KYMERA
EST. 2016

INVENTING NEW MEDICINES

WITH TARGETED PROTEIN DEGRADATION

November 2021

Forward-Looking Statements

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Targeted Protein Degradation

Next Potential Breakthrough Modality to Expand Drugged Proteome

Targeted Protein Degradation

Human Proteome

Existing Modalities

✓	**Undruggable Targets** Scaffold, transcript factor, multiple functions	✓
✓	**Efficient Development / Manufacturing**	X
✓	**Systemic Exposure**	X
✓	**Oral Bioavailability**	X

Kymera: A Leading TPD Company

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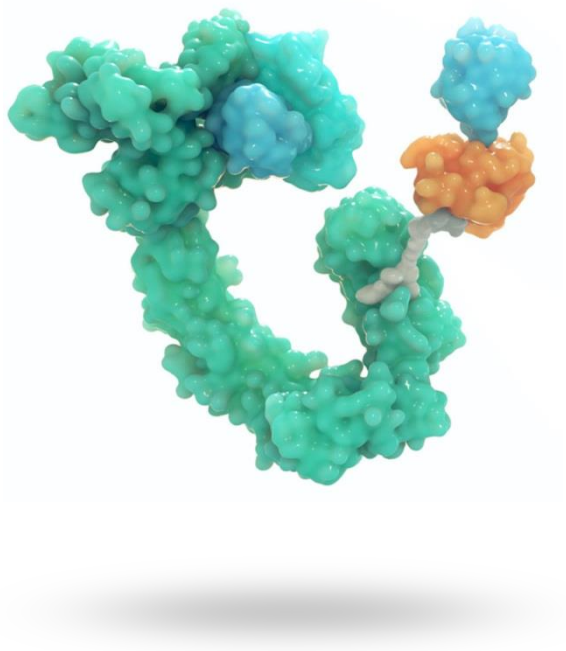
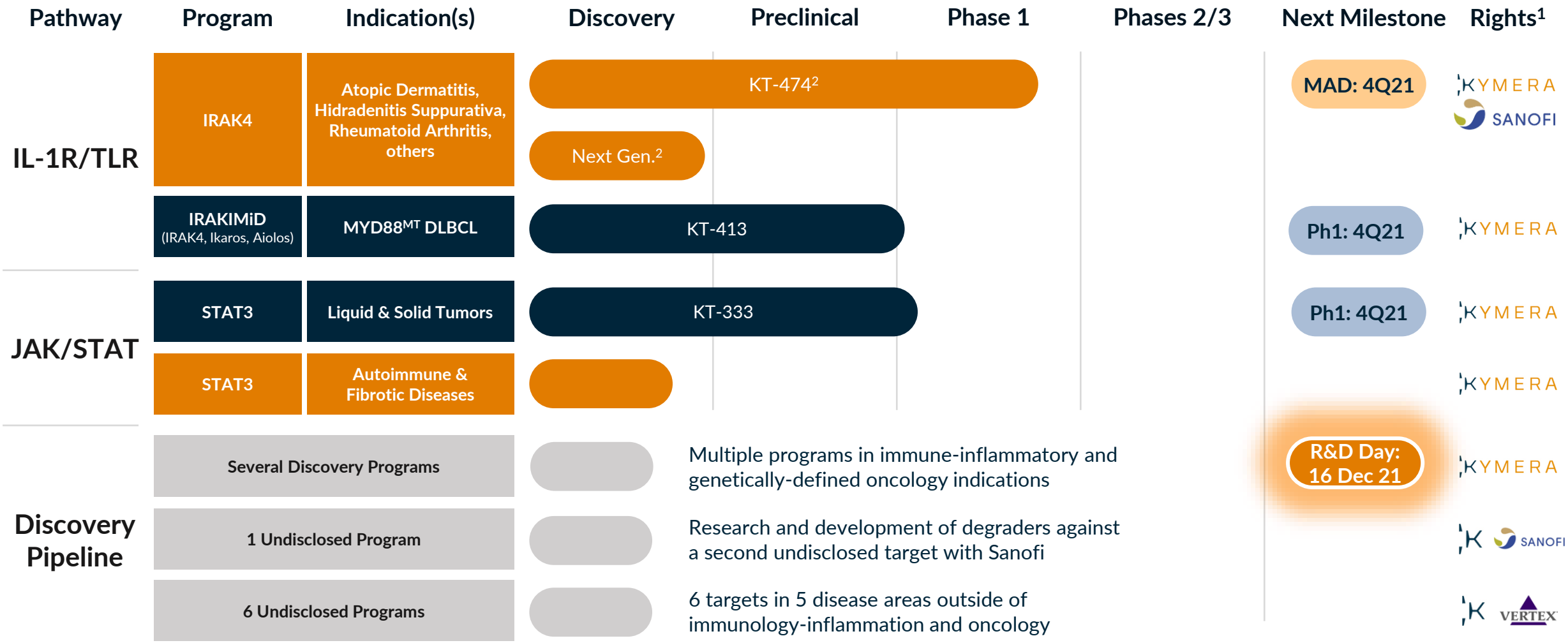


VISION	Fully integrated, **disease agnostic** protein degrader medicine company
KEY PARTNERSHIPS	SANOFI VERTEX gsk
INITIAL FOCUS	**Immunology-inflammation (I/I)** and **oncology**
FIRST-IN-CLASS	First **proof-of-mechanism/biology** (KT-474) and first **undrugged transcription factor** degrader in clinic (KT-333), **3 cleared IND's in 2021**
CLINICAL PIPELINE	**Expect 3 clinical stage programs by end 2021**, including I/I and Oncology programs
DISCOVERY PLATFORM	Multiple discovery programs against undrugged proteins, **targeting ≥ 1IND/Year** beyond 2021
WELL-POSITIONED	**$611M** cash balance

* Based on reported cash at September 30, 2021

Kymera's Pipeline of Novel Protein Degraders



1. Option to participate equally in the development and commercialization of Sanofi-partnered programs in the US.
2. Sanofi collaboration to develop IRAK4 degrader candidates, including KT-474 (SAR444656), outside of oncology and immuno-oncology fields.

● = Oncology ● = Immunology-Inflammation

Pegasus™ TPD Platform

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Targeted Protein Degradation

Biology

Co-opting a Naturally Occurring Process to Regulate Protein Levels

1. E3 ligase recognizes protein
2. Ubiquitin chain transferred
3. Protein is marked for elimination

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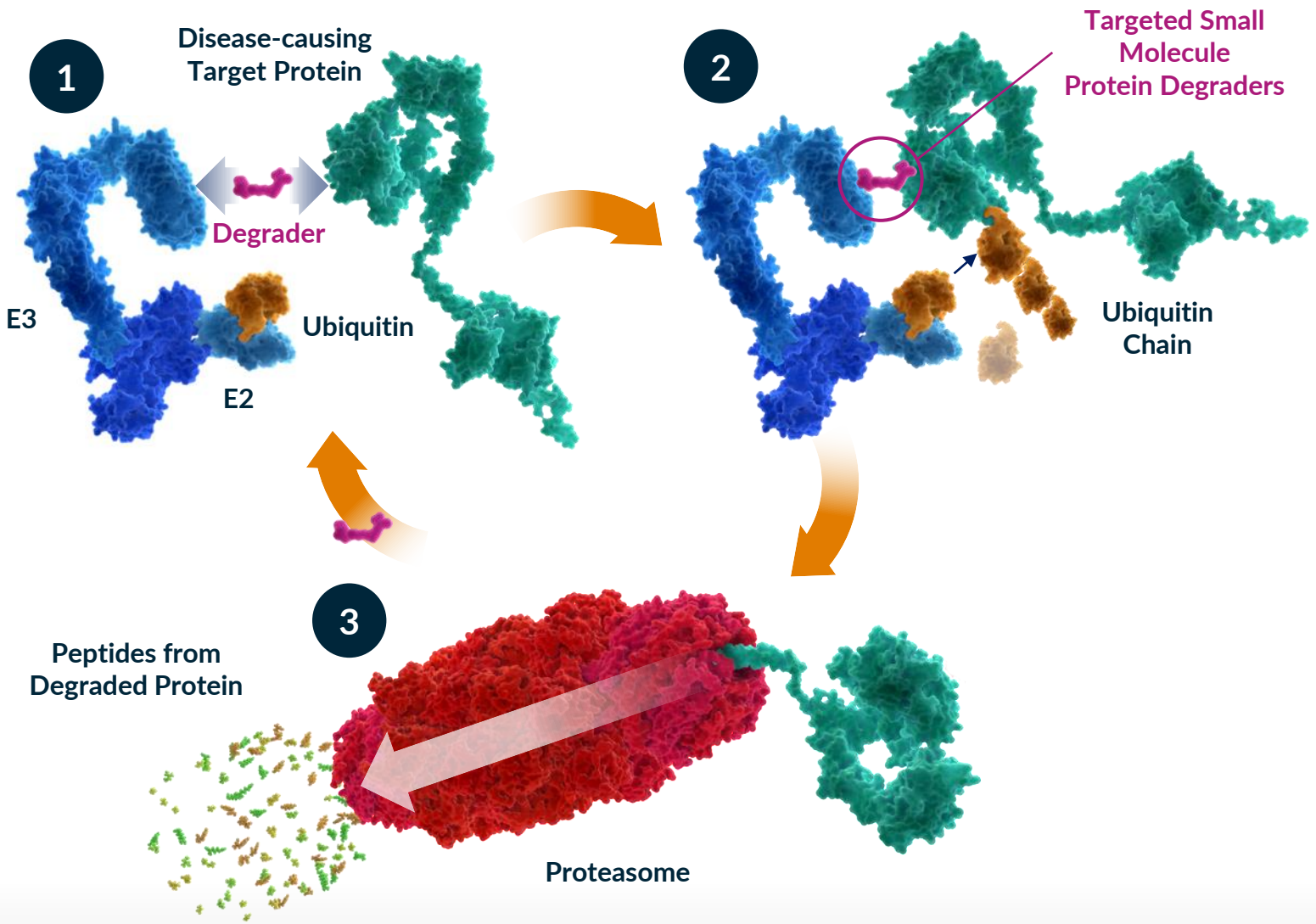
Broad Opportunity
Only Binding Site Required

Efficient
Catalytic

Prolonged Impact
Targeted Protein Degradation

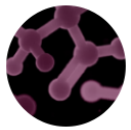


Proprietary Pegasus™ TPD Platform

Key Capabilities

Expanded E3 ligase toolbox

- **E3 ligase Whole-Body Atlas**: Identification of the **expression profiles of ~600 unique E3 ligases**
- Match target protein with appropriate E3 ligase based on expression, distribution, intracellular localization, and biology
- **Toolbox of proprietary ligands** leverages the E3 Ligase Whole-Body Atlas



Understanding degradation (PK/PD) across tissue types

- **Ternary complex modeling tool optimizes the development** of highly efficient and selective degrader therapeutics
- **Quantitative System Pharmacology Model** measures and predicts diverse sets of parameters that impact protein levels
- Based on understanding of PK/PD, both *in vitro* and *in vivo*, and across different tissues and cell types

Proprietary chemistry

- **Comprehensive hit finding technologies toolbox**: chemoproteomics, DEL, fragment screens, *in silico*
- **Proprietary chemistry expertise** enables the design and optimization of both E3 ligases and target protein binders
- Ability to convert into degraders with optimal pharmaceutical properties tailored to specific patient populations

Pegasus: E3 Ligase Whole-Body Atlas

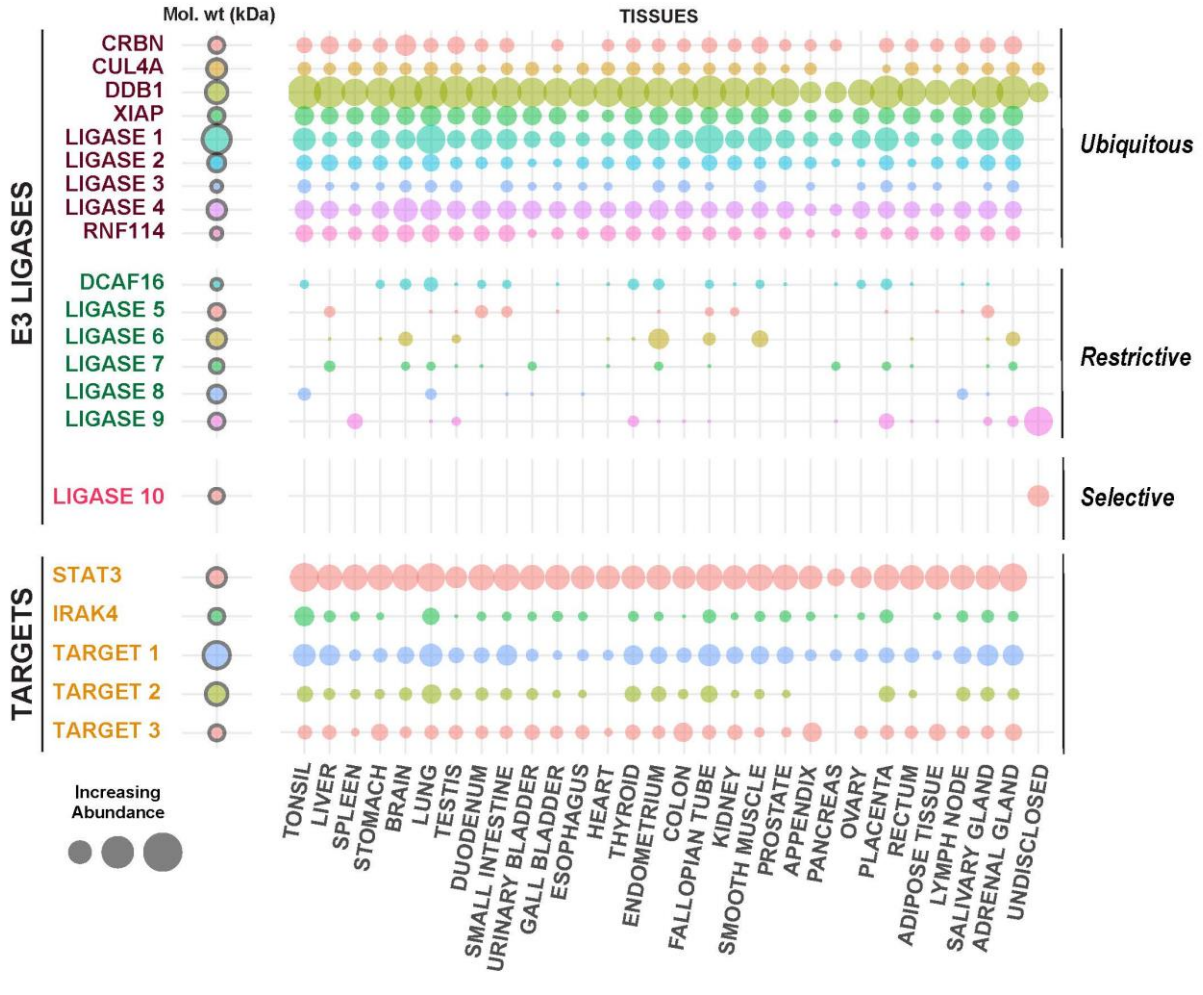
Different Expression Profiles of E3's Provide Opportunity for Tissue-selective/restricted Degradation

Expanded E3 ligase toolbox

Understanding degradation (PK/PD) across tissue types

Proprietary chemistry

- Focused on determining the expression profiles of ~600 unique E3 ligases
- Patterns mapped in both disease and healthy contexts
- Ability to match a target protein with appropriate E3 ligase based on expression and biology
- Vision to develop tissue-selective or tissue-restricted degraders to enable novel therapeutic opportunities



Novel Cullin Ring E3 Ligase Characteristics and Ligandability Assessment

E3 Ligase Type:	Cullin-RING
Known Substrates:	Endogenous substrates
Function:	Confidential
Crystal Structures:	Structure solved
Expression:	Expressed in selected tissues; broadly expressed in cancer cells

Precedence and Datamining

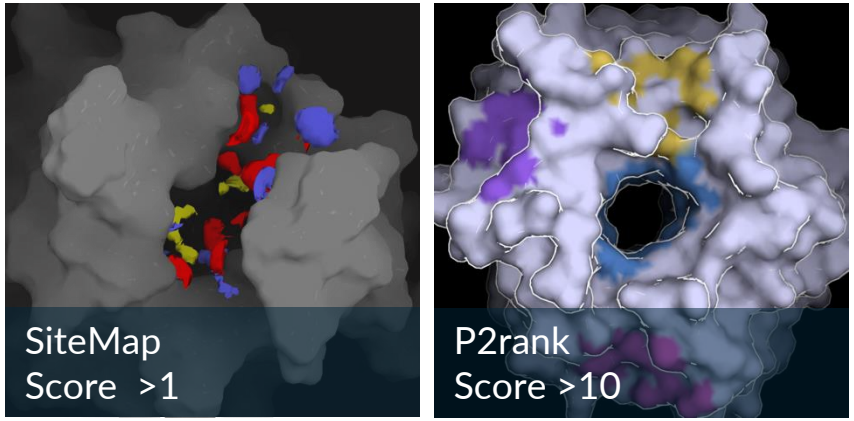
- ✓ ☑ Contains ligandable domains/protein family analysis
- ✓ ☑ Known substrate(s)
- ☐ Known and validated small-molecule

Structure-based Assessments

- ✓ ☑ Ligandability score
- ☐ Cryptic pocket available

Experimental/Biophysical

- ✓ ☑ Identified hits from pilot screens



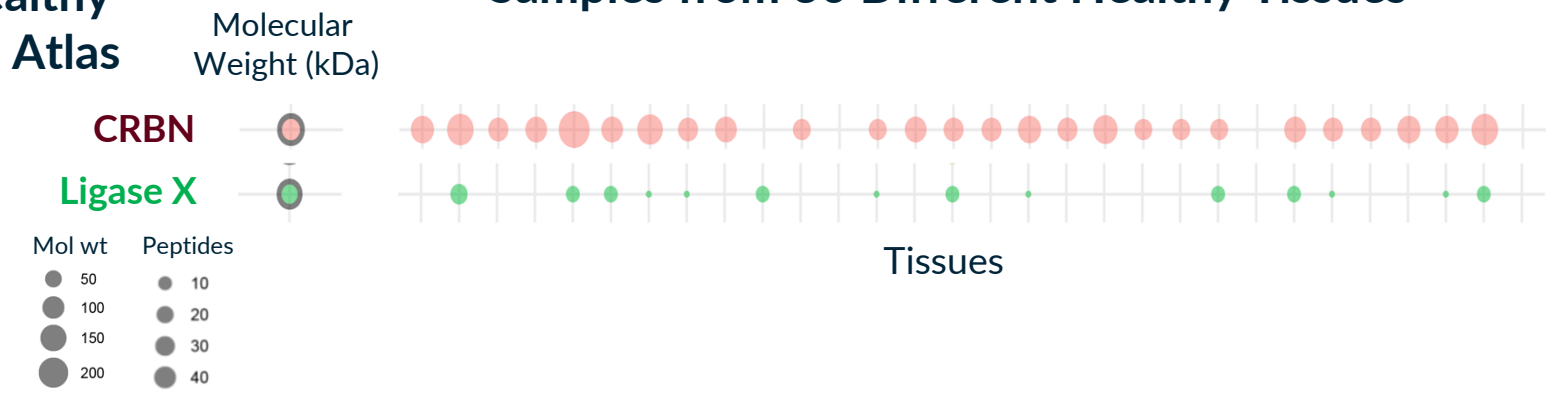
2 orthogonal *in silico* methods suggest pocket is ligandable

- SBDD/Hit-finding activities initiated based on **ligandability** assessment and X-ray system established

E3 Ligase X is a Low Abundant and Tissue Selective Protein, Broadly Expressed in Multiple Cancer Cell Lines

E3 Healthy Tissue Atlas

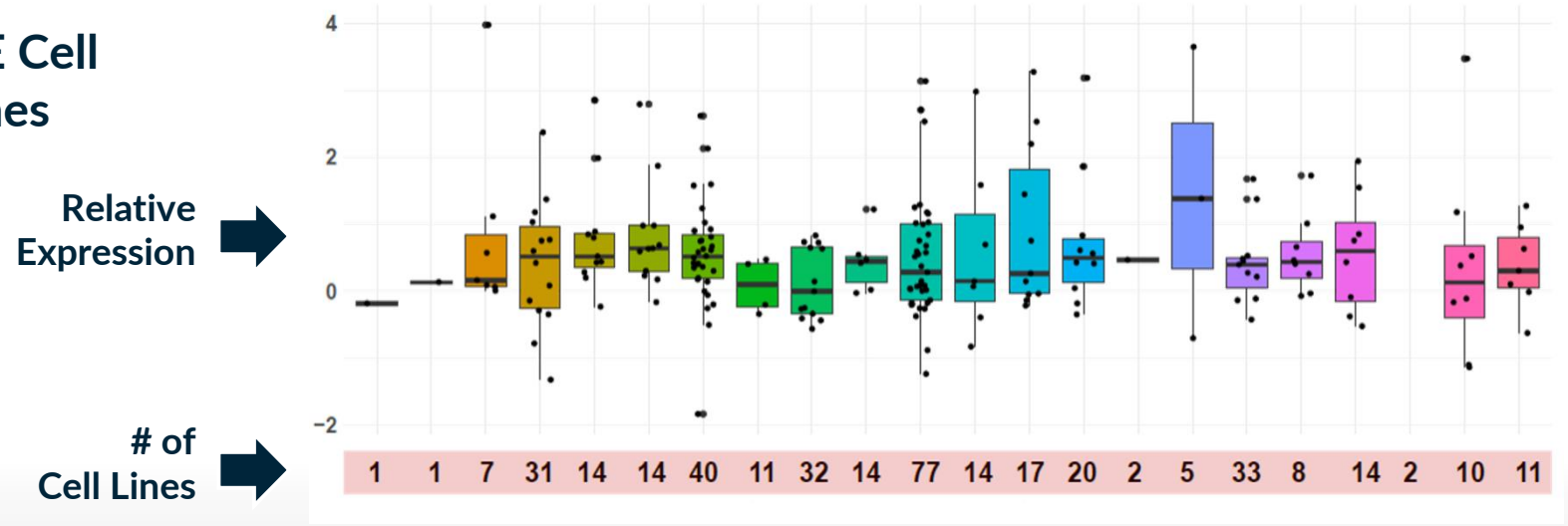
Samples from 30 Different Healthy Tissues



E3 Healthy tissues atlas confirms ubiquitous expression of CRBN and restrictive expression for **Ligase X**

CCLE Cell Lines

Cancer Lines Originated from 22 Different Tissues

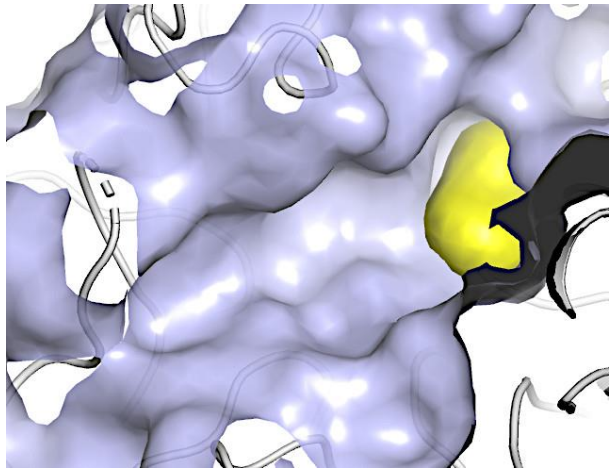


Ligase X is expressed in majority of CCLE cancer cell lines at low levels

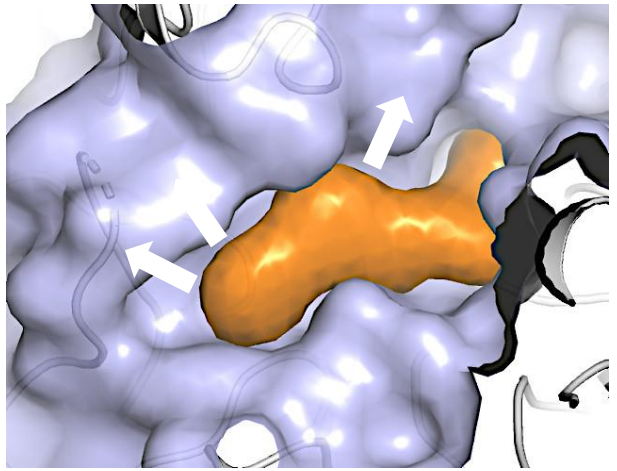
An Early Fragment X-ray Structure Solved along with Virtual Library Evaluation Led to Very Potent Binders of this Target

	HTRF
Fragment bound X-ray structure	IC_{50} > 1 mM
Rational design to explore SAR	IC_{50} < 30 µM
In silico library evaluation and synthesis	IC_{50} < 5 µM
3x	
Rational design to optimize library hits	IC_{50} < 0.1 µM MW <400; clogP 0.7

Total # of virtual compounds evaluated	40K
Total # of crystal structures	18
Total # of compounds made	195



