UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 4, 2024

KYMERA THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-39460**	**81-2992166**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

Kymera Therapeutics, Inc.
200 Arsenal Yards Blvd., Suite 230
Watertown, Massachusetts 02472
(Address of principal executive offices, including zip code)

(857) 285-5300
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	KYMR	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 4, 2024, Kymera Therapeutics, Inc. (the "Company") held a virtual immunology research and development day event to provide an overview of the Company's emerging pipeline of high-value immunology programs, including new target disclosures, supporting preclinical data and timing to clinical study initiation. A form of the slide presentation is being furnished as Exhibit 99.1 to this Current Report on Form 8-K. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

The information in this Item 7.01, including Exhibit 99.1 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such filing.

Item 9.01. Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Kymera Therapeutics, Inc. R&D Day Presentation, dated January 4, 2024, furnished herewith.
104	Cover Page Interactive Data (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Kymera Therapeutics, Inc.

Date: January 4, 2024

By: /s/ Nello Mainolfi
Nello Mainolfi, Ph.D.
Founder, President and Chief Executive Officer

Exhibit 99.1

KYMERA

2024 IMMUNOLOGY R&D DAY

January 4, 2024

Welcome

Justine Koenigsberg
Vice President, Investor Relations

Forward Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. These statements include, but are not limited to, implied and express statements about our strategy, business plans and objectives for our programs; plans and timelines for the preclinical and clinical development of our product candidates, including the therapeutic potential, clinical benefits and safety profiles of such product candidates; expectations regarding timing, success and data announcements of ongoing preclinical studies and clinical trials; our ability to initiate new clinical programs, including plans to submit investigational new drug (IND) applications; the initiation, timing, progress and results of our current and future preclinical studies and clinical trials of our current and prospective product candidates; our plans to develop and commercialize our current and any future product candidates and the implementation of our business model and strategic plans for our business, current and any future product candidates. All statements other than statements of historical facts contained in this presentation, including express or implied statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "assume," "believe," "could," "estimate," "expect," "goal," "intend," "may," "milestones," "objective," "plan," "predict," "potential," "seek," "should," "target," "will," "would" and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. You should not rely upon forward-looking statements as predictions of future events and actual results or events could differ materially from the plans, intentions and expectations disclosed herein.

Any forward-looking statements are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements including, without limitation, risks associated with: the timing and anticipated results of our current and future preclinical studies and clinical trials, supply chain, strategy and future operations; the delay of any current and future preclinical studies or clinical trials or the development of our drug candidates; the risk that the results of prior preclinical studies and clinical trials may not be predictive of future results in connection with current or future preclinical studies and clinical trials, including those for KT-474, KT-333, KT-253, KT-621, and KT-294; our ability to successfully demonstrate the safety and efficacy of our drug candidates; the timing and outcome of any interactions with regulatory authorities; obtaining, maintaining and protecting our intellectual property; our relationships with existing and future collaboration partners; the impacts of current macroeconomic and geopolitical events. In addition, any forward-looking statements represent Kymera's views only as of today and should not be relied upon as representing its views as of any subsequent date. Kymera explicitly disclaims any obligation to update any forward-looking statements, except as required by law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. As a result of these risks and others, including those set forth in our filings with the SEC, actual results could vary significantly from those anticipated in this presentation, and our financial condition and results of operations could be materially adversely affected.

Certain information contained in this presentation and statements made orally during this presentation relate to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party studies, publications, surveys and other data to be reliable as of the date of the presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent sources have evaluated the reasonableness or accuracy of the Company's internal estimates or research, and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research. This presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners.

Agenda

Welcome Justine Koenigsberg, Vice President, Investor Relations	10:00 - 10:05
Revolutionizing Immunology with Small Molecule Oral Degraders Nello Mainolfi, Ph.D., Founder, President and CEO	10:05 - 10:25
Paving the Way: KT-474, a First-in-Class Oral IRAK4 Degrader Jared Gollob, M.D., Chief Medical Officer	10:25 - 10:35
Dupilumab-like Activity in a Pill: KT-621, a First-in-Class Oral STAT6 Degrader Amy Wang, Ph.D., Senior Director and Program Lead, Immunology	10:35 - 10:55
Degrading a Proven Target: KT-294, a First-in-Class Oral TYK2 Degrader Juliet Williams, Ph.D., Head of Research	10:55 - 11:15
Closing Remarks: Solving Big Problems with Small Molecules Nello Mainolfi, Ph.D., Founder, President and CEO	11:15 - 11:20
Q&A	11:20 - 12:00

Revolutionizing Immunology with Small Molecule Oral Degraders

Nello Mainolfi, Ph.D.,
Founder, President and CEO

KYMERA

Mission

Build a global medicines company that harnesses novel modalities to revolutionize healthcare

What I Will Cover

- Targeted Protein Degradation: Harnessing a Game-Changing Novel Modality
- Demonstrating Reproducible and Scalable Clinical Innovation
- Our Target Selection Strategy
- Why Oral Degraders in Immunology
- Our Two New Programs

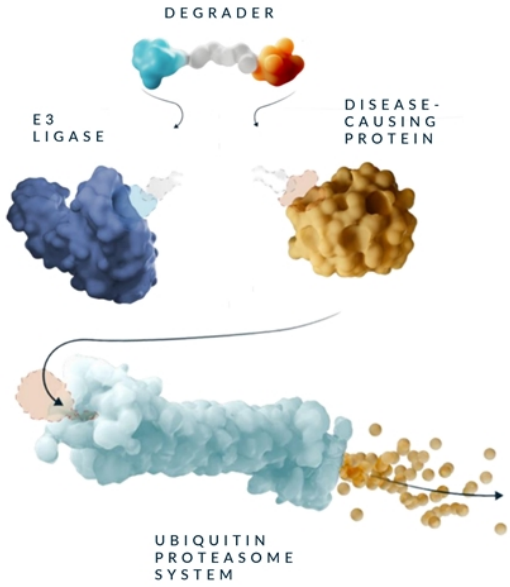
Harnessing a Game-Changing, Novel Modality

Kymera, a Leader in Targeted Protein Degradation

- Focused on unlocking high value, undrugged targets using TPD
- Highly productive and reproducible platform for discovery of innovative medicines
- Leading platform and pipeline IP, developed internally
- Well-capitalized, enabling expansion into areas with large clinical and commercial opportunities

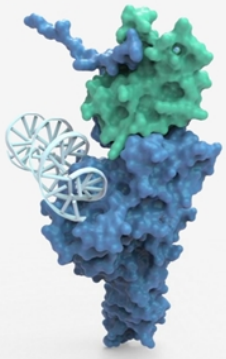
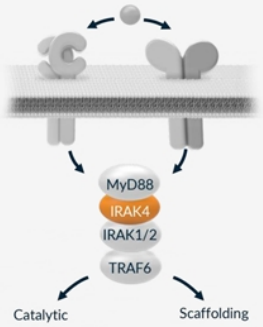
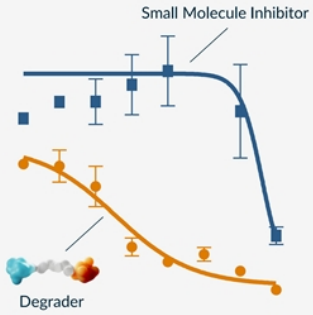
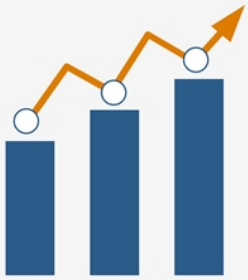
Industry Leading Execution

- Since founding Kymera in 2016:
  - Advanced four first-in-class programs to the clinic
  - Demonstrated clinical translation of degradation and safety
  - Achieved early clinical POC in I&I and oncology programs
- Extensive validation of target selection and molecular design
- Successful track record delivering multiple new drug mechanisms in clinic, expecting up to 10 novel INDs within first 10 years



Target Selection Strategy

Focus on First- or Best-in-Class Opportunities

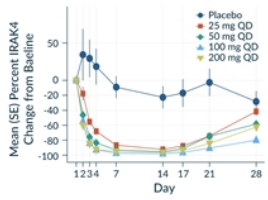
Undrugged or Inadequately Drugged targets	Strong Genetic/Pathway Validation	Clear Path to Early Clinical Differentiation	Large Clinical/Commercial Opportunities
			
TRANSCRIPTION FACTORS & SCAFFOLDING PROTEINS	APPROVED DRUGS IN SAME PATHWAY	SUPERIORITY VS PATHWAY DRUGS	AREAS OF SIGNIFICANT VALUE CREATION

Demonstrating Reproducible and Scalable Clinical Innovation

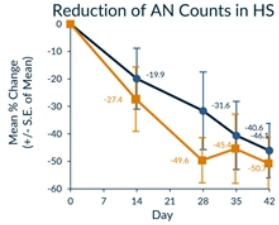
IRAK4 KT-474

IRAK4 Degradation leads to Early POC in HS and AD

IRAK4 Levels



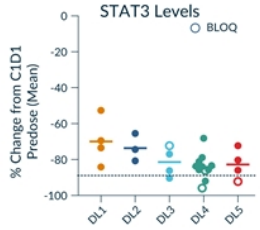
Reduction of AN Counts in HS Patients



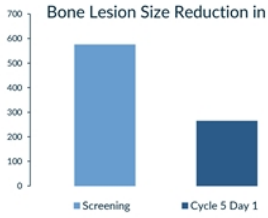
STAT3 Degradation Leads to Major Response in cHL Patient

STAT3 KT-333

STAT3 Levels

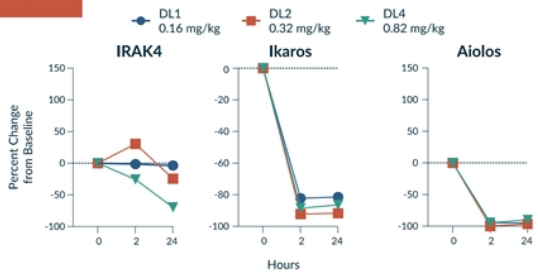


Bone Lesion Size Reduction in cHL Patient



IRAKIMID KT-413

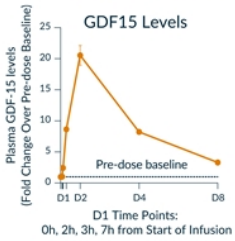
Degradation of IRAK4 and Ikaros/Aiolos in Humans was Well Tolerated



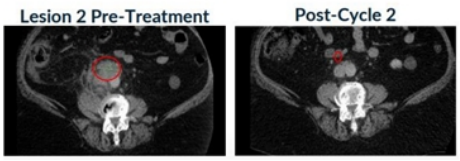
MDM2 Degradation Leads to Major Response in MCC Patient with no Heme-tox

MDM2 KT-253

GDF15 Levels

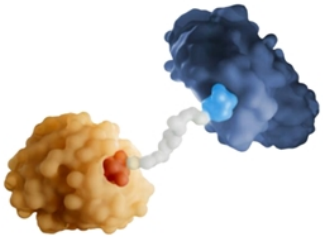


Lesion Size Reduction in MCC Patient



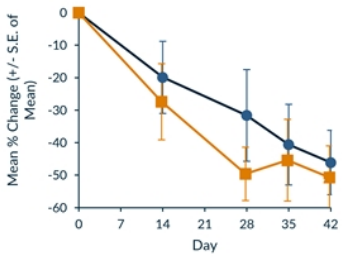
Building a Global Medicines Company

Pioneering a new modality 2016-2020



- Focused on undrugged targets within clinically validated pathways
- Forged multiple strategic partnerships to forward integrate (>$3B total value)
- Developed industry leading capabilities in TPD and novel E3s

Demonstrating early POC 2021-2023

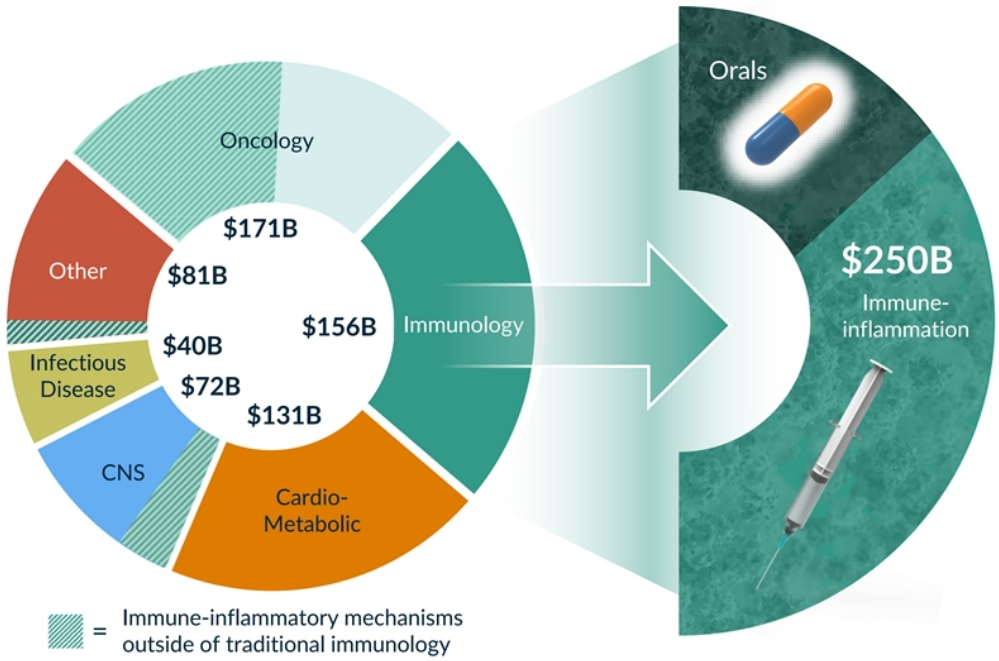


- Advanced four drug candidates into clinic demonstrating clinical activity in oncology and immunology
- Initiated two Phase 2 studies in significant immunology indications with Sanofi
- Demonstrated biological and clinical superiority of degrader vs. SMIs

Delivering a new generation of medicines 2024-2028

- Focus on large clinical/commercial opportunities with oral degraders
- Increase investments in I&I
- Complete multiple POC studies in large indications and launch several registrational studies
- Build towards a fully integrated global biotech

The Opportunity in Immunology

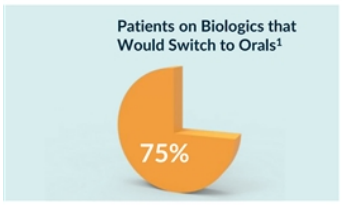


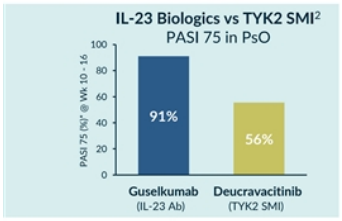
Immune-inflammation is a **$250B WW market**[1] spanning multiple therapeutic areas.

