KYMERA
EST. 2016

INVENTING NEW MEDICINES

WITH TARGETED PROTEIN DEGRADATION

JP Morgan Healthcare Conference, January 11th 2022

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Proteome Editing is the New Frontier of Medicine

Genome

- Essentially **static**
- Alterations are responsible for **some** diseases
- Editing is **irreversible**

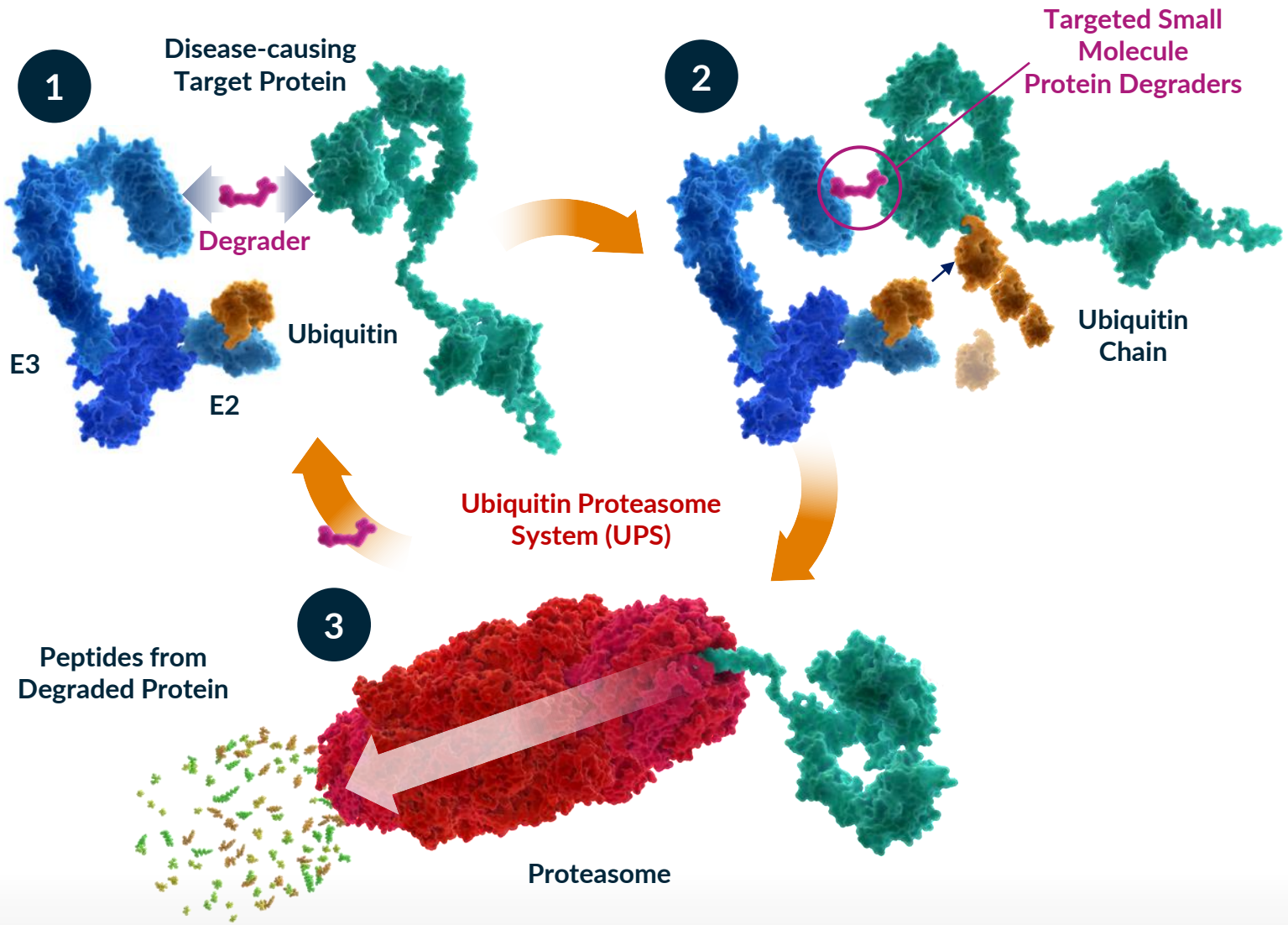
Encodes

Proteome

- **Changes** based on internal (genetic) and external (epigenetic) events
- Alterations are responsible for **all** diseases
- Editing is **reversible**

Proteome Editing with Targeted Protein Degradation

A Nobel Prize (2004) Inspired Technology

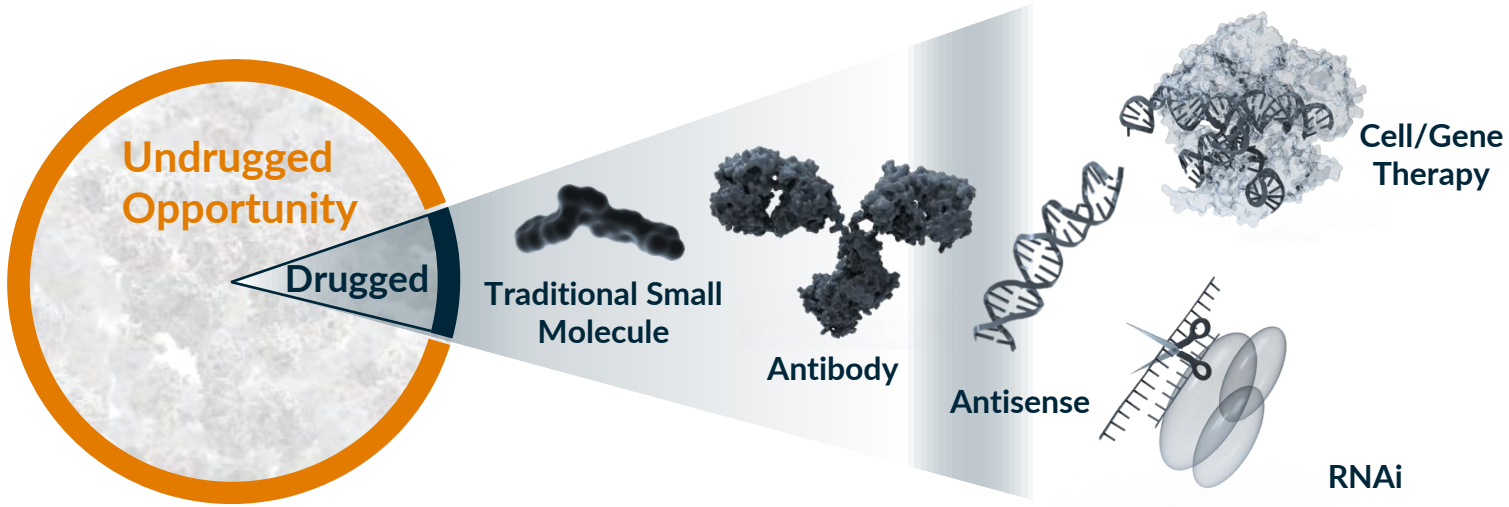


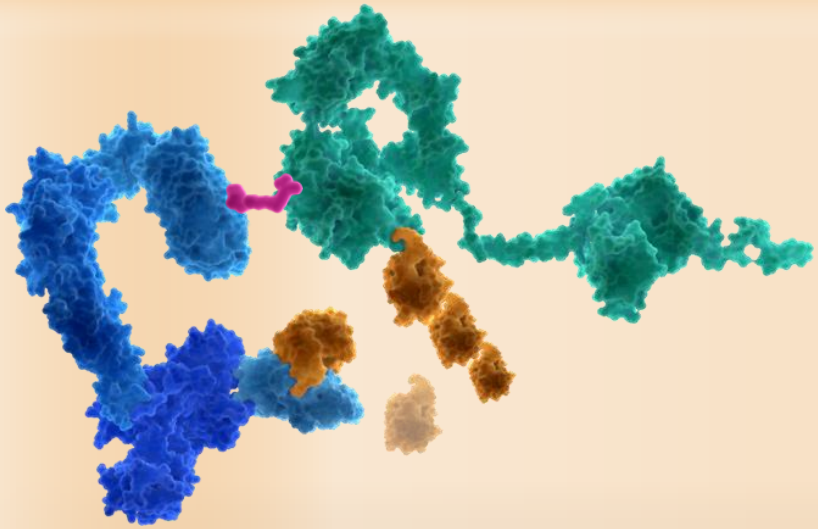
Expanded Opportunities

- Small molecule binds to E3 and target protein to effect its degradation
- Small Molecule only needs to "weakly" bind to protein:
  Not inhibit function
- Highly potent/catalytic:
  Small amount of drug needed
- Highly specific
- Genetic–like knock-down effects
- Advantage of small molecule development:
  Route of administration, manufacturing
- Agnostic to protein type and disease

Expanding Druggable Proteome with Targeted Protein Degradation

All therapeutic modalities to date **only drug up to 20%** of proteome

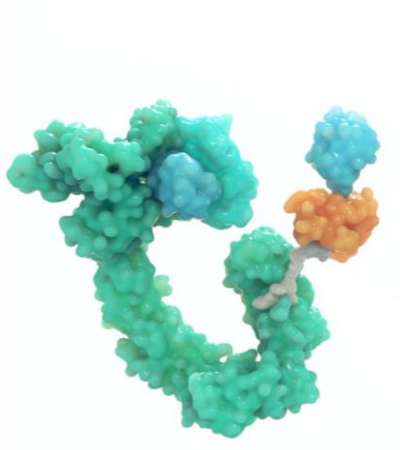




Kymera **is expanding the drugged proteome** with Targeted Protein Degradation (TPD)

Introduction to Kymera

KYMERA



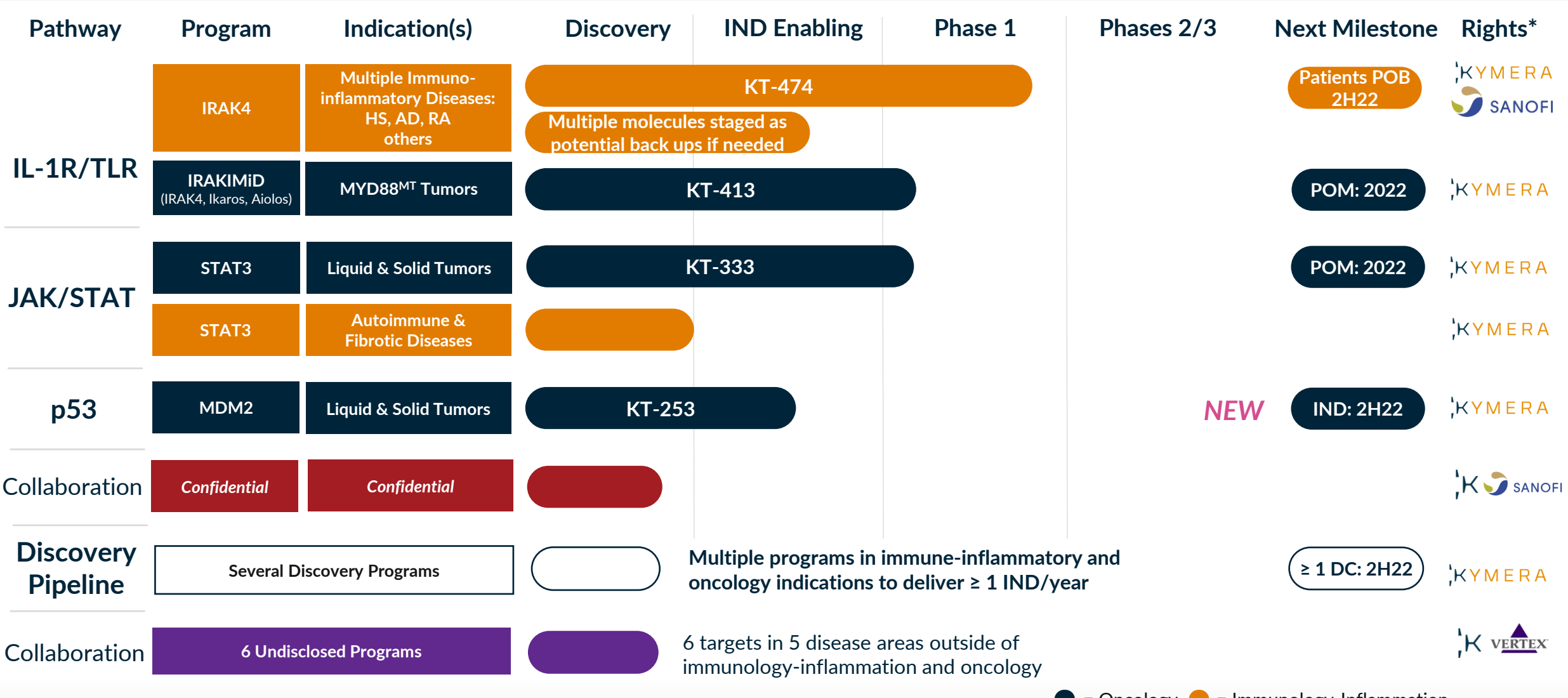
OUR VISION

To be a disease- and technology-agnostic, fully integrated global biopharmaceutical company, using targeted protein degradation to deliver medicines that will transform patients' lives

- **Leader** in Targeted Protein Degradation (TPD)
- Building a **fully-integrated**, global biotech company
- Initial focus in **Immunology/Inflammation and Oncology**, but already a **disease-agnostic platform**
- Accelerating forward integration through **key strategic partnerships**
- Establishing **many "firsts"** for TPD with initial programs
- Three clinical stage programs and **a deep pipeline positioned to deliver ≥1 IND/year**
- Focused on **continued innovation** in platform and discovery
- Well-capitalized with **$611 million of cash***

* Based on reported cash at Sep. 30th, 2021

Kymera's Pipeline of Novel Protein Degraders



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

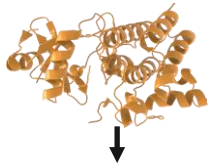
We Want to Drug All Target Classes

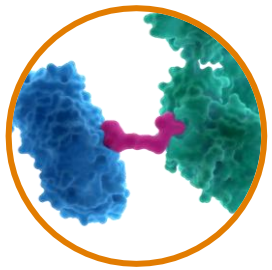
Expanding the Druggable Proteome with TPD