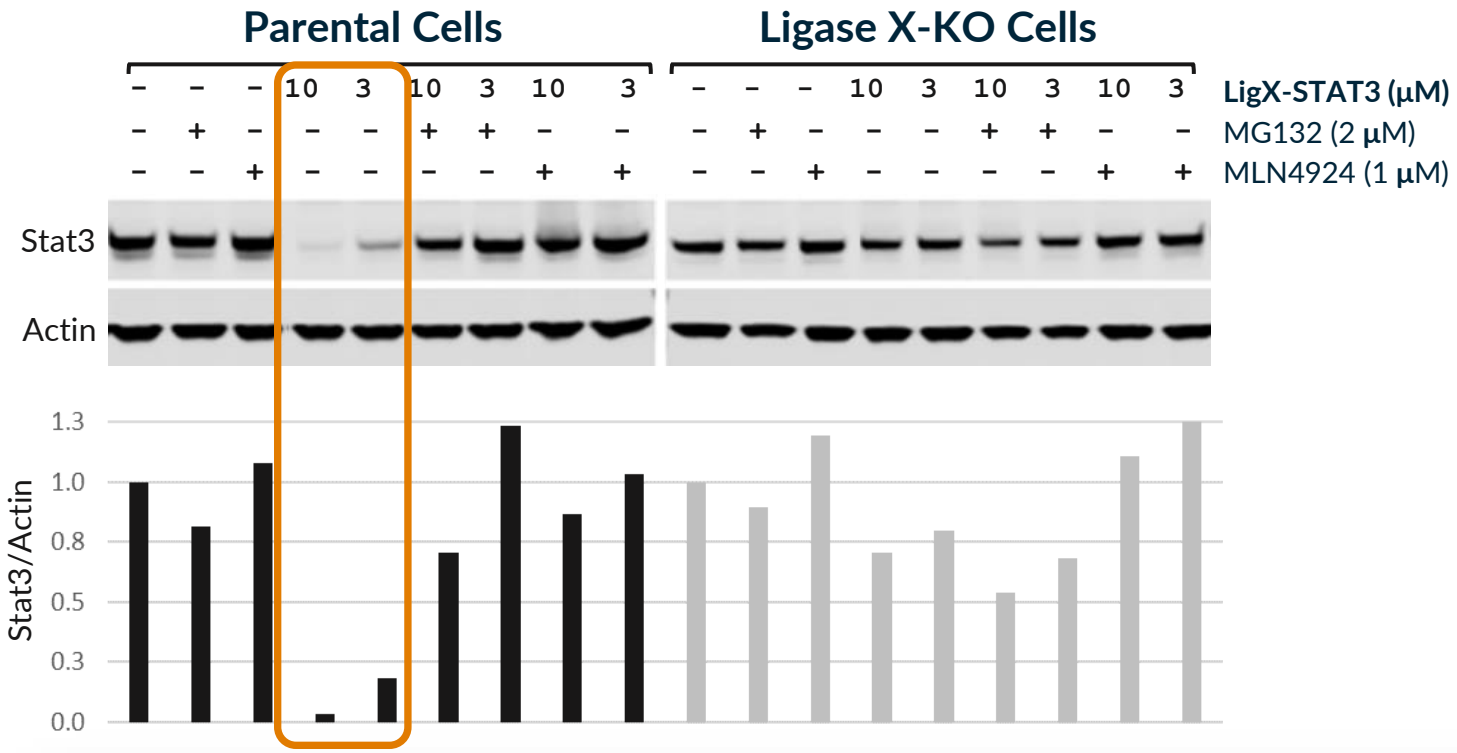
X-ray with Fragment



X-ray with Optimized Ligand

- Successfully applied SBDD to rapidly identify diverse E3 ligase ligands
- Multiple exit vectors identified and confirmed via chemistry, molecular modeling and X-ray
- Degraders synthesized for BRD4 + additional Kymera targets including STAT3 and IRAK4

STAT3 Degrader Based on Ligase X Demonstrates Broad Degradation Across Multiple Cancer Cell Types



Cells (Assay)	DC_{50} (μM)
A549 (HiBiT)	**0.20**
Su-DHL-1 (MSD)	**0.82**
Uveal Melanoma 92-1 (WB)	**<1**
OVCAR-3 (WB)	**0.6**
OVCAR-8 (WB)	**1.0**

- Degrader LigX-STAT3 demonstrated dose-dependent degradation of STAT3, achieving >50% STAT3 degradation at 1 μM.
- STAT3 degradation was rescued by proteasome inhibitor MG-132 or neddylation inhibitor MLN4924, indicating UPS mediated protein degradation
- Knockout of ligase X abolished STAT3 degradation, indicating the degradation is ligase X dependent.

IRAK4 Degrader KT-474

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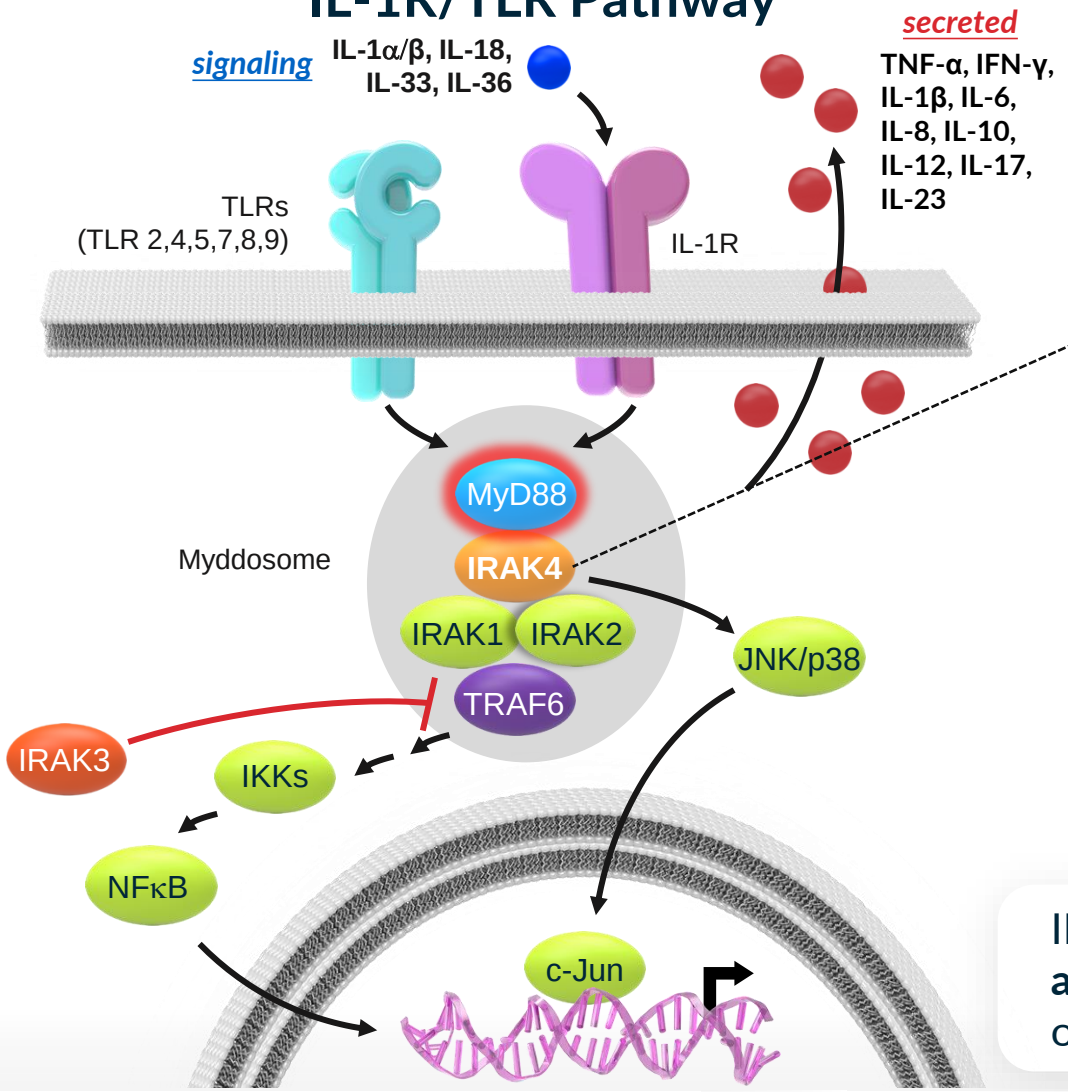
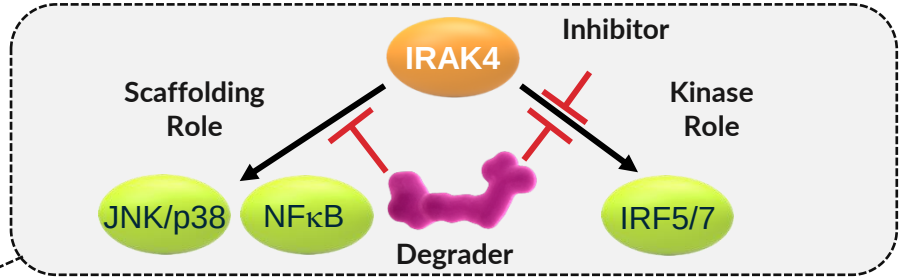
IRAK4 Targeting: Degrader Advantage, Clinical Validation, and Human Genetics De-risking

IL-1R/TLR Pathway



Degrader Advantage



Clinical Pathway Validation

IL-1α/IL-1β : Rheumatoid Arthritis, CAPS, Hidradenitis Suppurativa
IL-1α: Atopic Dermatitis
IL-1β: Gout; CANTOS Outcomes Data in Atherosclerosis and Lung Cancer
IL-18: Macrophage Activation Syndrome
IL-36: Generalized Pustular Psoriasis, Atopic Dermatitis
IRAK4 SMI: Rheumatoid Arthritis

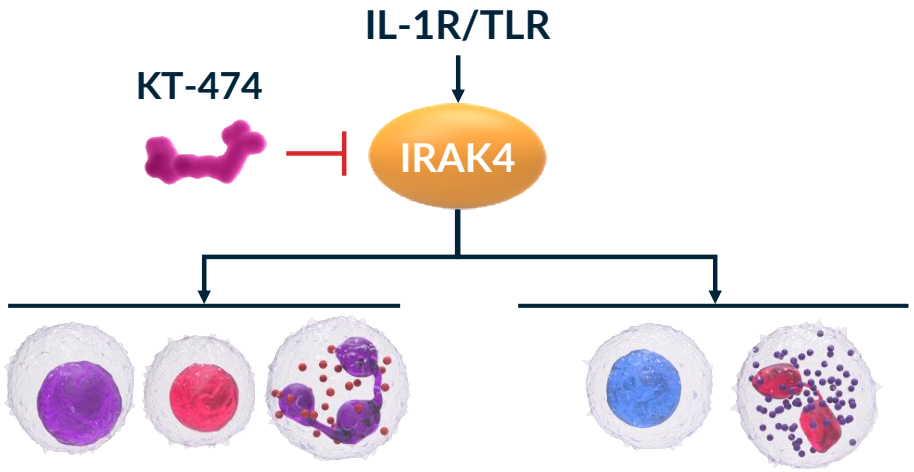
Human Genetics

Humans with **IRAK4 Null Mutation are healthy**

IRAK4 degrader has potential to achieve a **broad, well-tolerated anti-inflammatory effect,** providing multiple development opportunities in autoimmune inflammatory diseases

Development Opportunities for IRAK4 Degrader in Inflammation

Potential for Broad Activity Across Th1-Th17 and Th2 Diseases



Th1-Th17/Neutrophils

- **Hidradenitis Suppurativa**
- **Rheumatoid Arthritis**
- Lupus
- IBD
- Gout
- Psoriasis

Th2/Eosinophils

- **Atopic Dermatitis**
- Asthma
- COPD
- CRSwNP

$ 150B Combined global drug sales

Indication	2021 Prevalence US/EU5/JP	2021 Global Sales
AD	~82.5 M	$5,760 M
HS	~785 K	$1,106 M
RA	~385 K	$27,634 M
SLE	~580 K	$1,333 M
IBD	~3.2 M	$21,710 M
Gout	~18.2 M	$1,319 M
Psoriasis	~15.8 M	$23,268 M
Asthma	~87.3 M	$15,664 M
COPD	~61.7 M	$9,960 M
CRSwNP	~20.4 M	$2,622 M

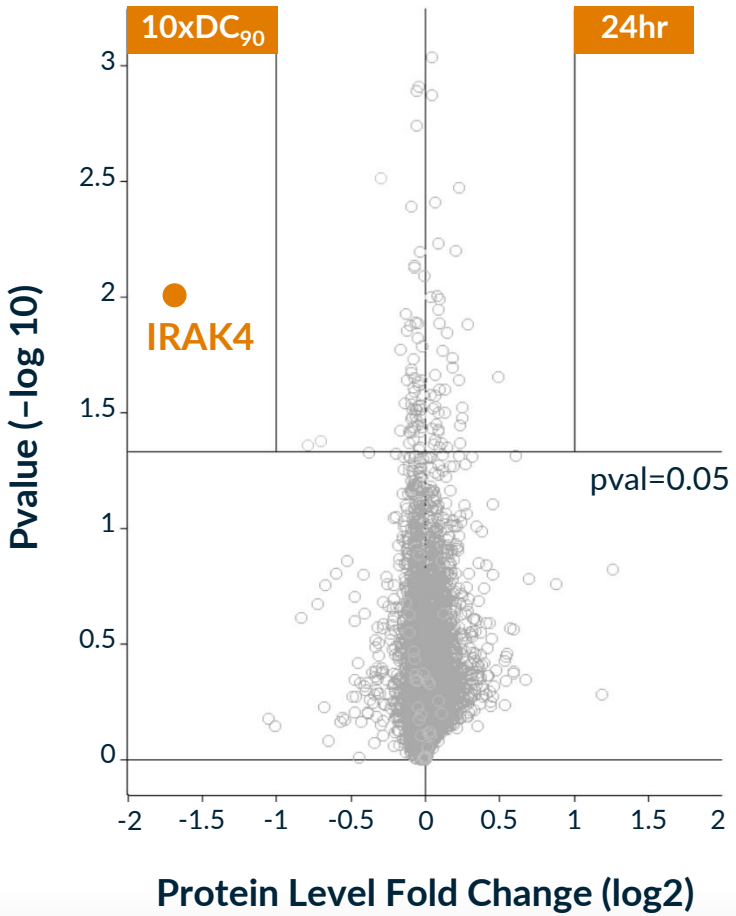
Limitations of Current Therapies

- **Anti-Cytokine/Cytokine Receptor Antibodies**
  - Target only 1-2 cytokines
  - Require injection
- **Small Molecule Inhibitors**
  - Limited pathway blockade (IRAK4 SMI)
  - Safety issues (JAK family)

Source: EvaluatePharma; GlobalData; Dash. Allied Market Research. 2021; Koto. Modern Rheumatology. 2021; Ahn. JAMA Otolaryngol Head Neck Surg. 2016; UC: Ulcerative Colitis; CD: Crohn's Disease.

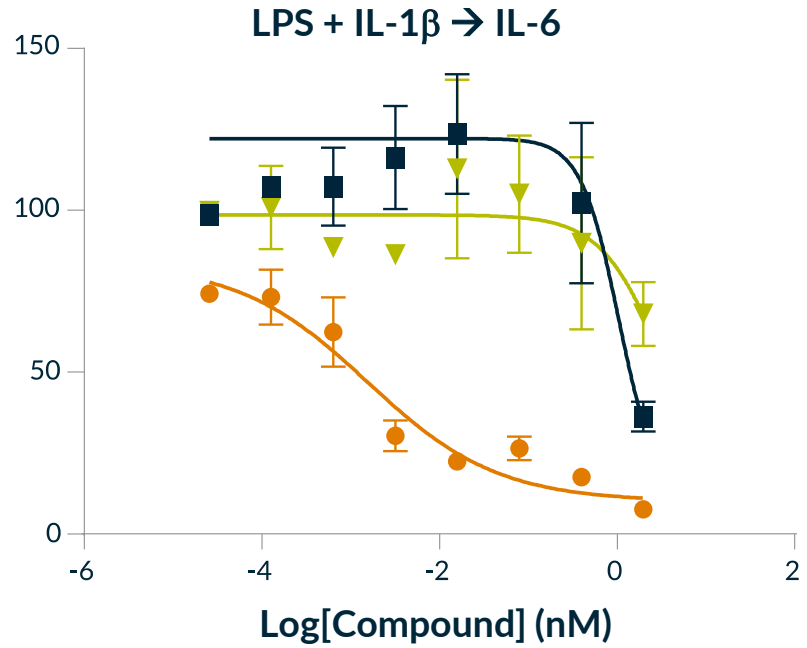
KT-474: Potent and Specific IRAK4 Degradation with Impact on Cytokines Superior to Kinase Inhibition

Degradation and Selectivity



- KT-474 DC_{50} = 2.1 nM in human immune cells
- KT-474 only degraded IRAK4 in human immune cells at concentration 10-fold above the DC_{90}
- KT-474 better able to inhibit IL-6 under both LPS and LPS + IL-1β than clinically active IRAK4 SM kinase inhibitor PF-06550833

Superiority over SM kinase Inhibitor

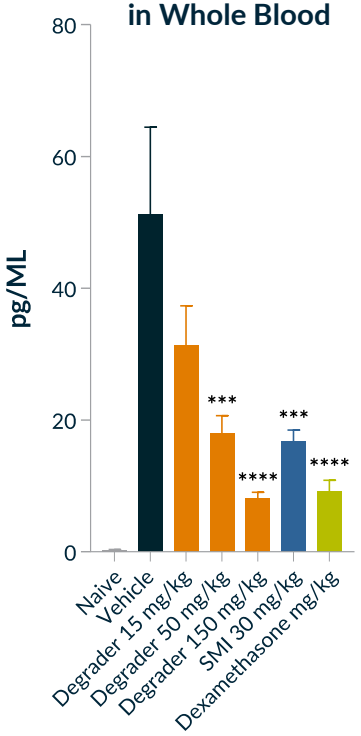


Legend	Compound	IL-6 IC_{50} (nM)
	IRAK4 Degrader	0.8
	Negative control	450
	IRAK4 SMI *(PF-06550833)*	N/A

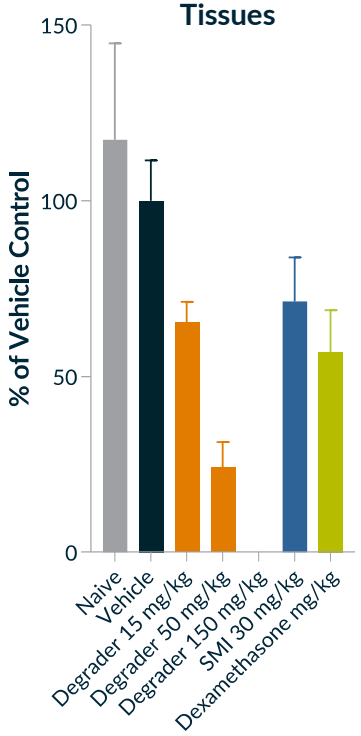
KT-474 is Superior to IRAK4 Small Molecule Inhibitor (SMI) Across Multiple Preclinical Immune-inflammatory *In Vivo* Models

rmIL-33 Intradermal Challenge Model

In vivo IRAK4 Degradation in Whole Blood

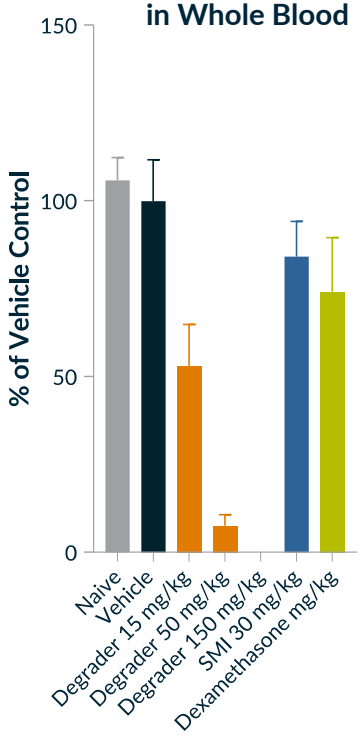


IL-5 in Ear Tissues

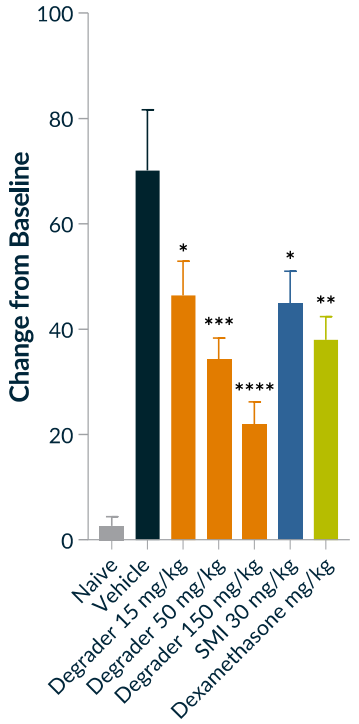


rhIL-36αβγ Intradermal Challenge Model

In vivo IRAK4 Degradation in Whole Blood

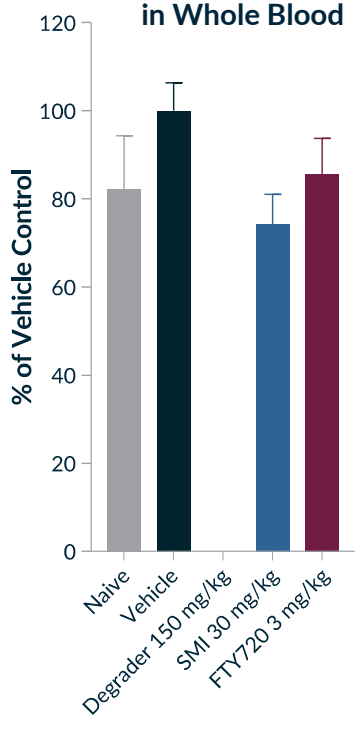


Ear Thickness

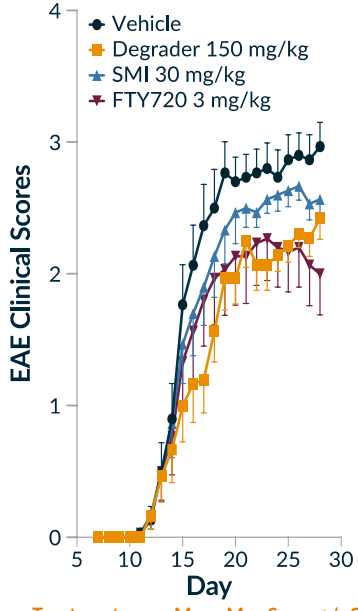


Th17-mediated Multiple Sclerosis Model

In vivo IRAK4 Degradation in Whole Blood



MOG-EAR[1]



Treatment	Mean Max Score +/- SD	p value
Vehicle	3.40 +/- 0.54	-
Degrader 150 mg/kg	**2.69 +/- 0.52**	0.0018
SMI 30 mg/kg	3.07 +/- 0.42	0.0822
FTY720 3 mg/kg	**2.70 +/- 1.28**	0.0271

IRAK4 knockdown of **≥85%** in whole blood achieved anti-inflammatory effect **comparable to potent corticosteroids** or **approved standard of care drugs** in these models as well as in models of TLR4 (MSU-Gout) or TLR7/8 (Imiquimod-Psoriasis) activation that was **superior to IRAK4 small molecule inhibitor**

1. Myelin oligodendrocyte glycoprotein-induced experimental autoimmune encephalomyelitis (MOG-EAR) model

KT-474 Phase 1 Trial Design

Double-blind, Placebo-controlled, Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) trial

Three-part Phase 1 Design

1 SAD Portion
Healthy Volunteers

- **7** cohorts (up to 56 adult healthy subjects)
- **8** per cohort (6:2 randomization)
- **Single** dosing (starting dose 25 mg)

2 MAD Portion
Healthy Volunteers

- **5** cohorts (up to 60 adult healthy subjects)
- **12** per cohort (9:3 randomization)
- **14x** daily doses (starting dose 25 mg)

3 MAD Portion
Patient Cohort

- **1** cohort (up to 20 AD and HS patients)
- Open-label
- **14x** daily doses

Endpoints

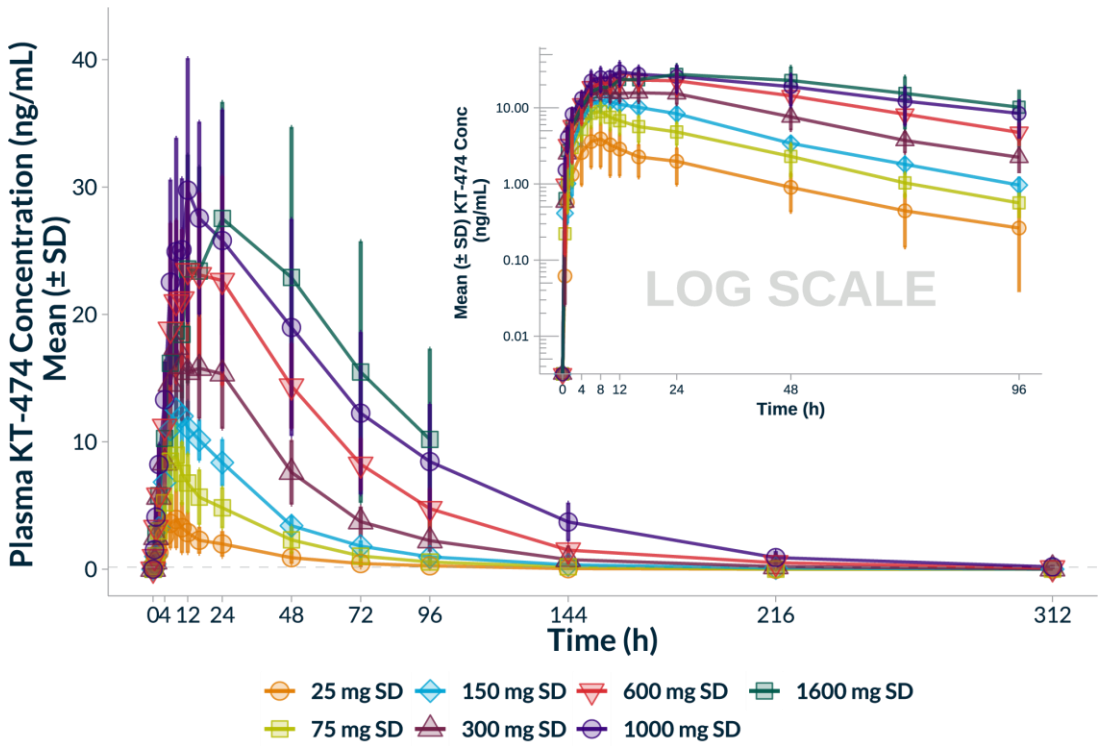
Primary
- Safety & tolerability

Secondary/ Exploratory (SAD & MAD)
- Pharmacokinetic measures (half-life, bioavailability)
- IRAK4 knockdown in PBMC