Injectables dominate, comprising >75% of the established market.

[1]Revenues from Top 1,000 worldwide brands by revenue; Source: GlobalData; 2022 Non-Covid, Non-Vaccine Rx Market

Why Small Molecule Oral Degraders in Immunology





Key pathways/cytokines validated as drivers of many diseases in I&I

Biologics blocking these pathways/cytokines have revolutionized treatment

Biologics are injected, can be inconvenient for patients and costly to manufacture

Traditional small molecule inhibitors insufficiently block these pathways, limiting efficacy

Oral Degraders Can Offer Biologic-like Efficacy in a Pill

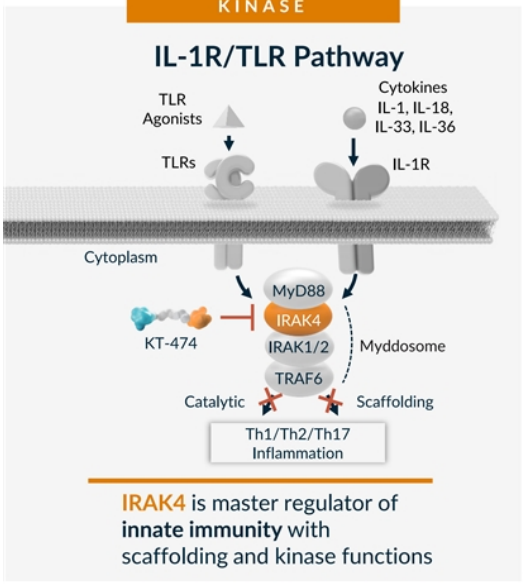
Degraders can provide **comparable pathway inhibition to biologics**, convenience of **oral dosing**, **ease of manufacturing** and potentially access **broader populations**

[1]J&J Business Review Dec '23 (survey of N=395 patients with moderate-to-severe psoriasis); [2]Tremfya (IL-23 biologic) package insert, Sotyktu (TYK2 SMI) package insert

Revolutionizing Immunology with Oral Degraders

Our IRAK4 Example

IRAK4
SCAFFOLDING KINASE



IRAK4 is master regulator of **innate immunity** with scaffolding and kinase functions

BEST-IN-PATHWAY MECHANISM

Clinical pathway validation	>	IL-1, IL-18, IL-33, IL-36 biologics
Human genetics	>	IRAK4 null adults: healthy
Undrugged/inadequately drugged by other technologies	>	Scaffolding kinase, only TPD can address
Best-in-pathway profile opportunity	>	Superior to single cytokine upstream blockers: IL-1/18/33/36
Clear path to early clinical de-risking	>	Superiority in Phase 1/2
Access large clinical and commercial opportunities	>	HS, AD, RA, Asthma, COPD, IBD, others[1]

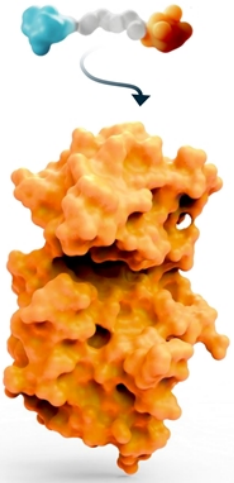
[1]Current indications; HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities

Revolutionizing Immunology with Oral Degraders

WHAT WE HAVE LEARNED FROM KT-474

Strong PK/PD Correlation

Early Signs of Clinical Activity

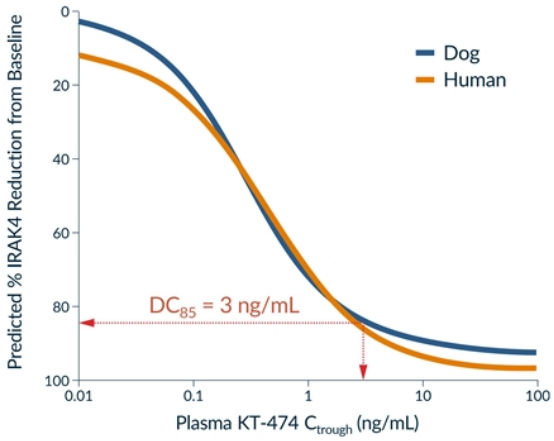


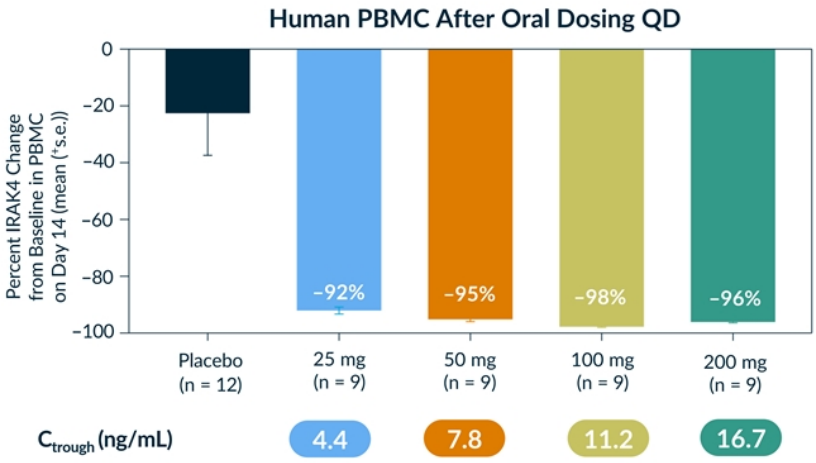
IRAK4 SCAFFOLDING KINASE

Safety

Differentiated vs. SMI

KT-474: Fidelity of Translation from Preclinical to Clinical Profile





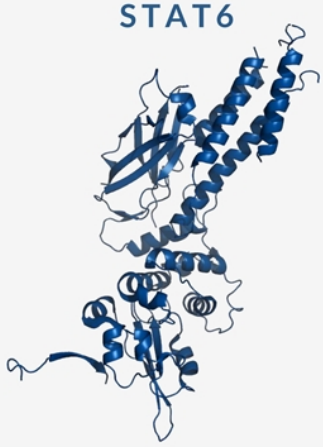
PK/PD modeling of observed data predicts **comparable DC_{85} (~3 ng/mL) in dog and human** showing excellent preclinical to clinical translation and predictability of IRAK4 degradation

Revolutionizing Immunology with Small Molecule Oral Degraders

Our Two New Programs

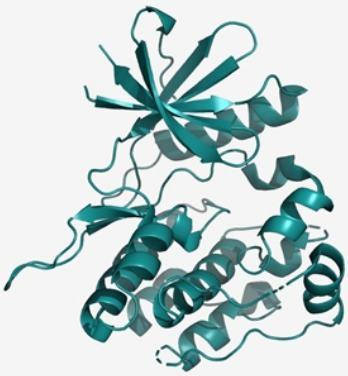
SPECIFIC IL-4/13 TRANSCRIPTION FACTOR

STAT6

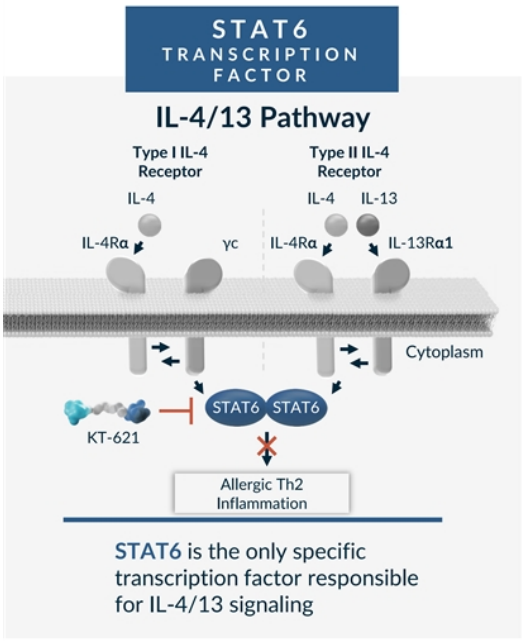


SPECIFIC IL-23/IFN SCAFFOLDING KINASE

TYK2



STAT6 Degrader: Dupilumab-like Activity in a Pill

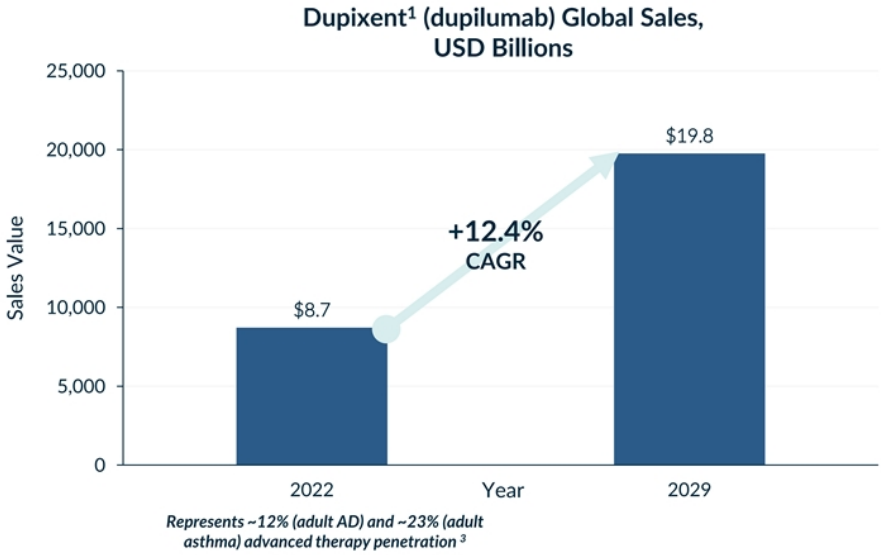


STAT6 is the only specific transcription factor responsible for IL-4/13 signaling

BEST-IN-PATHWAY MECHANISM

Clinical pathway validation	>	Dupilumab
Human genetics	>	Gain of function variants cause severe allergic diseases; KO phenotype (mouse) normal
Undrugged/inadequately drugged by other technologies	>	Transcription factor, TPD can fully block target/pathway
Best-in-pathway profile opportunity	>	Dupilumab-like activity with oral small molecule profile
Clear path to early clinical de-risking	>	Phase 1/2 efficacy
Access large clinical and commercial opportunities	>	Dupilumab indications (AD, Asthma, COPD, CRSwNP, EoE, PN, others), mega-blockbuster potential

STAT6: Significant Potential Across Multiple I&I Indications



MARKET OPPORTUNITY

Total IL-4/IL-13 biologics[2] sales expected to double by 2029

- >$10B in 2023
- >$23B by 2029

Currently approved indications of IL-4/IL-13 agents are dominated by biologics

Oral STAT6 degrader has potential for dupilumab-like activity with convenience of an oral pill

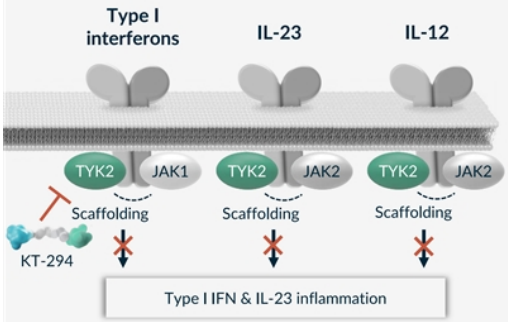
Oral STAT6 degrader could have broader access beyond biologics-eligible patients and impact much larger populations

[1]dupilimab/Dupixent indications: Approved – Atopic Dermatitis, Asthma, CRSwNP, EoE, PN; Investigational – COPD, CSU, BP, CPUO, EoG, UC; [2]IL-4/IL-13 = dupilumab, tralokinumab, and lebrikizumab; [3]Sanofi 2Q23 Earnings; GlobalData

TYK2 Degrader: Degrading a Proven Target for a Best-in-Class Profile

TYK2 SCAFFOLDING KINASE

IL-12/23/IFN Pathways

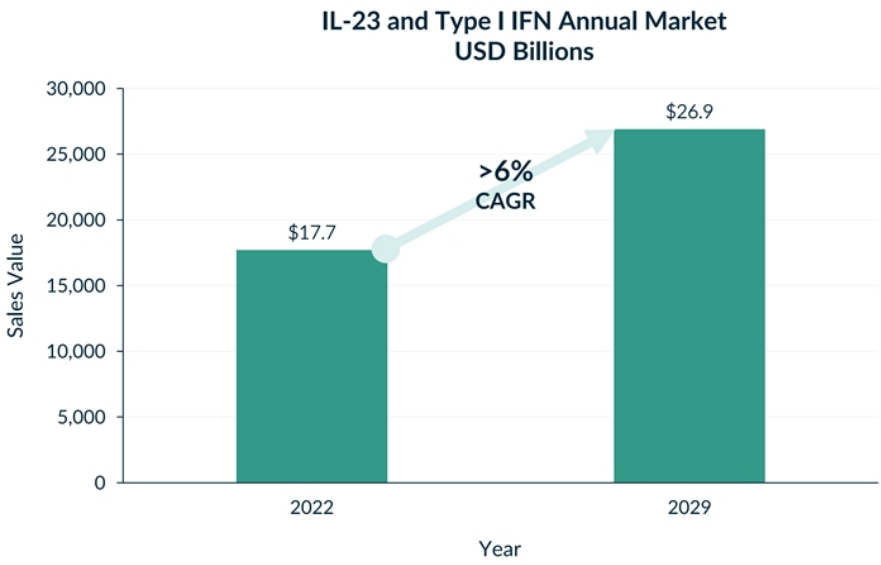


TYK2 is a JAK family scaffolding kinase required for Type I IFN, IL-12 and IL-23 cytokine signaling

BEST-IN-PATHWAY MECHANISM

Clinical pathway validation	>	IL-23 biologics (ustekinumab), TYK2 inhibitor (deucravacitinib) approved, others
Human genetics	>	LOF variant is protective in immunological diseases and generally normal
Undrugged/inadequately drugged by other technologies	>	Scaffolding kinase, SMIs do not fully block pathway
Best-in-pathway profile opportunity	>	TYK2 degrader recapitulates LOF phenotype: biologic-like activity and convenience of oral pill
Clear path to early clinical de-risking	>	Phase 1 differentiation
Access large clinical and commercial opportunities	>	IL-23, IFN indications, beyond: IBD, PsO, PsA, Lupus, others

TYK2: Significant Potential Across Multiple I&I Indications



MARKET OPPORTUNITY

Total IL-23 and Type I IFN biologics[1] sales expected to grow by over $9B by 2029

