



# Corporate Presentation

July 2025

## **Rēclūdo (Latin)**

*transitive verb III conjugation*

*1 to open*

*2 to open up, to disclose, to reveal, to unlock*

# Unlocking New Therapeutic Possibilities



# Unlocking Previously Undruggable SH2 Domains of High Value Targets in Inflammatory Diseases



**Differentiated candidates in validated pathways & blockbuster markets**



**STAT6 inhibitor**

- Sanofi partnership
- Validated by IL-4R $\alpha$  and IL-13 biologics



**BTK SH2 inhibitor**

- Wholly-owned
- Validated by BTK kinase inhibitors

**Undisclosed Programs**

- Additional SH2 domain high value targets

## OPERATIONAL STRENGTH

Experienced drug developers | Well-capitalized to value-driving milestones |  
Sanofi option: 50-50 US profit share

**Leading Investors**  
Supported \$102M Series A



**Nick Lydon**

## PROPRIETARY PLATFORM DRIVES OPTIONALITY

120 human SH2 domains; coveted targets previously considered “undruggable” |  
Fuels robust pipeline and multiple partnering opportunities

# Experienced Leadership Team



**Nancy Whiting**  
**Pharm.D.**  
President and CEO



Adcetris®, Tukysa®, Padcev®, Tivdak®



**Ajay Nirula**  
**M.D., Ph.D.**  
EVP, Head R&D



Rituxan®, Tecfidera®, Siliq®, Taltz®,  
Olumiant®, Omvoh®, Ebglyss®



**Matt Caldemeyer**  
**M.B.A.**  
CBO



**Brian Hodous**  
**Ph.D.**  
CSO



Ayvakit™



**Catherine Bovenizer**  
**C.P.A.**  
SVP, Finance



**Vivek Kadambi**  
**Ph.D.**  
SVP, Non-clinical  
Sciences & CMC



Adcetris®, Entyvio®, Ayvakit®, Gavreto®



**Paul Smith**  
**Ph.D.**  
SVP, Biology



Opzelura™, Gilenya®, Kesimpta®



**Daniel Treiber**  
**Ph.D.**  
SVP, Discovery  
Technology



Vanflyta®



**Nick Lydon,**  
**Ph.D.**  
Co-founder,  
Board Member



Gleevec®  
Lasker-DeBakey Award, Japan Prize

# Strategic Collaboration with Sanofi for STAT6 Inhibitor



**50%**

Option to participate  
in 50% U.S. profit share

**>\$1.3B**

Upfront payments  
and potential future  
development and sales  
milestones

**Significant  
royalties**

Up to double-digit  
royalties on  
future sales

**Recludix**  
Pharma

- Preclinical research and early clinical development
- Certain U.S. co-promotion activities

**sanofi**

- From Phase 2 onwards, WW clinical development
- U.S. co-promotion and ROW commercialization

# Significant Unmet Medical Needs in Inflammatory Disease Remain



**>60 M patients** diagnosed globally **each year** with immune-related inflammatory disease; potential for **rapid market expansion**

**Significant unmet needs** persist to close **efficacy gaps** and elevate standard of care

Risk of **infection** and **other serious events** with current therapies pose major **safety barriers** that limit addressable population

Self-injection can be **burdensome** and **reduces compliance for many patients**

A diverse range of sub-populations have **no suitable therapeutic option** and remain untreated



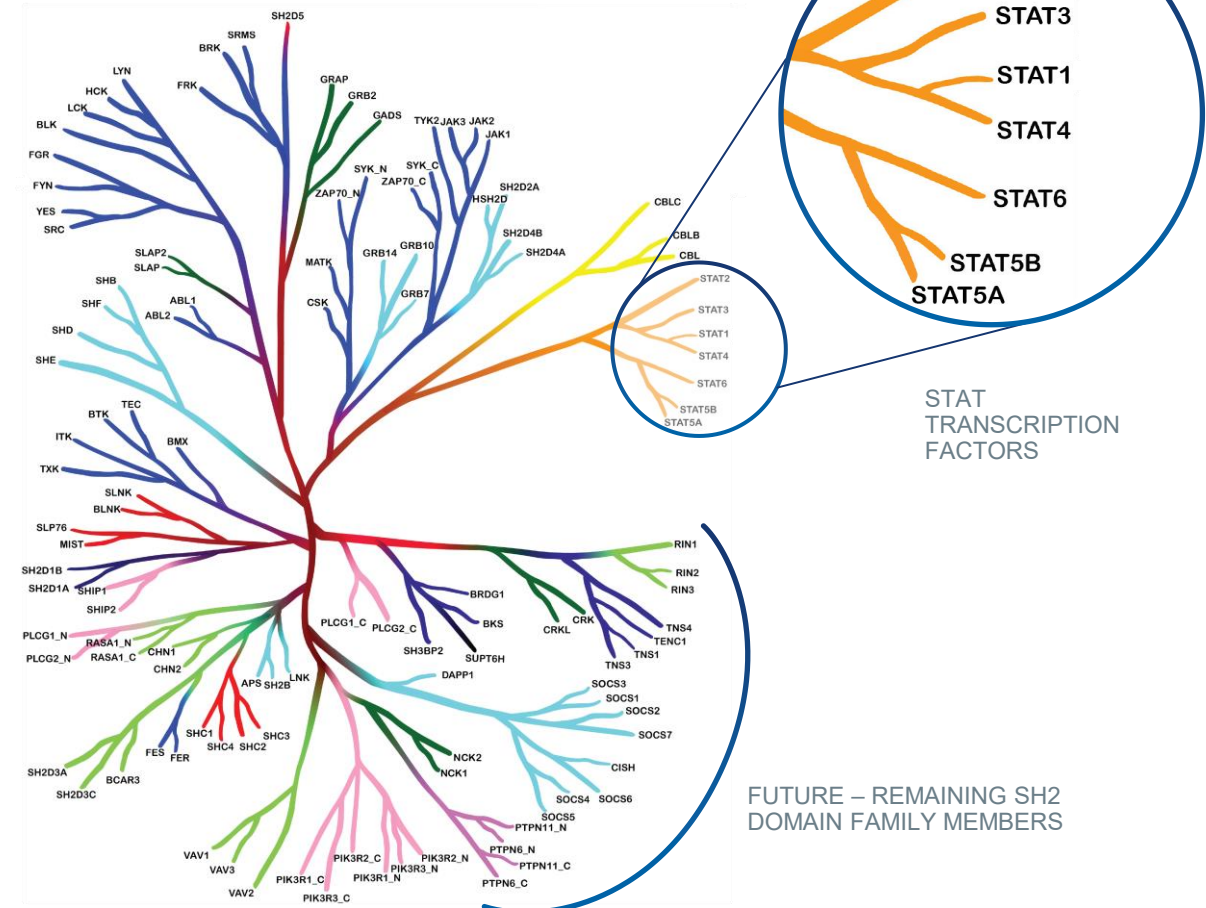
# SH2 Domains Have Previously Been Deemed “Undruggable”

Significant opportunity in targeting SH2 domain proteins

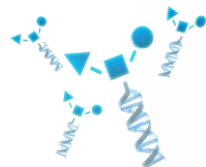
Src Homology 2 (SH2) domains are highly conserved protein domains that have long been recognized as attractive drug targets

- Small protein modules made up of ~100 amino acids
- 120 human SH2 domains
- Play a key role in mediating protein-protein interactions
- The SH2 domain of STAT proteins is required for:
  - Binding to cytokine receptors
  - Dimerization of STAT proteins

Human SH2 Domain Family Tree



# Recludix Platform: Integrated Proprietary Technologies & New Chemical Approaches

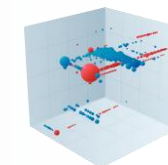


## Custom SH2 Domain Targeting DNA-Encoded Libraries

Discovery and SAR DELs | Hundreds of millions of molecules

## Proprietary DEL Selection & SAR Analysis

Rapid massively parallel determination of structure-activity relationships



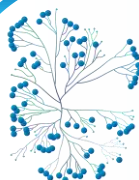
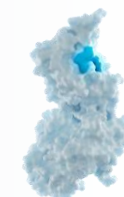
## Prodrug Modality Expertise