Exploratory (SAD & MAD)
- *Ex vivo* response of whole blood to TLR agonists (SAD & MAD) and IL-1β (MAD only)

Exploratory (MAD Only)
- IRAK4 knockdown in skin biopsies
- Proinflammatory cytokine and chemokine levels in skin biopsies (Patients only)
- Plasma C-reactive protein (HV and Patients) and cytokine levels (Patients only)

SAD Study: Favorable PK after Single Oral Dosing



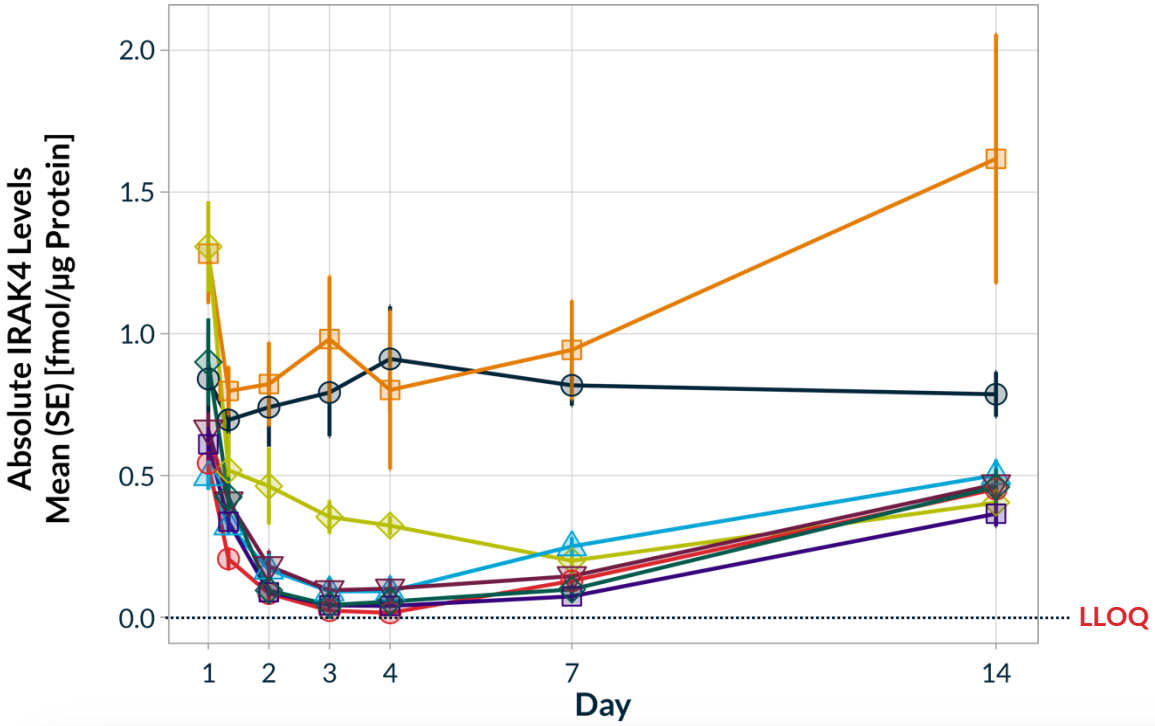
SAD #	Dose	Cmax (ng/mL)	t_{max} (h)	AUC (ng.h/mL)	$t_{1/2}$ (h)
1	25 mg	3.49 (61.2)	8.0 (6.0-8.0)	112 (65.4)	25.2 (27.0)
2	75 mg	9.08 (36.6)	7.0 (6.0-8.0)	288 (36.7)	28.7 (10.1)
3	150 mg	12.7 (25.7)	9.0 (8.0 - 10.0)	483 (21.9)	31.6 (22.1)
4	300 mg	17.4 (29.6)	8.0 (8.0 – 24.0)	869 (31.4)	36.4 (13.1)
5	600 mg	24.2 (27.5)	12.0 (6.00 – 24.0)	1530 (18.6)	40.9 (18.2)
6	1000 mg	27.8 (34.4)	20.0 (6.0 – 24.0)	1890 (60.8)	38.8 (7.0)
7	1600 mg	27.3 (36.2)	24.0 (12.0 – 48.0)	1920 (43.0)	36.4 (46.9)

Geometric Mean (%CV) reported for all parameters, except tmax where median (range) are presented

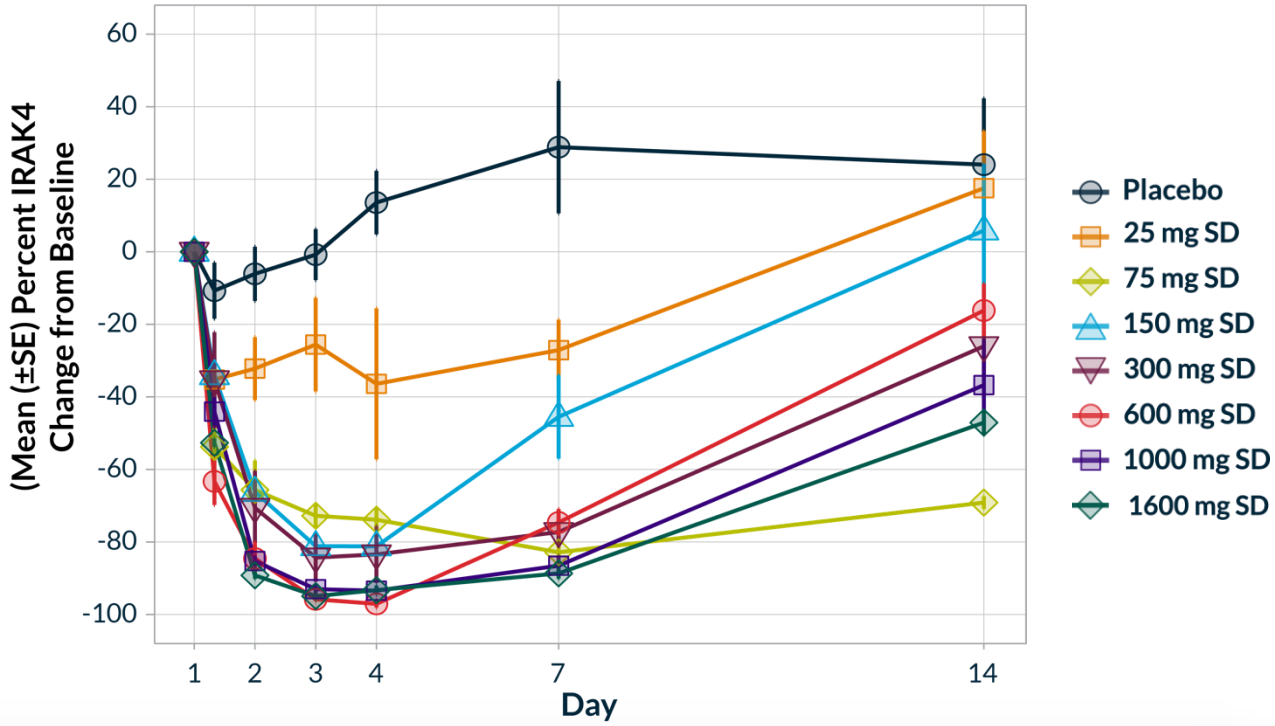
- Consistent PK after single dosing: Cmax achieved between 7-24 hours, half-life = 25-40 hours
- Dose dependent exposure increases, plateauing after the 1000 mg dose
- Low to moderate inter-subject variability in exposure

KT-474 Achieved Deep and Dose-Dependent IRAK4 Degradation after Single Oral Doses that Lasted for at Least 6 Days

Absolute IRAK4 Levels

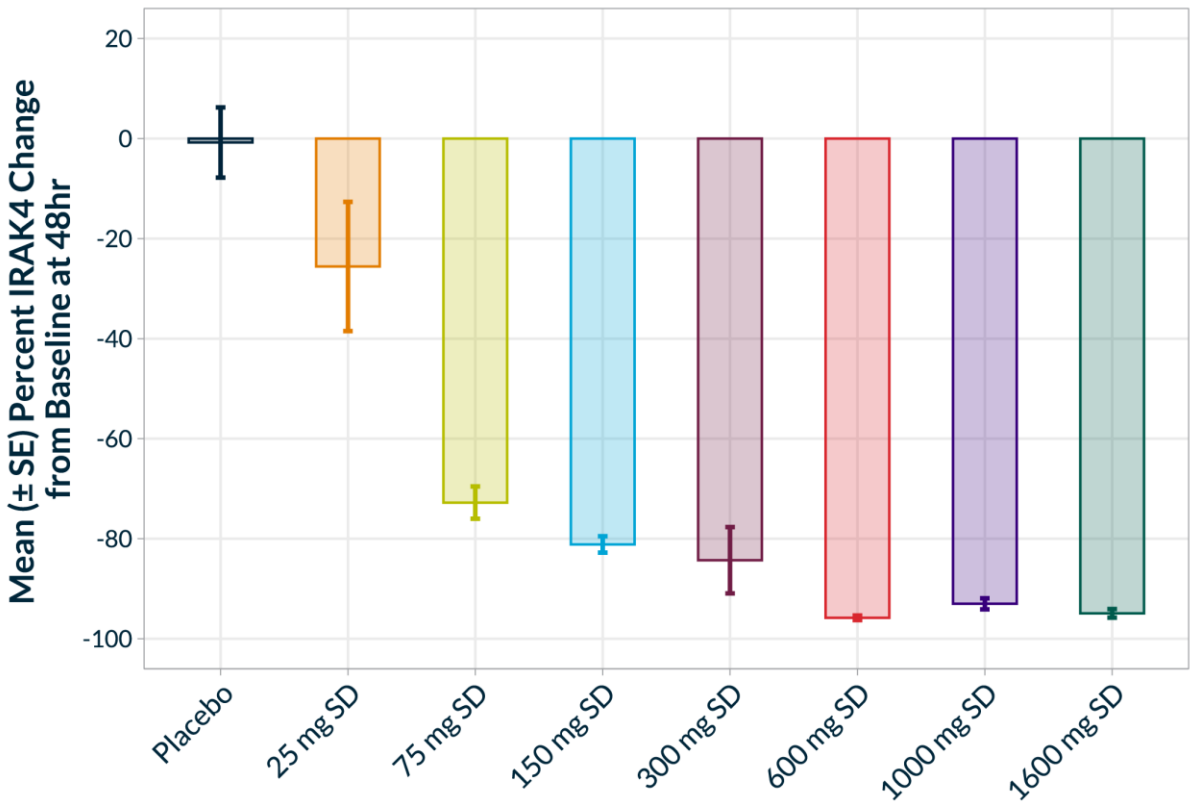


Mean % Reduction of IRAK4



- Detected by Mass Spectrometry in circulating PBMC
- IRAK4 levels nadired at 48-72 hours (Day 3-4)
- IRAK4 reduction lasted for at least 6 days post-dose in all dose groups
- SAD 5 through 7 approached or exceeded Lower Limit of Quantitation (LLOQ)

KT-474 Achieved >95% IRAK4 Degradation After Single Dose



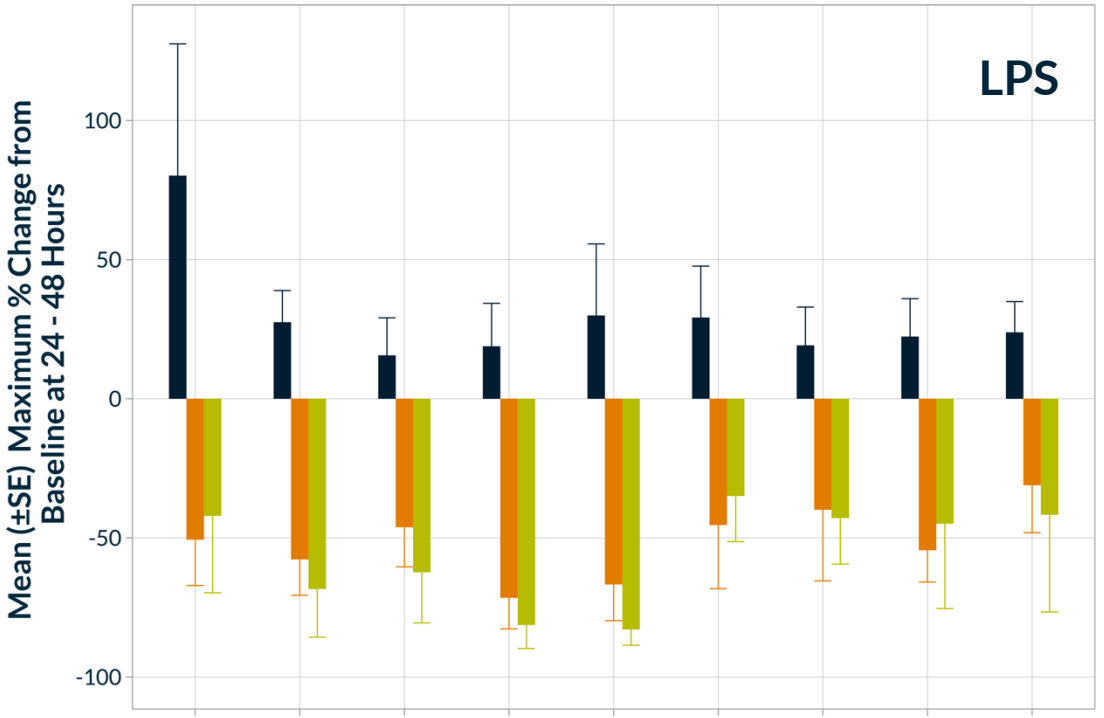
Percent IRAK4 Reduction in PBMC at 48 Hours Post-Dose using Mass Spectrometry

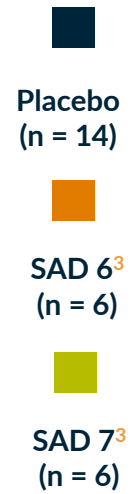
	N	Mean IRAK4 Change	Median IRAK4 Change	*p value*
Placebo	13	-1%	-2%	--
25 mg	6	-26%	-39%	*0.1*
75 mg	6	-73%	-75%	*<0.0001*
150 mg	6	-81%	-82%	*<0.0001*
300 mg	6	-84%	-89%	*<0.0001*
600 mg	7	-96%	-96%	*<0.0001*
1000 mg	5	-93%	-94%	*<0.0001*
1600 mg	6	-95%	-95%	*<0.0001*

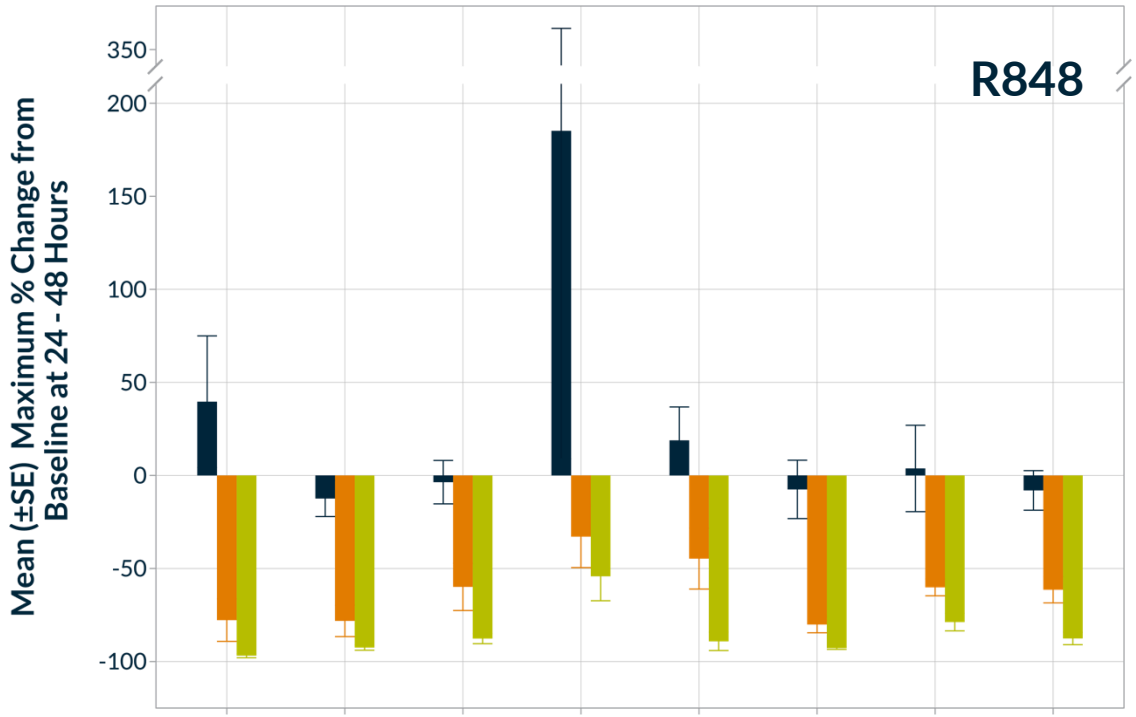
* p-values relative to placebo

Up to 97% Maximum *Ex Vivo* Cytokine Inhibition 24-48h Post-Dose

Effect Against LPS (TLR4)- or R848 (TLR7/8)-Stimulated Cytokine Induction in Whole Blood







	IFNγ	IL1β	IL6	IL8	IL10	IL12	IL17	IL23	TNFα
Pbo	80%	27%	16%	19%	30%	29%	19%	22%	24%
SAD 6 85-93% Degr*	-51%	-58%[1]	-46%[2]	-72%[1]	-67%[2]	-45%[2]	-40%[2]	-54%[2]	-31%
SAD 7 89-95% Degr*	-42%	-68%[1]	-62%[1]	-81%[1]	-83%[1]	-35%[2]	-43%[2]	-45%[2]	-42%[2]

	IFNγ	IL1β	IL6	IL8	IL10	IL12	IL17	TNFα
Pbo	40%	-12%	-4%	185%	19%	-7%	4%	-8%
SAD 6	-78%	-78%[1]	-60%[1]	-33%	-45%	-80%[1]	-60%[1]	-61%
SAD 7	-97%[2]	-92%[1]	-88%[1]	-54%	-89%[1]	-93%[1]	-79%[1]	-88%[2]

[1] = p value < 0.01; [2] = p value < 0.05

*Mean IRAK4 degradation in PBMC at 24-48h

[3]Ex vivo cytokine assay was performed at 48h nadir (maximal degradation) only in cohorts 6-7

KT-474 Demonstrates Broadest Anti-inflammatory Effect Compared to Other Clinical Agents

Inhibition of *Ex Vivo* Disease Relevant Cytokine/Chemokine Stimulation by Anti-Inflammatory Agents in Ph1 Studies

Agent/Stimulus	Target	IFNγ	TNFα	IL-1β	IL-6	IL-8	IL-17	IL-12	IL-23	IL-10
KT-474/LPS	**IRAK4 (degrader)**	✓	✓	✓	✓	✓	✓	✓	✓	✓
KT-474/R848	**IRAK4 (degrader)**	✓	✓	✓	✓	✓	✓	✓		✓
CA-4948/R848	IRAK4* (inhibitor)				✓					
ATI-450/LPS	MK2		✓	✓	✓	✓				
ATI-450/IL-1β	MK2		✓		✓	✓				
LY2775240/LPS	PDE4		✓							
Iberdomide/LPS	Ikaros/ Aiolos			✓						
JNJ-61803534/ T cell activation	RORγ						✓			

* Non-selective

Iberdomide: Schafer PH, et al. *Ann Rheum Dis* 2018;77:1516–1523; **LY2775240**: Patel DR, et al. *Clin Transl Sci.* 2021;14:1037–1048. ; **JNJ61803534**: Xue X, et al. Sci Rep 2021;11:11066-80, **MK2**: Aclaris 2021 Company Overview; **CA-4948**: Booher RN, et al. ASH Annual Meeting 2018, Poster #4168

Blinded SAD Safety Summary

- No SAEs
- Treatment-related AEs observed only in SAD 5 and SAD 6; all were self-limiting and resolved
  - *No treatment-related AEs in SAD 7*
- No significant ECG changes

Possibly or Probably Treatment-Related AEs* (>1 Subject)

AE Term	#AEs (subjects)	Severity	Cohort
Headache	**4 (3)**	Moderate (x2)	SAD 5, SAD 6
		Mild (x2)	SAD 5
Nausea	**2 (2)**	Mild (x2)	SAD 6

* per investigator assessment

SAD Summary

KT-474 SAD Phase 1 Results Demonstrate Degrader Proof-of-mechanism and Proof-of-biology, First Time for TPD in a Placebo-controlled Study

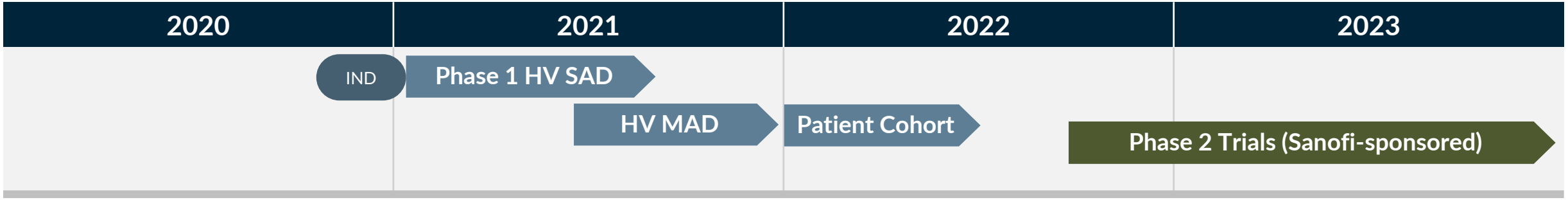
SAD Dose Escalation Complete

- Proof-of-mechanism and proof-of-biology established
  - Robust, dose-dependent IRAK4 reduction in PBMC maintained for at least 6 days, with mean **93-96% KD**
  - Up to **97% inhibition** of R848 or LPS induction of 8 different pro-inflammatory cytokines
  - Maximum cytokine effects seen with KT-474 exposures corresponding to ≥*85%* degradation in PBMC
- **Well-tolerated**, with side effects being mild-moderate self-limiting headache and GI symptoms (none at highest dose)

MAD Dose Escalation Ongoing

- Data to be presented at Kymera R&D Day on 12/16/21
- Expectation during multi-dosing is to reach IRAK4 degradation and cytokine inhibition levels at much lower doses

KT-474 Phase 1 Trial: Next Steps



Data readouts:
- Oct 2021: HV SAD POM/POB
- Before end of 2021: HV MAD POM/POB
- Mid 2022: Patients POM/POB

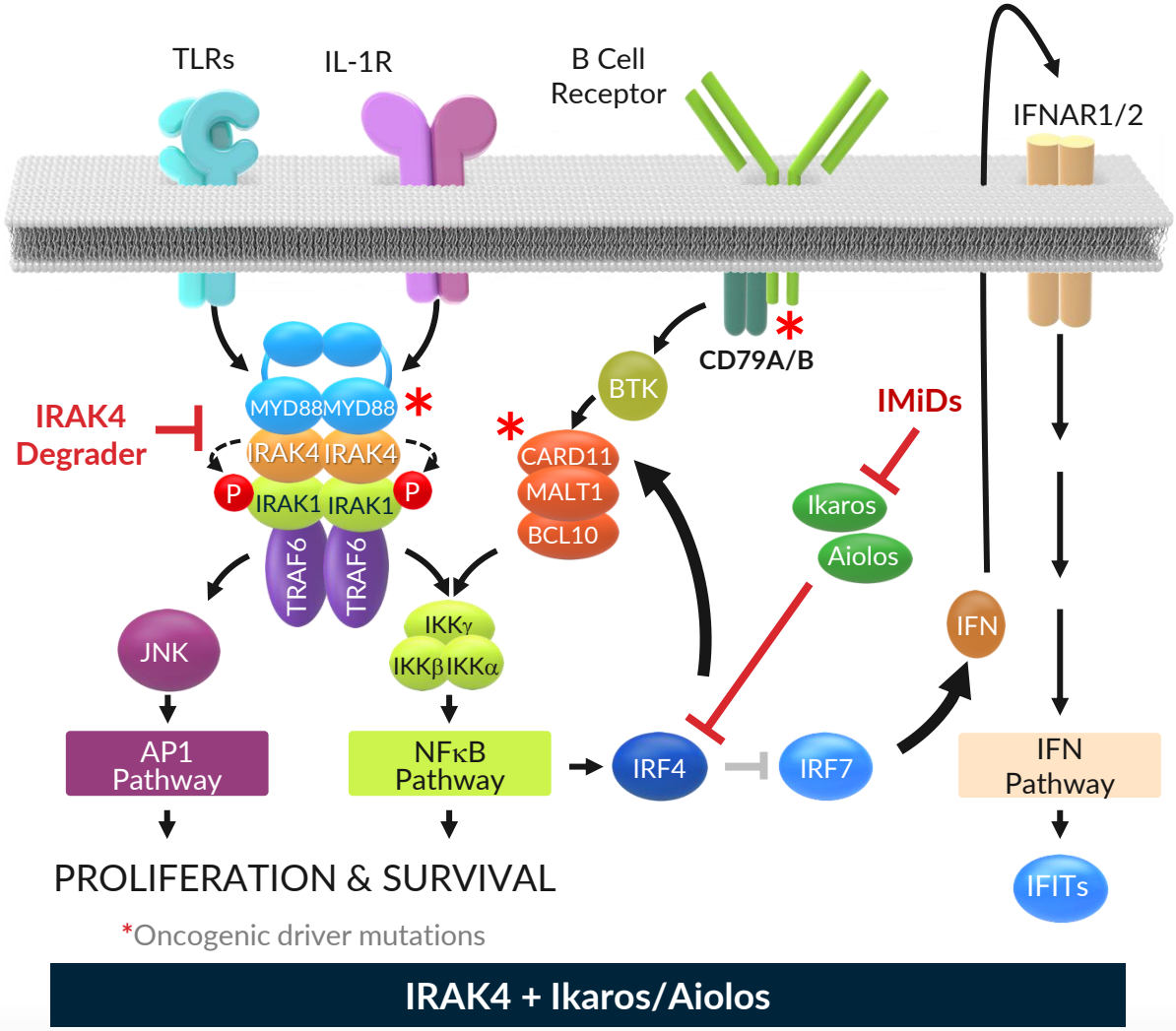
- Healthy volunteer MAD enrollment ongoing
  - Anticipate maximizing **IRAK4 knockdown and impact on downstream biomarkers at substantially lower doses** with daily dosing based on PK and PD and as shown in preclinical models
  - On track to complete by year-end
  - Plan to present safety, PK, and PD data at R&D Day, 12/16/21
  - PD includes: IRAK4 levels in blood and skin, *ex vivo* cytokine stimulation, plasma hsCRP
- Cohort of AD and HS patients (up to 20) to start enrolling in Q1'22
  - Data readout planned for mid-year 2022


IRAKIMiD
KYMERA

IRAKIMiD

A Combo in a Single Molecule

- MYD88 mutation drives differentiation and proliferation in ~25% of diffuse large B cell lymphoma (DLBCL)
- IMiDs downregulate IRF4, increasing IFN signaling and further suppressing NFkB activation and show activity in lymphoma
- Inhibiting both MYD88 and IRF4-dependent NFkB and activating IFN signaling drive cell death in MYD88-mutant lymphomas and leads to full and durable responses *in vivo*
- Combining two therapeutically relevant pathways in a single molecule has the potential to be first single agent targeted therapy agent in lymphoma (MYD88-mut)



Indications/Expected Timeline

MYD88-mutant DLBCL

IND Cleared: 4Q 2021
Current: Ph1
Phase 1 proof-of-mechanism in patients: 2022

Adapted from Yang, et al. (2012) *Cancer Cell*, 6:723-737.

