Abstract #9820

Results of first-in-human, Phase 1 study of KSQ-001EX, an autologous tumor infiltrating lymphocyte therapy engineered to inactivate the SOCS1 gene, in patients with select advanced solid tumors

Rodabe N. Amaria[1], Hussein A. Tawbi[1], Alexandra Ikeguchi[1], Isabella C Glitza Oliva[1], Jennifer L McQuade[1], Michael A. Davies[1], Youlia Petrova[1], Cara Haymaker[2], Chantale Bernatchez[3], Marie-Andrée Forget[3], Karrie Wong[4], Erica Tobin[4], Micah J. Benson[4], Anna Truppel-Hartmann[4], and Patricia M. Harris[4]

1. Department of Melanoma Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX
2. Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX
3. Cell Therapy Manufacturing Center (CTMC), Houston, TX
4. KSQ Therapeutics, Inc., Lexington, MA

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Disclosure Information

AACR American Association for Cancer Research
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AACR.ORG/AACR2026 | #AACR26

I have the following relevant financial relationships to disclose:

Employee of: MD Anderson Cancer Center

Consultant for: Obsidian, Immatics, KSQ

Research support: Obsidian, Immatics, KSQ, Erasca, Regeneron

KSQ-001EX phase I study: key takeaways from melanoma cohort

eTIL therapy engineered to overcome tumor immunosuppression

No dose limiting toxicity and manageable safety profile with and without IL2

Tumor reduction in 100% of patients treated above median cell dose -/+ IL2 with a target dose range (1-10B cells) below unmodified TIL

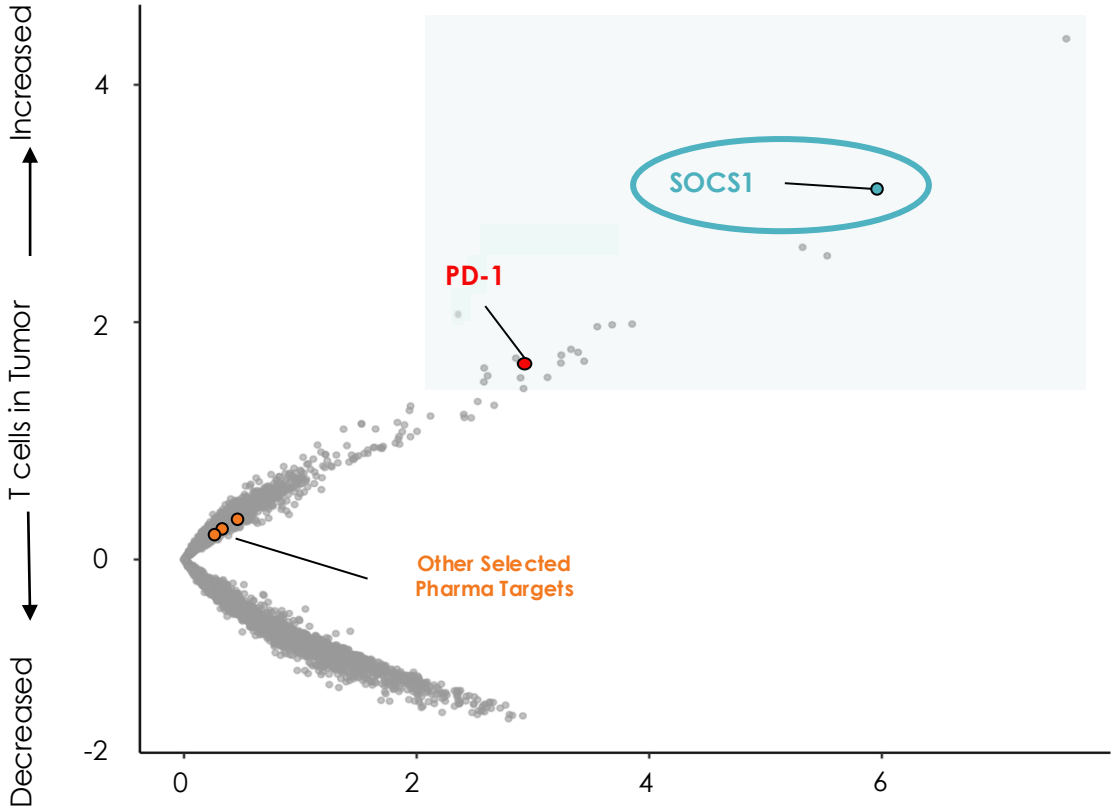
Evidence of SOCS1 inactivation, a novel T cell target, impacting TIL functionality

