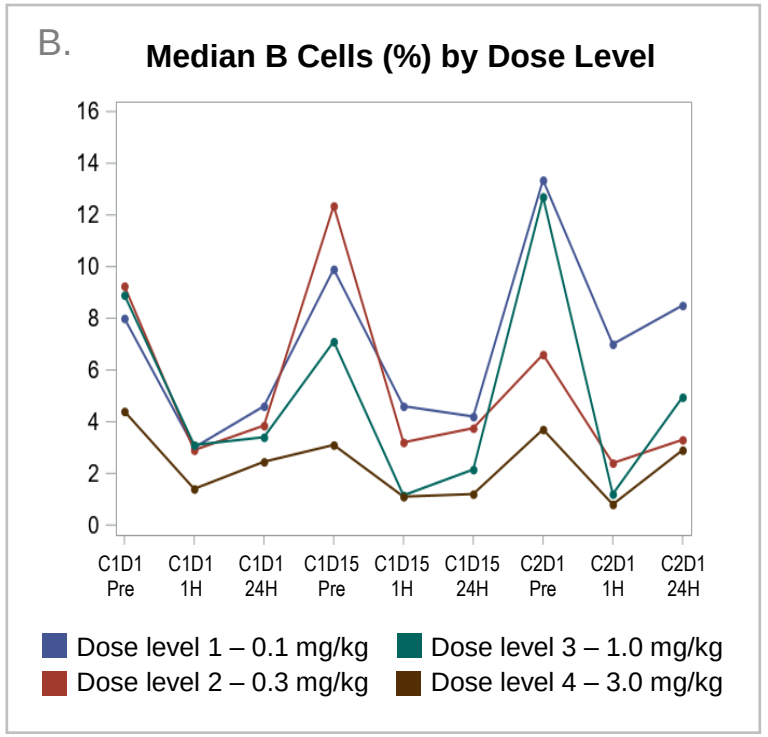
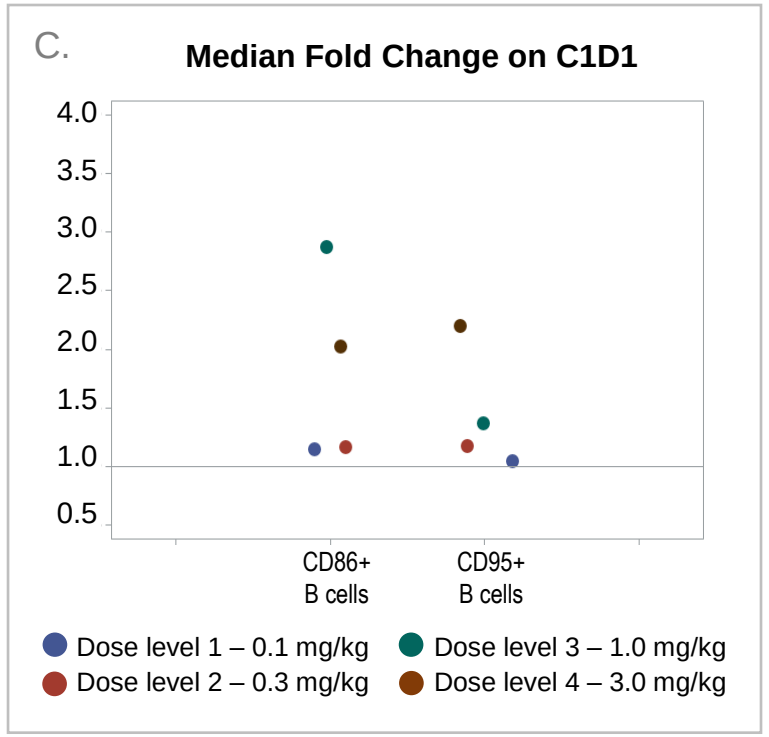
Evidence of CD40 Activation

SL-172154 Stimulates Dose-Dependent B Cell Margination and Activation







➔ Dose-dependent margination of CD40+ B cells and monocytes observed following each weekly dose

➔ SL-172154 doses ≥ 1 mg/kg associated with ~2-fold increased expression of activation markers

Lakhani et al., *SITC*, 2021
Data cut off: October 6, 2021

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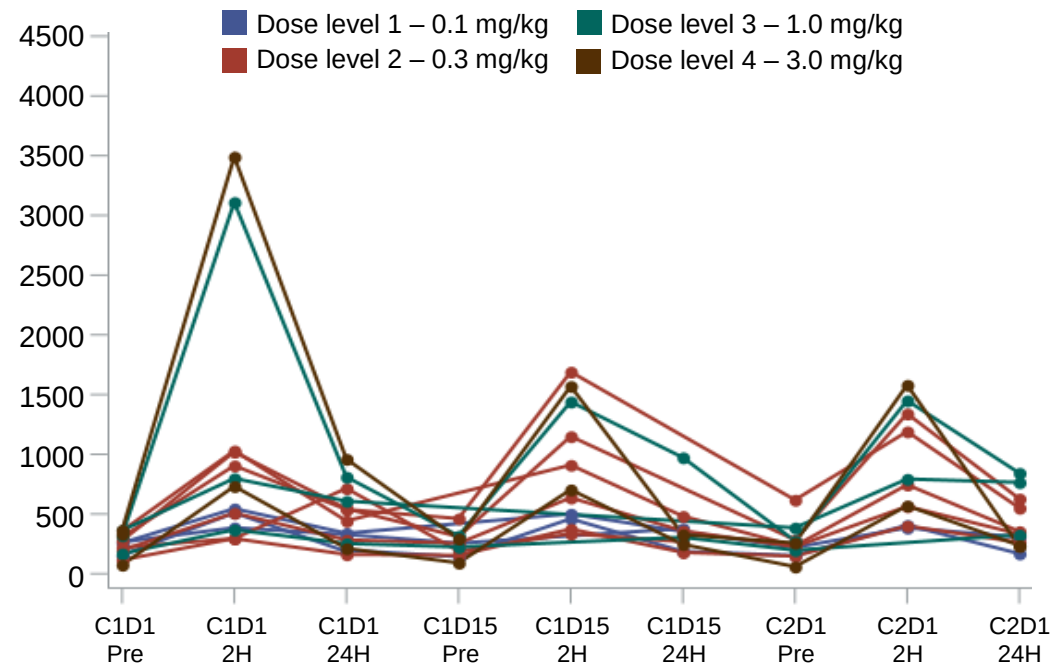
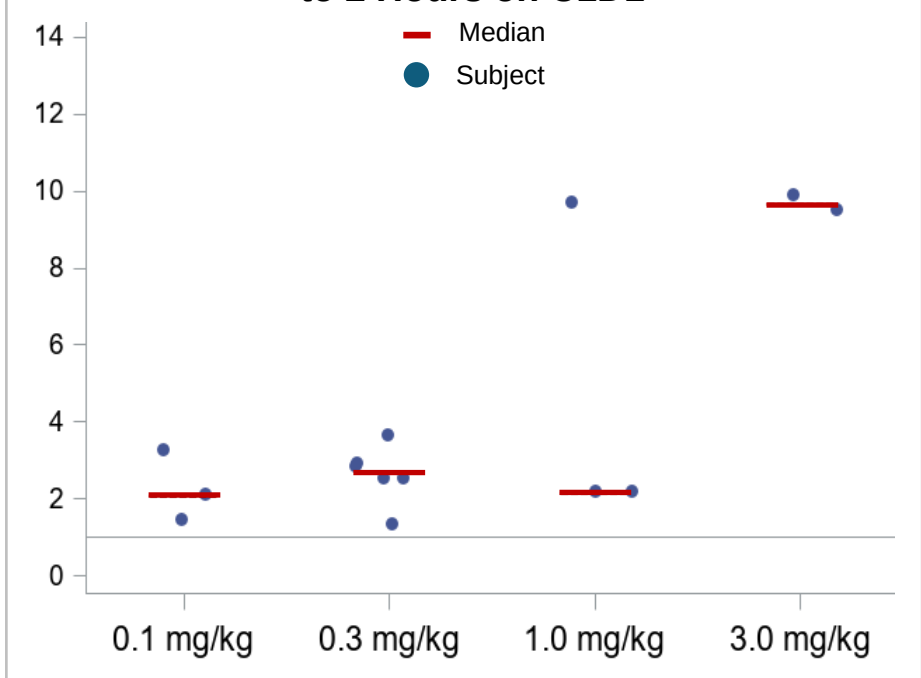
SL-172154 Stimulates Dose-Dependent and Reproducible Increases in Serum Interleukin-12 (IL-12)

A.



B.