ID Inadequately Drugged Targets with Clear Degrader Advantage

Small molecule binders exist but unable to drug target fully

e.g. IRAK4, MDM2…



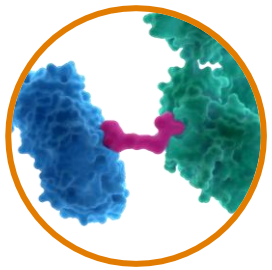


Heterobifunctional Degraders

UD Undrugged Targets

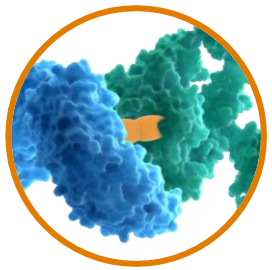
No other technology can drug

Ligandable Proteins
e.g. STAT3…



Heterobifunctional Degraders

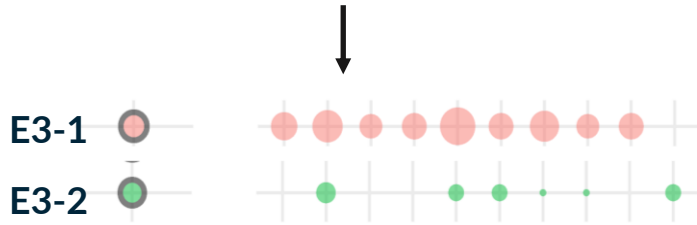
Un-ligandable Proteins
e.g. other transcription factors



Molecular Glues

TR Clinically Validated Targets Enabled by E3 Ligase Tissue Restricted Expression

On target unwanted pharmacology limits clinical application



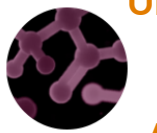
Tissue sparing or selective E3 ligases eliminate unwanted toxicity and allow full clinical potential

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
- **Toolbox of proprietary ligands** leverages the E3 Ligase Whole-Body Atlas



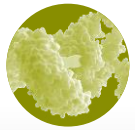
Understanding Degradation (PK/PD) Across Tissue Types

- **Quantitative System Pharmacology Model**
- Understanding and **Translating PK/PD** from preclinical systems into humans

Proprietary Chemistry

- **Comprehensive hit finding technologies toolbox**
- **Proprietary chemistry expertise, AI enabled optimization**
- Ability to convert into **degraders with optimal pharmaceutical properties**

NEW



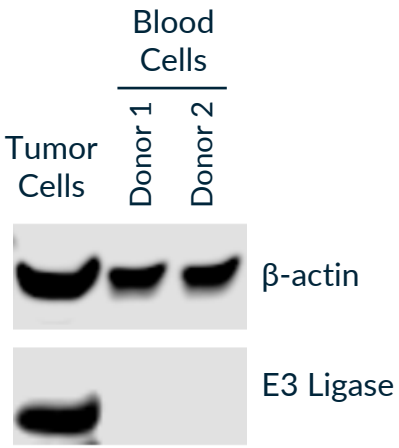
Center for Molecular Glue Discovery

- **Identification of novel E3 ligases** to degrade high value “undrugged and un-ligandable” proteins
- **With external collaborators** enable differentiated approach to molecular glues discovery

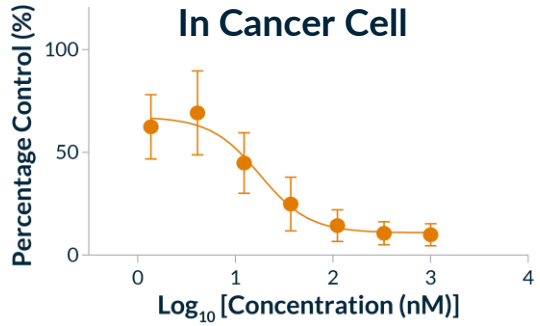
Tissue-Selective Degradation Drives Increase of Therapeutic Index

- Kymera has characterized an E3 ligase that is expressed broadly but NOT in ONE blood cell type
- A clinically validated oncology target has dose limiting toxicity driven by on-target pharmacology in the same blood cell type where this E3 ligase is absent/very low

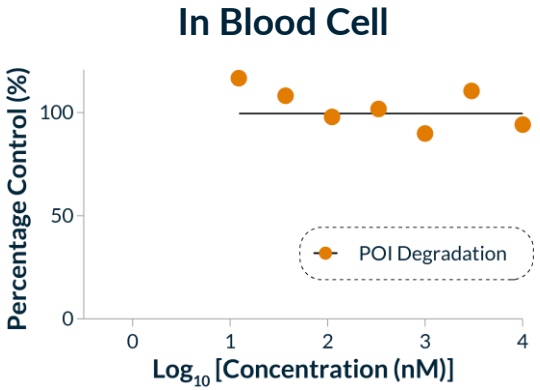
E3 Ligase is Almost Absent in One Blood Cell Type



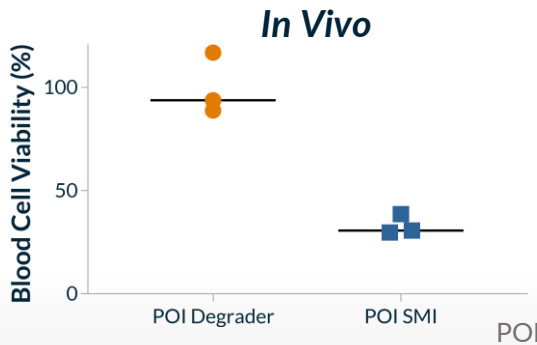
Optimization and Degrader Program



Kymera's degrader using this E3 ligase **degrades target in cancer cells**



Kymera's degrader using this E3 ligase **DOES NOT degrade target in one blood cell type**



In a pharmacologically active dose *in vivo* a **degrader allows blood cells to survive** while SMI leads to substantial cell death

- This program is projected to nominate a development candidate in 2022

POI = protein target of interest

Rationally Designing Molecular Glues to Drug Historically Undrugged/Unligandable Targets

To drug all genetically validated but **undrugged and un-ligandable** proteins through the discovery of novel E3 ligases and small molecule glues

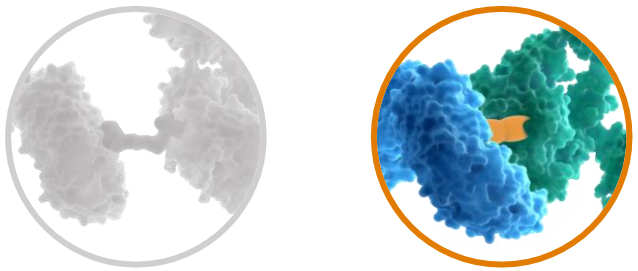
UD

Undrugged Targets

No other technology can drug

Ligandable Proteins
e.g. STAT3

Un-ligandable Proteins
e.g. other transcription factors



Heterobifunctional Degraders

Molecular Glues

Our Approach:

- We are **NOT** iterating on CRBN/IMiD Scaffold
- Identifying the best matched pairs between targets of interests and E3 ligases exploiting **natural affinity augmented with small molecule glues**
- Established a platform that uses high content genetic-based screens, structural insights, biological pathways deconvolution, degron discovery, computational knowledge expansion
- Multiple programs in discovery stage
- Strategic partnerships with:

A-ALPHA BIO

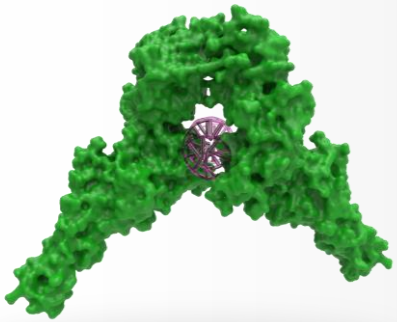
UNIVERSITY of WASHINGTON

NYU

Kymera's Differentiated Approach to TPD

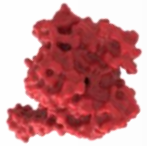
TARGET SELECTION

Unique approach focused on undrugged or not fully drugged targets with broad indication potentials



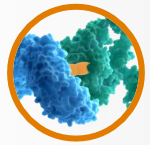
PLATFORM

Significantly differentiated investments



Tissue-selective E3 Ligases

Enabling a whole new generation of clinical programs

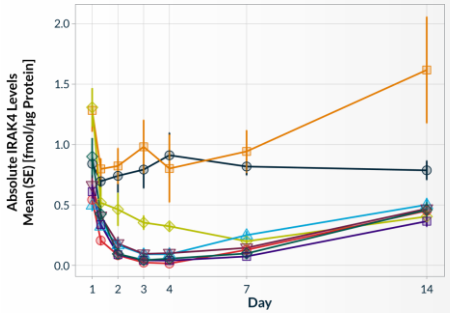


New Molecular Glue Approach

Novel strategy to address undrugged/ un-ligandable targets

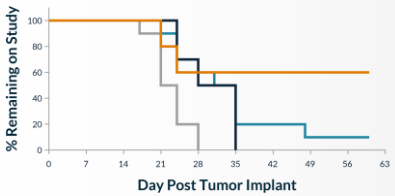
CLINICAL

Innovative clinical trial designs for degrader development



TPD "FIRSTS"

Kymera has accomplished several "firsts" in TPD



KT-474/ IRAK4

FIRST randomized, placebo-controlled trial in healthy volunteers

KT-333/ STAT3

FIRST Hetero-bifunctional degrader against an undrugged transcription factor in clinic

INNOVATION

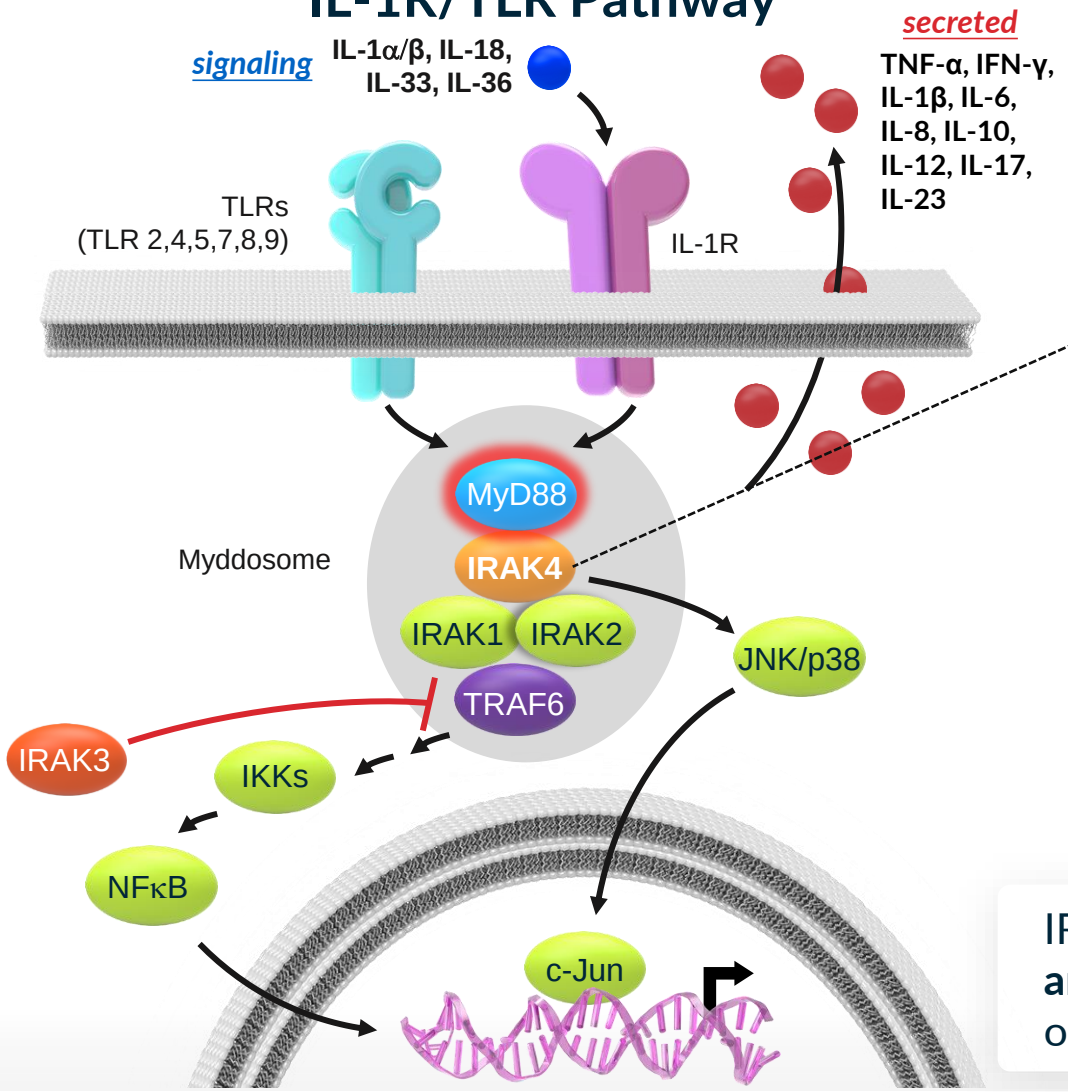
Serious commitment to constant evolution of our science

