KYMERA
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INVENTING NEW MEDICINES

WITH TARGETED PROTEIN DEGRADATION

KT-474 Phase 1 Clinical Trial Update

June 28, 2021

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Kymera: A Leading TPD Company

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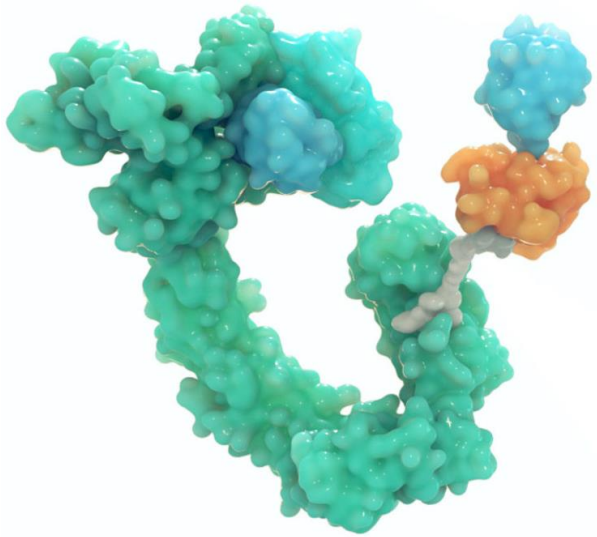
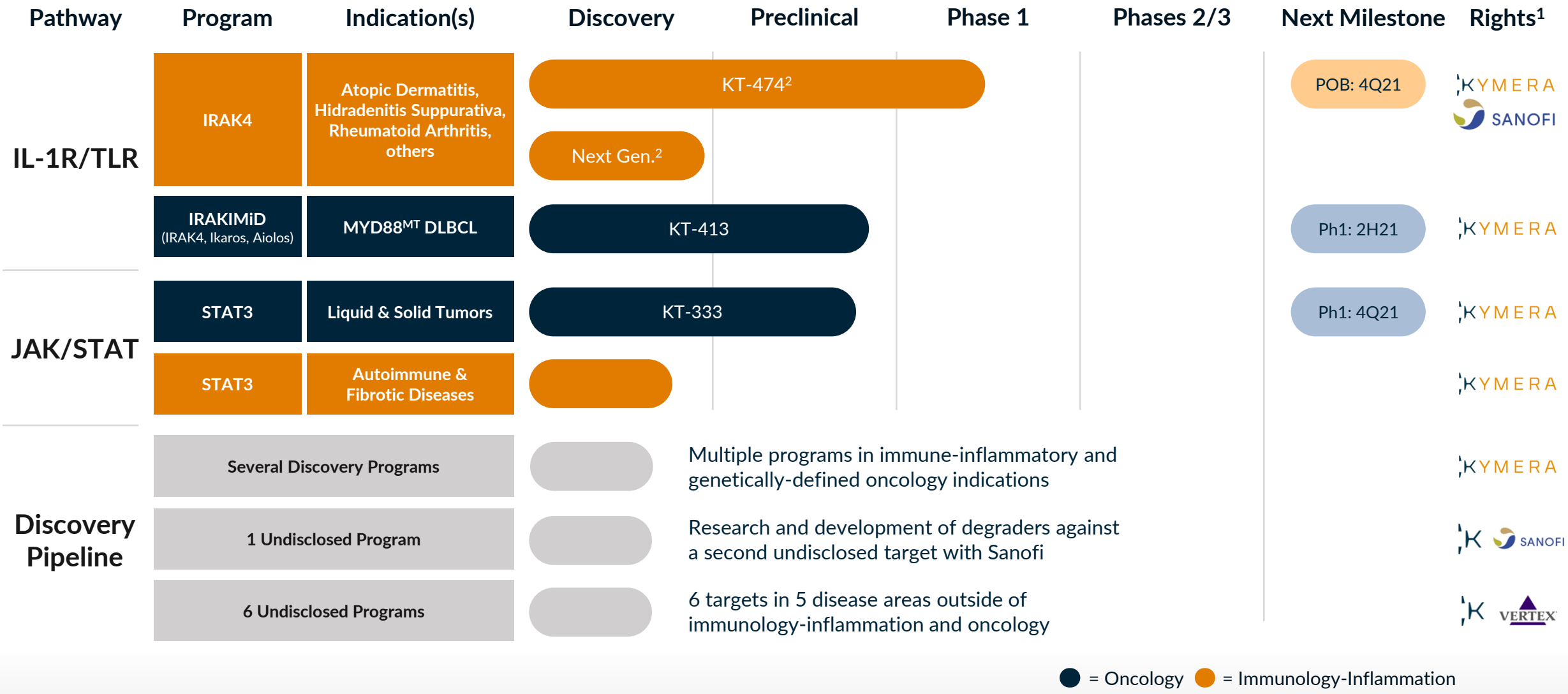


VISION	Fully integrated, **disease agnostic** protein degrader medicine company
KEY PARTNERSHIPS	SANOFI VERTEX gsk
INITIAL FOCUS	**Immune inflammation (I/I)** and **oncology**
FIRST-IN-CLASS	**First** to show **placebo-controlled** degrader **proof-of-mechanism**
CLINICAL PIPELINE	**2** additional **INDs** and clinical initiations expected by end of **2021**
PROOF-OF-BIOLOGY	To be established in humans in **2021**
WELL-POSITIONED	**$435M** cash balance at **Q1 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.

