



JP Morgan Healthcare Conference

January 15, 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 α 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

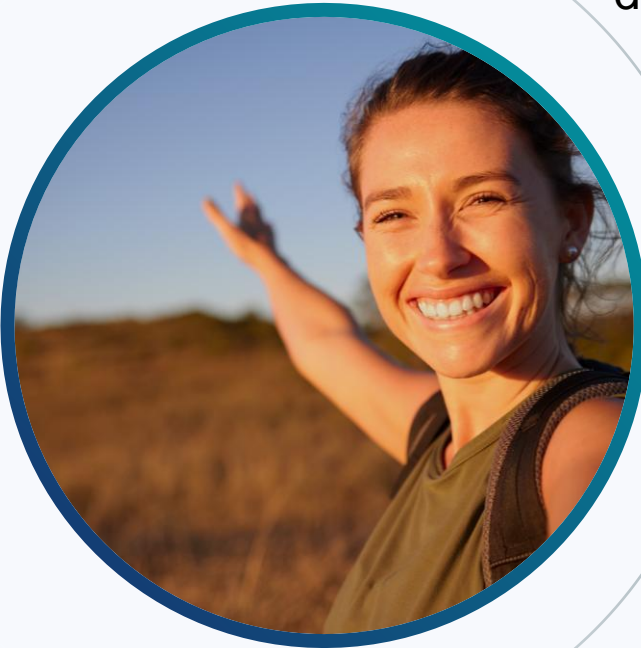
Recludix
Pharma

- 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

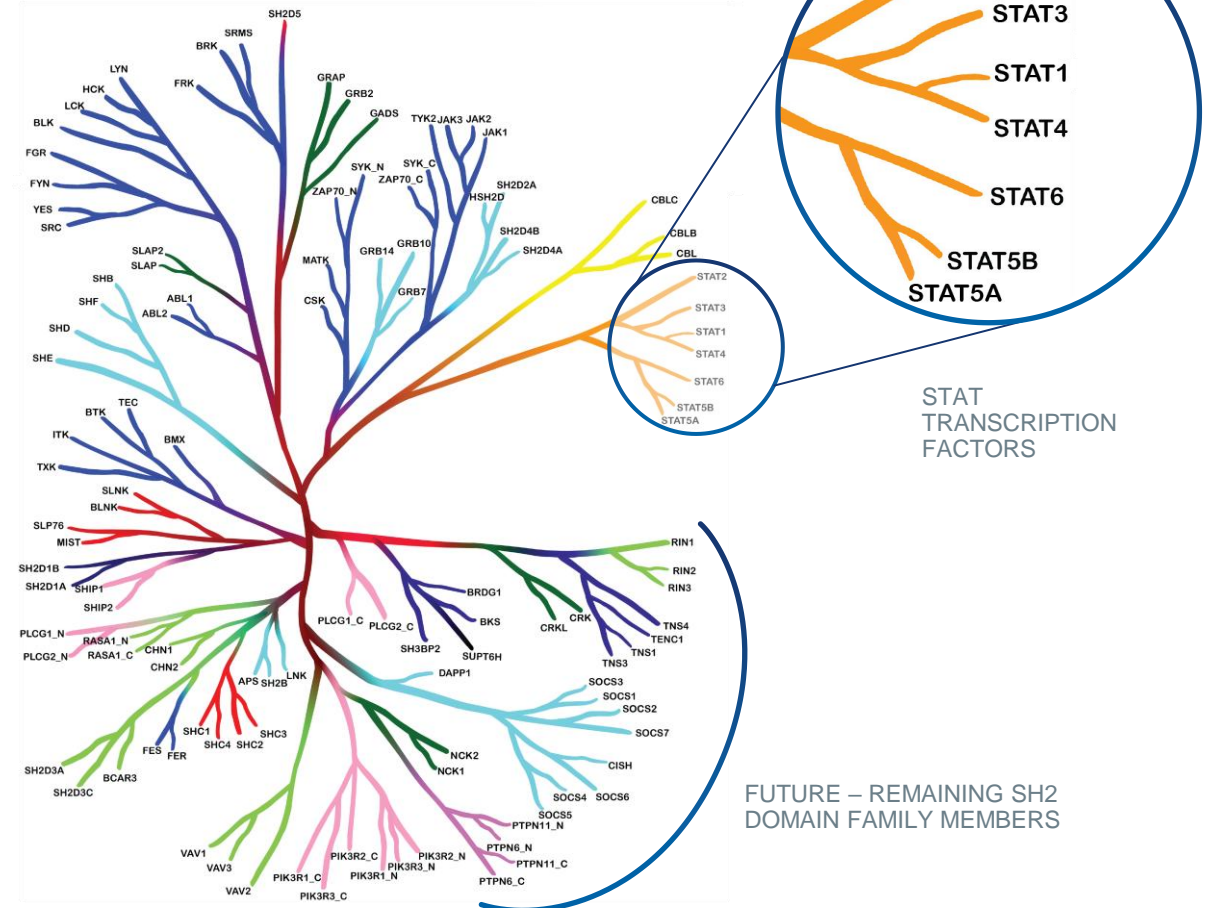
SH2 Domains Have Previously Been Deemed “Undruggable”

