



# Corporate Presentation

January 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



**STAT3 inhibitor**

- Wholly-owned
- Validated by JAK & TYK2 inhibitors



**BTK SH2 inhibitor**

- Wholly-owned
- Validated by BTK kinase inhibitors

## **OPERATIONAL STRENGTH**

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

## **PROPRIETARY PLATFORM DRIVES OPTIONALITY**

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

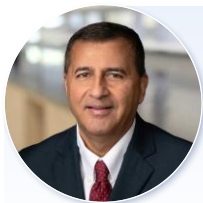
# Experienced Leadership Team



**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,  
MBA**  
CBO



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



**Brian Hodous,  
Ph.D.**  
SVP, Chemistry



Ayvakit™



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



Vanflyta®



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



Opzelura™, Gilenya®, Kesimpta®



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



Kinetix Novartis/CIBA-GEIGY  
Gleevec®  
Lasker-DeBakey Award, Japan Prize

## \$102M Series A



**Nick Lydon**

# 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

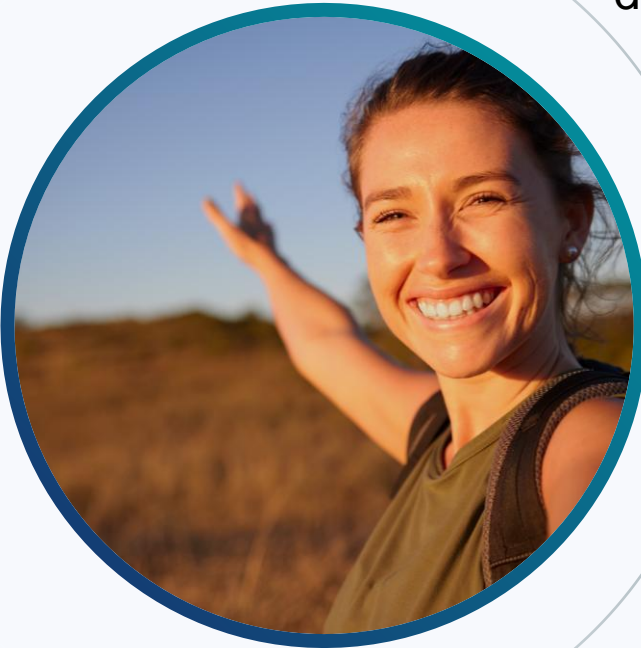
**Recludix**  
Pharma

- 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



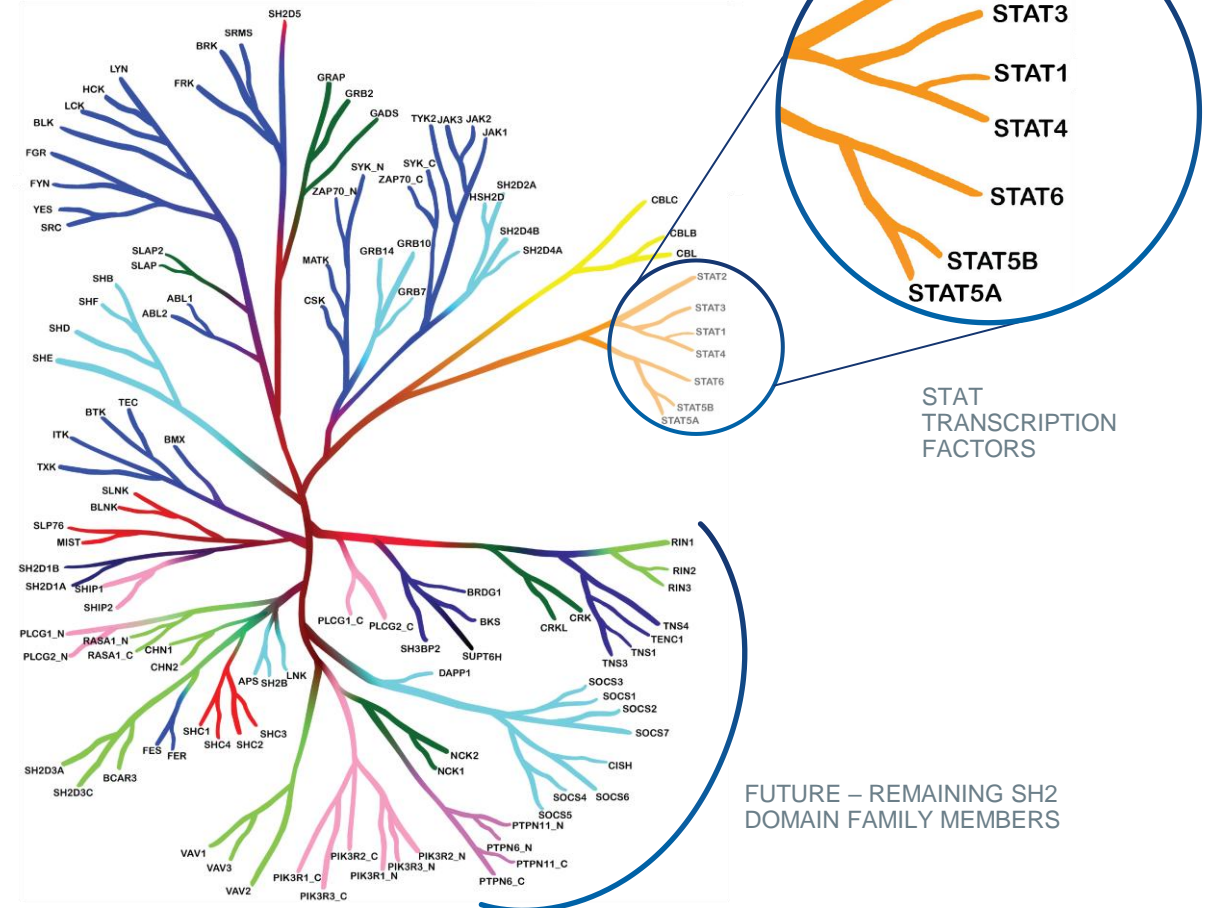
# SH2 Domains Have Previously Been Deemed “Undruggable”

Significant opportunity in targeting SH2 domain proteins

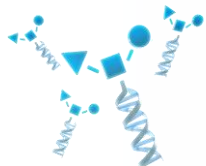
Src Homology 2 (SH2) domains are highly conserved protein domains that have long been recognized as attractive drug targets

- 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

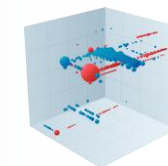


## Custom SH2 Domain Targeting DNA-Encoded Libraries

Discovery and SAR DELs | Hundreds of millions of molecules

## Proprietary DEL Selection & SAR Analysis

Rapid massively parallel determination of structure-activity relationships



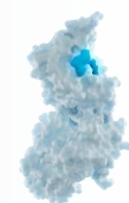
## High Quality Lead Compounds

### Prodrug Modality Expertise

Drives enhanced target coverage

### Structure-Based Design

Proprietary co-crystallography systems



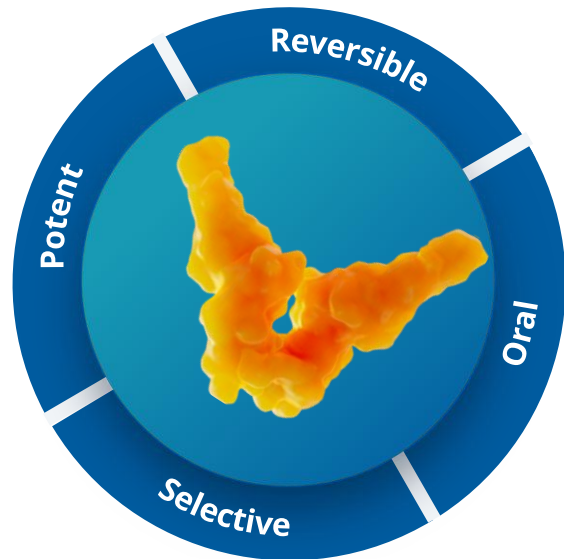
## SH2 Domain Screening Tool

Unique panel of SH2 domain assays | Drives selectivity

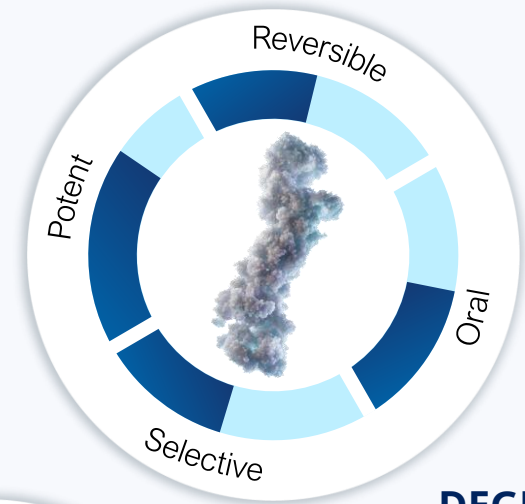
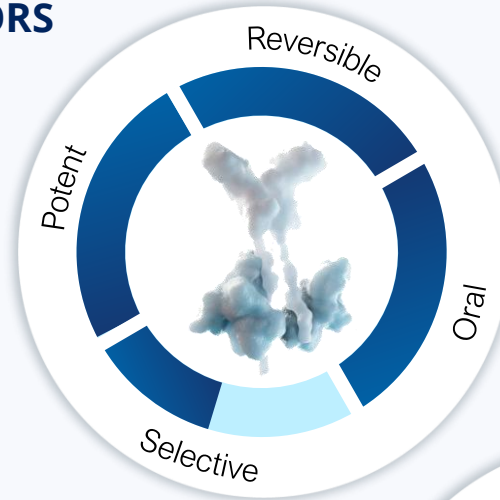
# STAT SH2 Domain Inhibition Enables a Best-in-Class Product Profile