Near-Term Milestones Provide Significant Opportunity

Program	Compound	Indication(s)	Expected Upcoming Milestones
IRAK4	KT-474	AD, HS, RA, others	✓ Initiated SAD portion of Phase 1 trial in healthy volunteers (Feb 2021) ✓ 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) • Present data from atopic dermatitis cohort in non-interventional study (2H21) • Establish Phase 1 proof-of-biology in healthy volunteers (4Q21) and in patient cohort (1H22)
IRAKIMiD (IRAK4, Ikaros, Aiolos)	KT-413	$MYD88^{MT}$ DLBCL	✓ Presentation of preclinical data updates at AACR, ICML meetings (2Q21) • Submit IND to 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	✓ Nominated development candidate for liquid & solid tumor indications (1Q21) • Present additional preclinical data in liquid & solid tumor indications (2H21) • Submit IND to initiate Phase 1 clinical trial in liquid and solid tumors (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

IRAK4 Degrader KT-474

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

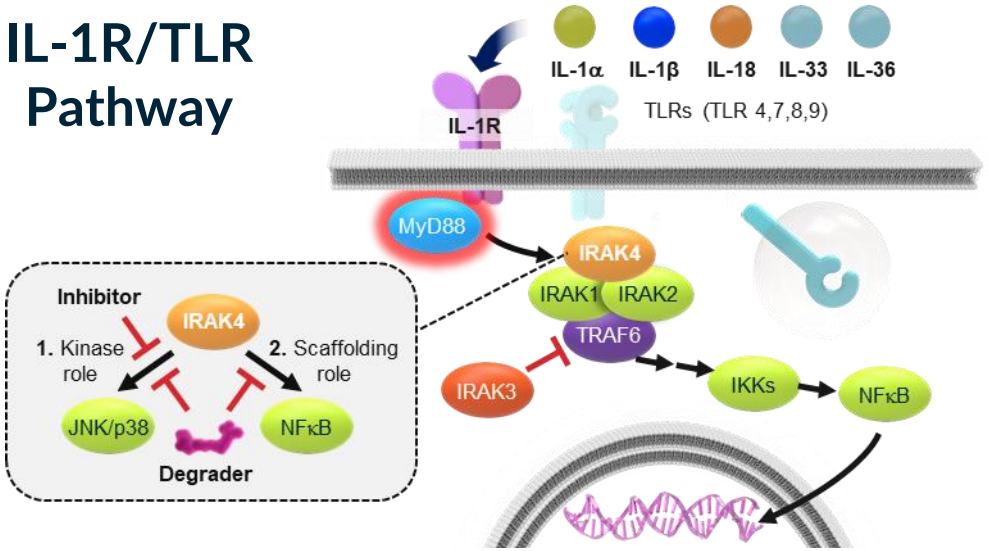
Unmet Medical Need

Validated Biology

Undrugged Node

Precision Medicine Approach

IL-1R/TLR 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

- IRAK4 is a key component of the myddosome protein complex involved in innate immunity that mediates signals through IL-1R and TLRs
- Several commercial and clinical stage drugs have validated this pathway in multiple diseases
- Degrading IRAK4, and fully blocking IL-1R/TLR signaling, is expected to be superior to antibody-based therapies that block only single cytokines, with convenience of a daily oral therapy
- IRAK4 degradation can block pathway fully vs kinase inhibitors that partially block signaling
- Human genetics de-risk safety: adults that lack IRAK4 are healthy