- IL-12 response post-infusion occurs with repeated dosing
- IL-12 is a mediator of TH1 effector cytokine responses

- Fold increases in IL-12 by dose level

Lakhani et al., *SITC*, 2021
Data cut off: October 6, 2021

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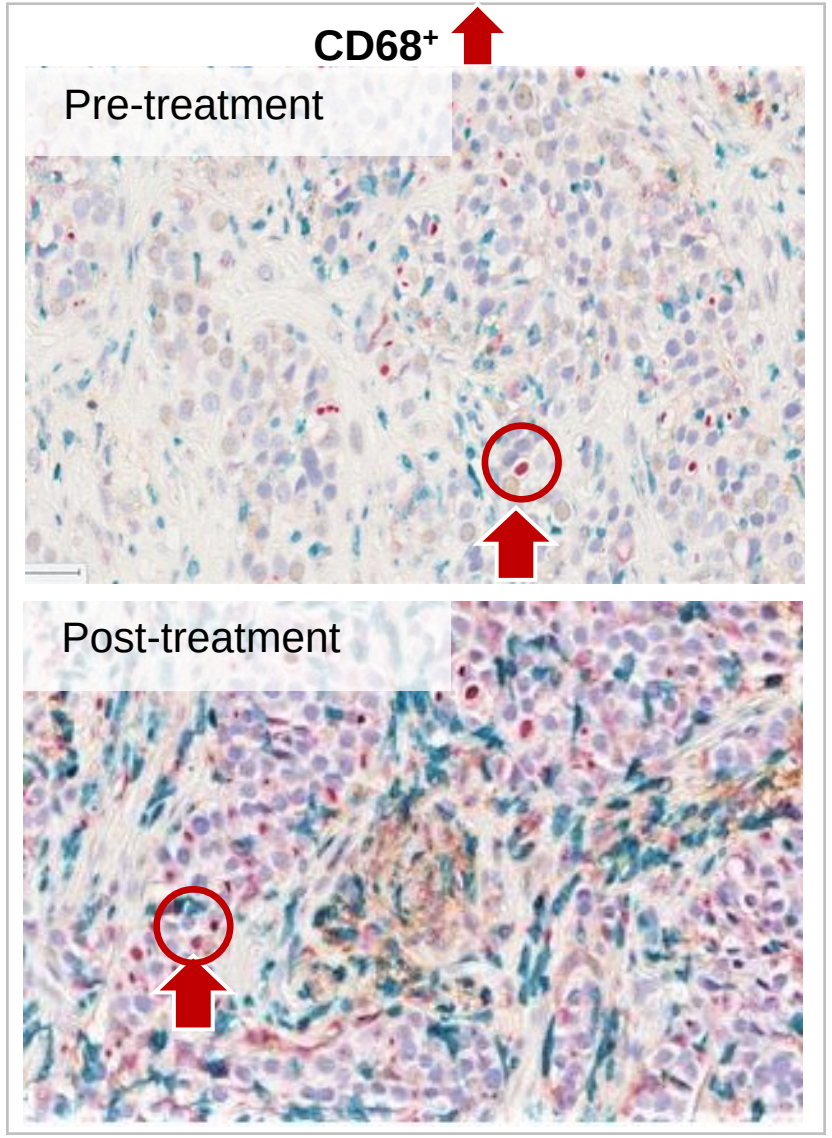
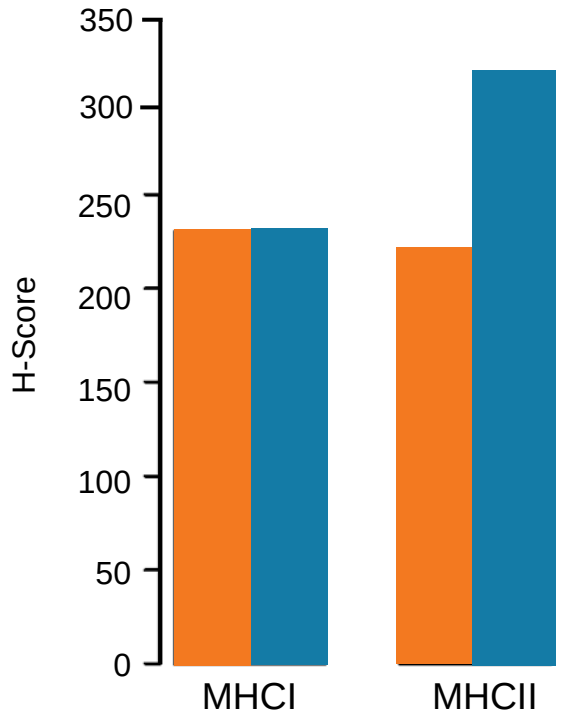
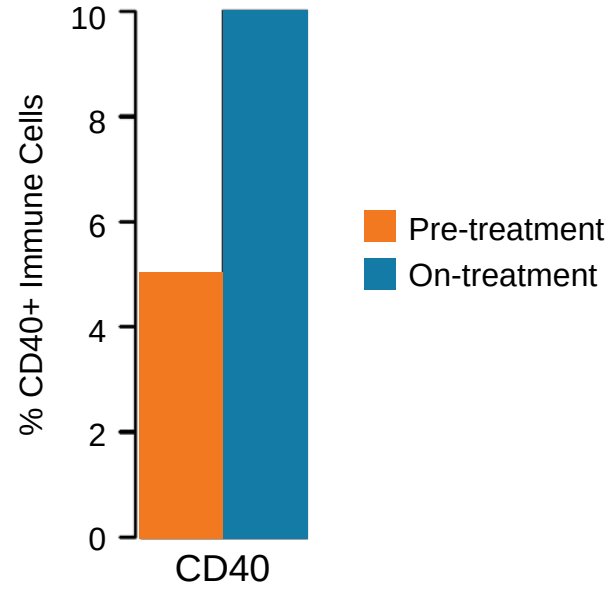
SL-172154 Induces Innate Immune Response in TME

Individual Case Study: Patient A







➔ SL-172154 increases CD68+ macrophages and upregulates activation markers, CD40 and MHC Class II in TME

TME = tumor microenvironment

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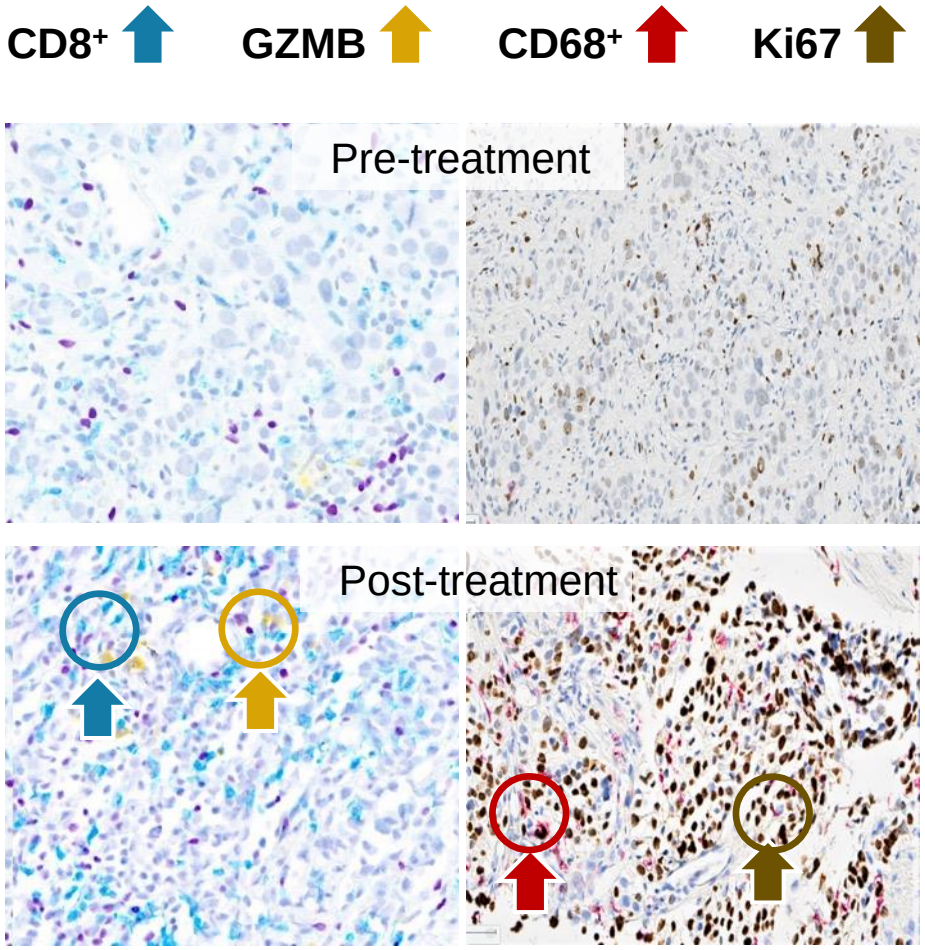
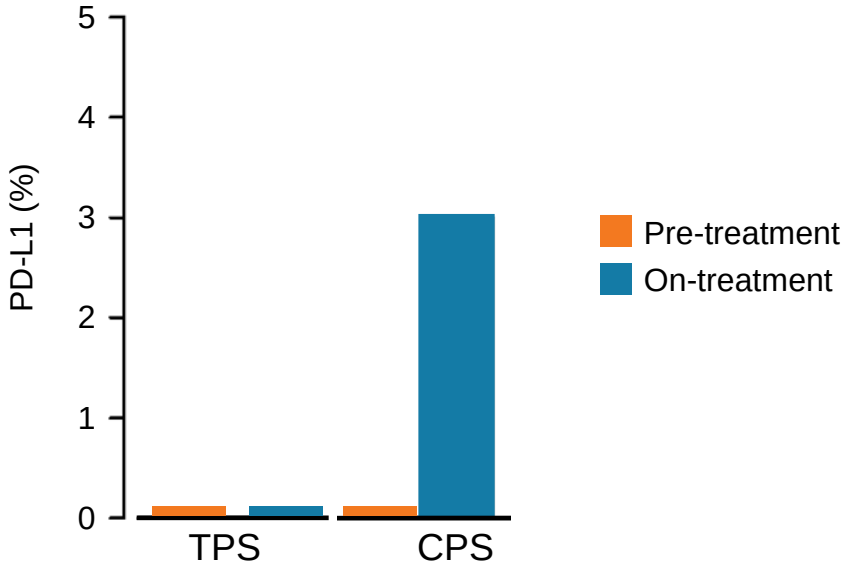
SL-172154 Induces Adaptive Immune Response in TME