IRAK4

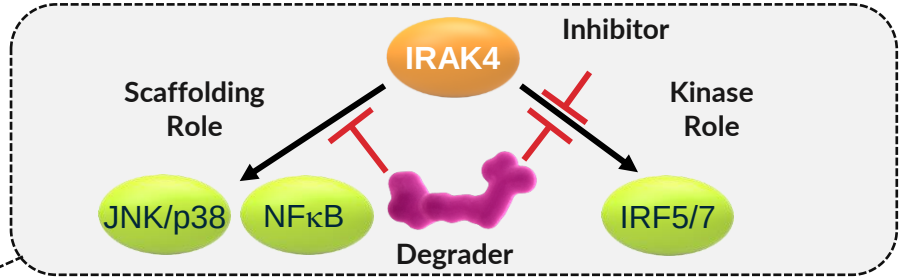
KYMERA

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

IL-1R/TLR Pathway



Degrader Advantage



Clinical Pathway Validation

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

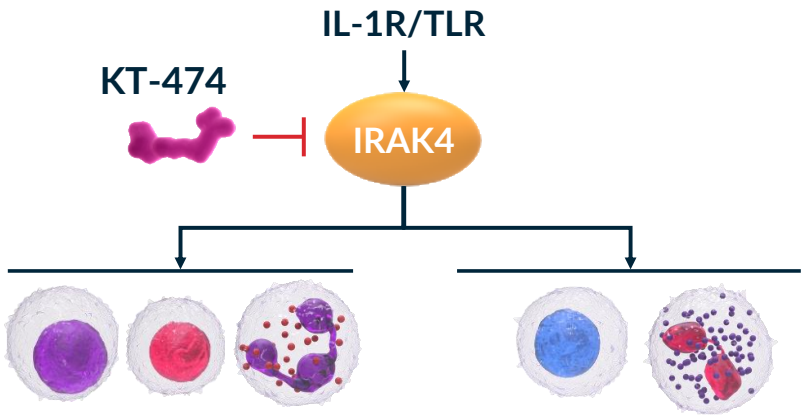
Human Genetics

Adult humans with **IRAK4 Null Mutation are healthy**

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

Development Opportunities for IRAK4 Degrader in Inflammation

Potential for Broad Activity Across Th1-Th17 and Th2 Diseases



Th1-Th17/Neutrophils

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

Th2/Eosinophils

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

$ 150B Combined global drug sales

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

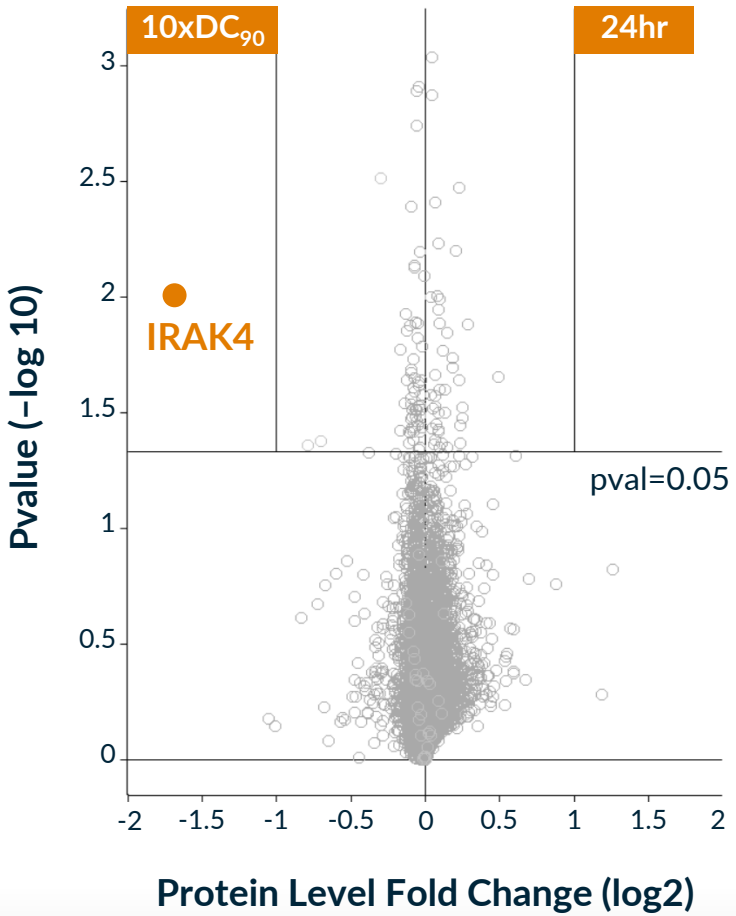
Limitations of Current Therapies

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

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

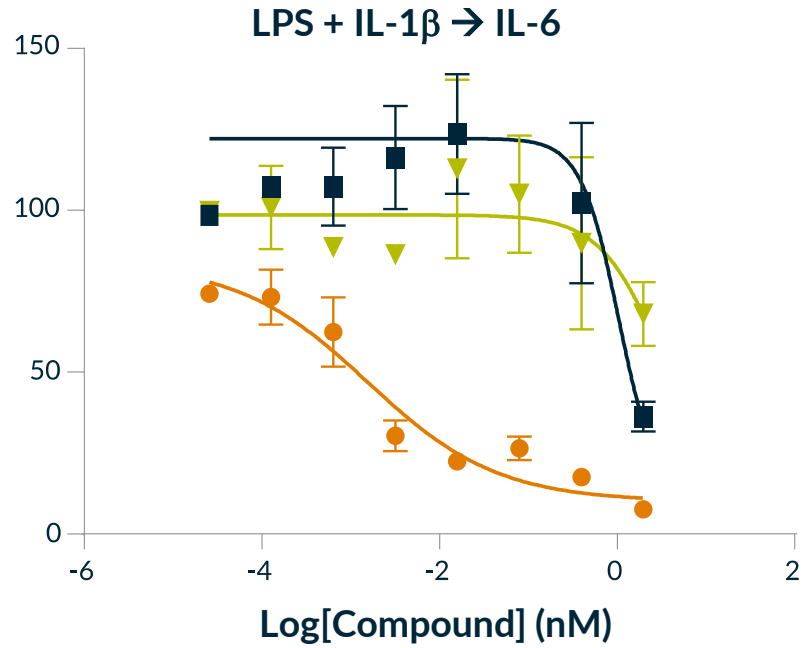
KT-474: Potent and Specific IRAK4 Degradation with Impact on Cytokines Superior to Kinase Inhibition

Degradation and Selectivity



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

Superiority over SM kinase Inhibitor



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

KT-474 Phase 1 Trial Design Includes HV and Patients

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

2 MAD Portion
Healthy Volunteers

- **4** cohorts (48 adult healthy subjects)
- **12** per cohort (9:3 randomization)
- **14x** daily doses (starting dose 25 mg)

3 MAD Portion
Patient Cohort

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

Endpoints

Primary
- Safety & tolerability

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

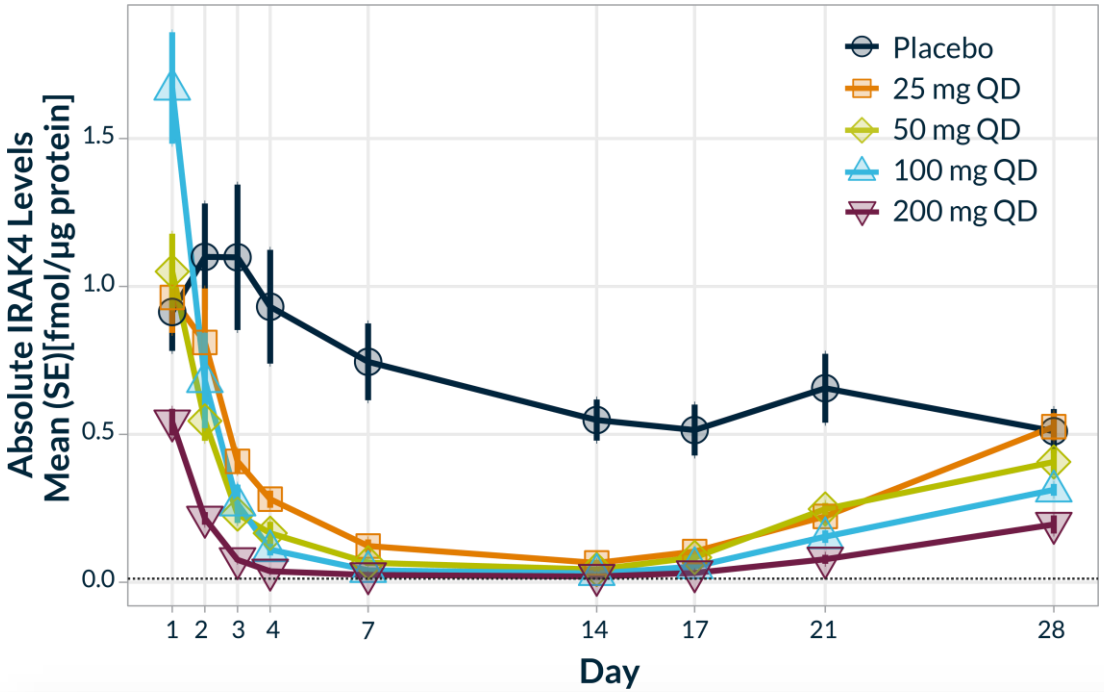
Exploratory
SAD & MAD
- *Ex vivo* response of whole blood to TLR agonists (SAD & MAD) and IL-1β (MAD only)

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

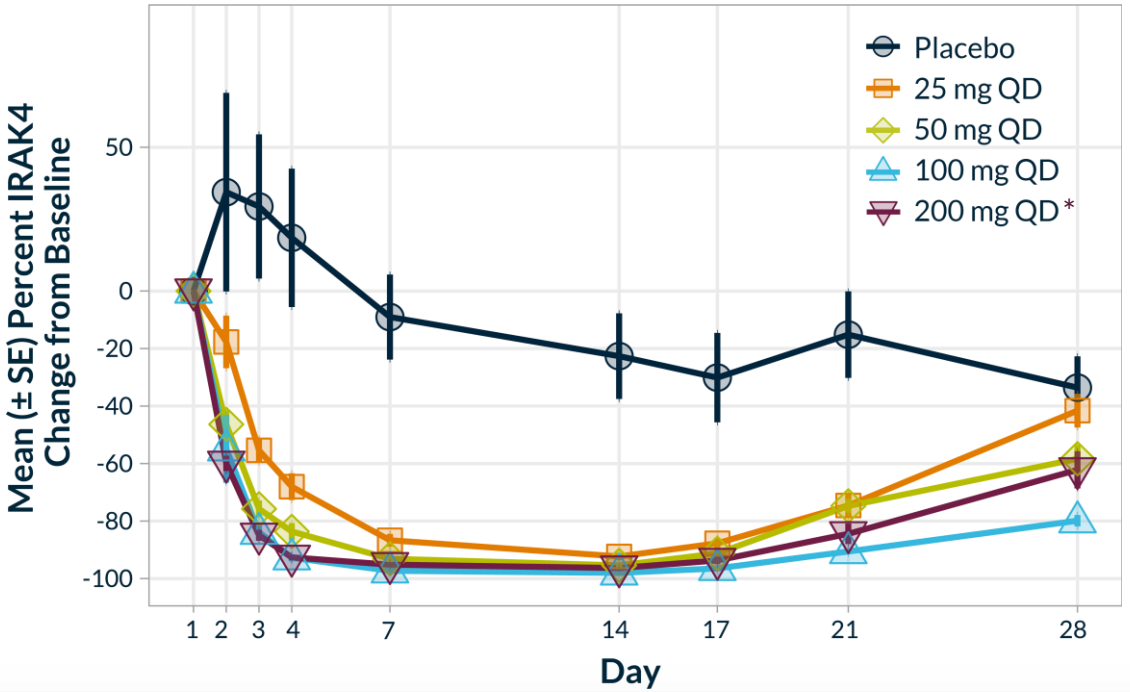
2
MAD Portion
Healthy Volunteers

KT-474 Achieved Robust and Sustained IRAK4 Degradation with Multiple Daily Oral Doses (14 Days)

Absolute IRAK4 Levels



Mean % Reduction of IRAK4

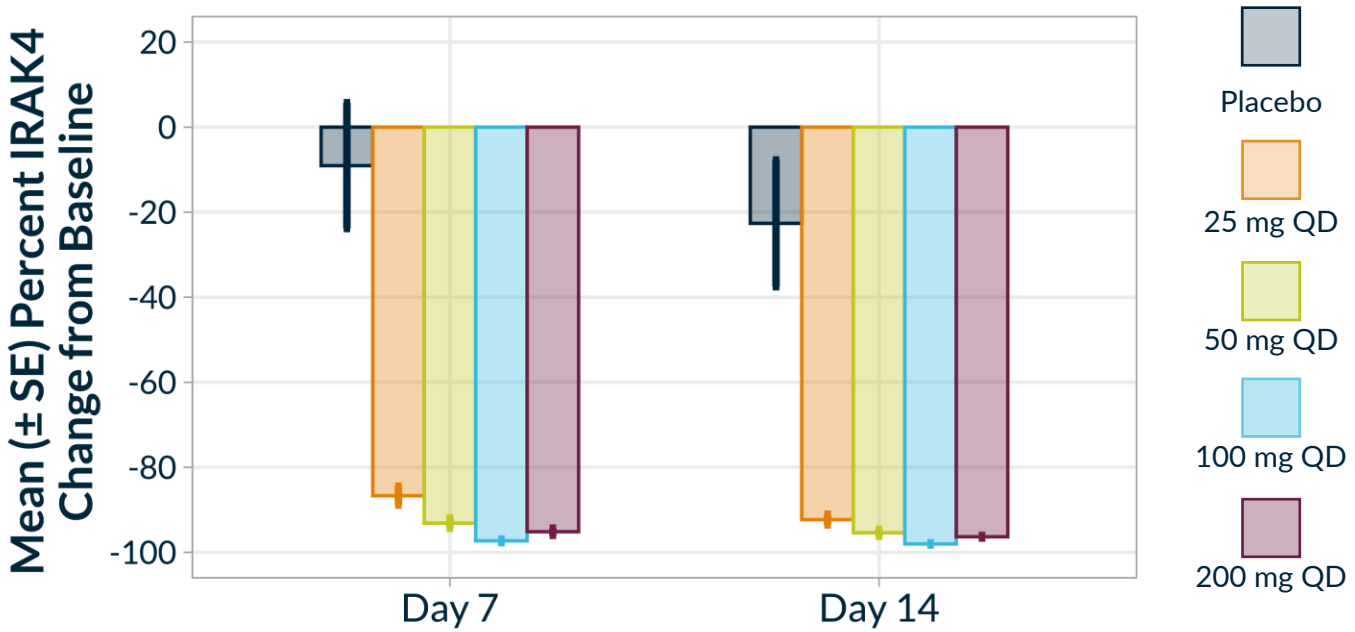


- Detected by mass spectrometry in circulating PBMC
- Steady state IRAK4 reduction achieved between Days 7 and 14
- Recovery towards baseline by Day 28 (2 weeks after last dose)
- MAD 2 through 4 approached Lower Limit of Quantitation (LLOQ)

Lower Daily Doses of KT-474 Achieved >98% IRAK4 Degradation (MS)

Plateau in IRAK4 Reduction after 14 days in PBMC after 100 mg

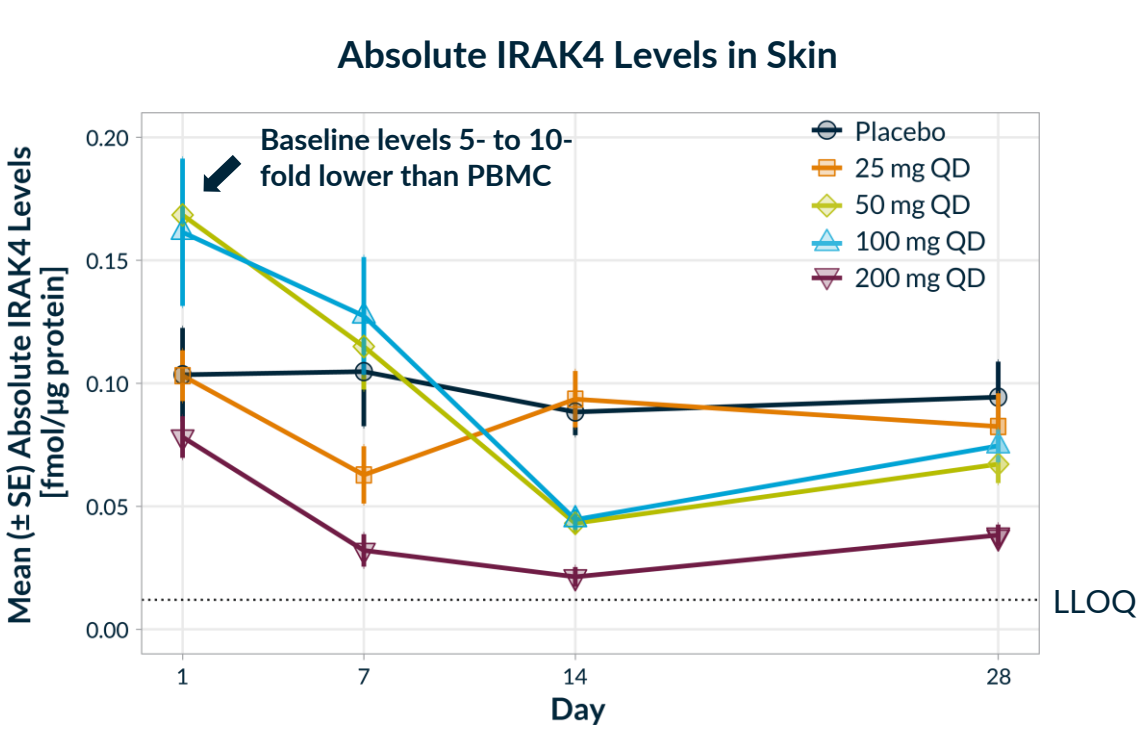
Percent IRAK4 Reduction in PBMC by Mass Spectrometry