Overcoming challenges in the treatment of solid tumors

KSQ-001EX, an engineered TIL (eTIL®) with inactivation of SOCS1

- Patients with advanced melanoma resistant or refractory to ICI have a poor prognosis
- An autologous tumor infiltrating lymphocyte (TIL) therapy has recently been approved by FDA with ORR 31.5% (23/73) with a cell dose between 7.5-72 billion with IL-2 (Amtagvi USPI)
- **Tumor antigen heterogeneity** and the **immunosuppressive tumor microenvironment** are key challenges in treating solid tumors
- **KSQ-001EX is a SOCS1 edited, functionally enhanced eTIL therapy, polyclonal by nature, engineered to overcome tumor immunosuppression**

Genome-wide CRISPR screens identify SOCS1 as one of the strongest targets enhancing T cell function in solid tumors



Schlabach MR et al, JCI, 2023

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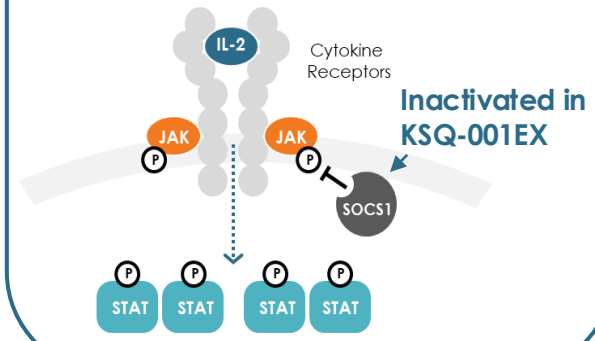
KSQ-001EX designed to enhance T cell function in solid tumors

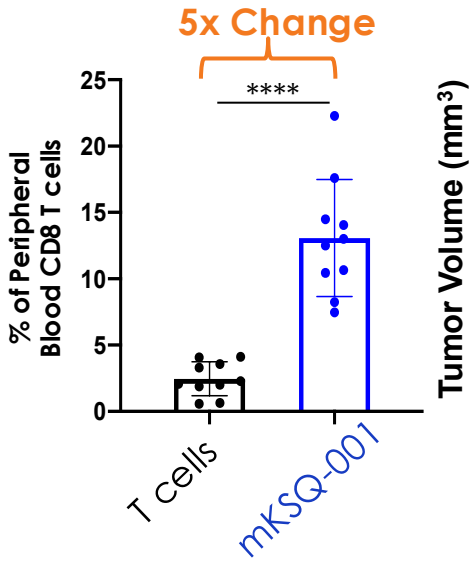
SOCS1 is a negative regulator of cytokine signaling and T cell function

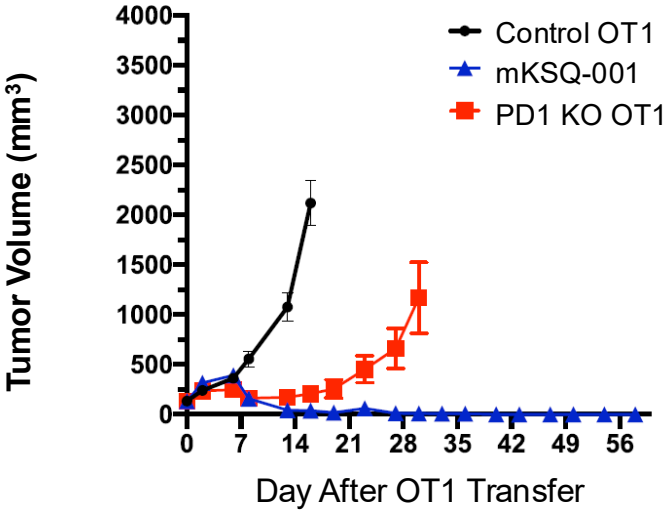
SOCS1 inactivation in T cells leads to:

- Increased engraftment & persistence
- Increased accumulation in tumor
- Superior tumor-killing functionality
- Increased formation of central memory

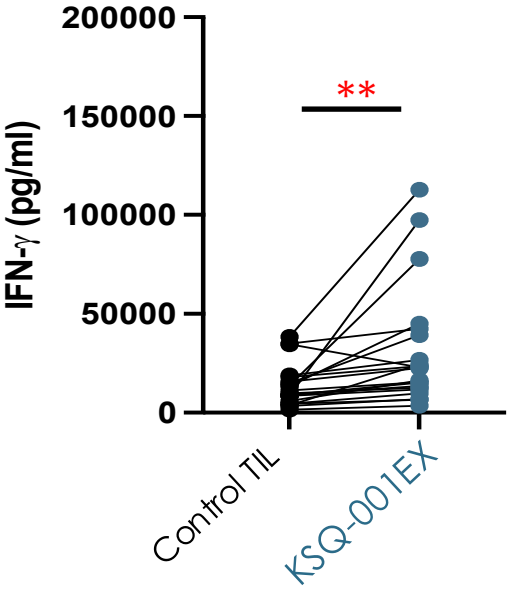


Mouse KSQ-001 (mKSQ-001) Showed Enhanced In Vivo Expansion and Efficacy in B16-OVA Tumor Model





Human KSQ-001EX Showed Increased IFNγ Release against A375 Tumor Spheroids



Based on the observed increase in TIL activity by SOCS1 editing, a dose range of 1-10 x 10^9 KSQ-001EX cells was selected for the safety lead-in phase of the clinical trial.