Individual Case Study: Patient A





- SL-172154 increases cytotoxic CD8+ T cells in TME
- Induction of PD-L1 on immune cells is a consequence of CD8+ T cell activation

TPS = tumor proportion score
CPS = combined positive score

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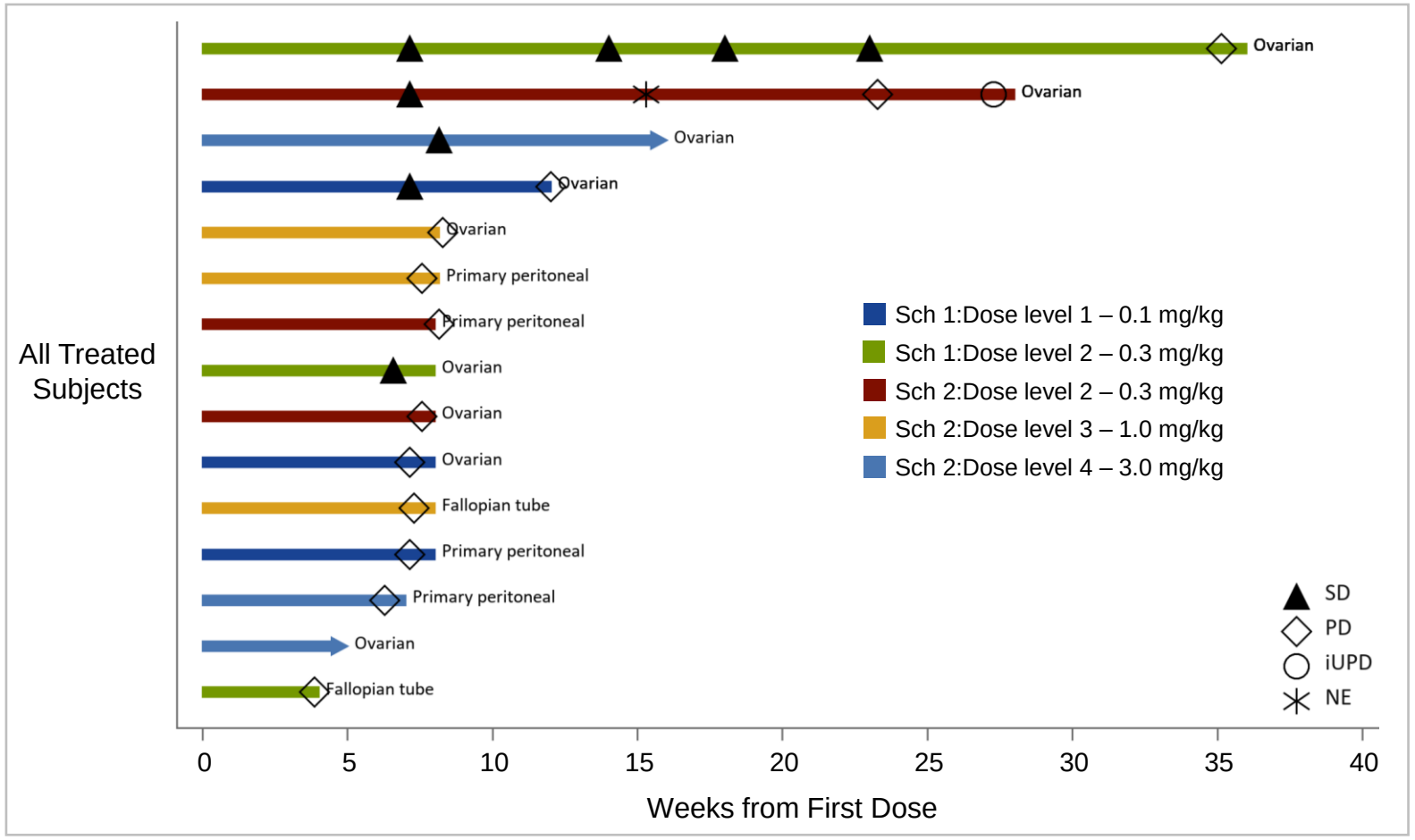
SL-172154: Best Overall Response

Dose Escalation Continues



- Best response among 14 subjects with post-baseline scan
  - SD, n=4
  - PD, n=9
  - NE, n=1
- 1 subject (3 mg/kg, Schedule 2) had not completed the first on-treatment disease assessment at week 8

iUPD = unconfirmed progressive disease (iRECIST)
NE = non-evaluable
PD = progressive disease
SD = stable disease of ≥ 8 weeks

Lakhani et al., *SITC*, 2021
Data updated on October 7, 2021

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SL-172154: Ovarian Dose Escalation

CD47 Inhibition Combined with Potential Best-In-Class CD40 Agonist

Key Takeaways

High Target Engagement	✓ **High target occupancy on CD47; preferential binding to leukocytes** ✓ **High target engagement on CD40+ leukocytes**
Active PD Profile	✓ **Binding to CD40+ B cells and monocytes led to rapid activation** and margination post infusion ✓ **Cyclical increases in innate and adaptive serum cytokines** with CD40 receptor engagement and activation ✓ **No evidence of a bell-shaped dose response curve** to date ✓ Evidence of **innate and adaptive immune response** in the TME ✓ **On-target PD activity** has not plateaued
Unique Safety Profile	✓ **No DLTs reached** to date through 3 mg/kg; continuing to dose escalate to 10 mg/kg ✓ **No evidence of CRS or pneumonitis** ✓ **No notable increases in IL-6 or TNFα**

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Overall Clinical Development Strategy for SL-172154

Rapidly Expanding Strategy in 2022

PHASE 1A
Monotherapy Ovarian Trial

SL-172154 IV Dose Level (DL)

- DL5 – 10.0 mg/kg
- DL4 – 3.0 mg/kg
- DL3 – 1.0 mg/kg
- DL2 - 0.3 mg/kg
- DL1 - 0.1 mg/kg

Development Programs
in 2022 and Beyond

- **Ovarian cancer** **[+ liposomal doxorubicin]**
- **AML** **[+ azacitidine + venetoclax]**
- **HR-MDS** **[+ azacitidine]**
- **TP53 mutant AML** **[+ azacitidine]**
- **Evaluating other combinations in solid tumors**

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ABSTRACT #494

SL-279252 (PD1-Fc-OX40L)

Phase 1 Dose Escalation and Dose Expansion Study of an Agonist Redirected Checkpoint (ARC) Fusion Protein, SL-279252 (PD1-Fc-OX40L), in Subjects with Advanced Solid Tumors or Lymphomas

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SL-279252: Novel PD-1 Inhibitor + OX40 Agonist

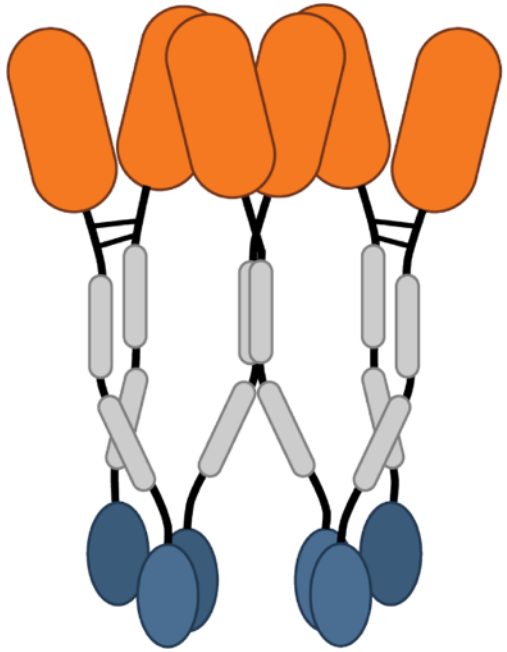
Rationally Designed to Increase Clinical Responses to PD-1 Blockade

SL-279252
(PD1-Fc-OX40L)