**Recludix**  
Pharma

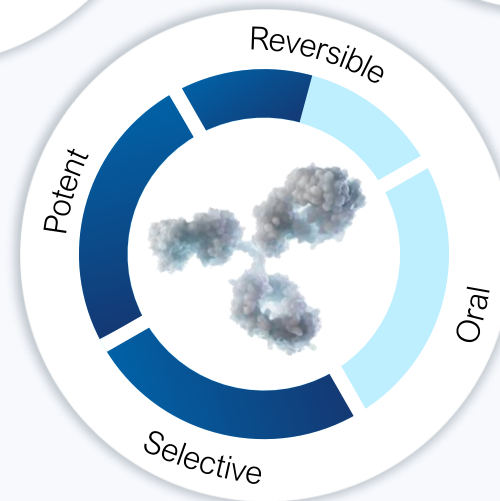


**JAK/TYK2  
INHIBITORS**



**DEGRADERS**

**BIOLOGICS**



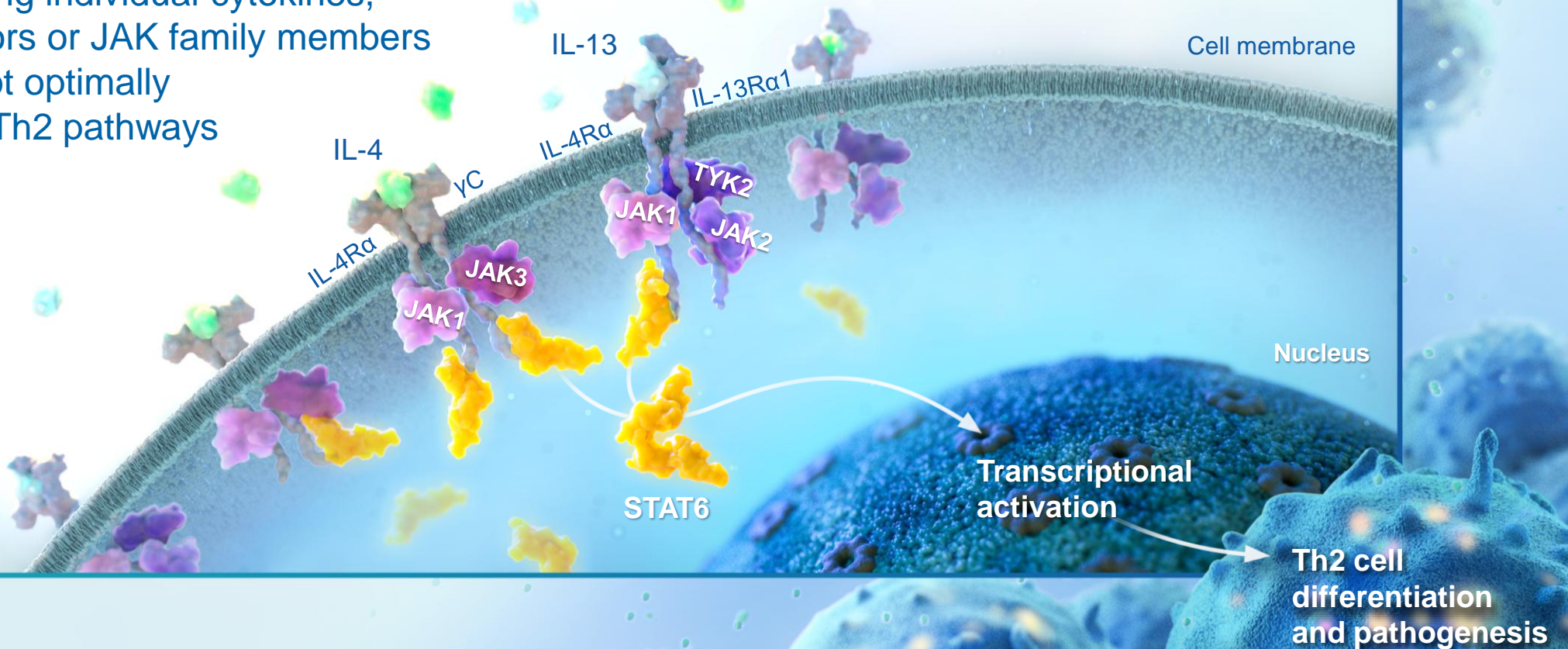


# STAT6

# 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



# 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

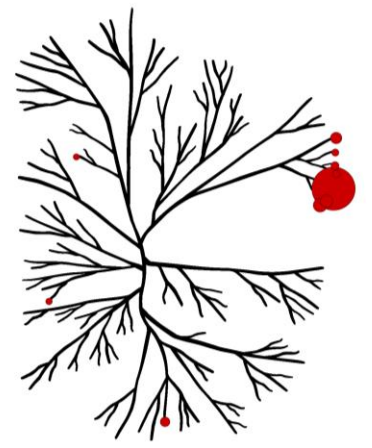
Patient-friendly oral formulation may enable treatment beyond those currently served by injectable agents

# STAT6 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
<b>STAT6 Inhibitor</b>	<b>REX-8756</b>	>3,000 nM	>1,000 nM	>2,500 nM	<b>19 nM</b>	>10,000 nM	>10,000 nM
<b>IL-4 / IL-13 Antagonist</b>	<b>Dupilumab</b>	>10,000 nM	>1,000 nM	>1,000 nM	<b>26 nM</b>	>1,000 nM	>1,000 nM
<b>JAK Inhibitors</b>	<b>Abrocitinib</b>	1,300 nM	900 nM	73 nM	<b>80nM</b>	3,200 nM	2,800 nM
	<b>Upadacitinib</b>	39 nM	36 nM	7.4 nM	<b>4.3 nM</b>	69 nM	20 nM
	<b>Baricitinib</b>	110 nM	210 nM	25 nM	<b>15 nM</b>	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