Schlabach MR et al, JCI, 2023

First in human study of KSQ-001EX in solid tumors

Evaluating KSQ-001EX at doses ≤ 10B cells in patients with melanoma

Phase 1: Dose Confirmation

Key eligibility criteria:

- Advanced cutaneous, acral or unknown primary melanoma that has progressed following ≥1 line of prior systemic therapy (including anti-PD-1/anti-PDL1 inhibitor alone or in combination)
- Resectable lesion for manufacturing
- At least one measurable lesion following resection

Primary Objective: To evaluate the safety and tolerability of KSQ-001EX

Primary and key Secondary Endpoints:

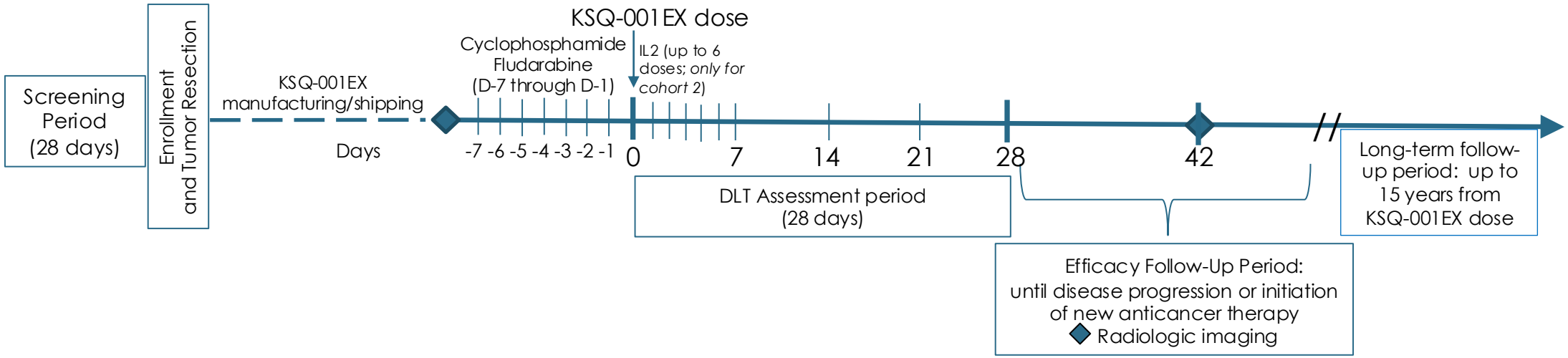
- Incidence of DLTs;
- Incidence/severity of TEAEs
- ORR, DOR, TTR per RECIST
- Manufacture success rate

Safety Lead-in Cohort 1 (n=6)
KSQ-001EX
up to 10 x 10^9
(1 x 10^9 – 10 x 10^9 cells)
No IL-2
Advanced Melanoma

→

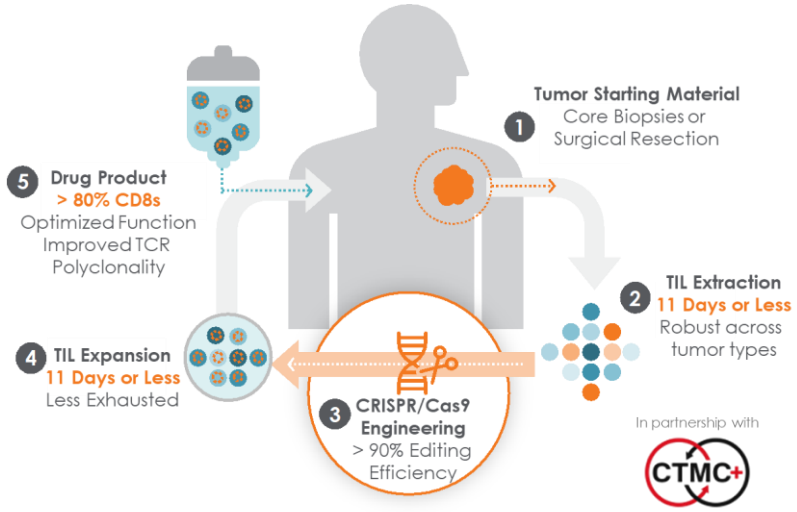
Safety Lead-in Cohort 2 (n=6)
KSQ-001EX
up to 10 x 10^9
(1 x 10^9 – 10 x 10^9 cells)
High-dose IL2 (up to 6 doses)^
Advanced Melanoma
^IL-2 dose: 600,000 IU/kg q 8-12 hrs