Shattuck's First **Product Candidate**

Significant **Platform Risks Discharged**

Dual Mechanism of Action



6 PD-1 Receptor Domains
Blocks PD-1/PD-L1 Pathway

Inert IgG4 Fc

2 OX40L Trimers
Costimulation to OX40+ T Cells

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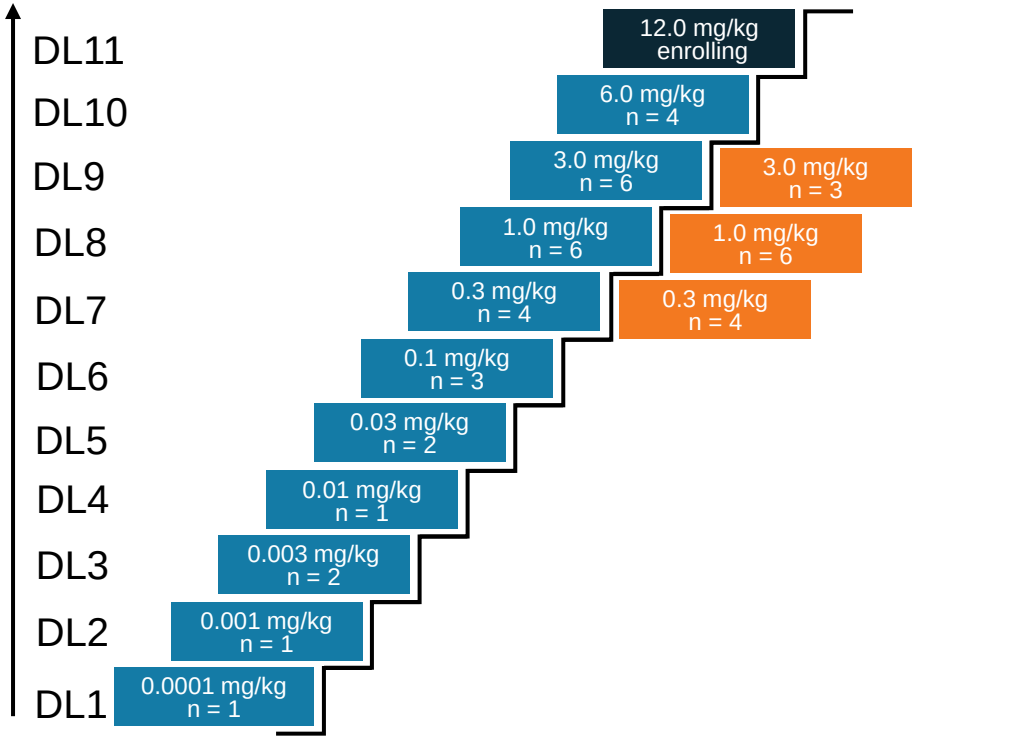
SL-279252: Study Design and Objectives

Dose Escalation per Keyboard Design (N=43)



❖ Eligible subjects must have PD-L1 tumor expression ≥ 1% according to tumor proportion score (TPS) and/or combined proportion score (CPS).

Schedule 1 (D1, D8, D15) Q2W; cycle length = 28d

Schedule 2 QW; cycle length = 28d

Study Objectives: Evaluate the safety, identify a dose and schedule, and characterize the PK, immunogenicity, PD, and anti-tumor activity of SL-279252

Key Inclusion Criteria

- Locally advanced or metastatic solid tumors or lymphomas including: melanoma, non-small cell lung cancer (NSCLC; squamous, adenocarcinoma or adeno-squamous), urothelial carcinoma, head and neck squamous cell carcinoma (SCC), cervix SCC, gastric or gastro-esophageal junction adenocarcinoma, SCC of the anus, cutaneous SCC, renal cell carcinoma, Hodgkin's lymphoma, diffuse large B-cell lymphoma, microsatellite instability-high (MSI-H) or mismatch repair deficient (MMRD) solid tumors
- Must have received all standard of care options
- Age 18 years or older
- ECOG performance status of 0 or 1
- Measurable disease as defined by iRECIST (solid tumors) or RECIL 2017 (lymphoma)

Johnson et al., *SITC*, 2021
Data cut off: June 11, 2021

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SL-279252: Study Population and Tumor Characteristics

Tumor Characteristics (All Treated Subjects)	Total (N = 43)
Cancer Type, n (%)	
Ocular Melanoma	7 (16)
Adeno NSCLC	6 (14)
Gastric Adenocarcinoma	5 (12)
Renal Cell Cancer	4 (9)
SCC of Head and Neck	4 (9)
Squamous Cell Cervical	3 (7)
MSI-H or MMRD Solid Tumors*	3 (7)
Mucocutaneous Melanoma†	2 (5)
Urothelial Cancer	2 (5)
Gastro-esophageal Junction	2 (5)
Esophageal Adenocarcinoma	1 (2)
Diffuse Large B cell lymphoma	1 (2)
SCC of the Skin	1 (2)
SCC of the Anus	1 (2)
Squamous NSCLC	1 (2)

* Endometrial, upper gastrointestinal track, and ileum and appendix

- Age: 64 (median), 31-82 (range)
- 56% male
- Prior lines of systemic therapy: 3 (median), 0-5 (range)
- 58% checkpoint inhibitor experienced

Johnson et al., *SITC*, 2021
Data cut off: June 11, 2021
† Mucosal melanoma of the vulvar (n=1) and cutaneous melanoma of the toe (=1)

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SL-279252: Summary of Safety in All Treated Subjects

All Causality AEs in >10% of Subjects

Total number of subjects	**N = 43**
All causality AEs (any grade)	**n (%)**
Any AE	40 (93)
Constipation	11 (26)
Back pain	8 (19)
Anemia	7 (16)
Decreased appetite	7 (16)
Abdominal pain	6 (14)
Cough	6 (14)
Fatigue	6 (14)
Insomnia	6 (14)
Nausea	6 (14)
Diarrhea	5 (12)
Rash maculo-papular	5 (12)

- No dose-limiting toxicities
- Most common TRAEs were maculo-papular rash (n =4; 9%), infusion-related reaction (IRR; n=3; 7%), asthenia, constipation, decreased appetite, fatigue, hypothyroidism, night sweats and pruritis (remainder were n=2; 5%)
- G3 TRAEs were neutropenia (2%) and hypercalcemia (2%); each occurred in 1 subject
- No G4/5 TRAEs occurred
- IRRs occurred in 3 subjects (7%), were manageable and did not prevent completion of dosing or lead to discontinuation

Johnson et al., *SITC*, 2021
Data cut off: June 11, 2021

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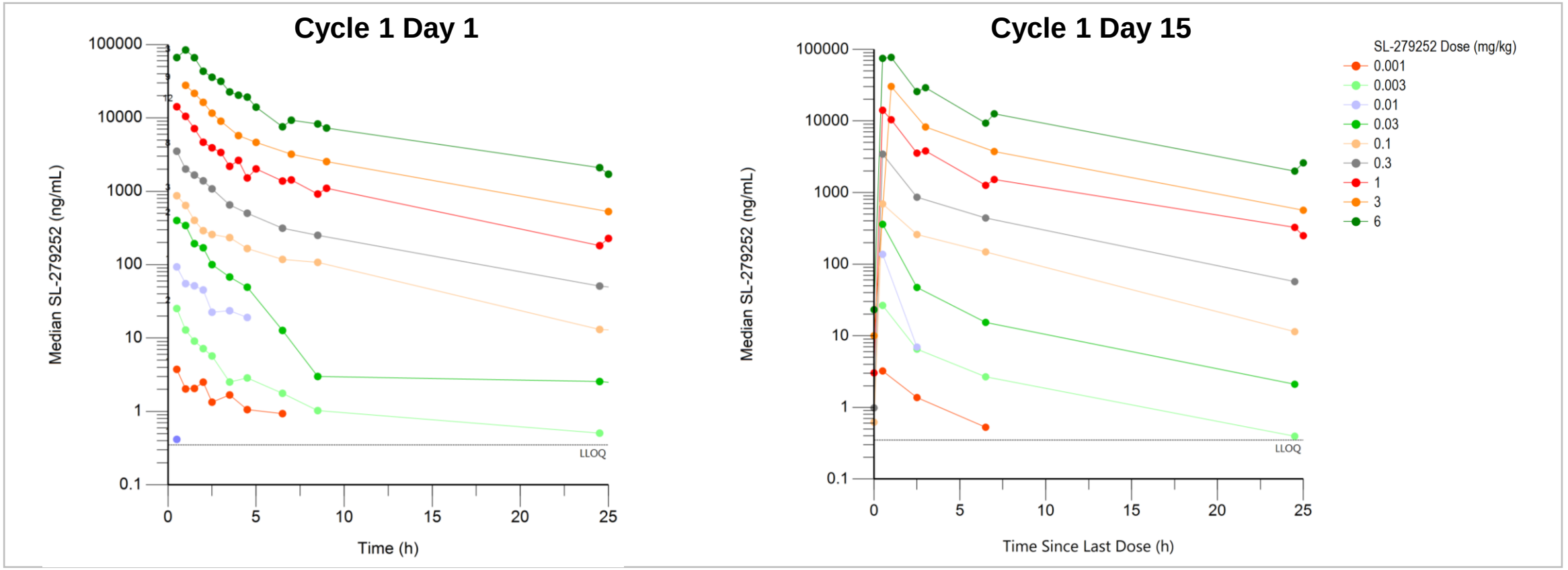
SL-279252: Pharmacokinetics