Drives enhanced target coverage

## High Quality Lead Compounds

## Structure-Based Design

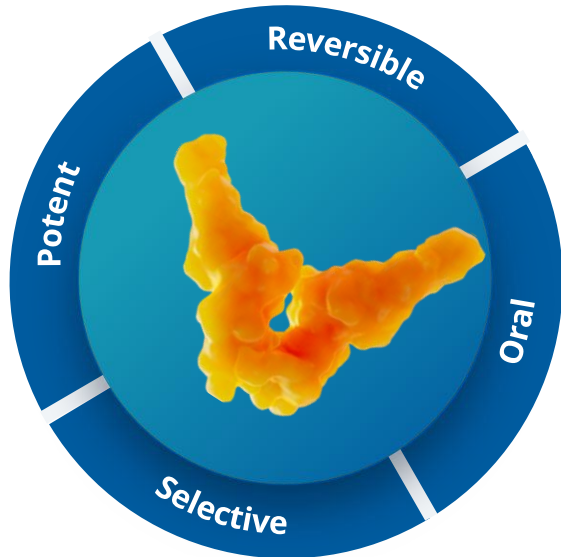
Proprietary co-crystallography systems



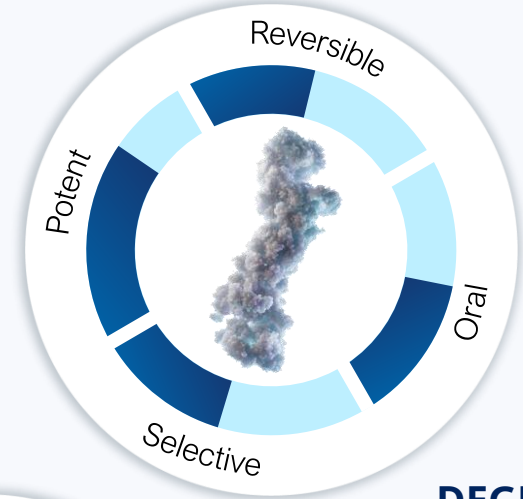
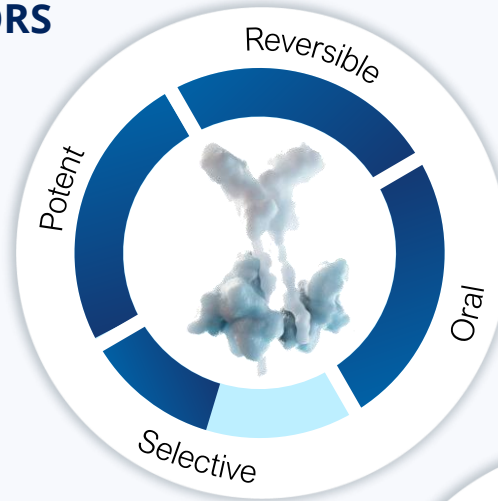
## SH2 Domain Screening Tool

Unique panel of SH2 domain assays | Drives selectivity

# STAT SH2 Domain Inhibition Enables a Best-in-Class Product Profile

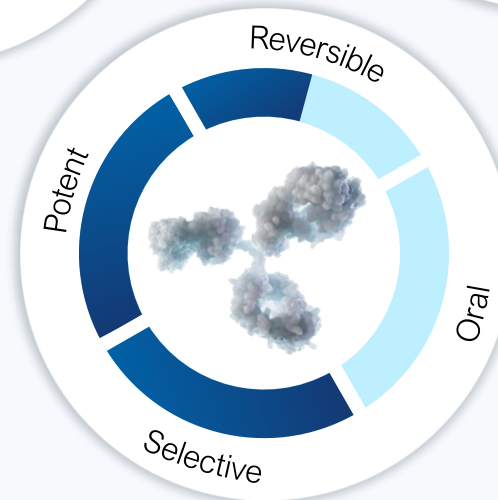


## JAK/TYK2 INHIBITORS



## DEGRADERS

## BIOLOGICS





**STAT6**

# Opportunity to Serve Large Patient Populations in High-Value Markets with a Uniquely Differentiated Product



**Atopic  
dermatitis  
42M**

**PN  
0.5-1M**

**Asthma  
46M**

**COPD  
63M**

**CRSwNP  
0.5-1M**

## >150M

TOTAL PATIENT IMPACT

### LARGE POPULATIONS

Targeting broad, established patient populations with persistent unmet needs

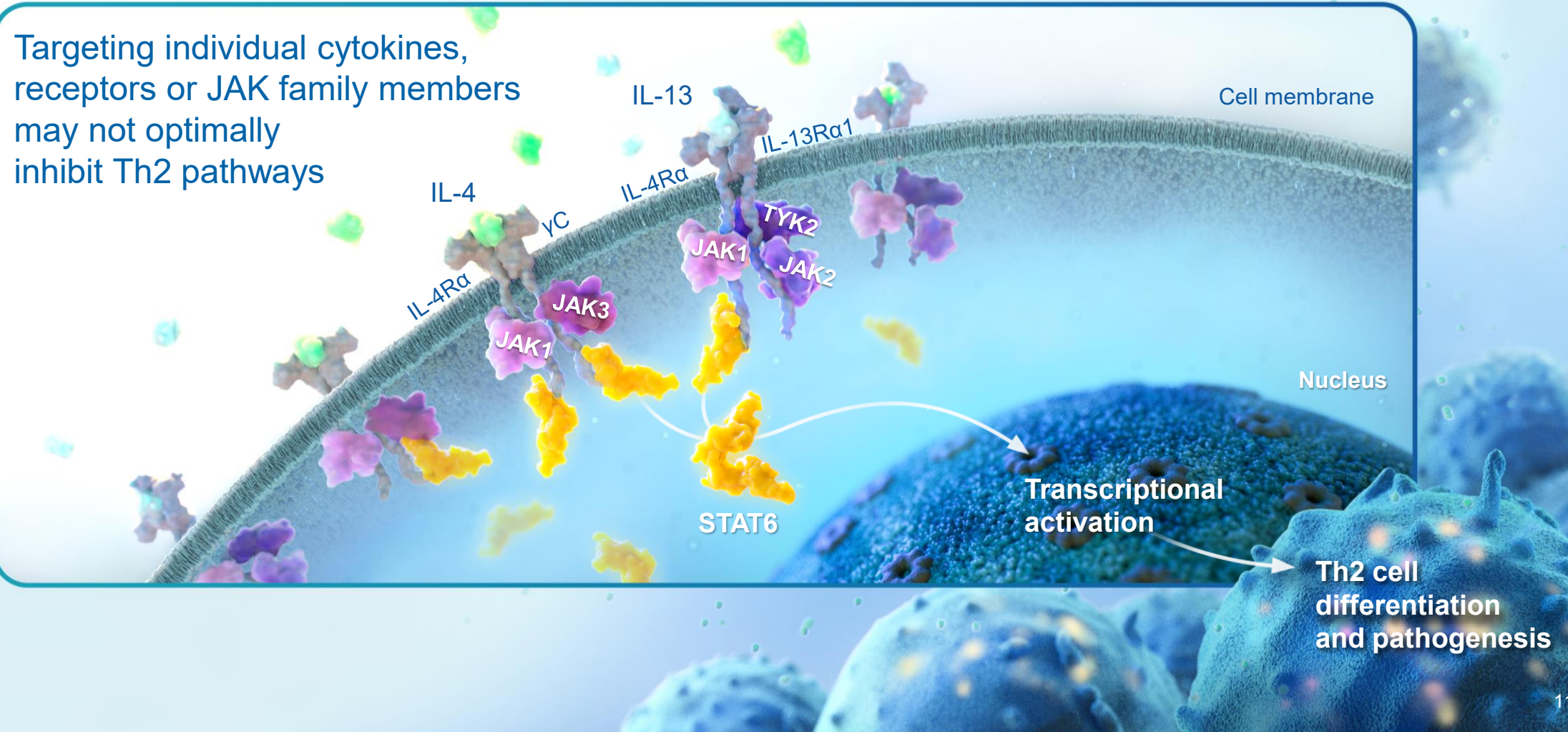
### DIFFERENTIATED PRODUCT

Patient-friendly oral formulation may enable treatment beyond those currently served by injectable agents

# STAT6 is a First- and Best-In-Class Opportunity to Selectively Target Th2 Inflammatory Disease Pathways



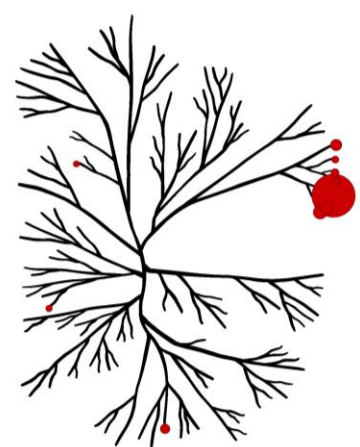
Targeting individual cytokines, receptors or JAK family members may not optimally inhibit Th2 pathways