Study Treatment Schema



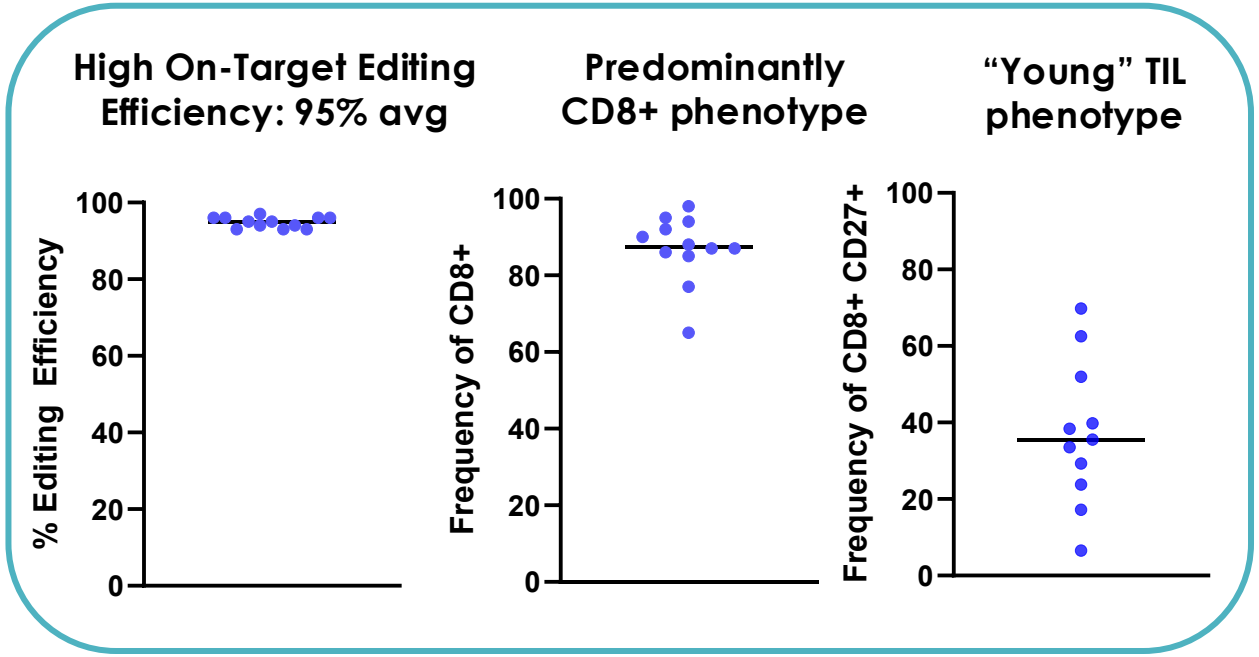
Clinicaltrials.gov: NCT06237881

ExPRESS™, a proprietary eTIL® manufacturing process leads to consistent drug product phenotypes



- ExPRESS: A 22 Day, PBMC feeder cell-free manufacturing process
- DP characteristics remained consistent: high editing efficiency and CD8 rich phenotype – regardless of starting material

KSQ-001EX Clinical Drug Product



*Data inclusive of all DPs dosed

Abstract#3721: Anti-tumor function and long-term persistence of KSQ-001EX, a SOCS1-edited eTIL therapy, independent of IL-2 co-administration
Poster presentation on Monday, 20 April from 2-5pm
(Clinical Research/Adoptive Cell Therapy 1, poster section #40)

Heavily pretreated ICI resistant advanced melanoma

KSQ-001EX target dose range below unmodified TIL

Baseline Patient and Disease Characteristics	Cohort 1 (no IL2) n=4	Cohort 2 (w/IL2) n=8	All Patients N = 12
Median Age (range); years	56 (47 – 67)	39.5 (29 - 65)	46.5 (29 – 67)
Male / Female, n (%)	2 (50) / 2 (50)	5 (62.5) / 3 (37.5)	7 (58) / 5 (42)
BRAF Mutation, n (%)	3 (75)	6 (75)	9 (75)
Median # Prior Therapies (range)	3 (2 – 5)	2 (1 – 5)	2 (1 – 5)
Primary refractory to ICI, n (%)	1 (25)	3 (37.5)	4 (33)
Bridging therapy, n (%)	1 (25)	3 (37.5)	4 (33)
Baseline LDH > ULN, n (%)	1 (25)	4 (50)	5 (42)
Median Baseline SOD, cm (range	7.5 (1.3 – 10.6)	6.2 (2.7 – 21.9)	6.2 (1.3 – 21.9)
Median KSQ-001EX Cell dose*	6B (4.1B – 8.4B)	4.65B (500M -10.7B)	5.25B (500M – 10.7B)

15 patients with tumor harvest: 2 manufacturing failures and 3 pts with dose <1x10^9 cells (2 infused)

* Manufacturing process allowed starting material from core biopsies and resections

