INVENTING NEW MEDICINES

WITH TARGETED PROTEIN DEGRADATION

April 2021

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Targeted Protein Degradation

What if you could remove disease causing proteins…

…with a small molecule-based technology?

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**

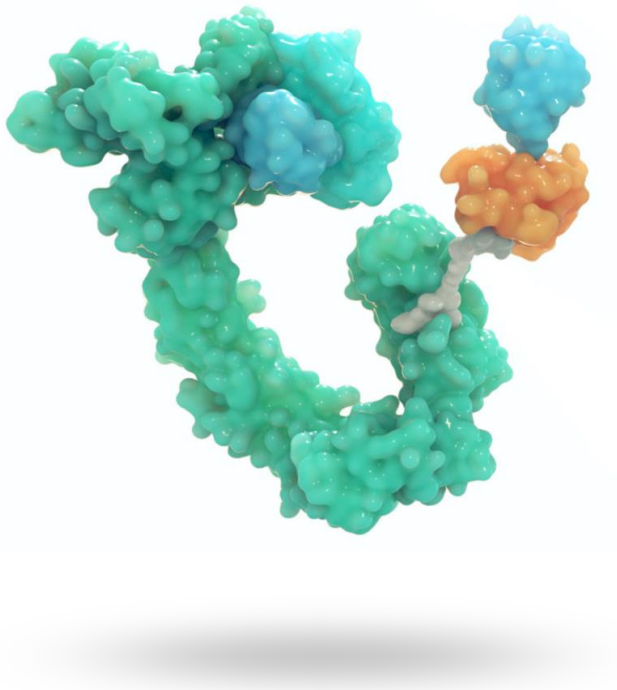
Team

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

Kymera: A Leading Targeted Protein Degradation Company

Founded:	2016
Stage:	Clinical
NASDAQ:	KYMR
Employees:	~100
Cash balance at Q4'20*:	$459M

KYMERA



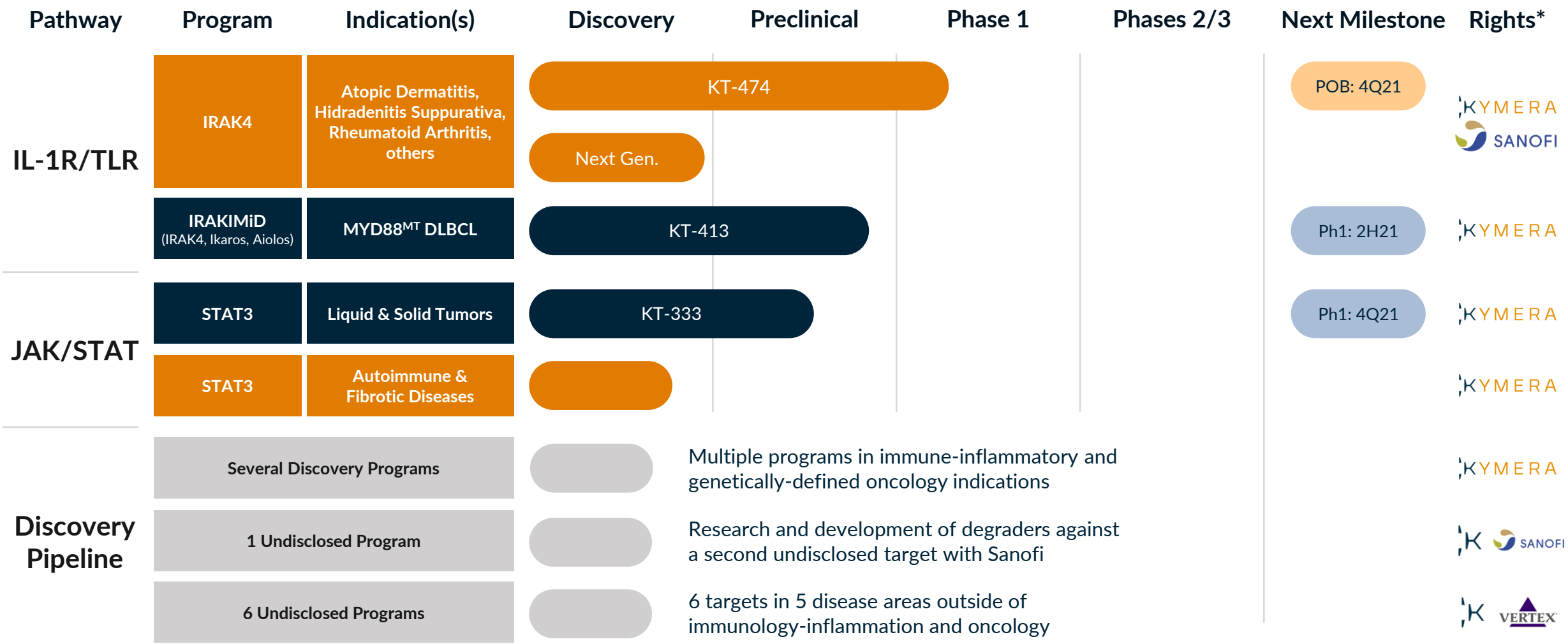
- Premier, **disease agnostic** protein degrader discovery platform
- Key **enabling partnerships**:

SANOFI VERTEX gsk

- Initial focus in **immune-inflammation and oncology**
- First company set to dose degrader to **healthy volunteers and I/I patients**
- Expect **3 INDs** and clinical initiations by end of **2021**
- First proof-of-biology established in humans in **2021**

* Kymera expects that its cash, cash equivalents, and investments as of 12/31/2020, excluding any future potential milestones from collaborations, will enable the Company to fund its operational plans into 2025.

Kymera's Pipeline of Novel Protein Degraders



*Option to participate equally in the development and commercialization of Sanofi-partnered programs in the US

Pegasus™ Platform and R&D Approach

KYMERA

Targeted Protein Degradation

Biology

Co-opting a Naturally Occurring Process to Regulate Protein Levels

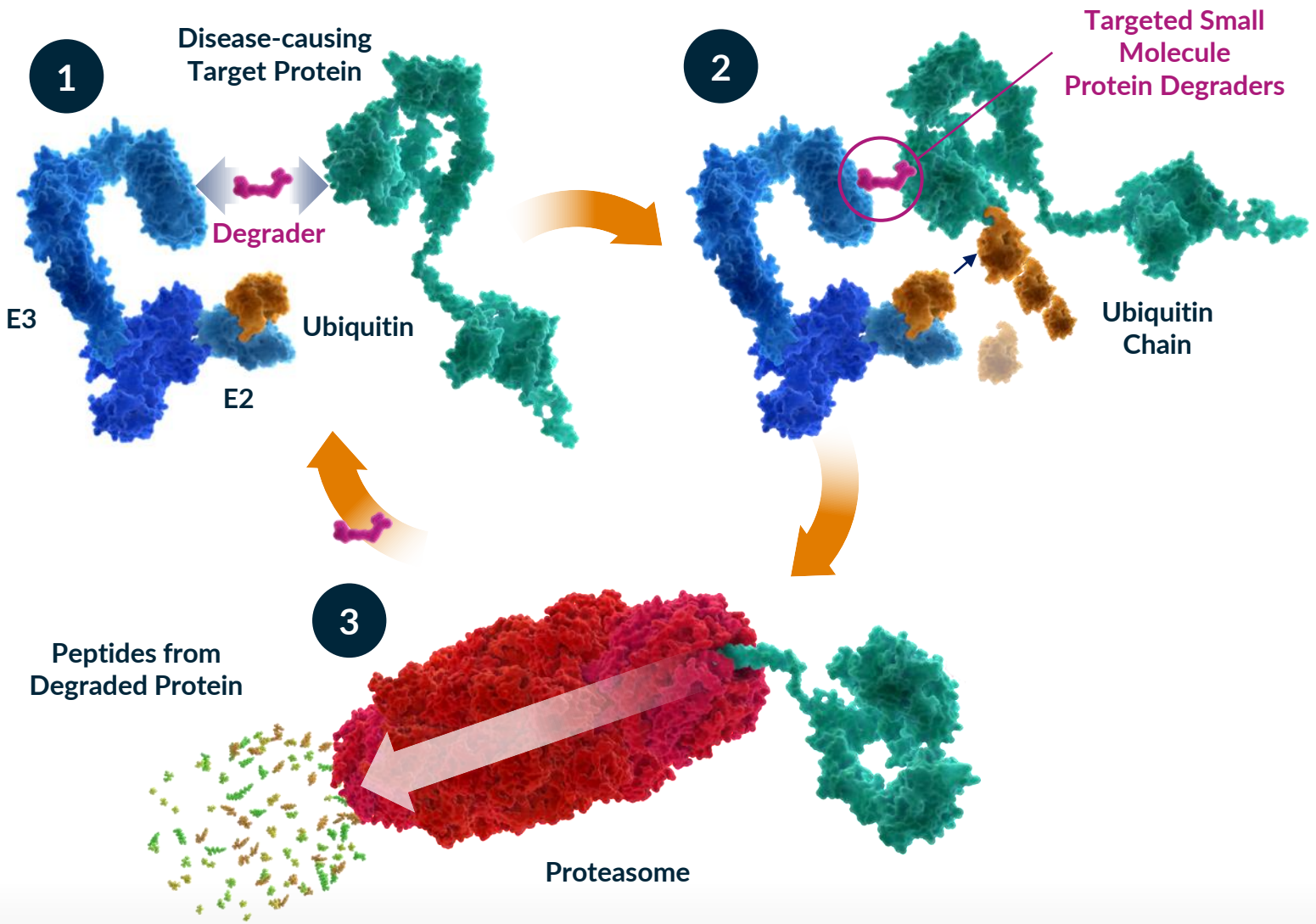
1. E3 ligase recognizes protein
2. Ubiquitin chain transferred
3. Protein is marked for elimination

KYMERA

Broad Opportunity
Only Binding Site Required

Efficient
Catalytic

Prolonged Impact
Targeted Protein Degradation



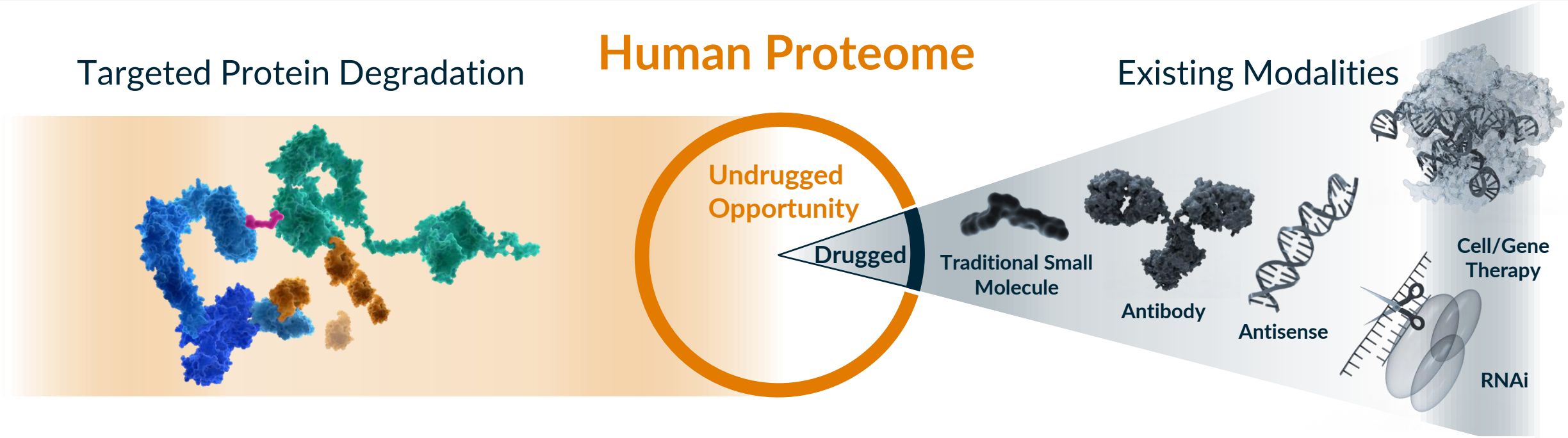
Targeted Protein Degradation

Next Potential Breakthrough Modality to Expand Drugged Proteome

Targeted Protein Degradation

Human Proteome

Existing Modalities



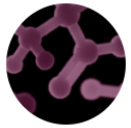
✓	**Undruggable Targets** Scaffold, transcript factor, multiple functions	✓
✓	**Efficient** Development / Manufacturing	X
✓	**Systemic** Exposure	X
✓	**Oral** Bioavailability	X

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

Leading the Evolution of Targeted Protein Degradation

What if you could remove disease causing proteins…

…only where it matters?

Pegasus: E3 Ligase Whole-Body Atlas

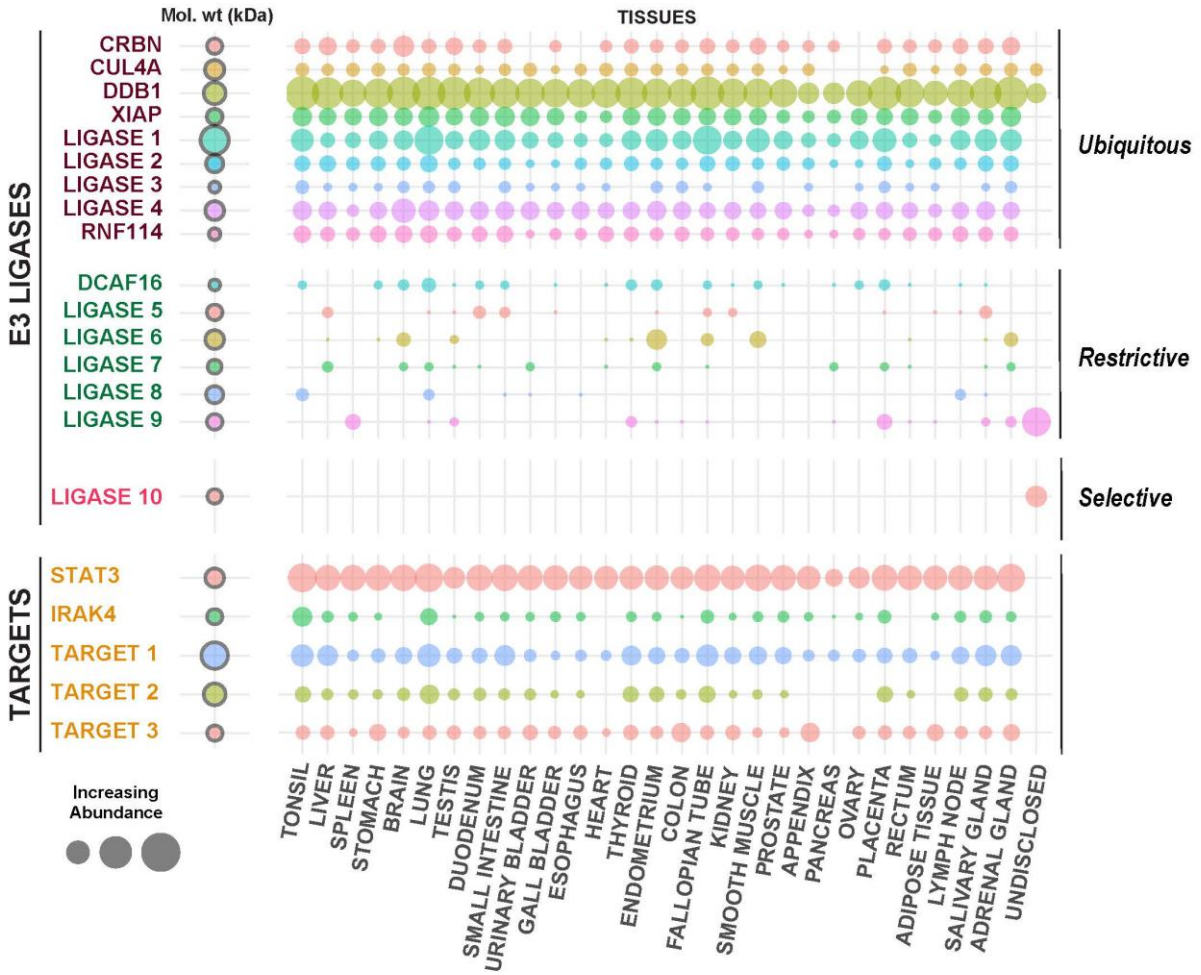
Different expression profiles of E3's provide opportunity for tissue selective/restrictive degradation

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-restrictive degraders to enable novel therapeutic opportunities