KT-474 Opportunity

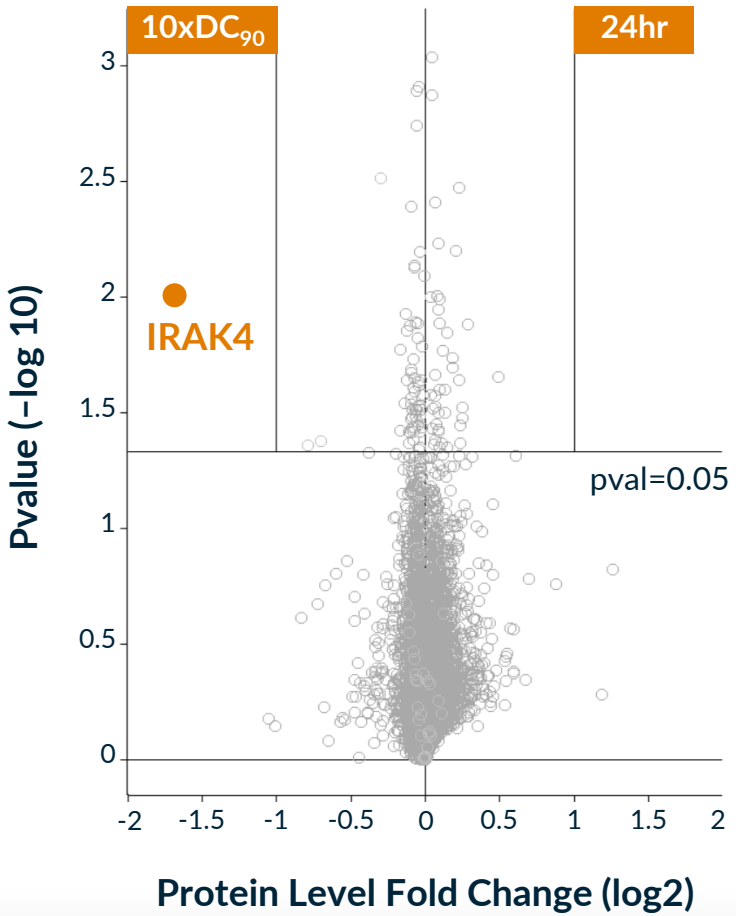
Immune-inflammatory disorders collectively impacting millions of patients in the U.S.

	Total Prevalence (U.S.)	
Atopic Dermatitis (AD)	>16.0M[1]	• Chronic, pruritic **inflammatory skin disease** • Large unmet need for safe and effective oral agents for patients with AD
Rheumatoid Arthritis (RA)	>1.3M[2]	• Chronic, systemic **autoimmune disease** that can cause irreversible joint damage • Multiple therapies targeting the **IL-1R/TLR pathway** are approved
Hidradenitis Suppurativa (HS)	>325K[3]	• Chronic and debilitating inflammatory skin disease • **~25%** of patients with moderate-to-severe disease[4] • Adalimumab is approved, which provides some benefit to **~50% of patients** with moderate-to-severe disease[5]
Additional Opportunities	→	• Immune-inflammatory diseases impacted by **IL-1R/TLR pathway**

1. Chiesa Fuxench et al. J Invest Dermatol. 2019 Mar;139(3):583-590.
2. Hunter et al. Rheumatol Int . 2017 Sep;37(9):1551-1557.
3. Garg et al. JAMA Dermatol. 2017;153(8):760-764.
4. Calao et al. PLoS One. 2018; 13(7): e0200683.
5. Kyriakou et al. Dermatol Reports. 2018 Oct 1; 10(2): 7859.

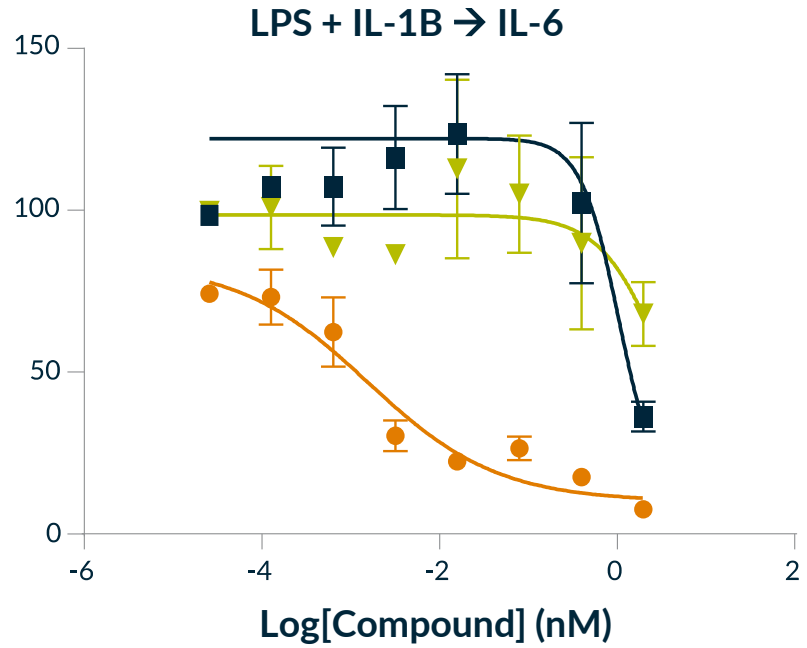
KT-474: Potent and Specific IRAK4 Degradation Superior to Kinase Inhibition

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-1B than clinically active IRAK4 SM kinase inhibitor PF-06550833