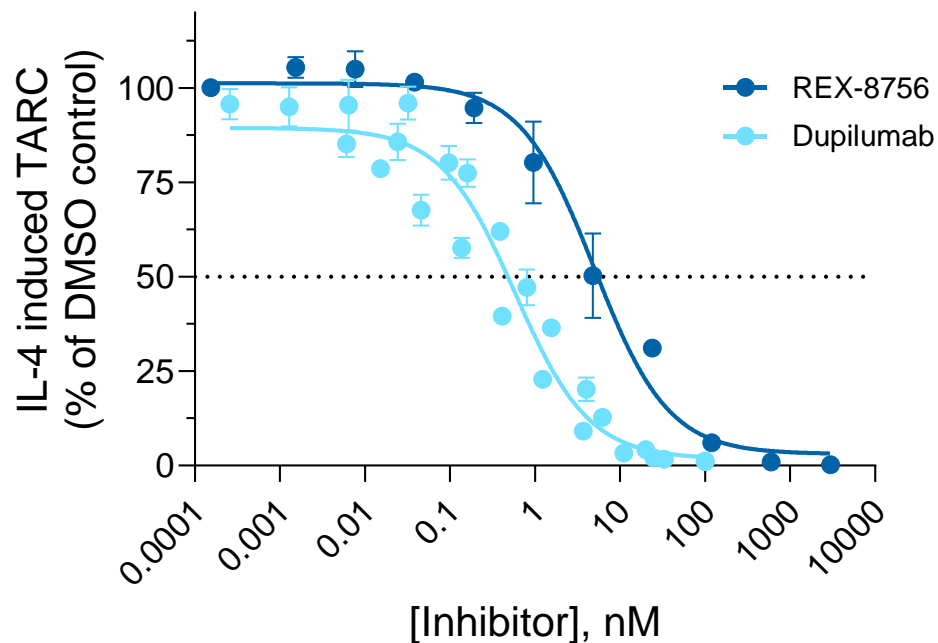
<10X



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

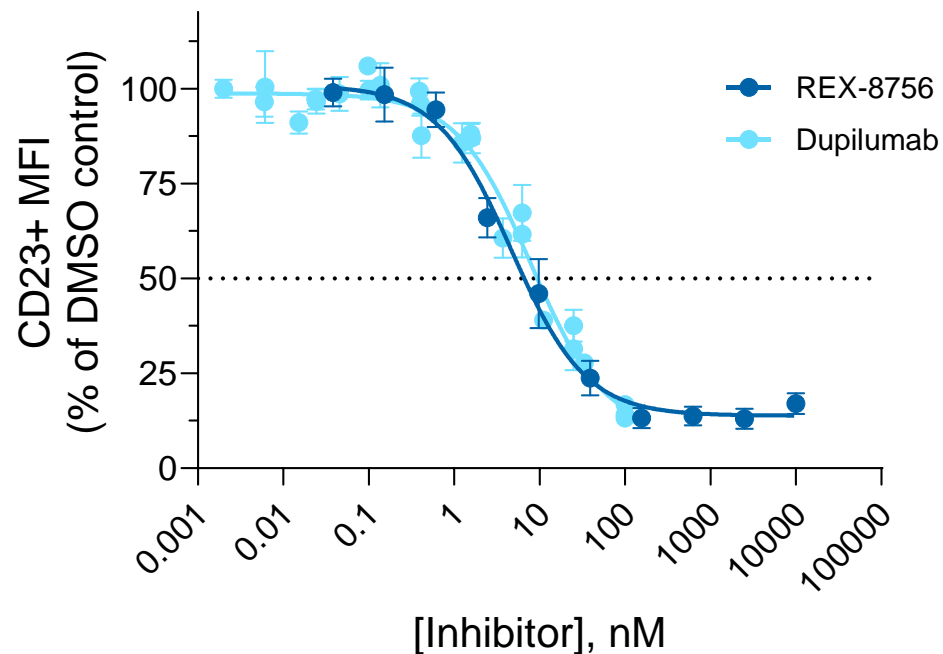


## IL-4 induced TARC



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

## IL-4 induced CD23 activation



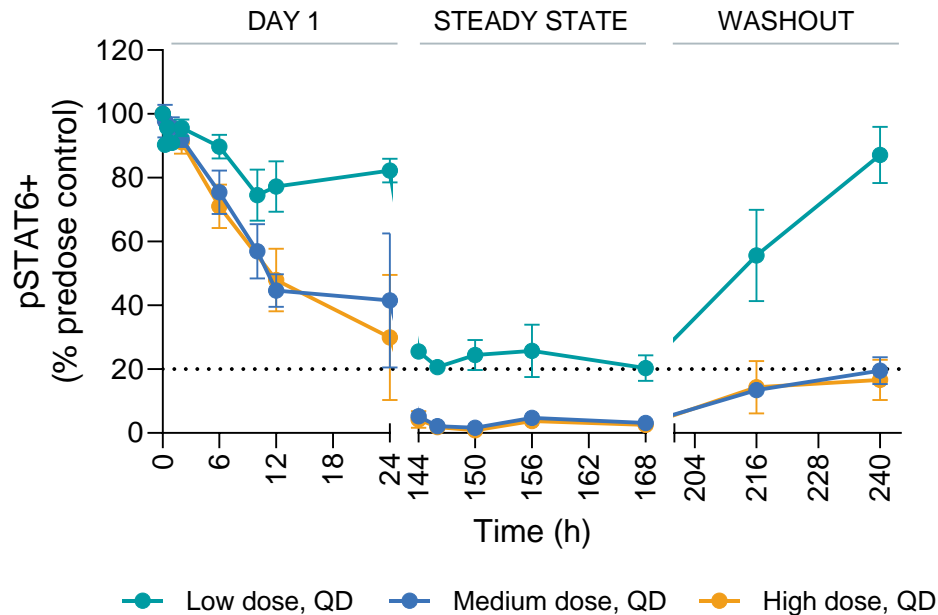
	REX-8756	Dupilumab
<b>IC<sub>50</sub></b>	5.1 nM	11 nM

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

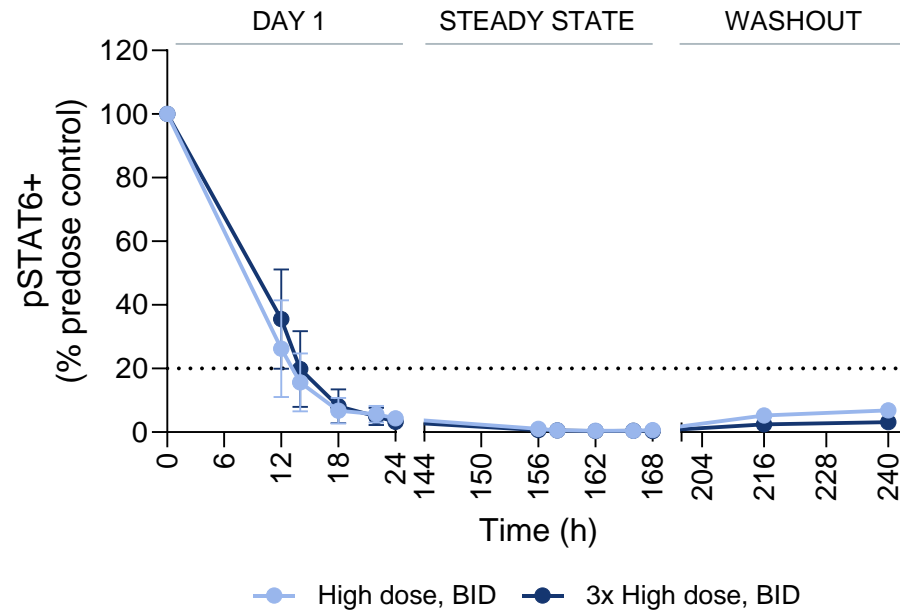


Efficacious dose at >80% pSTAT6 PD modulation

## 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

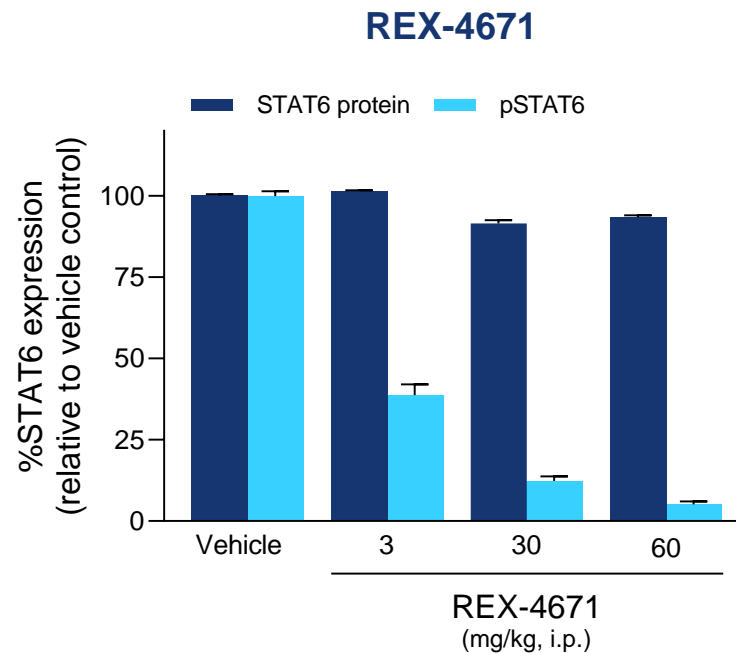
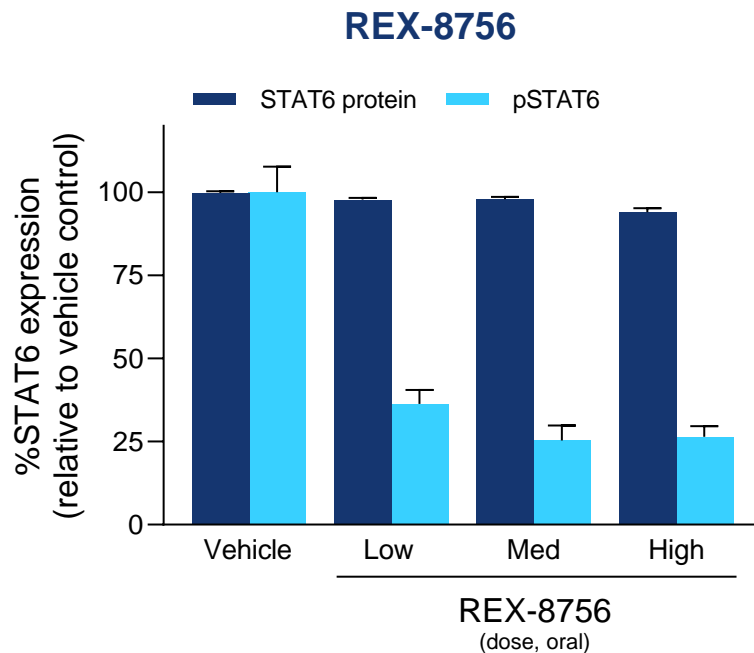
- Highly selective pSTAT6 inhibition, no off-target pSTAT1 or pSTAT3 impact observed
- Well tolerated at all dose levels

# 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

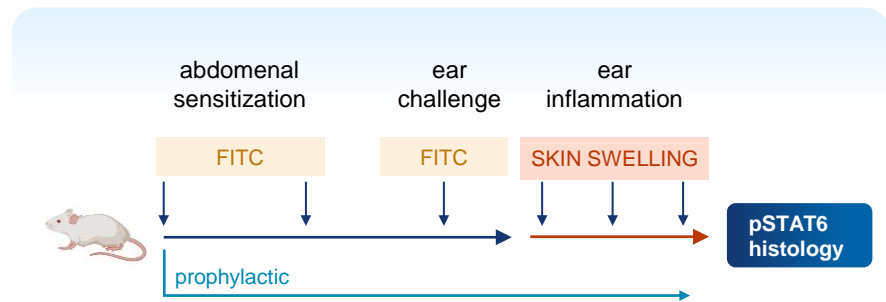


### Single dose PK/PD study

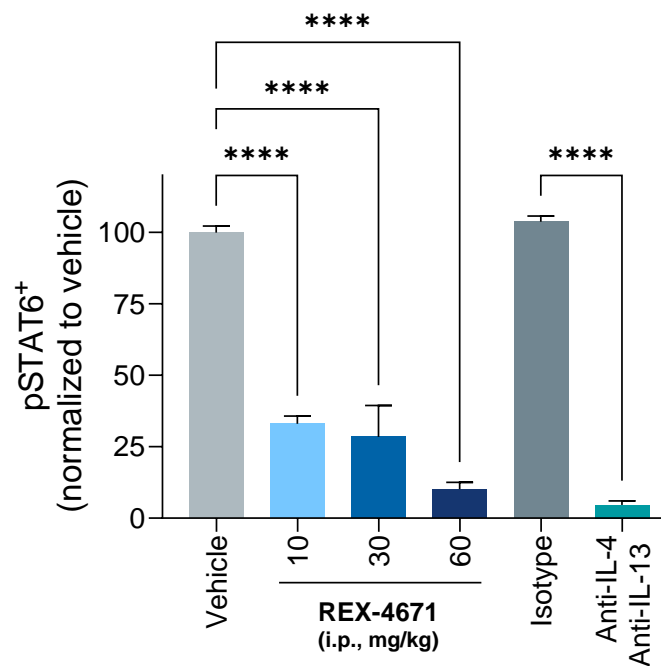
- Samples collected 4hr post single dose
- Whole blood and splenocytes ex vivo stimulated with IL-4 to induce STAT6 pathway activation
- Total STAT6 and pSTAT6 quantified by flow cytometry