Pegasus: E3 Ligase Whole-Body Atlas

A Bone Marrow Sparing E3 Ligase

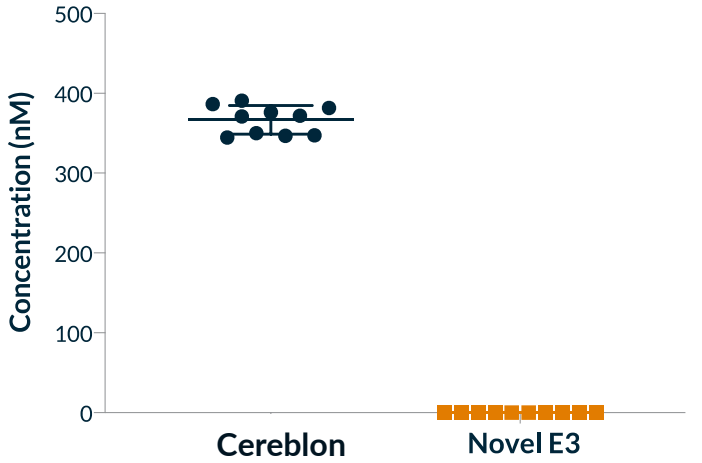
Expanded E3 ligase toolbox

Understanding degradation (PK/PD) across tissue types

Proprietary Chemistry

- E3 Ligase Whole-Body Atlas queried to identify a tissue sparing E3 ligase based on target protein unwanted pharmacology (i.e. bone marrow for a particular target of interest)
- A bone marrow sparing E3 ligase identified
- Screening and optimization lead to a novel binder to a previously unliganded E3 ligase (E3 ligase binders toolbox)
- A novel degrader based on a bone marrow sparing E3 ligase demonstrated target degradation

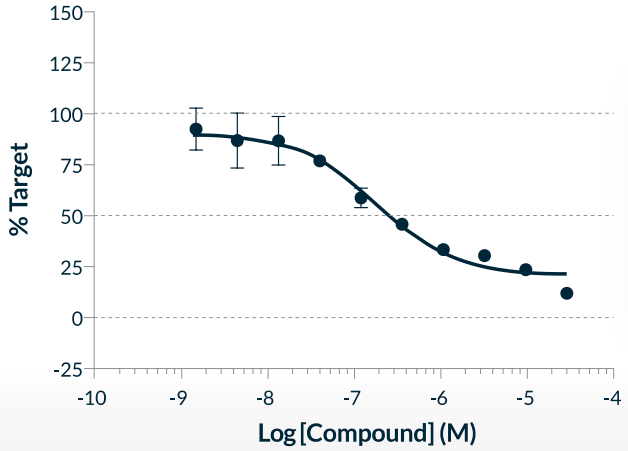
This E3 Ligase is Not Expressed in Bone Marrow



Bone marrow: CD34+ from five donors

Ligand Identification

TPD with Bone Marrow Sparing Novel E3 Ligase



Target	Target Protein
DC_{50} (nM)	206
Dmax (%)	88

Pegasus

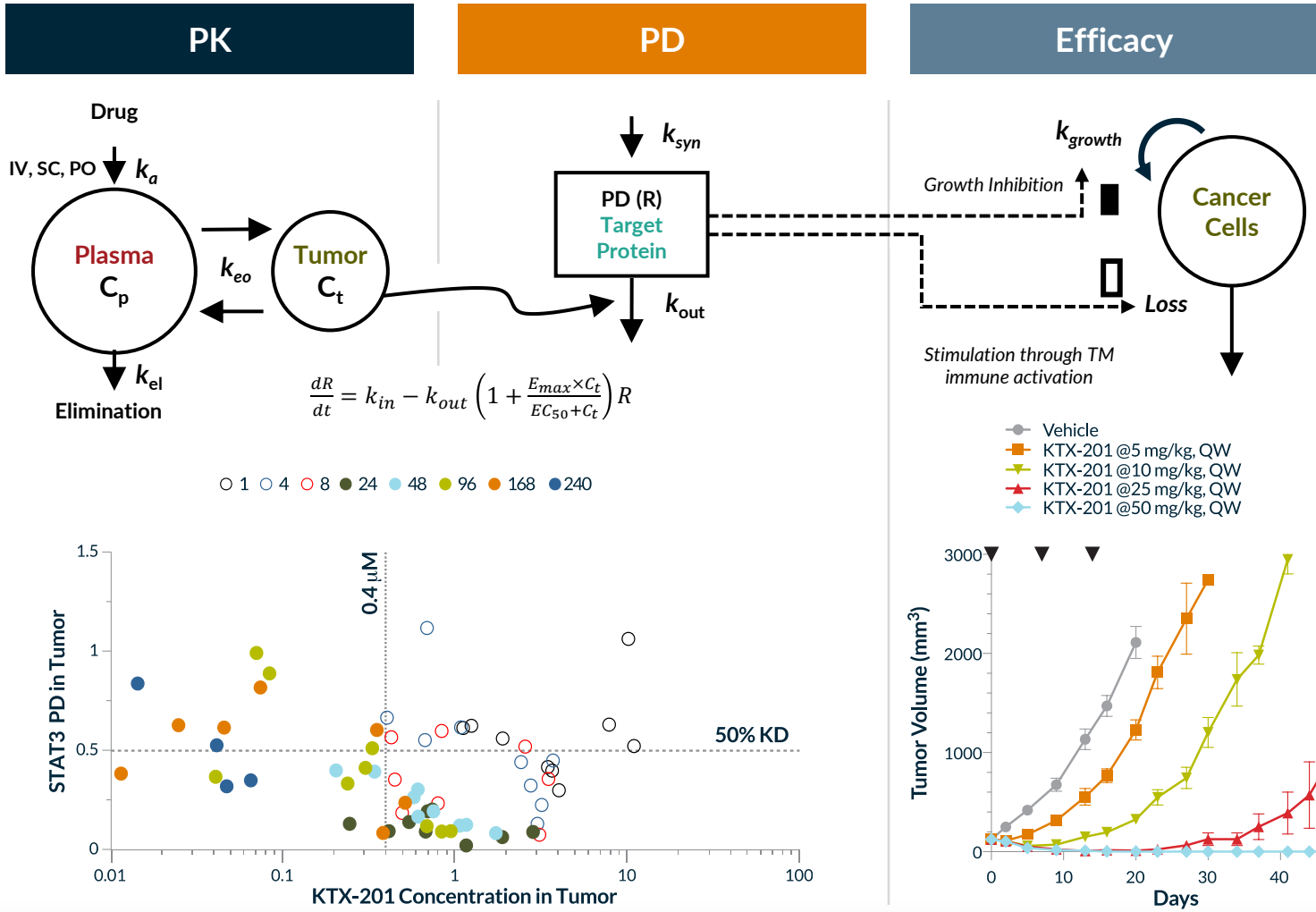
Ternary Complex Modeling / Quantitative System Pharmacology Model

Expanded E3 ligase toolbox

Understanding degradation (PK/PD) across tissue types

Proprietary Chemistry

- Refined understanding of each parameter impacting degradation profiles
- Modeling predicts how relative E3 ligase and protein concentrations impact degradation
- Designed to solve complex equations to accurately translate PK/PD into optimal human dosing



Pegasus
Proprietary Chemistry

Expanded E3 ligase toolbox

Understanding degradation (PK/PD) across tissue types

Proprietary Chemistry

- A comprehensive approach that allows for rapid hit finding and the rational design and optimization of targeted protein degraders (TPDs)
- A large, chemically diverse toolbox of privileged linkers that can confer favorable pharmacokinetic properties to enable oral absorption
- A collection of proprietary ligands to known and novel E3 ligases that allow for degradation in desired tissues of interest and establish a strong intellectual property position
- Computational chemistry expertise, including a novel and proven approach for predicting ternary complexes, to expedite all activities from hit finding to late lead optimization
- Leveraging binary and ternary complexes to rationally guide potency and selectivity
- Process chemistry expertise with demonstrated ability to rapidly deliver kg quantities of TPDs

Development Candidate Profile

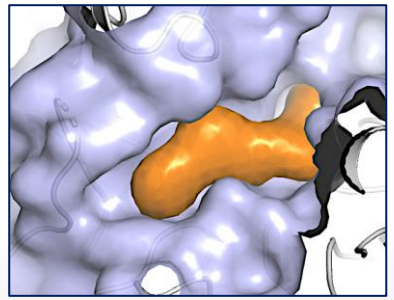
Characteristic	Metric	KT-413
Potency	IRAK4 DC_{50} (nM)	***8***
Human *in vitro* clearance	HLM (µL/min/mg)	***3.5***
***In vivo* clearance**	Monkey CL (mL/min/kg)	***3.2***
Bioavailability	Monkey PO PK (%F)	***41***

Ligand to Novel Tissue Restricted E3 Ligase

Fragment Screening Hit
E3 Ligase IC_{50}: >1 mM

Lead Ligand
E3 Ligase IC_{50}: 30 nM
cLogP: 0.74
MW: 399

E3 Ligase X Ray Co-crystal



Kymera Drug Development Principles

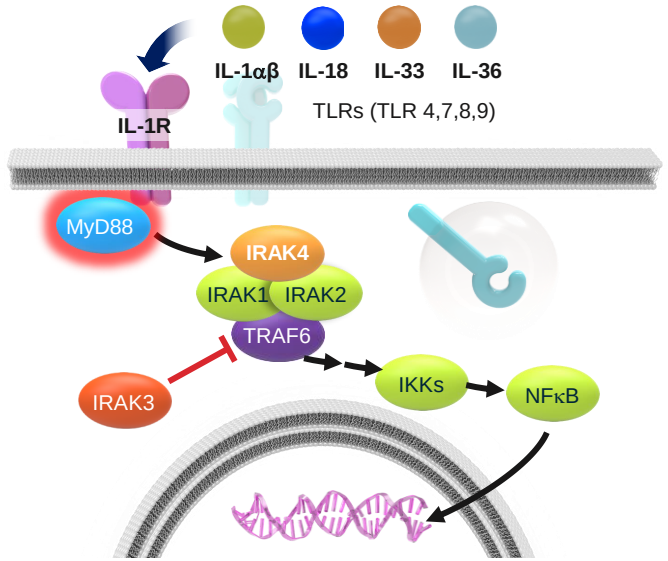
Unmet Medical Need	Many unmet medical needs across various cancers and rheumatological, dermatological disorders
Validated Biology	Clinically validated across several disease areas: oncology, immunology, fibrosis
Undrugged Node	Key undrugged or inadequately drugged nodes that TPD can unlock
Precision Medicine Approach	Targeted to a genetically defined patient population

Kymera Drug Development Principles

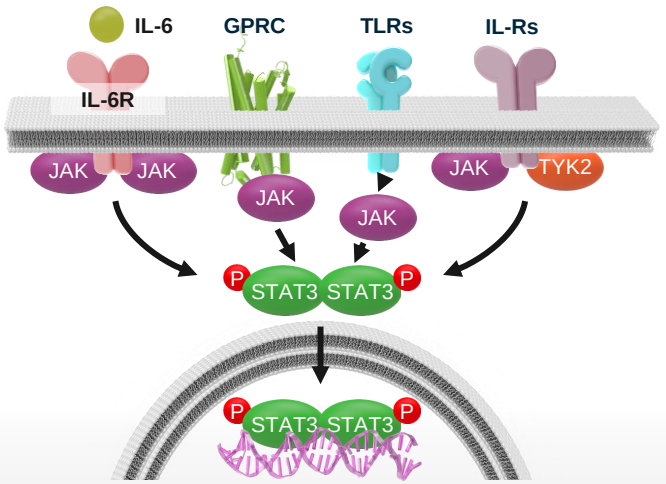
Initial focus on pathways that have been clinically and commercially validated with undrugged nodes

- **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-18: Macrophage Activation Syndrome
IL-1β: CANTOS Data, Atherosclerosis, Lung Cancer
IL-33: Atopic Dermatitis
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

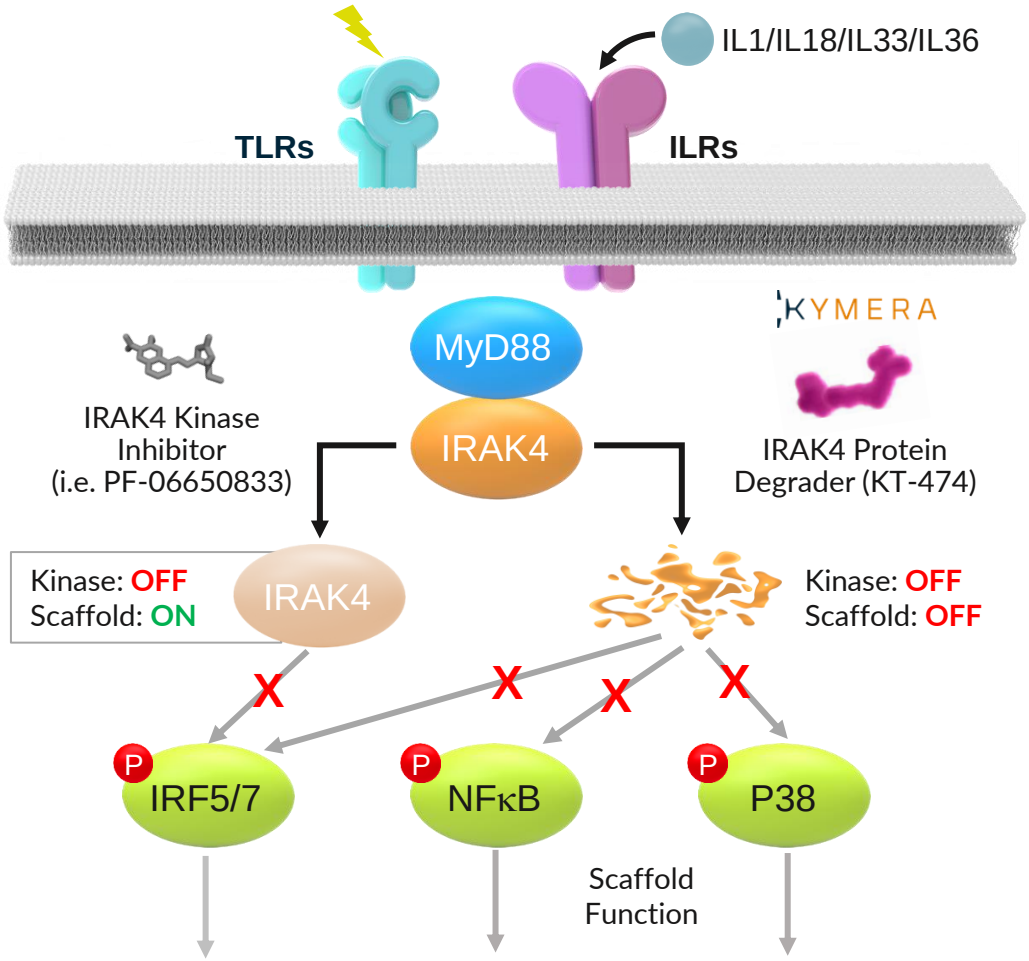
KYMERA

IRAK4 Biology and Degrader Rationale

- IRAK4 is a key component of the myddosome protein complex
- Myddosome is involved in innate immunity that mediates signals through IL-1R and TLRs
- IL-1R/TLR signaling through the myddosome complex is dependent on IRAK4 kinase and scaffolding functions
- Believe degrading IRAK4 can provide a single oral small molecule solution to many diseases impacted by this pathway
- Sanofi collaboration on development of degraders targeting IRAK4 outside oncology and immuno-oncology

Indications/Expected Timeline

HS, AD, RA, others
Phase 1 SAD initiation: 1Q 2021 ✔
Phase 1 MAD enrollment: 2H 2021*
Phase 1 proof-of-biology in healthy volunteers: 4Q 2021



IFNα/β, Inflammatory Cytokines (IL-6, TNF) & Mediators

* Initiation of MAD portion of Phase 1 trial is on partial clinical hold pending FDA review of interim SAD data.