Manageable safety profile independent of IL2 dosing

No Dose Limiting Toxicities

Frequent Adverse Events (> 2 patients) SOC; Preferred Term, n (%)	Cohort 1 (no IL2) N=4	Cohort 2 (w/ IL2) N=8	Total N=12
Blood and lymphatic system disorders			
Anemia	3 (75)	8 (100)	11 (92)
Cardiac disorders			
Sinus tachycardia	0	4 (50)	4 (33)
Gastrointestinal disorders			
Nausea	3 (75)	6 (75)	9 (75)
Diarrhea	2 (50)	1 (12.5)	3 (25)
Immune system disorders			
Fever	2 (50)	6 (75)	8 (67)
Investigations			
Platelet count decreased	4 (100)	5 (62.5)	9 (75)
Neutrophil count decreased	4 (100)	4 (50)	8 (67)
Alanine aminotransferase increased	1 (25)	4 (50)	5 (42)
Aspartate aminotransferase increased	2 (50)	3 (37.5)	5 (42)
Lymphocyte count decreased	3 (75)	1 (12.5)	4 (33)
White blood cell decreased	3 (75)	0	3 (25)
Nervous system disorders			
Chills	1 (25)	7 (87.5)	8 (67)
Fatigue	4 (100)	3 (37.5)	7 (58)
Headache	3 (75)	2 (25)	5 (42)
Respiratory, Thoracic, and Mediastinal disorders			
Dyspnea	1 (25)	2 (25)	3 (25)
Skin and subcutaneous tissue disorders			
Rash maculo-papular	1 (25)	3 (37.5)	4 (33)

- Majority of AEs are hematologic, consistent with lymphodepletion safety profile
- Grade 3 nonhematologic AEs in ≥ 1 patient:
  - Hypertension, hyponatremia, hypoxia (2 each)
  - Abdominal pain, bronchospasm, dyspnea, headache, rash, and syncope (1 each)
- No CRS or ICANS
- No potential SOCS1 specific toxicities identified
- 4 patients with SAEs (unrelated to eTIL)
- No Grade 5 AEs

Data as of March 9, 2026

Dose dependent reduction in target lesions irrespective of IL2

Tumor reduction in 100% and 33% ORR in patients treated > median cell dose*

	101-011	101-014	101-002	101-006	101-005	101-003	101-010	101-004	101-016	101-015
Cell dose (cells)	2.3 x 10^9	4.1 x 10^9	4.1 x 10^9	5.2 x 10^9	5.3 x 10^9	6. 7 x 10^9	8.2 x 10^9	8.4 x 10^9	9 x 10^9	10.7 x 10^9
# of IL2 doses	6	6	n/a	6	n/a	n/a	6	n/a	4	5
Best reduction in tumor burden, % (Target lesion SOD)	+ 2	n/a	+ 2	+ 4	- 10	- 30	- 11	- 27	- 48	- 41
Non-Target Lesion Response	Non-CR/ non-PD	unk	Non-CR/ non-PD	PD	CR	N/A	PD	CR	SD	SD
Best Overall Response	SD	PD	SD	PD	SD	PD due to isolated BM	PD	SD	**PR**	**PR**
Time to progression (weeks)	12	4	12	6	12	4	6	15 months	n/a **(ongoing > 12 months)**	12

Partial Response (PR)
Stable Disease (SD)
Progressive Disease (PD)

- **100% of tumor reduction in patients above median cell dose(>5.25 x 10^9 cells)**
  - 33% ORR (2/6) in patients treated with above median cell dose
    - 1 patient ongoing with PR > 12 months

** 2 patients dosed with <1B x 10^9 cells non efficacy evaluable and efficacy data not displayed*

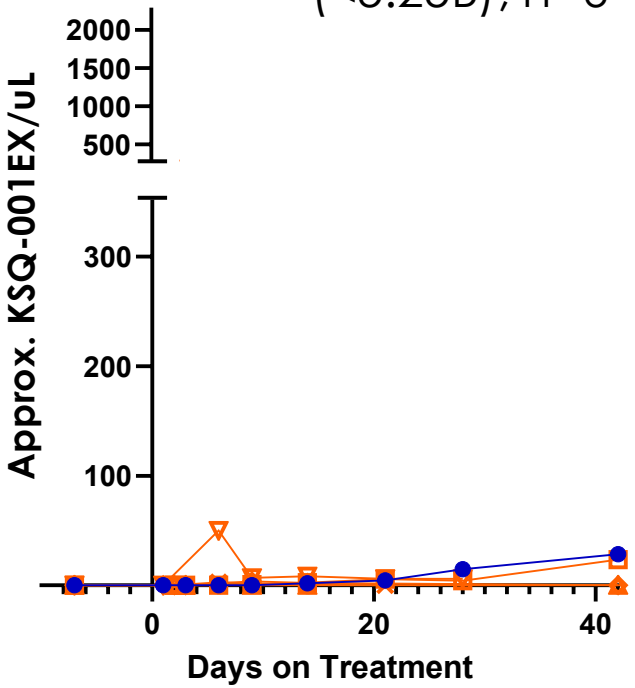
CR: Complete Response; ORR: Overall Response Rate