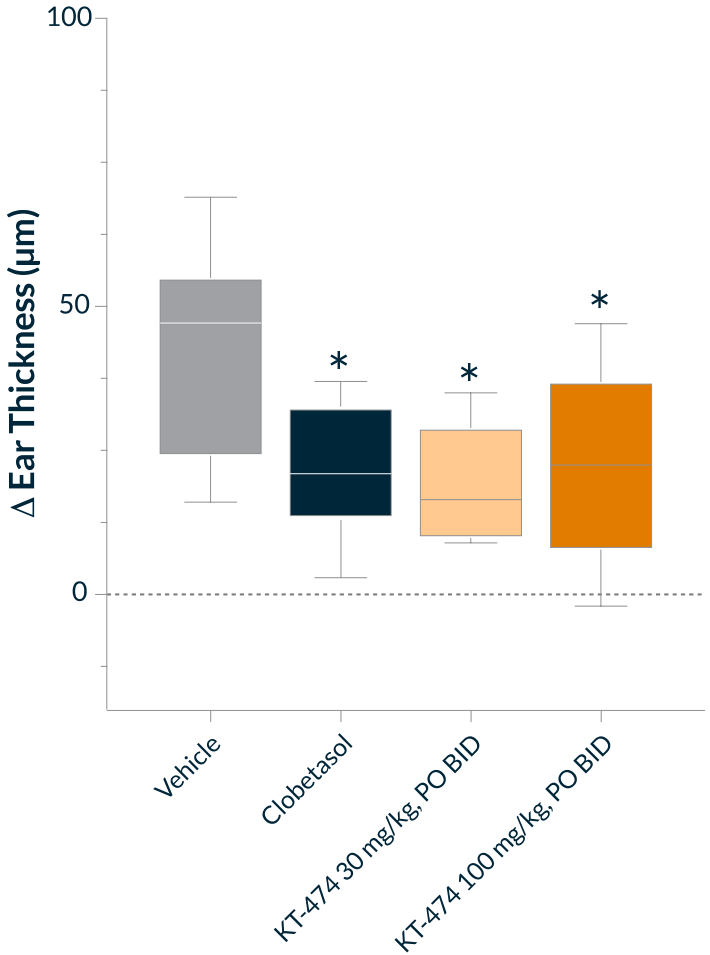
Superiority over SM kinase Inhibitor

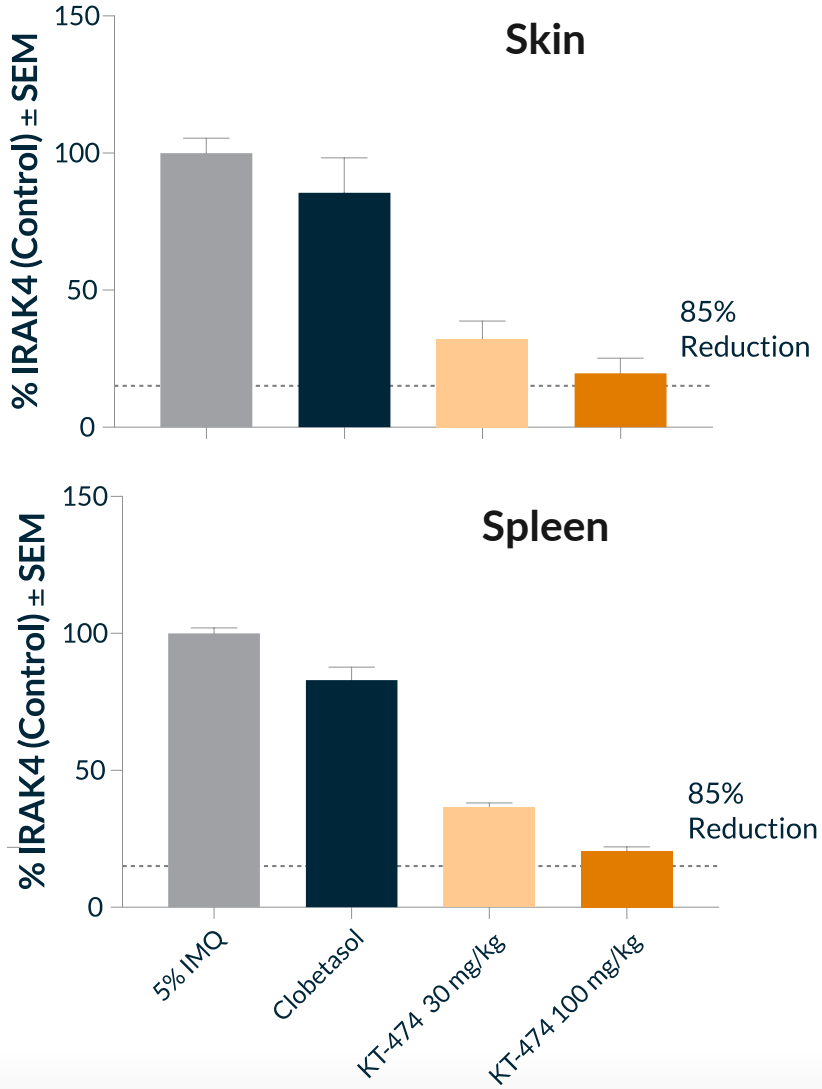


Legend	Compound	IL-6 IC_{50} (nM)
	IRAK4 Degrader	0.8
	Negative control	450
	IRAK4 SMI *(PF-06550833)*	N/A