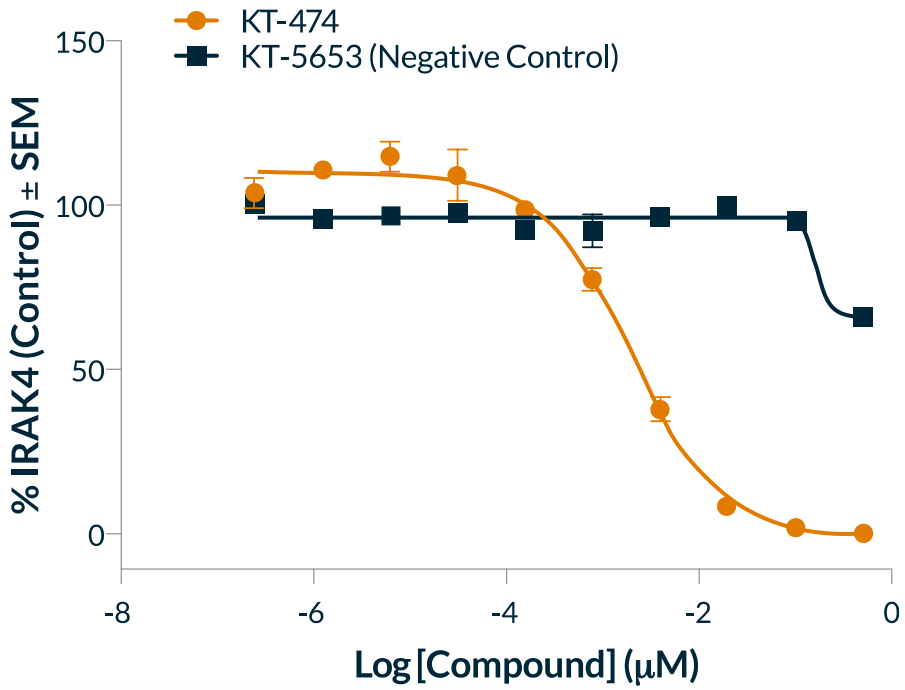
KT-474 Opportunity

Immune-inflammatory disorders collectively impacting millions of patients in the U.S.

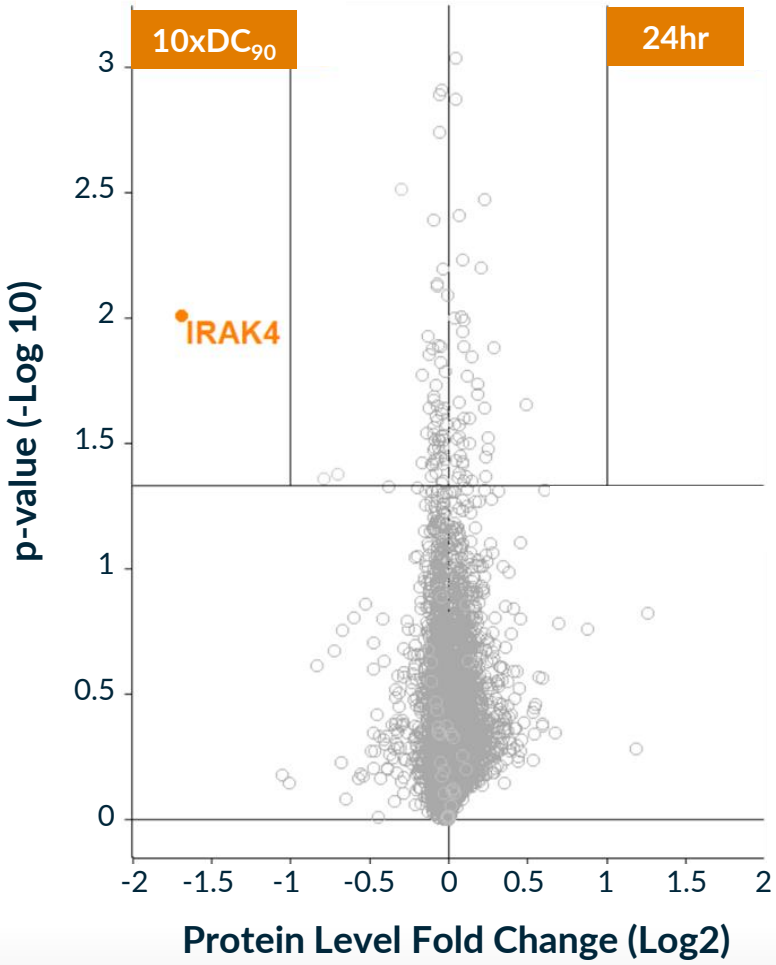
	Patient Impact (U.S.)	
Hidradenitis Suppurativa (HS)	>325K	• Chronic and debilitating inflammatory skin disease • **~25%** of patients with moderate-to-severe disease • Adalimumab (anti-TNF antibody) is approved, which provides some benefit to **~50% of patients** with moderate-to-severe disease
Atopic Dermatitis (AD)	>11.0M	• Chronic, pruritic **inflammatory skin disease** • Dupilumab (IL-4Rα targeting antibody) approved with only **40% of patients** meeting primary endpoint in Phase 3 trials
Rheumatoid Arthritis (RA)	>1.3M	• Chronic, systemic **autoimmune disease** that can cause irreversible joint damage • Multiple therapies targeting the **IL-1R/TLR pathway** are approved
Additional Opportunities	→	• Immune-inflammatory diseases impacted by **IL-1R/TLR pathway**

KT-474: Specific IRAK4 Degradation

Degradation in Human Monocytes



Selectivity in Human PBMC

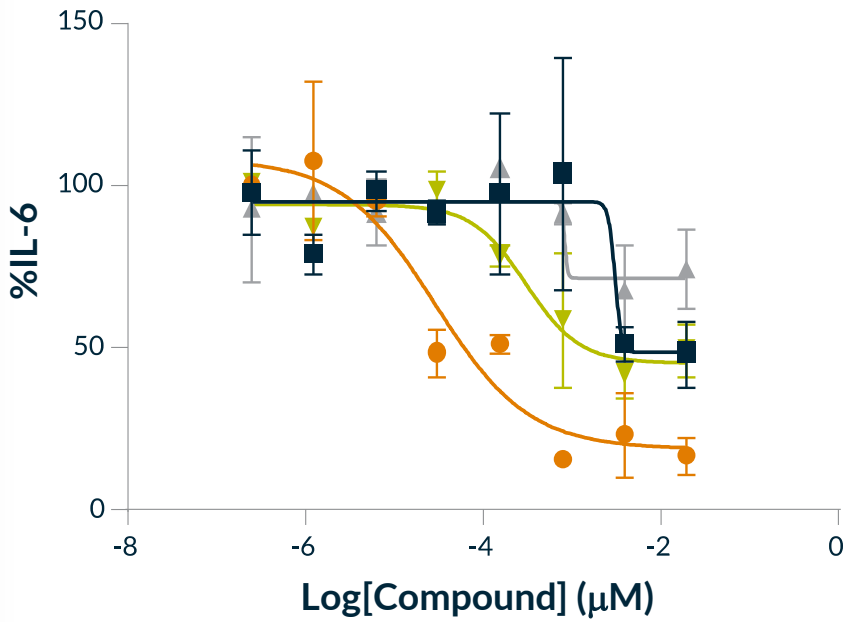


- Calculated DC_{50} of 2.1 nM and E3 ligase dependent degradation of IRAK4 in human immune cells
- IRAK4 was only protein of over 10,000 to be degraded by KT-474 in human immune cells at concentration 10-fold above the DC_{90}

IRAK4 Degradation Superior to Kinase Inhibition in Cytokine Production

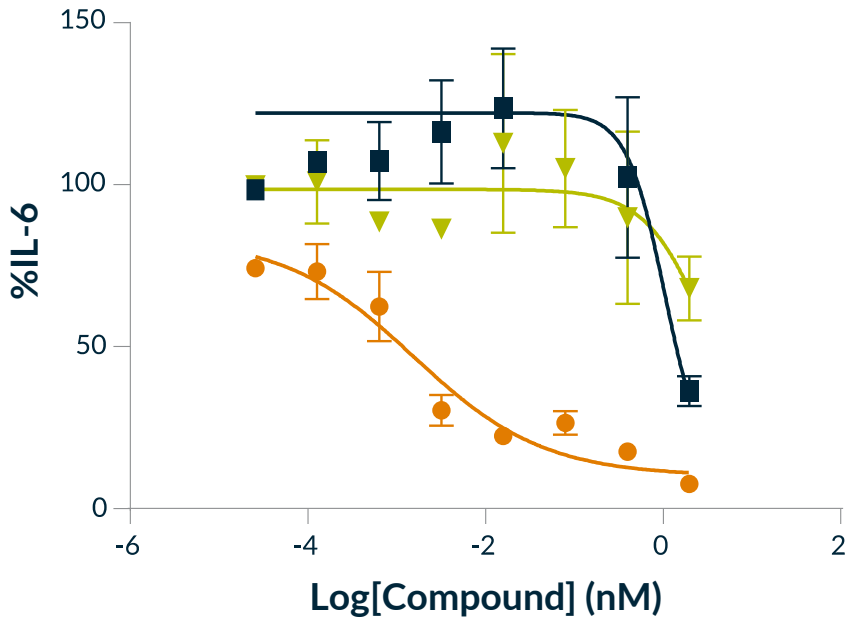
- Functional activity of KT-474 assessed by measuring pro-inflammatory cytokine levels upon activation
- Cells pre-treated with KT-474, a negative control, and small molecule IRAK4 kinase inhibitors
- KT-474 better able to inhibit IL-6 under both LPS and LPS + IL-1B than clinically active IRAK4 SM kinase inhibitor PF-06550833

LPS → IL-6



Legend	Compound	IL-6 IC_{50} (nM)
	KT-474	3
	Negative control	335
	IRAK4 SMI *(PF-06550833)*	N/A
	IRAK4 SMI *(other)*	N/A

LPS + IL-1B → IL-6

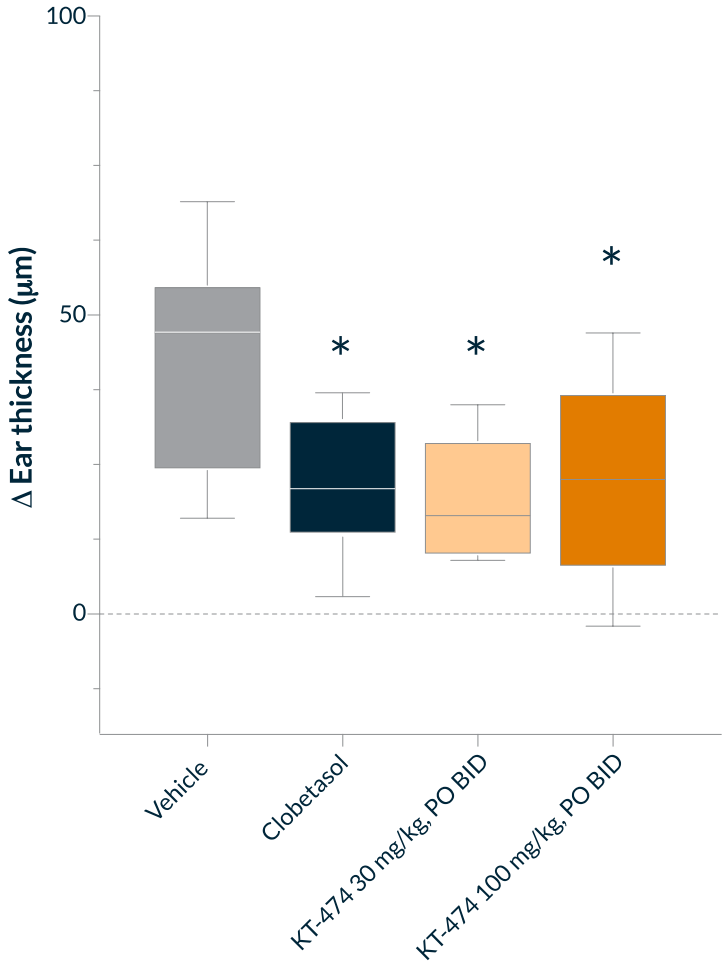


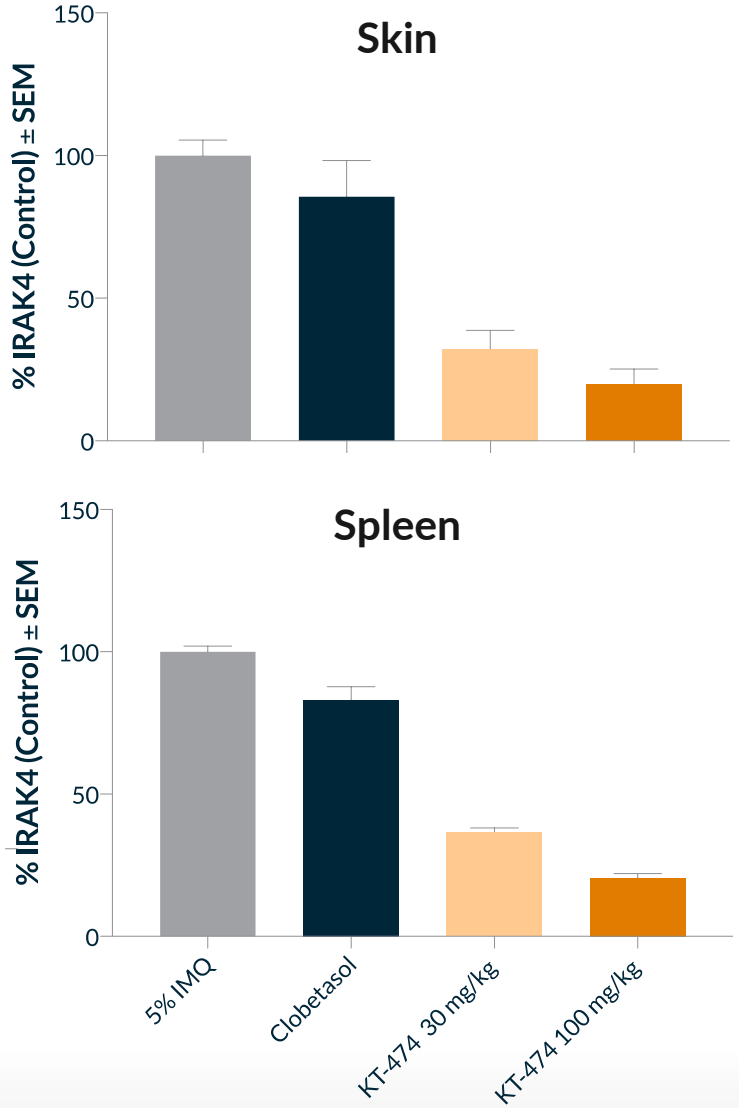
Legend	Compound	IL-6 IC_{50} (nM)
	IRAK4 Degrader	0.8
	Negative control	450
	IRAK4 SMI *(PF-06550833)*	N/A