- ~$18B in 2022
- ~$27B by 2029

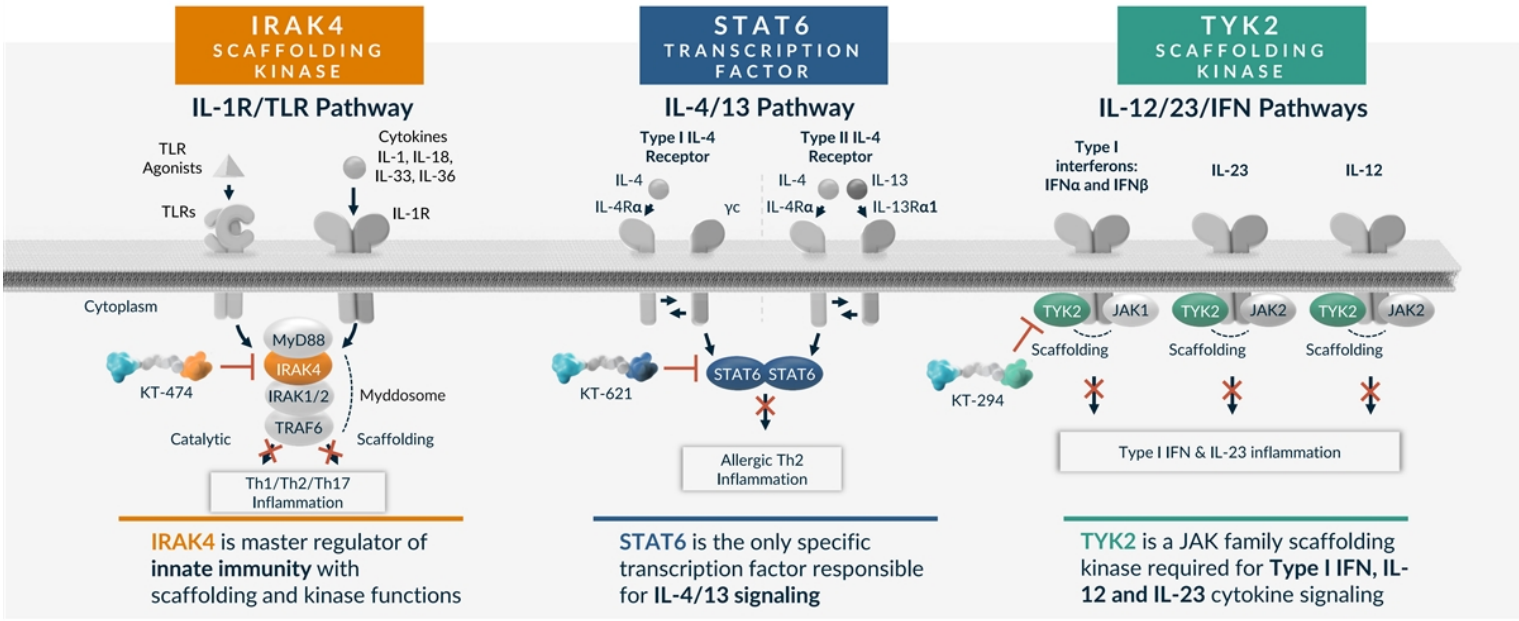
Currently approved indications dominated by biologics, with oral options challenged by efficacy and/or safety

TYK2 degrader has potential for biologic-like efficacy with convenience of oral pill

[1]IL-23 = ustekinumab, risankizumab, guselkumab and tildrakizumab; Type 1 interferon = anifrolumab; GlobalData

Kymera Immunology Oral Degrader Portfolio

Complementary, First-in-class Mechanisms



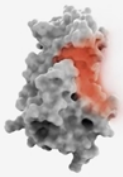
IRAK4 is master regulator of **innate immunity** with scaffolding and kinase functions

STAT6 is the only specific transcription factor responsible for **IL-4/13 signaling**

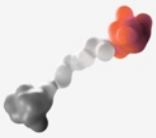
TYK2 is a JAK family scaffolding kinase required for **Type I IFN, IL-12 and IL-23** cytokine signaling

Industry-leading Oral Immunology Pipeline

Three Fundamental Immune-inflammatory Pathways with Large Market Potential



High value undrugged/ inadequately drugged targets



Next generation oral drugs with potential best-in-class profiles

Building the industry-leading oral immunology portfolio

	IRAK4 (KT-474) SCAFFOLDING KINASE	STAT6 (KT-621) TRANSCRIPTION FACTOR	TYK2 (KT-294) SCAFFOLDING KINASE
Potential Indications	• HS, AD, RA, Asthma, COPD, IBD, others[1]	• AD, Asthma, COPD, CRSwNP, EoE, PN, others	• IBD, PsO, PsA, Lupus, others
Opportunity	• **First-in-class broad anti-inflammatory oral degrader**	• **Dupilumab-like activity in a pill**	• **Biologic-like activity in a pill**
Commercial Rights	• Up to 50% US with Sanofi, tiered royalties in ROW[2]	• Wholly owned	• Wholly owned

[1]Current indications; HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities; [2]KT-474 (SAR444656) partnered with Sanofi, with Kymera option to participate in the development and commercialization, and 50/50 profit split, in the United States. Double digit tiered royalties in ROW.

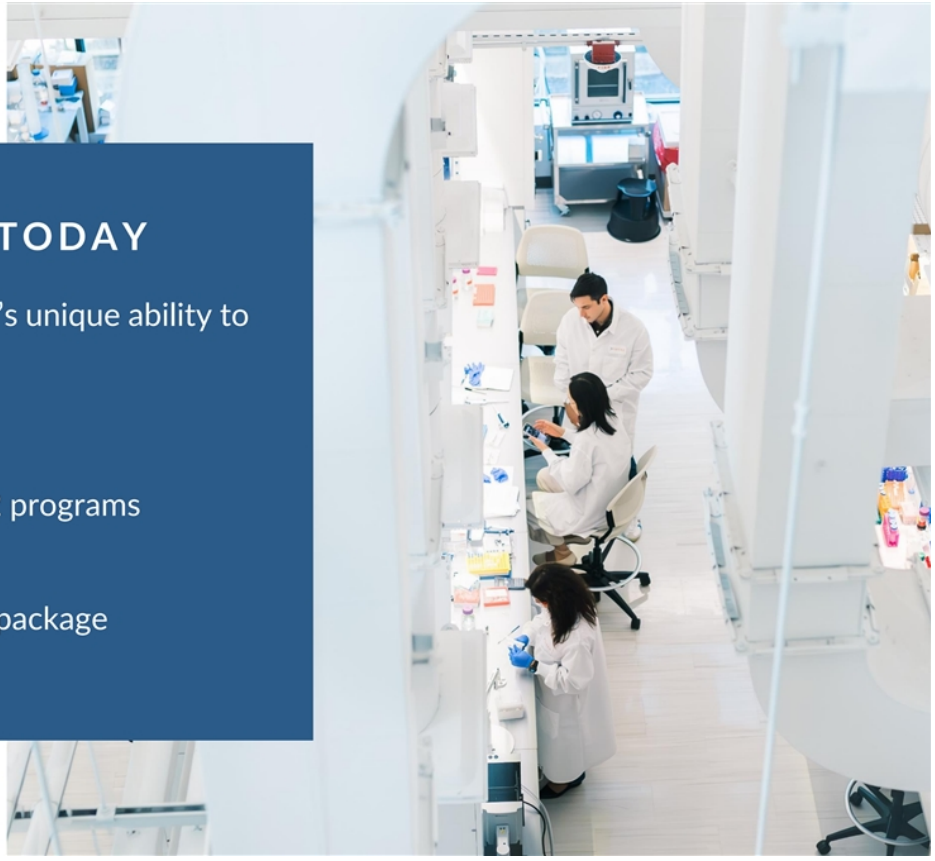
WHAT TO EXPECT TODAY

Vision for our I/I portfolio and Kymera's unique ability to capitalize on power of TPD

Update on IRAK4 program

Detailed overview of STAT6 and TYK2 programs

- Clinical opportunities
- Degrader advantage
- Compelling preclinical data package
- Timelines to clinic



Paving the Way: KT-474, a First-in-Class IRAK4 Oral Degrader

Jared Gollob, M.D.,
Chief Medical Officer

IRAK4: What We Will Cover

- Pathway Biology and Validation
- Clinical Development/Commercial Opportunities
- Degrader Profile and Advantage
- Our Clinical Data and Fidelity of Translation
- Our Ongoing Phase 2 Studies

IRAK4 Biology and Target Rationale

Target Rationale

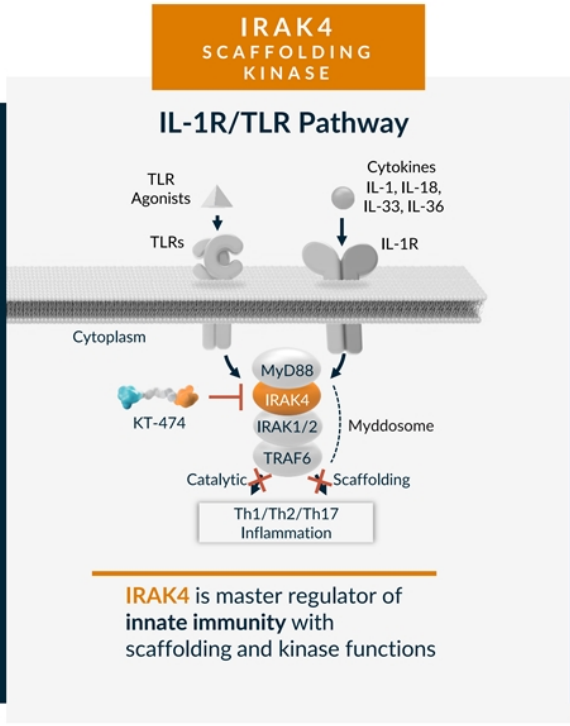
- IRAK4 is an obligate node in IL-1R/TLR signaling, and its degradation is the only approach to fully block the pathway

Human Genetics

- Adult humans with IRAK4 null mutation are healthy

Clinical Pathway Validation

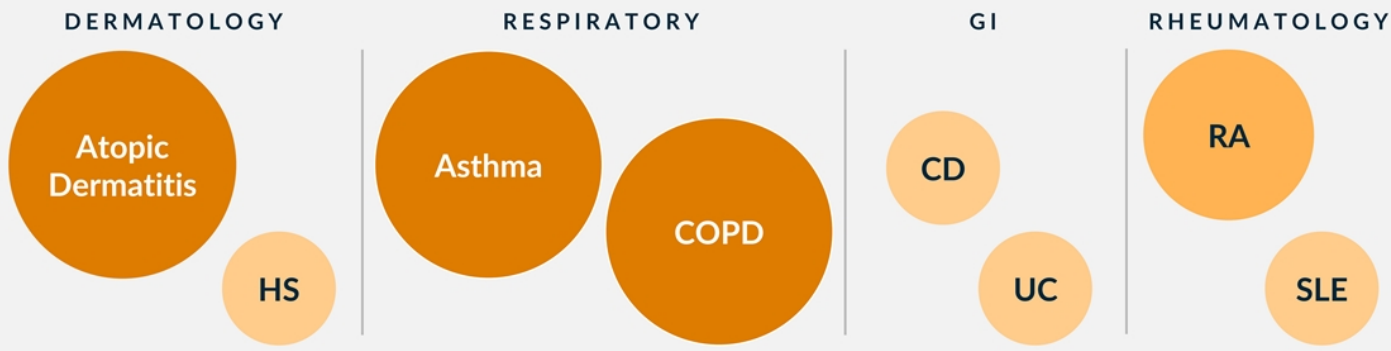
- IRAK4 degradation has the potential to achieve a broad, well-tolerated anti-inflammatory effect
- Multiple development opportunities in immune-inflammatory diseases which signal through MyD88/IRAK4 have been validated[1]:
  - IL-1α/IL-1β : RA, CAPS, HS, AD, Gout
  - IL-18: AD, Macrophage Activation Syndrome
  - IL-36: Generalized Pustular Psoriasis, AD
  - IL-33: Asthma
  - IRAK4 SMI: RA



Adapted from West NT. Front Immunol 2019

[1]Current indications; HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities

IL-1R/TLR Pathway Potential Impact Across Multiple Immune-Inflammatory Diseases

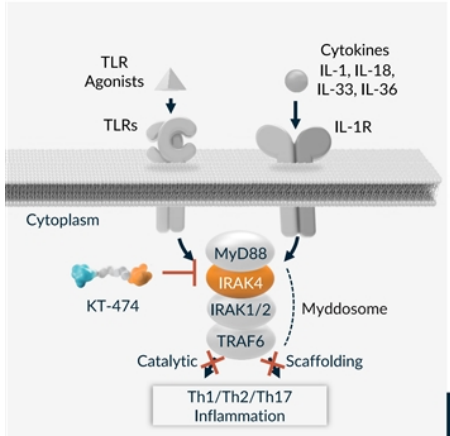


Total Potential Patient Impact[1]: **>150M patients**

- Numerous indication opportunities across multiple therapeutic areas validated by sub-optimal pathway inhibitors
- IRAK4 degradation leading to full pathway inhibition has the potential to deliver superior profile to upstream biologics
- Oral degrader medicines offer opportunity to reach broader patient populations

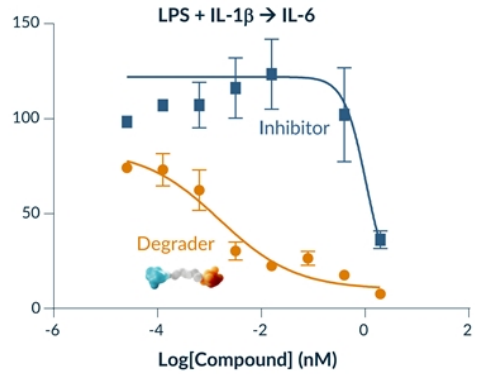
[1]GlobalData (2022 diagnosed prevalent patient population for US/EU5/JP)

IRAK4 Degrader Advantage



IRAK4 caps the oligomer size of MYD88 to trigger myddosome formation

Only Degrader Can Fully Block Inflammation



Preclinical Data *(Kymera IRAK4 Backgrounder)*

- IRAK4 KO is able to block TLR activation unlike the kinase dead rescue
- IRAK4 **scaffolding function** is critical in Myddosome formation and pathway signaling
- IRAK4 degradation, but not kinase inhibition, can **block TLR induced NF-κB translocation** and **IL1R+TLR activation**
- IRAK4 degradation is superior to kinase inhibition at **blocking downstream phosphoproteome**
- IRAK4 degradation is superior to inhibition in a **variety of preclinical efficacy models**