# STAT6 Inhibitor REX-8756 is Highly Potent and Selective in Biochemical and Cellular Assays



**REX-8756**

Biochemical potency (SH2scan $K_D$ )	Cellular potency (pSTAT6 $IC_{50}$ in human PBMCs)	Biochemical STAT family selectivity	Cellular selectivity (PBMCs)	SH2 domain selectivity
0.04 nM	0.72 nM (IL-4) 0.19 nM (IL-13)	>1,000X vs. STAT1/2/3/4/5	>1,000X vs. STAT1/2/3/4/5	

# STAT6 Inhibitor Demonstrates Biologic-Like Selectivity and Differentiates from JAK Inhibitors

Direct selective STAT6 inhibition provides greater selectivity than currently approved JAK inhibitors



		T CELL FUNCTION				HEMATOLOGIC HOMEOSTASIS	
		General adaptive immune response	Defense against viruses and bacteria	Defense against extracellular pathogens	Defense against parasites and mediation of antibody responses	Erythropoiesis	Thrombopoiesis
		T Cell Activation (CD25)	Th1 Cell Function (IFN $\gamma$ )	Th17 Cell Function (IL-17A)	Th2 Cell Function (IL-5)	EPO-Induced STAT5-Driven Transcription	TPO-Induced STAT5-Driven Transcription
STAT6 Inhibitor	REX-8756	>3,000 nM	>1,000 nM	>2,500 nM	19 nM	>10,000 nM	>10,000 nM
IL-4 / IL-13 Antagonist	Dupilumab	>10,000 nM	>1,000 nM	>1,000 nM	26 nM	>1,000 nM	>1,000 nM
JAK Inhibitors	Abrocitinib	1,300 nM	900 nM	73 nM	80nM	3,200 nM	2,800 nM
	Upadacitinib	39 nM	36 nM	7.4 nM	4.3 nM	69 nM	20 nM
	Baricitinib	110 nM	210 nM	25 nM	15 nM	56 nM	42 nM

Recludix Pharma JPM Morgan Healthcare Conference 2023  
Recludix Pharma data on file, March 2023

Selectivity relative to Th2 inhibition:

>30X

10-30X

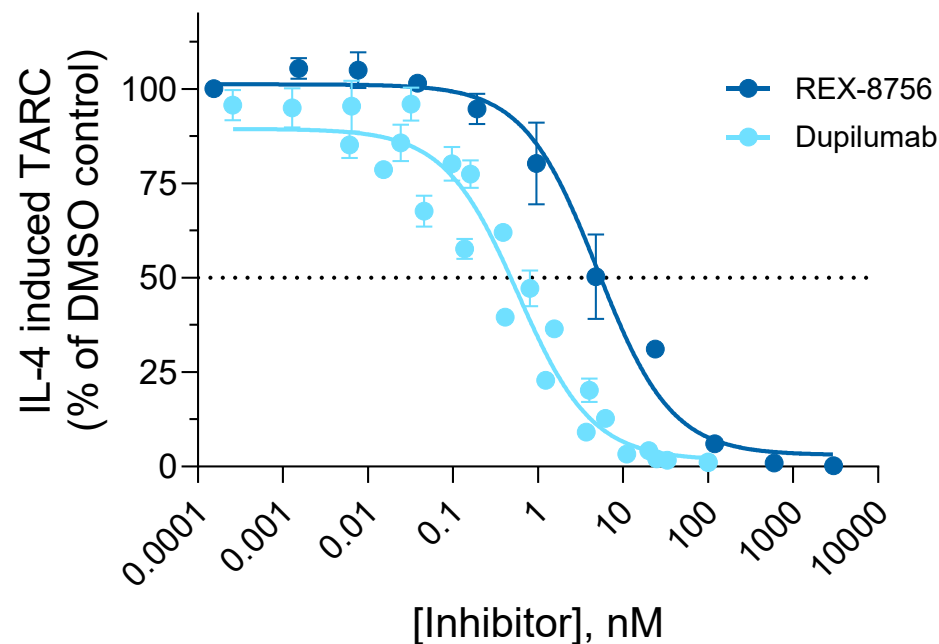
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# STAT6 Inhibitor Fully Inhibits IL-4/13 Stimulated STAT6-Driven Biomarkers in Human PMBCs

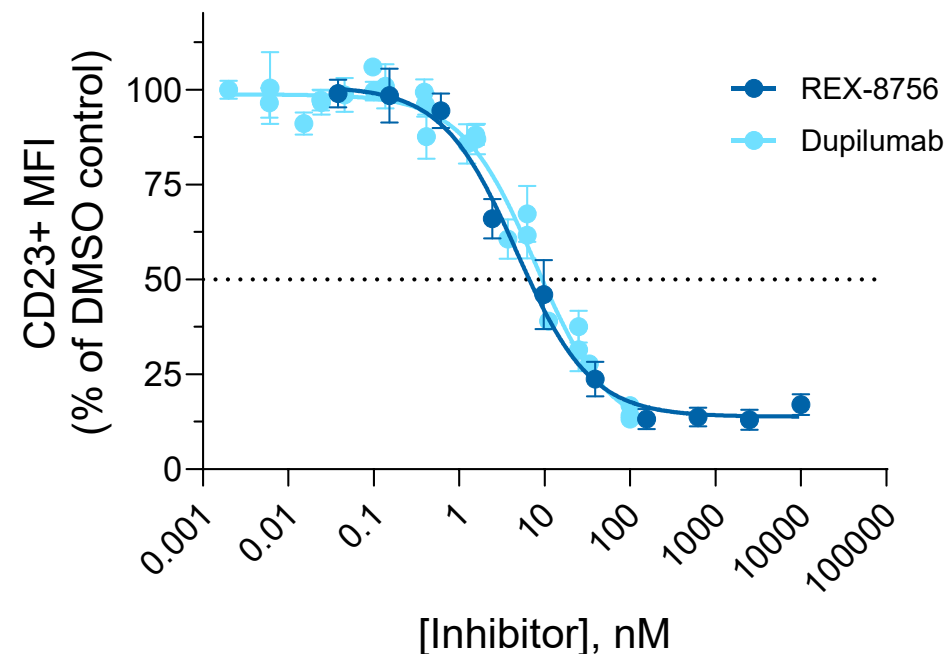


## IL-4 induced TARC



	REX-8756	Dupilumab
IC <sub>50</sub>	6.3 nM	0.8 nM

## IL-4 induced CD23 activation



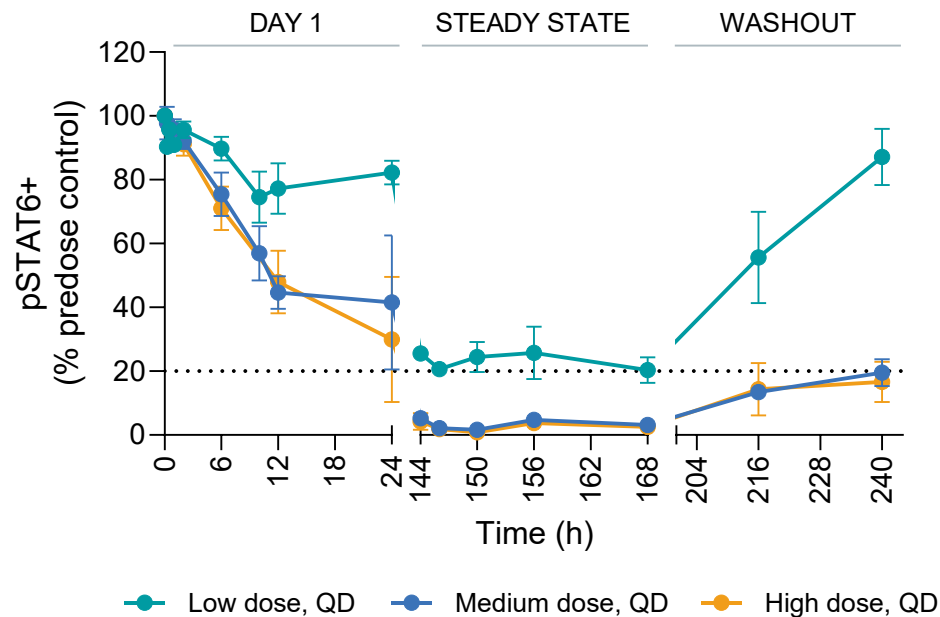
	REX-8756	Dupilumab
IC <sub>50</sub>	5.1 nM	11 nM