KT-413 Opportunity

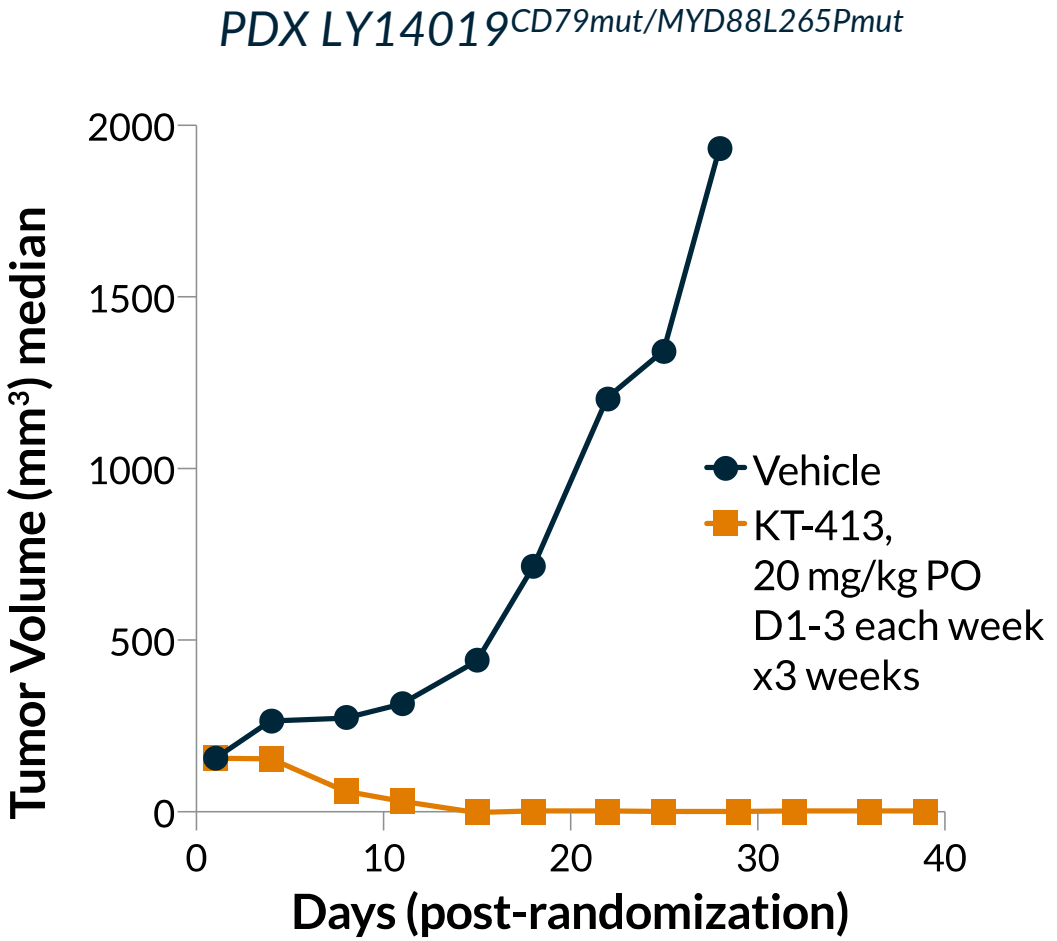
Potential to be First Precision Medicine in DLBCL to Target a Genetically-defined Population (MYD88-mut)

	Patient Impact (U.S.)	
MYD88-mutant DLBCL	~7.0k[1] per year	• MYD88 is mutated in at least 25% of DLBCL patients, the most common subtype of non-Hodgkin's lymphoma[1] • Front-line treatment includes **R-CHOP** (chemo/rituximab) • DLBCL **5-year survival rate is ~64%**, and MYD88 mutations in DLBCL are associated with poorer survival following frontline R-CHOP chemotherapy[3]
Other MYD88-mutant B cell Lymphomas	>1.0k[2] per year	• MYD88 is mutated in approximately 90% of **Waldenström's macroglobulinemia** cases and 70% of primary central nervous system lymphoma[4,5]
Additional Cancers	→	• **IL1R/TLR/NFκB**-driven cancers, AML & MDS subsets with long isoform of IRAK4 (IRAK4L)

1. Lee et al. Sci Rep. 2017; 7: 1785.
2. https://www.lls.org/sites/default/files/file_assets/waldenstrommacroglobulinemia.pdf
3. https://seer.cancer.gov/statfacts/html/dlbcl.html.
4. Varettoni et al. Blood (2013) 121 (13): 2522–2528.
5. Hattori et al. Cancer Sci. 2018 Jan; 109(1): 225–230.

KT-413 Shows Regressions in MYD88^{MT} Patient-Derived Xenograft Models

Model	MYD88	CD79B	TNFAIP3	Other	KT-413 (%TGI)
LY14019	L265P	MT	MT		**100**
LY2264	L265P	MT		IRF4	**100**
LY2298	L265P	MT		BCL2/BCL6	**90**
LY12699	L265P	MT			**87**
LY2345	WT		MT		**70**
LY2301	WT				**30**
LY0257	L265P			BCL2/BCL6/IKZF3	**0**



KT-413 dosed orally shows strong tumor growth inhibition (>85% TGI) in 4/5 MYD88-Mutated DLBCL PDX Models

- Activity is observed regardless of co-mutations that activate NFkB and IRF4 pathways
- The non-responsive MYD88^{MT} model LY0257 harbors a mutation in Aiolos and is reported to be insensitive to lenalidomide
- The functional consequence of Aiolos mutations in IRAKIMiD and IMiD response is being investigated

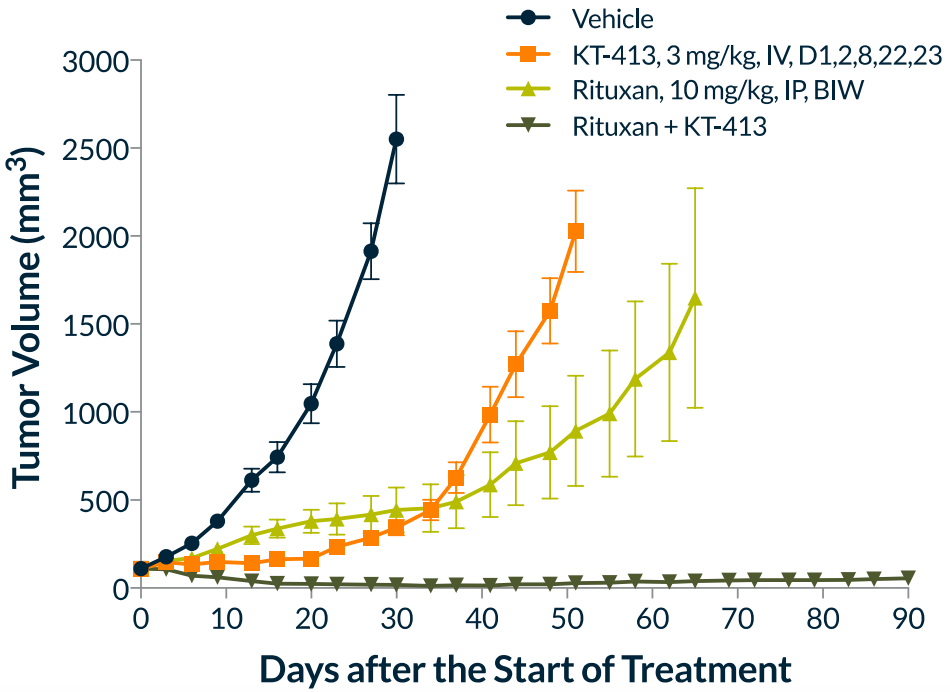
Some level of tumor growth inhibition observed in MYD88-WT PDX

- May be consistent with IMiD activity of KT-413

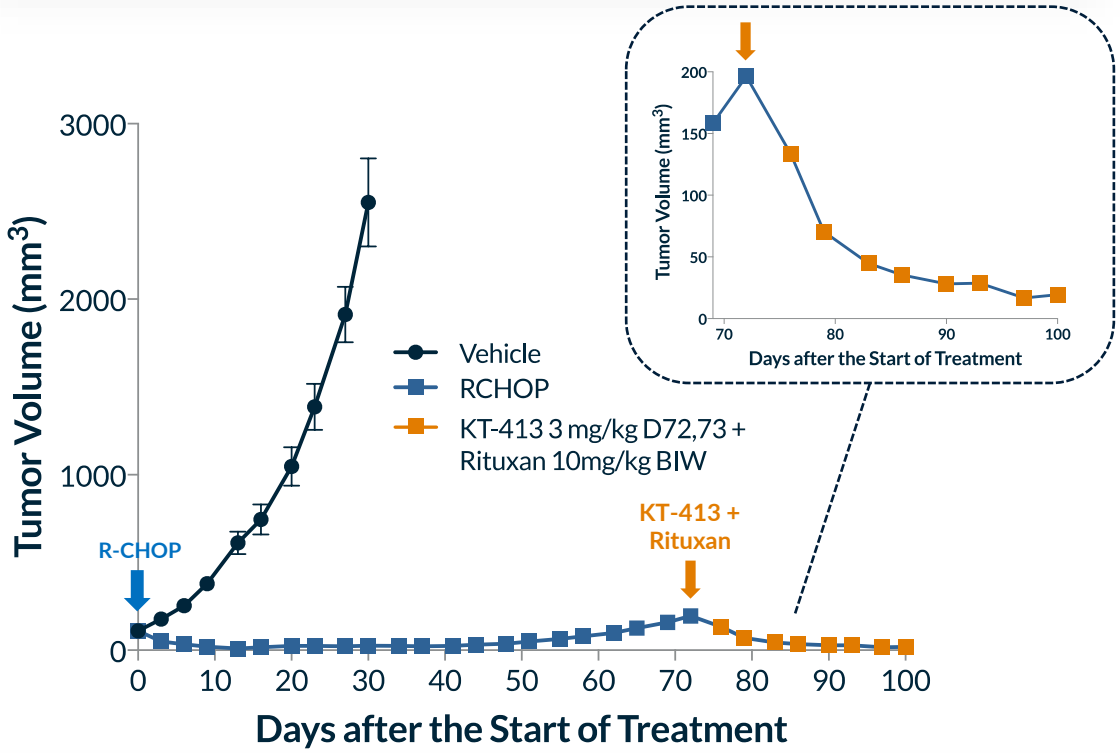
PDX models run at Crown Biosciences

KT-413 has Synergistic Activity in Driving Deep Tumor Regressions in Combination with Other Therapies in Preclinical Models

- KT-413 administered on intermittent schedules demonstrated deep and durable regressions in combination with rituximab in MYD88MT OCI-Ly10 xenografts



- KT-413 + rituximab showed strong tumor regressions in tumors that relapsed following initial R-CHOP treatment



*Determined by Bliss Independence method

KT-413 Phase 1 Trial Design

Multi-Center, Phase 1 Dose Escalation Trial

Two-part Phase 1 Design

Phase 1a (4Q21/1Q22)

- Dose escalation and MTD expansion
- R/R B cell lymphomas, including DLBCL
- Once every 3 weeks dosing
- **POM/POB in 2022**
- **POC in 2H22/1H23**

Phase 1b (2023)

- Expansion cohorts at recommended dose from Phase 1a
- R/R DLBCL: MYD88 mutant and wild-type

Endpoints

Primary
- Safety & tolerability

Secondary
- PK
- Clinical Activity

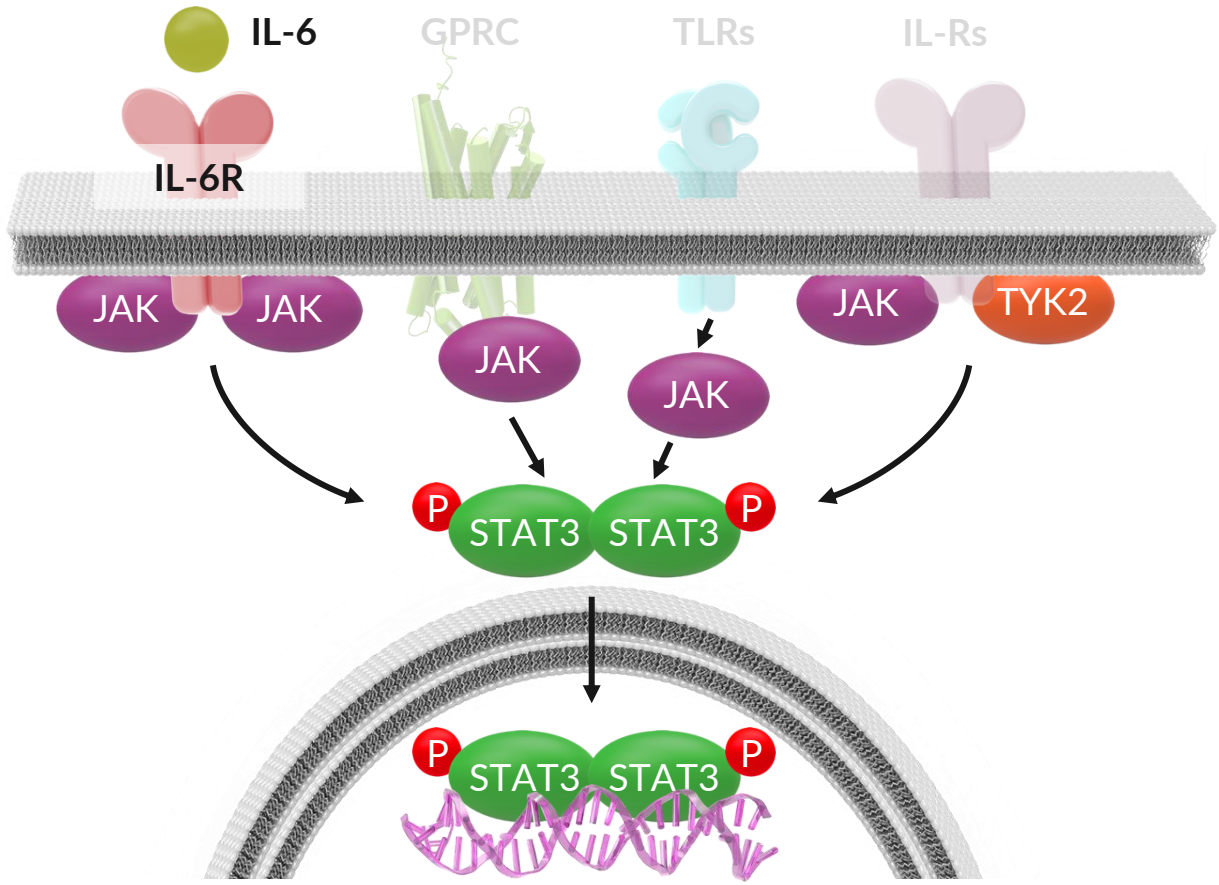
Exploratory
- PD effects including:
  - IRAK4/Ikaros/Aiolos KD in PBMC and tumor
  - Impact on NFkB and IRF4 pathways in tumor
- Relationship between tumor genotype and clinical activity

STAT3

KYMERA

STAT3 Biology and Degrader Rationale

- STAT3 is a traditionally largely undrugged transcription factor activated through cytokine and growth factor receptors via JAKs and non-JAKs mediated mechanisms
- High degree of validation of JAK-STAT pathway in oncology and immuno-oncology supported also by numerous publications
- STAT3 plays a role in tumor biology, evasion of immune surveillance and inflammation/fibrosis
- No known drugs specifically affect STAT3 broadly across all relevant cell types



Indications/Expected Timeline

Hematological Malignancies/Solid Tumors and Autoimmune/Fibrosis

IND Cleared: 4Q 2021
Current: Ph1
Phase 1 proof-of-mechanism in patients: 2022

STAT3 Opportunity in Oncology & Autoimmunity

First-in-class Opportunity to Address STAT3-driven Pathology Across Large and Diverse Indications

Patient Impact (U.S.)

Cancer

~5.0k per year[1]
Peripheral T-cell Lymphoma

~2.0k per year[2]
Cutaneous T-cell Lymphoma

~200.0k per year[3]
NSCLC

I/I Fibrosis

>40.0k[4]
Systemic Sclerosis

>16.0M[5]
Atopic Dermatitis

>40.0k[6]
Idiopathic Pulmonary Fibrosis

Liquid Tumors

Genetically-defined STAT3 mutation and/or hyperactivation
PTCL, CTCL, T-LGL leukemia

STAT3 activation and dependency
DLBCL, AML, multiple myeloma

Solid Tumors

Cell Intrinsic: STAT3 role in EMT/TKI resistance
Combinations in TKI / chemotherapy resistant settings

Cell Extrinsic: STAT3 role in IO
T-cell infiltrated tumors. Combinations with immune-modulators

Autoimmune

STAT3 GOF syndrome
Genetically-defined population characterized by enteropathy, arthritis, dermatitis, lung disease

Immune-inflammatory
Systemic sclerosis, atopic dermatitis, rheumatoid arthritis, Crohn's disease/ulcerative colitis

Fibrosis

Chronic inflammation / fibrosis
Idiopathic pulmonary fibrosis, CKD/renal fibrosis

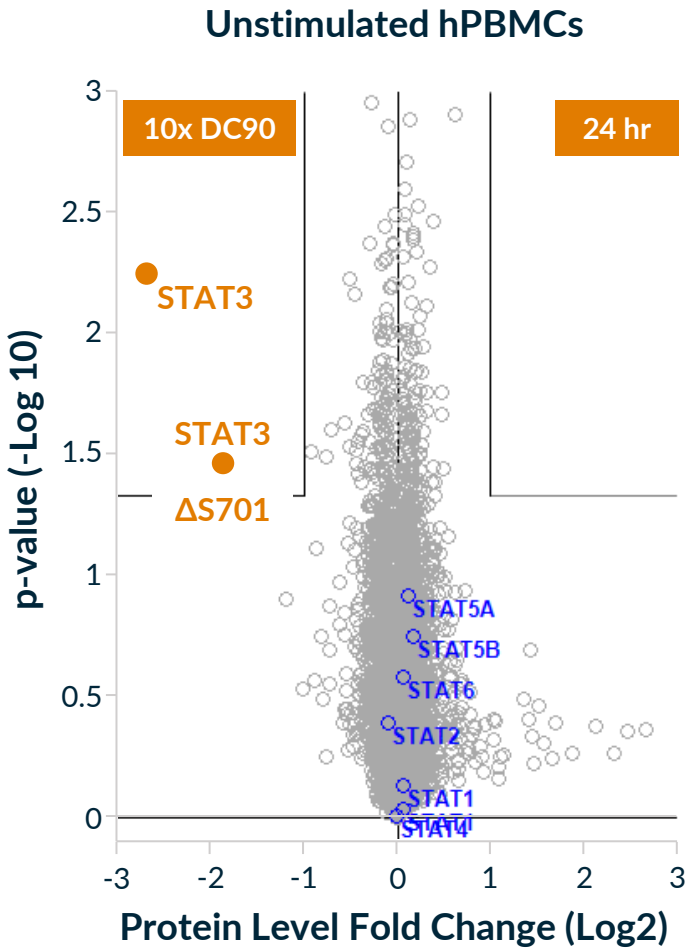
1. Marchi and O'Connor. CA CANCER J CLIN 2020;70:47–70.
2. Criscione and Weinstock. Arch Dermatol. 2007 Jul;143(7):854-9.
3. https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html.
4. Bergamasco et al. Clin Epidemiol. 2019; 11: 257–273.
5. Chiesa Fuxench et al. J Invest Dermatol. 2019 Mar;139(3):583-590.
6. Nalysynk et al. European Respiratory Review. 2012 21: 355-361.