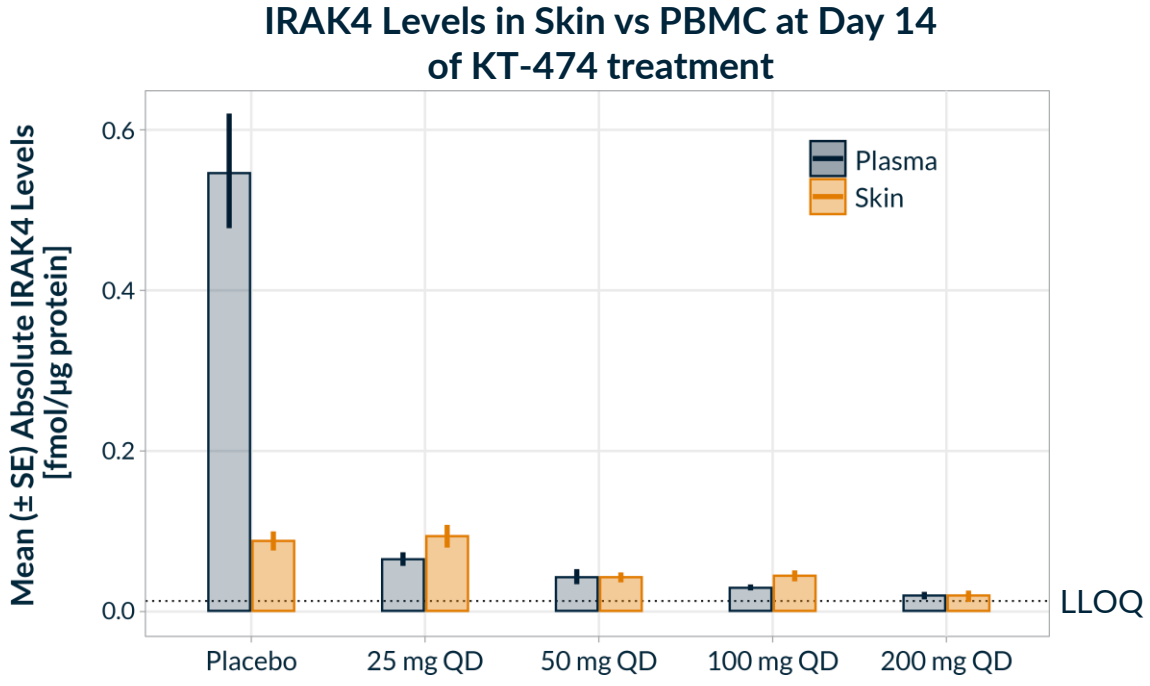


	Placebo (n=12)	25 mg QD (n=9)	50 mg QD (n=9)	100 mg QD (n=9)	200 mg QD (n=9)
Mean Day 7	-9%	-87%	-93%	-97%	-95%
Mean Day 14	-23%	-92%	-95%	-98%	-96%
*p value**		*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*

* p-values relative to placebo

KT-474 Reduced IRAK4 to Near LLOQ in the Skin (MS)

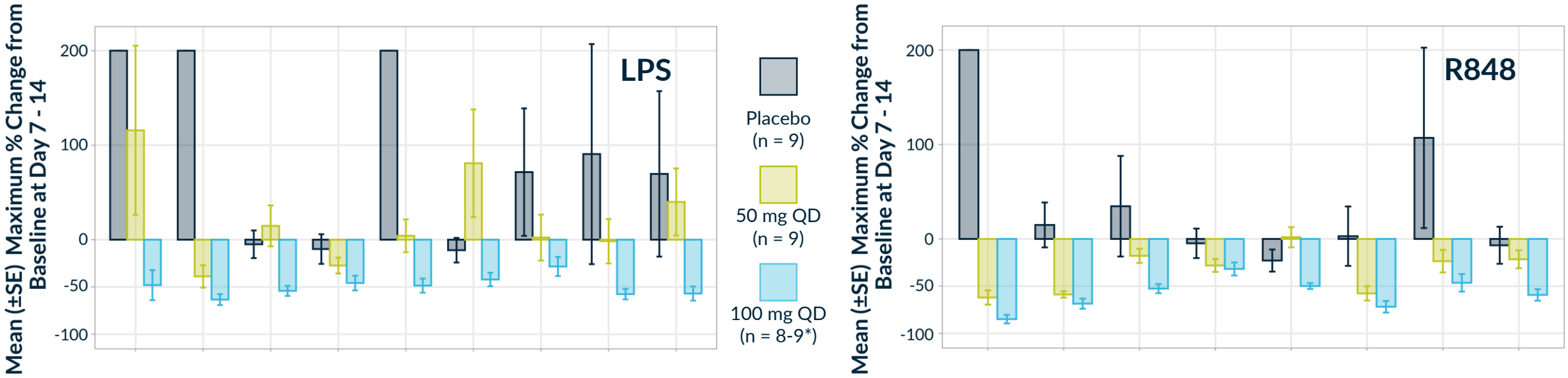




- Baseline IRAK4 levels in skin substantially lower compared to PBMC
- Dose-dependent IRAK4 degradation in skin by mass spectrometry
- Steady-state not yet reached at day 14
- Mean IRAK4 levels at 200 mg dose nearing LLOQ by Day 14, with knockdown up to 90% at 200 mg
- Comparable degradation in PBMC shows that effect of KT-474 is independent of baseline expression level

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

Results through MAD3 Showed Dose-Dependent Effect Tracking with Extent of Monocyte IRAK4 Degradation



	IFNγ	IL1β	IL6	IL8	IL10	IL12	IL17	IL23	TNFα
Pbo	357%	292%	-5%	-10%	880%	-11%	72%	91%	70%
50 mg QD	116%	-39%	15%	-27%	4%	81%	2%	-2%	40%
100 mg QD	-48%	-63%	-54%	-46%	-49%	-42%	-28%	-58%	-57%

	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%

50 mg QD: 93-95% PBMC degradation at Day 7-10; **87-90% Monocyte degradation at Day 7-14**
100 mg QD: 97-98% PBMC degradation at Day 7-10; **92-93% Monocyte degradation at Day 7-14**

*n=8 for LPS, n=9 for R848

Mean values > 200% have been replaced by 200 for visualization purposes

Blinded MAD Safety Summary

n=12 per cohort (9 drug/3 placebo)

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

AEs	#Subjects	Severity	Cohort
Headache	**6**	Moderate, Mild	MAD2
		Mild	MAD 3
		Mild (x3)	MAD 4
Palpitations**	**3**	Mild	MAD 2, MAD 4 (x2)
Nausea	**2**	Mild	MAD 2

- No SAEs
- Treatment-related AEs were self-limiting and resolved (table above)

* per investigator assessment;
** all were considered possibly-related, transient self-reported episodes during 21 days of in-patient observation in Phase 1 unit; **not associated with any objective findings** and did not lead to interruption in dosing; no AE's related to ECG changes including QTc across MAD cohorts 1-4

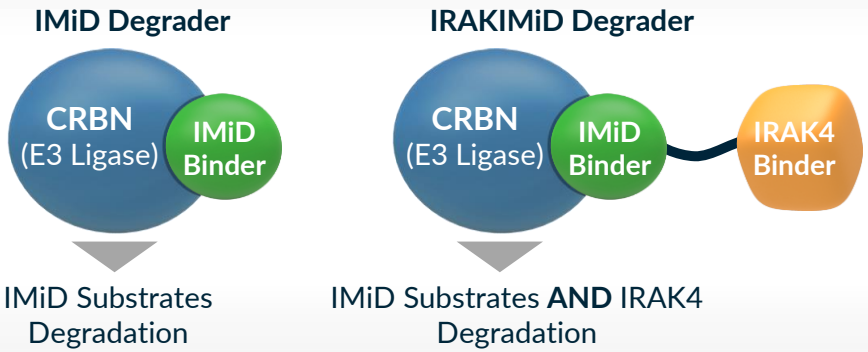
KT-474 Phase 1 Healthy Volunteer Summary

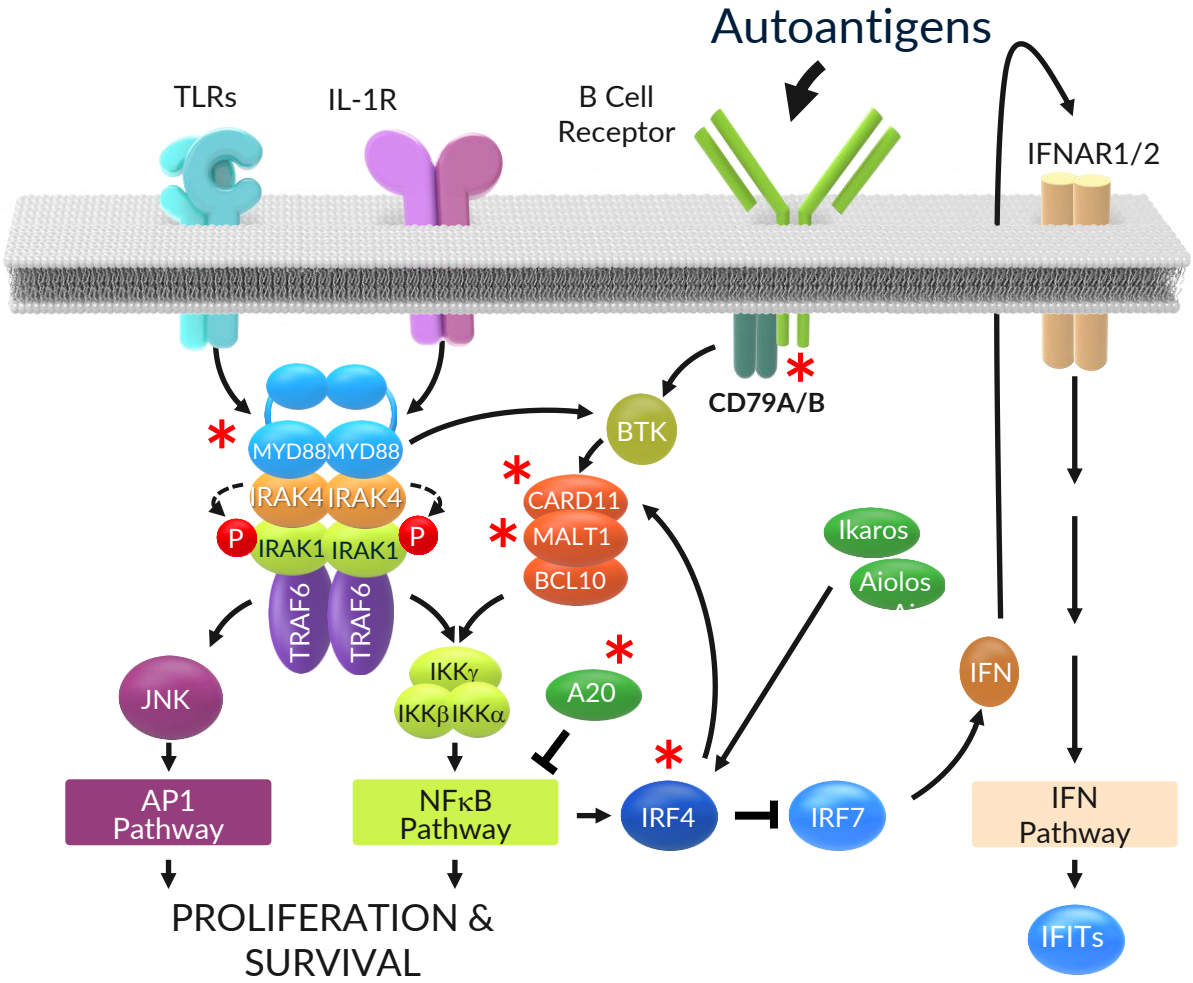
- Dose escalation completed for healthy volunteer portion of SAD and MAD portions of trial
- Proof of mechanism (POM) and proof of biology (POB) established in SAD, and at substantially lower doses in MAD
  - POM: **IRAK4 degradation in blood and skin to near LLOQ** of highly quantitative and sensitive mass spectrometry assay, with 95-98% mean IRAK4 reduction in blood at day 14 in top 3 MAD doses (50mg, 100mg, 200mg)
  - POB: **Strong and broad inhibition of whole blood *ex vivo* disease relevant cytokine induction**, with over 50% inhibition of up to 9 cytokines and maximum inhibition of 85% at 100 mg MAD dose
- Blinded safety analysis of cohorts showed KT-474 to be safe and well-tolerated, with no serious adverse events
- Upcoming planned milestones:
  - Initiate open-label cohort in HS and AD patients in 1Q22
  - POB in patients in 2H22
  - Phase 2 studies in multiple indications


IRAKIMiD
KYMERA

IRAKIMiDs are Potent Degraders of IRAK4 and IMiD Substrates Targeting Redundant Pro-survival Pathways in MYD88^{MT} DLBCL

- Single-agent therapies that target activated NFκB signaling in DLBCL show limited activity in preclinical or clinical settings
- Redundant NFκB pathway activation and downregulation of Type 1 IFN is common in MYD88^{MT} lymphoma, supporting need to seek combination therapies
- Targeting simultaneous degradation of IRAK4 and IMiD substrates Ikaros and Aiolos shows synergistic activity in MYD88^{MT} models, supporting this targeted combination





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

IRAKIMiD: First Precision Medicine in MYD-88 Mutated Cancers

- **MYD88 is mutated in ≥ 25% of DLBCL** patients, the most common subtype of non-Hodgkin's lymphoma
- DLBCL **5-year survival rate is ~64%**, and MYD88 mutations are associated with poorer survival
- SOC in relapsed/refractory DLBCL: CAR-T therapy, ADC's, and anti-CD19 and CD20, associated with ORR of 40-80%
- **There are no treatments indicated specifically in MYD88 mutant DLBCL**

- MYD88 is mutated in approximately 90% of **Waldenström's macroglobulinemia** (WM) cases.
- Standard therapy: ibrutinib-based or zanubrutinib, overall response rates of 80-90% and major response rates of approximately 73%

- MYD88 is mutated in approximately 70% of **primary central nervous system lymphoma (PCNSL)**
- Standard therapy in 1L: high-dose (HD) methotrexate combinations, overall response rates (ORR) 53-87%, complete response (CR) 23-49%, and 2-year PFS rates of 36-61%.
- Approximately 20-30% of patients with PCNSL experience tumor progression within first 6 months of treatment.
- There is no standard of care therapy in relapsed disease