➔ Cmax and AUC increase with increasing dose up to 6 mg/kg

➔ A trend towards non-linear increase in exposure is apparent for AUC and reflected by a decrease in CL with increasing dose

➔ Preliminary observations suggest saturation of target mediated drug disposition

Johnson et al., *SITC*, 2021
Data cut off: June 11, 2021

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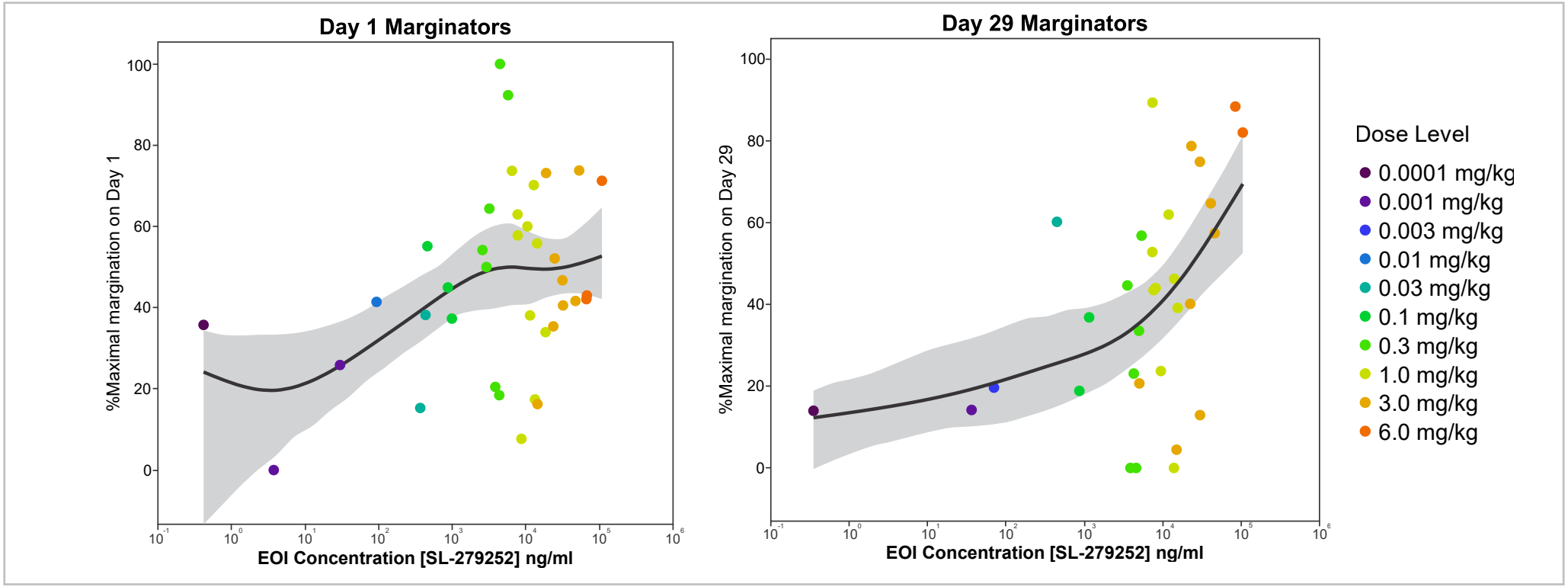
SL-279252: Maximal OX40 Receptor Engagement by Dose



- Dose-dependent binding and margination of CD4+OX40+ T cells observed through 6 mg/kg
  - PD effect was observed following each dose of SL-279252 and has not yet plateaued
    - PD effects of OX40 binding may continue to increase at 12 mg/kg DL

Gonzalez et al., *SITC*, 2021
EOI = end of infusion

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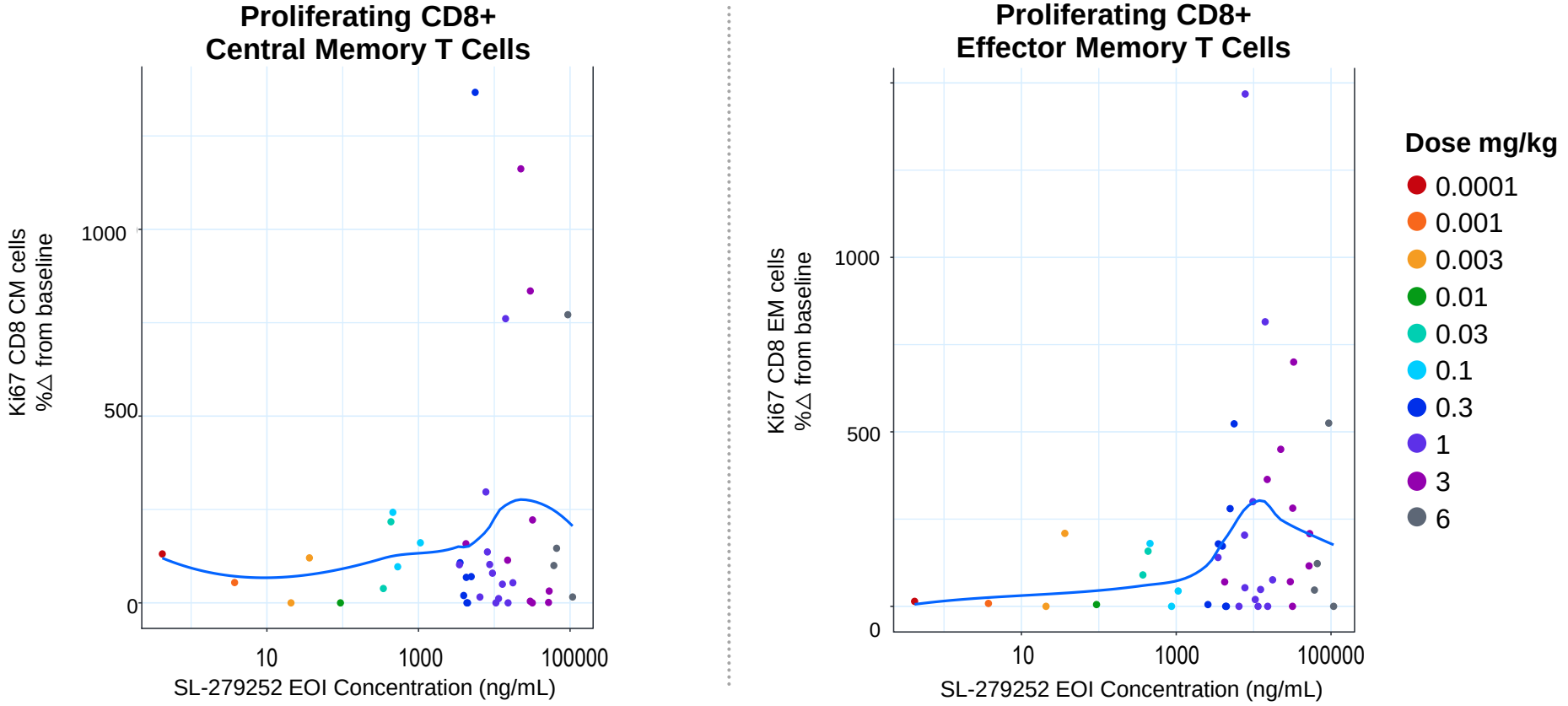
SL-279252: Dose Dependent Increases in CD8+ T cells



➔ 5-10X increases in proliferating and total CD8 CM and EM T cells at doses ≥ 1.0 mg/kg in some subjects

➔ No significant trends in cytokine or chemokine changes observed

CM = central memory
EM = effector memory
% △ from BL= percent change from baseline