Expansion and long-term persistence of KSQ-001EX

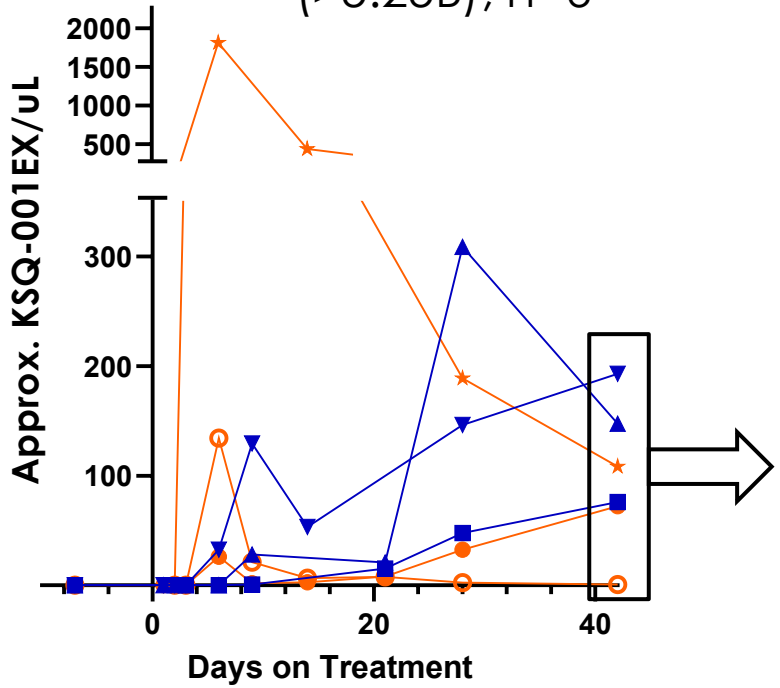
In patients receiving above median cell dose regardless of IL-2