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

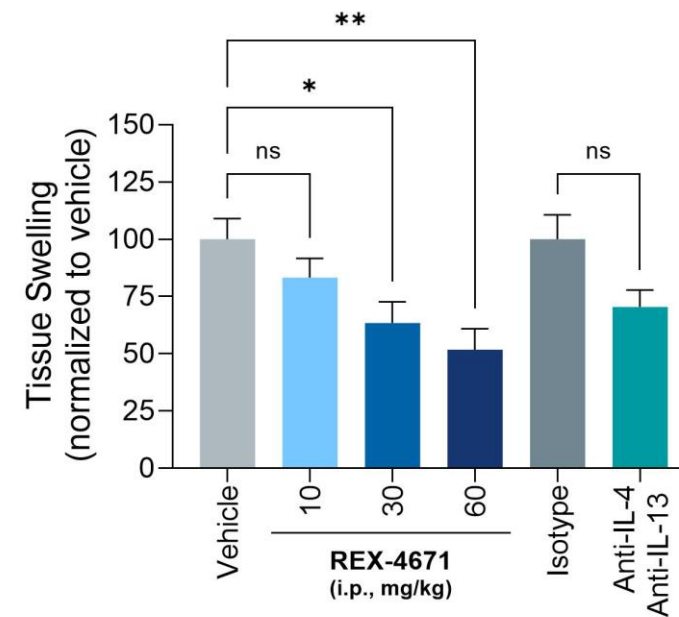
- REX-4671 dose dependently inhibits pSTAT6 and significantly reduced skin inflammation in chemical-induced dermatitis model
- Comparable in vivo efficacy to the combination of anti-IL-4/13 surrogate antibodies



Spleen pSTAT6 inhibition



Skin inflammation

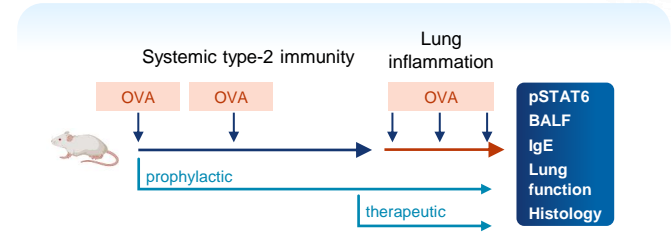


\*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001

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



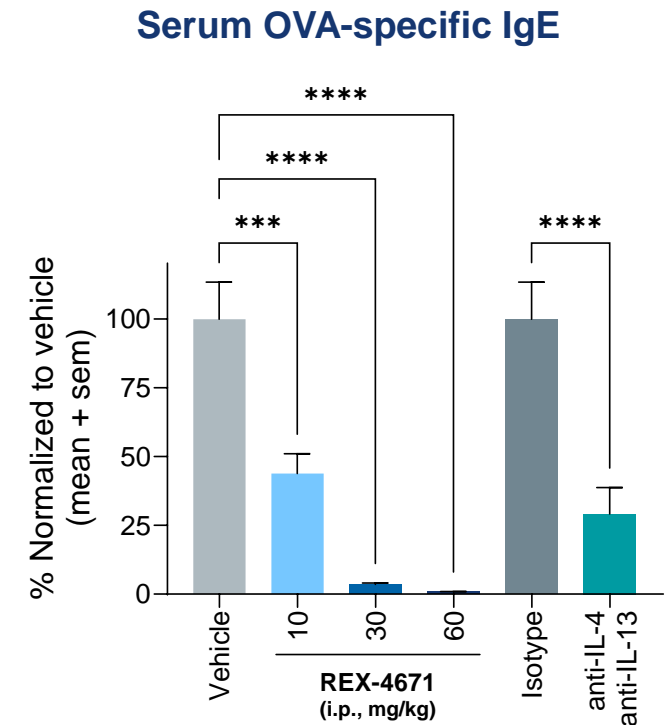
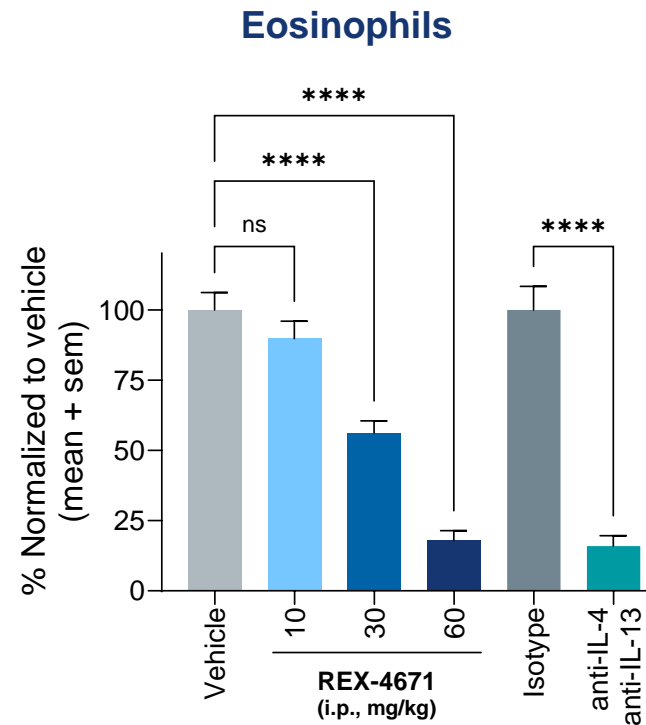
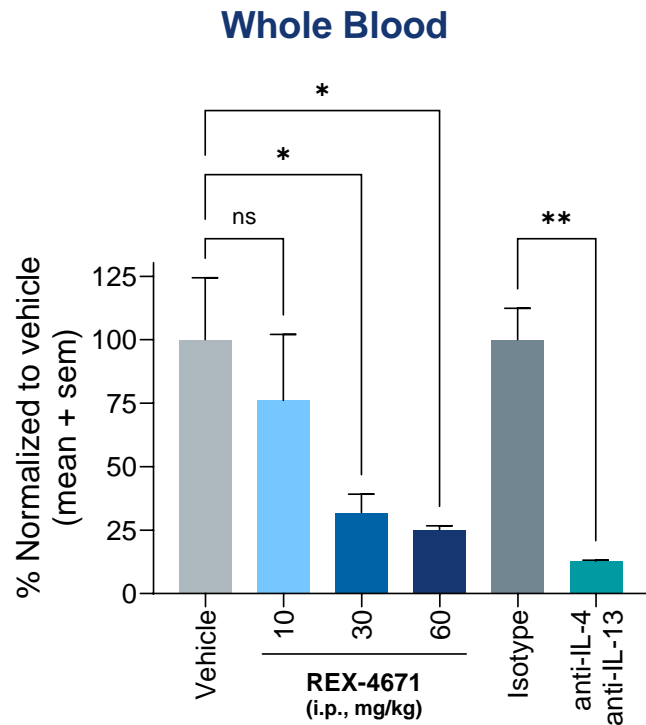
- REX-4671 demonstrates comparable efficacy to combined anti-IL-4/13 rodent surrogate antibodies