KT-333 Highly Specific Degradation of STAT3

CANCER
- Liquid Tumors
- Solid Tumors

I/I FIBROSIS
- Autoimmune
- Fibrosis

- Deep mass spectrometry-based proteomics to assess STAT3 specificity performed
- hPBMC and tumor cells (SU-DHL-1) treated with KT-333 degrader
- STAT3 was the only protein to be degraded with statistical significance
- Data demonstrate highly selective degradation profile



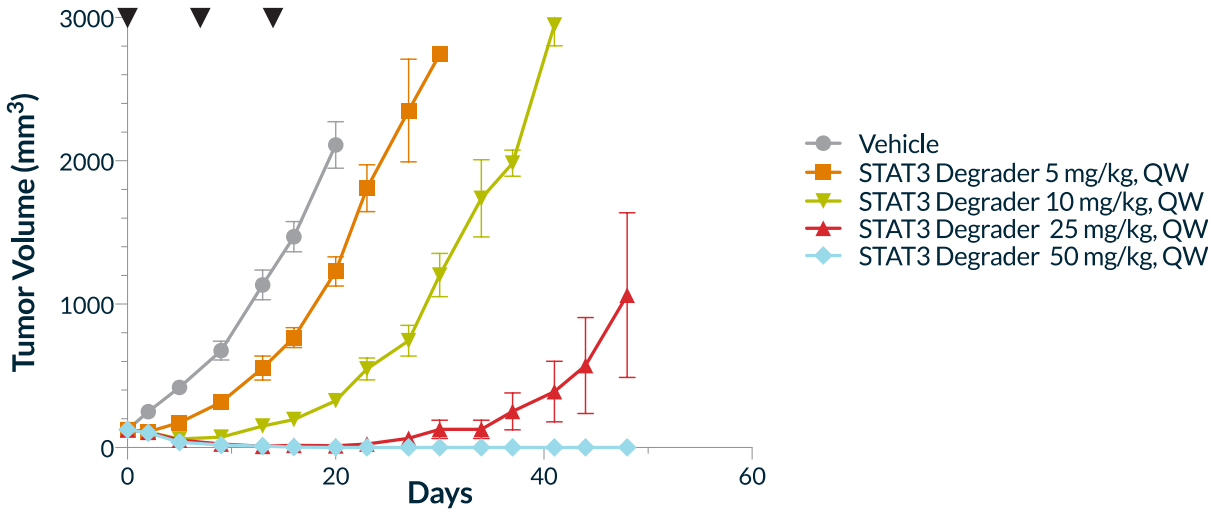
● STAT Family Members: **STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B, STAT6**

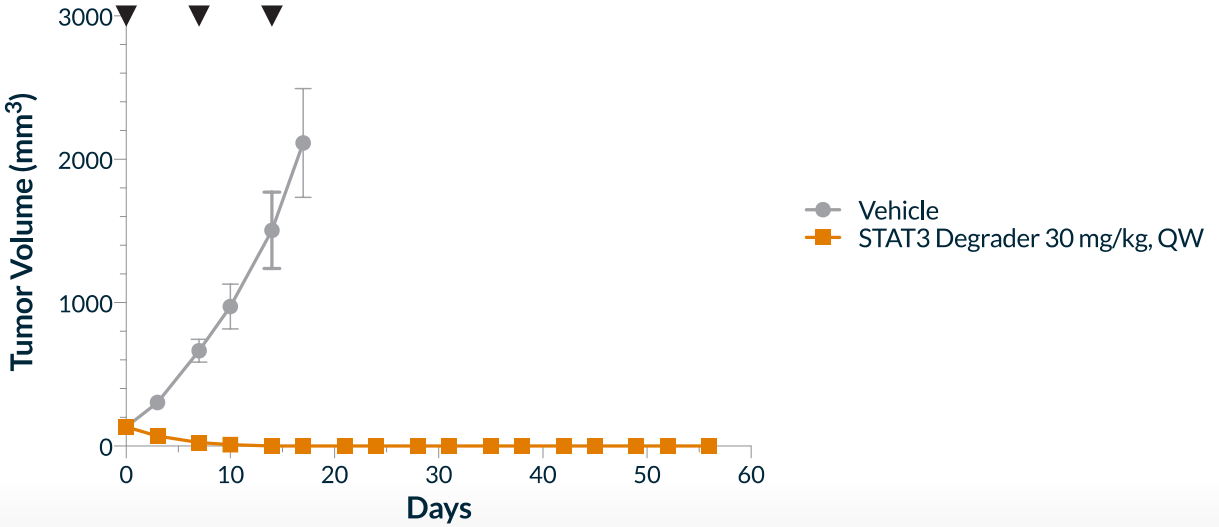
Full and Durable Regressions Across Multiple *in vivo* Preclinical Tumor Models

CANCER
- Liquid Tumors
- Solid Tumors

I/I FIBROSIS
- Autoimmune
- Fibrosis

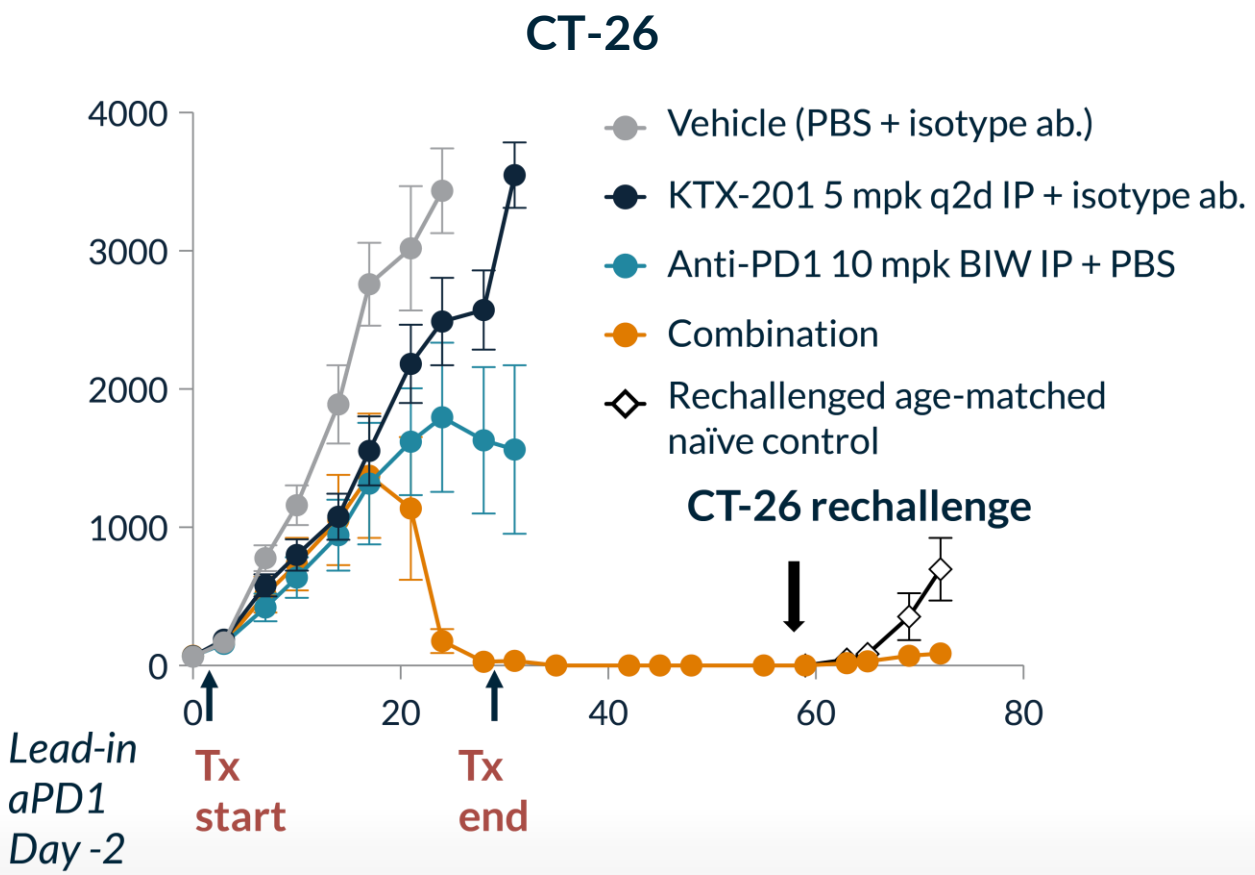
- Mice bearing STAT3-dependent ALK+ ALCL SU-DHL-1 (above) and STAT3-driven ALK+ ALCL xenograft model SUP-M2 (below) tumors dosed with STAT3 degrader
- Dose and degradation dependent tumor growth inhibition observed with once-a-week IV dosing
- 30 mg/kg sufficient to drive full tumor regression that was durable for multiple weeks after the last dose



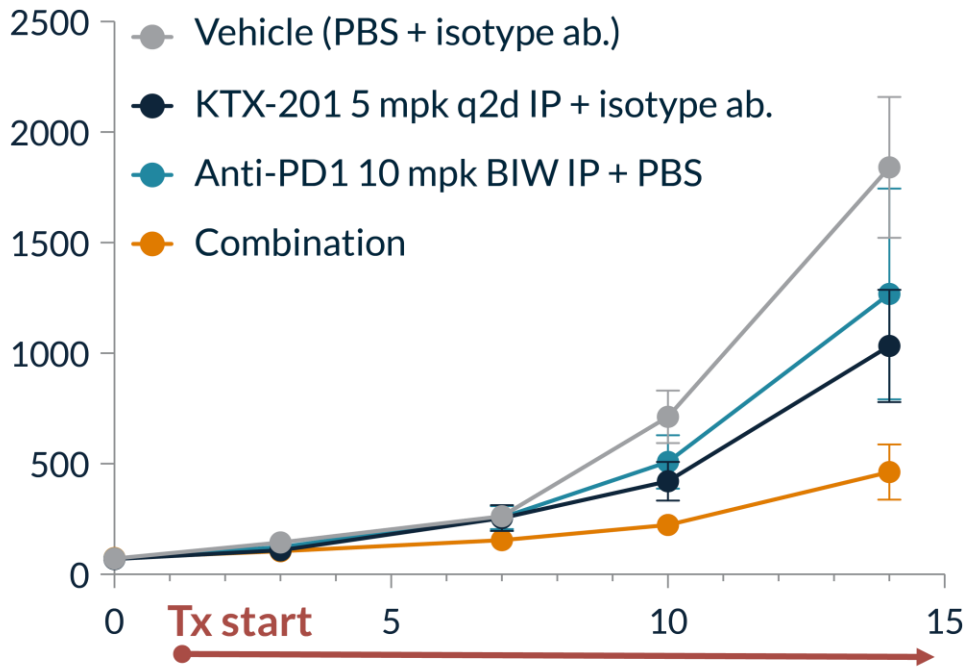


STAT3 Degradation Enhances Anti-PD-1 Responses in Mouse Models of Solid and Hematologic Cancers

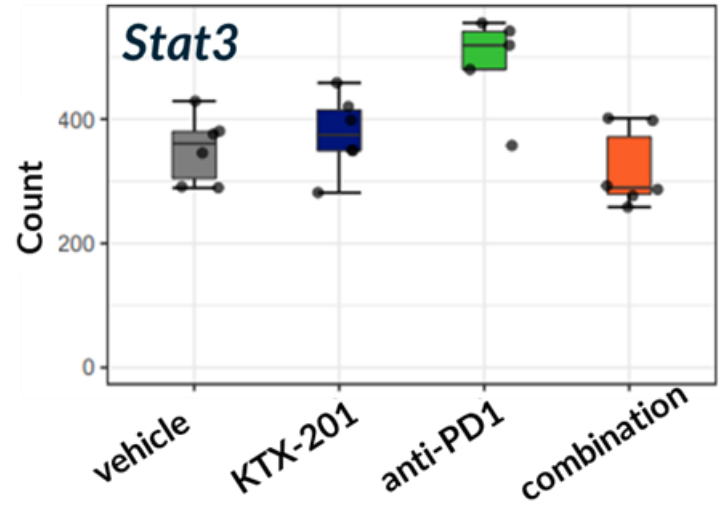
STAT3 degradation synergizes with anti-PD-1 leading to 60% CR and development of long-term immunological memory in CT-26 tumors

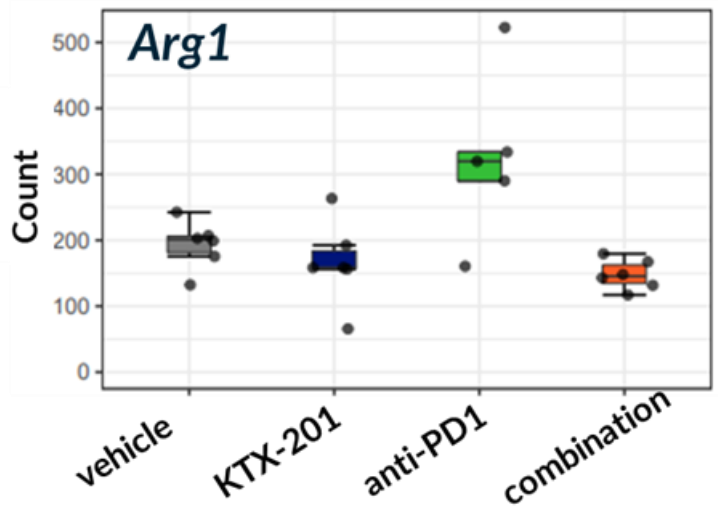


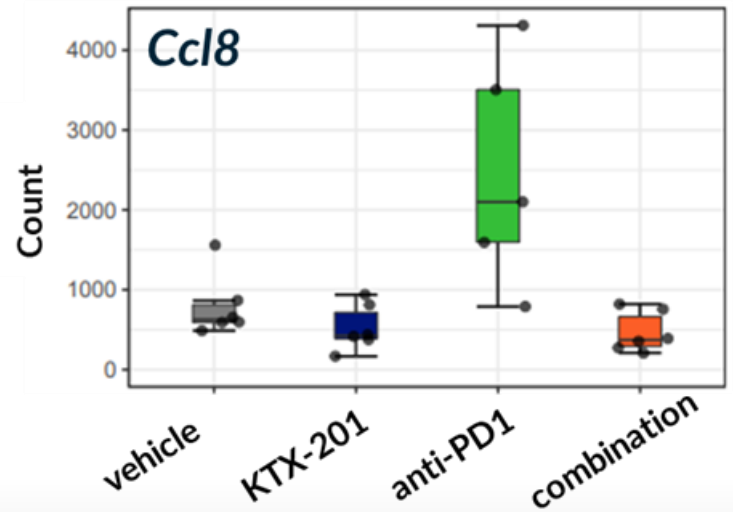
STAT3 Degrader + anti-PD-1 show a combination effect in A20 mouse lymphoma

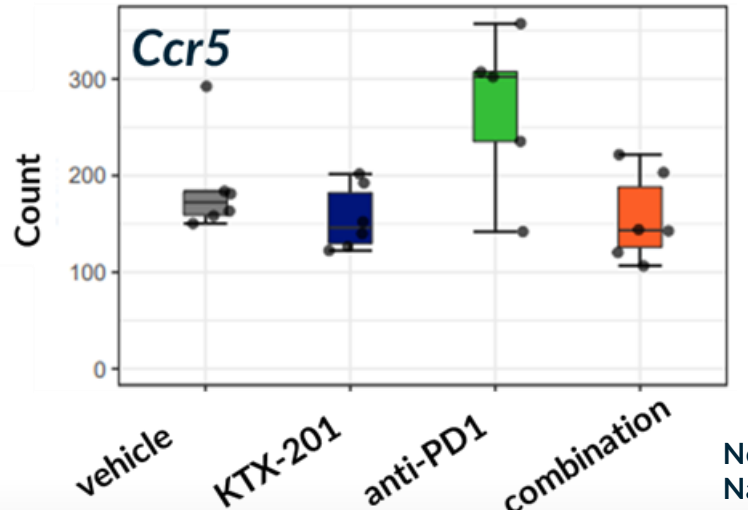


Anti-PD-1 Upregulates STAT3 and Other Immunosuppressive Genes Effect Neutralized when Combined with STAT3 Degrader









Note: Transcriptomic analysis using Nanostring IO 360 n=6/grp; t = Day 11.
KTX-201 = STAT3 Tool Degrader

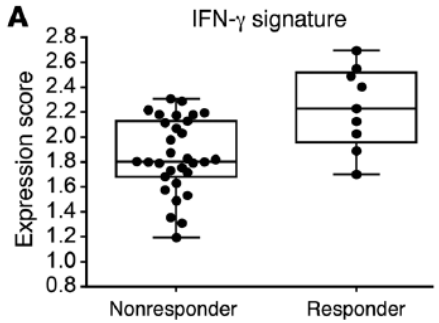
STAT3 Degradation Enriches for an IFNγ-dependent Gene Signature Predictive of Sensitivity to anti-PD-1

IFNγ related signature predicts clinical response to PD-1 blockade

220 patients, 9 cancer types from clinical studies of pembrolizumab

Table 2. IFN-γ and expanded immune gene signatures

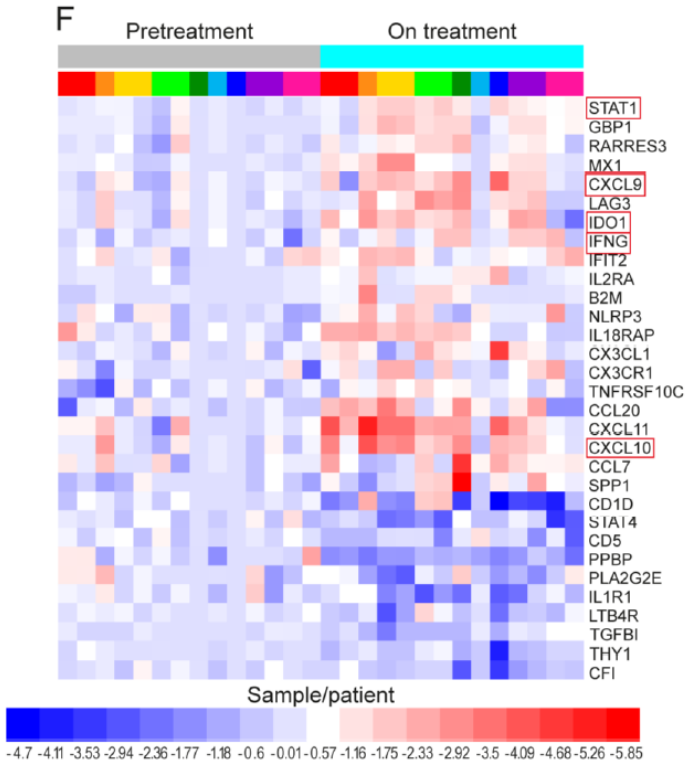
IFN-γ
IDO1
CXCL10
CXCL9
HLA-DRA
STAT1
IFNG



Ayers et. al. JCI 2017

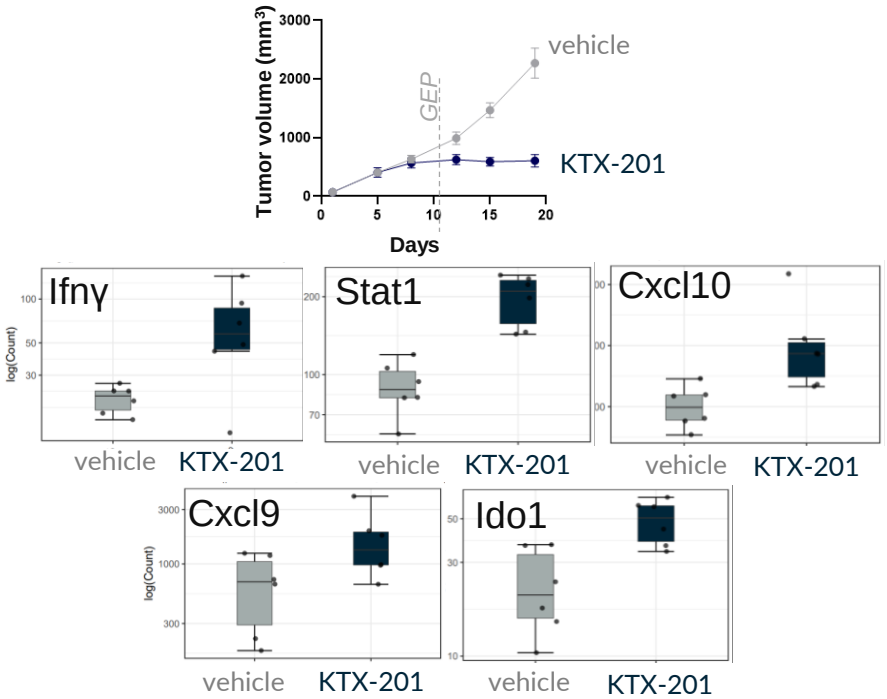
STAT3 ASO treatment leads to upregulation of IFNγ signature in DLBCL patients

(IFNγ, STAT1, CXCL10, CXCL9, IDO1)



Proia et. al. Clin Can Res 2020

STAT3 degrader treated CT-26 tumors show increased expression of Ifnγ signature genes associated with PD-1 sensitivity



On treatment - Day 11; n=6/grp

KT-333 Phase 1 Trial Design

Multi-Center, Phase 1 Dose Escalation Trial

Two-part Phase 1 Design

Phase 1a (4Q21)

- Dose escalation and MTD expansion
- R/R lymphomas and solid tumors
- Weekly dosing
- **POM/POB in 2022**
- **POC in 2H22/1H23**

Phase 1b (2023)

- Expansion cohorts at recommended dose from Phase 1a
- R/R PTCL, CTCL, LGL leukemia, solid tumors

Endpoints

Primary

- Safety & tolerability

Secondary

- PK
- Clinical Activity

Exploratory

- PD effects, including:
  - STAT3 KD and impact on STAT3 pathway activation in PBMC and tumor
  - Impact on circulating inflammatory biomarkers
- Relationship between tumor genotype/STAT3 activation status and clinical activity

2021 and Near-Term Milestones Across Pipeline

● Oncology ● Immunology-Inflammation

Program	Compound	Indication(s)	Expected Upcoming Milestones
IRAK4	KT-474	AD, HS, RA, others	• **Established degrader proof-of-mechanism** in healthy volunteer SAD portion of Phase 1 trial (**June 2021**) ✓ • **Initiate enrollment in MAD** portion of Phase 1 trial (**July 2021**) ✓ • **Established degrader proof-of-biology** in healthy volunteer SAD portion of Phase 1 trial (**Oct 2021**) ✓ • Establish Phase 1 proof-of-biology and Ph2 dose selection in MAD healthy volunteers (**4Q21**) • Establish Phase 1 proof-of-biology in patient cohort (**mid-22**)
IRAKIMiD (IRAK4, Ikaros, Aiolos)	KT-413	$MYD88^{MT}$ DLBCL	• **Presentation of preclinical data updates at AACR, ICML** meetings (**2Q21**) ✓ • **IND clearance to initiate Phase 1** clinical trial in r/r B cell lymphomas (**4Q21**) ✓ • Present additional KT-413 preclinical data and potential expansion strategies (**4Q21**) • Establish Phase 1 proof-of-mechanism and biology in patients (**2022**)
STAT3	KT-333	Liquid & Solid Tumors	• **Nominated development candidate** for liquid & solid tumor indications (**1Q21**) ✓ • **IND cleared to initiate Phase 1** clinical trial in liquid and solid tumors (**4Q21**) ✓ • Present additional preclinical data in liquid & solid tumor indications (**2H21**) • Establish Phase 1 proof-of-mechanism and biology in patients (**2022**)

R&D Day – Dec 16th, 2021

- **Release KT-474 MAD data**: degradation in blood/skin, disease biomarkers, safety
- **New programs in Development**: pathway, target, data, clinical/commercial opportunities
- **Platform advancements**: new data, new investments and opportunities
- **Kymera 2026** – vision, goals, plans

Appendix

KYMERA

What We Are Building

Vision

A fully integrated **degrader medicines company** that discovers, develops, and commercializes transformative medicines while leading the evolution of targeted protein degradation (TPD)

Opportunity

- Potential to **expand the druggable proteome dramatically**

Platform

- Advancing **TPD beyond current opportunities**

Strategy

- Focusing on undrugged targets and clinical indications with **high unmet medical need and franchise potential**

Team

- Driven by a **culture of scientific innovation**

Strategic Partnerships to Accelerate Growth

Supports Discovery, Development, and Commercialization Within and Outside of Core Therapeutic Areas

Strategic Collaborators

SANOFI

- Established July 2020; **$150M** upfront; **>$2B** of potential milestones, plus tiered royalties
- Focused on **IRAK4 in I/I** + 2nd program; KYMR advances IRAK4 through Ph 1; Sanofi Ph 2 and beyond
- KYMR retains U.S. co-dev and co-co opt-in rights, and rights to IRAK4 in oncology

VERTEX

- Established May 2019; **$70M** total upfront; **>$1B** of potential milestones, plus tiered royalties
- **6 targets** in 5 disease areas
- Outside of Kymera's core focus areas in oncology and immune-inflammatory

gsk

- Established April 2018
- Gained access to GSK's **DEL capabilities** to screen for ligands to targets and E3 ligases

LEUKEMIA & LYMPHOMA SOCIETY®

- Blood-based cancers
- Leveraging patient network and access

Academic Collaborators

COLUMBIA UNIVERSITY

The Rockefeller University 1901

UCSF

Yale

UNIVERSITY OF CAMBRIDGE

NATIONAL INSTITUTES OF HEALTH

MAYO CLINIC

Pegasus™ Platform and R&D Approach

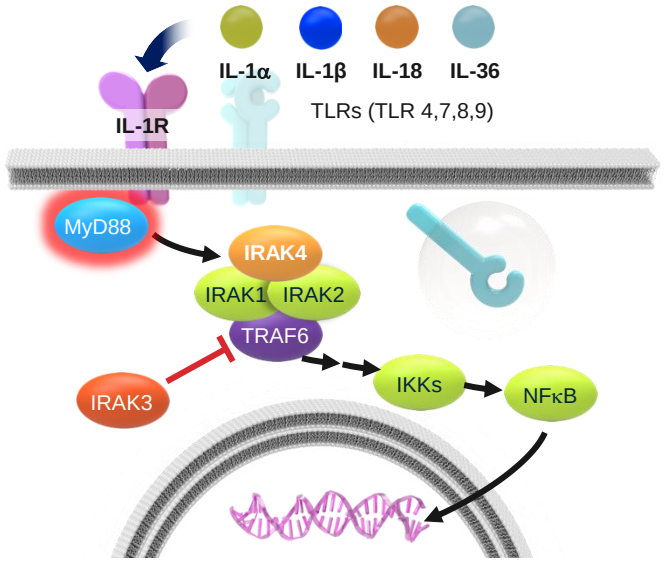
KYMERA

Kymera Drug Development Principles

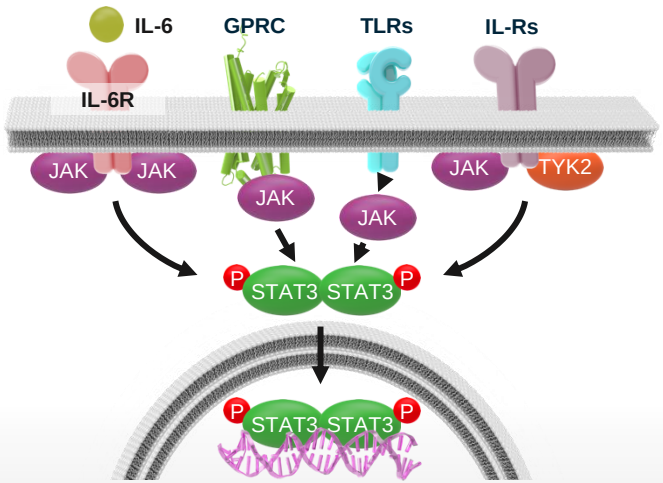
Initial Focus on Pathways that have Been Clinically and Commercially Validated with Undrugged Nodes

- **Unmet Medical Need**
- **Validated Biology**
- **Undrugged Node**
- **Precision Medicine Approach**

IL-1R/TLR Pathway



JAK-STAT Pathway



Clinical Pathway Validation

IL1-Rα/IL-1β : Rheumatologic Diseases
IL-1α: Atopic Dermatitis
IL-1β: CANTOS Data, Atherosclerosis, Lung Cancer
IL-18: Macrophage Activation Syndrome
IL-36: Generalized Pustular Psoriasis
IRAK4 SMI: Rheumatoid Arthritis