KT-413 is a Potent Degrader of IRAK4 and IMiD Substrates with Potent Activity in MYD88^{MT} Cell lines and *In Vivo*

KT-413

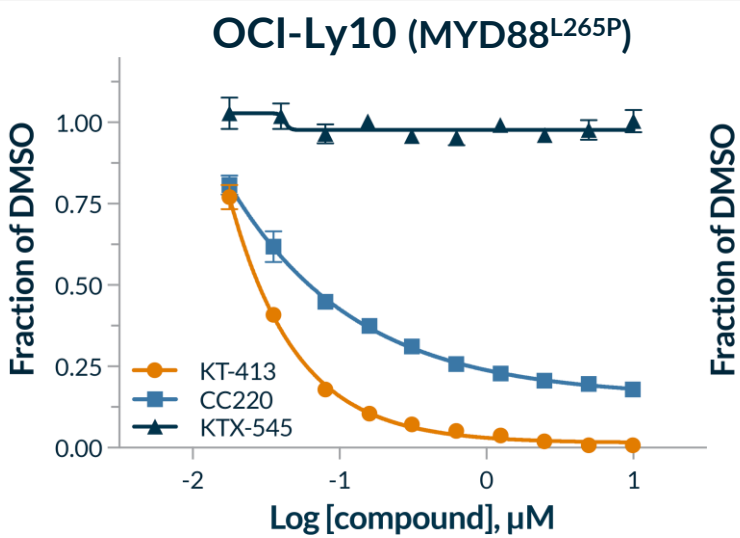
IRAK4 DC_{50} = 6 nM

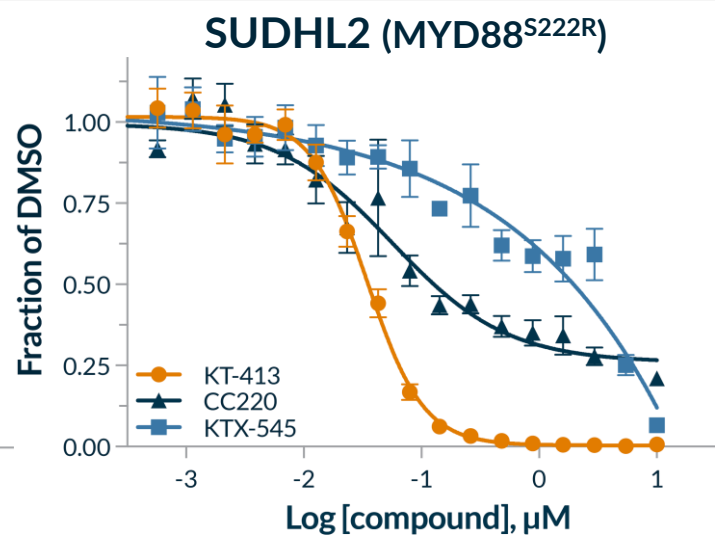
Ikaros DC_{50} = 2 nM

Aiolos DC_{50} = 2 nM

OCI-Ly-10 (MYD88^{MT} DLBCL)

- KT-413 is more active in MYD88^{MT} DLBCL cells than the clinically active IMiD, CC-220, and IRAK4-selective degrader, KTX-545

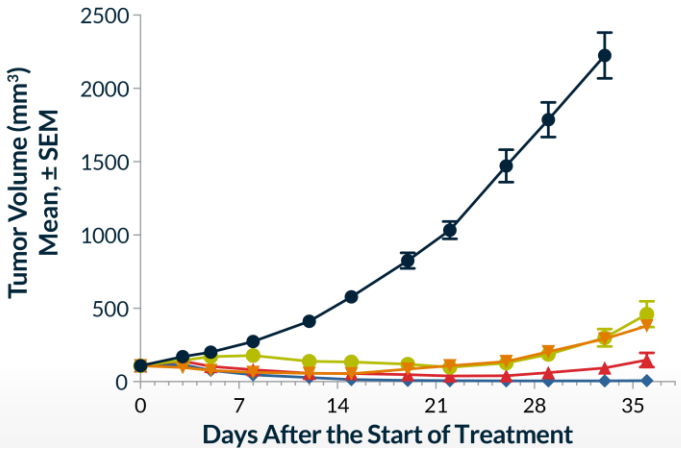




- In the OCI-LY10 MYD88^{MT} xenograft model, intermittent dosing of KT-413 induced strong antitumor activity, including complete or partial regressions.
  - **Superior activity compared to the clinically active IRAK4-inhibitor CA-4948 or the IMiD CC-220 alone**

Superior Anti-tumor activity

OCI-Ly-10 Tumor Volume

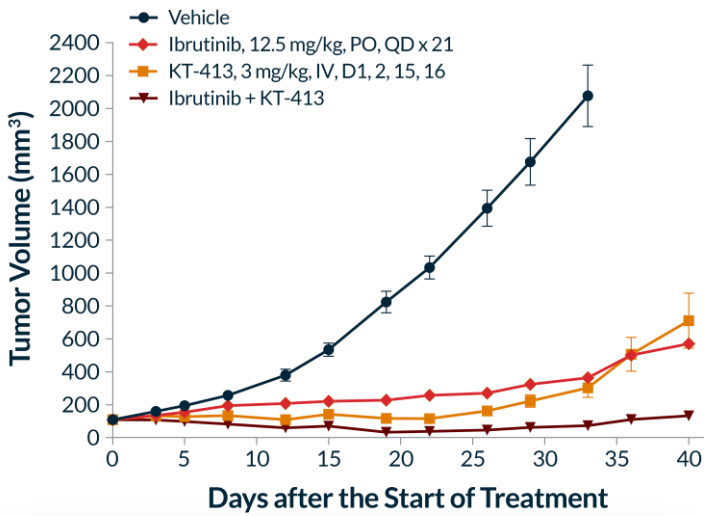


- IV Vehicle
- CA-4948, 150 mg/kg, PO, QD x 37
- CC-220, 3 mg/kg, PO, QD x 21
- KT-413, 5 mg/kg, IV, D1,2,15,16
- KT-413, 10 mg/kg, IV, D1,2,21,22

Drug (day 33)	T/C% (REG%)	CR	PR	SD	PD
CA-4948	9	0	0	0	7
CC-220	9	0	0	0	7
KT-413 5mg/kg	(14)	1	0	3	3
KT-413 10 mg/kg	(94)	5	2	0	0

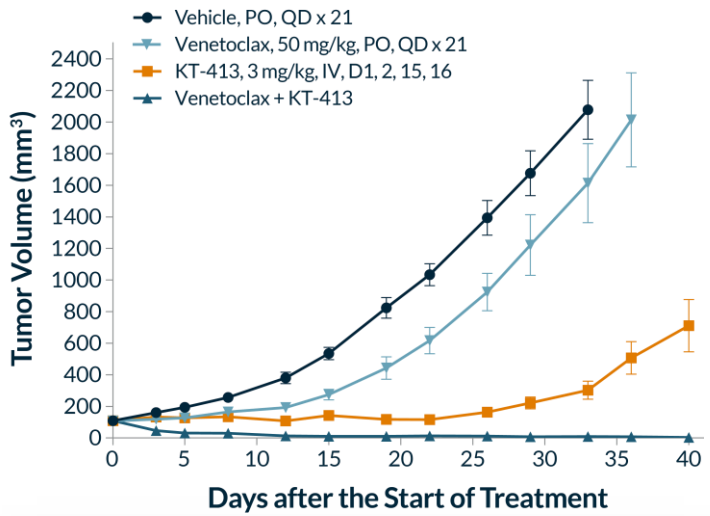
KT-413 Has Strong Activity in Combination in MYD88^{MT} OCI-Ly10 Xenografts

with BTK Inhibitor



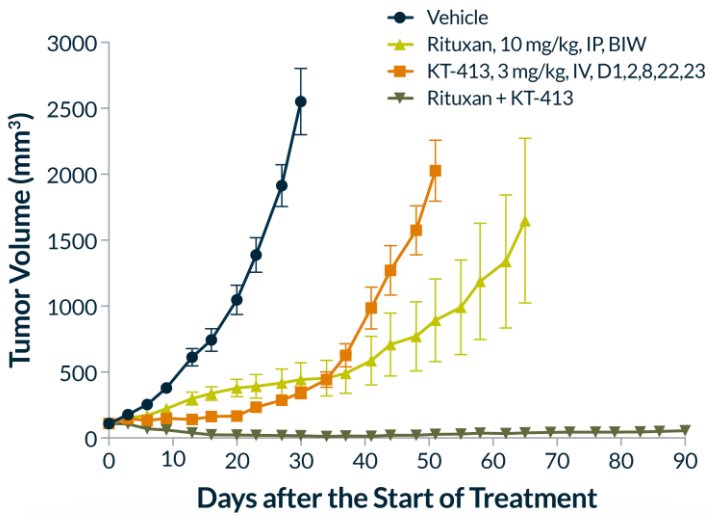
- KT-413 administered on intermittent schedules leads to strong regressions in combination with the BTK inhibitor Ibrutinib

with BCL-2 Inhibitor



- KT-413 administered on intermittent schedules leads to deep and durable regressions in combination with the BCL-2 inhibitor, Venetoclax

with Rituxan



- KT-413 administered on intermittent schedules leads to deep and durable regressions in combination with Rituxan

Data support potential for KT-413 in combination in earlier lines of therapy

IRAKIMiD Degrader KT-413 has Potential to be First Precision Medicine in DLBCL to Target a Genetically-defined Population (MYD88MT)

- Profound **antitumor activity** in preclinical models both **in single agent** and **combination**
- Clinical strategy in place to enable accelerated approval:

Monotherapy

  - $MYD88^{MT}$ DLBCL for most direct path to registration
  - Other $MYD88^{MT}$ lymphomas of interest include PCNSL, WM

Combinations

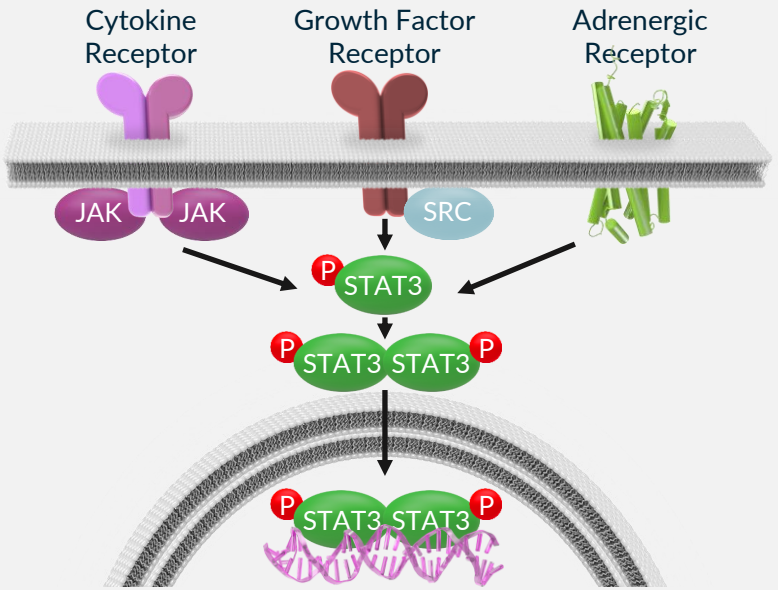
  - With SOC agents in $MYD88^{MT}$ DLBCL to enable earlier line therapy

STAT3

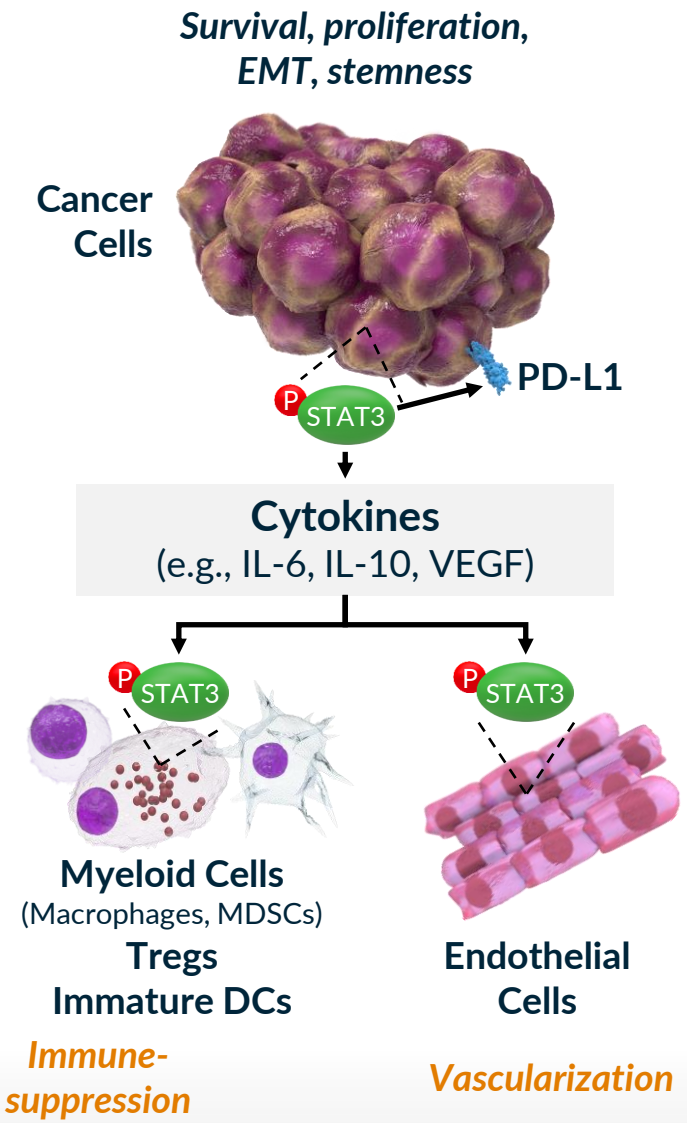
KYMERA

STAT3 Has Unique Tumor Cell Intrinsic and Extrinsic Mechanisms

STAT3 as a Target



- High degree of validation of JAK-STAT pathway in oncology and immuno-oncology supported by >25k publications
- Traditionally undrugged target
- First-in-class opportunity to address STAT3 driven pathology across large and diverse indications