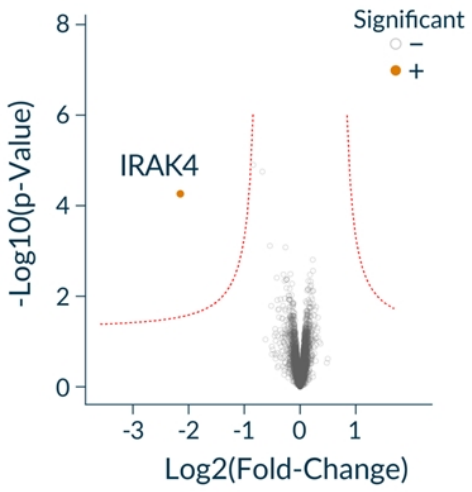
Clinical Data *(Nature Medicine*)*

- IRAK4 degradation **reduces signs and symptoms of HS and AD**, while IRAK4 SMI inactive in Phase 2 HS trial
- IRAK4 blocks inflammation in blood and skin of HS and AD patients

**Ackerman, et al.*, Nature Medicine (2023).

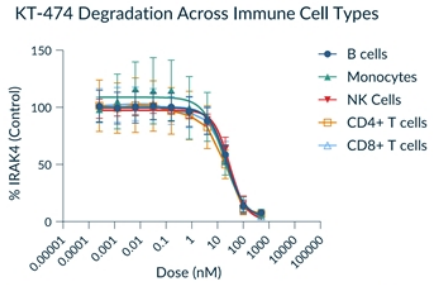
KT-474: Selective and Potent IRAK4 Degrader Active in Multiple Cell Types

Selectivity in PBMC



- KT-474 selectively degrades IRAK4 in human immune cells at concentration 10-fold above the DC_{90}
- Potent degradation in PBMC subsets and skin cells including fibroblasts, with single-digit nM DC_{50}
- Associated with functional inhibition of TLR- and IL-1β-stimulated cytokine production
- Comprehensive understanding of degradation kinetics across cell types to enable human translation

Potency in Blood and Skin Cells



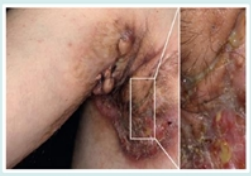
Cell type (Human)	Source	KT-474 DC_{50} (nM)
Monocytes	Blood	2.6
B cells	Blood	2.7
CD4 T cells	Blood	1.5
CD8 T cells	Blood	1.5
NK cells	Blood	1.8
Fibroblasts	Skin	1.5
Keratinocytes	Skin	7.8

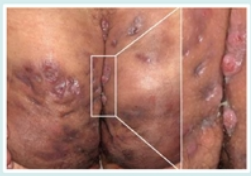
Initial Clinical Focus for KT-474: Moderate to Severe HS and AD

Hidradenitis Suppurativa (HS)

Chronic and debilitating skin disease with painful nodules, abscesses and draining fistulae/tunnels

Major QoL impact: Pain, itching, depression, social isolation





Many diagnosed in their 20s/30s; more common in females (~3:1); prevalence estimated to be up to 1-3% of population in US and EU

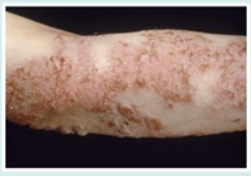
Lesions characterized by pleotropic inflammation with Th1/Th17 skewing; bacterial infection and tissue destruction leading to TLR activation; IL-1 and IL-36 production

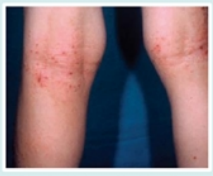
Active agents approved or in development target TNF-α, IL-17 and JAK/STAT pathways

Atopic Dermatitis (AD)

Chronic inflammatory skin disease with scaly, dry, erythematous lesions; intense itching/scratching, predisposition to infections

Major QoL impact: Itching, pain, sleep disturbance





Onset usually in early childhood; affects an estimated 98 million adults in US/EU5/JP[1]

Lesions characterized by pleotropic inflammation with Th2 skewing; bacterial infection and skin barrier breakdown leading to TLR activation; IL-33 and IL-1 production

Active agents approved or in development target IL-4/IL-13, JAK/STAT and OX40/OX40-L pathways

KT-474 Opportunity: Potential for broad anti-inflammatory effect, competitive efficacy vs. pathway biologics and convenience of once-daily oral dosing

[1]GlobalData – undiagnosed, all-age prevalence

KT-474 Phase 1: Compelling Data and Early POC in HS and AD

Healthy Volunteers (HV): SAD and MAD

- Evaluated safety, tolerability and pharmacokinetics in 105 healthy volunteers
  - SAD: Oral doses of 25-1600 mg
  - MAD: Escalating doses up to 200 mg were administered for 14 consecutive days
- Robust (>95%) and sustained IRAK4 degradation with single and multiple daily doses
- Broad inhibition of *ex vivo* TLR-mediated cytokine induction
- Generally well-tolerated across all dose groups

HS and AD Patient Cohort

- Open label study in 21 patients with HS and AD
- Dose: 75 mg QD with food (equivalent exposure to 100 mg fasted), administered for 28 consecutive days
- Safety, PK and PD comparable to healthy volunteers
- Robust IRAK4 degradation in blood and skin with associated systemic anti-inflammatory effect in HS and AD patients
- Promising clinical activity observed in HS and AD


nature medicine

Article

IRAK4 degrader in hidradenitis suppurativa and atopic dermatitis: a phase 1 trial


News & views

Targeted therapy

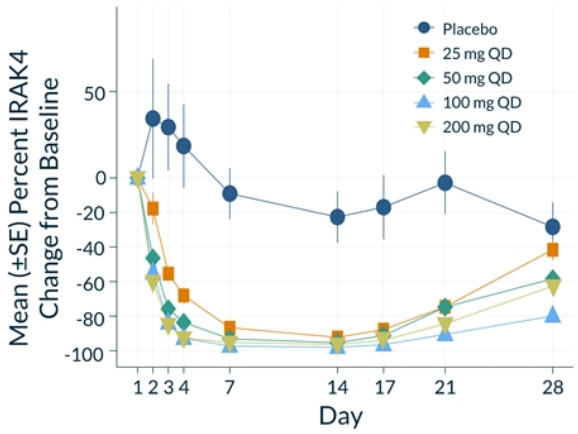
PROTACs reach clinical development in inflammatory skin disease

Fleur M. Ferguson

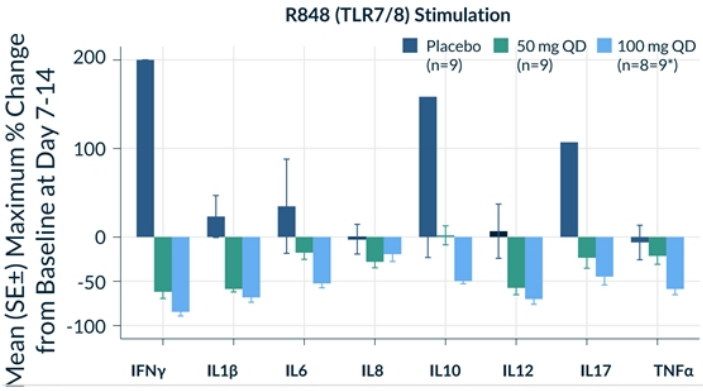
A phase 1 trial of an IRAK4-targeted protein degrader in patients with chronic inflammatory skin diseases hits an important milestone for the safe application of this drug class beyond oncology.

Near-Complete Degradation and Broad Cytokine Impact in Healthy Volunteers

Mean % Reduction of IRAK4
(Daily oral doses for 14 days)



***Ex Vivo* Inhibition of 9 Disease-Relevant Cytokines, Day 7-14**

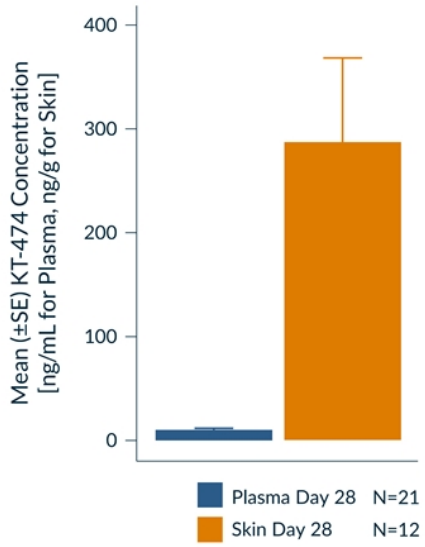


	IFNγ	IL1β	IL6	IL8	IL10	IL12	IL17	TNFα
Pbo	>500%	15%	35%	-5%	-23%	3%	107%	-7%
50 mg QD	-62%	-59%	-18%	-28%	2%	-58%	-24%	-21%
100 mg QD	-85%	-68%	-53%	-32%	-50%	-72%	-46%	-59%

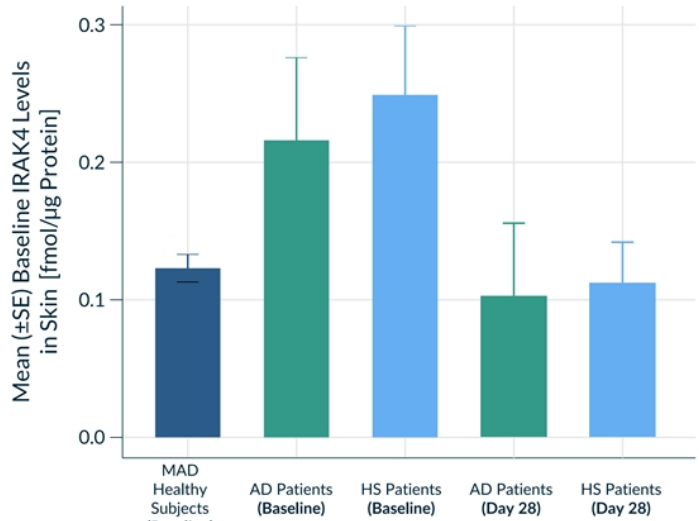
- High fidelity of PKPD translation from preclinical species to humans.
- Human efficacious concentrations (C_{trough} 3 ng/mL) and doses (50-200 mg) were correctly predicted

High Skin Exposure and Degradation in Skin of HS and AD Patients

High KT-474 Exposure in HS and AD Patients Skin

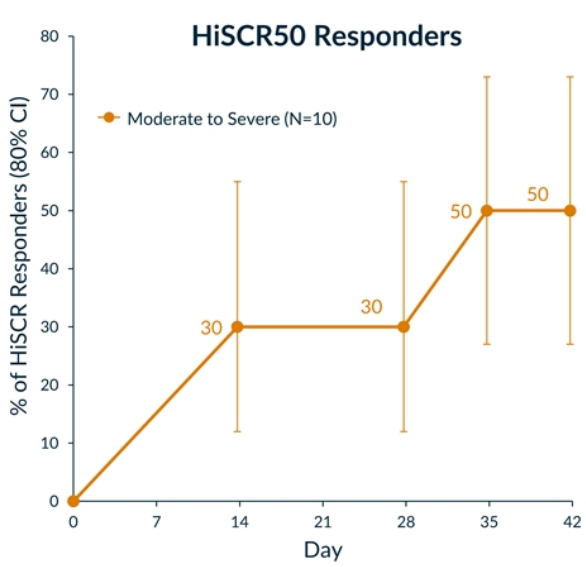


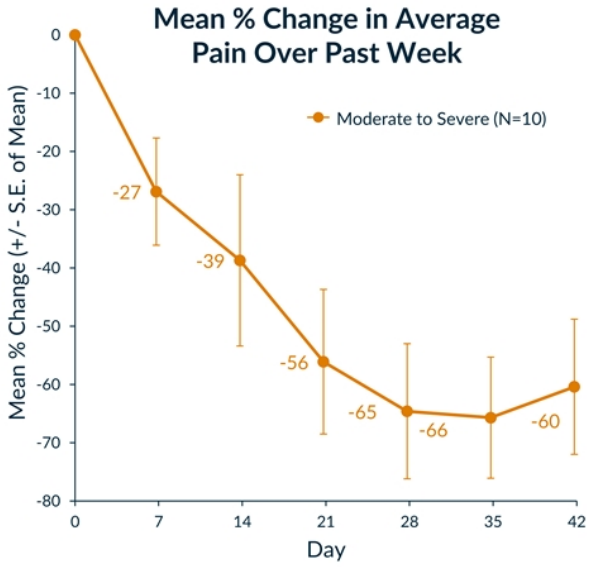
Reduced IRAK4 in Skin Lesions of AD and HS Patients



	MAD Healthy Subjects (Baseline)	AD Patients (Baseline)	HS Patients (Baseline)	AD Patients (Day 28)	HS Patients (Day 28)
N	46	7	11	6	9
Mean	0.12	0.22	0.24	0.1	0.11

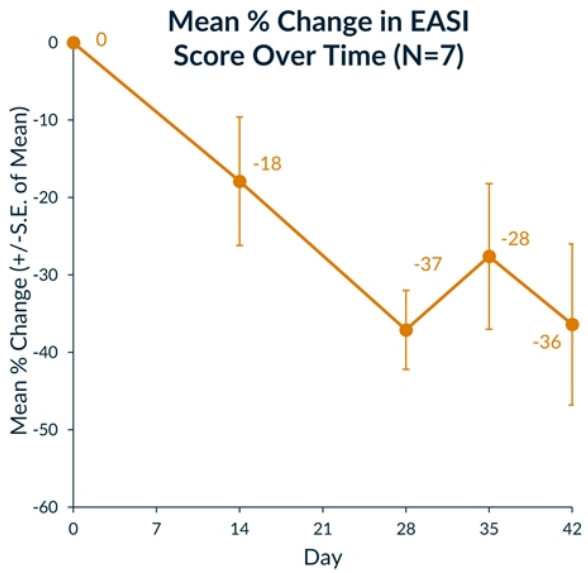
Robust Clinical Impact in HS After Only 28 Days of Dosing

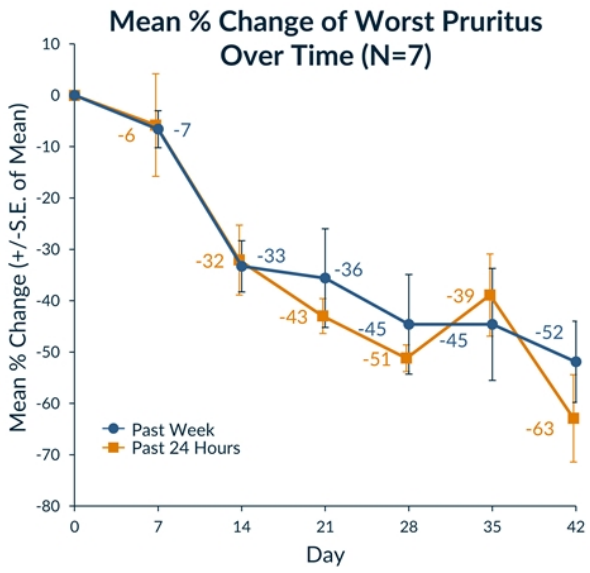




HiSCR50 response rate of up to 50% and pain reduction of up to 66% in moderate to severe HS patients