# REX-8756 Achieves Complete pSTAT6 Inhibition with Once Daily Dosing and is Well Tolerated in Dog 7-Day Study

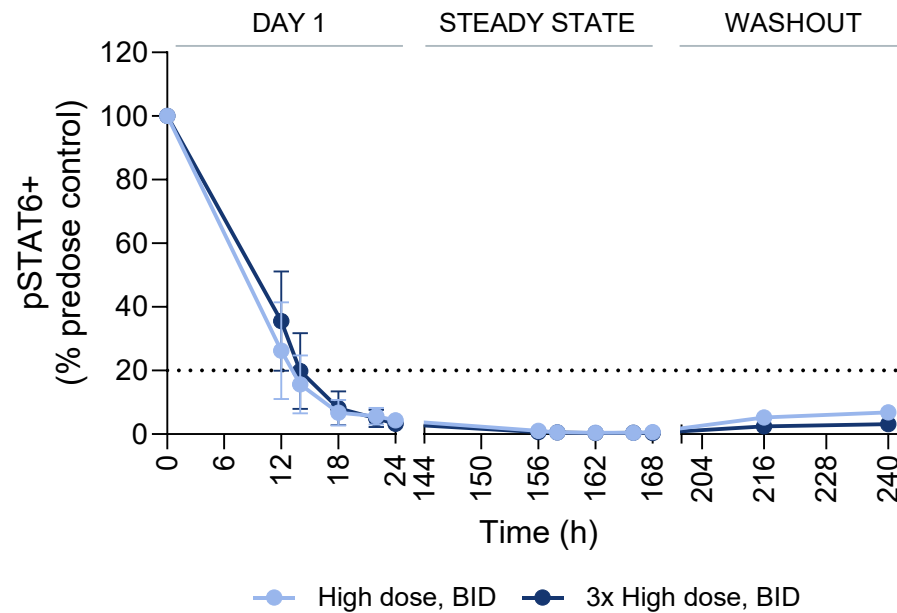


Efficacious dose at >80% pSTAT6 PD modulation

## Oral, QD dosing



## Oral, BID dosing



### Multi-day PK/PD & Hazard ID study

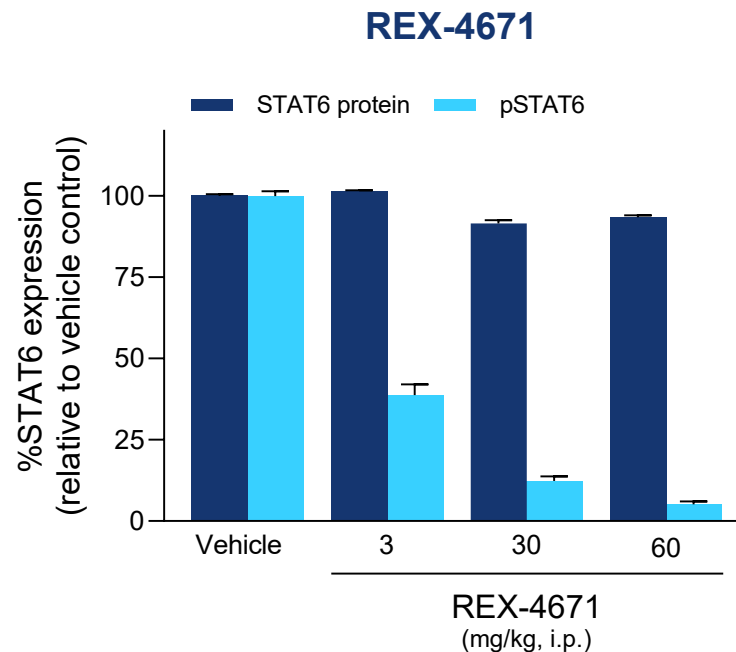
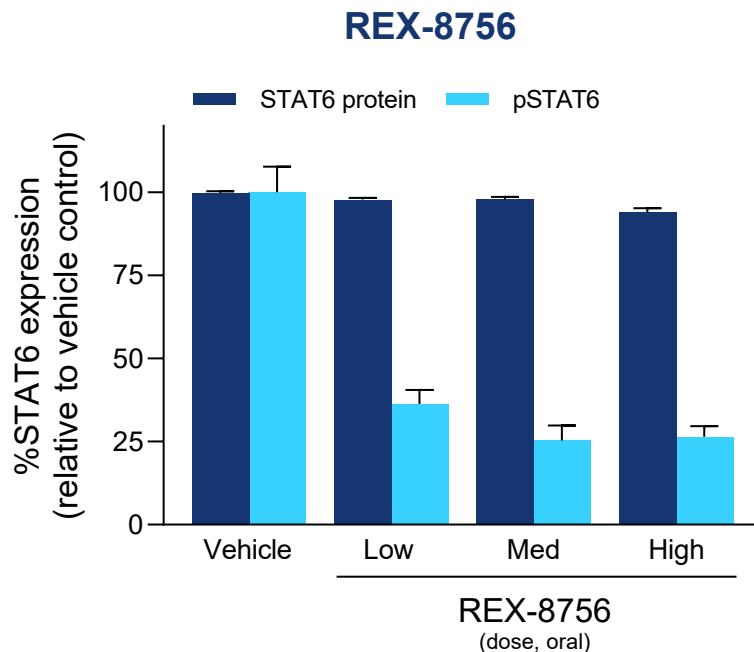
- Once or twice daily oral administration
  - Day 1
  - Day 7: Steady State
  - Day 9-10: Washout
- Clinical observations, hematology, serum chemistry, coagulation

- Highly selective pSTAT6 inhibition, no off-target pSTAT1 or pSTAT3 impact observed
- Well tolerated at all dose levels

# Recludix STAT6 Inhibitors Achieve Deep and Durable pSTAT6 Inhibition In Vivo without STAT6 Protein Degradation in Mice

- Recludix compounds achieve dose-dependent, rapid, and durable pSTAT6 inhibition in blood and tissues
- Reversible pSTAT6 inhibition achieves exquisite targeting of type-2 inflammation without STAT6 protein degradation

## In vivo pSTAT6 inhibition without protein degradation

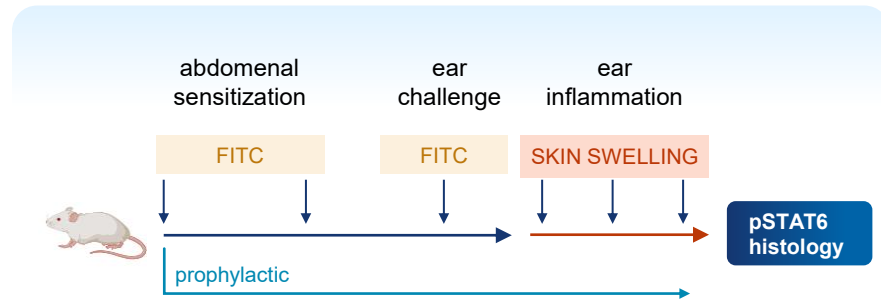


### Single dose PK/PD study

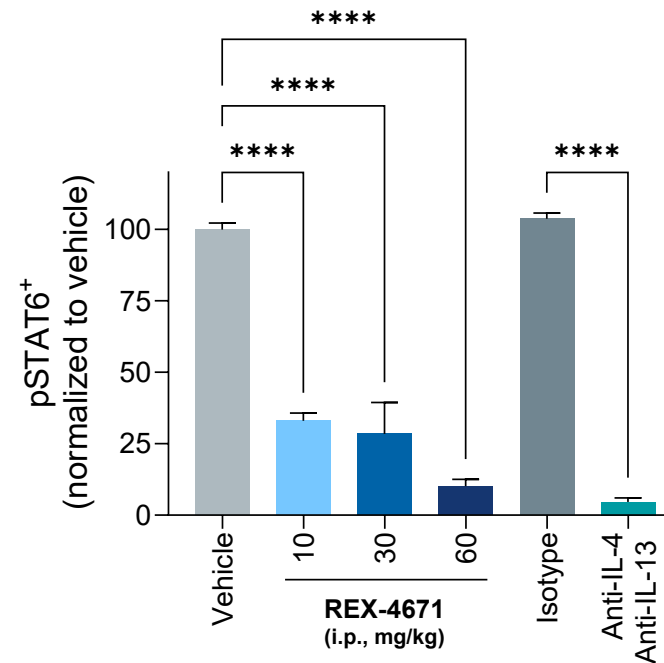
- Samples collected 4hr post single dose
- Whole blood and splenocytes ex vivo stimulated with IL-4 to induce STAT6 pathway activation
- Total STAT6 and pSTAT6 quantified by flow cytometry