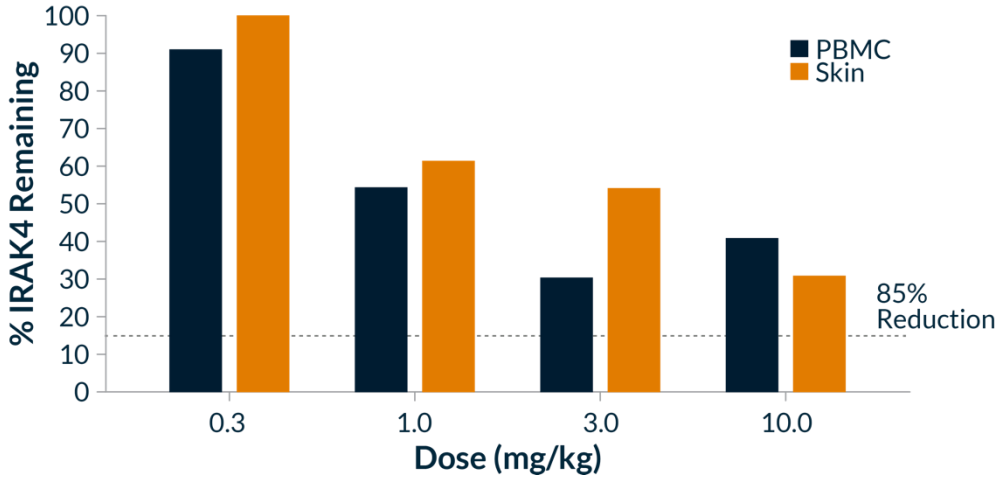
IL-6R: Rheumatoid Arthritis
IL-6: Multicentric Castleman's Disease
JAK1/2: Myelofibrosis
JAK3: Alopecia Areata
TYK2: Autoimmune Diseases
STAT3 ASO: AZD9150 in Oncology

IRAK4

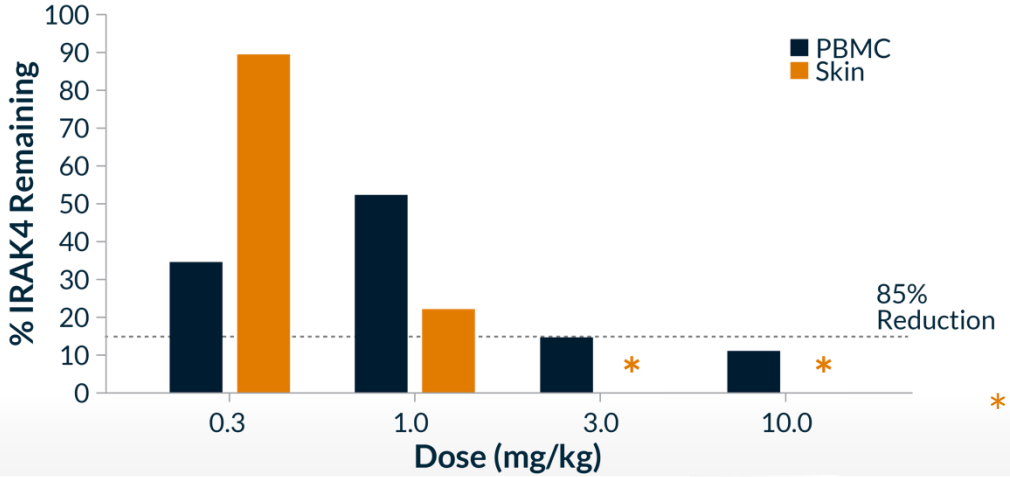
KYMERA

KT-474 Multi-dosing (Daily x 7 Days) Maximizes IRAK4 Degradation at Lower Doses in Dogs

IRAK4 Knockdown 24h after Day 1 Dose



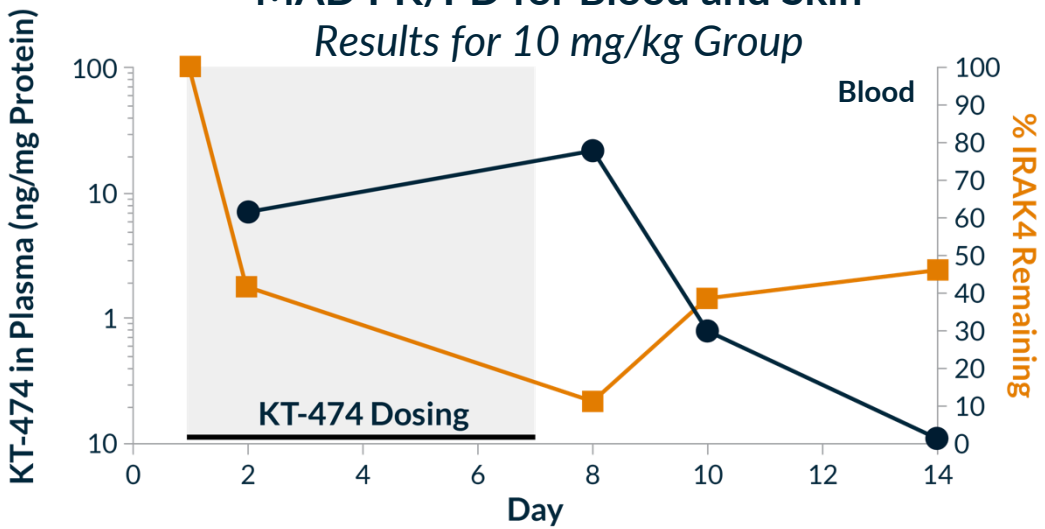
IRAK4 Knockdown 24h after Day 7 Dose

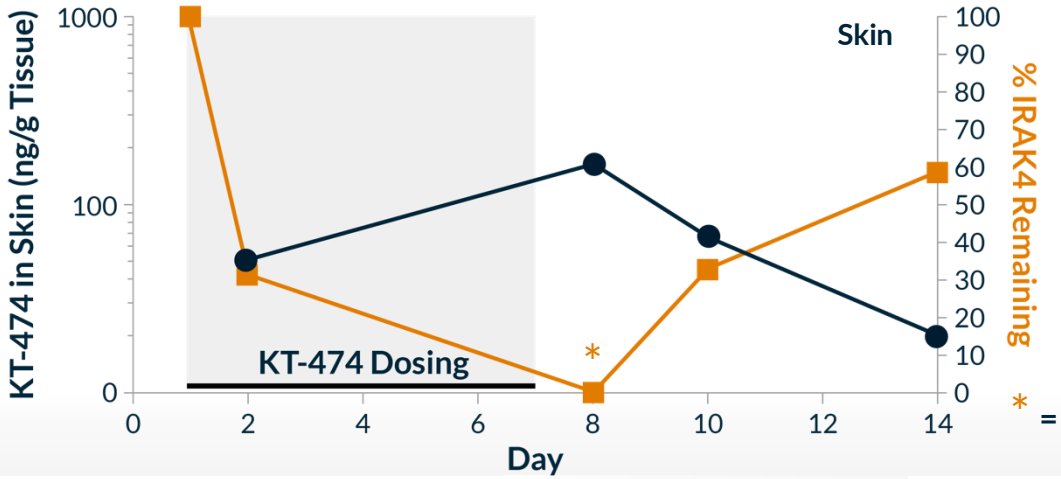


* = BLQ

MAD PK/PD for Blood and Skin

Results for 10 mg/kg Group

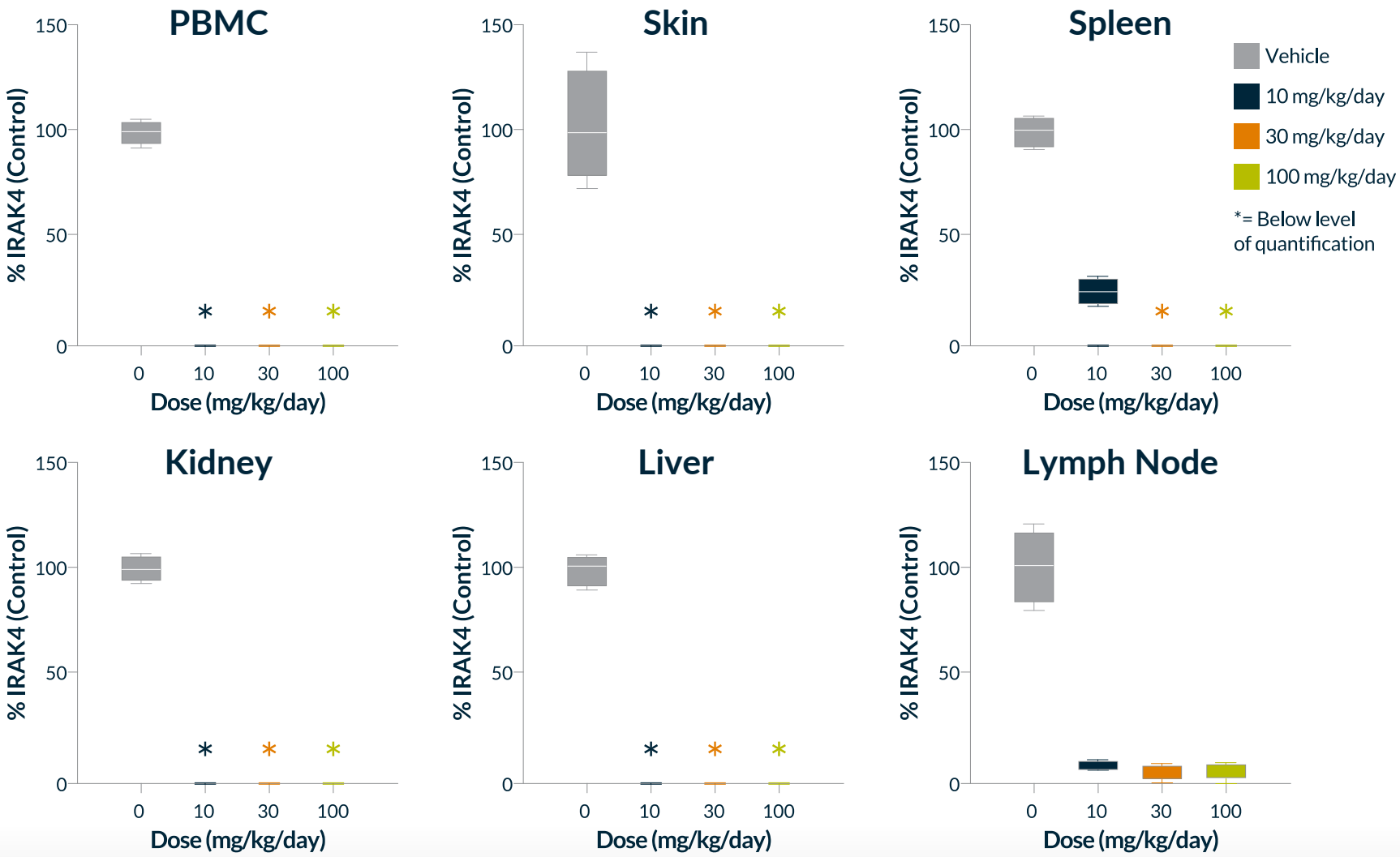




* = BLQ

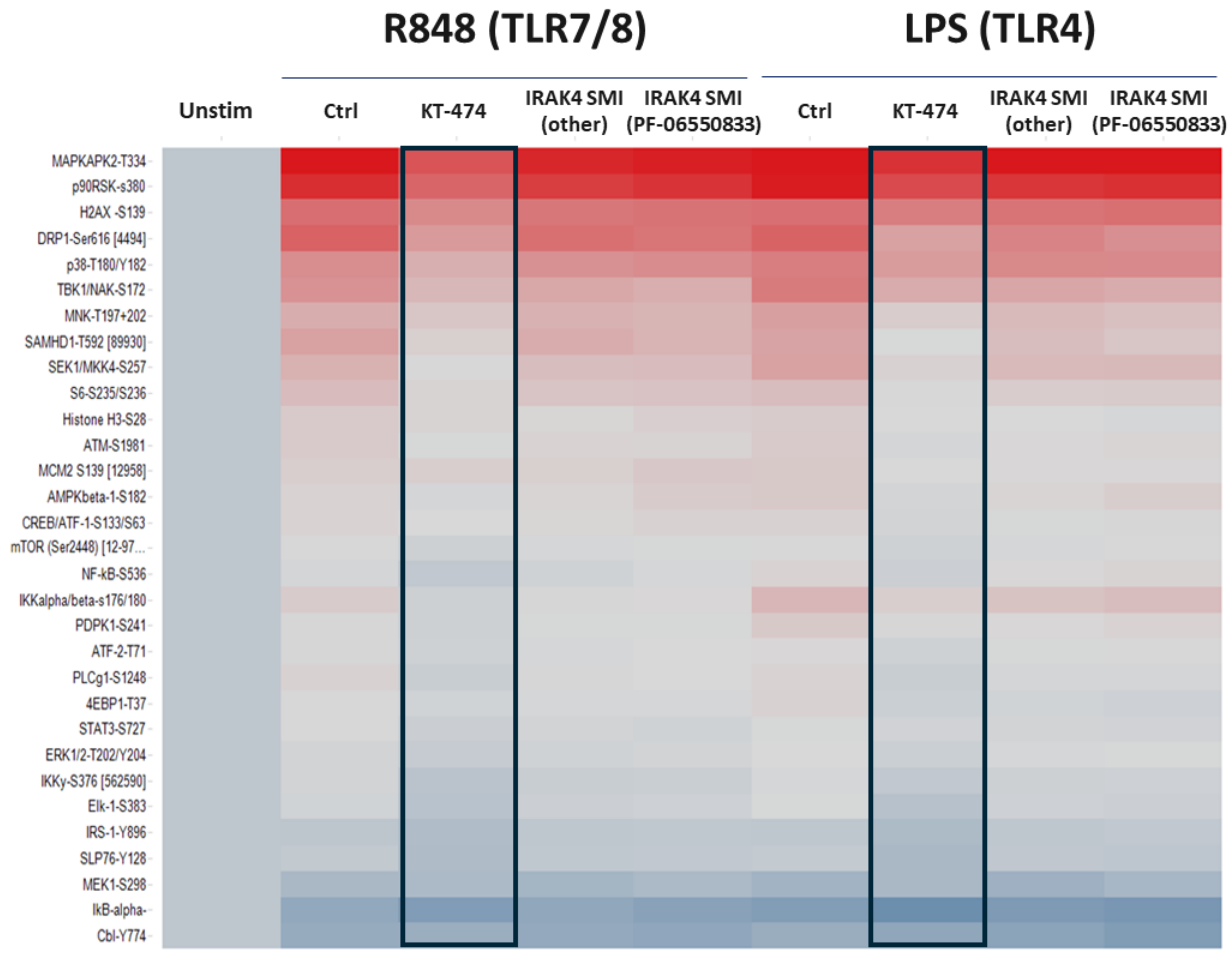
KT-474: Near Complete Systemic IRAK4 Degradation is Well Tolerated in Preclinical Non-rodent Model

- Orally-administered KT-474 evaluated in a 14-day non-GLP tox and PKPD study in rodent and non-rodents (shown).
- Almost complete knockdown demonstrated across multiple tissues at multiple doses
- Compound well-tolerated at all doses up to 600 mg/kg for rodents and 100 mg/kg for non-rodents



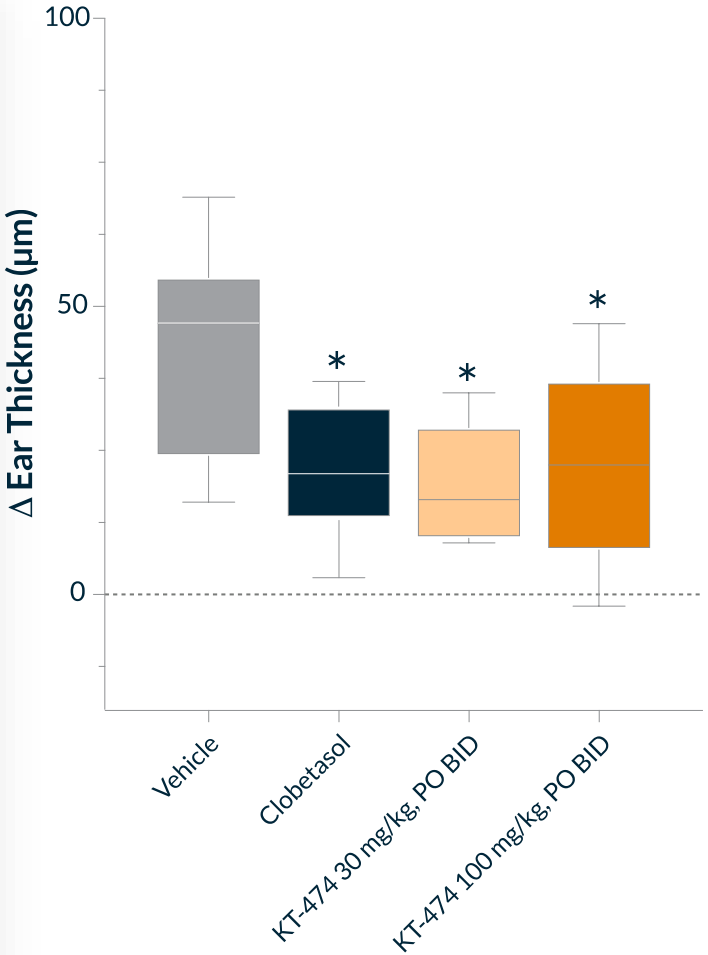
IRAK4 Degradation Superior to Kinase Inhibition in Intracellular Signaling

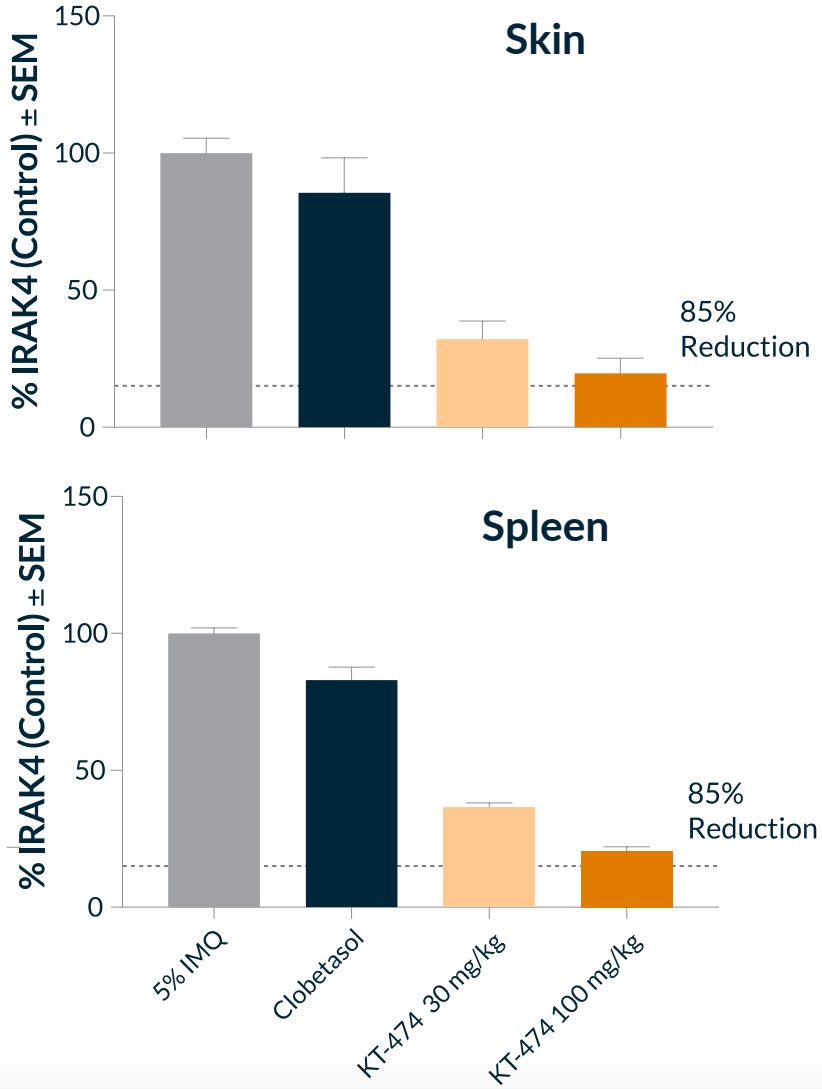
- Phosphorylation events upon TLR activations monitored using flow cytometry
- KT-474 inhibited pro-inflammatory phosphorylation events in a superior manner to small-molecule inhibitors including clinically active PF-compound



85% IRAK4 Degradation Sufficient for Maximal *In Vivo* Efficacy in Preclinical Models

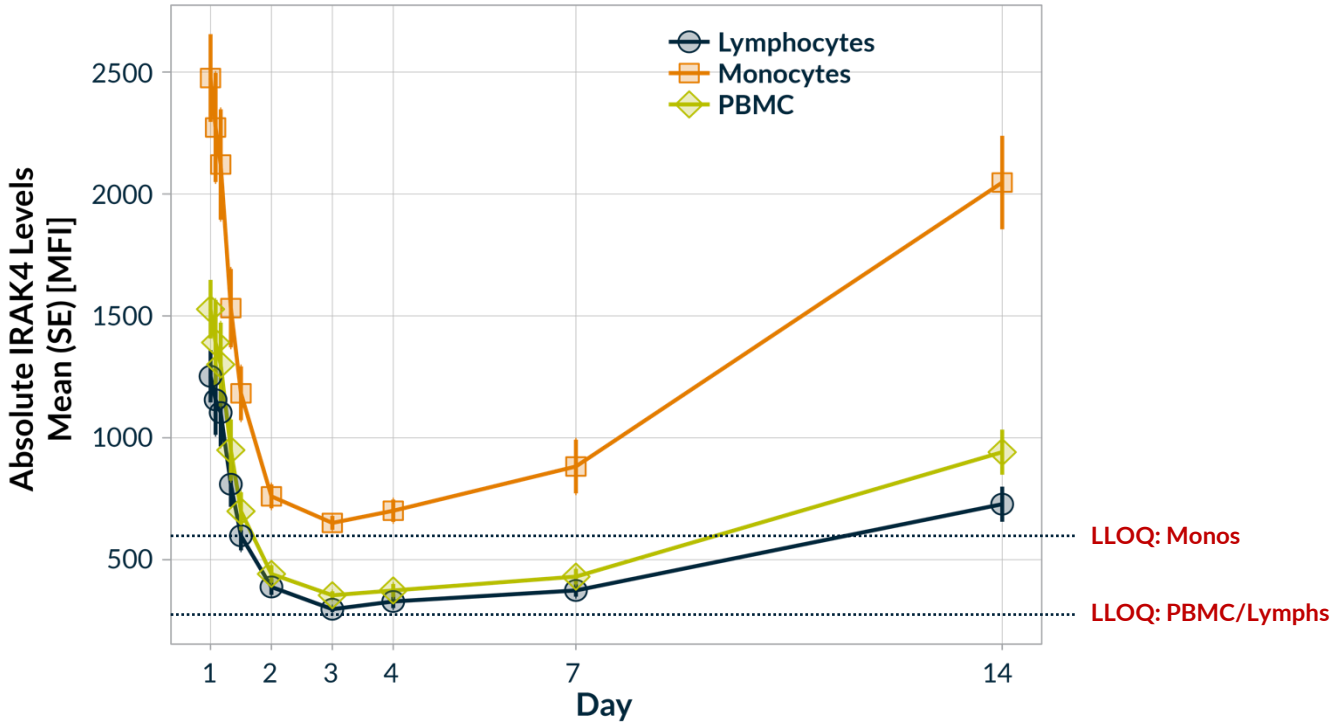
- Ability to inhibit topical skin thickening induced by imiquimod was measured in a mouse model of psoriasis
- Orally dosed KT-474 inhibited thickening, a reflection of local and systemic inflammation, comparable to a topic corticosteroid after 2 or 4 days of dosing
- Full efficacy at doses achieving at 65-80% IRAK4 reduction in skin and spleen. In other models KT-474 has demonstrated full efficacy with 85% degradation



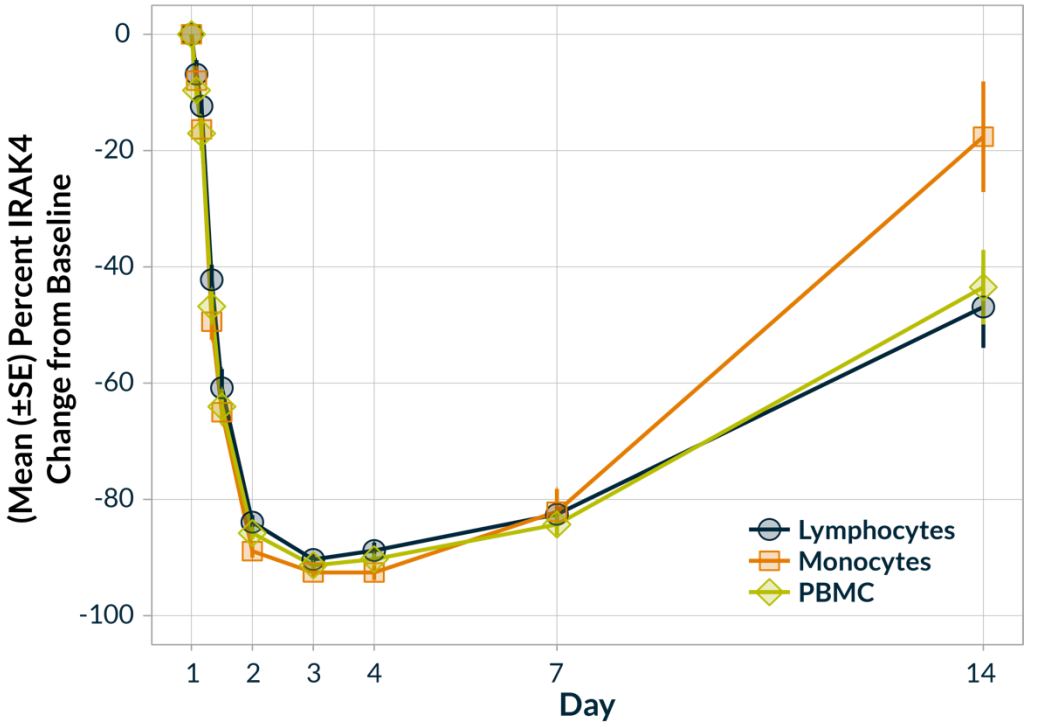


Robust IRAK4 Degradation Observed in Lymphocytes and Monocytes: Flow Cytometry Results at SAD 7