Robust Clinical Impact in AD After Only 28 Days of Dosing





EASI score reduction of up to 36% and pruritus reduction of up to 63% in moderate to severe AD patients

KT-474/SAR444656: Positioned for Clinical Success

Phase 2 HS Trial
(ZEN)

- Double-blind, placebo-controlled
- Up to 99 patients, dosed for 16 weeks
- 1 KT-474 dose arm, 1 placebo arm
- Primary endpoint: % Change in AN Count
- Additional endpoints (select):
  - HiSCR50, IHS4, HS-Skin Pain-NRS30
- Primary completion (est.): February 2025

Phase 2 AD Trial
(ADVANTA)

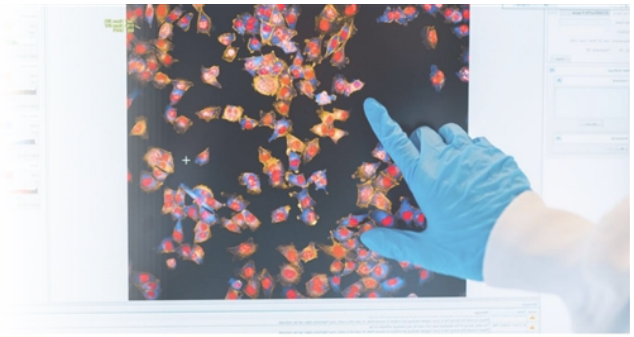
- Double-blind, placebo-controlled
- Up to 115 patients, dosed for 16 weeks
- 2 KT-474 dose arms, 1 placebo arm
- Primary endpoint: % Change in EASI
- Additional endpoints (select):
  - EASI 50/75/90, vIGA-AD, PP-NRS
- Primary completion (est.): January 2025

Topline data expected 1H 2025

Additional information on the Phase 2 studies can be found at www.clinicaltrials.gov; identifier NCT06028230 (HS) and NCT06058156 (AD); Study Sponsor: Sanofi

Oral IRAK4 Degrader: KT-474

A best-in-pathway broad oral anti-inflammatory agent for multiple inflammatory diseases



Validated Biology

Mediates signaling through IL-1 and toll-like receptors

Upstream cytokine blockers with proven clinical activity across many diseases

Scaffolding kinase at the interface of innate and adaptive immune responses with a variety of functions

Competitive Profile

Potential for Broad Activity Across Th1-Th17 and Th2 Diseases

>$50B in combined global drug sales[1] opportunity

Large potential for oral degraders with best in pathway efficacy

KT-474 Progress/Next Steps

Phase 1 complete:
- Robust IRAK4 degradation
- Favorable safety profile
- Systemic suppression of proinflammatory cytokines and chemokines
- Early signs of strong clinical activity

Partner Sanofi conducting Phase 2 trials in HS and AD

Phase 2 data expected in 1H 2025

Activity and fidelity of translation of TPD platform in KT-474 Phase 1 trial informs probability of success with STAT6 and TYK2 immunology programs

[1]GlobalData (2022 sales for AD, HS, Asthma, COPD, UC, CD, RA, SLE)

Dupilumab-like activity in a pill: KT-621, a First-in-class Oral STAT6 Degrader

Amy Wang, Ph.D.,
Senior Director, Biology Project Lead

What We Will Cover

- STAT6 Biology and Target Rationale
- Clinical Development/Commercial Opportunities
- Degrader Advantage
- Preclinical Data
- Next Steps

STAT6 Biology and Target Rationale

Target Biology and rationale

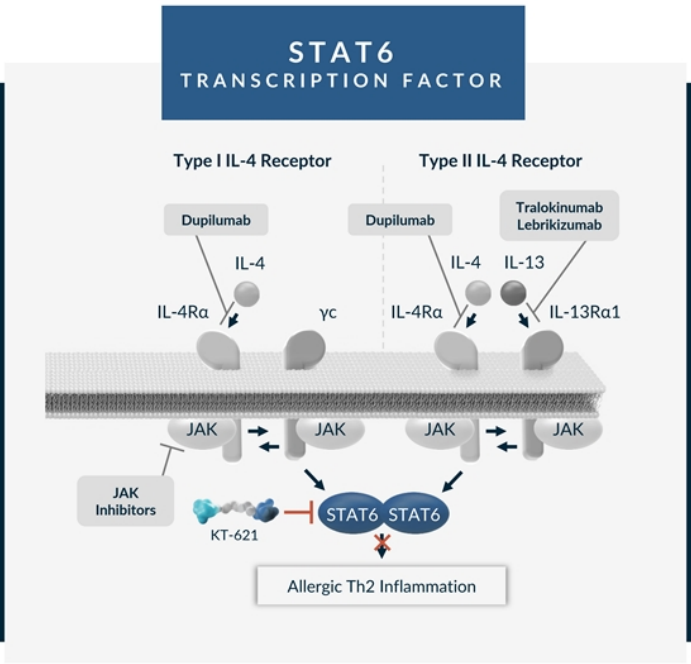
- STAT6 is the specific transcription factor required for IL-4 and IL-13 cytokine signaling
- STAT6 regulated cytokines are clinically validated targets for allergic diseases

Human and Mouse Genetics

- Gain of function (GOF) mutations of STAT6 cause severe allergic diseases in human
- STAT6 KO mice develop normally, are viable and fertile

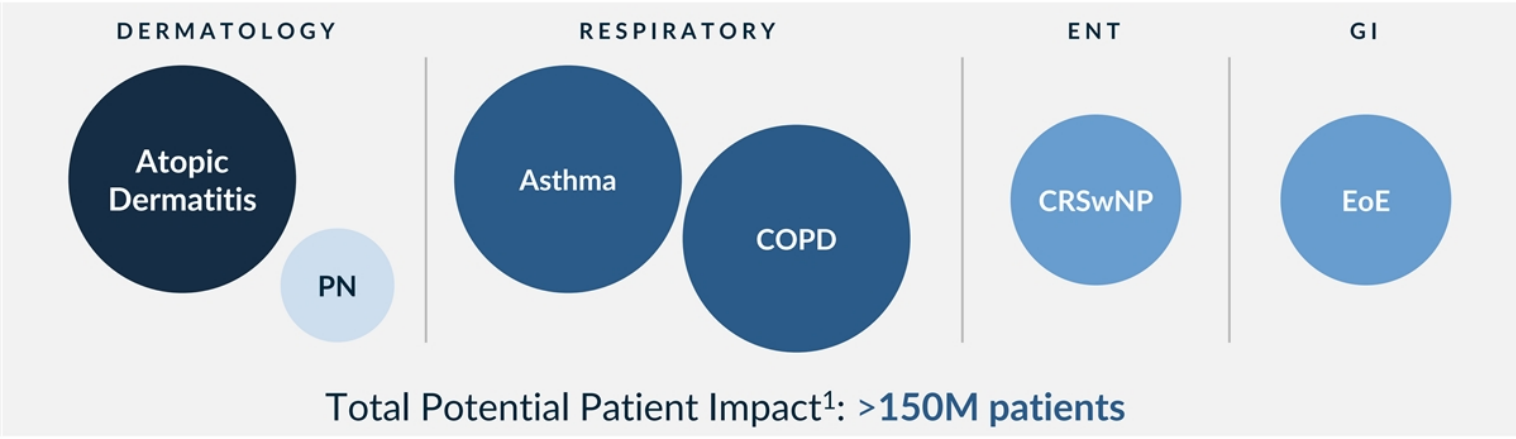
Clinical Pathway Validation

- Dupilumab, an IL-4Rα monoclonal Ab has been approved in: Atopic dermatitis, Asthma, CRSwNP, Eosinophilic Esophagitis, Prurigo Nodularis, has positive Phase 3 data in COPD and is in development for multiple additional indications
- STAT6 degradation can achieve dupilumab–like pathway inhibition



Adapted from Junttila. Front Immunol. 2018; Sharma et al. J Exp Med. 2023; Suratannon et al. J Allergy Clin. Immunol. 2022; Takeuchi et al. J Allergy Clin Immunol. 2022

Oral STAT6 Degraders Can Transform Treatment Paradigm in Multiple Indications De-risked by Dupilumab

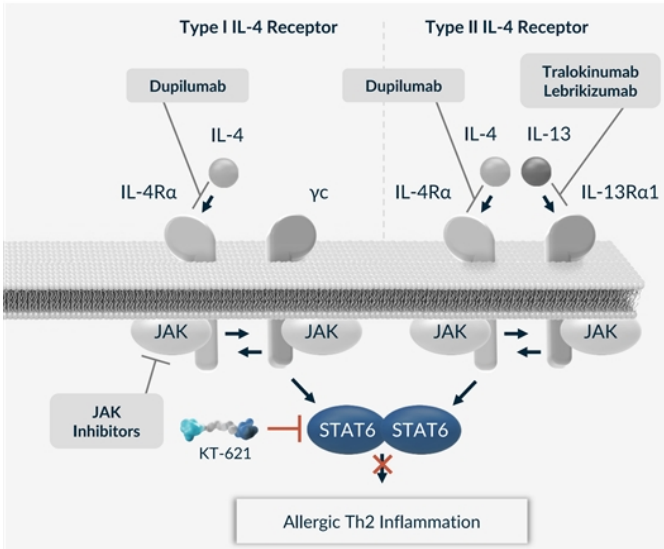


Total Potential Patient Impact[1]: **>150M patients**

- Numerous indication opportunities across multiple therapeutic areas de-risked by dupilumab
- STAT6 degradation leading to full pathway inhibition has the potential to deliver dupilumab-like activity
- Oral degrader medicines offer opportunity to reach broader patient populations

[1]GlobalData (2022 diagnosed prevalent patient population for US/EU5/JP)

STAT6 Degrader Advantage



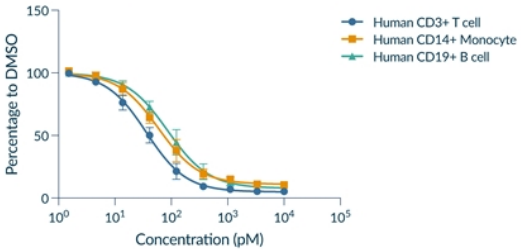
- STAT6 is the specific and essential transcription factor in the IL-4/13 pathway
- Occupancy based approaches (e.g., SMI) unlikely to block pathway fully in a pharmacologically relevant manner
- Only degradation of STAT6 can block its activity fully and match dupilumab pathway blockade *in vitro* and *in vivo*

KT-621: A Picomolar Degrader of STAT6

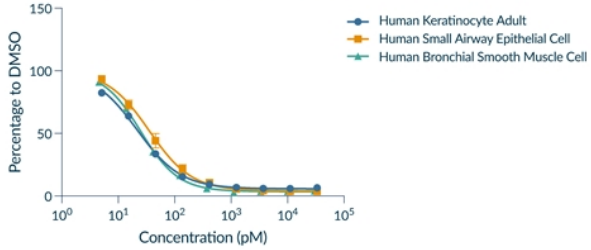
Consistent Degradation Across All Disease Relevant Cell Types Evaluated

	Human Primary Cell Type	KT-621, DC_{50} (pM)
Blood	**Hematopoietic cell (all TH2 diseases)**	
	Human PBMC	13
	Human CD3 T cell	36
	Human CD14 monocyte	60
	Human CD19 B cell	86
	Human eosinophil	99
Skin	**Epithelial cell (AD, CPG, CU, asthma, COPD)**	
	Human keratinocyte (adult)	22
	Human keratinocyte (neonatal)	18
Lungs	Human bronchial tracheal epithelial cell	33
	Human small airway epithelial cell	35
Throat/ Airway	**Smooth muscle cell (asthma, COPD, EoE)**	
	Human bronchial smooth muscle cell	25
	Human esophageal smooth muscle cell	33
Blood Vessels	**Endothelial cell (all TH2 diseases)**	
	Human vascular endothelial cell	46

STAT6 Degradation in Hematopoietic Cells



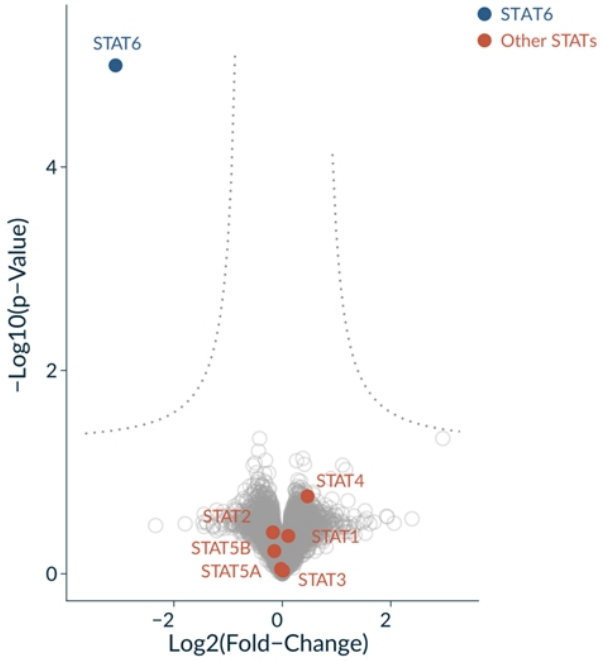
STAT6 Degradation in Tissue Cells



KT-621: Exquisite Degradation Selectivity for STAT6

Complete STAT6 degradation selectivity in human PBMC proteome at 100 x DC_{90}

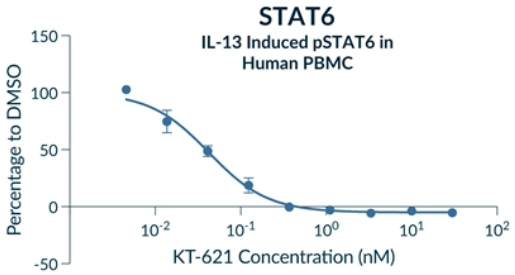
No other STATs are degraded to any extent

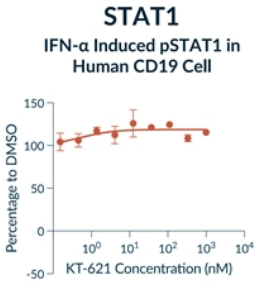


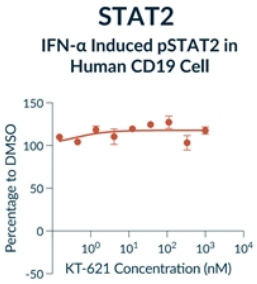
KT-621: Exquisite Pathway Selectivity for STAT6