IRAK4 Degradation *In Vivo* Active in Preclinical Mouse Psoriasis Model

IL-1R/TLR driven

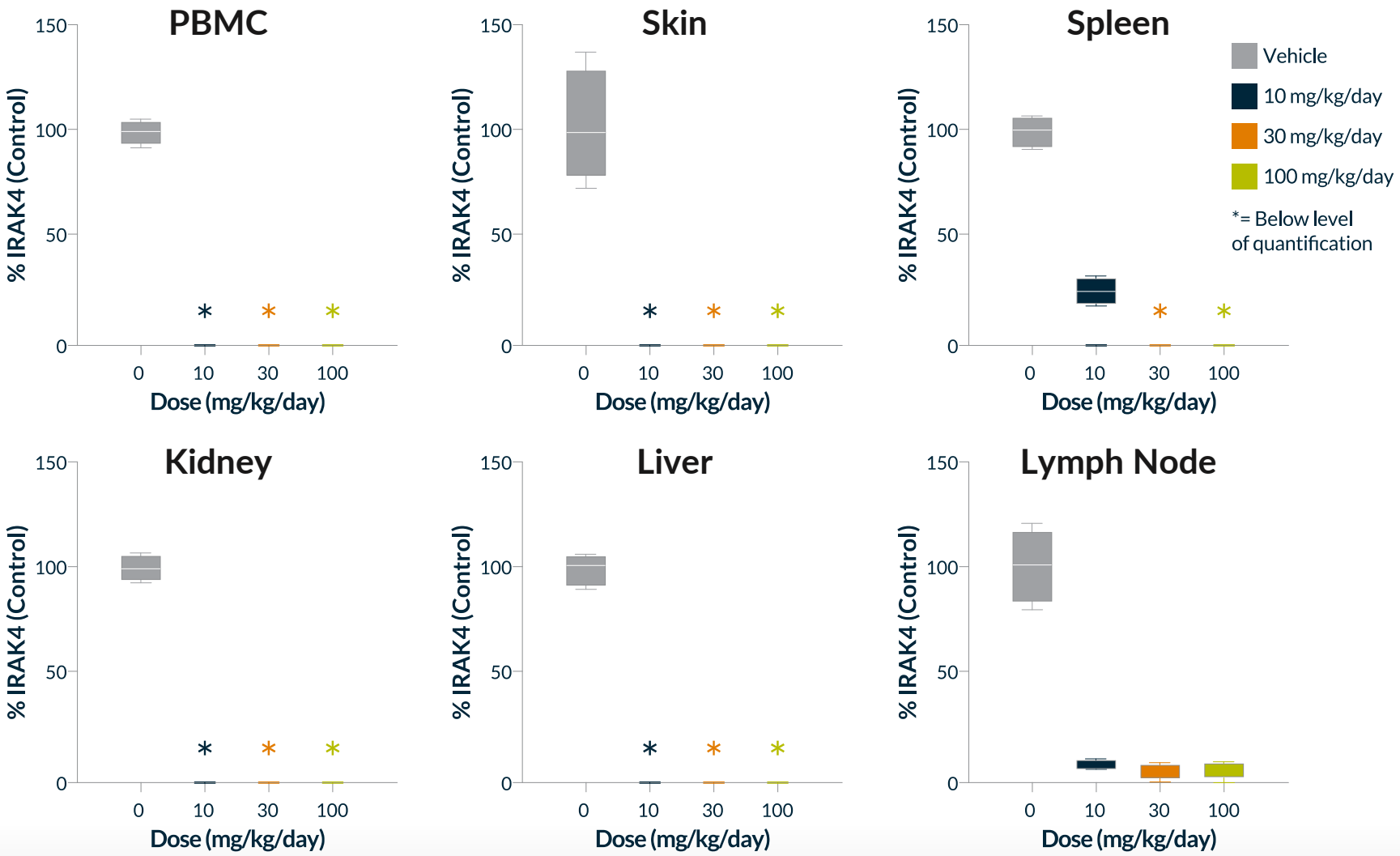
- Ability to inhibit topical skin thickening induced by imiquimod was measured in a mouse model of psoriasis
- Orally dosed KT-474 inhibited thickening, a reflection of local and systemic inflammation, comparable to a topic corticosteroid after 2 or 4 days of dosing
- Inhibition shown at doses achieving at least 60-70% IRAK4 knockdown in skin and spleen





KT-474: Close to Complete IRAK4 Degradation and Well Tolerated in Preclinical Non-rodent Model

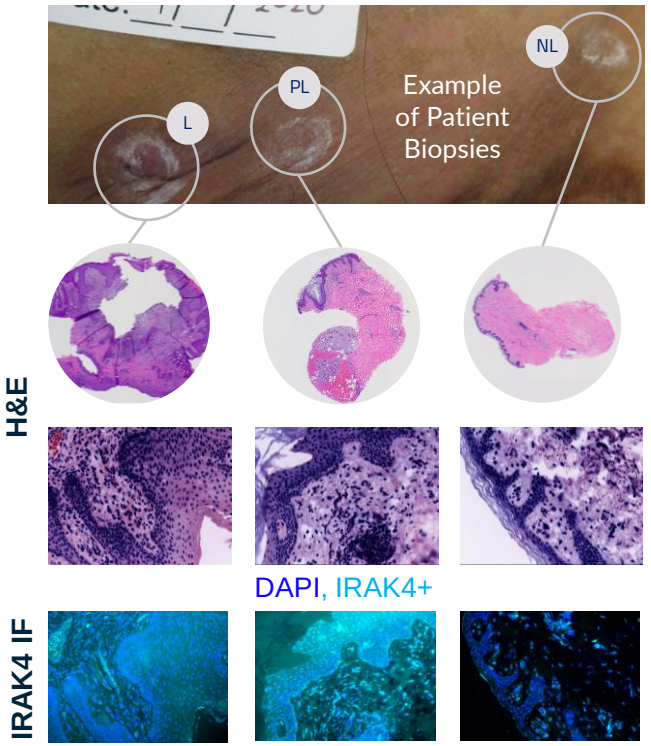
- Orally-administered KT-474 evaluated in a 14-day non-GLP tox and PKPD study in rodent and non-rodents (shown).
- Almost complete knockdown demonstrated across multiple tissues at multiple doses
- Compound well-tolerated at all doses up to 600 mg/kg for rodents and 100 mg/kg for non-rodents



Non-Interventional Study: IRAK4 Expression is Highest in Lesional (L) & Peri-Lesional (PL) Skin

IRAK4 Immunofluorescence (IF)

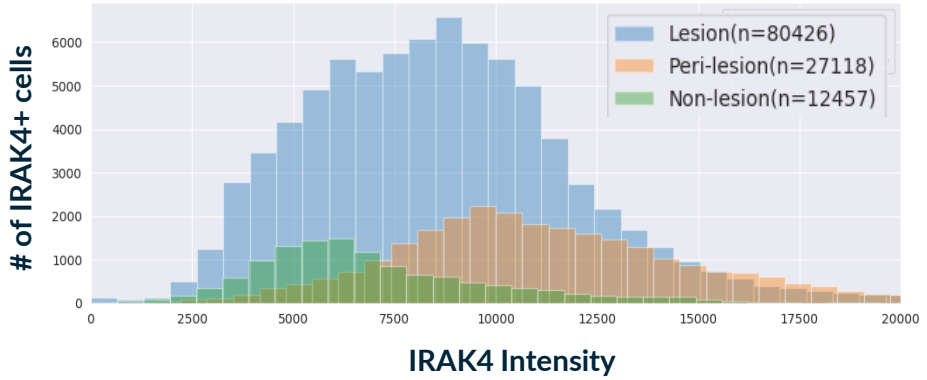
N=10 | **IHS4 severity:** 4 mild, 3 moderate, 3 severe



IF Analysis

- L, PL, NL IRAK4 positive cells counted and binned into intensity ranges as depicted by the horizontal bars below
- Cell counts per intensity bin were summed from the 3 biopsy locations

Cell Count by Intensity per Biopsy Location



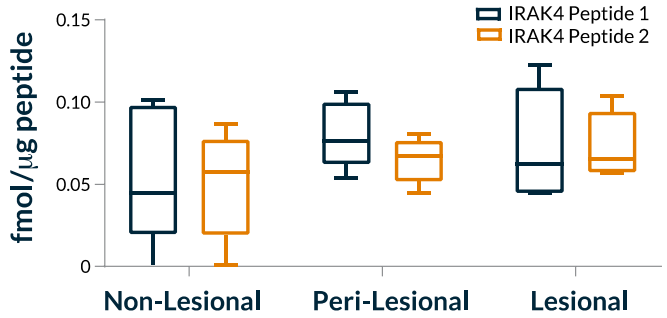
IRAK4 Mass Spectrometry (MS)

N=5 | **IHS4 severity:** 0 mild, 2 mod, 3 severe

MS Analysis

- Two peptides were chosen providing strong concordance in absolute quantification
- Plot represents the range of fmol/ug peptide across the 3 biopsy locations

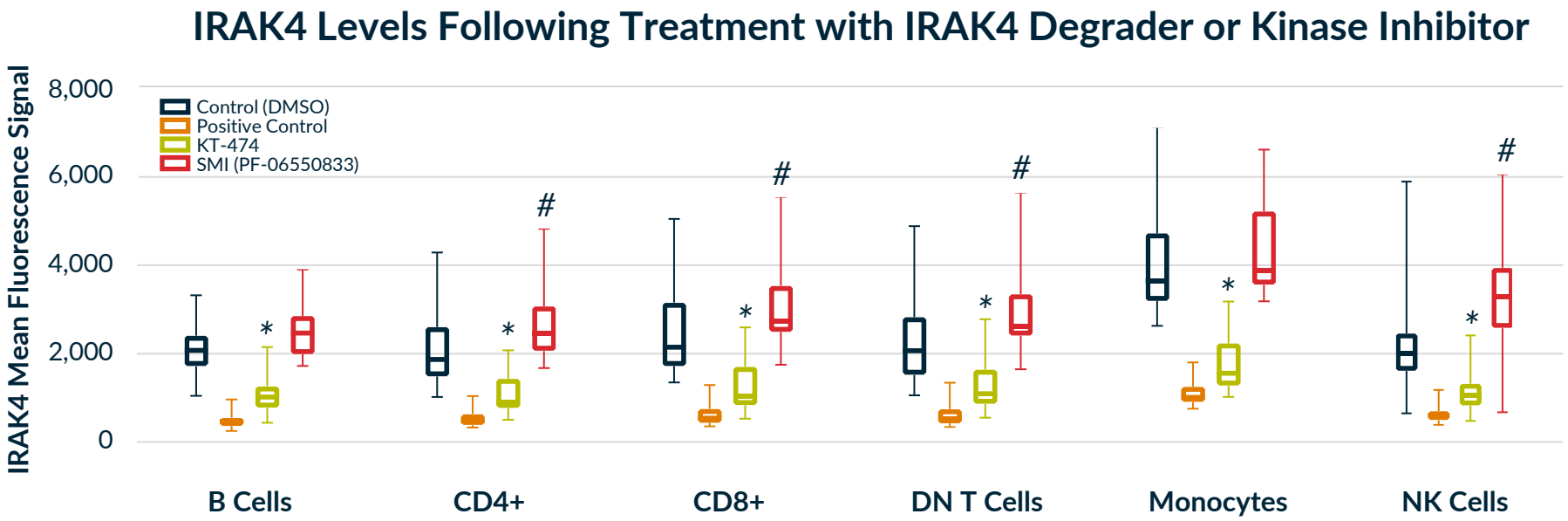
IRAK4 Absolute Quantification Normalized to PARK7



CONCLUSIONS

L and PL biopsies have more IRAK4+ cells and higher intensity IRAK4 staining than NL as measured by IF. MS with trend towards higher level of IRAK4 in L and PL compared to NL.

Non-Interventional Study: 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

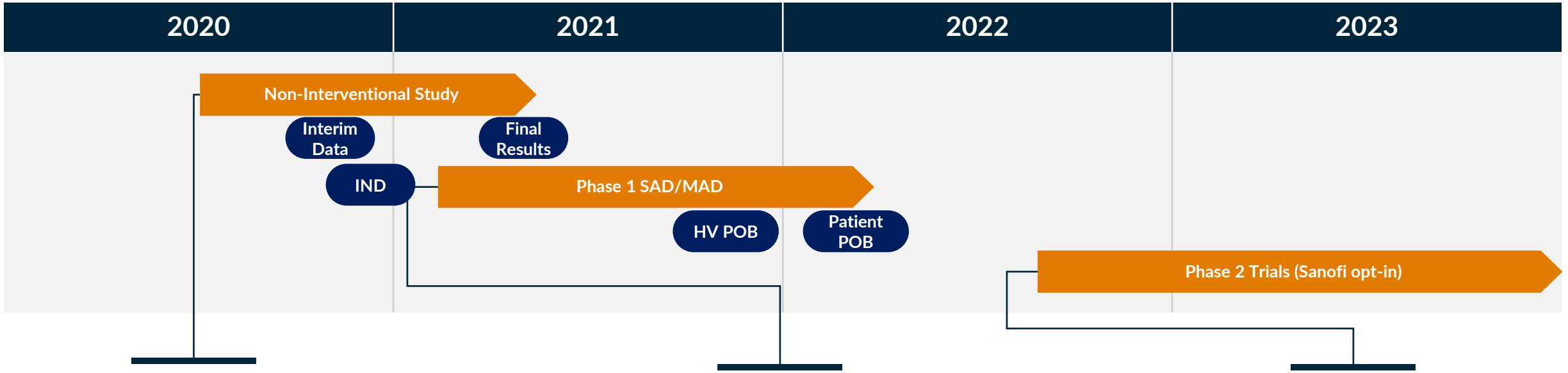
- Kymera demonstrated that **IRAK4 levels are higher in lesional and peri-lesional skin compared to non-lesional**
- ***Ex vivo* incubation of HS blood with KT-474 reduced IRAK4 to a level approaching the lower limits of detection across all PBMC** subsets, irrespective of baseline expression intensity, 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

KT-474 Phase 1 Trial to Establish Proof-of-Biology

Double-blind, placebo-controlled, Single Ascending Dose (SAD) and Multiple Ascending Dose (MAD) study

	SAD Portion	MAD Portion	
	Healthy Volunteers (HV)	Healthy Volunteers (HV)	Patient Cohort
Target Enrollment	• N = up to 56 adult HV	• N = up to 48 adult HV	• Up to 20 AD or HS patients • Moderate-severe disease
Primary Endpoint	• Safety and tolerability of KT-474 when administered as single and multiple oral doses at escalating dose levels in HVs and following multiple doses in patients with AD or HS		
Secondary Endpoints	• Pharmacokinetic measures (half-life, bioavailability, Cmax, Tmax) • IRAK4 knockdown in peripheral blood mononuclear cells (PBMC) • *Ex vivo* response of whole blood to TLR agonists and IL-1β		**SAD & MAD**
	• IRAK4 knockdown in skin biopsies • Proinflammatory cytokine and chemokine levels in skin biopsies • C-reactive protein and cytokine levels in plasma		**MAD only**

KT-474 Development Plan



- Evaluating 40 patients (HS n=30; AD n=10)
- Biomarker endpoints in blood and skin: IRAK4, cytokines, acute phase reactants
- Interim data presented 4Q20
- **Complete data to be presented in 2Q21**

- **Dosing in SAD portion initiated 1Q21**
- SAD and MAD studies in healthy volunteers (HV) and AD/HS patients
- Primary endpoint is safety
- Secondary endpoints to establish proof-of-biology (POB)
- **POB to be presented in 4Q21**

- Randomized, placebo-controlled trials in patients in indications such as AD, HS, RA, others

* Initiation of MAD portion of Phase 1 trial is on partial clinical hold pending FDA review of interim SAD data.

IRAK4 Conclusions

- IRAK4 is a key undrugged node in a pathway with demonstrated clinical impact in several immune-inflammatory diseases
- IRAK4 degradation is superior to small molecule kinase inhibition and/or upstream pathway blockade through mAb thanks to the ability to fully block the broader family of IL-1 family cytokine and TLR agonists in a context-independent manner
- Kymera has developed a first-in-class potent, selective and orally active IRAK4 degrader, KT-474, with franchise potential across a wide variety of immune-inflammatory diseases such as HS, RA, AD and others
- KT-474 is more potent and more broadly active than leading IRAK4 small molecule kinase inhibitors and has demonstrated activity in a variety of preclinical models with a promising activity and safety profile
- In a Non-Interventional study in HS patients, Kymera has demonstrated that IRAK4 levels are higher in lesional and peri-lesional skin compared to non-lesional
- *Ex vivo* incubation of HS blood with KT-474 reduces IRAK4 to a level approaching the lower limits of detection across all PBMC subsets, irrespective of baseline expression intensity, whereas an IRAK4 kinase inhibitor increases IRAK4 levels in T and NK cells
- Kymera has initiated the SAD portion of the Phase 1 trial of KT-474 in healthy volunteers


IRAKIMiD
KYMERA

IRAKIMiD

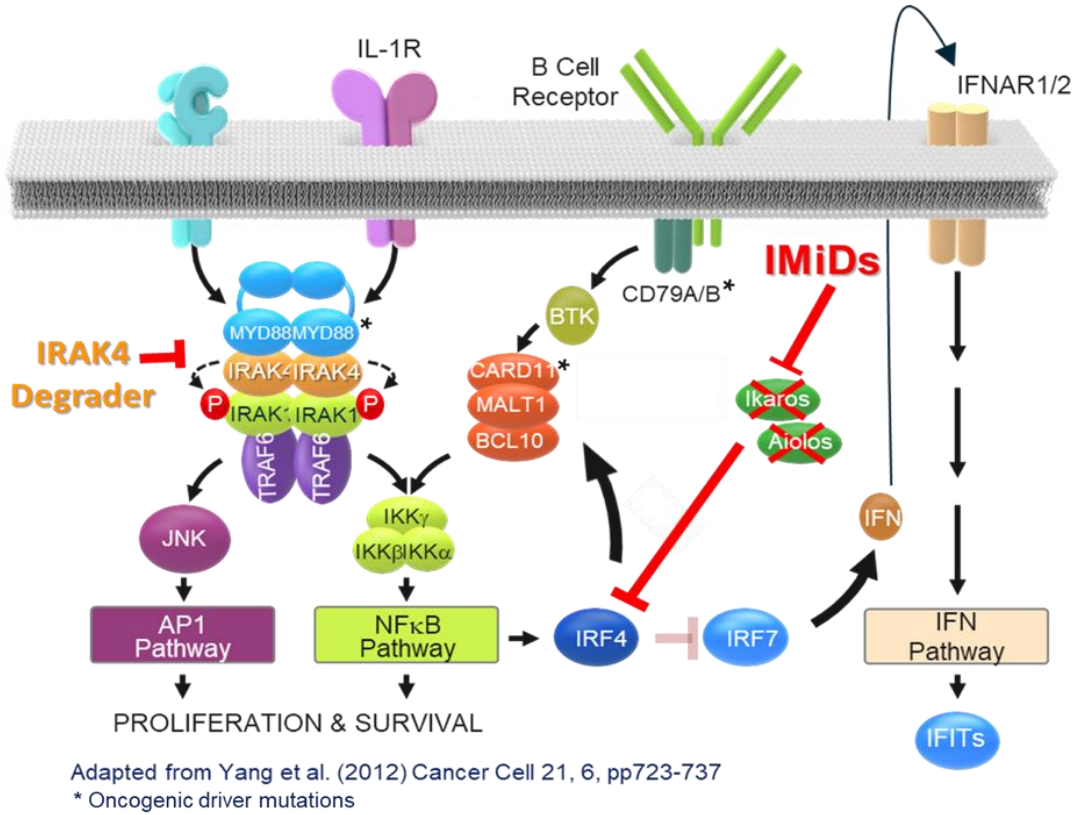
A combo in a single molecule

- 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 (MYD-88 mut)