## pSTAT6 inhibition

## Lung immune cell infiltration

## Humoral immunity

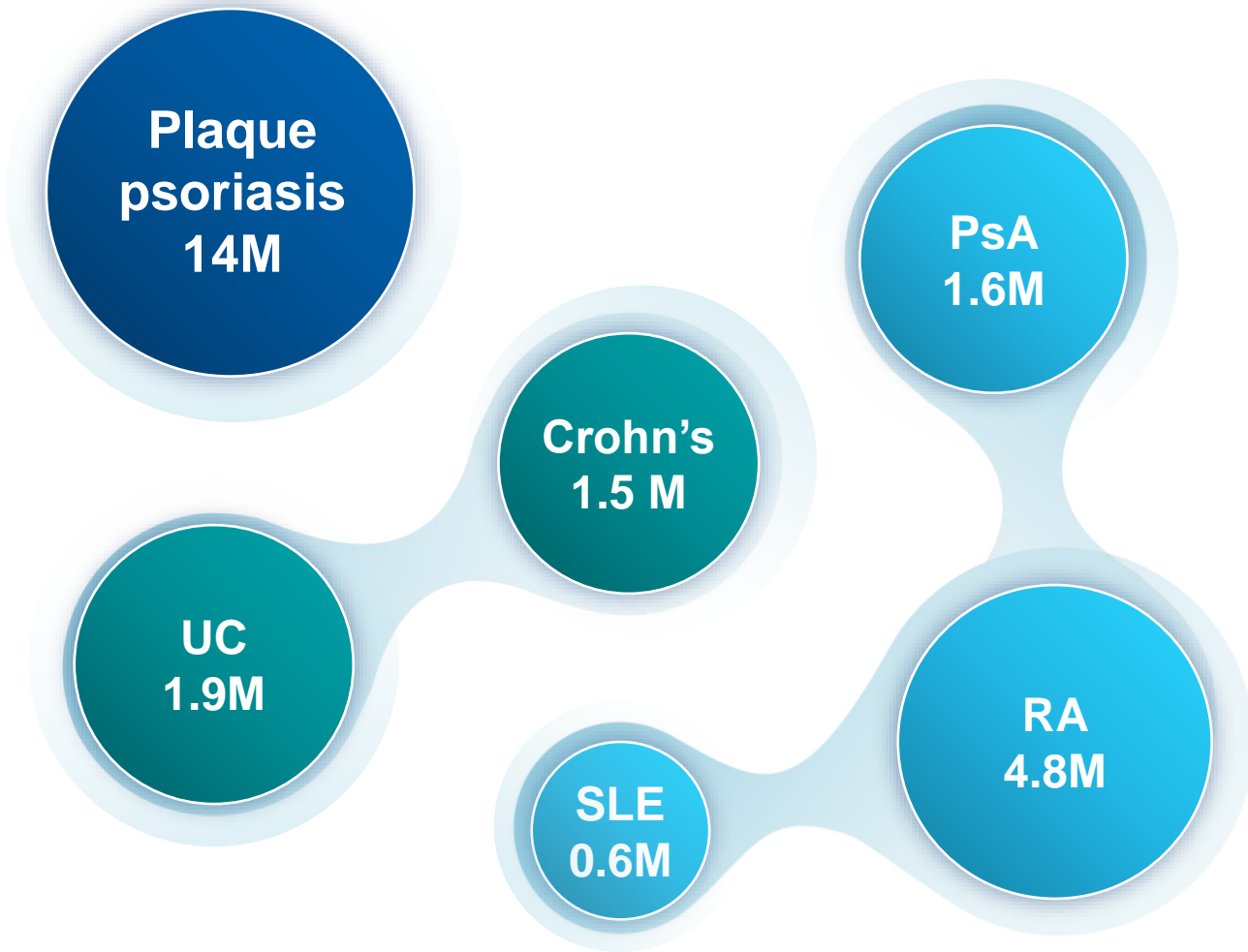


\*p<0.05, \*\*p<0.01, \*\*\*p<0.001, \*\*\*\*p<0.0001



**STAT3**

# Highly Potent Therapy Inhibiting Validated Inflammatory Pathways Through a Selective and Safe Approach



## >24M

TOTAL PATIENT IMPACT

### POTENTIAL FOR TRANSFORMATIVE SAFETY

Avoids long-standing safety concerns with less specific pathway inhibition of JAK and TYK2 inhibitors

### COMPELLING EFFICACY

Robust efficacy potential in both Th17 mediated and broader IL-6 driven diseases

### FAVORABLE DOSING

Oral administration competes favorably with current standard of care

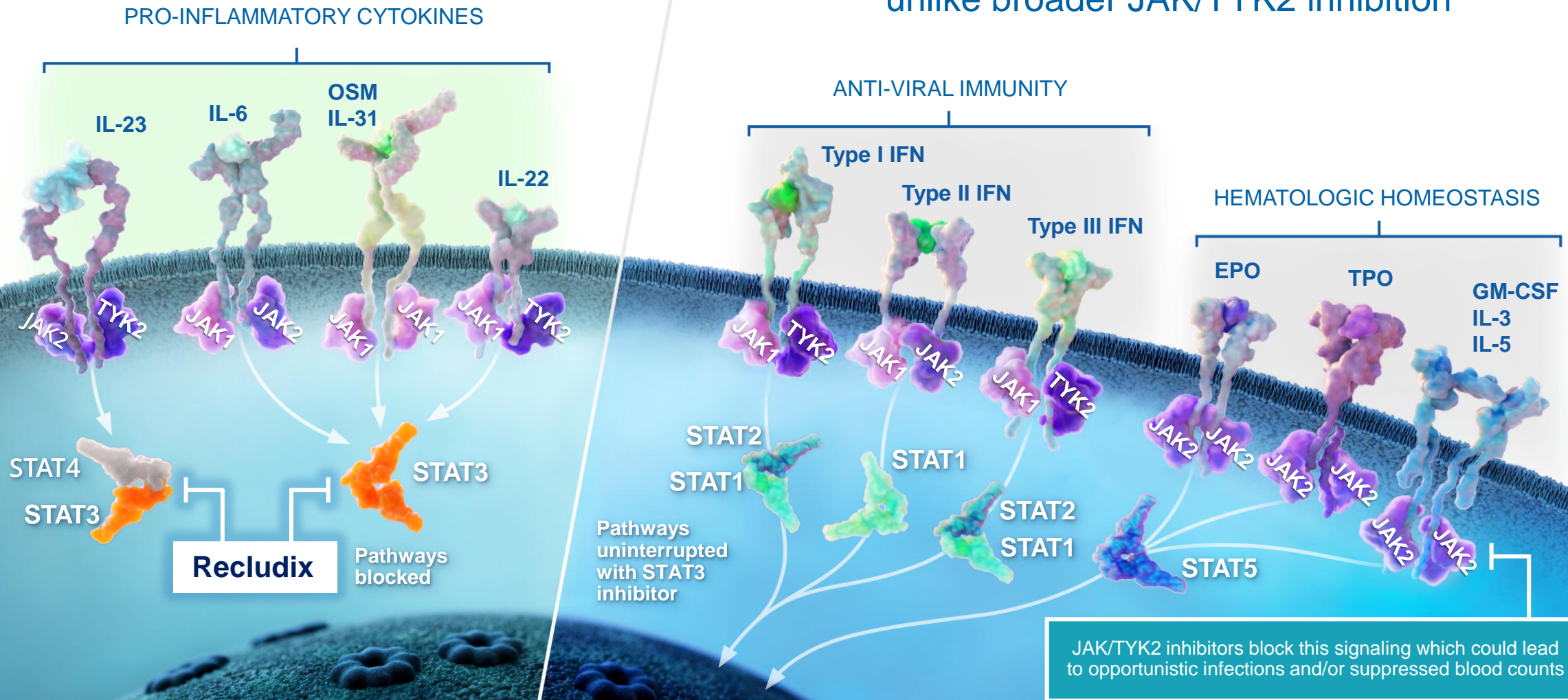
Source: GlobalData 2023, ClearView HealthCare Partners

UC: Ulcerative colitis, PsA: Psoriatic arthritis, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus

# STAT3 is a First- and Best-In-Class Opportunity to Inhibit Clinically Validated Inflammatory Disease Pathways

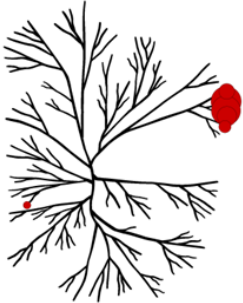
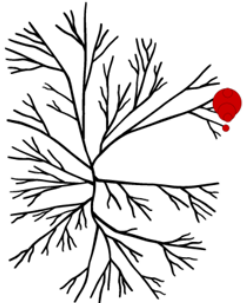


STAT3 targeting avoids pathways important for viral immunity and hematologic homeostasis, unlike broader JAK/TYK2 inhibition



# Recludix Has Identified Multiple Highly Potent, Selective and Orally Bioavailable STAT3 Inhibitors



	REX-5376	REX-7117
<b>Biochemical potency</b> (SH2scan $K_D$ )	0.15 nM	0.16 nM
<b>Cellular potency</b> (pSTAT3 $IC_{50}$ in human PBMCs)	0.72 nM	1.2 nM
<b>Biochemical STAT family selectivity</b>	~2X vs. STAT1 >150X vs. STAT2/4/5/6	~20X vs. STAT1 >500X vs. STAT2/4/5/6
<b>Cellular selectivity</b> (PBMCs)	~2X vs. STAT1 ~20X vs. STAT2 >300X vs. STAT4/5/6	>20X vs. STAT1 >500X vs. STAT2/4/5/6
<b>SH2 domain selectivity</b>		

# STAT3 Inhibition Impairs Th17 Cells and Differentiates From JAK/TYK2 Inhibitors in Functional T Cell Assays



		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
STAT3 inhibitors	REX-5376	>10,000 nM	>2,000 nM	11 nM	>3000 nM	>10,000 nM	>10,000 nM
	REX-7117	>10,000 nM	>2,000 nM	14 nM	>3000 nM	>10,000 nM	>10,000 nM
IL-6 mAb	Tocilizumab	>1,000 nM	>1,000 nM	Not established	>1,000 nM	>1,000 nM	>1,000 nM
IL-23 mAb	Risankizumab	>1,000 nM	>1,000 nM	Not established	>1,000 nM	>1,000 nM	>1,000 nM
TYK2 inhibitor	Deucravacitinib	>3,000 nM	260 nM	34 nM	~3,300 nM	3,200 nM	250 nM
JAK inhibitors	Tofacitinib	340 nM	74 nM	20 nM	20 nM	340 nM	200 nM
	Upadacitinib	39 nM	36 nM	8.0 nM	4.4 nM	69 nM	20 nM
	Baricitinib	110 nM	210 nM	15 nM	15 nM	57 nM	40 nM