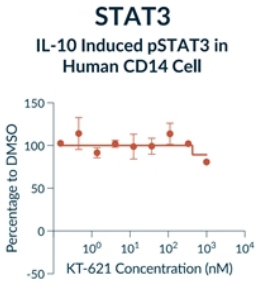
No Impact on Any Other STAT Pathway Observed

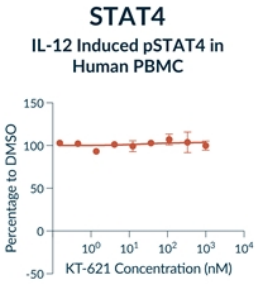
STAT assays	KT-621, IC_{50} (nM)
IFN-α induced pSTAT1	> 1000
IFN-α induced pSTAT2	> 1000
IL-10 induced pSTAT3	> 1000
IL-12 induced pSTAT4	> 1000
IL-2 induced pSTAT5	> 1000
IL-13 induced pSTAT6	0.042

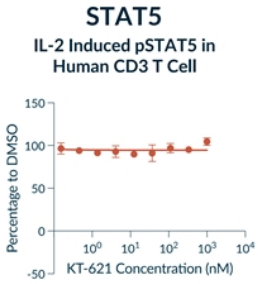








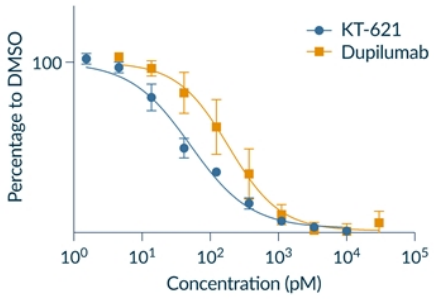




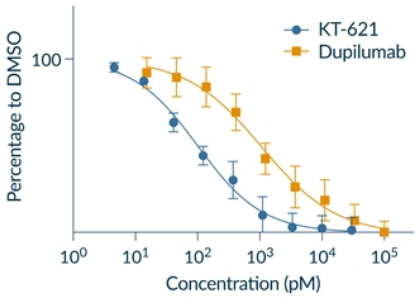
KT-621 Fully Blocks IL-4/13 Pathway, More Potently than Dupilumab

		Cellular Functional Assay	KT-621 IC_{50} (pM)	Dupilumab IC_{50} (pM)
TARC	Serum Th2 biomarker, chemoattractant for Th2 cell	IL-4 TARC release in human PBMC	**62**	194
		IL-13 TARC release in human PBMC	**43**	113
CD23	B cell activation marker, correlates with IgE class switch	IL-4 CD23 expression in human CD19 B cell	**125**	354
		IL-13 CD23 expression in human CD19 B cell	**98**	1070
PERIOSTIN	Serum Th2 biomarker and ECM protein associated with tissue remodeling in atopic diseases	IL-13 Periostin release in human bronchial smooth muscle cell	**24**	637
		IL-13 Periostin release in human esophageal smooth muscle cell	**39**	431

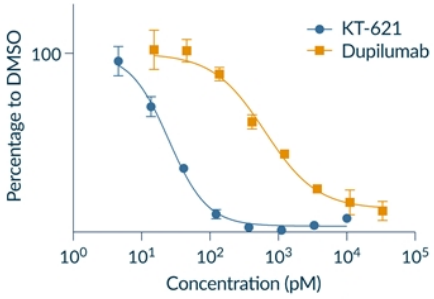
IL-4 Induced TARC Release in Human PBMC



IL-13 Induced CD23 Expression in Human CD19 B Cell



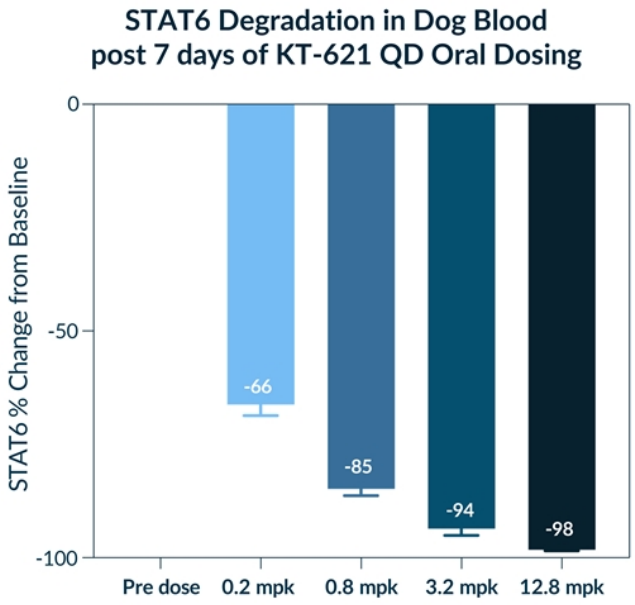
IL-13 Induced Periostin Release in Human Bronchial Smooth Muscle Cell



KT-621 Achieves Dose Dependent Deep Degradation of STAT6 *in vivo* with Low Oral Doses

KT-621 potently degrades STAT6 across multiple preclinical species

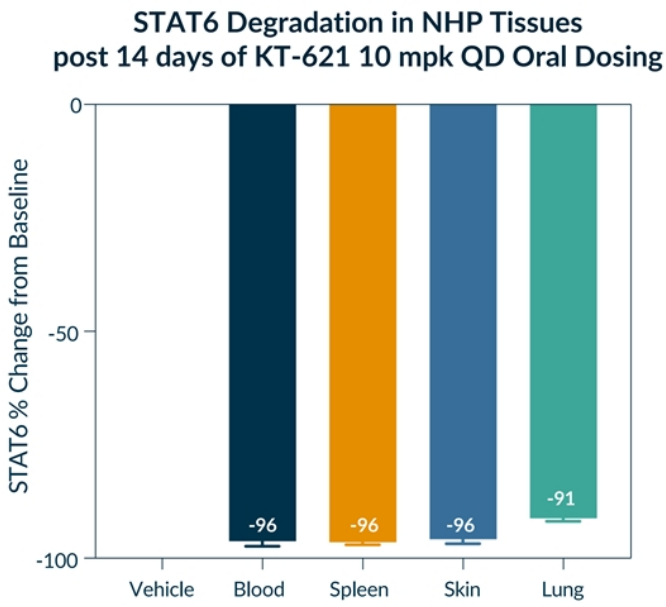
KT-621 can degrade STAT6 to depletion with low oral doses



KT-621 Degrades STAT6 in Disease Relevant Tissues in NHP

Deep degradation of STAT6 in NHP after 14 days of daily oral dosing

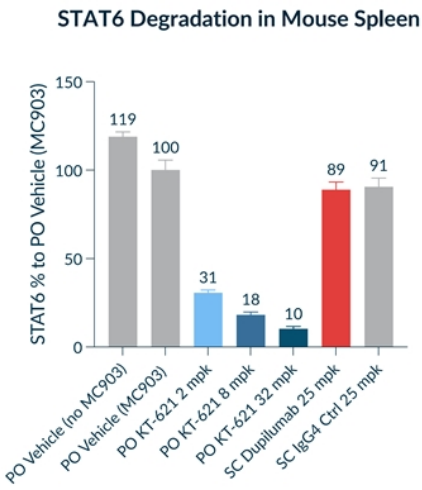
STAT6 is degraded in key disease-relevant tissues: blood, spleen, skin and lung

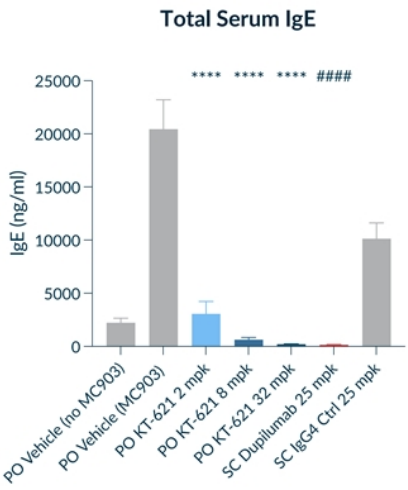


KT-621 Has Comparable *in vivo* Efficacy to IL-4Rα Saturating Dose of Dupilumab in the MC903 Atopic Dermatitis Model

An atopic dermatitis model induced by topical application of low-calcemic vitamin D3 analog MC903 with prominent Th2 inflammation in the IL4/IL4RA humanized mice:

- **KT-621 dosed QD orally for 11 days**
- **Dupilumab dosed 4 times subcutaneously**, 25 mpk twice a week (IL-4Rα saturating dose); **effect equivalent to 300 mg every other week in human**



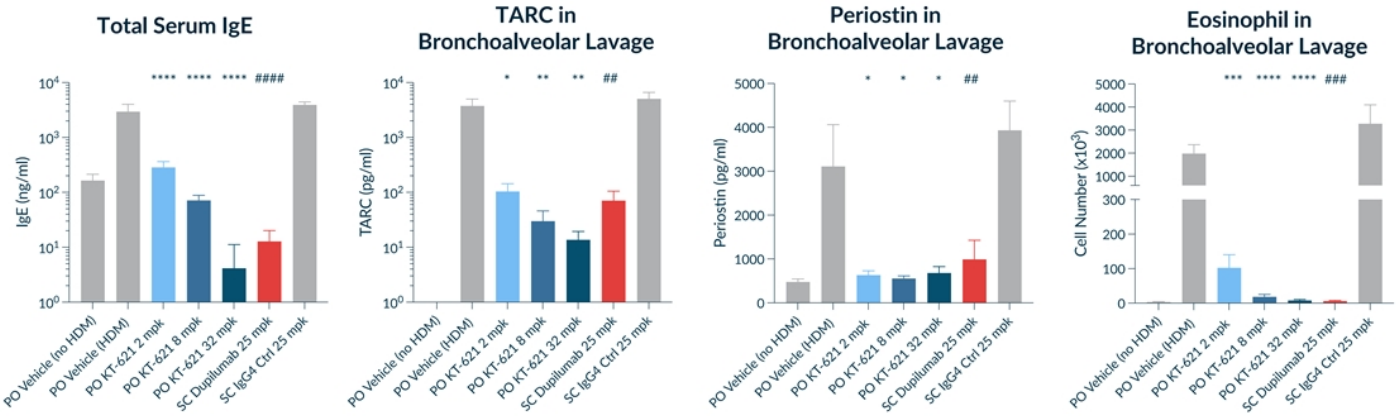


* Significance to PO vehicle (MC903); # Significance to SC IgG4 25 mpk BIW

KT-621 Has Comparable or Superior *in vivo* Efficacy to IL-4Rα Saturating Dose of Dupilumab in the Intranasal HDM Asthma Model

A lung inflammation model induced by intranasal house dust mite administration with dominant Th2 inflammation **in the IL4/IL4RA humanized mice** (Le Floc'h et al. *Allergy*. 2020)

- **KT-621 dosed QD orally for 31 days. 2/8/32 mpk** doses showed **72/85/91% STAT6 degradation** respectively in mouse spleen
- **Dupilumab dosed 9 times subcutaneously,** 25 mpk BIW (IL-4Rα saturating dose), **effect equivalent to 300 mg every other week in human**



*Significance to PO vehicle (HDM); # Significance to SC IgG4 Ctrl 25 mpk

Oral STAT6 Degrader: KT-621

Dupilumab-like efficacy with oral small molecule profile

Validated Biology

Specific and essential transcription factor in IL-4 and IL-13 signaling pathways

Central driver of Th2 inflammation

STAT6 validated by human genetics

Pathway validated by human genetics and dupilumab across multiple indications

Competitive Profile

WW IL-4/IL-13 biologic market currently $10B+ annually

Estimated to grow to $23B+ with expanded indications and new entrants

Mega-blockbuster potential for oral degraders with dupilumab-like efficacy and good safety

Potential to access beyond biologics-eligible patients and much larger population

KT-621, FIH: 2H 2024

Full IL-4 and IL-13 functional inhibition with picomolar IC50s superior to dupilumab

Robust efficacy shown in *in vivo* models of atopic dermatitis and lung inflammation equal or superior to dupilumab

STAT6 degradation was well-tolerated in multiple preclinical safety studies at >40x efficacious concentration

Currently in IND enabling studies

Degrading a Proven Target: KT-294, a First-in-Class Oral TYK2 Degrader

Juliet Williams, Ph.D.,
Head of Research

What We Will Cover

- TYK2 Biology and Target Rationale
- Clinical Development/Commercial Opportunities
- Degrader Advantage
- Preclinical Data
- Next Steps

TYK2 Biology and Target Rationale

Target Biology and Rationale

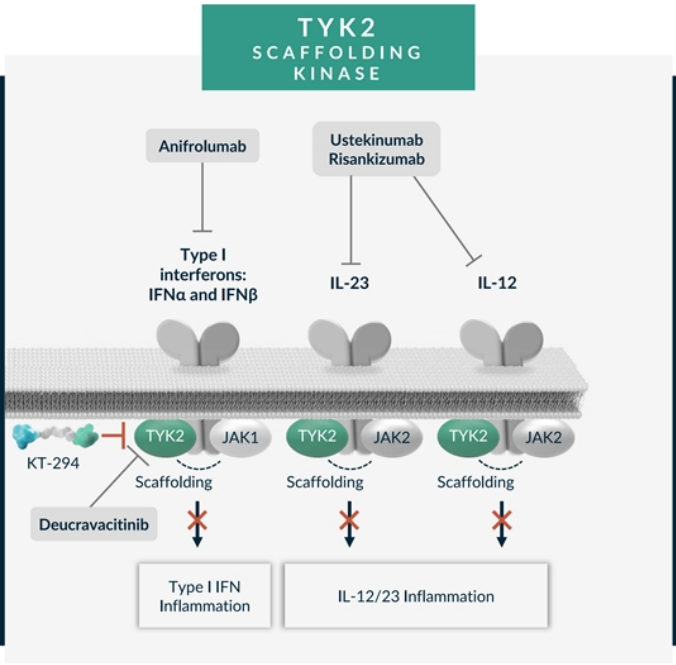
- TYK2 is a member of the JAK family required for Type I IFN, IL-12 and IL-23 cytokine signaling
- TYK2 regulated cytokines are clinically validated targets for autoimmune and inflammatory diseases