# STAT6 Tool Compound REX-4671 Has Comparable Efficacy to Combined Anti-IL-4/13 Biologics in Dermatitis Model

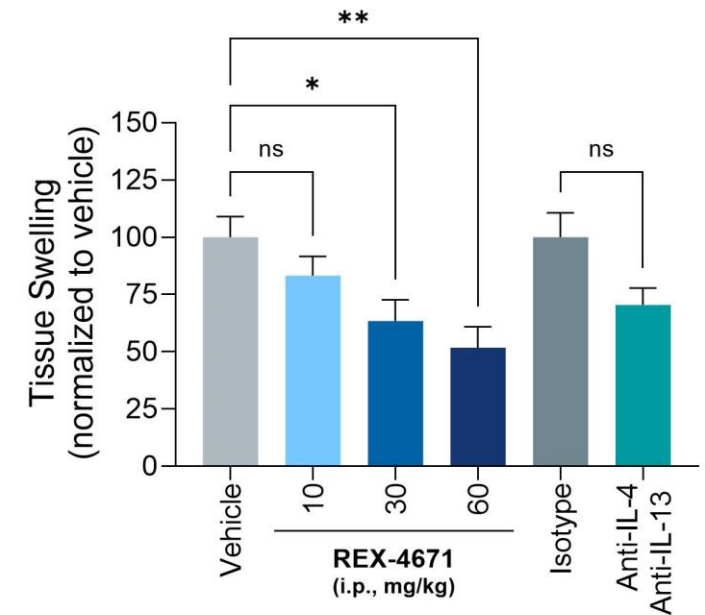
- REX-4671 dose dependently inhibits pSTAT6 and significantly reduced skin inflammation in chemical-induced dermatitis model
- Comparable in vivo efficacy to the combination of anti-IL-4/13 surrogate antibodies



Spleen pSTAT6 inhibition



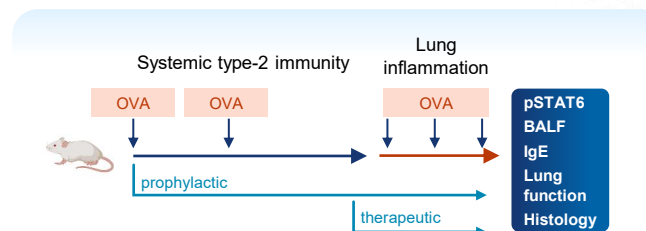
Skin inflammation



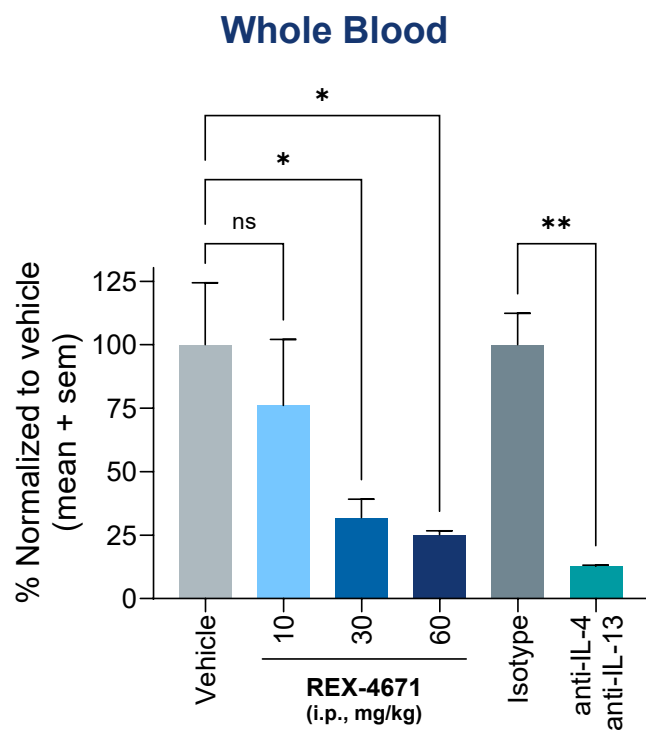
\*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001

# Prophylactic REX-4671 Demonstrates Comparable Efficacy to Combined Anti-IL-4/13 Biologics in OVA-Asthma Model

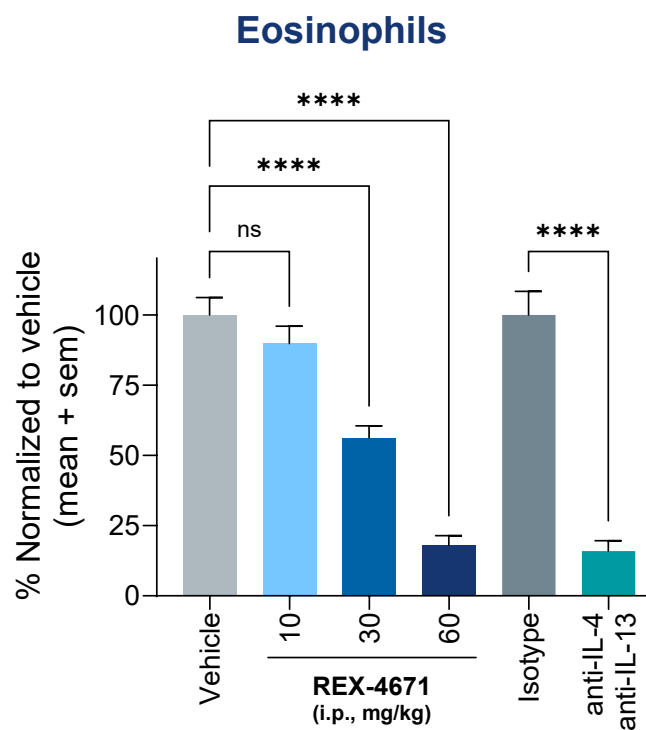
- REX-4671 demonstrates comparable efficacy to combined anti-IL-4/13 rodent surrogate antibodies



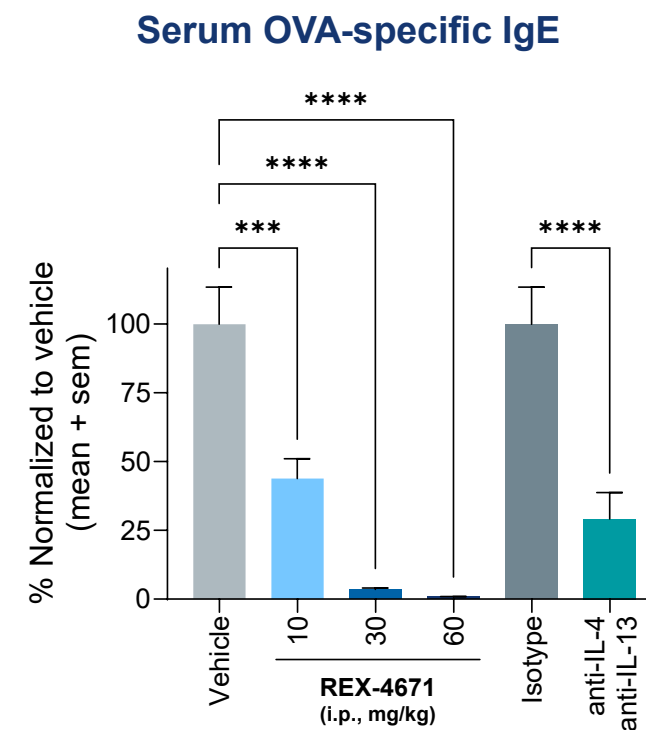
## pSTAT6 inhibition



## Lung immune cell infiltration



## Humoral immunity



\*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001



# Summary and Next Steps

- REX-8756 is a potent and selective oral STAT6 inhibitor that demonstrates complete pathway inhibition and is well tolerated in preclinical studies
- Completion of GLP toxicology studies and Development Candidate nomination associated with a \$50 million payment to Recludix under the collaboration with Sanofi
- Investigational New Drug (IND) enabling activities ongoing to support IND submission 2H 2025

**BTK**

# Selective Targeting BTK Has the Potential to Yield Superior Efficacy and Safety in Chronic Inflammatory Diseases



**CSU**  
**6.5M**

**RA**  
**4.8M**

**SLE**  
**0.5M**

**MS**  
**1.5M**

## >13M

TOTAL PATIENT IMPACT

**DIFFERENTIATED RELATIVE TO  
TRADITIONAL TKI APPROACH**

Targeting SH2 domain leads to best-in-class selectivity to enable improved safety margins

SH2 approach disrupts the central scaffolding function of BTK to deeply inhibit pro inflammatory signaling and widen the therapeutic window