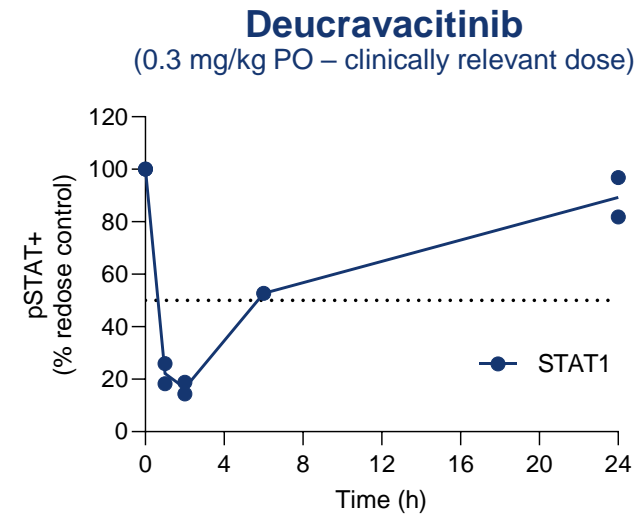
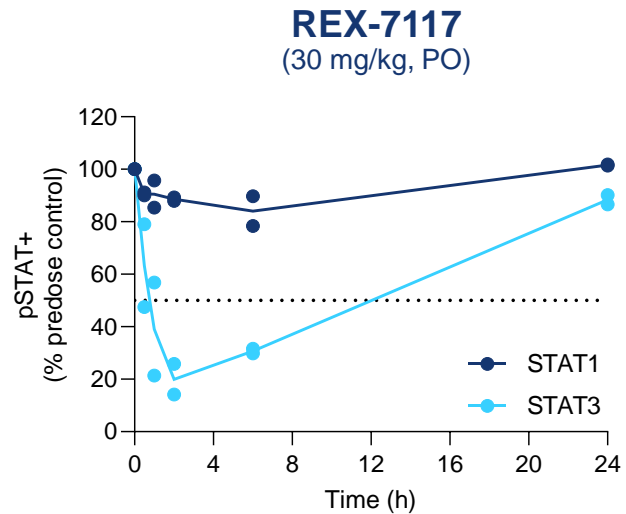
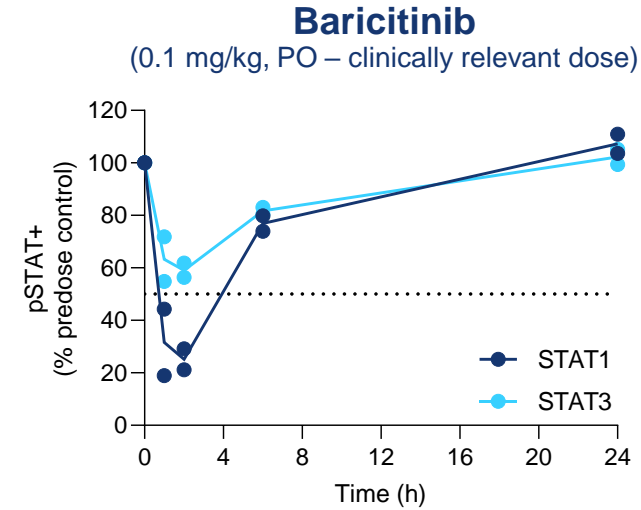
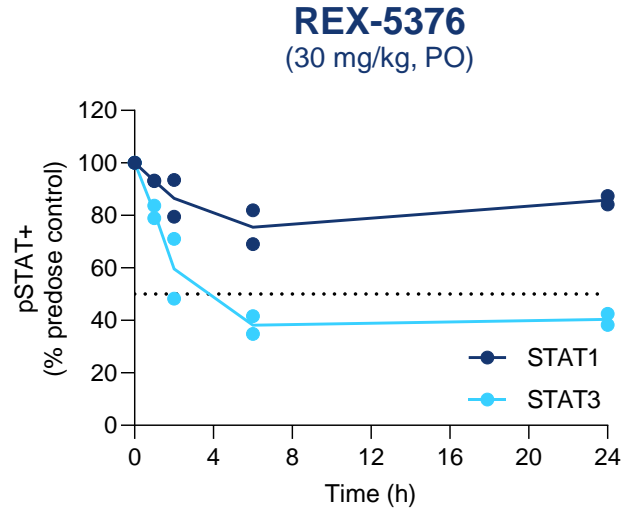
Selectivity relative to Th2 inhibition: >30X 10-30X <10X



# Recludix Oral STAT3 Compounds Characterized by Selective and Sustained Target Inhibition



Dog PBMCs evaluated for ex vivo pSTAT1/3 activity following single day oral dosing



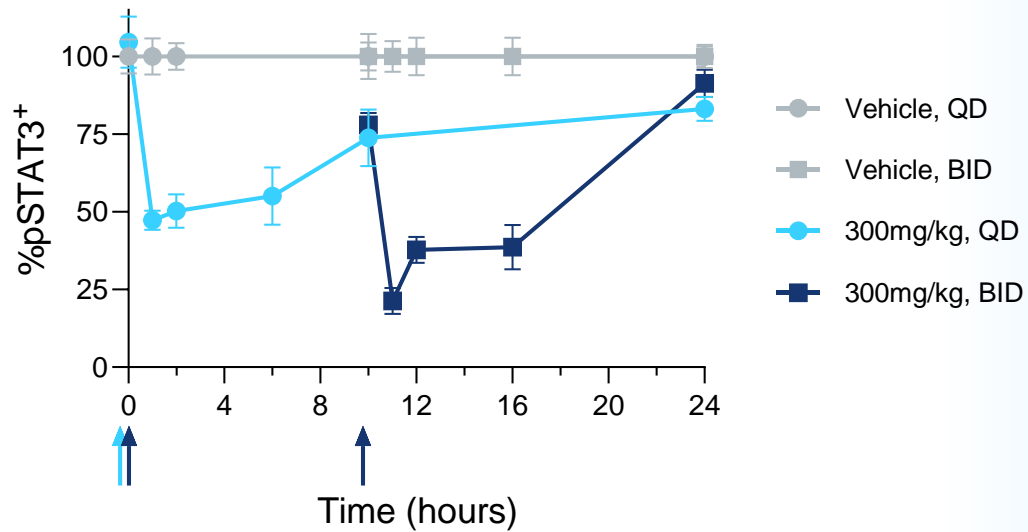
# REX-7117 Demonstrates Efficacy After Oral Dosing in a Murine IL-23-Induced Th17 Model of Psoriasis



REX-7117 efficacy comparable to anti-IL-17A biologic and improved relative to deucravacitinib

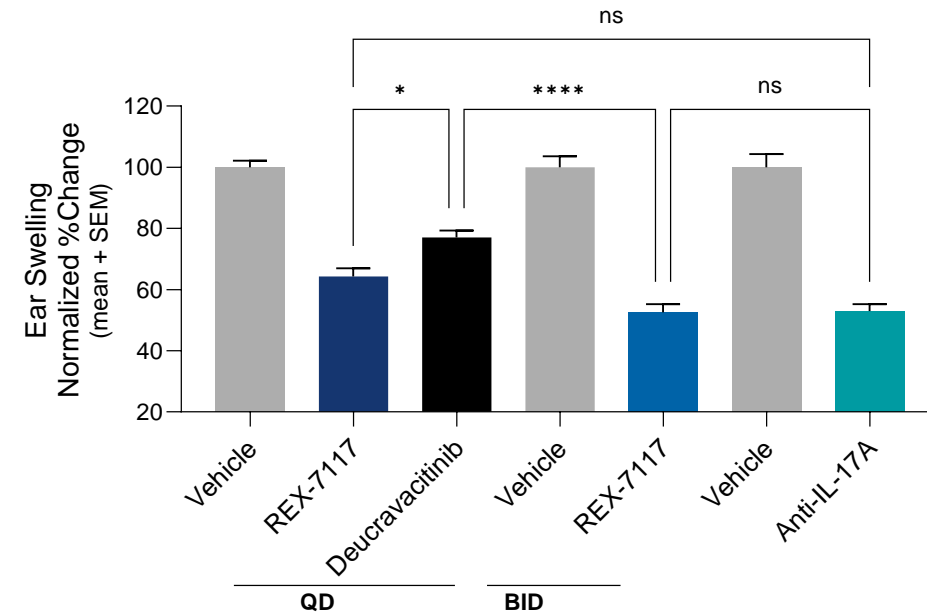
- Preclinical model used in the development of anti-IL-17 and anti-IL-23 biologics therapies
- REX-7117 dose was selected to match PD profile to that observed in dog at 15 mg/kg QD
- Deucravacitinib clinically relevant dose determined from regulatory filings and publications

### Mouse pSTAT3 Inhibition



n = 8-13 per timepoint

### IL-23 Induced Psoriasis Model

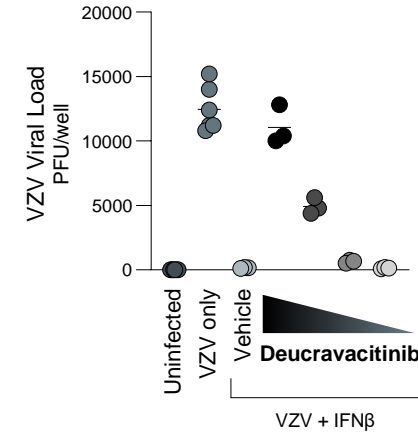
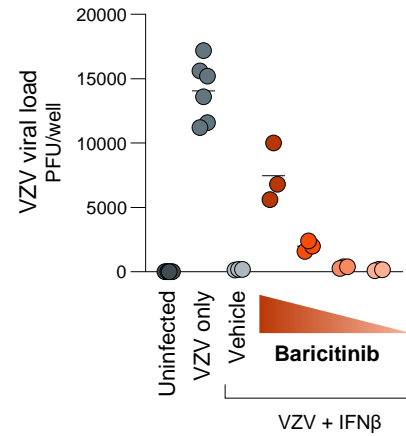
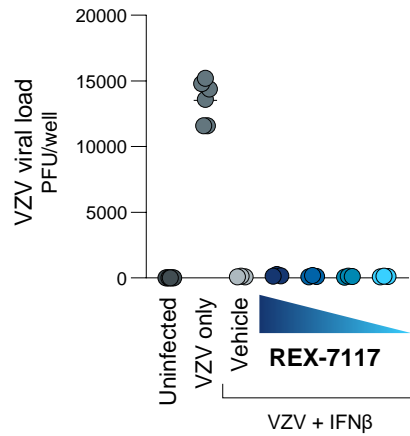
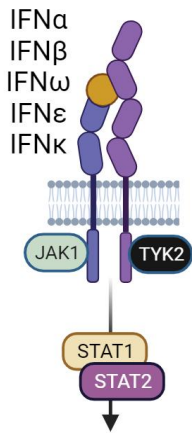