Human Genetics

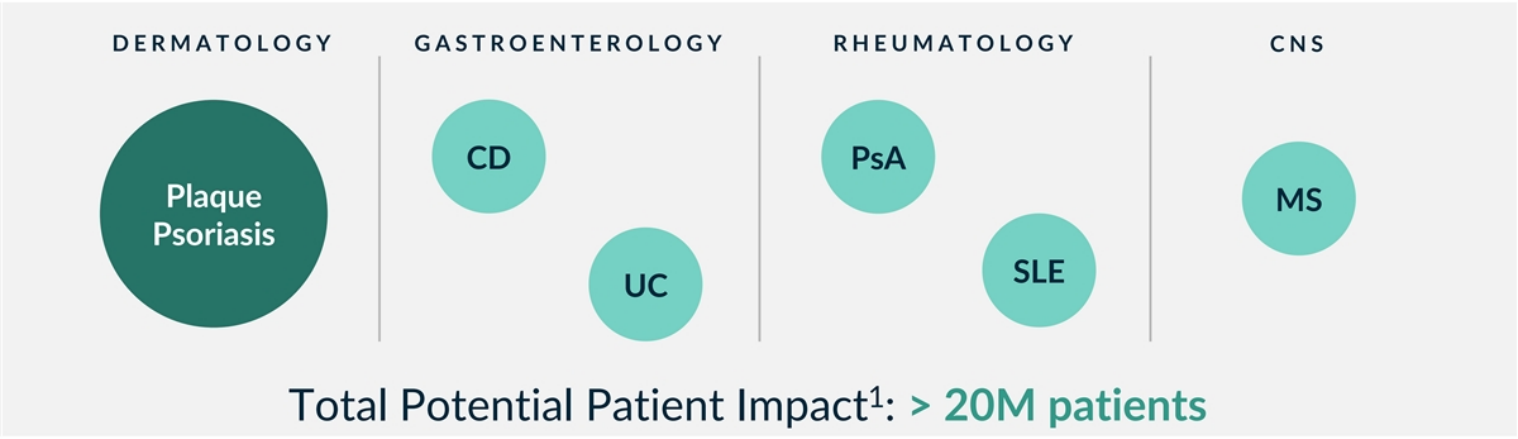
- Loss-of-function variant of TYK2 is protective in autoimmune and inflammatory diseases

Clinical Pathway Validation

- IL-23 (± IL-12)-targeting agents include ustekinumab, risankizumab, guselkumab, and tildrakizumab, with approvals in PsO, PsA, CD, UC
- Type I IFN-targeting agents include anifrolumab with approval in SLE
- TYK2 SMI deucravacitinib recently approved in PsO



Patient Impact of TYK2: Potential Best-In-Class Opportunity in I&I



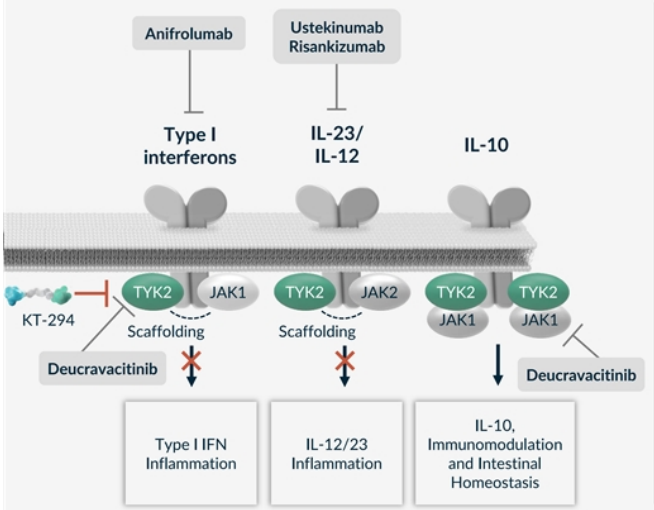
Total Potential Patient Impact[1]: > 20M patients

- Numerous indication opportunities across multiple therapeutic areas de-risked by biologics and deucravacitinib
- TYK2 degradation, differentiated from inhibition, leads to full pathway inhibition with potential to deliver biologic-like activity
- Oral degrader medicines offer opportunity to reach broader patient populations

[1]GlobalData (2022 diagnosed prevalent patient population for US/EU5/JP)

TYK2 Degrader Advantage

Only TYK2 Degraders Can Reach Biologics-like Activity



- TYK2 has a well-established scaffolding function that is responsible for cytokine receptor surface expression and activation
- Unlike SMIs, only TYK2 degradation recapitulates the human LOF phenotype of full pathway inhibition of Type I IFN, IL-12 and IL-23 and sparing of IL-10
  - Unlike deucravacitinib, which inhibits IL-10 through JAK1, KT-294 does not inhibit IL-10, which is important in IBD
  - Compared to TAK-279, KT-294 fully inhibits Type I IFN
- Full TYK2 degradation demonstrated by KT-294 leads to superior pathway inhibition to existing SMIs and potentially reach biologic-like activity

TYK2 Has Well-Established Scaffolding Function

- TYK2 complete deficiency severely impairs IL-23, Type I IFN, and IL-12 signaling but spares IL-10 in humans
- TYK2 scaffolding functions are demonstrated by differential pathway inhibitions in complete TYK2 deficiency vs a kinase dead variant in humans
- TYK2 deficient humans are generally healthy with only increased risk of some mycobacteria and viral infections that are relatively mild, curable and tend not to recur, de-risking safety for TYK2 degradation

Cytokine Pathway	IL-23	Type I IFN	IL-12	IL-10
WT TYK2	++++	++++	++++	++++
Complete deficiency TYK2 -/-	+	+	+	+++
TYK2 Kinase dead P1104A/P1104A	+	++++	++++	++++

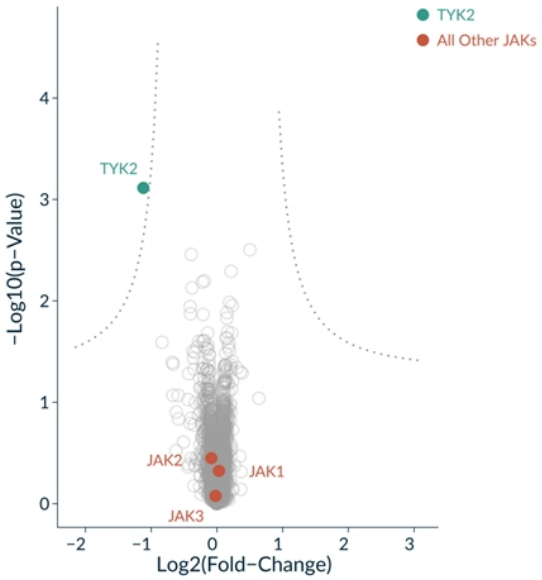
Degrading TYK2 is the only small molecule approach to eliminate all scaffolding and catalytic functions of TYK2, fully recapitulating the human TYK2-/- biology

Ogishi et al. JEM. 2022

KT-294, a Highly Selective Picomolar TYK2 Degrader, Recapitulates TYK2 Human Deficiency Biology

Fully Inhibits of Type I IFN and IL-12/23 and Spares IL-10/22

Selective TYK2 Degradation by KT-294 in hPBMC Proteome at 10x DC_{90}



Cellular Degradation/Functional Assay	KT-294 DC_{50}/IC_{50} (nM)
Human PBMC degradation	0.08
Human keratinocyte (neonatal and adult)	0.07
IL-23 pathway	
IL-23 pSTAT4 in human PBMC	0.7
IL-23 pSTAT3 in human CD3+CD161high TH17 cell	2.1
IL-23/IL-1β IFN-γ release in human PBMC	2.4
Type I IFN pathway	
IFN-α pSTAT1 in human CD19 B cell	13
IFN-α pSTAT2 in human CD19 B cell	15
IFN-α IP10 release in human PBMC	4.9
IL-12 pathway	
IL-12/IL-18 pSTAT4 in human PBMC	1.3
IL-12/IL-18 IFN-γ release in human PBMC	10
IL-10 and IL-22 pathways	
IL-10 pSTAT3 in human CD14 monocyte	> 1000
IL-22 pSTAT1 in HT29 cell	> 1000
IL-22 pSTAT3 in HT29 cell	> 1000

KT-294, Unlike Allosteric TYK2 Inhibitor Deucravacitinib, Does not Inhibit IL-10

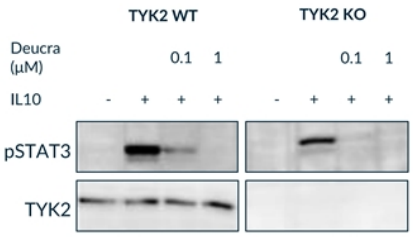
IL-10 has essential roles in intestinal homeostasis

- Loss of function mutations of the IL-10 pathway cause early onset refractory colitis in humans

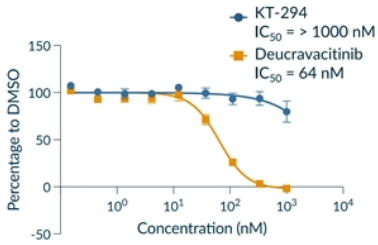
Deucravacitinib inhibits IL-10 through JAK1

- Deucra JAK1 Ki = 0.33 nM (Burke et al. Sci Transl Med. 2019)
- KT-294 JAK1 Ki = > 1000 nM

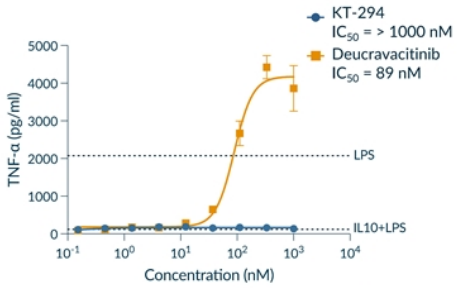
Deucra Inhibited IL-10 induced pSTAT3 in TYK2 KO EBV B Cell



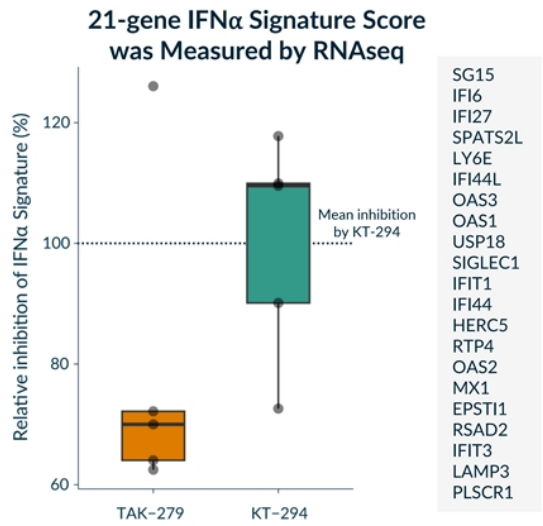
Deucra Inhibited IL-10 Induced pSTAT3 in Human CD14 Monocyte

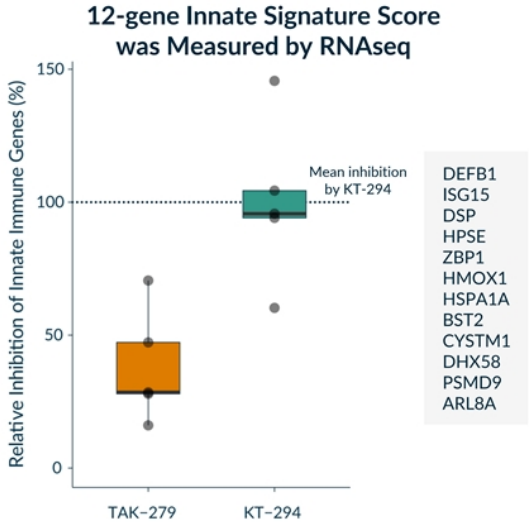


Deucra Inhibits IL-10's Function of Suppressing LPS Induced TNF-α Release in Human CD14 Monocyte



Superior Inhibition of Type I IFN Pathway and Innate Immunity by KT-294 vs TAK-279





Doses Used:

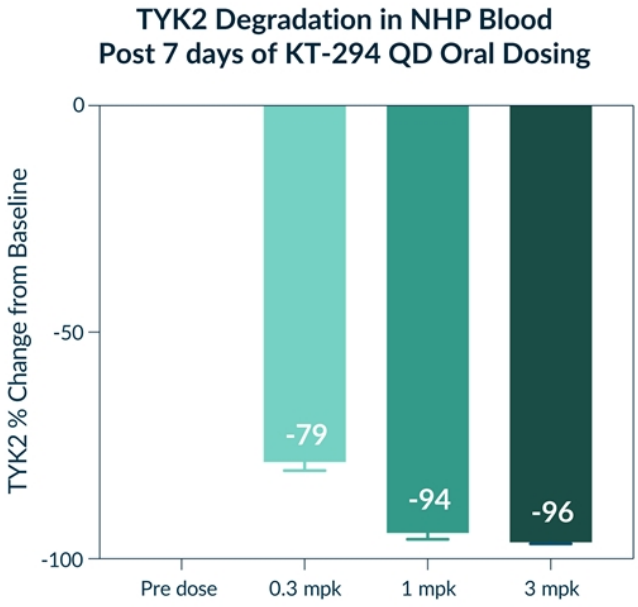
- TAK-279 = 422nM (IFNα stimulated pSTAT2 IC_{95}). Clinical exposure Cmax (free) at 35mg = ~ 77 nM
- KT-294 = 56nM (IFNα stimulated pSTAT2 IC_{95})

At concentrations where TAK-279 and KT-294 block pathway 95%, degrader demonstrates superior biological effect. (TAK-279 does not reach these exposures in clinic)

KT-294 Achieved Dose Dependent Deep Degradation of TYK2 *in vivo* with Low Oral Doses

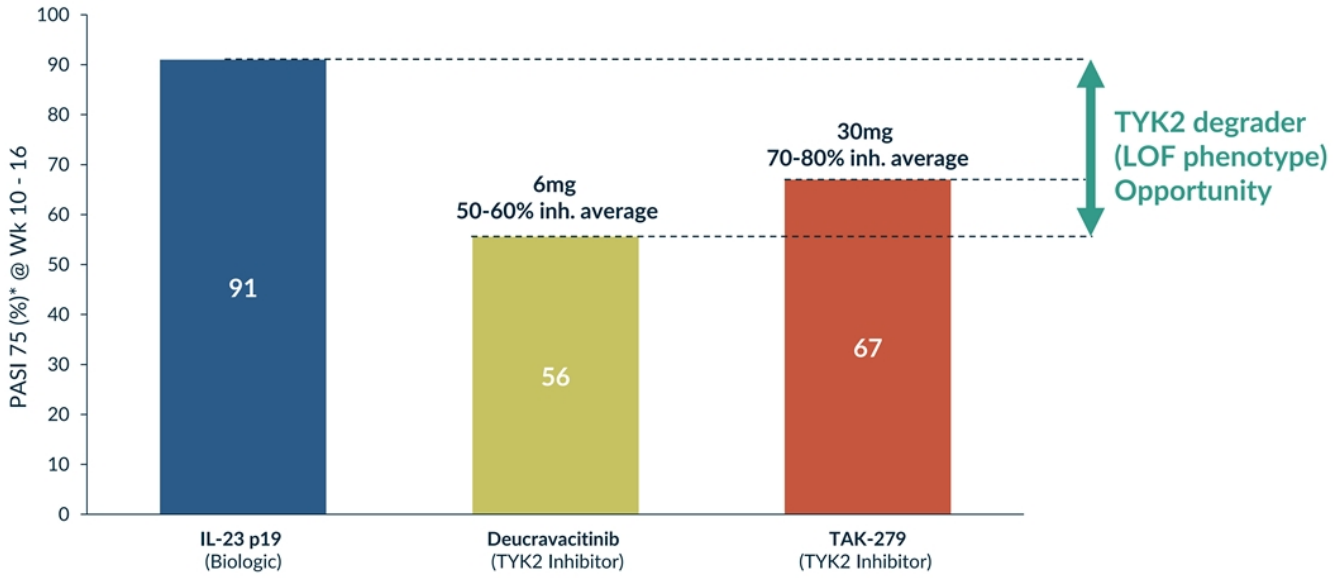
KT-294 potently degrades TYK2 across multiple preclinical species

In NHP, KT-294 can degrade TYK2 to depletion with low oral doses



TYK2 SMI's Do Not Reach Maximal Target Engagement

Clinical Efficacy In Psoriasis is Target Engagement Dependent



Company presentations and package inserts; * total observed response rate for primary endpoint cut-off ranges from Wk 10 to Wk 16.