Engraftment/Expansion by Dose

Infusion doses < median (<5.25B), n=6



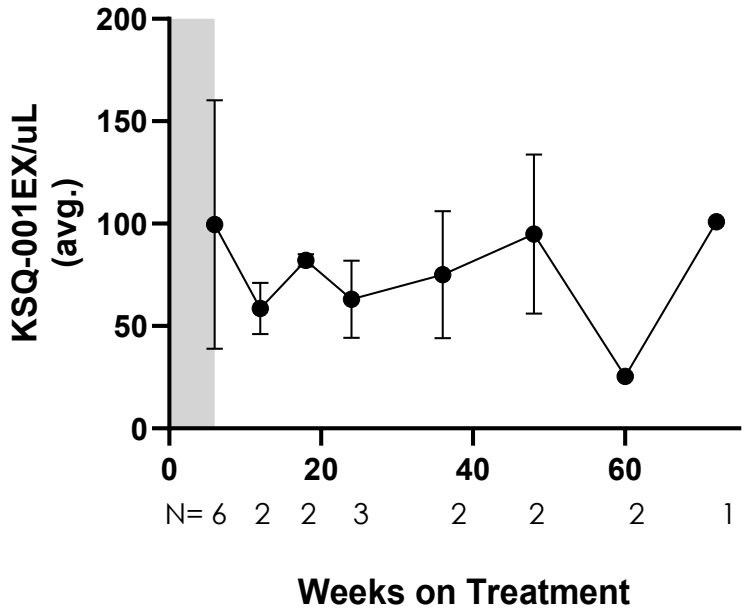
Infusion doses > median (>5.25B), n=6



Cohort 1: (-) IL-2 Cohort 2: (+) IL-2

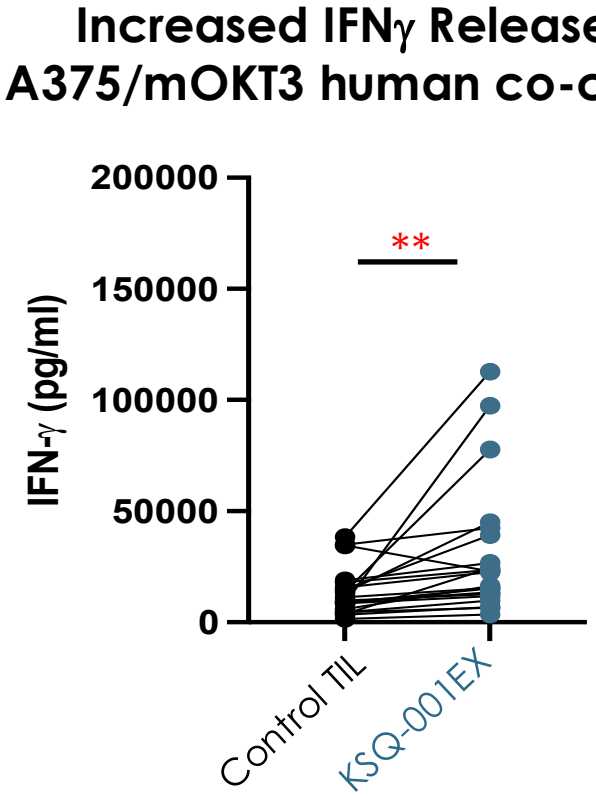
Persistence >6 weeks

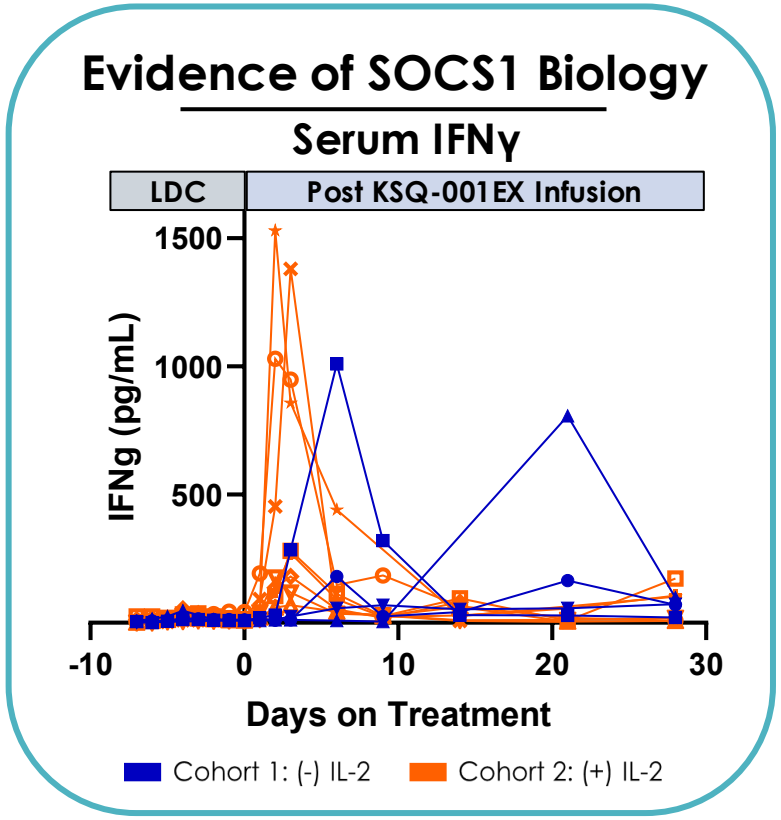
Persistence in Patients Receiving >5.25B Dose



IFNγ release reveals evidence of SOCS1 biology

Clinical data consistent with preclinical results





*Data inclusive of all patients dosed

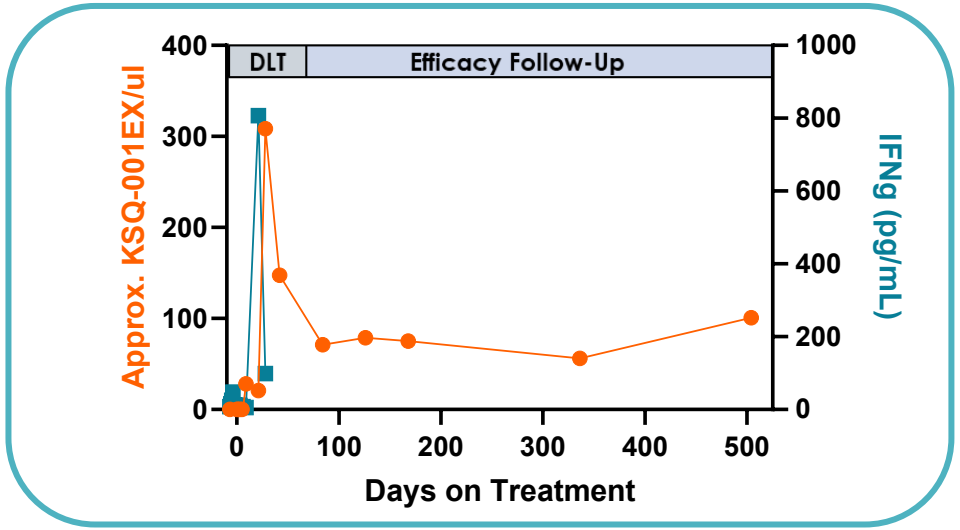
IFNγ peaks exceed levels reported in literature with unmodified TIL[1]