Significant opportunity in targeting SH2 domain proteins

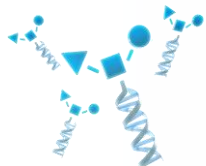
Src Homology 2 (SH2) domains are highly conserved protein domains that have long been recognized as attractive drug targets

- 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

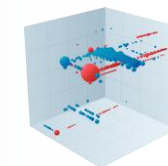


Custom SH2 Domain Targeting DNA-Encoded Libraries

Discovery and SAR DELs | Hundreds of millions of molecules

Proprietary DEL Selection & SAR Analysis

Rapid massively parallel determination of structure-activity relationships



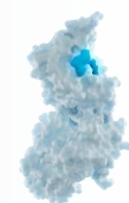
High Quality Lead Compounds

Prodrug Modality Expertise

Drives enhanced target coverage

Structure-Based Design

Proprietary co-crystallography systems



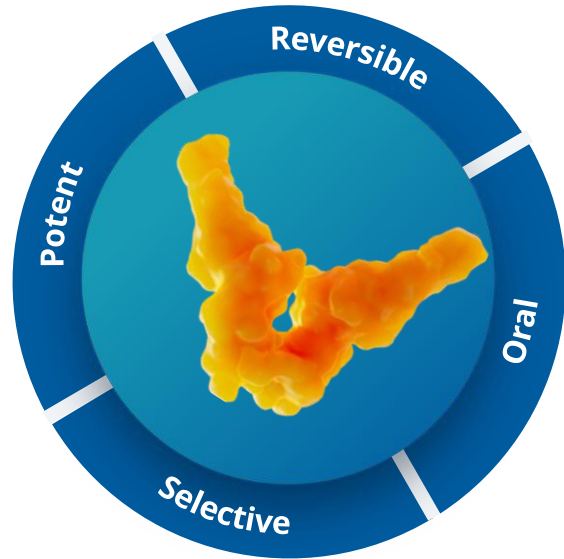
SH2 Domain Screening Tool

Unique panel of SH2 domain assays | Drives selectivity

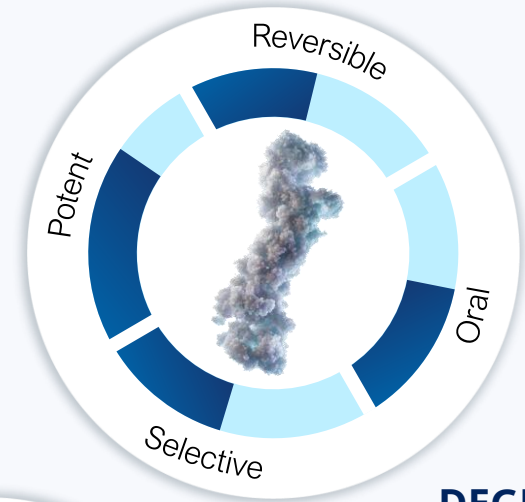
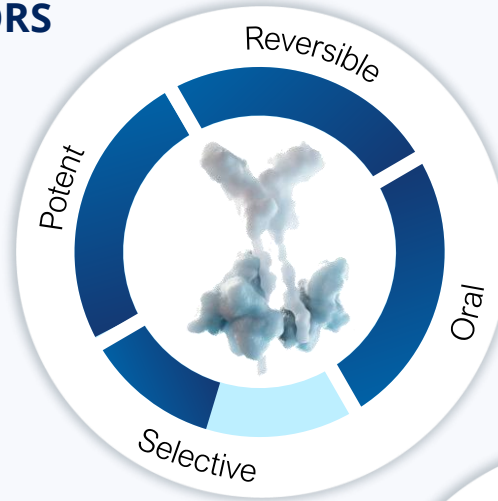
STAT SH2 Domain Inhibition Enables a Best-in-Class Product Profile