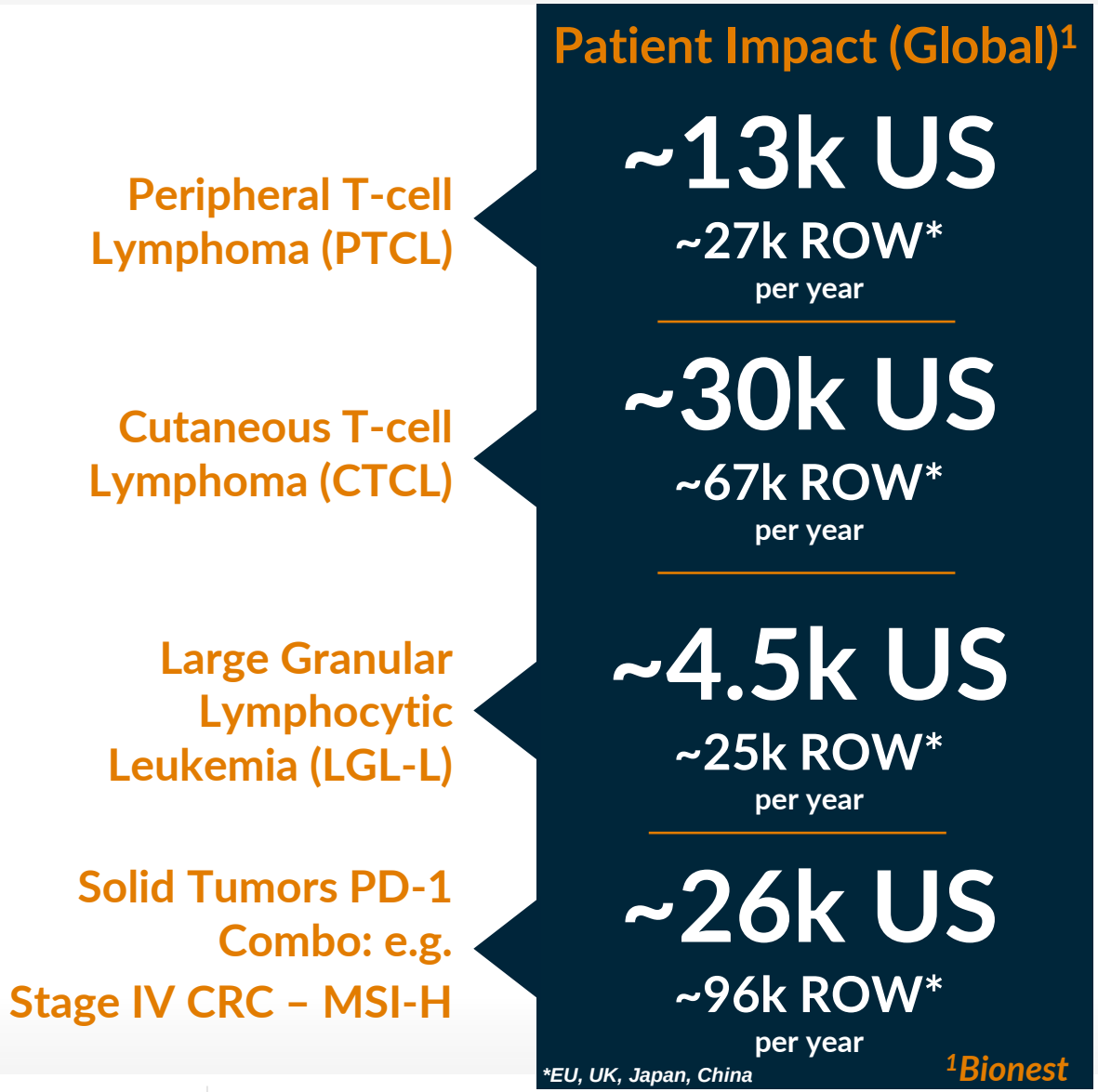
Tumor Cell Intrinsic

- Hyperactivation of STAT3 via either receptor signaling, or hotspot mutations promotes gene expression programs involved with survival, proliferation, stemness and metastasis of tumor cells
- Opportunities in STAT3-dependent malignancies (e.g., T cell malignancies, DLBCL, AML) and drug resistant tumors (e.g., TKI resistant oncogene-driven solid tumors)

Tumor Cell Extrinsic

- STAT3 promotes the differentiation and activity of immunosuppressive and endothelial cells, resulting in an immunosuppressive tumor microenvironment.
- Opportunities in multiple heme and solid tumor indications that are not responsive to immune checkpoint inhibitors.

First-in-class Opportunity to Address STAT3-driven Pathology Across Diverse indications



- Abnormal activation of **JAK/STAT pathway occurs in nearly all T-cell lymphomas**
- **STAT3 is most frequent mutation** among JAK/STAT pathway
- Standard therapies in relapsed/refractory PTCL including result in ORRs ~25%, CR rate of ~10% and mDOR of approximately 9 months

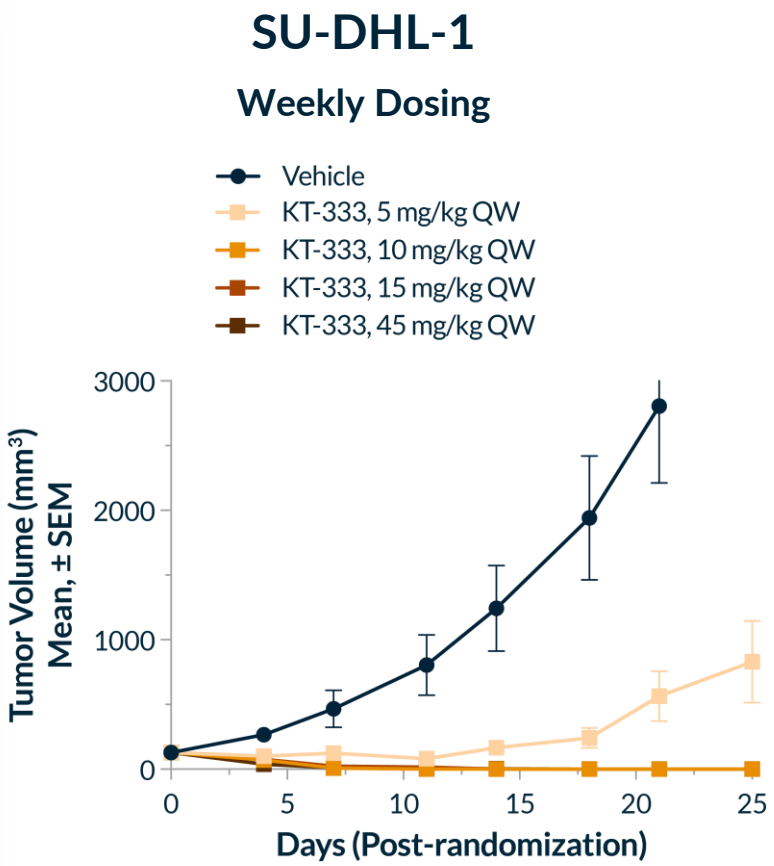
- **Advanced stages of disease associated with constitutively activated STAT3**
- Standard therapies in relapsed/refractory CTCL result in ORRs of ~30% with few CRs and mPFS of 5-8 months

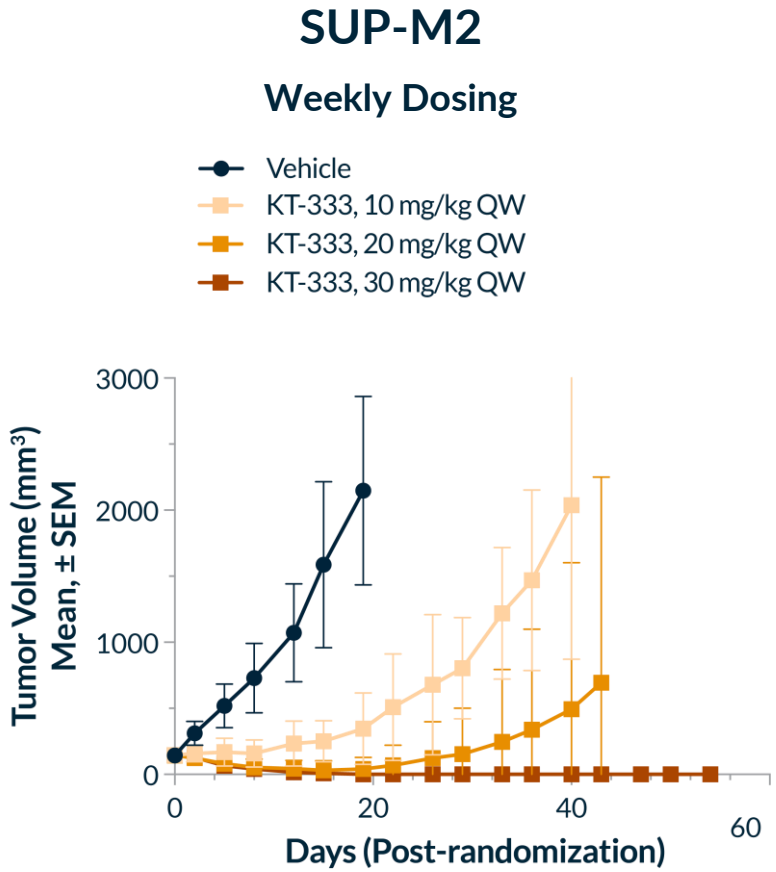
- **STAT3 mutations in up to 70% cases**
- **Constitutively active STAT signaling in nearly all cases**
- No approved agents in LGL-L; SOC in 1L which includes methotrexate and cyclophosphamide result in ORRs ~60%
- No SOC in ≥2L

- **STAT3 decreases inflammatory state in tumor, degradation of STAT3 sensitizes to PD1/L1 activity**
- PD1 inhibitors approved as single agents or in combination with CTLA4 inhibitor in 1L and in later lines following chemotherapy in patients with metastatic MSI-H CRC

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

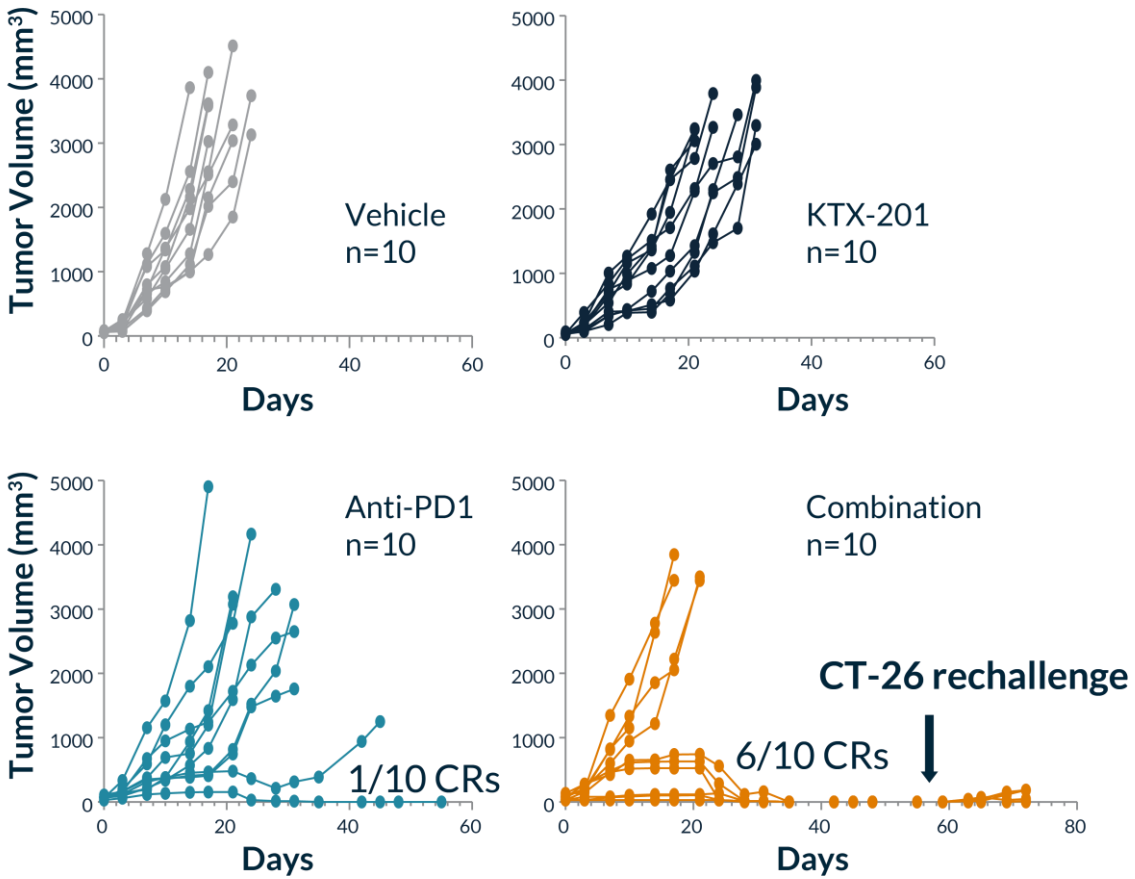
- Mice bearing STAT3-dependent ALK+ ALCL SU-DHL-1 or SUP-M2 tumor xenografts dosed with STAT3 degrader
- Dose- and degradation dependent tumor growth inhibition observed with once-a-week dosing
- 10 mg/kg sufficient to drive full tumor regression in SU-DHL- 1 that was durable for multiple weeks after the last dose (on day 14)

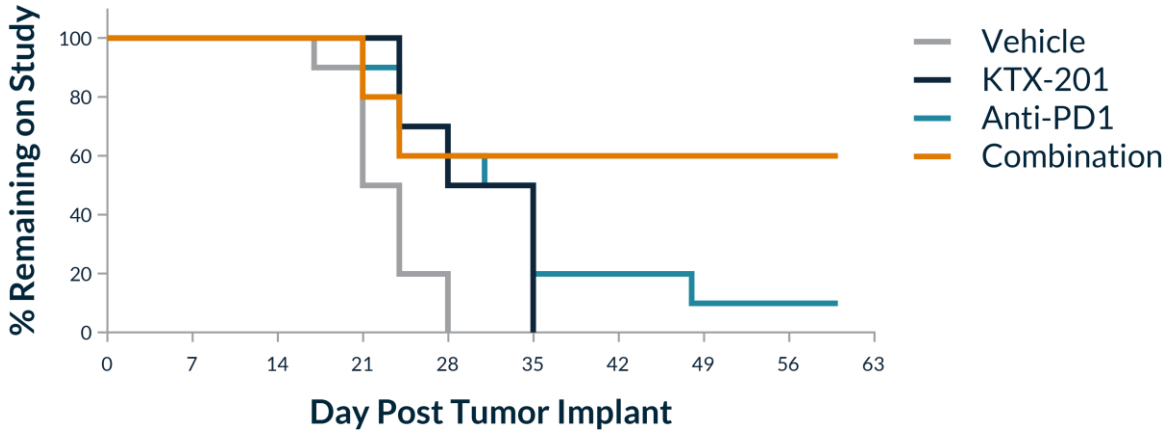




STAT3 Degrader's Role in Immuno-Oncology: Sensitization of Tumors to Anti PD-1

STAT3 Degradation and Anti-PD-1 Synergy





- KTX-201 synergizes with anti-PD-1 leading to 60% complete responses in CT-26 model
- Complete responders reject tumor rechallenge demonstrating development of long-term immune memory
- Combination extends survival