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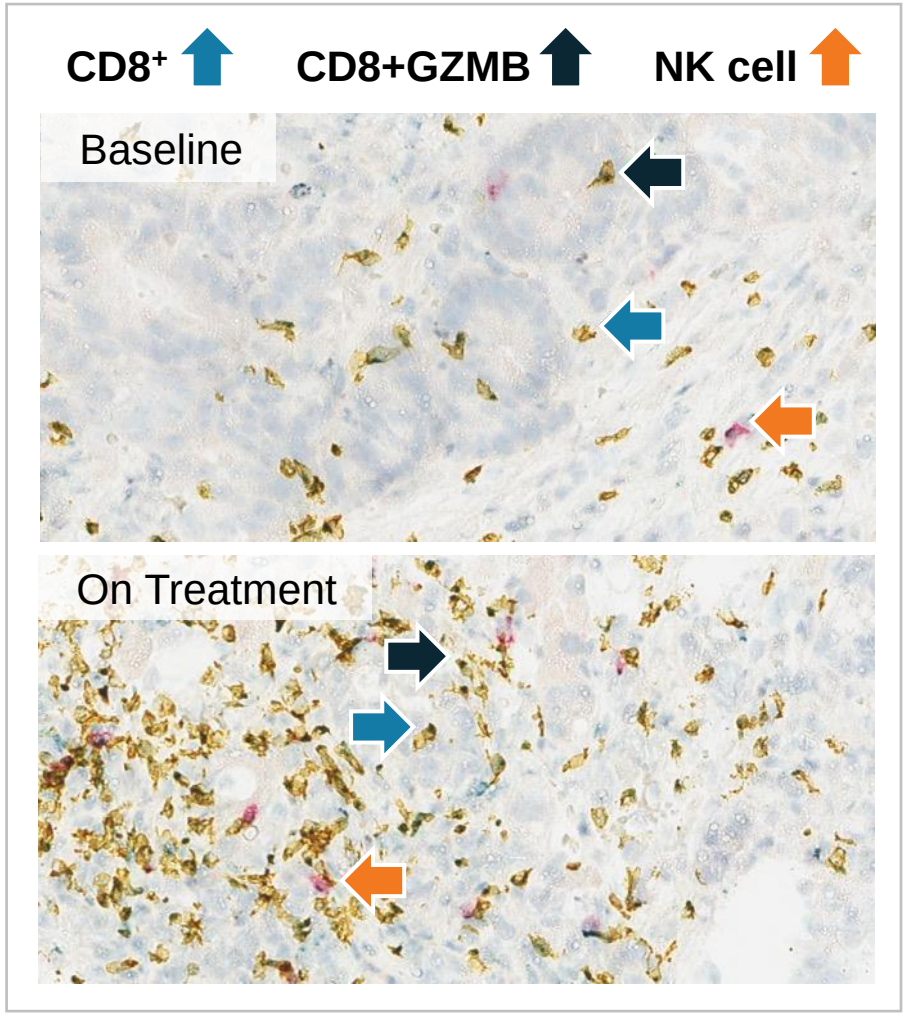
SL-279252: Increases CD8+/GZMB/Nkp46 in MSI-H CRC

Individual Case Study: Patient B



- SL-279252 causes local changes within the TME
- Increases in proliferating and granzyme-B expressing lymphocytes
- Similar increases observed in multiple treated subjects

Johnson et al., *SITC*, 2021
CRC = colorectal cancer
NK = natural killer

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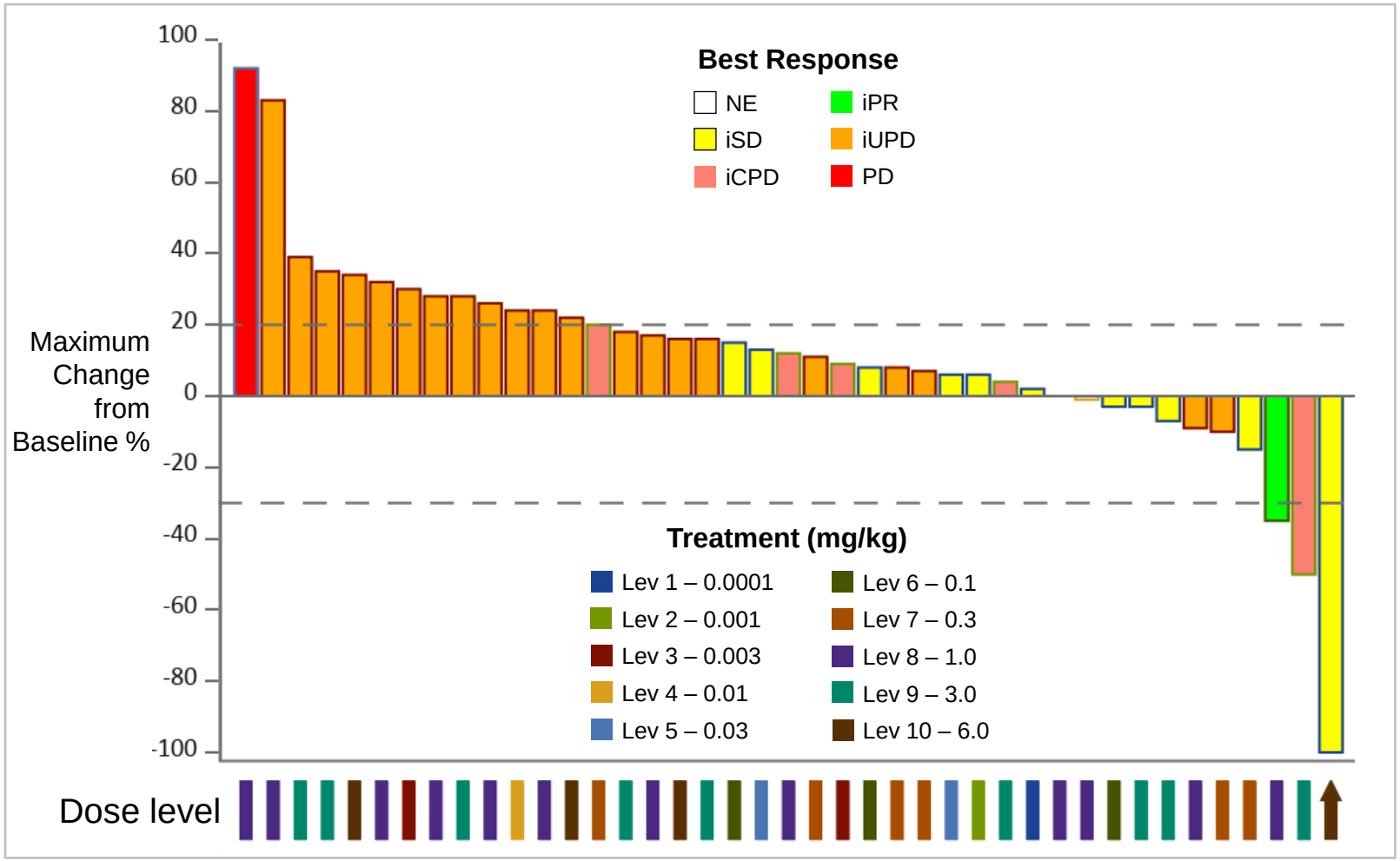
SL-279252: Percentage Change in Target Tumor Size from Baseline



- Best response was 1 confirmed iPR (ocular melanoma, 4 prior systemic regimens, CPI-experienced) in subject who remained on treatment for >1 year
- iSD in 12 subjects
  - 1 unconfirmed iPR in a CPI-experienced subject with vulvar melanoma
  - iSD for > 24 weeks occurred in 5/12 subjects (4 had received prior CPI therapy targeting PD-1, PD-L1, or CTLA-4)

iCPD = confirmed progressive disease per iRECIST
iPR = partial response per iRECIST
iSD = stable disease per IRECIST
iUPD = unconfirmed progressive disease per iRECIST
NE = non-evaluable
PD = progressive disease per RECIL 2017
↑ = ongoing subjects, updated post SITC data cut off

Johnson et al., *SITC*, 2021
Data updated on October 20, 2021

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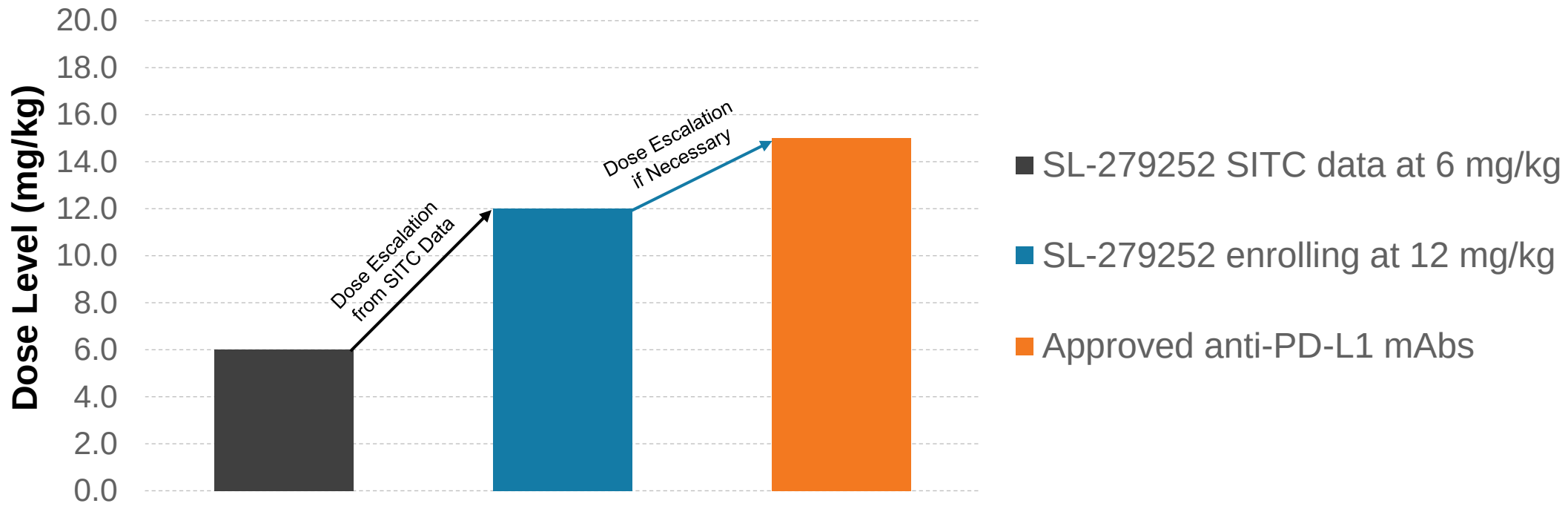
SL-279252: Dosing in Context with Traditional mAbs