[1]*Sarnaik et al. ASCO (2024)*

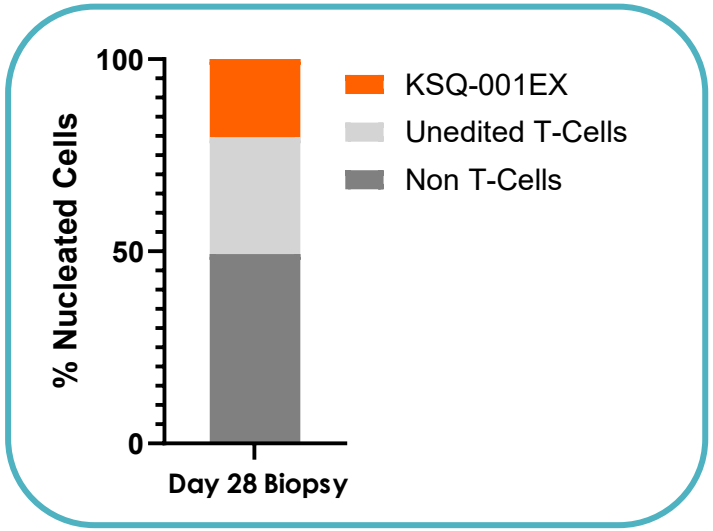
KSQ-001EX displays favorable kinetics and tissue homing

Case Study: Patient in Stable Disease for >12 months

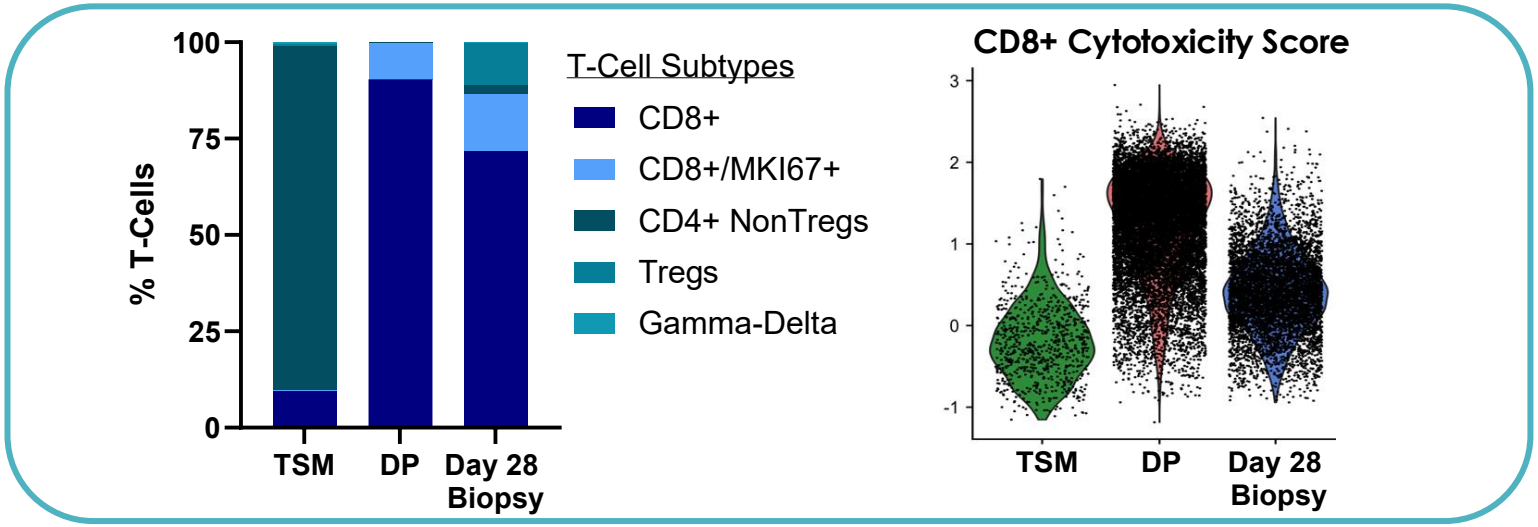
Expansion preceded by IFNγ with long-term persistence



~20% tumor infiltration



Reigniting the tumor microenvironment (CD8+)



DP: Drug Product
TSM: Tumor Starting Material

KSQ-001EX demonstrates anti-tumor activity

Evidence of SOCS1 inactivation impacting TIL functionality

- **Favorable drug product phenotype** with high CD8+/CD27+ "young" TIL population
- **No DLTs and manageable safety profile**, with most AEs attributed to lymphodepleting chemotherapy
- Dose dependent target lesion reduction at target dose range (1-10B cells) below unmodified TIL
  - **Tumor reduction in 100% of patients treated above median cell dose (5.25B)**
- KSQ-001EX **expansion, tumor infiltration, and long-term persistence** with one time treatment with and without IL-2
- Reigniting the tumor microenvironment with cytotoxic CD8+ cells
- Phase I/II study with **SOCS1 and Regnase-1 dual edited eTIL**, KSQ-004EX currently enrolling (clinicaltrials.gov: NCT06598371)

We would like to thank all patients and caregivers for their participation in this study

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