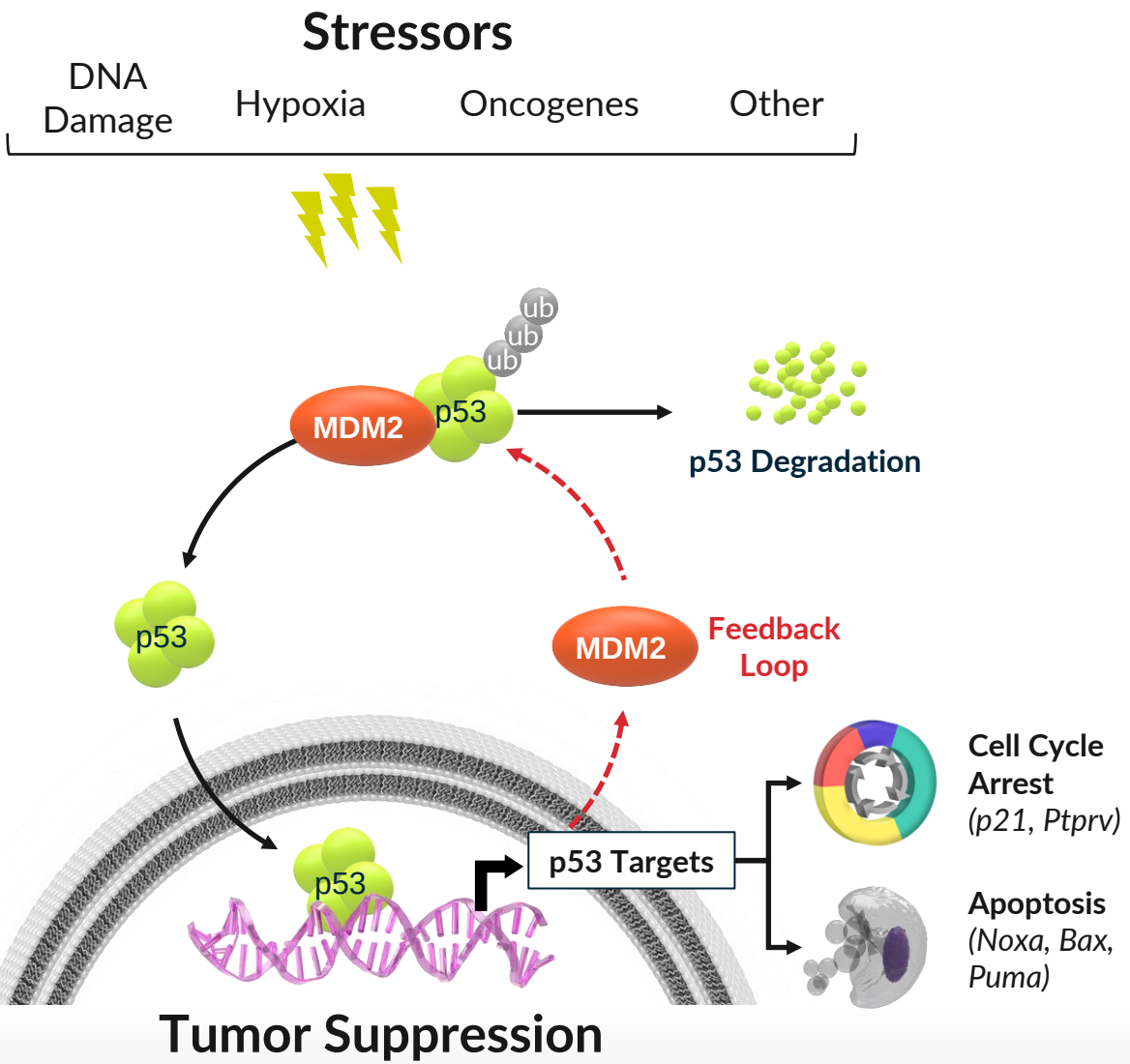
STAT3 Degrader KT-333, First-in-class Opportunity to Address STAT3-driven Pathology Across Diverse Indications

- First heterobifunctional degrader against an **undrugged target in the clinic**
- Profound **single agent activity** in liquid tumor and **promising combo activity** with anti-PD1 in liquid and solid tumors
- Clinical development strategy includes **direct registrational path in STAT3 pathway** activated heme malignancies
- Opportunity for **expansion into solid tumors** in combination with immune checkpoint inhibitors

MDM2

KYMERA

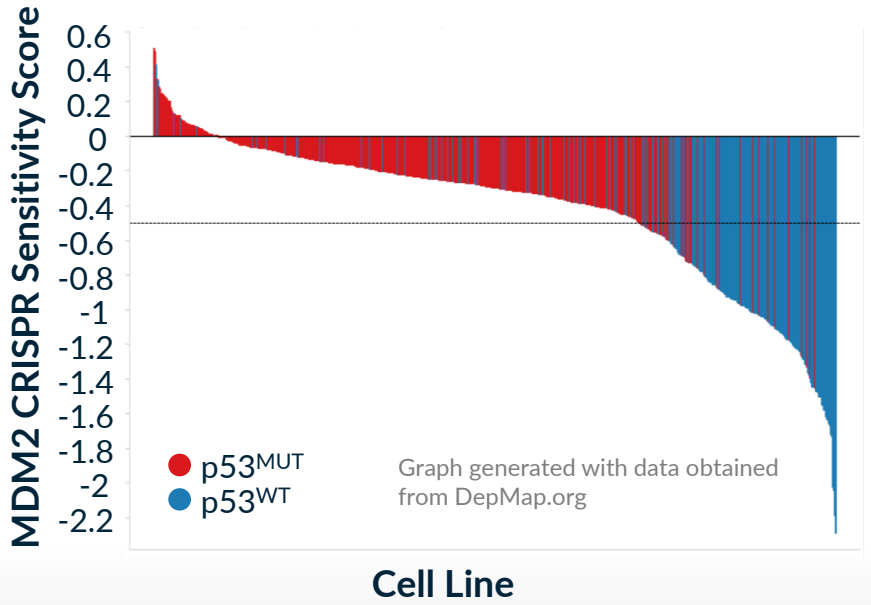
MDM2 is the E3 Ligase that Modulates P53, the Largest Tumor Suppressor



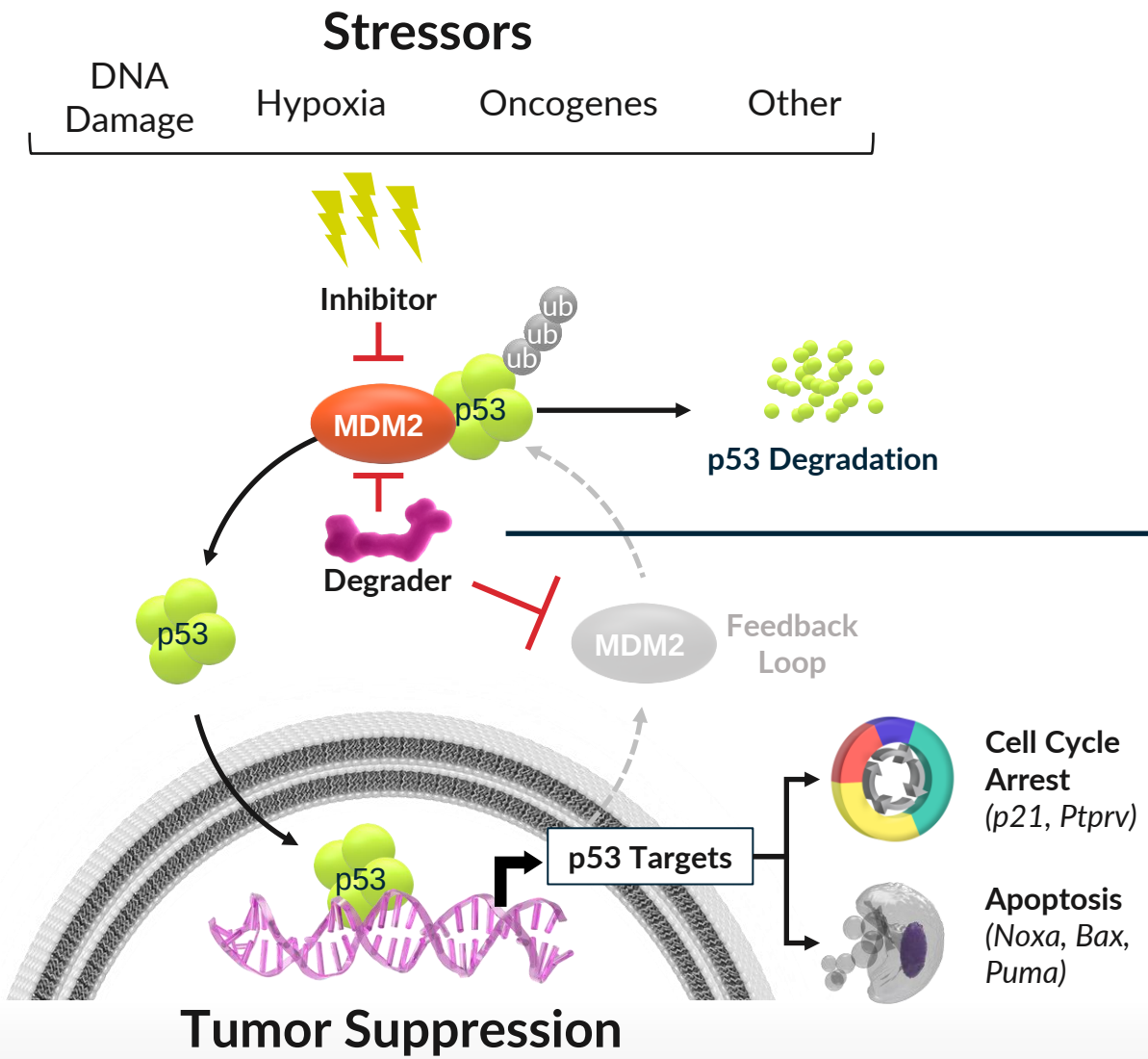
Cancer Genetics

- p53 is **NOT mutated** in almost 50% of tumors
- MDM2 overexpression and amplification can inactivate p53
- Large opportunity in wide variety of cancers

Dependency of p53^{WT} cells on MDM2



MDM2 Degradation, Not Inhibition, Efficiently Restores p53



Clinical Validation

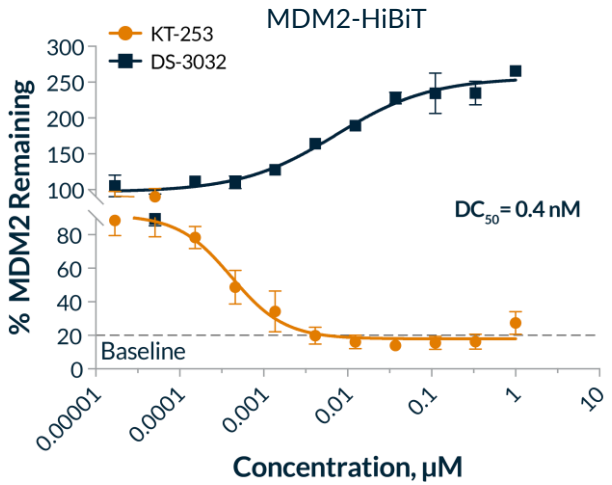
- **MDM2 small molecule inhibitors** of MDM2/p53 interaction **show activity in the clinic**..
- **...but they induce MDM2 feedback loop** resulting in limited impact on pathway

Degrader Advantage

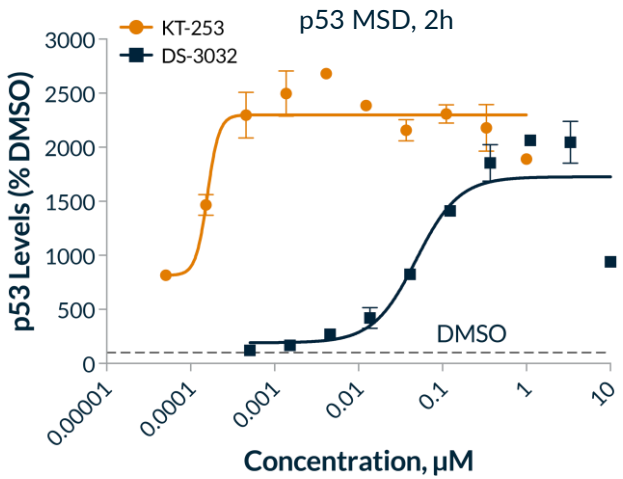
- **MDM2 degraders**, by removing the protein, **can overcome the p53-dependent feedback loop that upregulates MDM2**
- MDM2 degrader can induce an acute apoptotic response in tumor cells, **increasing efficacy and therapeutic index vs a small molecule inhibitor**

Kymera's MDM-2 Degrader Development Candidate, KT-253 is Superior to MDM2/p53 Small Molecule Inhibitors

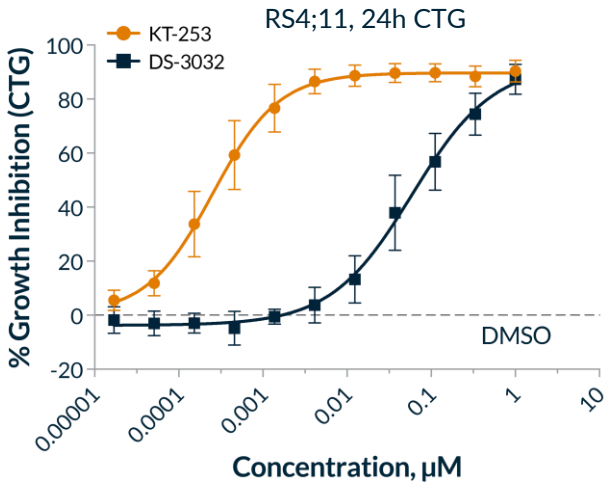
KT-253 is a potent MDM2 degrader



KT-253, unlike SMI's such as DS-3032, strongly stabilizes p53…



… which leads to superior tumor cell killing (pM range)

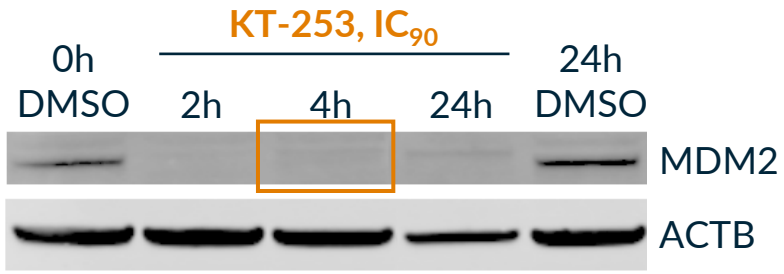


Compound	KT-253	DS-3032	RG7388	SAR405838	HDM201	AMG-232
Company	Kymera	Sankyo/Rain	Roche	Sanofi	Novartis	Amgen/Kartos
Clinical stage	IND enabling	Ph II / combo AML	Ph II / III	Paused	Ph I / II	Multiple Ph II; combo AML
RS4-11 IC_{50} (nM) (AML Cell Killing)	0.3	67	220	620	163	280
MDM2-HiBiT, DC_{50} (nM) (Degradation)	0.4	-	-	-	-	-