Recludix
Pharma

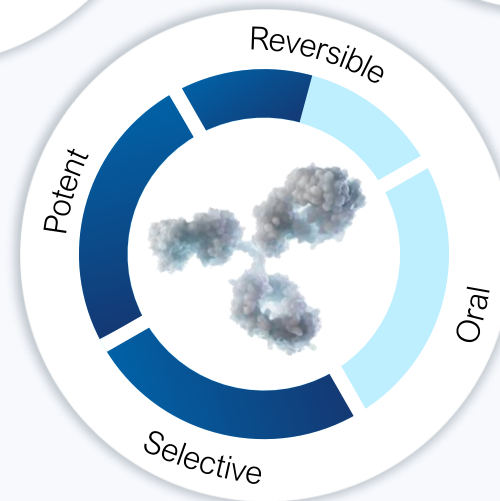


**JAK/TYK2
INHIBITORS**



DEGRADERS

BIOLOGICS

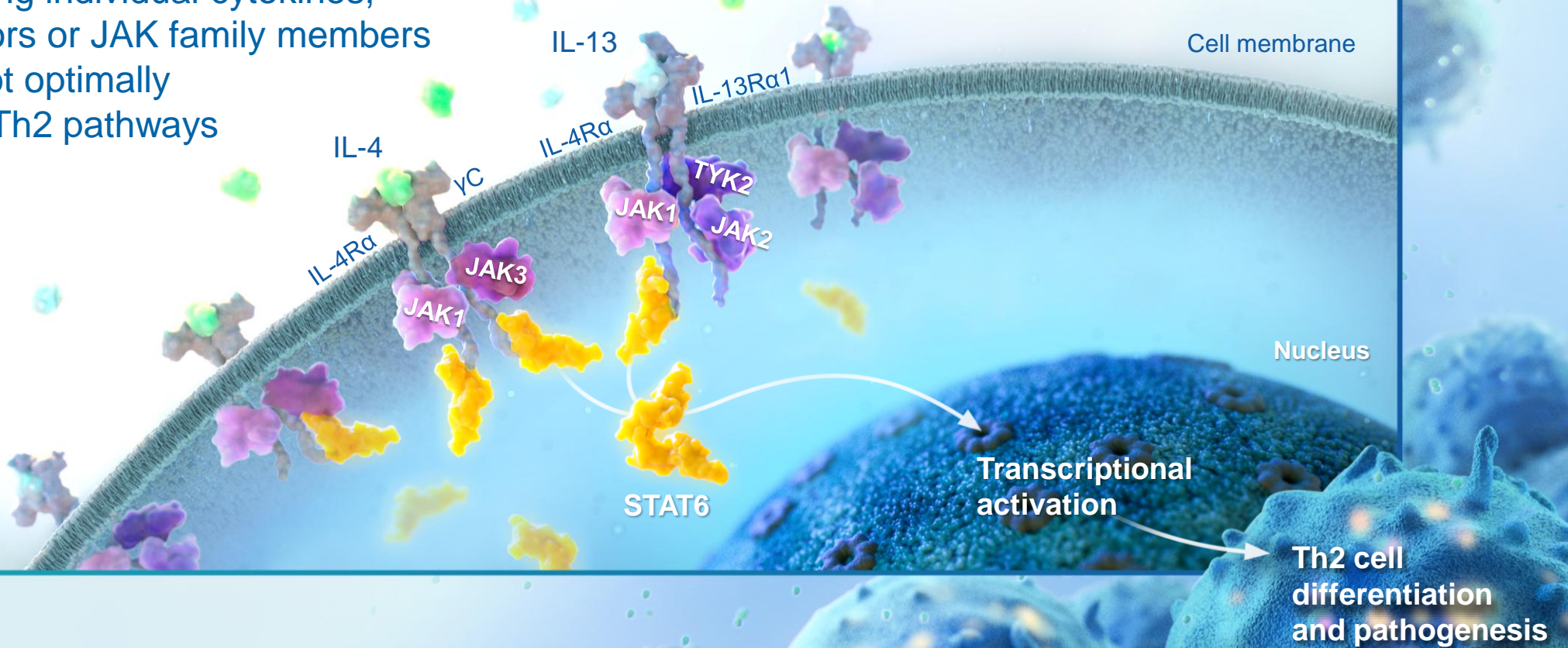


STAT6

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

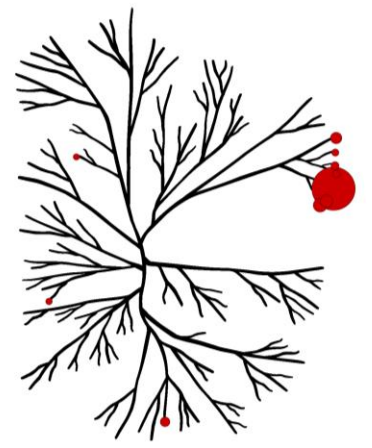
Patient-friendly oral formulation may enable treatment beyond those currently served by injectable agents

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 γ)	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