Prodrug mechanism enhances target coverage to drive improved efficacy

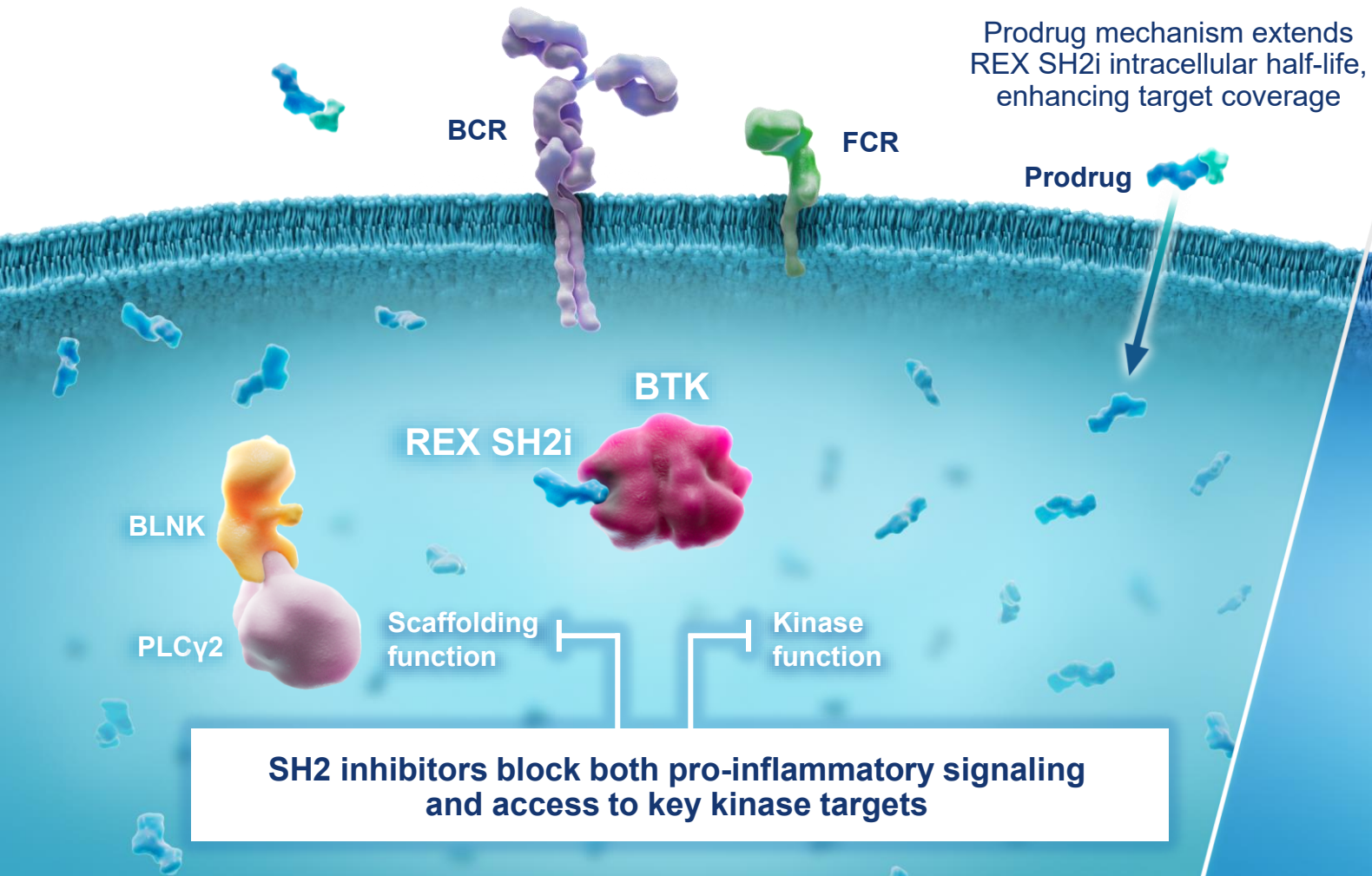
Source: GlobalData 2023, ClearView HealthCare Partners

CSU: Chronic spontaneous urticaria, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, MS: Multiple sclerosis

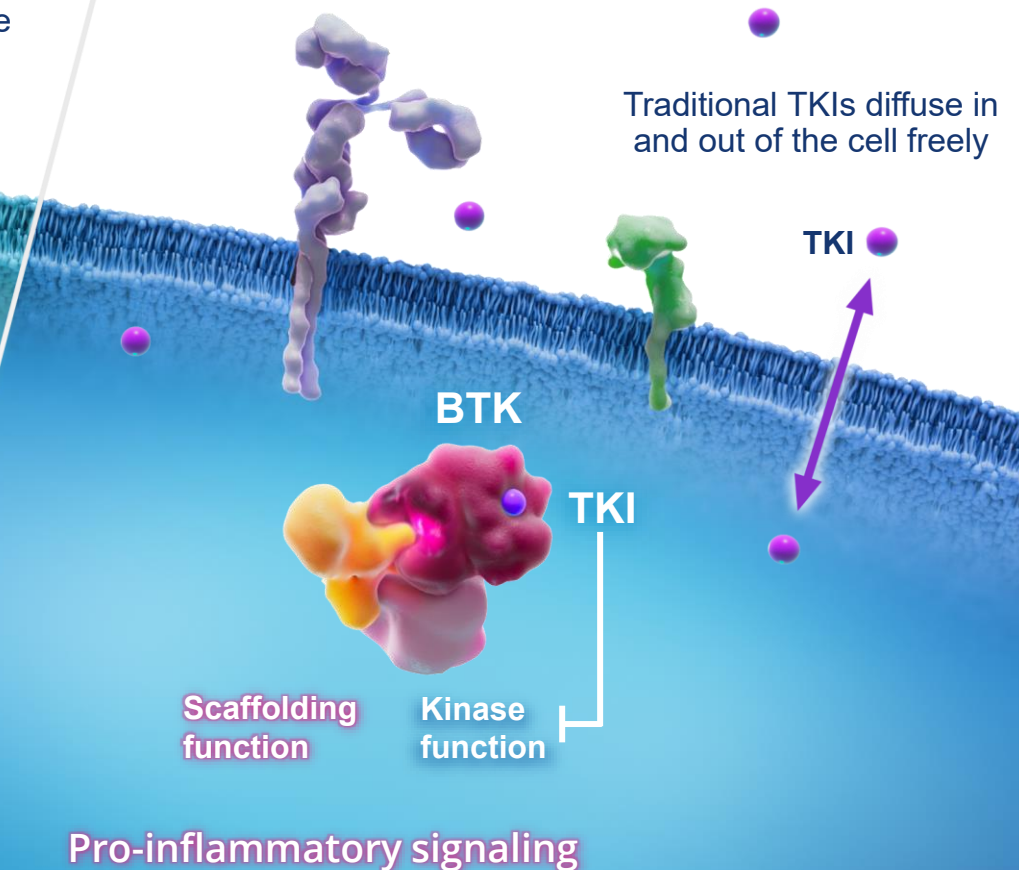
# BTK SH2 Inhibitor is First-In-Class with Differentiated Profile Relative to Traditional TKIs



## Recludix BTK SH2i Prodrugs



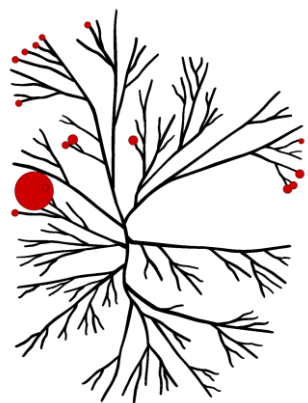
## Traditional BTK TKIs



# Recludix Has Developed Highly Potent and Selective BTK SH2 Domain Inhibitors in Biochemical Assays



Biochemical potency (SH2scan K <sub>D</sub> )	Biochemical Selectivity (TEC)	Biochemical Selectivity (SH2ome)	SH2 Domain Selectivity
0.055 nM	>69,000 × vs.TEC	>8000× vs SH2ome	