Absolute IRAK4 Levels

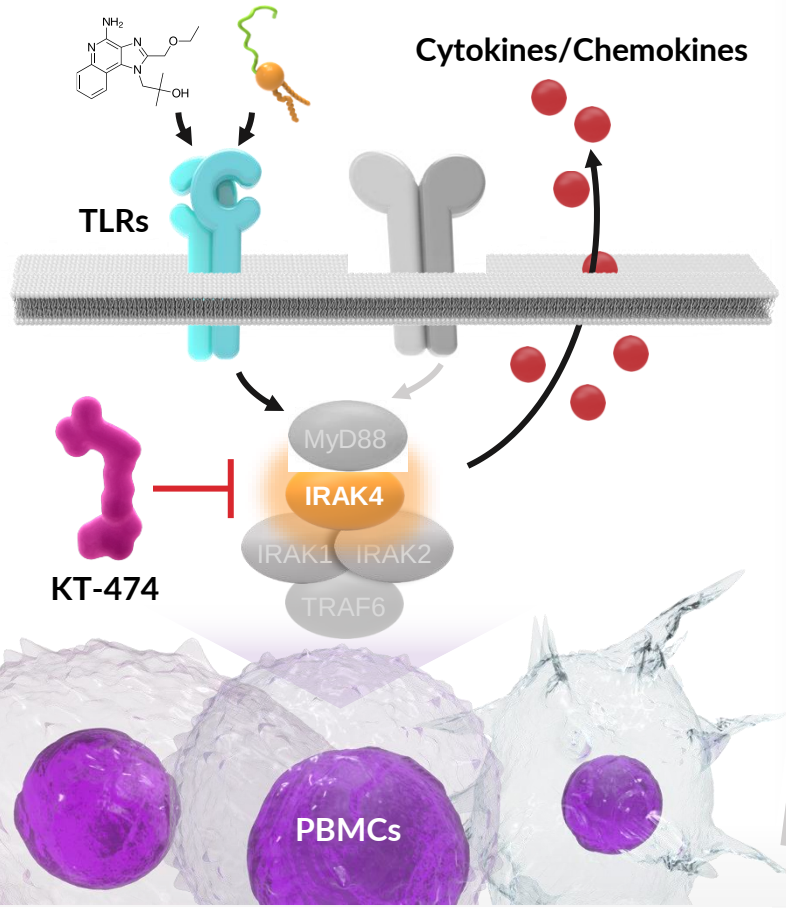


Mean % Reduction of IRAK4

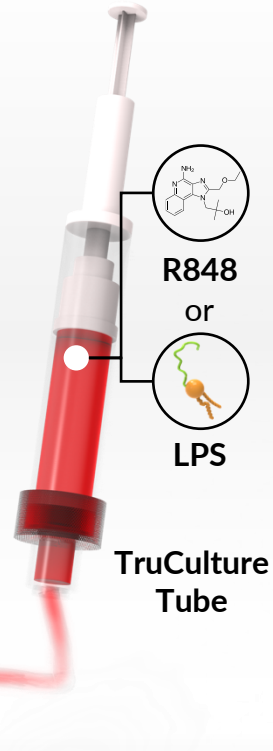


Ex Vivo Cytokine Stimulation: Methodology in KT-474 Phase 1 Trial

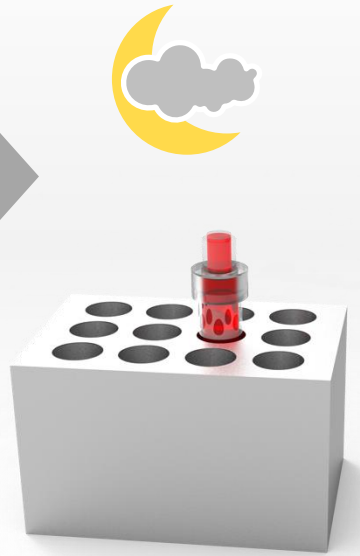
Impact of KT-474 on TLR-stimulated Cytokine/Chemokine Production



1 Blood Draw Pre-/Post-Dose



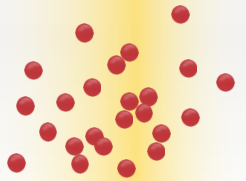
2 Overnight Incubation (37°)

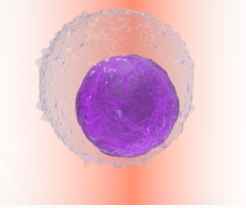


3 Plasma Isolation

4 Cytokine/Chemokine Measurement

TNF-α, IFN-γ, IL-1β, IL-6, IL-8, IL-10, IL-12, IL-17, IL-23





IRAK4 Non-Interventional Study

KYMERA

Non-interventional Study in HS and AD Patients

Designed to Characterize IRAK4 Expression and its Relationship to Inflammatory Biomarkers

Study Design

Patients Enrolled	• 30 HS: 9 mild, 10 moderate, 11 severe • 10 AD: 8 mild, 1 moderate, 1 severe
Inclusion Criteria	• Age 18 or older • Active Hidradenitis Suppurativa (HS) or Atopic Dermatitis (AD) • Mild, moderate, and severe HS (IHS4 score) or AD (EASI score)
Exclusion Criteria	• Patients currently on a biologic or other immunosuppressive treatment for HS or AD • Use of biologic treatment for HS or AD within 3 months or 5 half-lives, whichever is longer • Use of non-biologic immunosuppressive treatment in last 4 weeks
Biomarker Endpoints	• Targeted MS of IRAK4 in skin biopsies • IRAK4 immunofluorescence in skin biopsies • Proinflammatory gene transcripts in skin biopsies • Flow cytometry for IRAK4 in ex vivo treated whole blood • Cytokines from *ex vivo* treated whole blood • Plasma cytokines and acute phase reactants
Reporting Status	• Interim data on IRAK4 expression in HS skin and blood presented in October 2020 at SHSA Meeting • **Updated data presented in May 2021 at SID Meeting on full HS skin dataset for IRAK4 protein and proinflammatory gene transcripts as well as healthy skin and monocyte controls**

Non-interventional Study Methods

HS Skin Biopsies (N=30)

Lesion (L), Peri-lesion (PL), Non-lesion (NL)

IRAK4
Immunofluorescence (IF)
Localization/ Semi-quant

1. Expression in L vs PL vs NL
2. Expression by disease severity
3. Expression in Epidermis vs Dermis

IRAK4
Mass Spectrometry (MS)
Whole Tissue/Quantitative

1. Expression in L vs PL vs NL
2. Expression by disease severity

NanoString
Gene Expression Profiling (GEP)
Whole Tissue

1. Significantly elevated genes in L vs NL
2. Spearman correlation of elevated genes with IRAK4 protein levels by MS and IF

Control Methods

Healthy Subject Skin Biopsies (N=10)

IRAK4
Immunofluorescence (IF)

1. Expression in Healthy vs HS
2. Expression in Epidermis vs Dermis

IRAK4
Mass Spectrometry (MS)

1. Expression in Healthy vs HS

NanoString
Gene Expression Profiling (GEP)

1. Significantly elevated genes in HS vs Healthy
2. Spearman correlation of elevated genes with IRAK4 protein levels by MS and IF

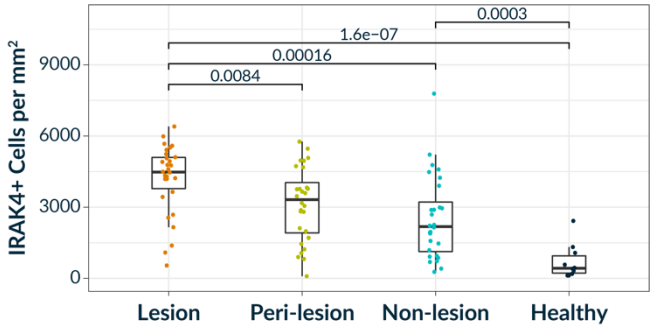
Ex-vivo R848-Stimulated Monocyte Methods

1. Mechanistic study designed to evaluate impact of IRAK4 degradation on response of healthy monocytes to TLR7/8 agonist R848
2. Monocytes isolated from blood of healthy donors (N=3), treated overnight with 500nM of IRAK4 degrader KT-474, and then stimulated with R848
3. For RNA-seq, cells were collected at 2 hours following stimulation
4. Analysis of KT-474 effect on R848 upregulation of subset of genes overexpressed in HS skin lesions that correlate with IRAK4 protein levels

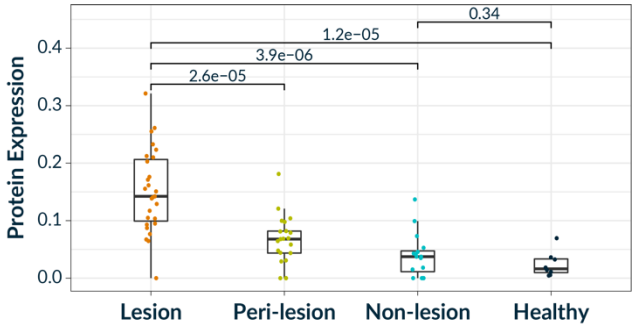
IRAK4 Protein Expression in Autoimmune Diseases: Upregulation in Skin of HS Patients Compared to Healthy Subjects

IRAK4 protein levels overexpressed in HS patient skin lesions

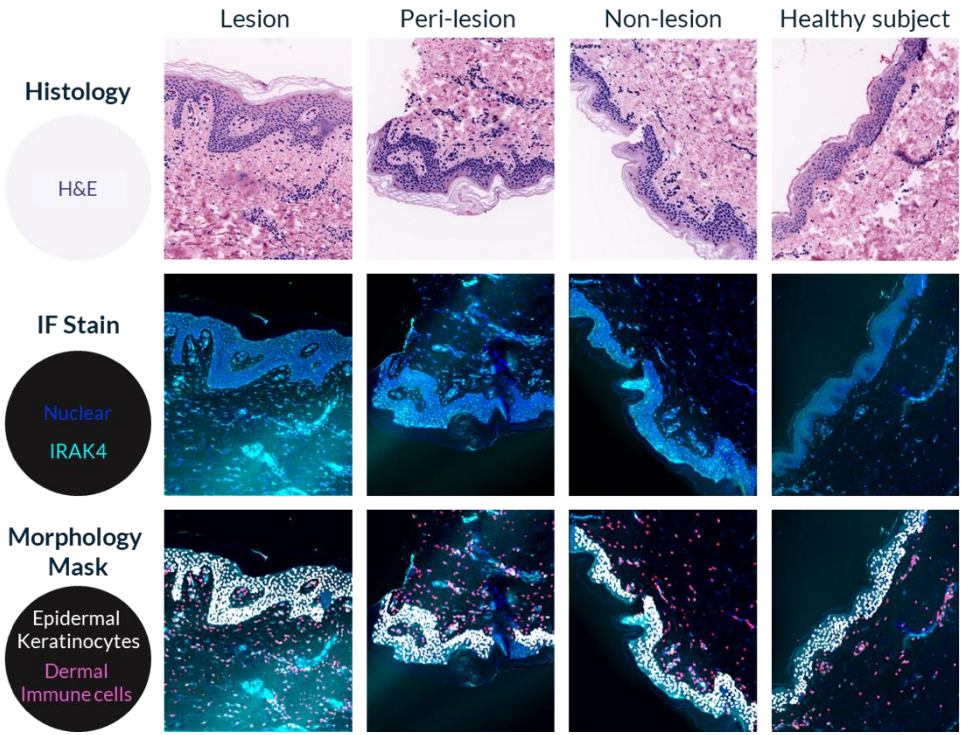
Immunofluorescence (IF)



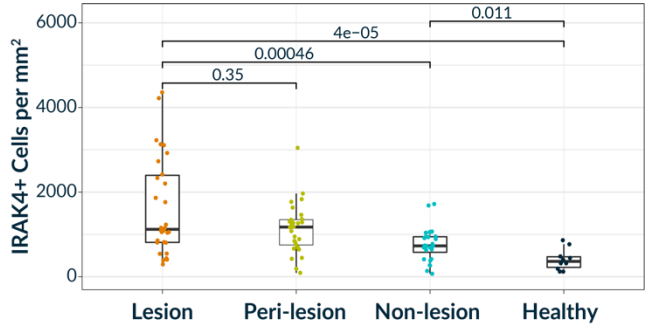
Mass Spectrometry (MS)



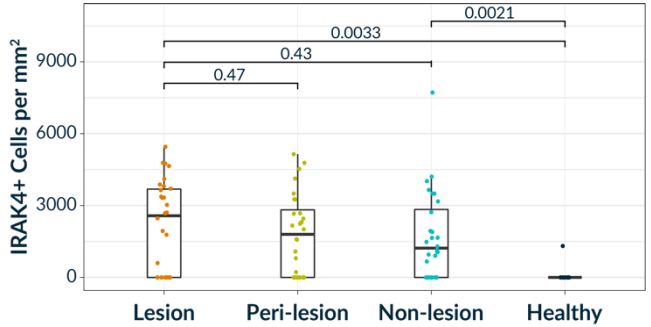
IRAK4 expression is upregulated in dermis and epidermis of HS patients relative to healthy subject skin



Dermal Immune Cells

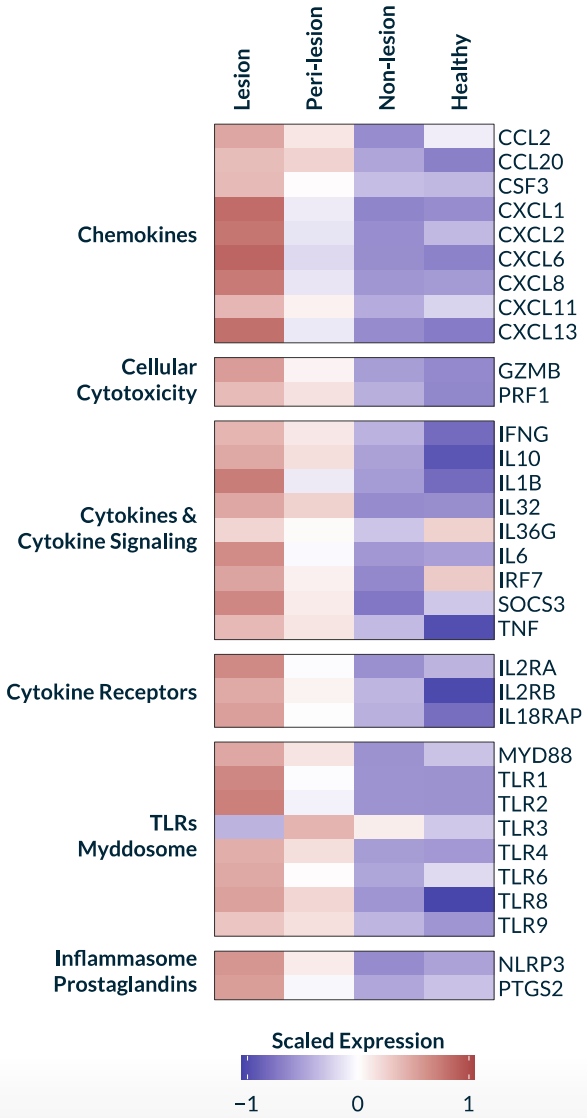


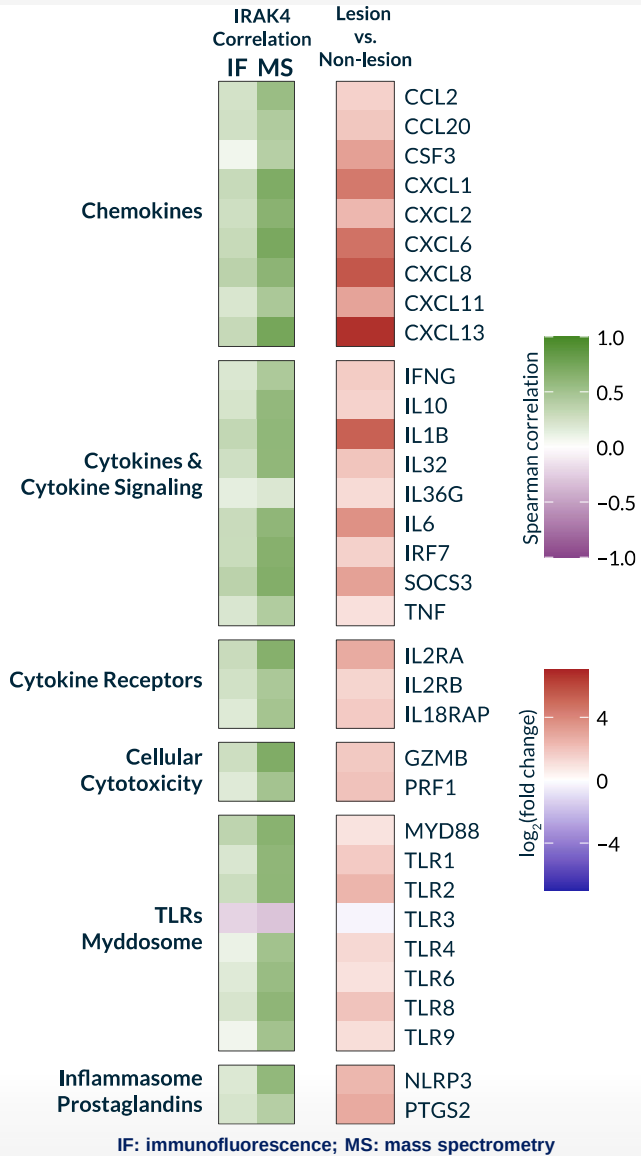
Epidermal Keratinocytes



Alavi et al., Society for Investigative Dermatology Annual Meeting, 2021

Multiple Proinflammatory Transcripts Are Upregulated and Correlate with IRAK4 Protein Levels in HS Skin Lesions

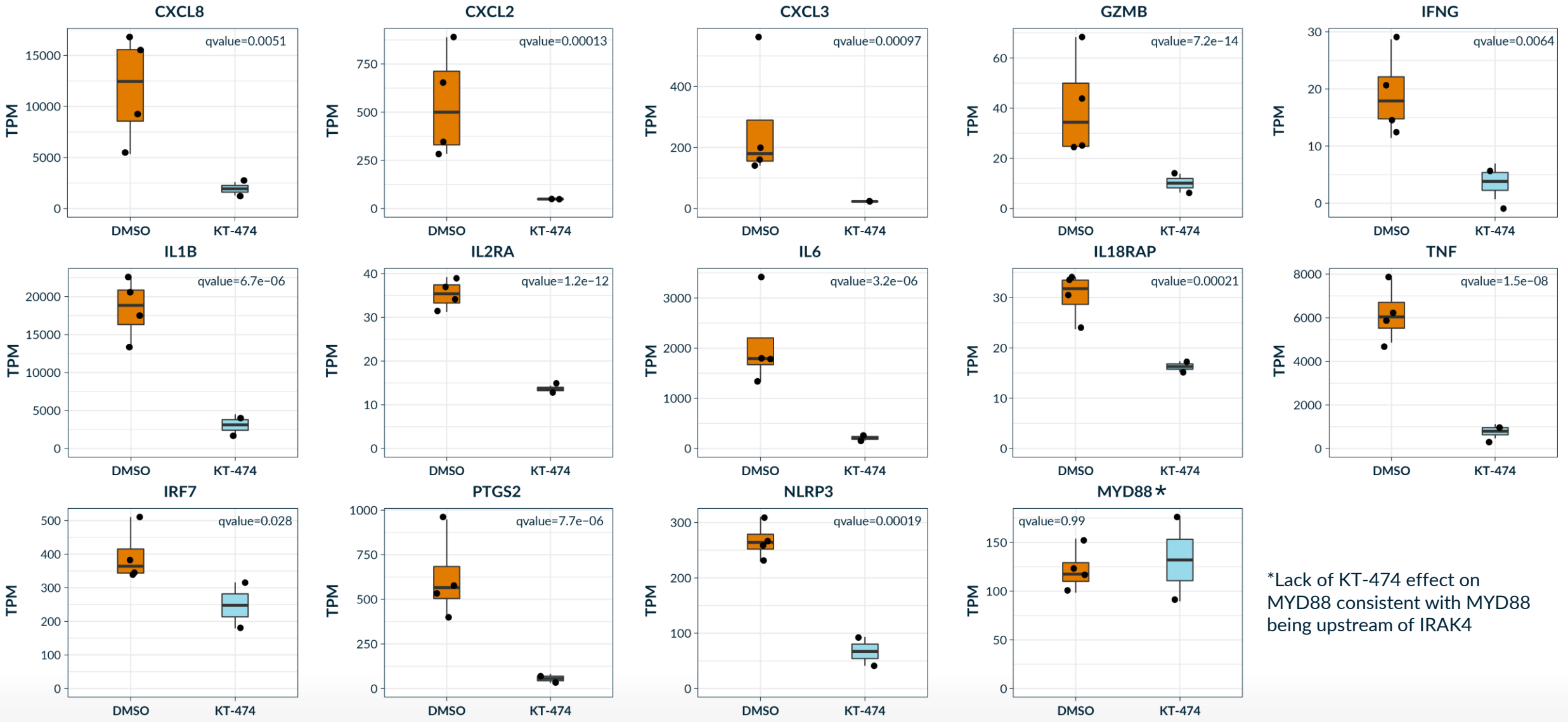




- Upregulation of TLRs, IL-1β/IL-36, MYD88, and multiple additional drivers of inflammation that all correlate with IRAK4 protein expression
- Highlights potential of IRAK4 targeting to treat diseases like HS characterized by marked pleiotropic inflammation

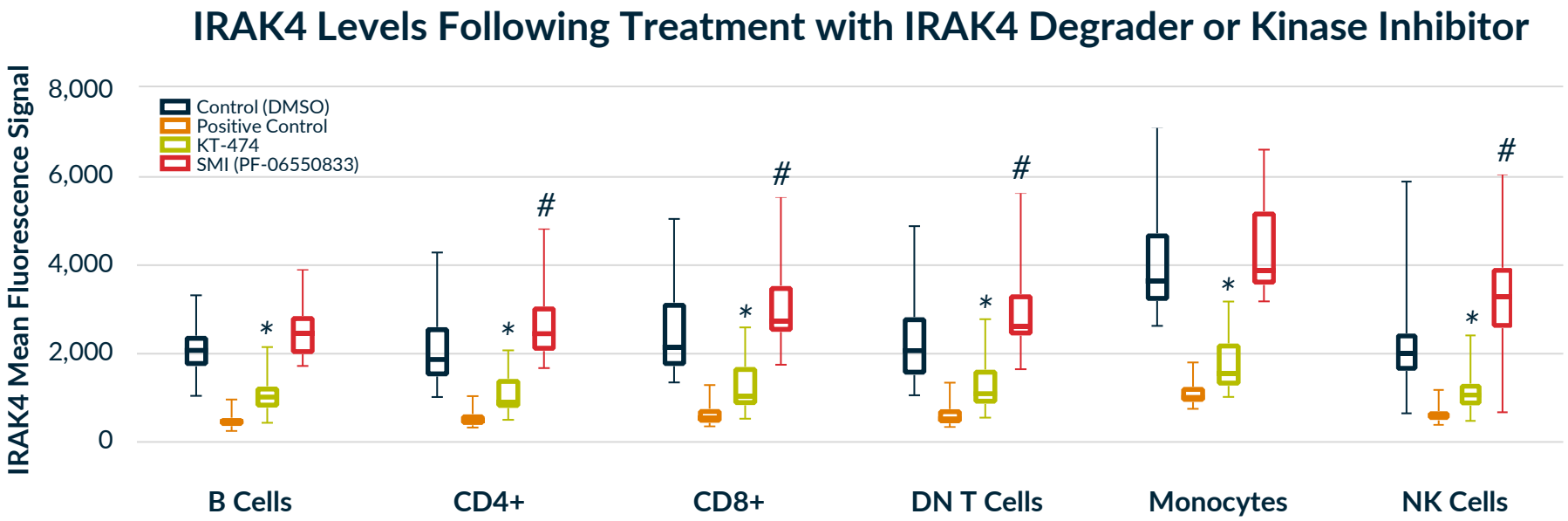
Alavi et al., Society for Investigative Dermatology Annual Meeting, 2021

IRAK4 Degrader KT-474 Inhibits TLR-Mediated Induction of HS-Overexpressed Proinflammatory Transcripts in Healthy Monocytes



*Lack of KT-474 effect on MYD88 consistent with MYD88 being upstream of IRAK4

IRAK4 Degrader Downregulates IRAK4 Expression Across All PBMC Subsets



N=30 patients, One-way ANOVA* KT-474 vs DMSO Control p≤0.0001, #SMI (PF-06550833) vs DMSO Control p≤0.02
Positive Control: cells treated with IRAK4 blocking antibody prior to IRAK4 staining

KEY TAKEAWAYS

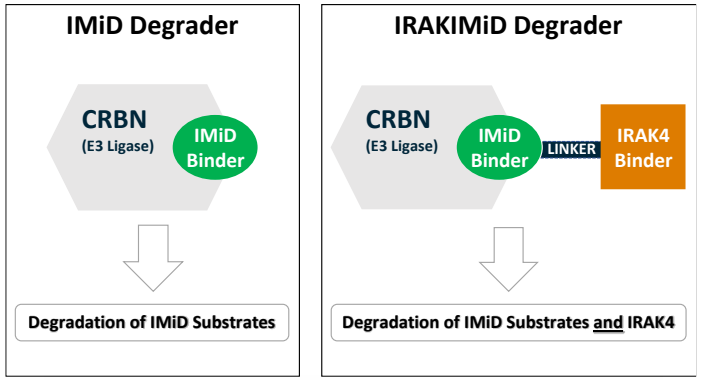
- *Ex vivo* incubation of HS blood with KT-474 reduced IRAK4 to a level approaching the lower limits of detection across all PBMC subsets, irrespective of baseline expression intensity, whereas an IRAK4 kinase inhibitor increased IRAK4 levels in T and NK cells
- Treatment with an IRAK4 kinase inhibitor led to an increase in IRAK4 levels of up to 2.6-fold in T and NK cells