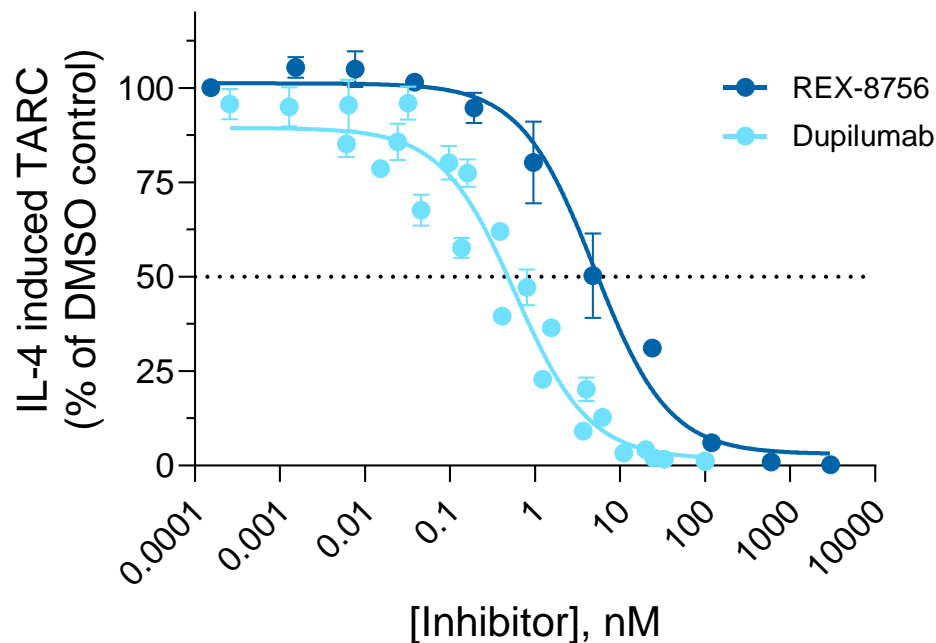
10-30X

<10X

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

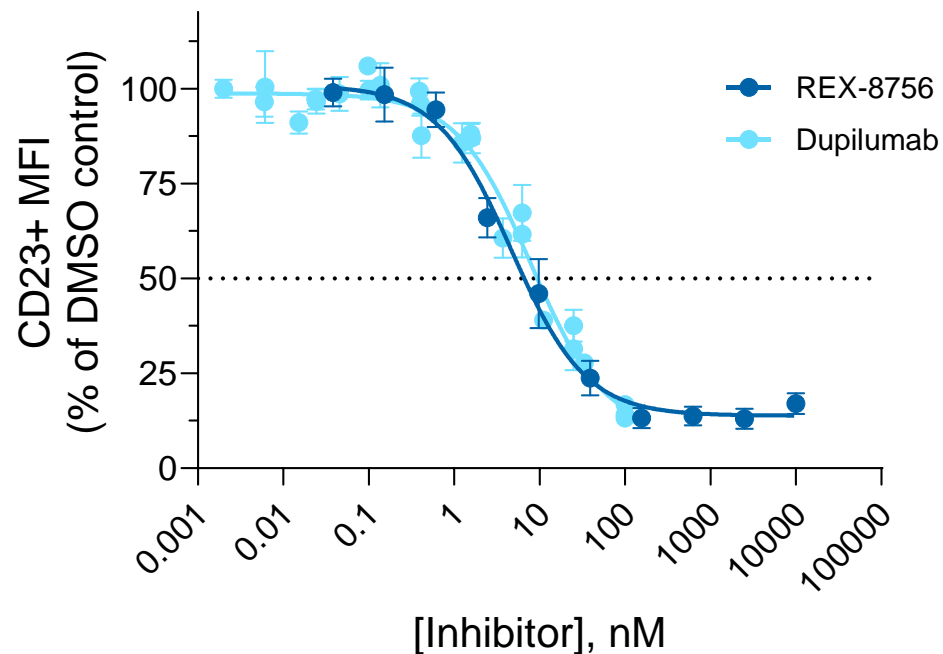


IL-4 induced TARC



	REX-8756	Dupilumab
IC₅₀	6.3 nM	0.8 nM

IL-4 induced CD23 activation