Indications/Expected Timeline

MYD88-mutant DLBCL
Current: KT-413 in IND-enabling activities
IND/Phase 1 initiation: 2H 2021
Phase 1 proof-of-biology in patients: 2022

Pathway



Adapted from Yang et al. (2012) Cancer Cell 21, 6, pp723-737
* Oncogenic driver mutations

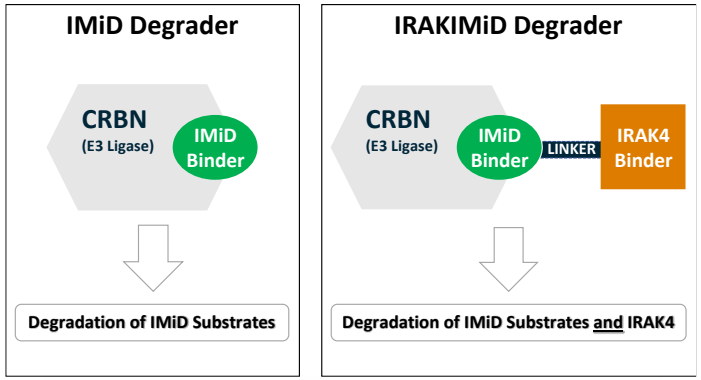
IRAK4 + Ikaros/Aiolos

KT-413 Opportunity

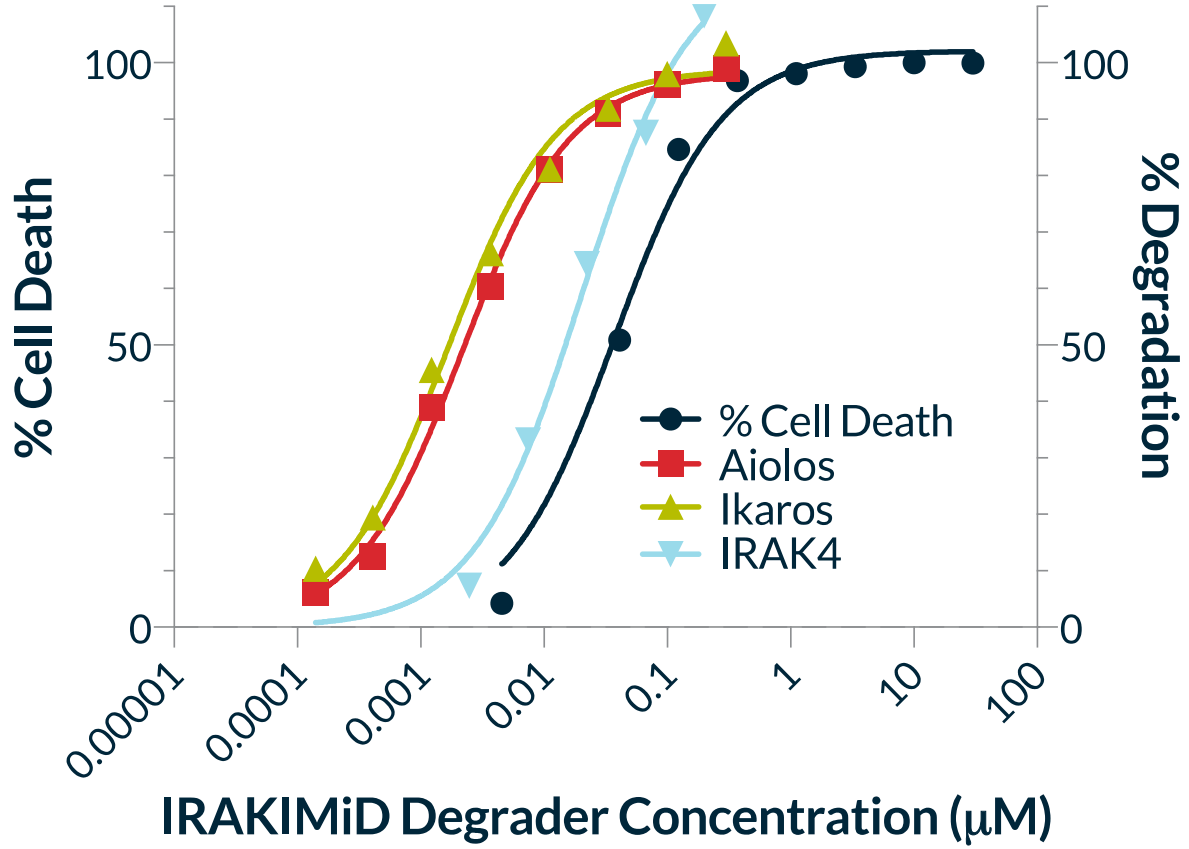
Potential to be first precision medicine in DLBCL to target a genetically defined population (MYD88-mut)

	Patient Impact (U.S.)	
MYD88-mutant DLBCL	**>7.0k** per year	• MYD88 is mutated in at least 25% of DLBCL patients, the most common subtype of non-Hodgkin's lymphoma • 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
Other MYD88-mutant B cell Lymphomas	**>1.0k** per year	• MYD88 is mutated in approximately 90% of **Waldenström's macroglobulinemia** cases and 70% of primary central nervous system lymphoma
Additional Cancers	→	• **IL1R/TLR/NFκB**-driven cancers, AML & MDS subsets with long isoform of IRAK4 (IRAK4L)

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: Selective for MYD88 Tumors Irrespective of Co-mutations

- KT-413 IRAKIMiD DC is a selective and efficient degrader of both IRAK4 and the IMiD substrates
  - *IRAK4 DC_{50} = 8 nM*
  - *Ikaros/Aiolos DC_{50} = 2 nM*
- Degradation leads to cell viability effects **preferentially in MYD88-mutant lines irrespective of other mutational status**
- Data support potential for broadly targeting tumors harboring MYD88 mutations

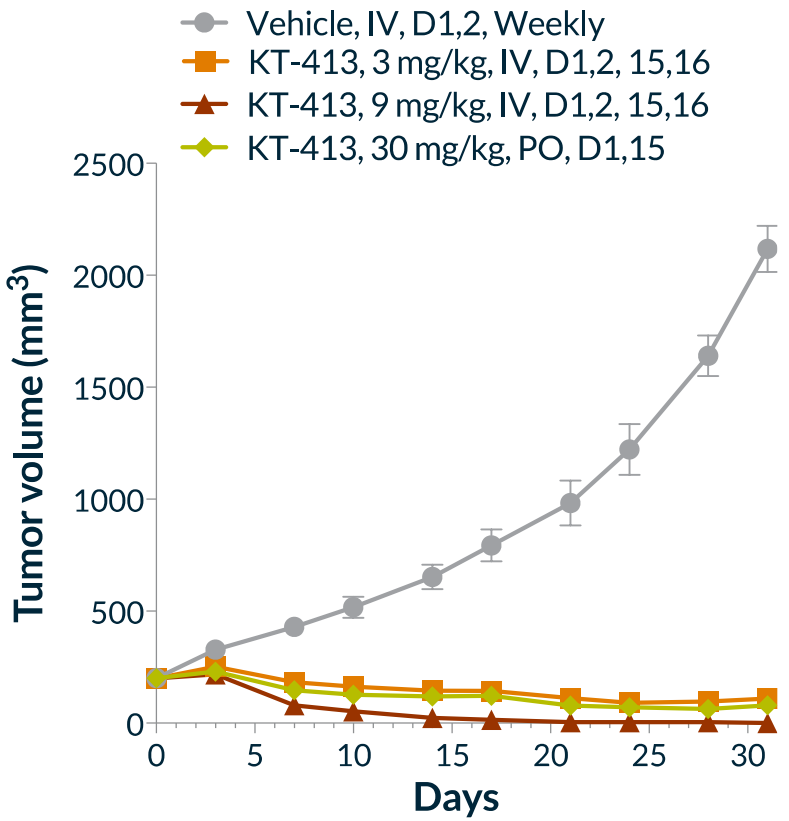
Substrate	DC$_{50}$ nM)
IRAK4	8
Ikaros/Aiolos	2/2

MYD88	Cell Line	Co-mutations	Cell (IC$_{50}$ nM)
mut	OCI-LY10 CTG IC$_{50}$ (nM)	CD79A	7
mut	SU-DHL2 CTG IC$_{50}$ (nM)	TNFAIP3, IRF4, BCL6	14
mut	TMD8 CTG IC$_{50}$ (nM)	CD79A, IRF4	29
Wild type	OCI-LY19 CTG IC$_{50}$ (nM)	None	3,400
Wild type	U2932 CTG IC$_{50}$ (nM)	BCL6	2,600

KT-413: Tumor Regressions from Intermittent Dosing in Preclinical Models

Both PO and IV

- KT-413 is active in both oral and IV dosing in OCI-Ly10 (MYD-88 mut) model
- KT-413 induced tumor regressions (including complete regressions) in intermittent (every other week) dosing regimens
- Significant activity supports potential to be first single-agent therapy for a targeted population in DLBCL



Dose	Schedule	D21 TGI
3 (IV)	D1,2 QW	94%
9 (IV)		99%
3 (IV)	D1,2 Q2W	95
9 (IV)		99%
12 (IV)	D1 Q2W	99%
30 (PO)		96%

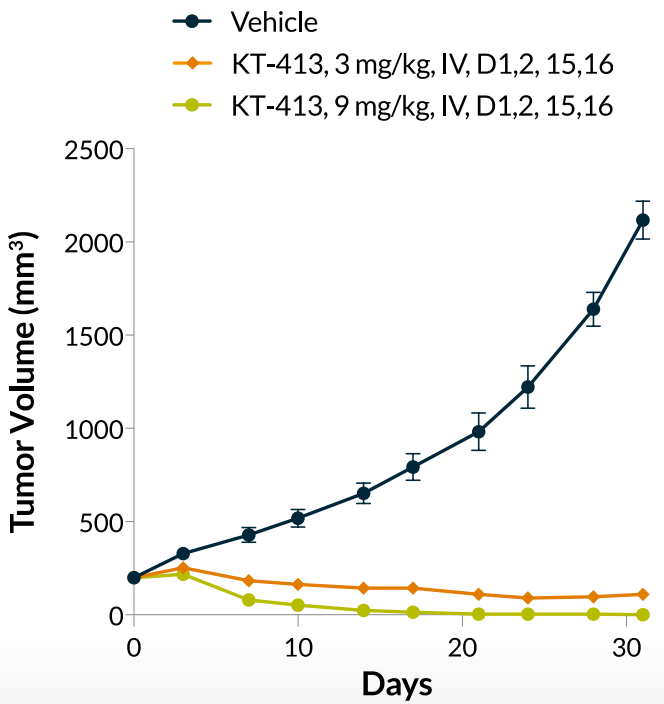
>90% Maximum Degradation of IRAK4 and Ikaros observed at 3 mg/kg D1,2 dosing

PK/PD in NHP is Consistent with Exposure and PD Associated with Efficacy

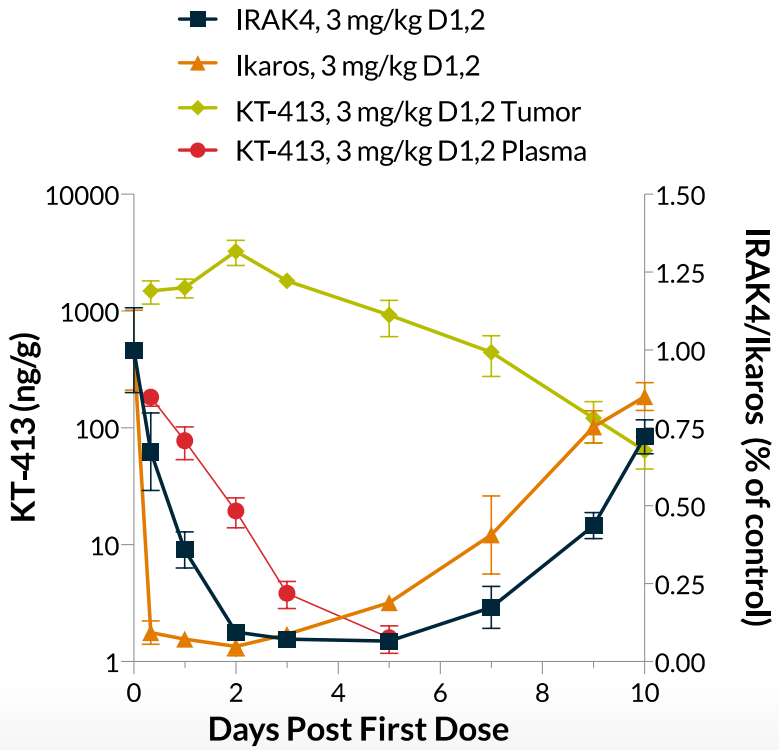
- Efficacy in OCI-Ly10 associated with >75% degradation in IRAK4 and IMiD substrates for >72h on intermittent (Q2W) dosing
- NHP doses on QW and Q2W dosing is associated with almost complete degradation of IRAK4 and IMiD substrates 3 days post dose