Deucravacitinib 1mg/kg is the estimated clinically relevant dose; Mouse surrogates of Cosentyx®

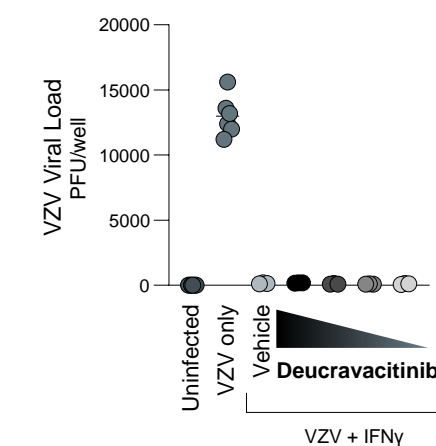
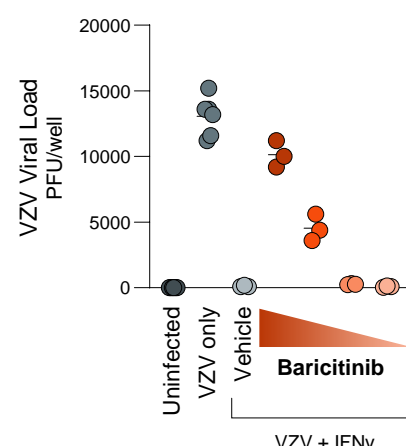
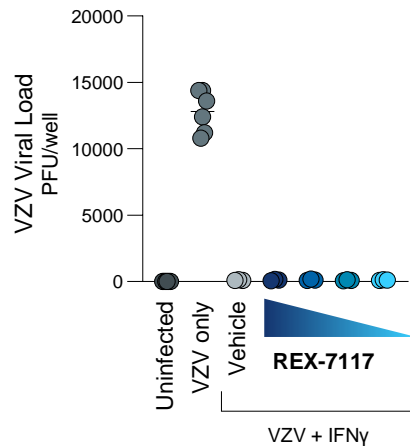
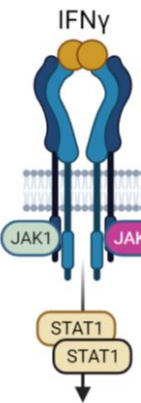
# Selectively STAT3 Inhibitors Do Not Impair Interferon-Mediated Inhibition of Viral Replication Unlike JAK/TYK2 Inhibitors



## Type I IFN $\beta$ : Varicella Zoster Virus (VZV)

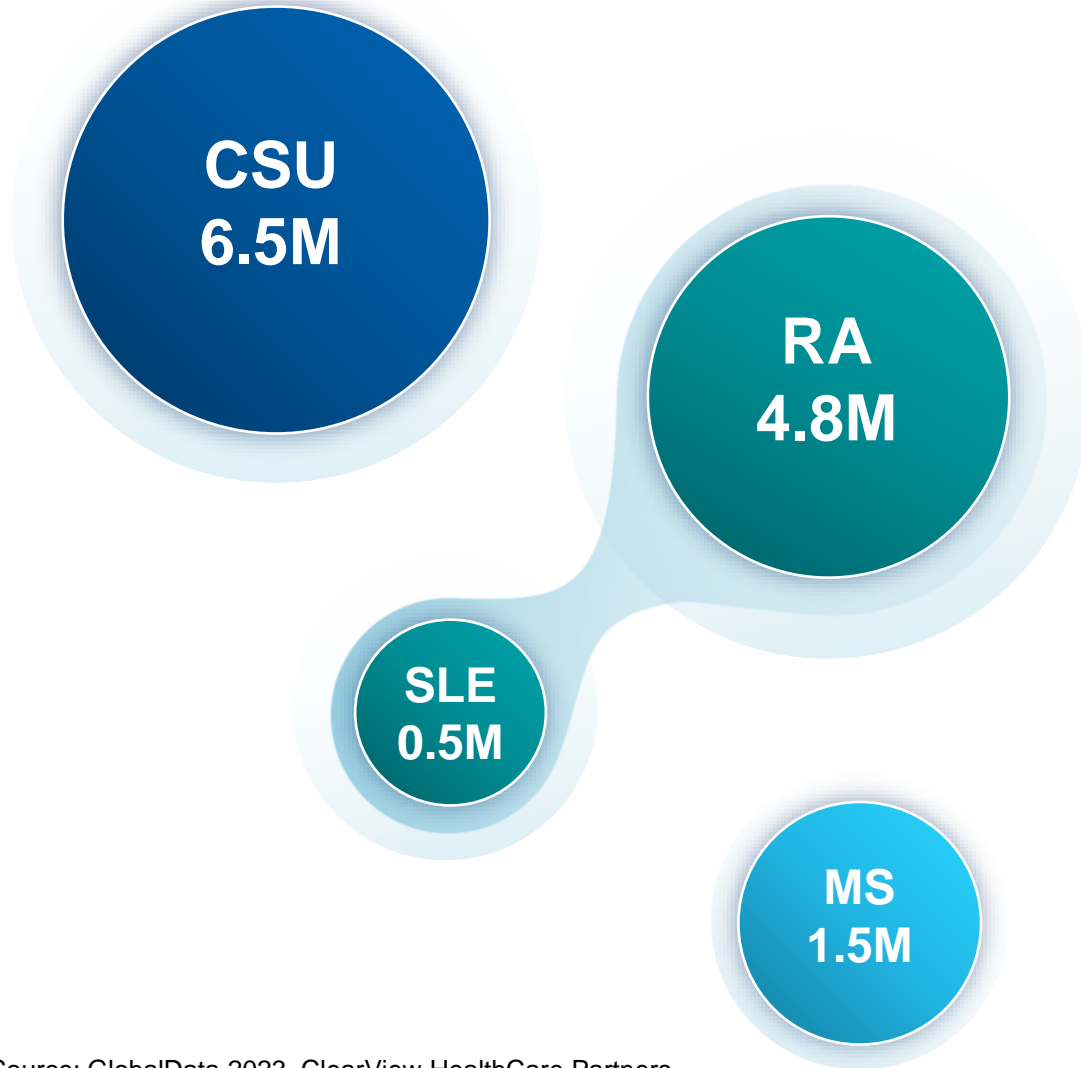


## Type II IFN $\gamma$ : Varicella Zoster Virus (VZV)



**BTK**

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



## >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

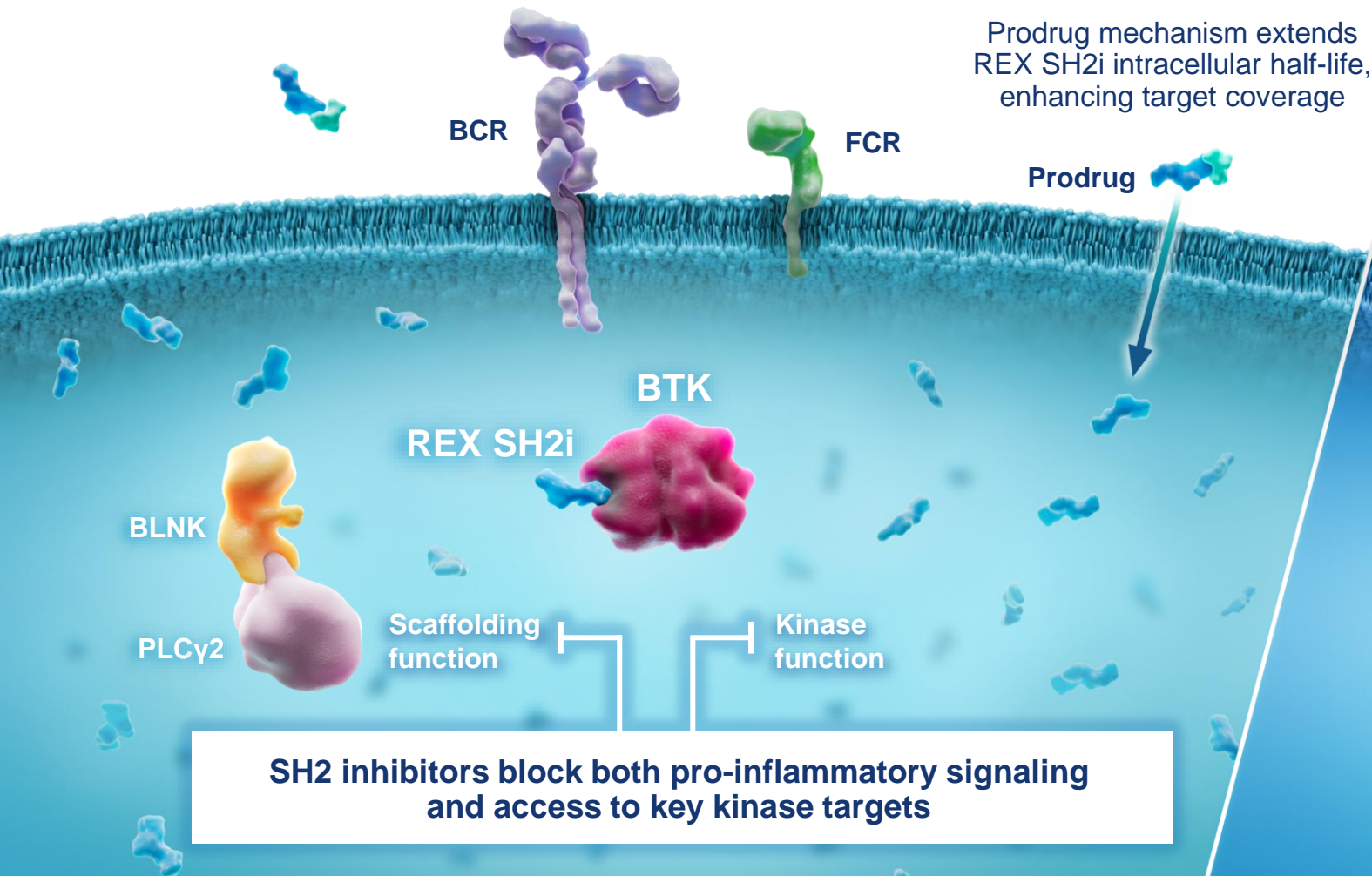
Source: GlobalData 2023, ClearView HealthCare Partners