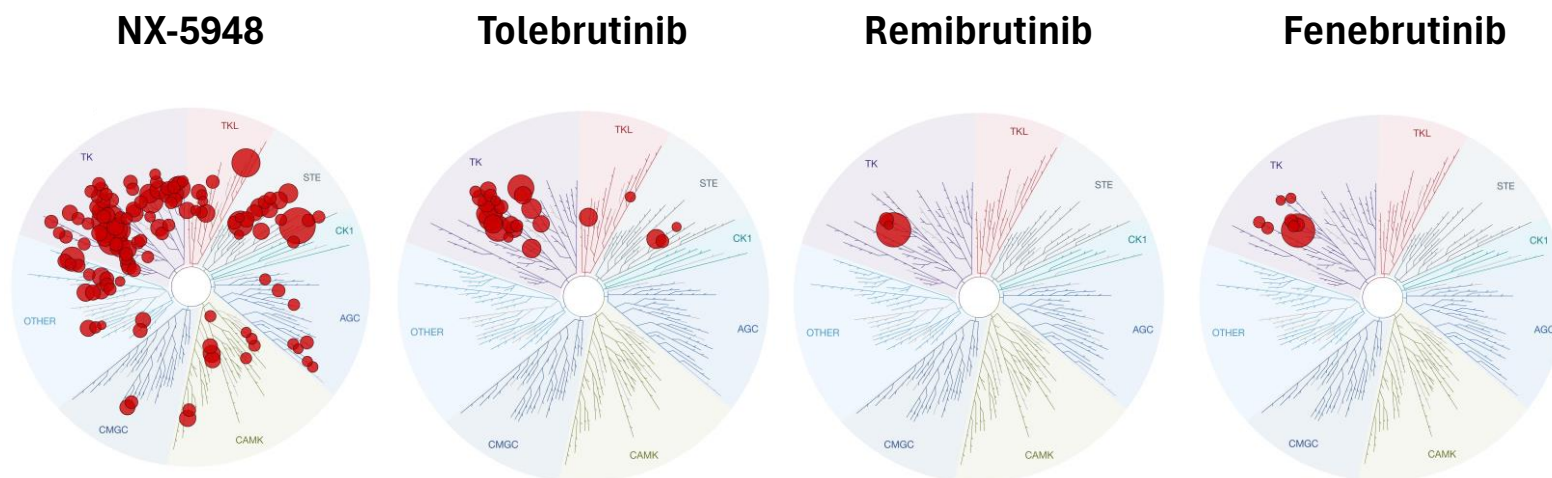


# BTK SH2 Domain Inhibitors are Differentiated Relative to Traditional BTK Tyrosine Kinase Inhibitors

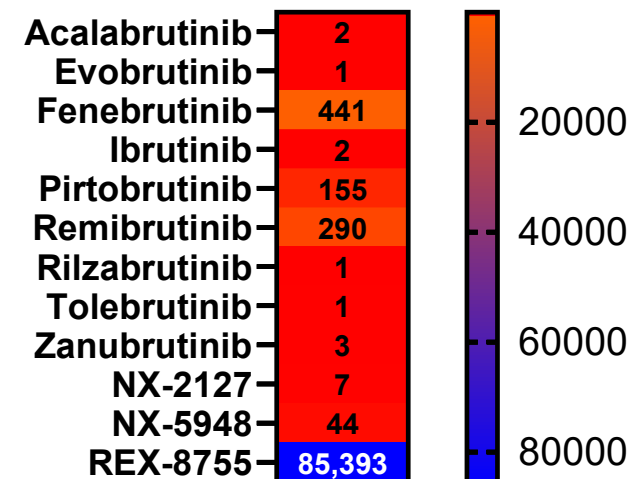
Selectivity difference is predicted to drive improved safety and efficacy outcomes

- Recludix BTK SH2 inhibitors:
  - Demonstrate exquisite selectivity
  - Do not inhibit TEC kinase, an important off-target involved in platelet dysfunction
  - Demonstrate TEC/BTK selectivity greater than 80,000x

Kinase selectivity



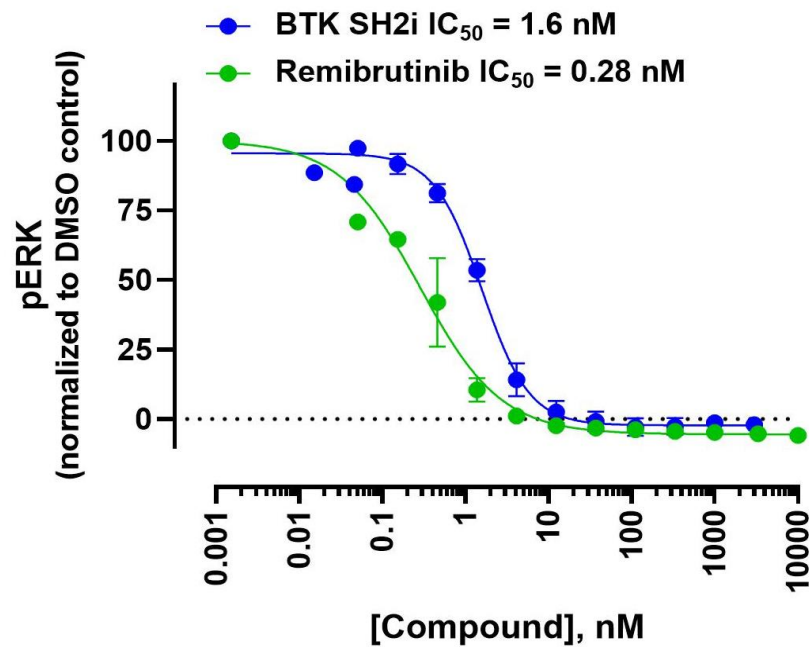
TEC/BTK selectivity



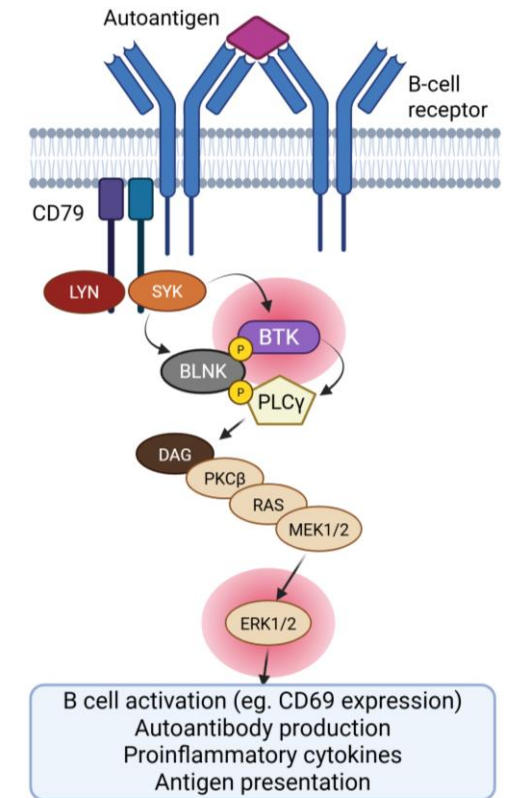
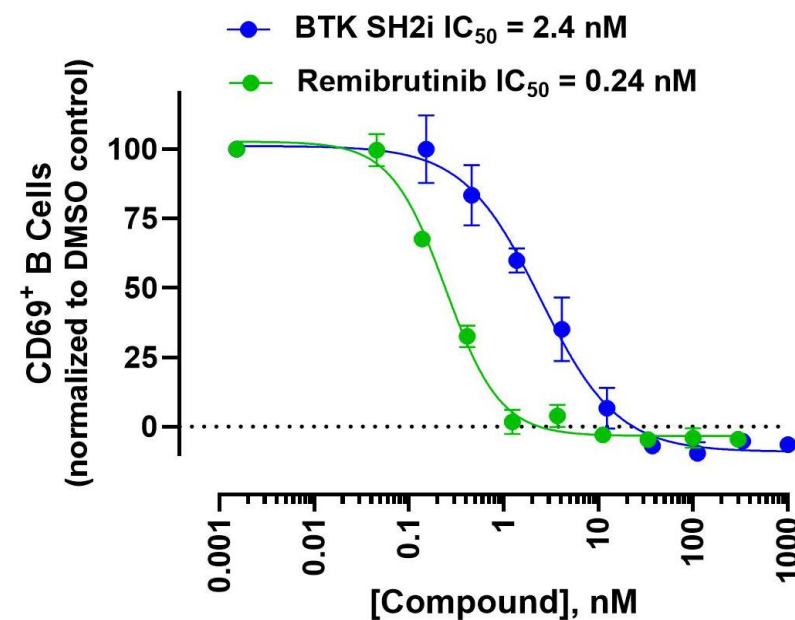
# BTK SH2 Domain Inhibitors Fully Block pERK Signaling and Downstream Immune Cell Activation