Xenograft Efficacy

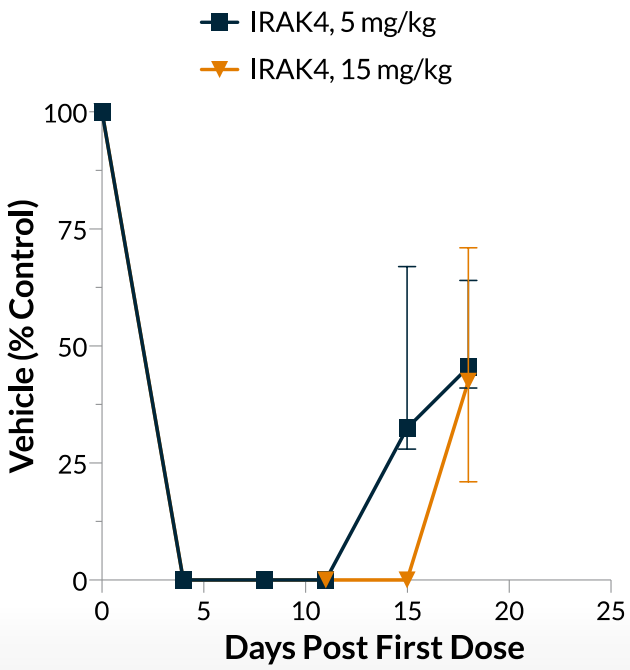
OCI-Ly10



KT-413 IV PK/PD in OCI-Ly10



PBMC PK/PD IRAK4 D1,2,8,9 Schedule



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

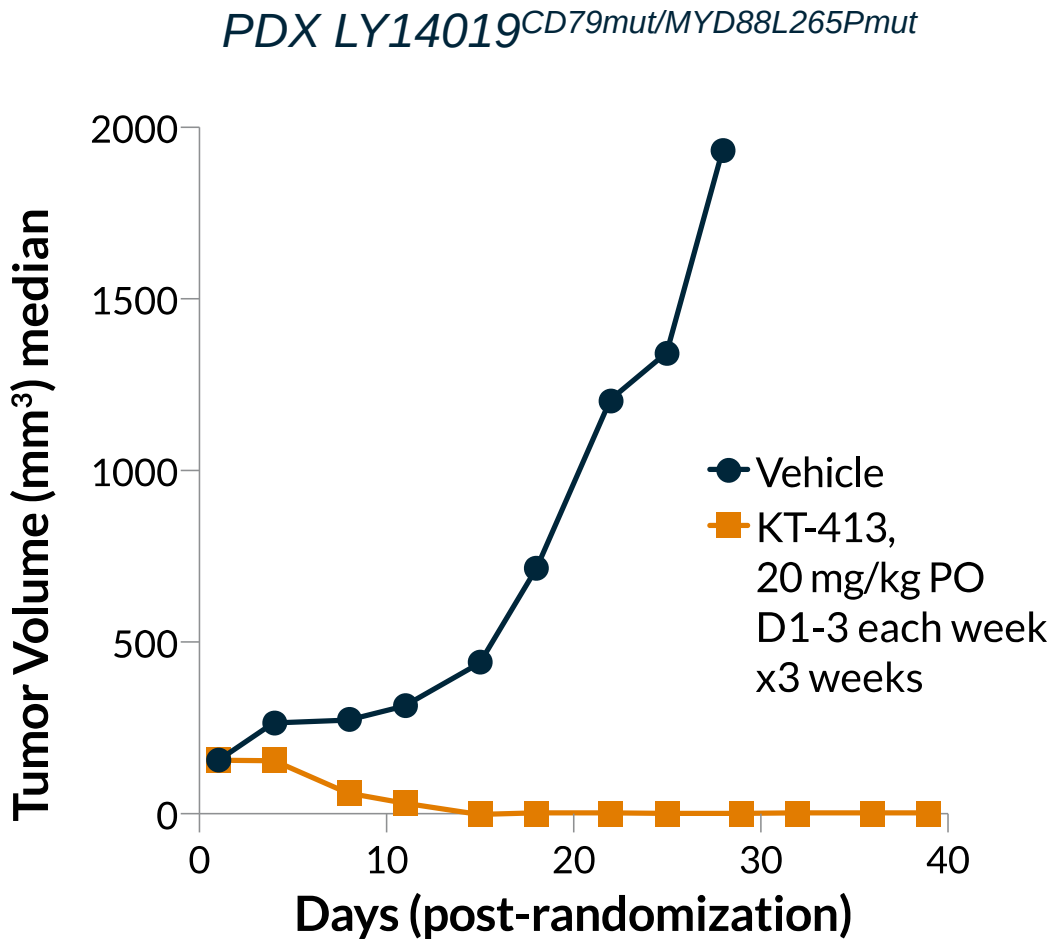
Model	MYD88	CD79B	TNFAIP3	Other	KT-413 (%TGI)
LY14019	L265P	MT	MT		**100**
LY2264	L265P	MT		IRF4	**100**
LY2298	L265P	MT		BCL2/BCL6	**90**
LY12699	L265P	MT			**87**
LY2345	WT		MT		**70**
LY2301	WT				**30**
LY0257	L265P			BCL2/BCL6/IKZF3	**0**

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

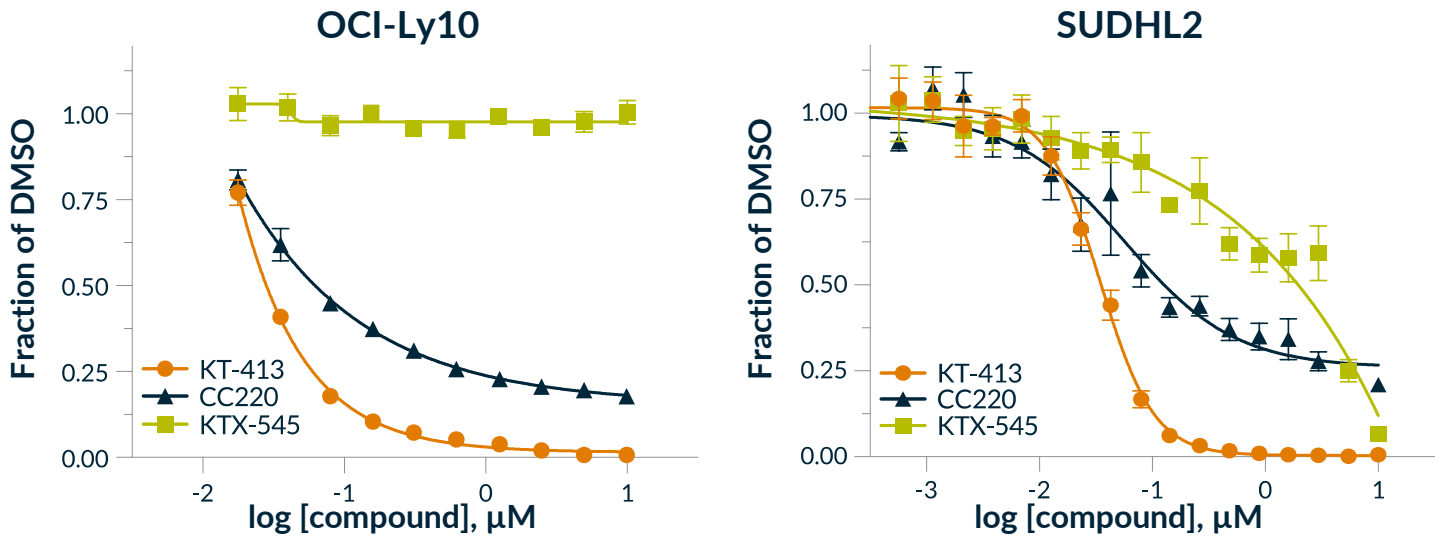
Some level of tumor growth inhibition observed in MYD88-WT PDX

- May be consistent with IMiD activity of KT-413



PDX models run at Crown Biosciences

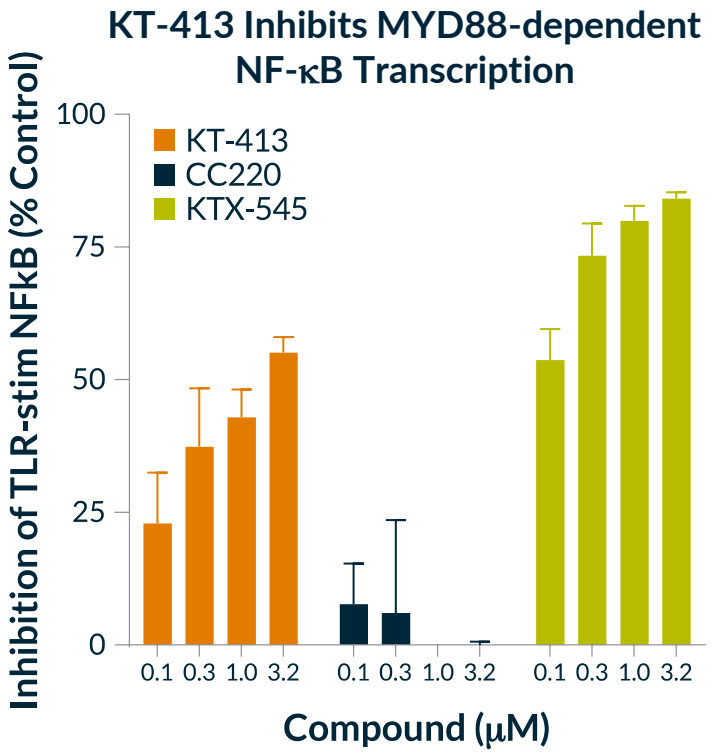
KT-413 is Active in MYD88^{MT} Lymphoma and Shows Greater Activity than either IRAK4-selective Agents or IMiDs Alone

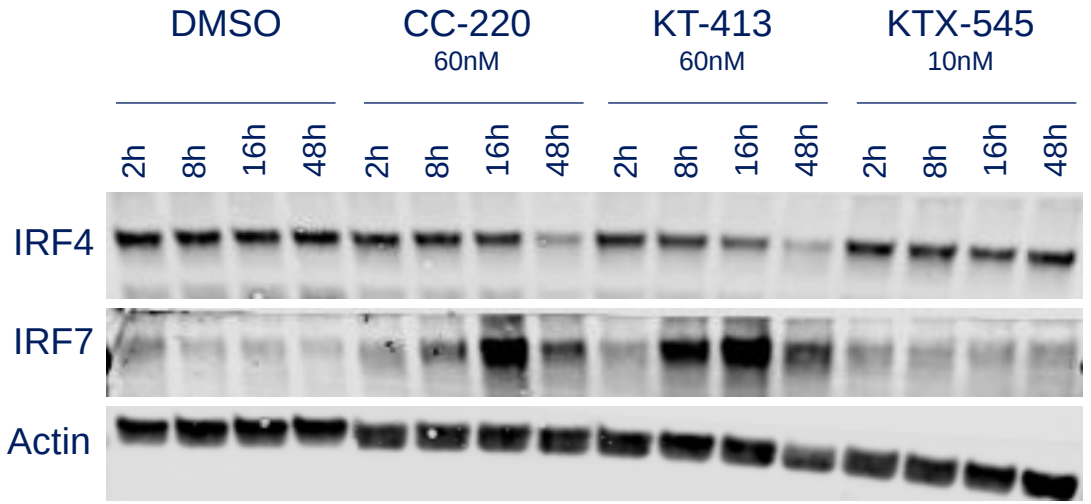


Compound	OCI-Ly10		SUDHL2	
	IC_{50} (nM)	CGI max (%)	IC_{50} (nM)	CGI max (%)
KT-413	28	99.3	35	99.9
CC-220	62	83.2	128	79
KTX-545	- -	5	1960	94

- We have previously disclosed that KT-413 shows strong and broad activity in MYD88 ^{MT} cell lines
- KT-413 is more active in MYD88^{MT} cells than CC220 and KTX-545, both in potency and in the maximal level of CGI achieved
  - In both cell lines KT-413 showed >98% maximal cell growth inhibition, whereas maximum cell growth inhibition by CC220 was <70% in both lines
  - As disclosed by Liu et al (ASH 2020), clinically active CA-4948 showed IC_{50}>3uM in both lines
- IRAK4 and known IMiD substrates (Ikaros [IKZF1], Aiolos [IKZF3], ZNF276) were significantly and selectively degraded
- No other proteins showed substantial and significant degradation

KT-413 Uniquely Inhibits Both IRAK4 and IMiD Dependent Pathways Demonstrating the Dual-targeting Activity of IRAKIMiDs





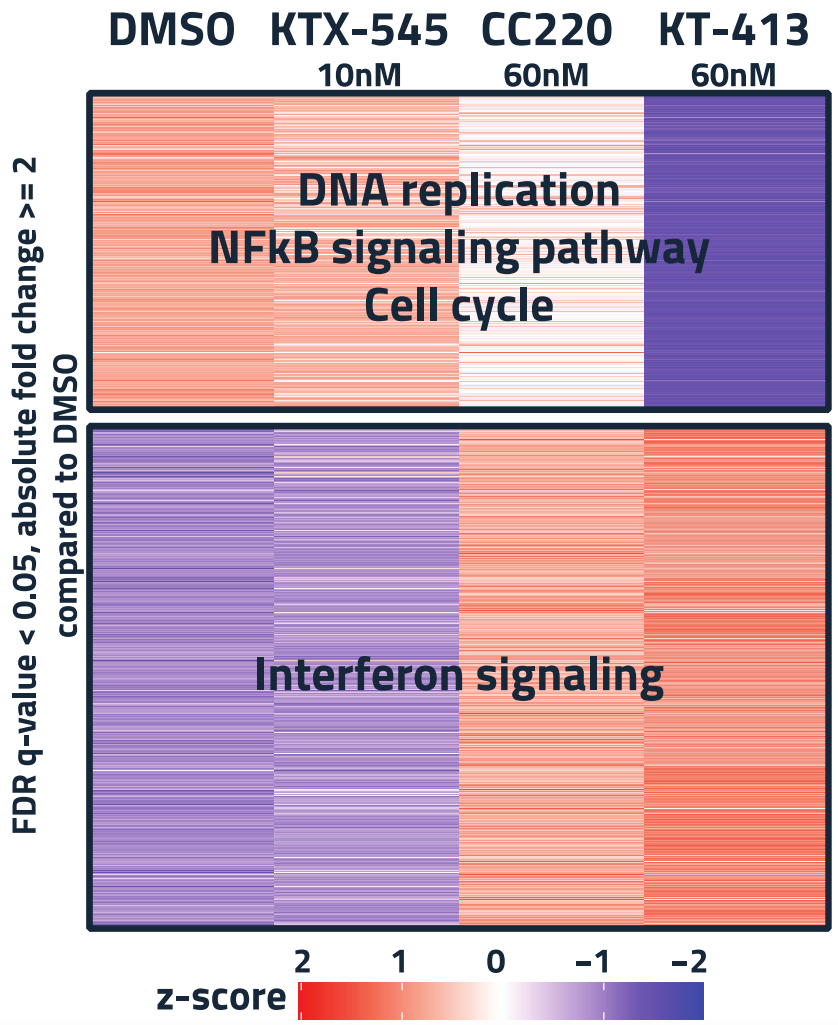
KT-413 and KTX-545 (IRAK4 degrader), but not CC220 inhibited MYD88-dependent NFkB transcription

- THP-1 Dual™ cells with a NFkB reporter were pretreated with KT-413, CC220, and KTX-545 for 24h, then stimulated with LPS for 24 hours in the continued presence of the compounds

KT-413 and CC220, but not KTX-545 activate Type1 IFN signaling in MYD88^{MT} OCI-Ly10 cells

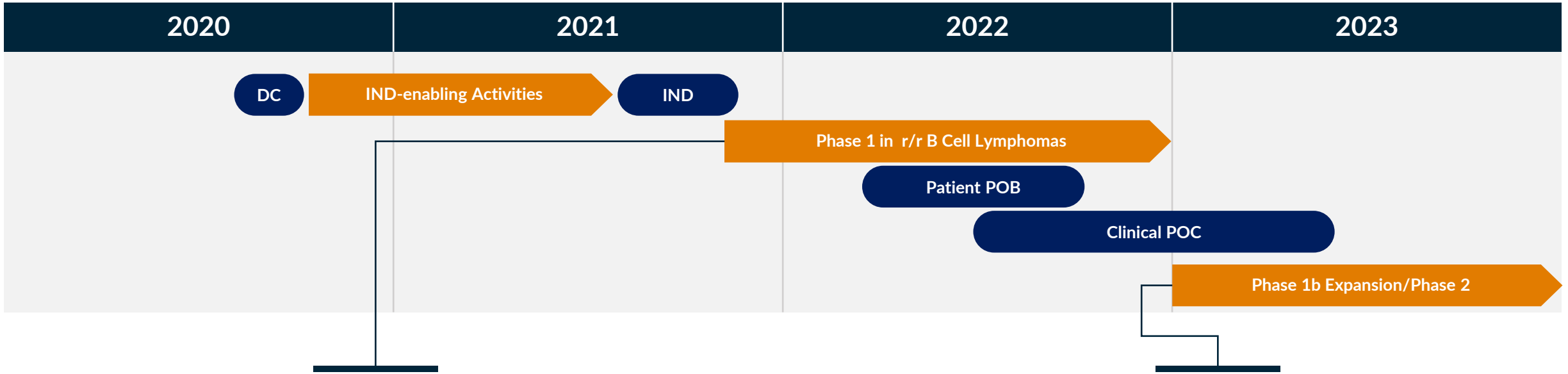
- KT-413 and CC220 downregulate IRF4 and upregulate IRF7, consistent with activation of Type1 IFN signaling in MYD88^{MT} lymphomas

KT-413 Preferentially Downregulates NFkB, Cell Cycle and Upregulates Apoptosis Pathways Compared to IMiDs or IRAK4-selective Degradation



- Genes involved in DNA replication, cell cycle, the NFkB signaling pathway, and phosphoproteins were strongly downregulated by KT-413, but not by CC220 or KTX-545
- KT-413 induced preferential upregulation of interferon signaling
- Preferential downregulation of NFkB and cell cycle pathways and upregulation of IFN signaling and apoptosis signals are consistent with greater and more potent KT-413 activity compared to IMiDs and IRAK4-selective targeting

KT-413 Development Plan



- **Multi-center Phase 1 dose escalation study (US sites) start in 2H21**
- Relapsed/refractory B cell lymphomas, including MYD88-mutant DLBCL
- Objectives include safety, tolerability, PK and PD (proof-of-biology) and preliminary clinical activity
- Clinical and biomarker endpoints