Current Dose Level Supports Continued Dose Escalation



- PD-L1 inhibitors historically dosed higher than PD-1 inhibitors, due to the more abundant expression of PD-L1
- Early anti-tumor activity and escalating PD activity of SL-279252 supports continuing dose exploration up to doses equivalent to those used for approved PD-L1 inhibitors

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SL-279252: Dose Escalation

PD-L1 Inhibition Combined with OX40 Agonist

Safety Profile	✓ **Well tolerated in heavily pretreated subjects** with refractory solid tumors with no MTD reached
PK Profile	✓ **Linear PK at doses up to 3.0 mg/kg**, and a greater than proportional increase in AUC was observed at 6.0 mg/kg suggesting potential receptor saturation ✓ **Preliminary half-life** (T½) is approximately 23 hours.
Target Engagement	✓ **Dose-dependent OX40 receptor engagement** on CD4+OX40+ T cells ✓ **OX40-dependent PD effects** have been observed in subjects dosed on Schedule 1 (D1, D8, D15, then Q2W in 28d cycles)
Efficacy	✓ **Anti-tumor activity in CPI-experienced subject** dosed on Schedule 1 • 1 confirmed iPR at 1.0 mg/kg • 12 iSD, including 5/12† with > 24-week duration • 1 unconfirmed iPR at 6 mg/kg (included in 12 iSD)

➔ Dose escalation of SL-279252 continues at 12.0 mg/kg to fully characterize PK, PD, and anti-tumor activity

Johnson et al., *SITC*, 2021

† Preliminary data reported in the abstract reported 6/12 iSD > 24-week duration, upon further analysis revised to 5/12 iSD > 24-week duration



Andrew Neill, M.B.A.
Chief Financial Officer

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SL-172154 Expansion Into Combination Studies

Deep Pipeline of Scientifically Validated and Novel Targets

PLATFORM	PROGRAM	DOMAINS: DOMAIN 1	DOMAINS: DOMAIN 2		INDICATIONS	COMBINATION(S)	STAGE OF DEVELOPMENT	ANTICIPATED MILESTONES / STATUS
CLINICAL-STAGE PIPELINE								
ARC	SL-172154	SIRPα	CD40L	Solid Tumors	Ovarian Cancer	Liposomal Doxorubicin	PRECLINICAL → PHASE 1	Initiating Combo Trial 1H'22
				Solid Tumors	CSCC and HNSCC	TBD	PRECLINICAL → PHASE 1	Initial Dose Escalation Data 1H'2022
				Hematology	AML and HR-MDS	Azacitidine +/- Venetoclax	PRECLINICAL → PHASE 1	Initial Dose Escalation Data 2H'2022
	SL-279252	PD-1	OX40L		Advanced Solid Tumors and Lymphoma	TBD	PRECLINICAL → PHASE 1	Dose Escalation Data 2H'2022

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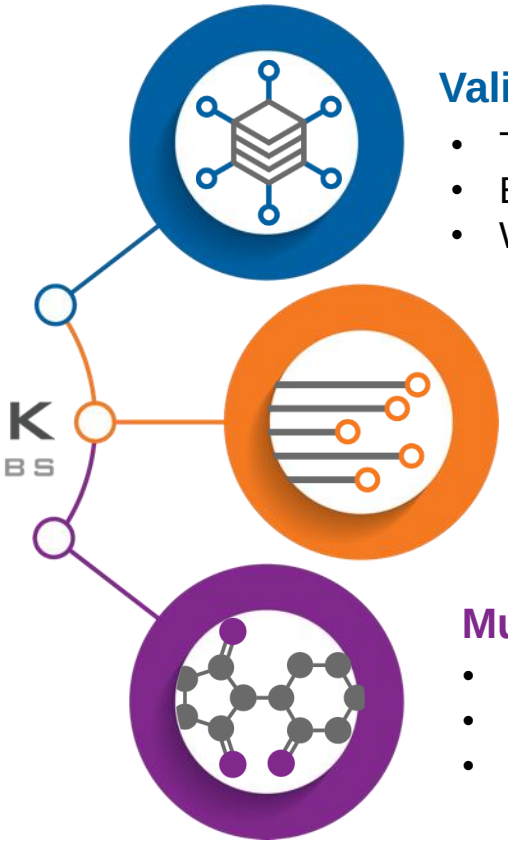
Well Positioned for High Growth



Validation of ARC Platform

- Two-clinical stage, immunologically active product candidates
- Evidence of CD40 and OX40-mediated immune activation
- Well tolerated to-date, with no DLTs

Expanding Clinical Development

- Five clinical trials in 2022
- Indications in solid tumor and hematologic malignancies
- Various combination strategies

Multiple Shots on Goal

- Focus on rapid execution of our ongoing and planned clinical trials
- Multiple data sets in combination
- Advance additional ARC molecules into clinical development

➔ $290.2 million Cash and cash equivalents and short-term investments of as September 30, 2021



Taylor Schreiber, M.D., Ph.D.
Chief Executive Officer

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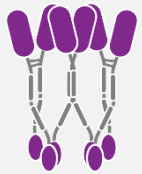
ARC Platform Proof of Concept

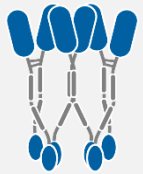
Key Clinical Observations

SL-172154
(SIRPα-Fc-CD40L)



- ✓ **Highly potent and best-tolerated CD40 agonist to date**
- ✓ **High occupancy of both CD47 and CD40 achieved by 3 mg/kg**
- ✓ **Evidence for intra-tumoral immune activation**
- ✓ **Recommended Phase 2 dose not yet reached**

SL-279252
(PD1-Fc-Ox40L)



- ✓ **Initial anti-tumor activity in CPI experienced melanoma**
- ✓ **OX40-dependent PD effects not previously reported for OX40 mAbs**
- ✓ **Evidence for intra-tumoral immune activation**
- ✓ **Recommended Phase 2 dose not yet reached**

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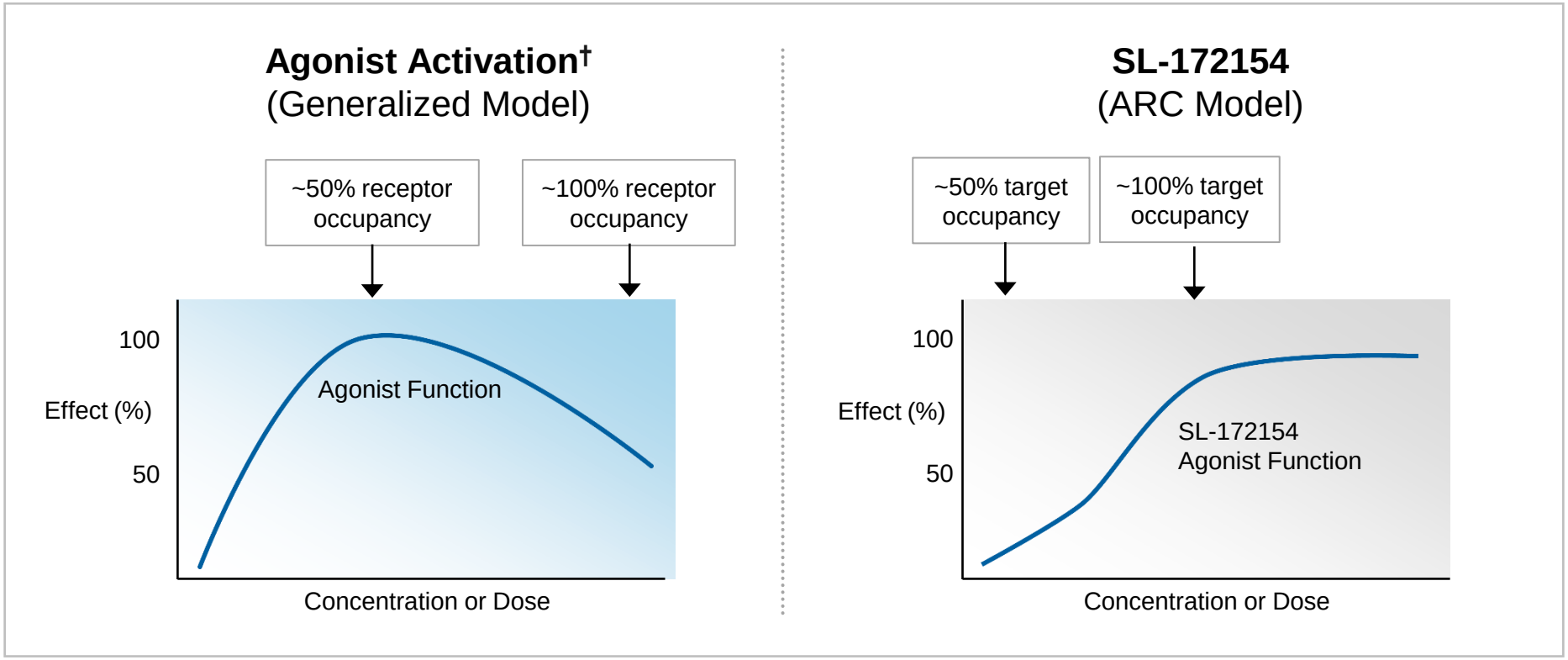
Clinical Data Support ARC Platform Thesis

TNF Activation Without Bell Shaped Dose Response



- ➔ CD40 mAbs encountered toxicity at doses that did not maximize CD40 biology
  - ➔ mAbs have shown a "bell shaped" dose response curve
  - ➔ ARCs have demonstrated dose-dependent activation of OX40 and CD40
- ➔ Clinical data suggest that ARCs may unleash the therapeutic potential of TNF receptors as agonistic targets in immuno-oncology

† Mayes et al. Nature 2018

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ARC Platform Positioned for Expansion

Major Takeaways

ARC Platform Validation

1. **Discharging Safety Risk**
   No DLTs observed to date while approaching nearly full target occupancy
2. **On-Target biology**
   Unique pharmacodynamic profiles consistent with on-target immune activation
3. **Unlocking TNF Superfamily**
   Initial clinical data targeting CD40 and OX40 validates ARC-based targeting of other TNF receptors (4-1BB, LTβR, etc.)