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

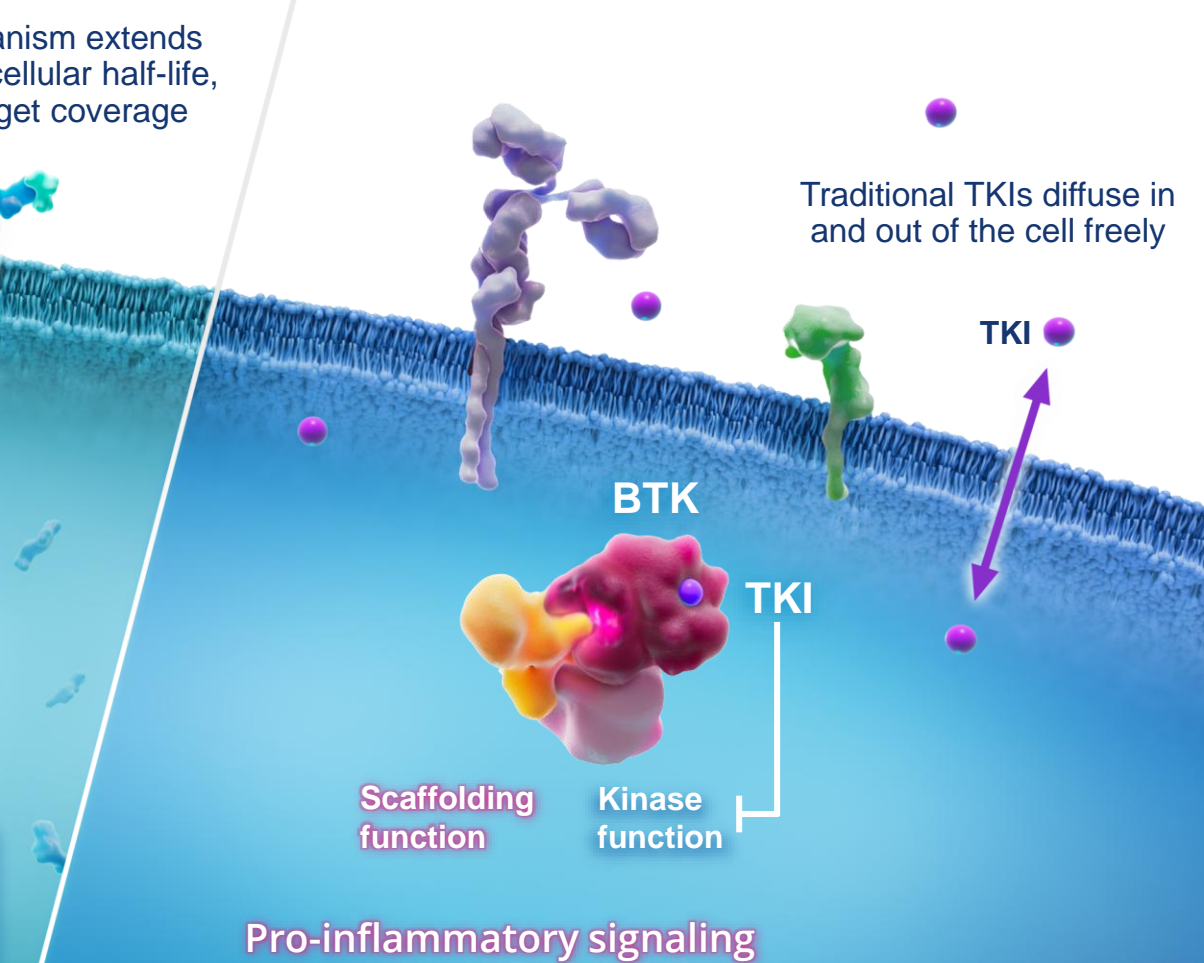
# BTK SH2 Inhibitor is First-In-Class with Differentiated Profile Relative to Traditional TKIs



## Recludix BTK SH2i Prodrugs



## Traditional BTK TKIs



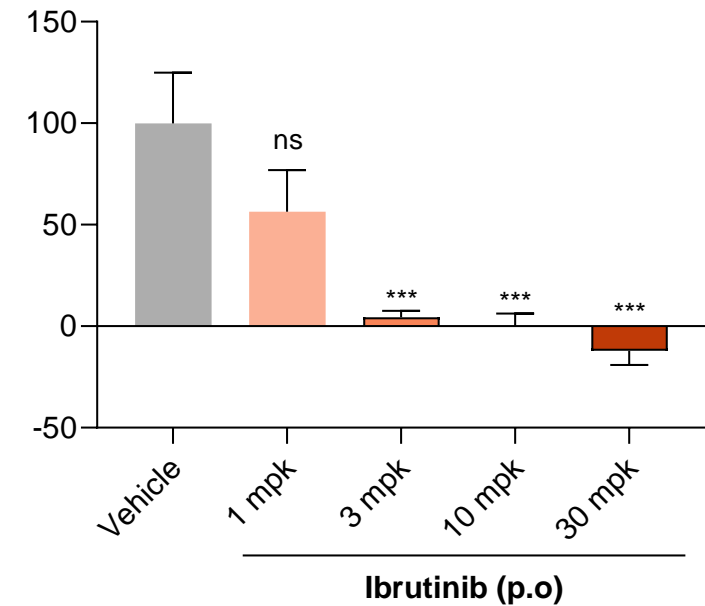
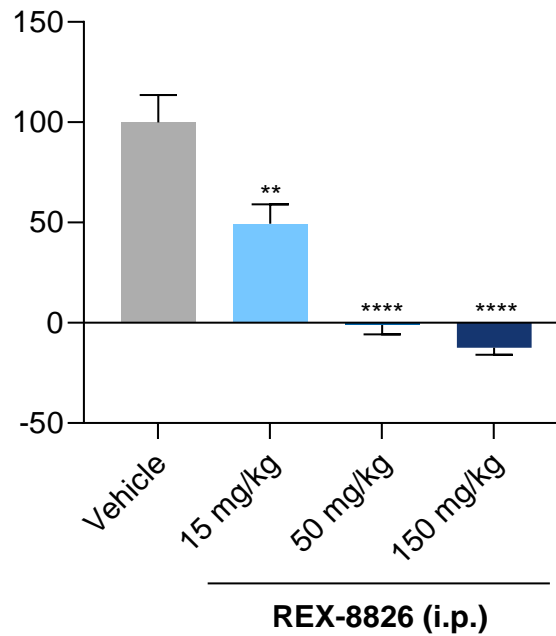
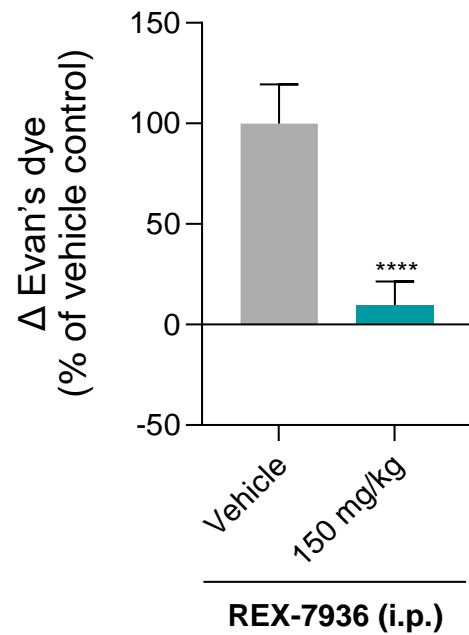
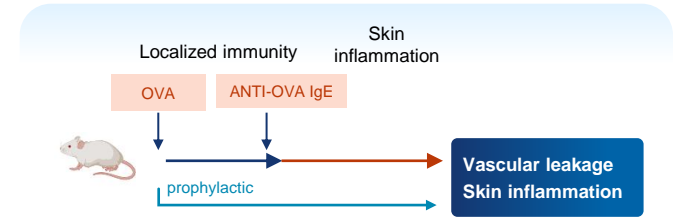


# BTK SH2 Inhibitors Abrogate Mast Cell Activation in In Vivo Model of Chronic Urticaria

BTK SH2 inhibitors demonstrate strong dose-dependent efficacy



## Vascular leakiness (Evan's dye extravasation)



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

# 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
- **Advancing STAT3 and BTK SH2 domain inhibitor programs towards the clinic**



## NEAR TERM MILESTONES

### STAT6

- GLP toxicology studies 1H25
- IND submission 2H25
- Phase 1 study initiation 2H25



**Thank you**

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Unlocking New Therapeutic Possibilities