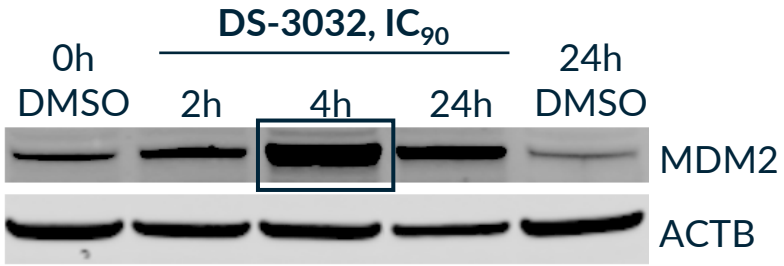
- KT-253 is **>200-fold more potent** in tumor cell killing assays than SMI's due to to its mechanism of action
- Proteomics show selective degradation of KT-253

KT-253, Unlike Small Molecule Inhibitors, Overcome the MDM2 and p53 Autoregulatory Feedback Loop

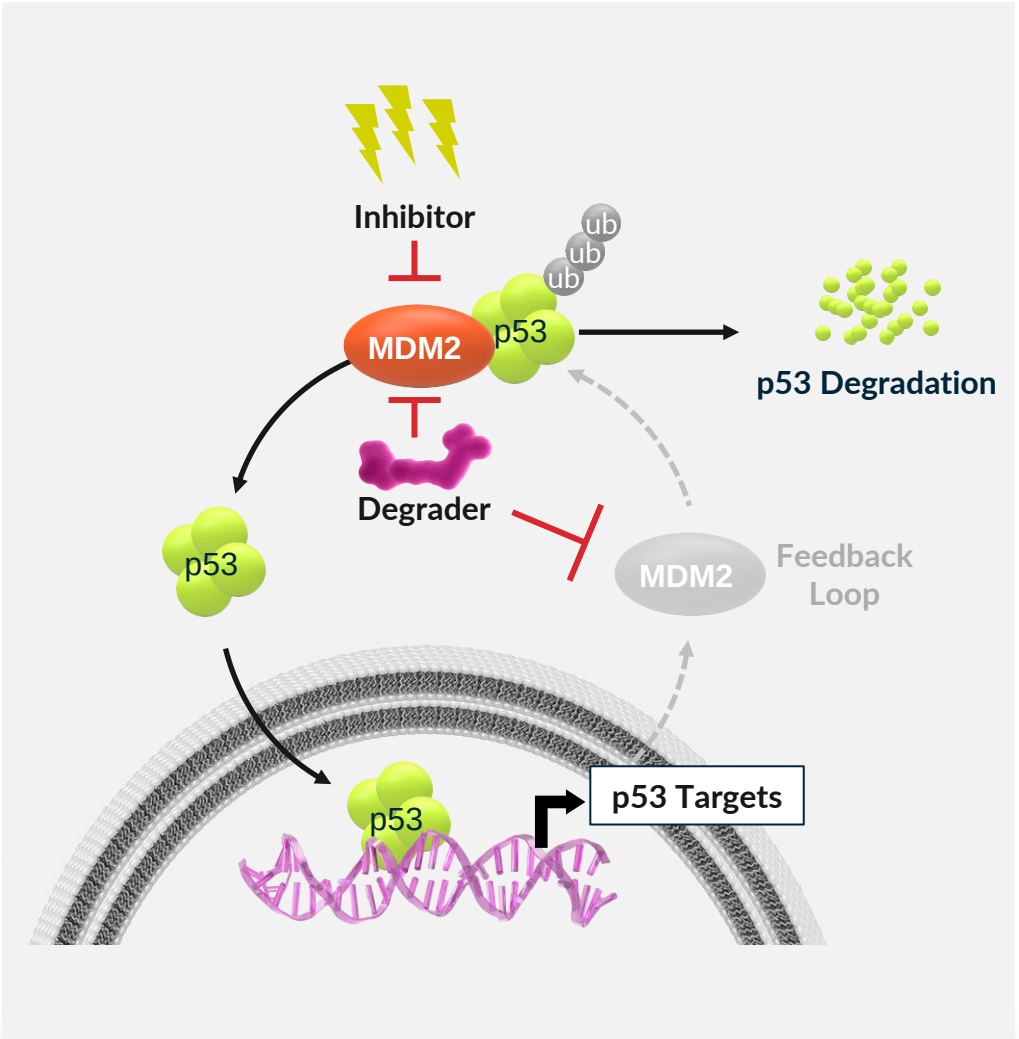
Degrader Overcomes MDM2 Feedback Loop



MDM2 levels are kept at undetectable levels with MDM2 degrader KT-253, leading to p53 stabilization



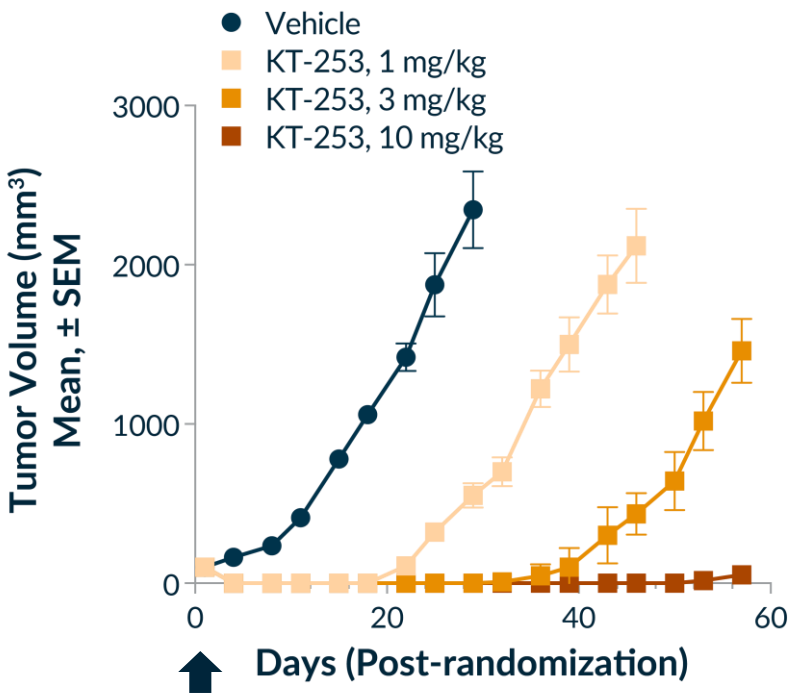
MDM2 levels are increased by the small molecule inhibitor (feedback loop), impairing p53 stabilization



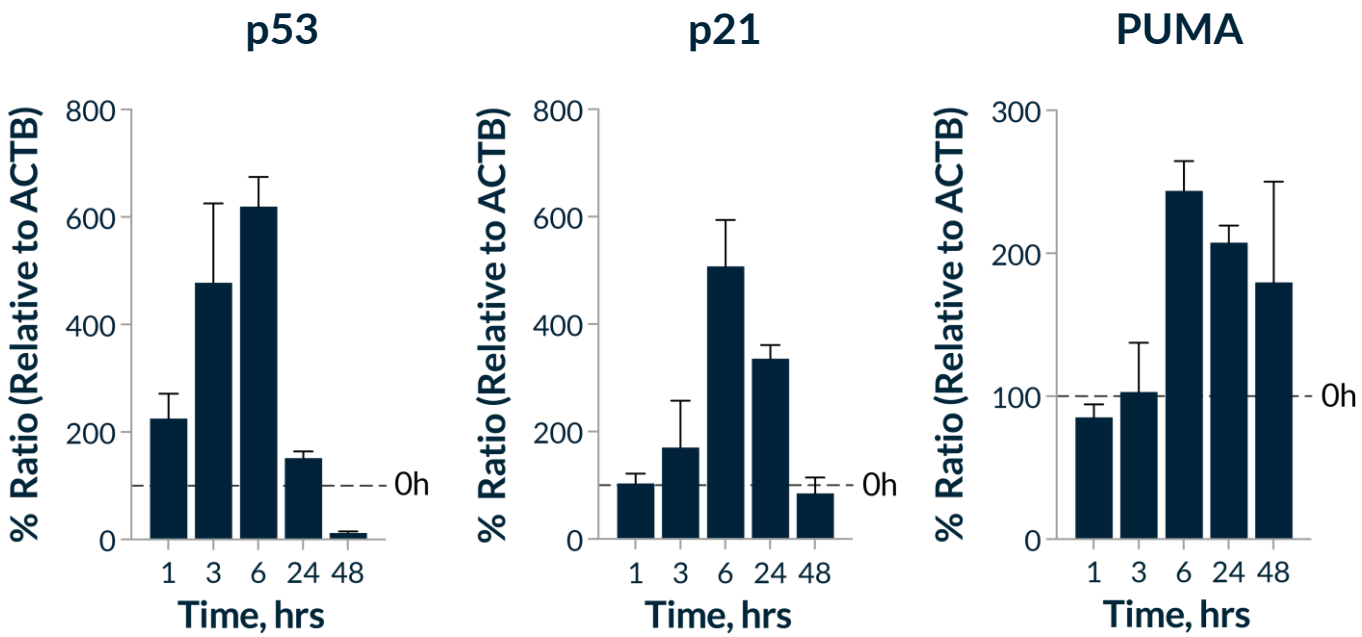
Single Dose of KT-253 Leads to Sustained Tumor Regression

Single Dose of KT-253 Achieves Sustained Tumor Regression

Rs4;11 XGs

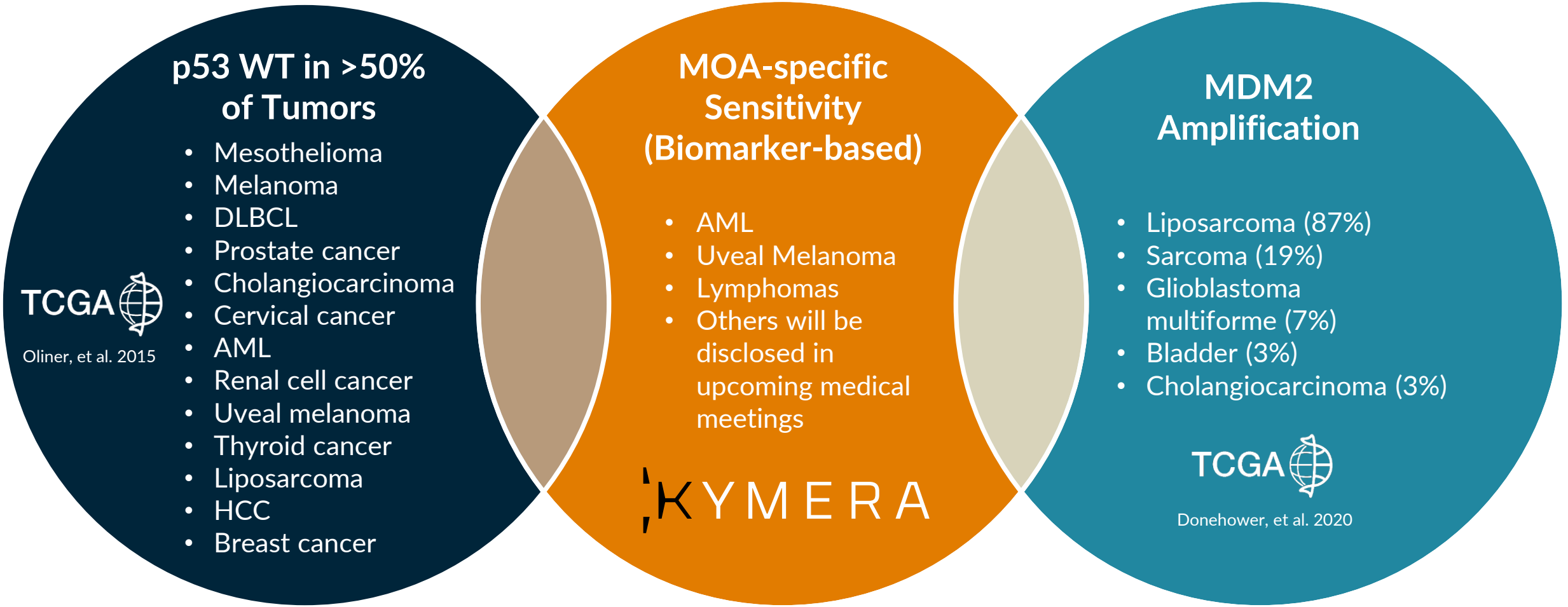


MDM2 Degradation (KT-253, 1 mg/kg) Leads to Fast Increase in p53, p21, and PUMA (Key Apoptotic Biomarker)



- Clinical equivalent doses of small molecule inhibitors have no significant *in vivo* impact in these xenograft models

Focus on Indications Where MDM2 Degradation Leads to Acute Apoptotic Response



KT-253 is a Potent MDM2 Degrader and a Best-in-Class p53 Stabilizer with Potential to Treat Numerous p53 WT Tumors

- KT-253 inhibits tumor cell growth with **picomolar potency** and is more **than 200-fold more potent** than clinically active MDM2 small molecule inhibitors
- KT-253, unlike small molecule inhibitors, **blocks the feedback loop** which up-regulates MDM2 production and in doing so more effectively stabilizes the tumor suppressor p53
- **Short term high exposures of KT-253** are enough to induce apoptosis in cell lines and *in vivo* xenografts, which ensures high activity and improved therapeutic index vs SMI's
- Broad franchise opportunities available for this mechanism (p53 WT is present in >50% tumors), Kymera is focused on indications with **specific sensitivity to degrader mechanism**, such as AML, Uveal melanoma and others through a biomarker strategy
- Projected IND filing in **2022**

What We Expect in 2022

- **Completion of Ph1 patient cohort for KT-474 and transition to Sanofi**
- **Proof of mechanism in patients for KT-413 and KT-333 oncology Ph1 studies**
- **IND filing for KT-253**
- **First tissue restricted E3 ligase enabled program in development**
- **Additional programs in oncology and immunology reaching development**
- Expanded recognition as a leader in TPD with a disruptive innovation engine across the biotech sector
- Multiple scientific contributions in medical meetings and in peer reviewed publications
- Continued investment in providing our employees, collaborator and partners the best experience

Our 5-year Vision: Where Kymera Will Be in 2026

KYMERA

A fully-integrated biotech company with a disease and technology agnostic pipeline and capabilities

Path to NDA for at least **1 program**

At least **8 clinical stage programs** across different development stages and disease areas

Pipeline positioned to deliver **at least 1 new IND per year**

Clinical proof-of-concept established in **tissue-selective/restricted degradation** and **undrugged** targets

Disease and technology-agnostic pipeline and capabilities

Expand technology platform to wholistically address undrugged proteome

Continued commitment to **innovation** and **first-in-class** science and medicines

Commercial organization **build up** in progress

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