- Phase 1b expansion cohorts in DLBCL (MYD88-mut and –wt) and other MYD88-mut lymphomas, including Waldenstrom's macroglobulinemia and primary central nervous system lymphoma
- Objectives include safety, tolerability and clinical activity of monotherapy and select combinations
- Clinical and biomarker endpoints
- Potential expansion in other indications
- **POB to be presented in 2022**

IRAKIMiD Conclusions

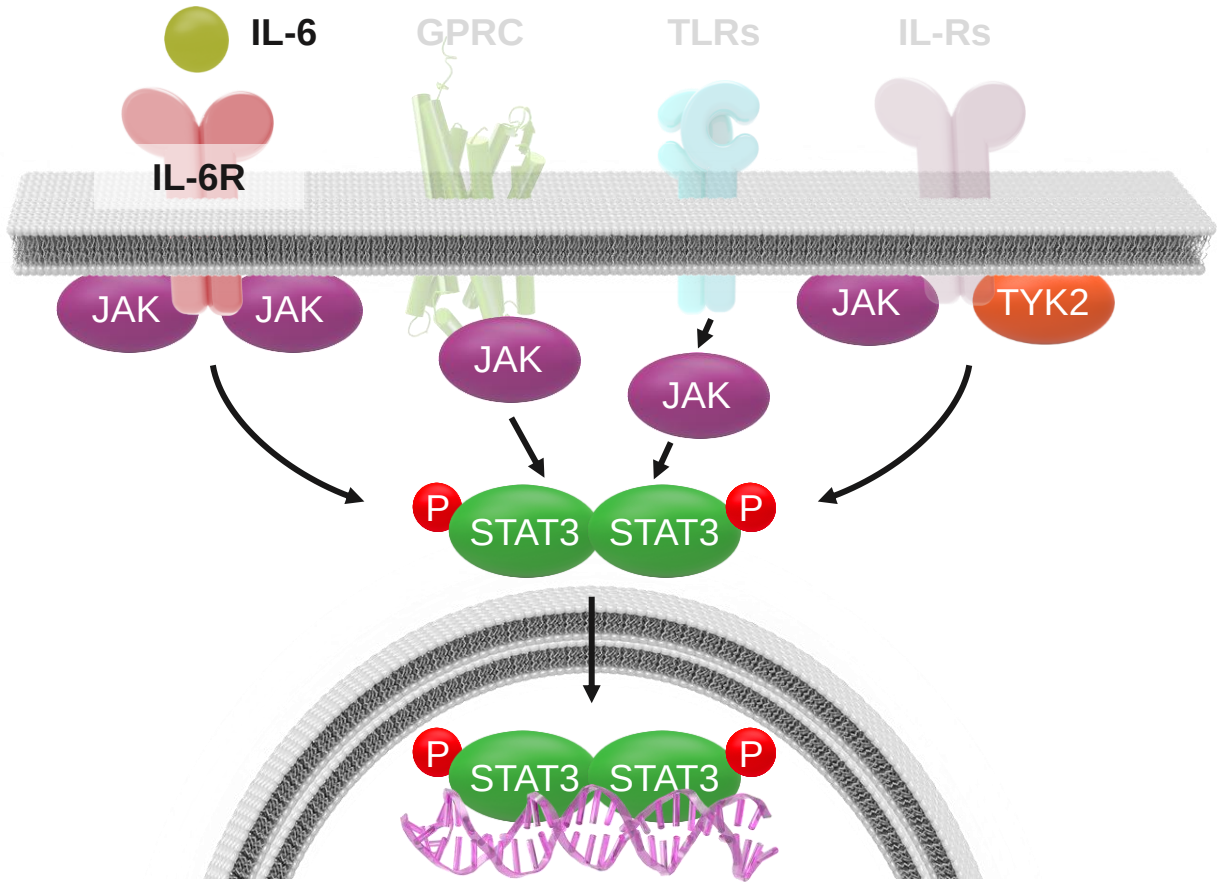
- Degradation of IRAK4 and IMID substrates in a single molecules confers an exclusively potent *in vivo* profile
- Promising DMPK characteristics - can be administered PO and IV, providing potential for flexibility in dosing; initial development in IV formulations
- Potent, selective degrader of IRAK4 and IMiD substrates
- Strong single agent activity in MYD88-MT DLBCL with strong tumor regressions in multiple models support potential for clinical responses as a single-agent in a selected population
- *In vivo* activity in both PO and IV schedules with intermittent dosing as little as QW or Q2W (D1 or D1,2) is efficacious
- Activity across multiple MYD88 CDX and PDX models, with different co-mutations, with complete and durable tumor regressions in several models
- Initial development for KT-413 is focused in MYD88-MT DLBCL as the potential first targeted agent in this patient population, to begin clinical development in 2H 2021, while further development opportunities are being prioritized

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

Nomination of development candidate: 1Q 2021 ✓

IND/Phase 1 initiation: 4Q 2021

Phase 1 proof-of-biology 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
Peripheral T-cell Lymphoma

>2.0k per year
Cutaneous T-cell Lymphoma

>200.0k per year
NSCLC

I/I Fibrosis

>40.0k
Systemic Sclerosis

>11.0M
Atopic Dermatitis

>40.0k
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

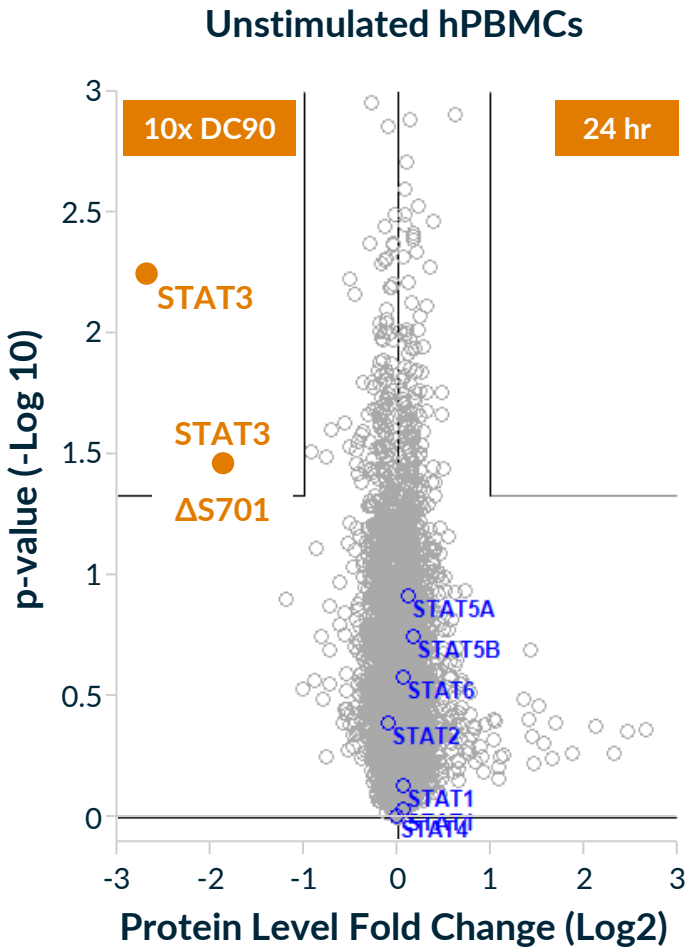
Chronic inflammation / fibrosis
Idiopathic pulmonary fibrosis, CKD/renal fibrosis

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**

STAT3 Degradation and Downstream Effects Across Tumor Cells

CANCER

Liquid Tumors

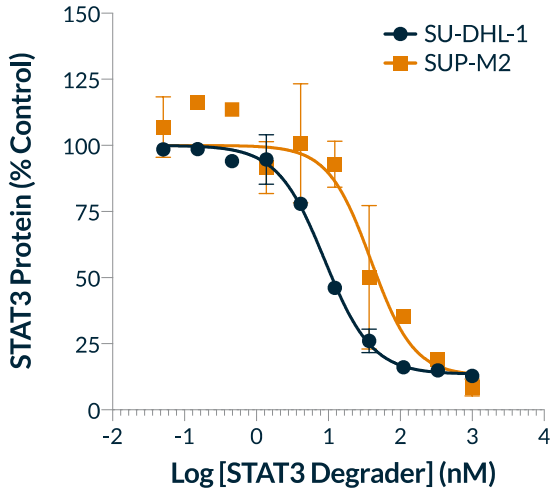
Solid Tumors

I/I FIBROSIS

Autoimmune

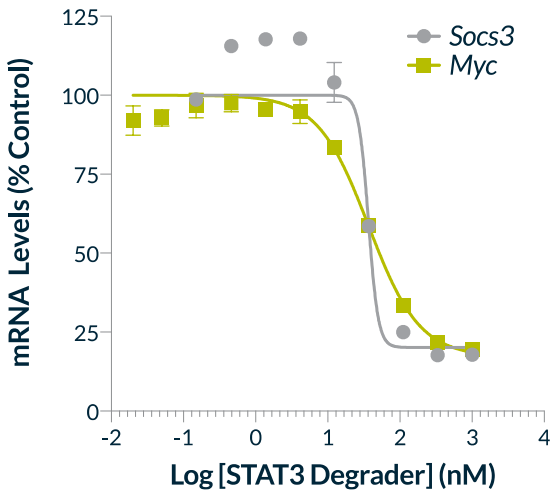
Fibrosis

STAT3 Degradation



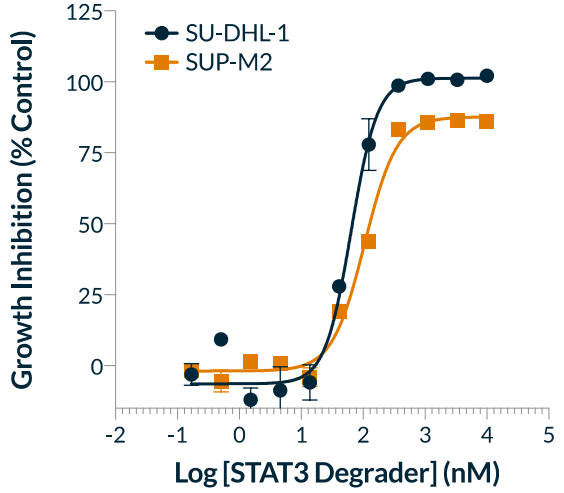
- STAT3 protein levels measured in two STAT3-dependent cell lines
- STAT3 degrader decreased levels of STAT3 by greater than 95% with DC_{50} of 15nM and 86 nM, respectively

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



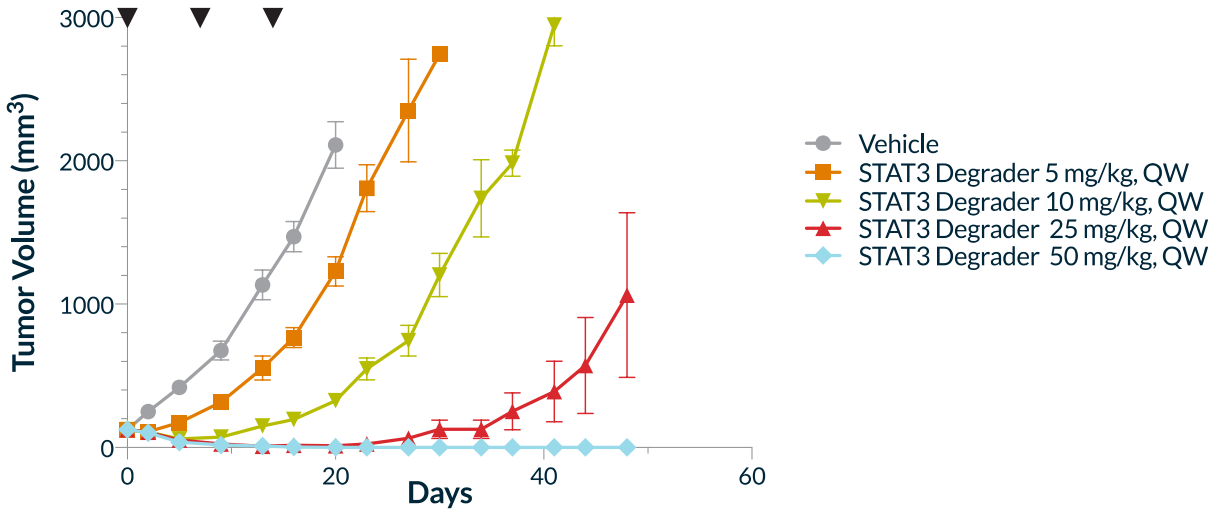
- Impact of STAT3 degradation on viability of lymphoma cells measured
- Inhibited growth of SU-DHL-1 and SUP-M2 cells with IC_{50} values of 64 and 105 nM, respectively

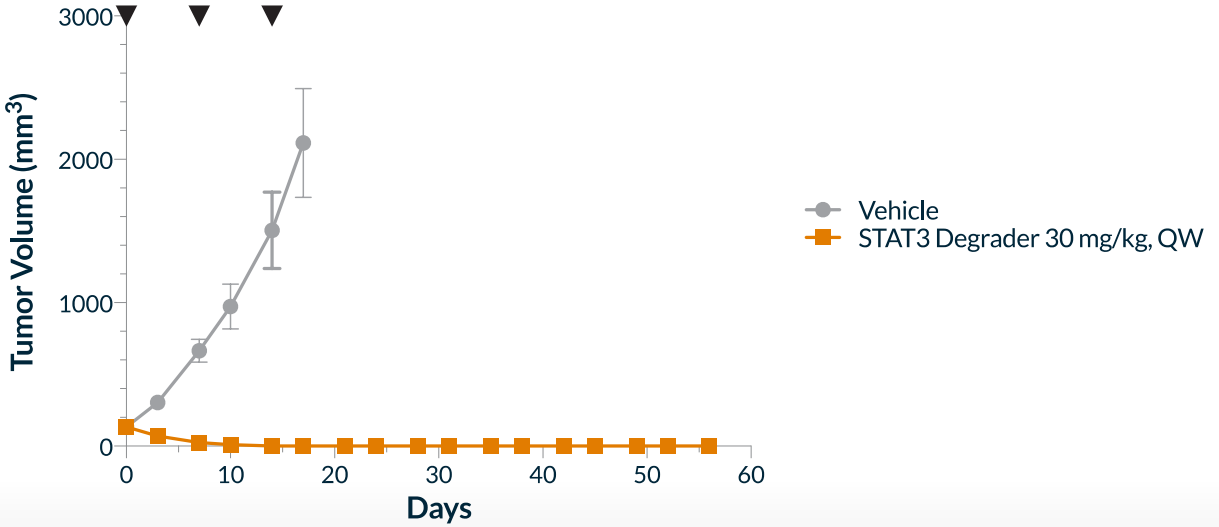
Full and Durable Regressions Across Multiple *in vivo* Preclinical Tumor Models