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

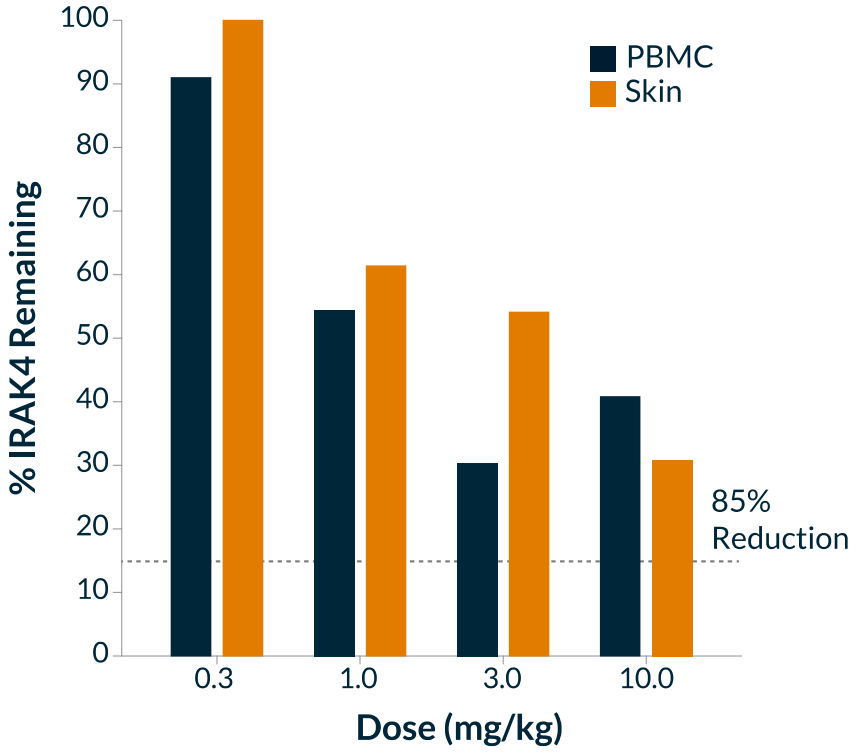




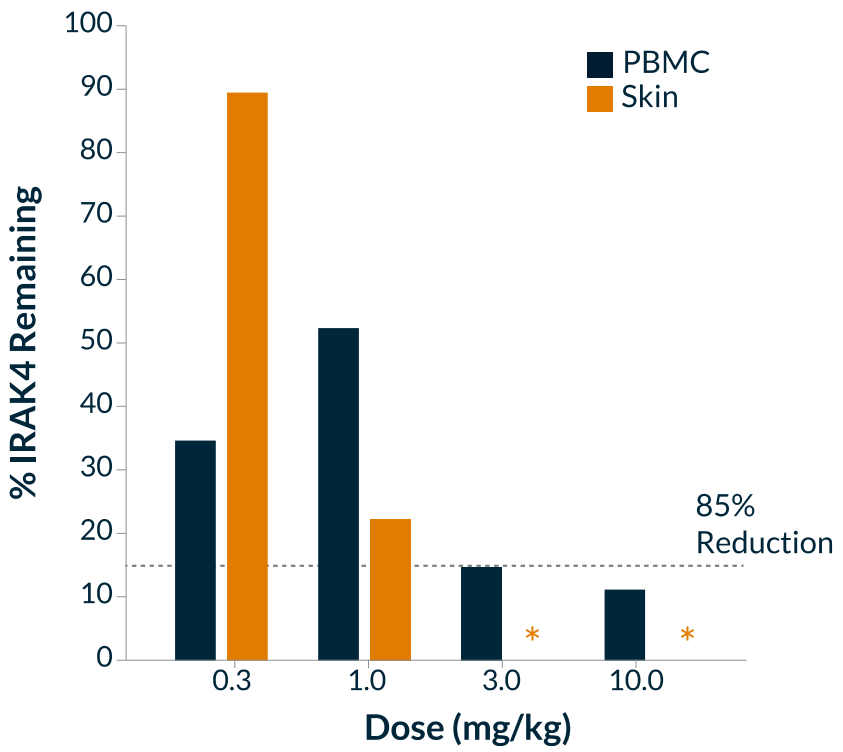
KT-474 in Dog: Multi-dosing Required to Achieve Target Degradation

- Orally-administered KT-474 achieves >85% knockdown of IRAK4 at Day 7 with repeat dosing in MAD study
- Multiple doses (MAD) lead to optimal degradation profile vs SAD upon reaching steady-state
- Consistency of IRAK4 knockdown observed across peripheral blood mononuclear cells (PBMC) and skin tissue

Dog Single Ascending Dose (SAD)
IRAK4 Knockdown at Day 1



Dog Multiple Ascending Dose (MAD)
IRAK4 Knockdown at Day 7



* = Below Limit of Quantitation

KT-474 Interim Phase 1 SAD Results

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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
MAD only