## pERK Assay



## CD69 Expression

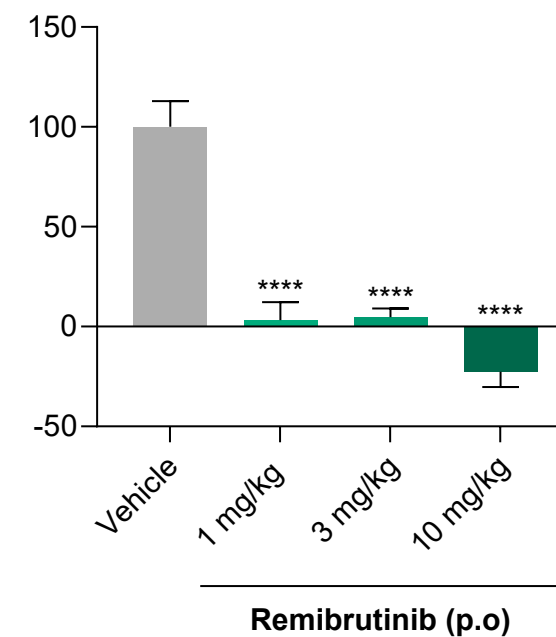
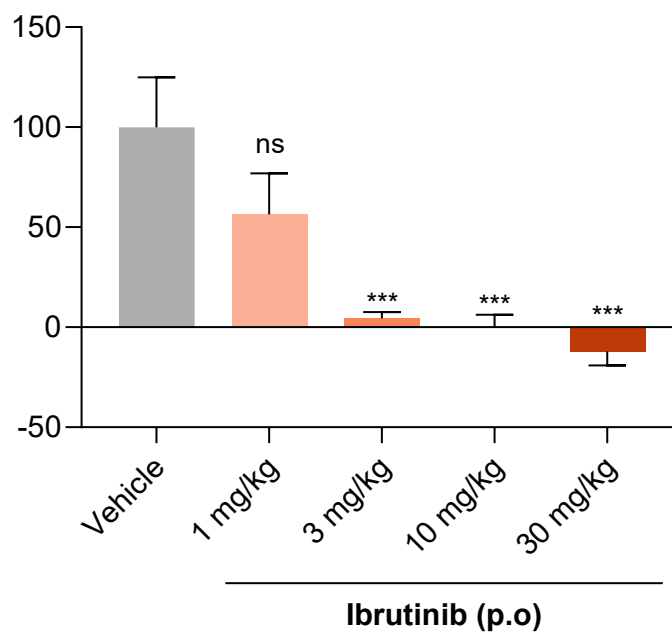
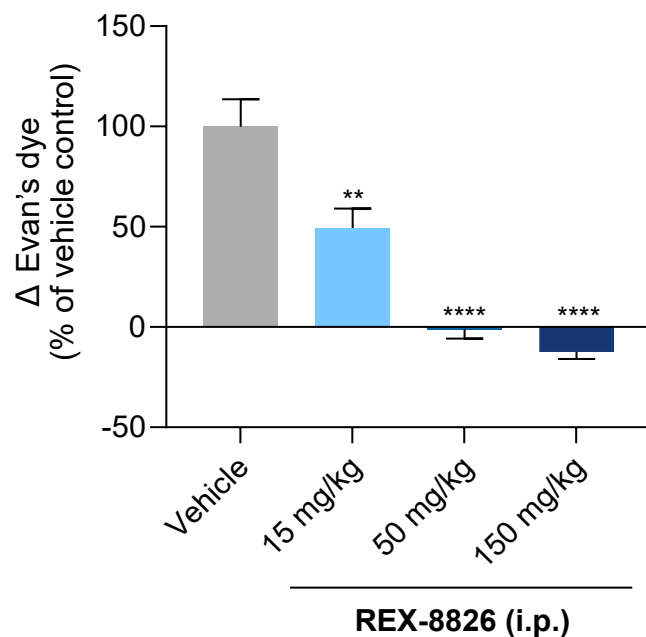
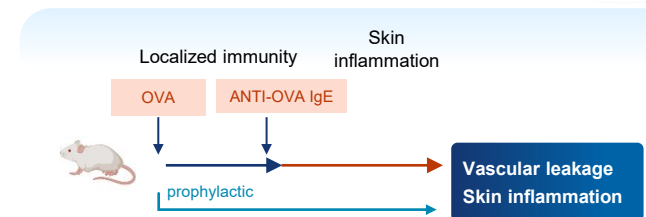


# BTK SH2 Domain Inhibitors Abrogate Mast Cell Activation in In Vivo Model of Chronic Urticaria

BTK SH2 domain inhibitors demonstrate strong dose-dependent efficacy



## Vascular leakiness (Evan's dye extravasation)

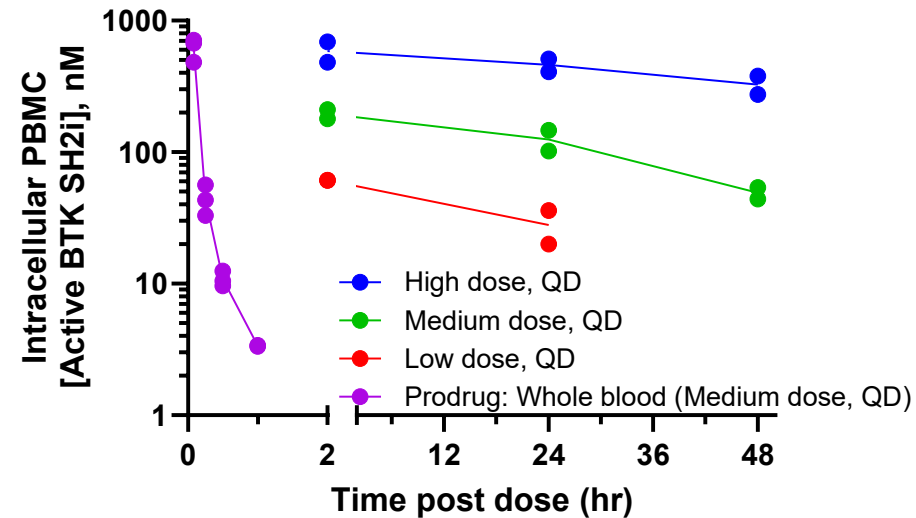


\*\* p < 0.1, \*\*\* p < 0.001, \*\*\*\* p < 0.0001

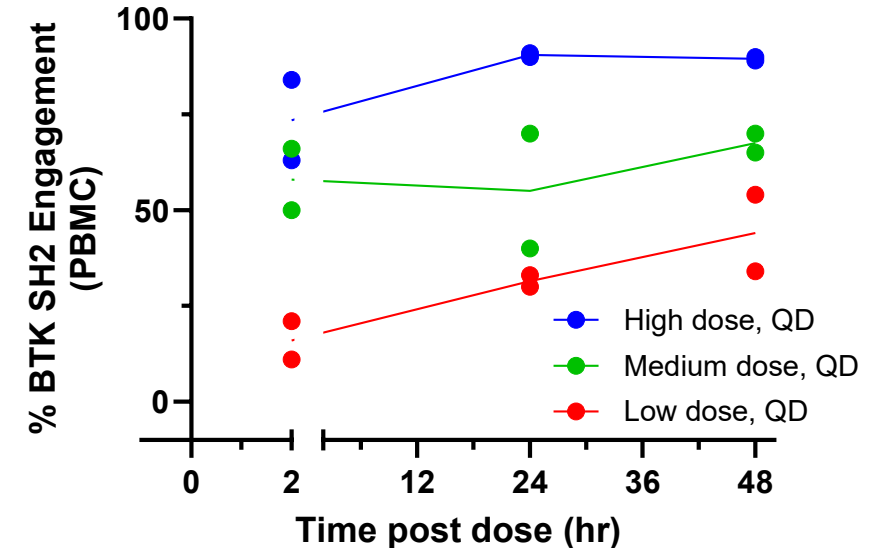
# BTK SH2 Domain Inhibitors Achieve Durable Intracellular PK Leading to Prolonged Target Engagement in Dog PBMCs



## BTK SH2i Pharmacokinetics



## BTK Target Engagement



- Following intravenous dosing in dogs, active BTK SH2i maintained durable intracellular exposures in target PBMCs while exposure of the prodrug was transient
- BTK SH2i exposure in PBMCs enabled deep, durable, and dose-dependent target engagement

# Highlights and Upcoming Milestones



# Highlights and Near-Term Milestones



## KEY ACCOMPLISHMENTS

- **Successfully drugged previously “undruggable” SH2 domains**
- **Advanced STAT6 inhibitor in global partnership with Sanofi**
  - Potent, selective, reversable, and orally bioavailable compounds
  - Favorable differentiation from IL-4/IL-13 biologics and JAK/TYK2 inhibitors
  - In vivo efficacy and target modulation, without protein degradation, in inflammation disease models
  - GLP toxicology studies completed and Drug Candidate nominated, triggering \$50 million milestone payment from Sanofi



## NEAR-TERM MILESTONES

### STAT6

- IND submission 2H25
- Phase 1 study initiation 2H25

### BTK

- Continue to advance program towards clinic



**Thank you**

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Unlocking New Therapeutic Possibilities