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





Effects of STAT3 Degradation on Tumor Microenvironment

CANCER

Liquid Tumors

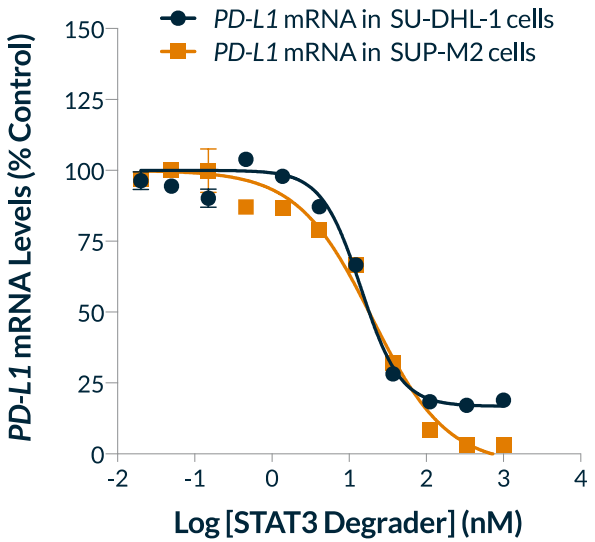
Solid Tumors

I/I FIBROSIS

Autoimmune

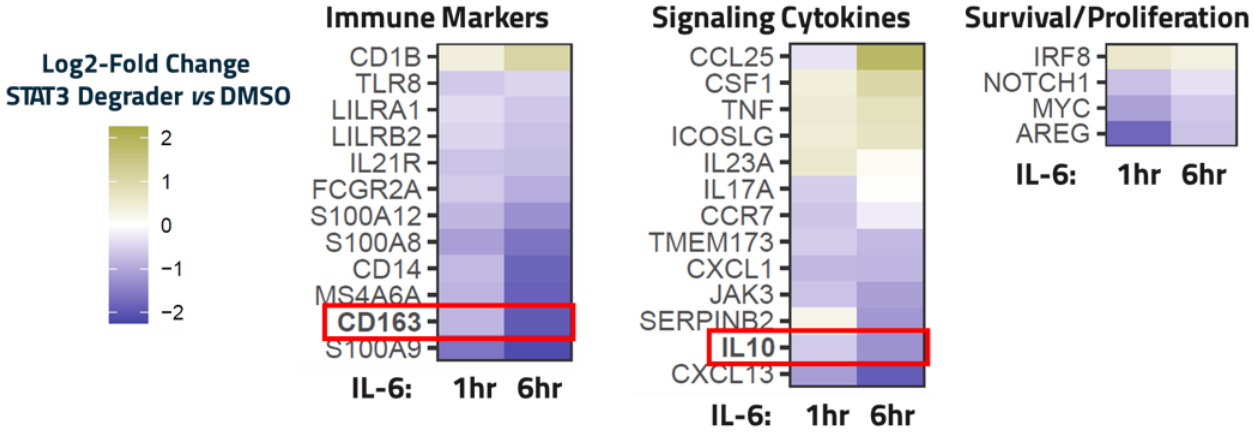
Fibrosis

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



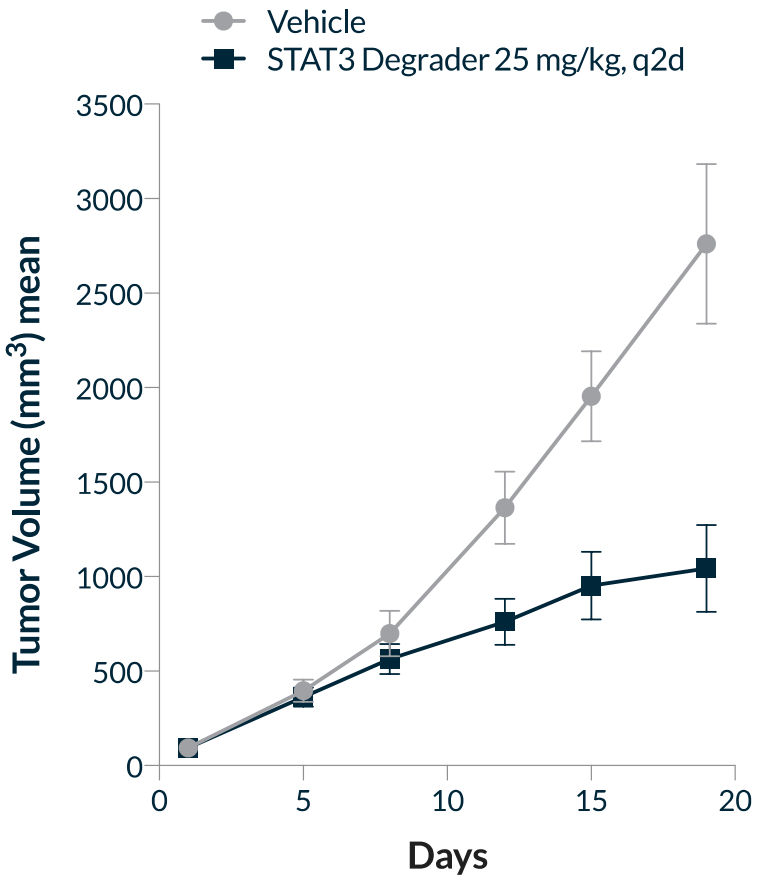
- STAT3 degrader blocked IL-6-induced increases in gene expression in hPBMC
- Data suggest degradation of STAT3 reverses expression of genes contributing to immune suppression

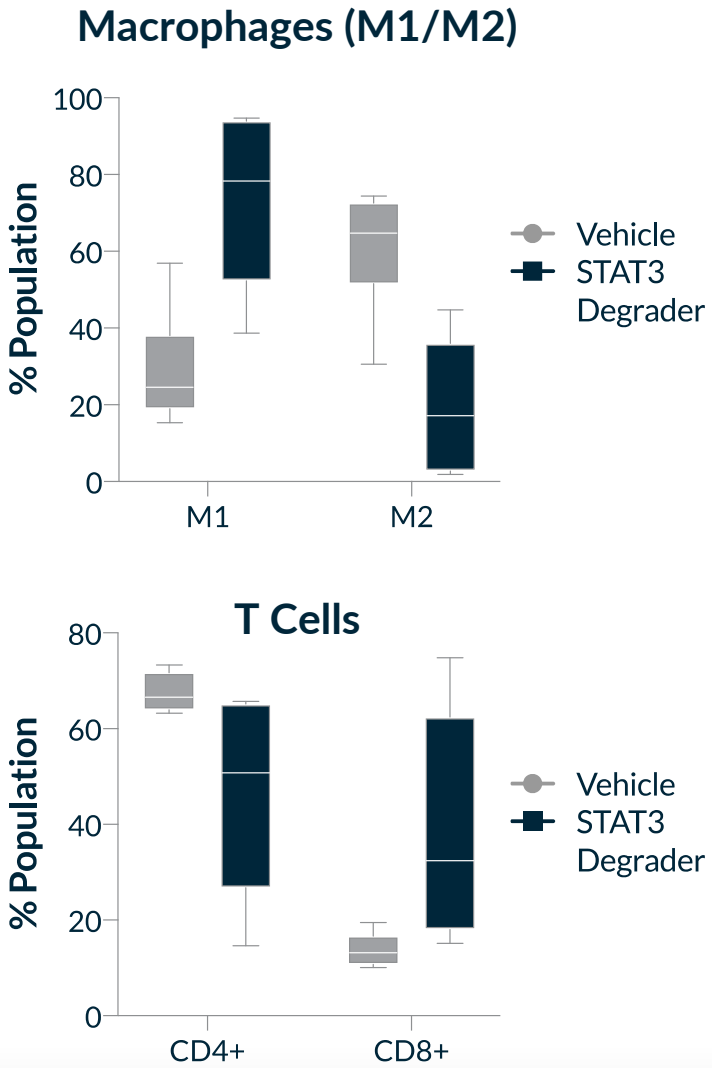
STAT3 Degrader *In Vivo* Active in Preclinical PD-1/L-1 Refractory Solid Tumor Model

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





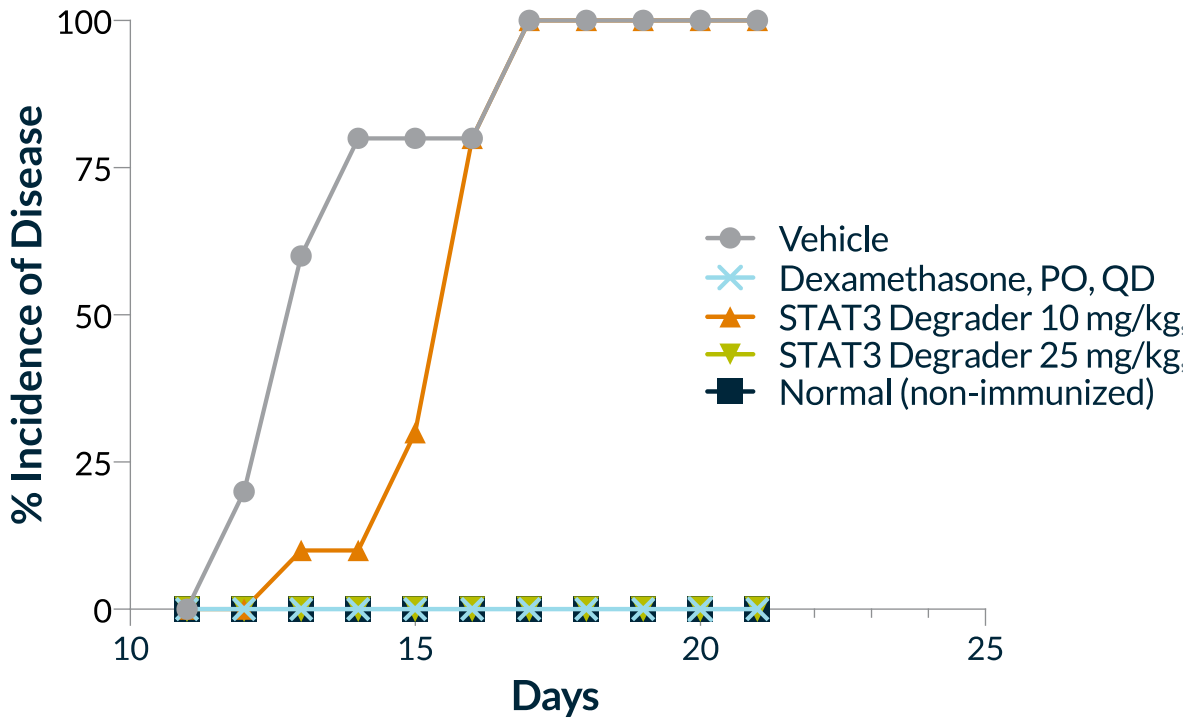
STAT3 Degrader Active in T Cell Activation Preclinical *In Vivo* Model

Multiple Sclerosis Model

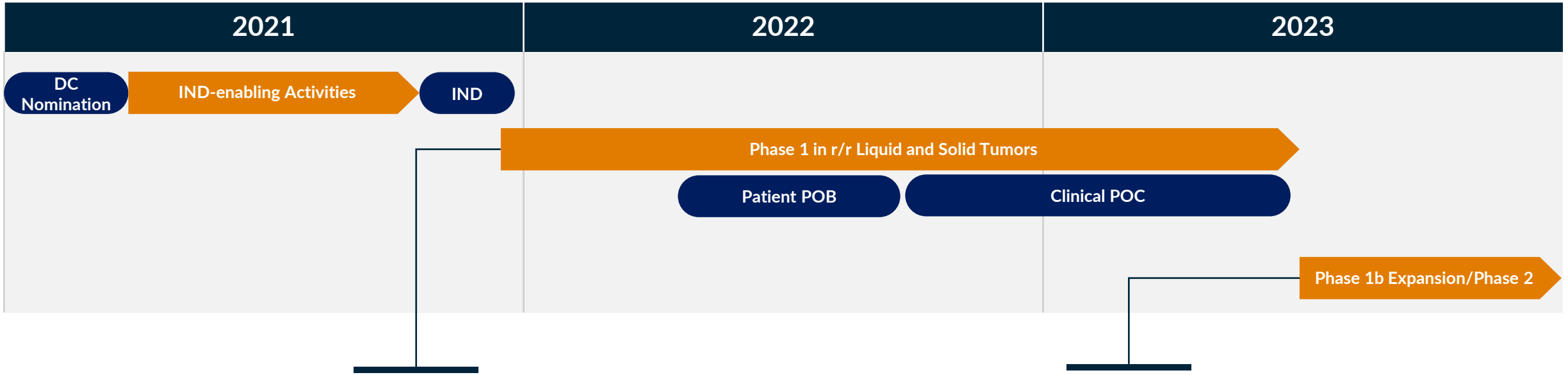
CANCER
- Liquid Tumors
- Solid Tumors

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 Degrader Development Plan in Liquid & Solid Tumors



- **Multi-center Phase 1 dose escalation study start in 4Q21**
- Safety, tolerability, PK and PD (proof-of-biology) and preliminary clinical activity
- Clinical and biomarker endpoints

- Phase 1b expansion cohorts in STAT3-dependent liquid tumors
- Objectives include safety, tolerability and clinical activity of monotherapy and select combinations
- Separate Phase 2 in solid tumors
- **POB to be presented in 2022**

Corporate Summary

KYMERA

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

Financial Summary

Well positioned to advance a leading TPD pipeline

Financial Highlights

- Over $600 million raised to date (equity and partnership)
- $220 million from partnerships upfronts
- IPO priced August 2020 at $20
- 44.8 million shares outstanding (2/26/2021)

Q4'20 Results

- Collaboration Revenues: $12.8 million
- R&D Expenses: $20.4 million
- G&A Expenses: $5.2 million
- Net Loss: $12.7 million

Cash and Financial Guidance

- $458.7 million in cash, cash equivalents and investments at Dec. 31, 2020
- Expect cash, cash equivalents, and investments to fund operational plans into 2025, excluding any future potential milestones from collaborations, while the Company continues to identify opportunities to accelerate growth and to expand pipeline, technologies and clinical indications

Near-Term Milestones Provide Significant Opportunity

Program	Compound	Indication(s)	Expected Upcoming Milestones
IRAK4	KT-474	AD, HS, RA, others	✔ Initiate SAD portion of Phase 1 trial in healthy volunteers (1Q 2021) • Present updated Non-Interventional trial results (2Q21) • Present KT-474 preclinical data vs. kinase inhibitors in immune-inflammatory preclinical models (2Q21) • Initiate enrollment in MAD portion of Phase 1 trial in HV, as well as AD and HS patients (2H21)* • Establish Phase 1 proof-of-biology in healthy volunteers (4Q 2021)
IRAKIMiD (IRAK4, Ikaros, Aiolos)	KT-413	$MYD88^{MT}$ DLBCL	✔ Presentation of KT-413 mechanism of action at the AACR Annual Meeting (April 2021) • Submit IND and, if cleared, initiate Phase 1 clinical trial in r/r B cell lymphomas (2H21) • Present additional KT-413 preclinical data and potential expansion strategies (2H21) • Establish Phase 1 proof-of-biology in patients (2022) • Establish Phase 1 initial clinical proof-of-concept in patients (2022)
STAT3	KT-333	Liquid & Solid Tumors	✔ Nominate development candidate for liquid & solid tumor indications (1Q21) • Present additional preclinical data in liquid & solid tumor indications (2021) • Submit IND, and if cleared, initiate Phase 1 clinical trial (4Q21) • Establish Phase 1 proof-of-biology in patients (2022) • Establish Phase 1 initial clinical proof-of-concept in patients (2022)
Discovery Programs & Platform			• Continue pipeline expansion by advancing early-stage discovery programs toward IND-enabling studies • Further expand Pegasus platform to generate novel degrader product candidates • Leverage Whole-Body Atlas to unlock new opportunities across broad therapeutic applications

● = Oncology ● = Immunology-Inflammation

* Initiation of MAD portion of Phase 1 trial is on partial clinical hold pending FDA review of interim SAD data.

THANK YOU

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Appendix

Non-Interventional Study: Trial Design and Baseline Demographics

Design

Number of Sites	Single center (York Dermatology Clinic and Research Center, Ontario, Canada) PI: Dr. Afsaneh Alavi, MD, MSch, FRCPC
Number of Patients	40 (30 HS and 10 AD)
Inclusion Criteria	1. Age 18 or older 2. Active Hidradenitis Suppurativa (HS) or Atopic Dermatitis (AD), diagnosed by PI 3. Mild, moderate, and severe HS patients (by IHS4 score), and moderate to severe AD (by EASI score)
Exclusion Criteria	1) Patients currently on a biologic or other immunosuppressive treatment for HS or AD 2) Use of biologic treatment for HS or AD within 3 months or 5 half-lives, whichever is longer 3) Use of non-biologic immunosuppressive treatment (eg. Cyclosporin) in the last 4 weeks.
Data Collection at Study Entry	Medical history, disease severity in HS (Hurley, PGA, IHS4, HASI) and AD (EASI), prior treatments, comorbidities, duration of disease
Sample Collection	Whole blood, plasma, skin (lesional, peri-lesional, non-lesional)

Baseline Demographics & Biomarkers

Study Duration	• FPI: 28May2020 • HS accrual completed; enrollment of AD patients ongoing
Patients Enrolled to Date	• 30 HS: 9 mild, 10 moderate, 11 severe • 2 AD
Demographics	• Age 19-56 yrs • 9 male, 23 Female • Duration of disease: 1-38 years • Race: 97% were non-Hispanic or Latino
Biomarker Endpoints	• Flow cytometry for IRAK4 in ex vivo treated whole blood • Targeted MS of IRAK4 in skin biopsies • IRAK4 immunofluorescence in skin biopsies • Cytokines from ex vivo treated whole blood • Plasma cytokines and acute phase reactants • Cytokines in skin biopsies

IRAKIMiDs Superior to IRAK4 Inhibition and IMiD Single Agents

- MYD88-mutated ABC-DLBCL cell lines OCI-Ly10 and SUDHL2 evaluated in a 4-day viability assay
- Activity of IRAKIMiD compared to an IMiD compound alone and IRAK4 kinase inhibitor alone assessed
- IRAKIMiD degrader (IC_{50} = 31 nM) significantly more selective and efficient than IRAK4 SM kinase inhibitor or a third generation clinically active IMiD CC-122 in cell viability