- IRAK4 knockdown in skin biopsies
- Proinflammatory cytokine and chemokine levels in skin biopsies
- C-reactive protein and cytokine levels in plasma
- *Ex vivo* response of whole blood to TLR agonists and IL-1β

KT-474 Phase 1 Trial Goals

Establishing proof-of-mechanism and proof-of-biology

De-risking Milestones

1
SAD Portion
Healthy Volunteers

Oral Bioavailability and Proof-of-Mechanism

- Efficacious plasma exposures that are safe and well-tolerated
- Proof-of-mechanism with IRAK4 knockdown following single KT-474 dose
- Predictable PK/PD supporting oral daily dosing regimen

2
MAD Portion
Healthy Volunteers

Optimal IRAK4 Reduction and Proof-of-Biology

- ≥85% IRAK4 knockdown in skin and blood with daily dosing x 14 days that is safe and well-tolerated
- Proof-of-biology with systemic anti-inflammatory effect: reduction in plasma hsCRP and inhibition of whole blood *ex vivo* response to TLR agonists and IL-1β
- Establishment of maximum effective dose

3
MAD Portion
Patient Cohort

Establish Proof-of-Biology in Patients

- ≥85% IRAK4 degradation in diseased skin and blood
- Anti-inflammatory effect in diseased skin and reduction of plasma cytokines and hsCRP
- Confirmation of dose for subsequent Phase 2 studies

KT-474 Interim Phase 1 Healthy Volunteer SAD Overview

Interim Results (Cohorts 1-4)

- **32** subjects randomized
- **24** subjects administered KT-474
- **8** subjects administered placebo

Dosing

- Single dose administration of oral KT-474 tablet
- Dose levels (mg):
  25
  75
  150
  300

Pharmacokinetic (PK) Features

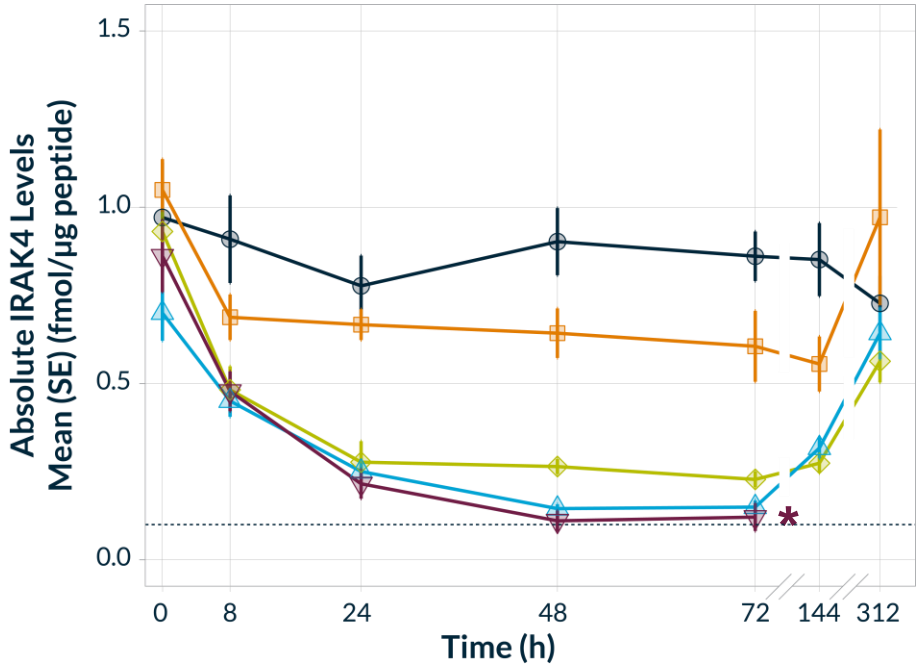
- PK profile consistent with oral daily dosing
- Predictable, dose-dependent plasma exposures after single oral dose of KT-474
- Half-life:
  25-32 hours