Non-interventional Study Conclusions

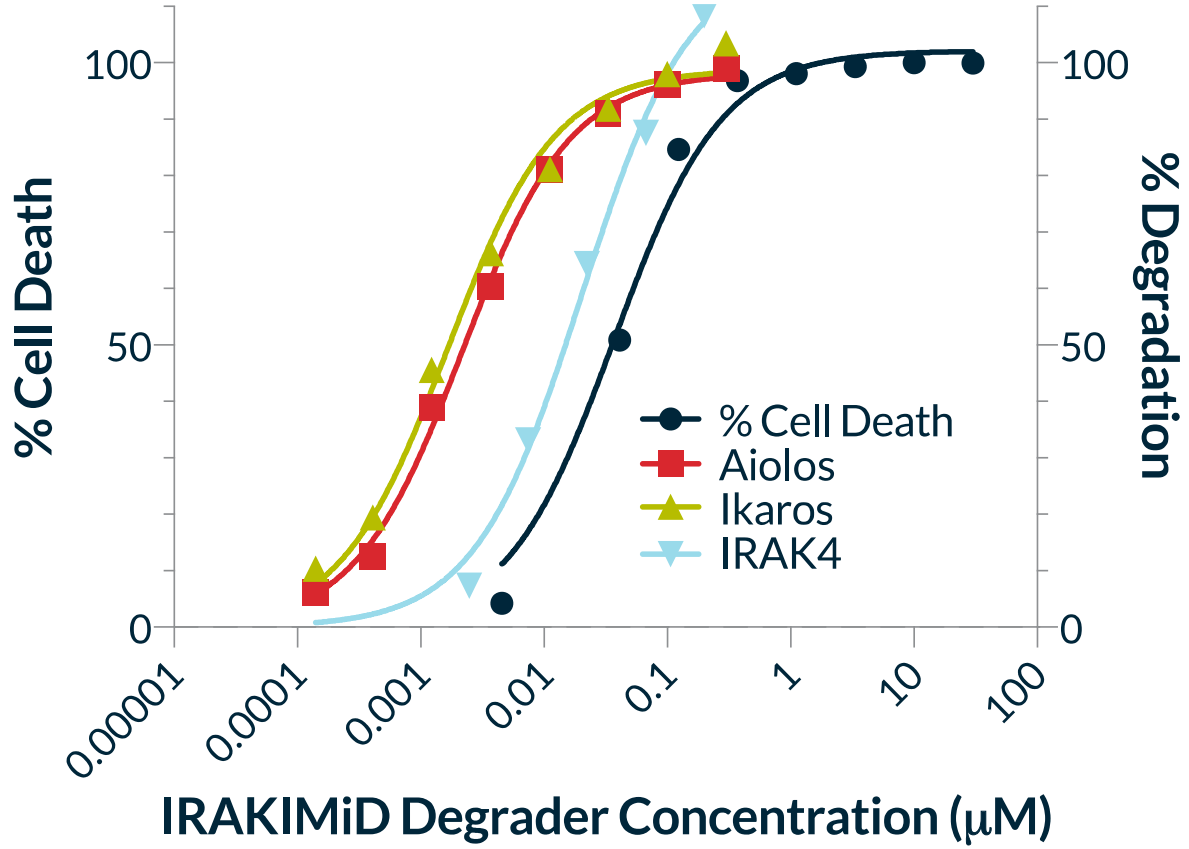
- **IRAK4 is overexpressed in HS skin relative to healthy subjects due to increase in number of IRAK4+ dermal immune cells and epidermal keratinocytes**
  - Higher expression in active HS skin Lesions compared to peri-lesion and/or non-lesion skin associated with increase in infiltrating IRAK4+ dermal immune cells
  - Higher expression in dermis and epidermis of non-lesion skin compared to skin of healthy subjects raises possibility that IRAK4 overexpression may predispose to inflammatory lesion formation in HS
- **Gene expression profiling shows upregulation of multiple mediators of inflammation in HS skin lesions that correlates with IRAK4 protein overexpression**
  - Includes genes involved in TLR/myddosome signaling, inflammasome activity, prostaglandin generation, Th1 and Th17 inflammation, and monocyte/neutrophil migration and activation, thereby linking IRAK4 to the pleiotropic inflammation in HS
  - Neither proinflammatory gene expression nor IRAK4 protein expression correlated with disease severity, suggesting common pathophysiology underlying inflammation in active lesions irrespective of disease stage
- **IRAK4 degrader KT-474 inhibits TLR-stimulated upregulation of HS-overexpressed inflammatory genes in monocytes from healthy subjects**
  - Provides further evidence for role of IRAK4 in overexpression of these mediators of inflammation in HS skin lesions and rationale for targeting IRAK4 with KT-474 for the treatment of patients with HS
  - Phase 1 trial of KT-474 in healthy volunteers and patients with HS or AD is ongoing and includes pre- and post-treatment skin biopsies and blood sampling to assess the effect of KT-474 on the expression of IRAK4 and associated biomarkers of inflammation


IRAKIMiD
KYMERA

Degradation of IRAK4, Ikaros and Aiolos Correlates to Cell Killing

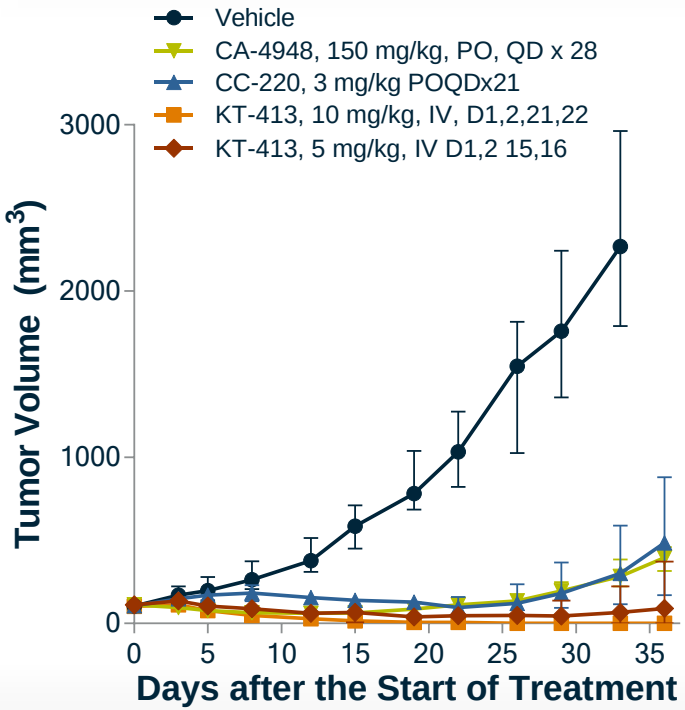


- IRAK4, Ikaros and Aiolos degradation measured in MYD-88-mutated OCI-Ly10 cells after 24 h of drug exposure
  - IRAK4 DC_{50} = 4 nM
  - Ikaros/Aiolos DC_{50} = 2/2 nM
- Degradation correlates with cell killing effects
  - IC_{50} = 31 nM



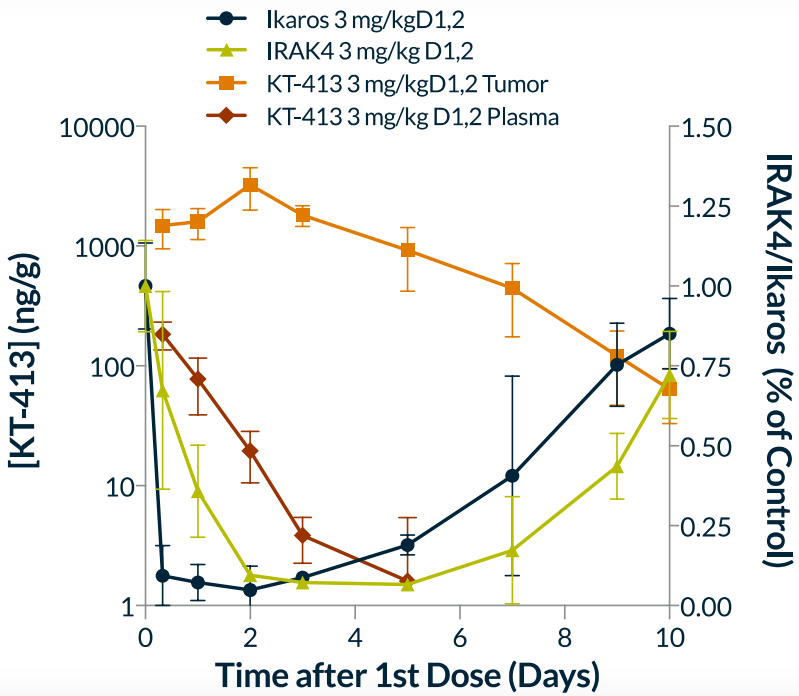
KT-413 is Highly Active on Intermittent Dosing Regimens and Superior to Clinically Active CA-4948 and CC-220

- In the OCI-Ly10 MYD88^{MT} xenograft model, intermittent dosing of KT-413 induced strong antitumor activity, including complete or partial regressions
  - Superior activity compared to the clinically active IRAK4-inhibitor CA-4948 or the latest generation IMiD CC-220 alone
- Minimally active dose of 3 mg/kg D1,2 showed extended tumor exposure and strong degradation of both IRAK4 and IMiD substrates that was maintained for at least 72h



Drug	CR	PR	SD	PD
CA-4948	0	0	3	4
CC-220	0	1	4	2
KT-413 (5 mpk)	2	2	3	-
KT-413 (10 mpk)	5	2	-	-

CR: <10mm^3 tumor on D26
PR: >50% regression from baseline
SD: <50% regression to 20% increase in tumor volume
PD: >20% tumor growth on D26



STAT3

KYMERA

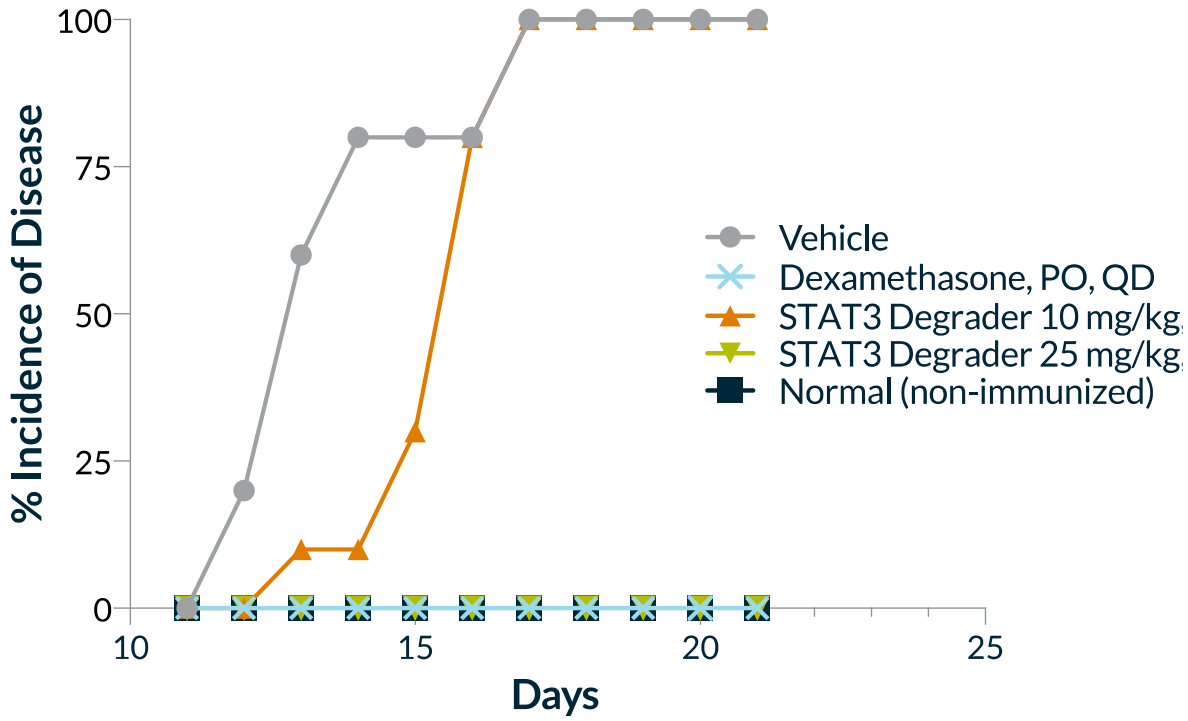
STAT3 Degrader Active in T Cell Activation Preclinical *In Vivo* Model

Multiple Sclerosis Model

CANCER
- Liquid Tumors
- Solid Tumors

I/I FIBROSIS
- Autoimmune
- Fibrosis

- A preclinical model of experimental autoimmune encephalomyelitis (T cell activation) was used to evaluate STAT3 degradation
- Kymera STAT3 Degrader completely prevented onset of the disease in mice



STAT3 Degradation and Downstream Effects Across Tumor Cells

CANCER

Liquid Tumors

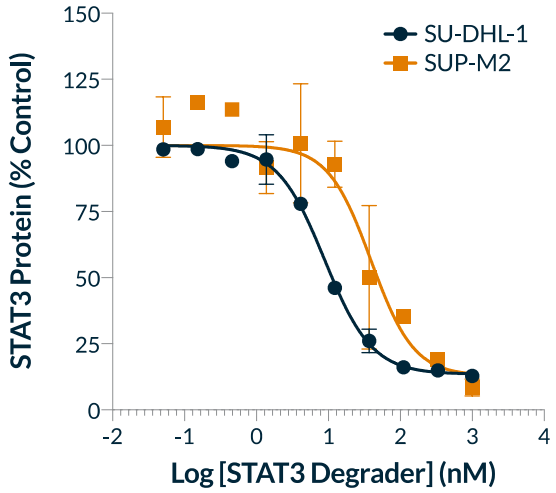
Solid Tumors

I/I FIBROSIS

Autoimmune

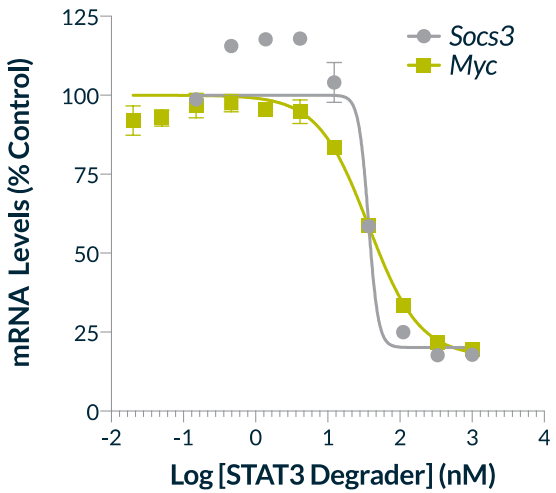
Fibrosis

STAT3 Degradation



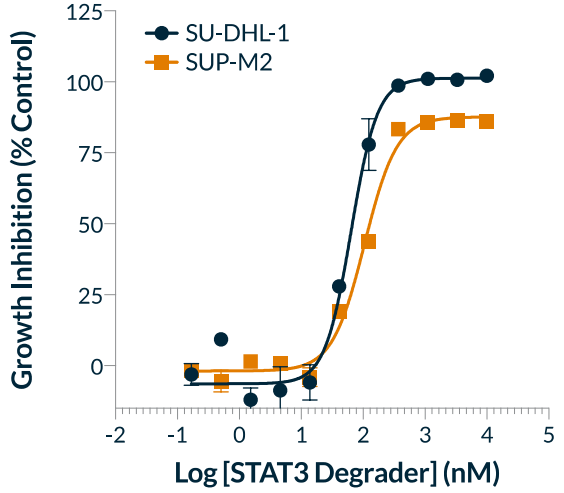
- STAT3 protein levels measured in two STAT3-dependent cell lines
- STAT3 degrader decreased levels of STAT3 by greater than 95% with DC_{50} of 15nM and 86 nM, respectively

Gene Transcription Effects



- Expression of STAT3 downstream target genes in SU-DHL-1 cells measured
- Treatment with STAT3 degrader for 24 hours led to significant downregulation of STAT3 target genes, including SOCS3 (IC_{50} = 36 nM) and MYC (IC_{50} = 37 nM)

Cell Viability Effects



- Impact of STAT3 degradation on viability of lymphoma cells measured
- Inhibited growth of SU-DHL-1 and SUP-M2 cells with IC_{50} values of 64 and 105 nM, respectively

Effects of STAT3 Degradation on Tumor Microenvironment

CANCER

Liquid Tumors

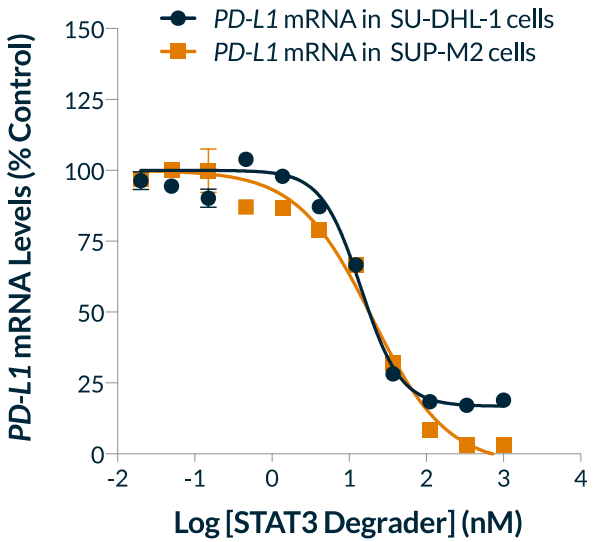
Solid Tumors

I/I FIBROSIS

Autoimmune

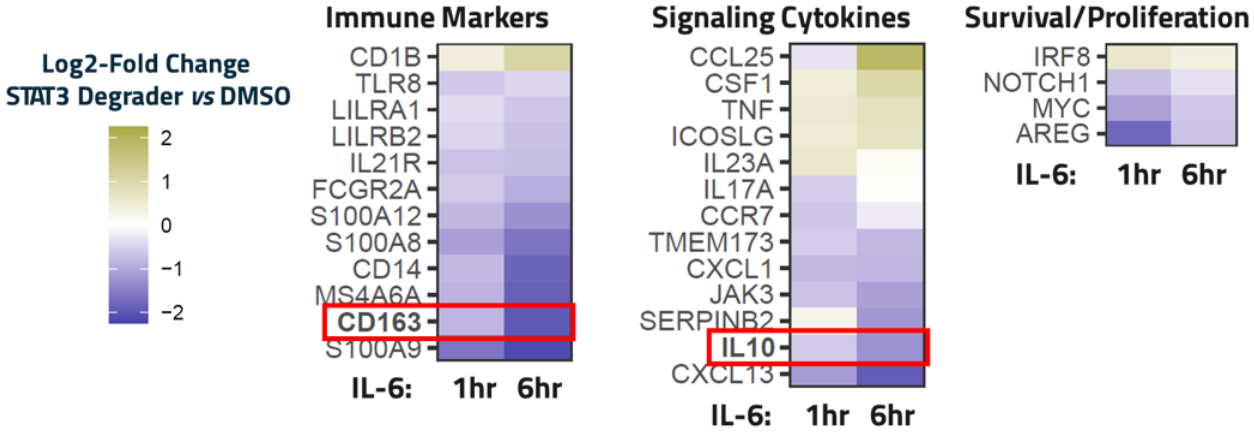
Fibrosis

PD-L1 Downregulation



- Treatment of cells with Kymera's STAT3 degrader reduced transcription of PD-L1 mRNA
- STAT3 degradation may reverse a key tumor intrinsic mechanism for immune suppression

Increased Inflammation in Tumor Associated Immune Cells



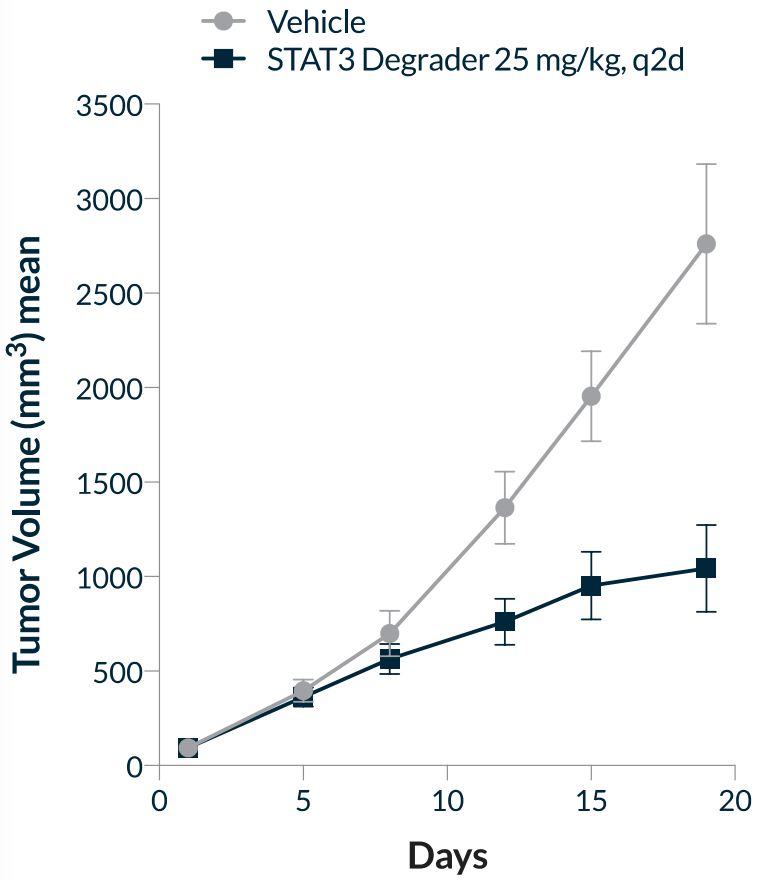
- STAT3 degrader blocked IL-6-induced increases in gene expression in hPBMC
- Data suggest degradation of STAT3 reverses expression of genes contributing to immune suppression

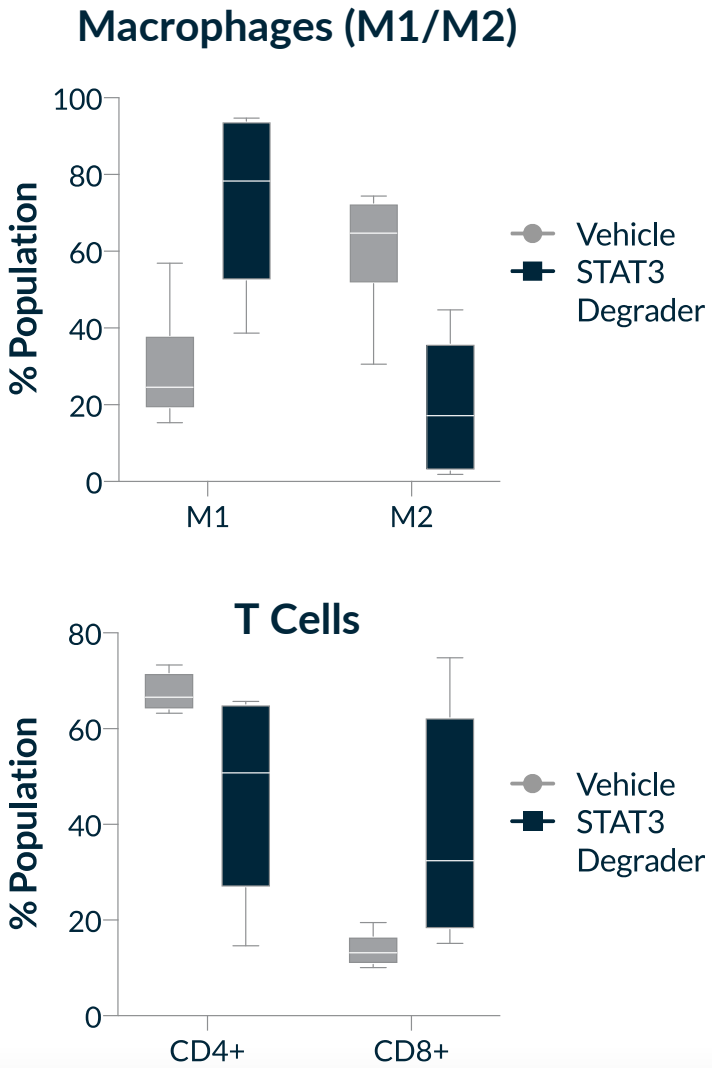
STAT3 Degrader *in Vivo* Active in Preclinical PD-1/L-1 Refractory Solid Tumor Model

CANCER
- Liquid Tumors
- Solid Tumors

I/I FIBROSIS
- Autoimmune
- Fibrosis

- Kymera's STAT3 degrader assessed in colorectal cancers (CT-26) known to be refractory to approved immunotherapies
- STAT3 degrader significantly reduced tumor growth when administered every two days
- Analysis of tumors showed synergistic modulation of immune cells (M2/M1 and T cells) within the tumor microenvironment to favor an anti-tumor response





THANK YOU

investors@kymeratx.com

media@kymeratx.com

inquiries@kymeratx.com