Rapidly Expanding Clinical Development

1. **SL-172154**
   CD47 inhibitor in solid tumors expanding into hematologic malignancies and combinations
2. **SL-279252**
   Exploring safety, PK, PD and anti-tumor activity at higher dose levels
3. **Clinical Pipeline Expansion**
   Extending the ARC platform reach with additional product candidates

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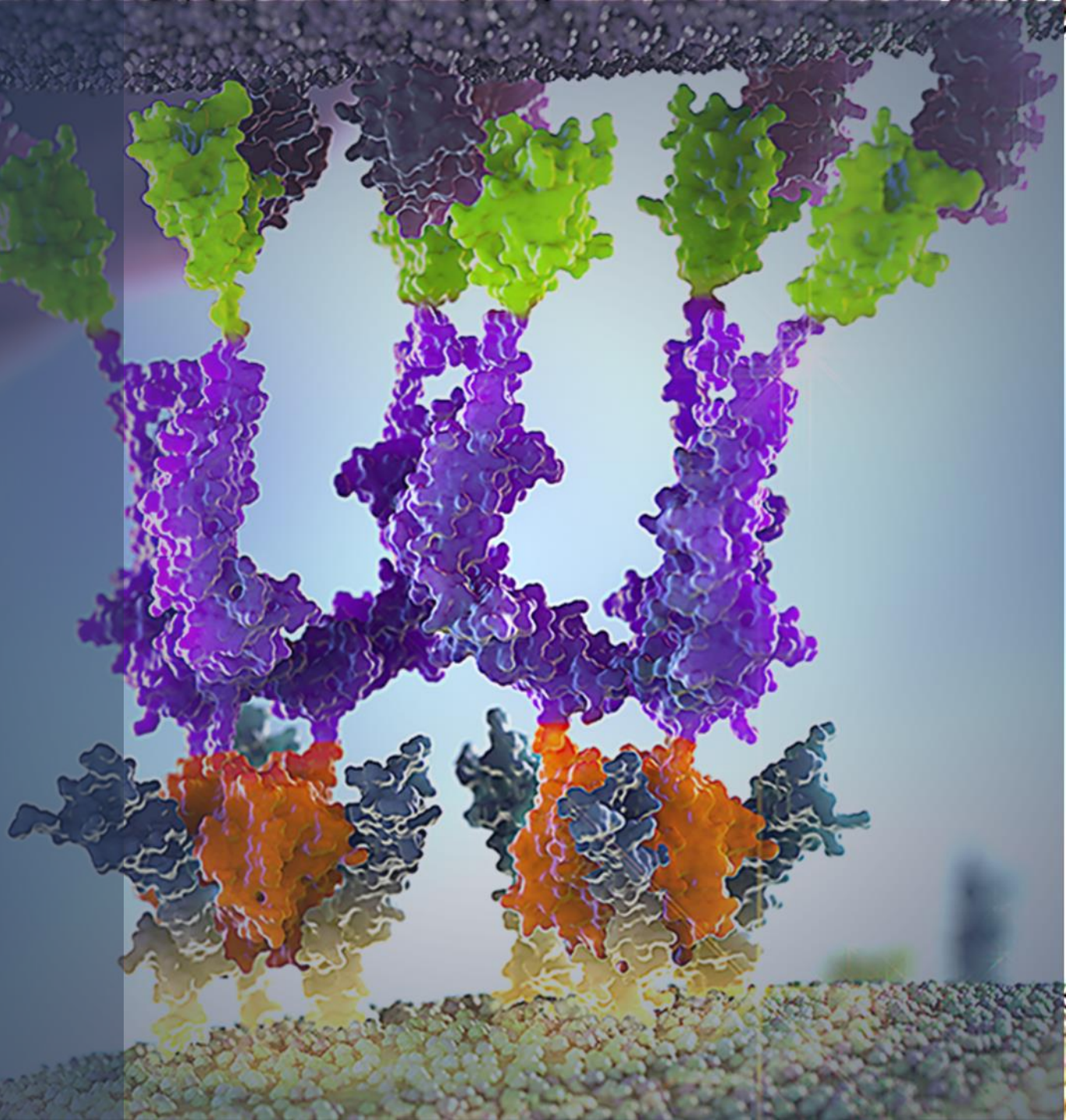
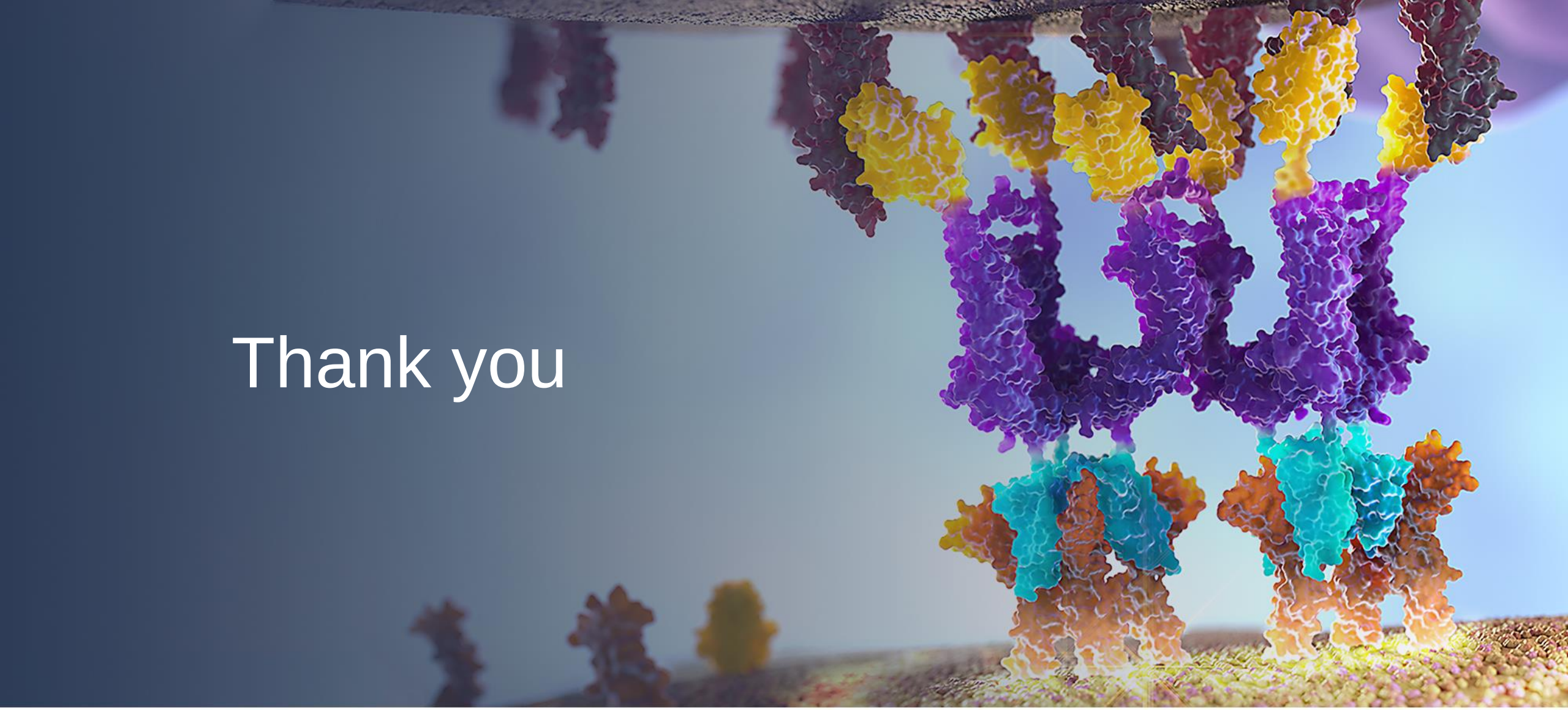
Q&A Attendees:

Dr. Taylor Schreiber, CEO

Dr. Lini Pandite, CMO

Andrew Neill, CFO





Thank you

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