Safety & Tolerability

- No treatment-related adverse events
- No Serious Adverse Events

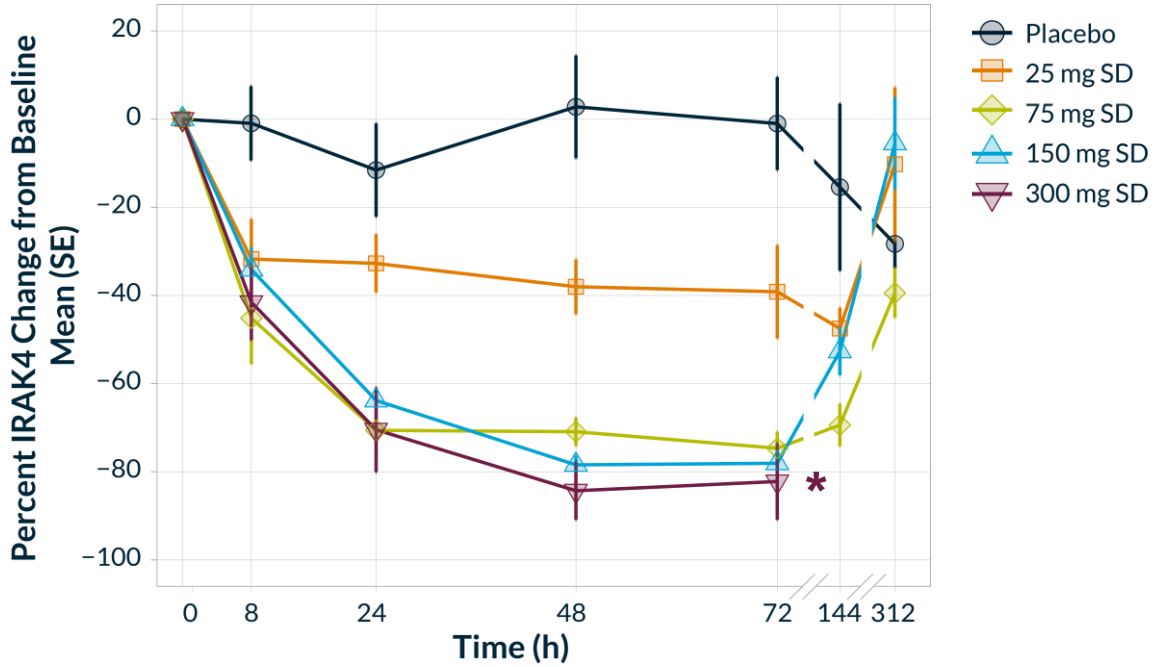
KT-474 Achieved Profound IRAK4 Degradation after Single Oral Dose that Lasted for at Least 6 Days

Absolute IRAK4 Levels



BLQ

Mean % Reduction of IRAK4

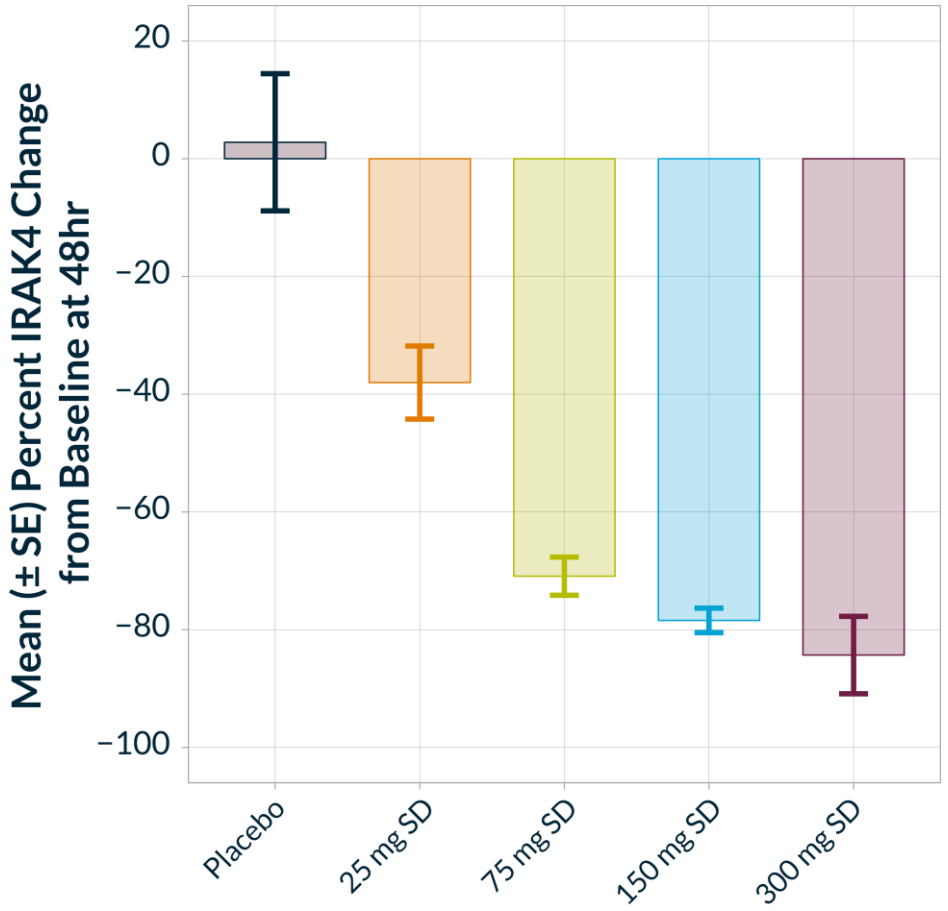


BLQ = Below Limit of Quantitation

* SAD4 144/312 h PD timepoints pending

- Measured by mass spectrometry in circulating PBMC
- IRAK4 levels nadired at 48-72 hours
- IRAK4 reduction lasted for at least 144h (6 days post-dose) in all dose groups