Biological and Clinical Differentiation

TYK2 Clinical Opportunities	Deucravacitinib IL12/23, IFN, IL10	TAK-279 IL12/23, ~IFN	KT-294 IL12/23, IFN	*KT-294, unlike TYK2 SMI, can replicate the TYK2 deficient phenotype and result: potent Type I IFN, IL-12/23 inhibition fully while sparing IL-10* **WITH FOLLOWING EXPECTED CLINICAL DIFFERENTIATION:**
Psoriasis	++	++	+++	**>90% degradation vs 70-80% inhibition at steady state (best anti-IL23 profile)**
Psoriatic Arthritis	++	++	+++	**>90% degradation vs 70-80% inhibition at steady state (best anti-IL23 profile)**
IBD	-	++	+++	**>90% degradation vs 70-80% inhibition at steady state (best anti-IL23 profile), + sparing IL-10**
Lupus & interferonopathies	++	+	+++	**>90% degradation vs 70-80% inhibition at steady state (best anti-IL23 profile) + best anti-IFN profile**

Oral TYK2 Degrader: KT-294

Potential Best-in-Class Opportunity with Biologic-like Profile

Validated Biology

TYK2 is a member of the JAK family required for Type I IFN, IL-12 and IL-23 cytokine signaling

Pathway validated by upstream biologics (i.e. ustekinumab) and TYK2 SMI across many diseases

TYK2 validated by human genetics

Competitive Profile

IL-23 and Type 1 IFN-based biologic market currently ~$18B annually

Estimated to grow to ~$27B with expanded indications and new entrants

TYK2 SM inhibitors have limitations due to selectivity (deucravacitinib) or lack of potent IFN-α activity (TAK-279) and limited clinical target engagement (both)

Mega-blockbuster potential for oral degrader with biologic-like activity that is superior to TYK2 SMI

KT-294, FIH: 1H 2025

Degrades TYK2 in human cells with pM potency

Recapitulates the phenotype of TYK2 human deficiency showing potent IFN-α, IL-12 and IL-23 inhibition and sparing IL-10

Dosed orally, shows complete TYK2 degradation in NHP providing a path to full target engagement in clinic, unlike current SMI

Currently in IND enabling studies

Solving Big Problems with Small Molecules

Nello Mainolfi, Ph.D.,
Founder, President and CEO

A Powerful Strategy That Puts Patients First

We focus on genetically validated targets/pathways that are either undrugged or inadequately drugged, where TPD is the best or the only solution

With a growing understanding of the underlying biology and many key pathways/targets validated by biologics, I&I offers large clinical/commercial opportunities

TPD can provide a unique solution with biologic-like specificity and efficacy, with the flexibility of oral small molecules

Our unique approach and capabilities have generated a best-in-industry oral I&I pipeline of first-in-class, highly valuable programs

Revolutionizing Immunology with Small Molecule Oral Degraders

	IRAK4 (KT-474) SCAFFOLDING KINASE	STAT6 (KT-621) TRANSCRIPTION FACTOR	TYK2 (KT-294) SCAFFOLDING KINASE
Status	• Phase 2 Trials in HS and AD with Sanofi	• IND-Enabling	• IND-Enabling
Potential Indications	• HS, AD, RA, Asthma, COPD, IBD, others[1]	• AD, Asthma, COPD, CRSwNP, EoE, PN, others	• IBD, PsO, PsA, Lupus, others
Next Milestone	• **HS and AD Ph2 data: 1H 2025**	• **FIH: 2H 2024**	• **FIH: 1H 2025**
Opportunity	• First-in-class broad anti-inflammatory oral degrader	• Dupilumab-like activity in a pill	• Biologic-like activity in a pill
Commercial Rights	• Up to 50% US with Sanofi, tiered royalties in ROW[2]	• Wholly owned	• Wholly owned

[1]Current indications; HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities; [2]KT-474 (SAR444656) partnered with Sanofi, with Kymera option to participate in the development and commercialization, and 50/50 profit split, in the United States. Double digit tiered royalties in ROW.

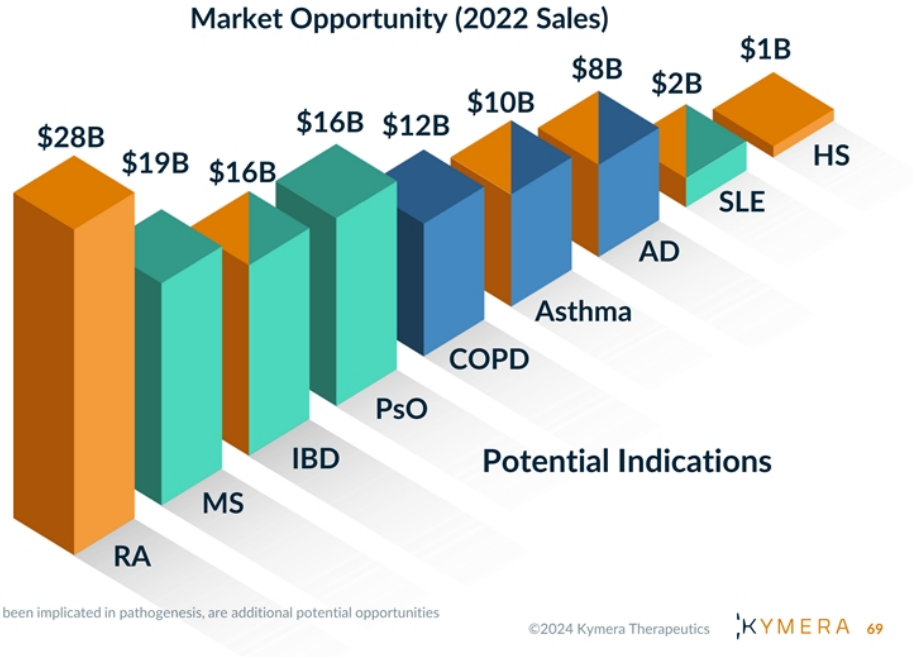
Kymera Immunology Oral Degrader Portfolio

Complementary Mechanisms Each with Mega-blockbuster Potential

IRAK4[1]: IL-1R/TLR pathway
Th1/17/Th2 biology

STAT6: IL-4/13 pathway
Th2 biology

TYK2: IL-23/IFN pathway



GlobalData, focused only on large markets based on 2022 sales of approved drugs

[1]Current indications; HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities

Immunology Pipeline with Clear Line of Sight to Large Value Creation

	Potential Indications	2024	2025	2026+	Upcoming Milestones	Rights
Oral QD Small Molecule Degraders						
IRAK4* **KT-474**	HS, AD, RA, Asthma, IBD, other[1]	HS Ph2 ▲ HS Late Development AD Ph2 ▲ AD Late Development			Ph2 HS & AD Data 1H 2025	sanofi KYMERA 50/50 US
STAT6 **KT-621**	AD, Asthma, COPD, PN CRSwNP, EoE	IND	Ph1 ▲ Mid-Late Development		Ph1 Start 2H 2024	KYMERA
TYK2 **KT-294**	Psoriasis, IBD, PsA, Lupus, other	IND	Ph1 ▲ Mid-Late Development		Ph1 Start 1H 2025	KYMERA

*KT-474 (SAR444656) partnered with Sanofi, with Kymera option to participate in the development and commercialization, and 50/50 profit split, in the United States. Double digit tiered royalties in ROW

Our Discovery Engine in Immunology

Areas of Focus:

- Humoral Immunity
- Rheumatology
- Plasma Cell Biology
- Respiratory Inflammation
- GI Inflammation
- Local Inflammation

▲ = key data readout

[1]Current indications; HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities

Pipeline with Clear Line of Sight to Large Value Creation

	Potential Indications	2024	2025	2026+	Upcoming Milestones	Rights
Immunology – Oral QD Small Molecule Degraders						
IRAK4* **KT-474**	HS, AD, RA, Asthma, IBD, other[1]	HS Ph2 / AD Ph2	HS Late Development / AD Late Development		Ph2 HS & AD Data 1H 2025	sanofi KYMERA 50/50 US
STAT6 **KT-621**	AD, Asthma, COPD, PN CRSwNP, EoE	IND	Ph1	Mid-Late Development	Ph1 Start 2H 2024	KYMERA
TYK2 **KT-294**	Psoriasis, IBD, PsA, Lupus, other	IND	Ph1	Mid-Late Development	Ph1 Start 1H 2025	KYMERA
Oncology						
STAT3** **KT-333**	PTCL, LGL-L, CTCL, Solid Tumors	Ph1		Mid-Late Development	Ph1 Data 2024	KYMERA
MDM2 **KT-253**	Liquid & Solid Tumors	Ph1		Mid-Late Development	Ph1 Data 2024	KYMERA

*KT-474 (SAR444656) partnered with Sanofi, with Kymera option to participate in the development and commercialization, and 50/50 profit split, in the United States. Double digit tiered royalties in ROW

**Assessment of STAT3 I/I opportunity is ongoing ▲ = key data readout

[1]Current indications; HS and AD. Other diseases shown, where IL-1R/TLR pathway has been implicated in pathogenesis, are additional potential opportunities

2024 PRIORITIES

- Completion of enrollment in IRAK4 oral degrader KT-474 Phase 2 trials in HS and AD by partner Sanofi (topline data 1H 2025)
- Initiation of oral STAT6 degrader KT-621 Phase 1
- IND ready for oral TYK2 degrader KT-294
- Additional oncology proof-of-concept data for the STAT3 degrader KT-333 and MDM2 degrader KT-253

Thank You

Q&A

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Abbreviations

Ab	Antibody
AD	Atopic Dermatitis
AN Count	Abscess and Inflammatory Nodule Count
CAGR	Compound Annual Growth Rate
CAPS	Cryopyrin-Associated Periodic Syndrome
CD	Crohn's Disease
cHL	Classic Hodgkin's Lymphoma
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
CRSwNP	Chronic Rhinosinusitis with Nasal Polyps
CTCL	Cutaneous T-Cell Lymphoma
Ctrl	Control
C_{trough}	Trough Concentration
CU	Chronic Urticaria
$DC_{\#}$	Degradation Concentration
DMSO	Dimethyl Sulfoxide
EASI	Eczema Area and Severity Index
EBV	Epstein-Barr Virus
ECM	Extracellular Matrix
ENT	Ear Nose Throat
EoE	Eosinophilic Esophagitis
EU	European Union
FIH	First-in-Human
GDF15	Growth Differentiation Factor 15
GI	Gastrointestinal
GOF	Gain of Function
HDM	House Dust Mite
HiSCR	Hidradenitis Suppurativa Clinical Response
hPBMC	Human Peripheral Blood Mononuclear Cells
HS	Hidradenitis Suppurativa
HV	Healthy Volunteers
I&I	Immunology and Inflammation
IBD	Inflammatory Bowel Disease
$IC_{\#}$	Inhibitory Concentration
IFN	Interferon
IHS4	International Hidradenitis Suppurativa Severity Score
IL	Interleukin
IND	Investigational New Drug Application
IP	Intellectual Property
IRAK4	Interleukin 1 Receptor Associated Kinase 4
IRAKIMiD	IRAK4 and IMiD substrates
JAK	Janus Kinase
JP	Japan
KO	Knockout
LGL-L	Large Granular Lymphocytic Leukemia
LOF	Loss of Function
LPS	Lipopolysaccharide Solution
MAD	Multiple Ascending Dose Study
MCC	Merkel Cell Carcinoma
MDM2	Mouse Double Minute 2
MS	Multiple Sclerosis
MYD88	Myeloid Differentiation Primary Response Protein 88
NF-kB	Nuclear Factor Kappa B
nM	Nanomolar
NRS	Numerical Rating Scale
PASI	Psoriasis Area and Severity Index
PBMC	Peripheral Blood Mononuclear Cells
Pbo	Placebo
Ph	Phase
PK/PD	Pharmacokinetics/Pharmacodynamics
PN	Prurigo Nodularis
POC	Proof-of-Concept
PP-NRS	Peak Pruritus Numerical Rating Scale
PsA	Psoriatic Arthritis

Abbreviations

PsO	Psoriasis
pSTAT	Signal Transducer and Activator of Transcription
PTCL	Peripheral T-Cell Lymphoma
QD	Once a day
QoL	Quality of Life
R&D	Research and Development
RA	Rheumatoid Arthritis
RNAseq	Ribonucleic Acid Sequencing
ROW	Rest of World
SAD	Single Ascending Dose study
SLE	Systemic Lupus Erythematosus
SMI	Small Molecule Inhibitor
STAT	Signal Transducer and Activator of Transcription
STAT3	Signal Transducer and Activator of Transcription 3
STAT6	Signal Transducer and Activator of Transcription 6
TARC	Thymus and Activation-Regulated Chemokine
Th1	Type 1
Th2	Type 2
Th17	Type 17
TLR	Toll-like Receptors
TPD	Targeted Protein Degradation
TYK2	Tyrosine Kinase 2
UC	Ulcerative Colitis
US	United States
vIGA	Validated Investigator Global Assessment for AD
WT	Wildtype
WW	Worldwide