IRAK4 Degradation >85% Achieved Following Single KT-474 Dose



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

	Placebo (n=8)	Cohort 1 (n=6)	Cohort 2 (n=6)	Cohort 3 (n=6)	Cohort 4 (n=6)
KT-474 dose	-	25 mg	75 mg	150 mg	300 mg
Mean IRAK4 Change	+3%	-38%	-71%	-78%	-84%
Median IRAK4 Change	+16%	-41%	-71%	-78%	-90%
*p value**		*0.0057*	*<0.0001*	*<0.0001*	*<0.0001*

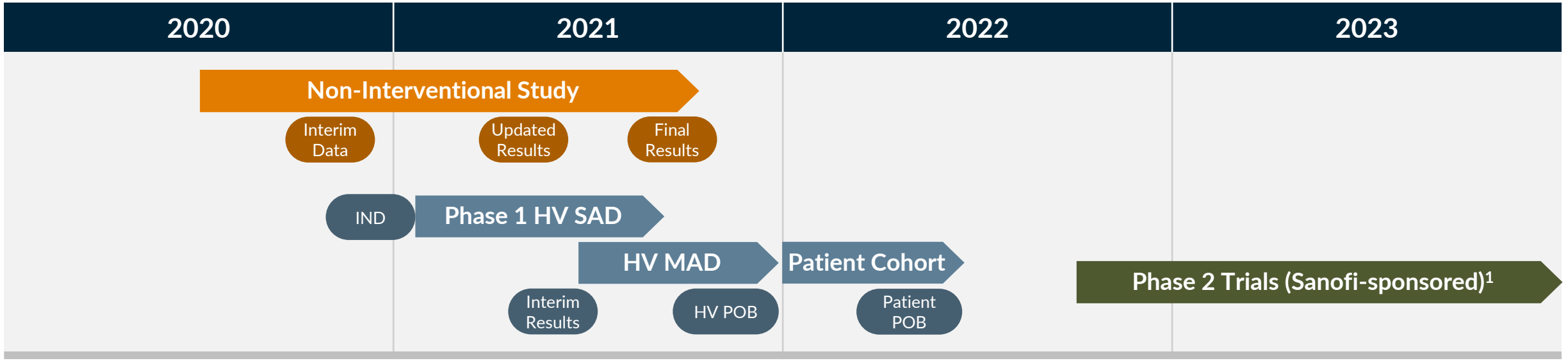
** p-values relative to placebo*

Interim Results from Phase 1 Healthy Volunteer SAD

Summary and Next Steps

- **KT-474 interim Phase 1 results demonstrate degrader proof-of-mechanism, first time for TPD in a placebo-controlled study**
  - Median IRAK4 reduction of 90% ($p<0.0001$ vs placebo) and maximum reduction of 94% at 48 hours following single dose of 300 mg, with sustained degradation that lasted for at least 6 days at all dose levels
  - Based on potency, PK and PD profiles with deep and sustained multiday degradation, expect to achieve biologically relevant (85%) level of degradation with repeat dosing at lower doses; selected MAD starting dose of 25 mg
  - Demonstrated predictable, dose-dependent and biologically active plasma exposures, and half-life that supports oral daily dosing
  - No treatment-related adverse events or serious adverse events observed to date
  - Demonstrating Phase 1 target degradation of >85% de-risks KT-474 ability to reach clinically relevant biological effects in future development as a potential best-in-class anti-inflammatory oral drug
- **FDA lifted partial clinical hold following review of interim healthy volunteer SAD results**
  - Dose escalation in SAD portion of Phase 1 to continue, including assessment of food-effect
  - In July, plan to initiate MAD portion of Phase 1 in healthy volunteers assessing daily dosing of KT-474 for 14 days
- **Expect to present updated results from healthy volunteer SAD/MAD portions in Q4'21**
  - Data to include IRAK4 degradation in skin and PBMC and effects on inflammatory biomarkers after repeat dosing
  - Optimal dose from MAD healthy volunteer portion to be evaluated in an open label cohort of patients with atopic dermatitis and hidradenitis suppurativa

KT-474 Development Plan



Non-Interventional

- 40 patients (HS n=30; AD n=10)
- Biomarker endpoints in blood and skin: IRAK4, cytokines, acute phase reactants
- Data updates:
  - Interim: **Oct 2020**
  - Updated HS: **May 2021**
  - Final AD: **2H21**

Phase 1

- SAD dosing initiated **1Q21**
- SAD/MAD studies: healthy volunteers (HV) and AD/HS patients
- Endpoints: primary - **Safety**; secondary - **Proof-of-Biology**
- Data updates:
  - Interim SAD proof-of-mechanism: **June 2021**
  - HV proof-of-biology: **4Q21**
  - Patient proof-of-biology: **1H22**

Phase 2

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

1. Estimated clinical development timeline.

THANK YOU

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