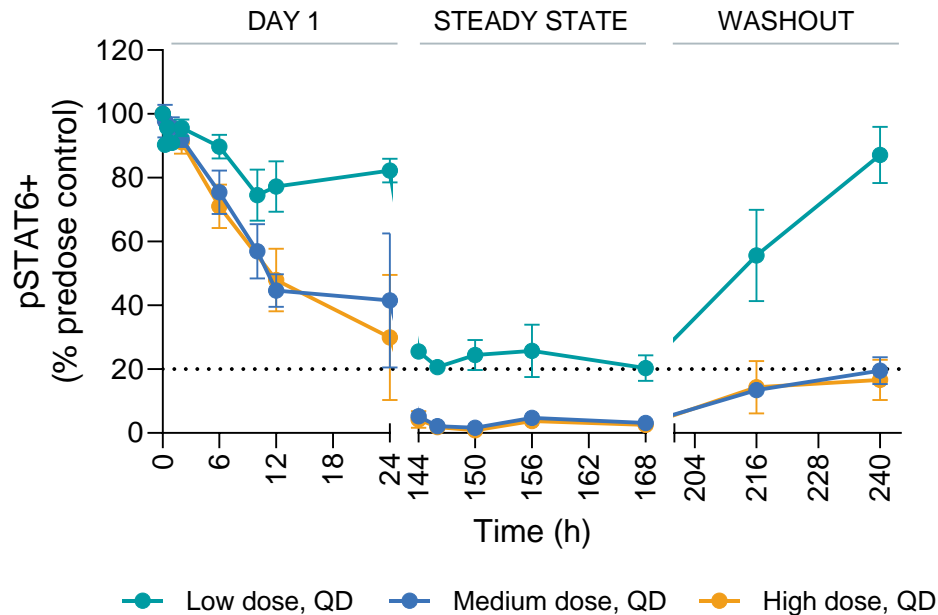
	REX-8756	Dupilumab
IC₅₀	5.1 nM	11 nM

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

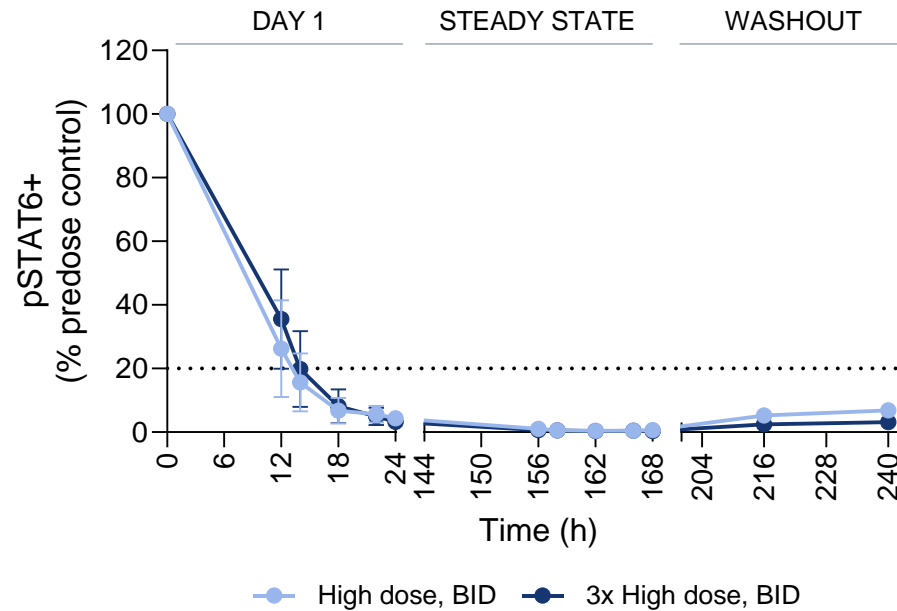


Efficacious dose at >80% pSTAT6 PD modulation

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

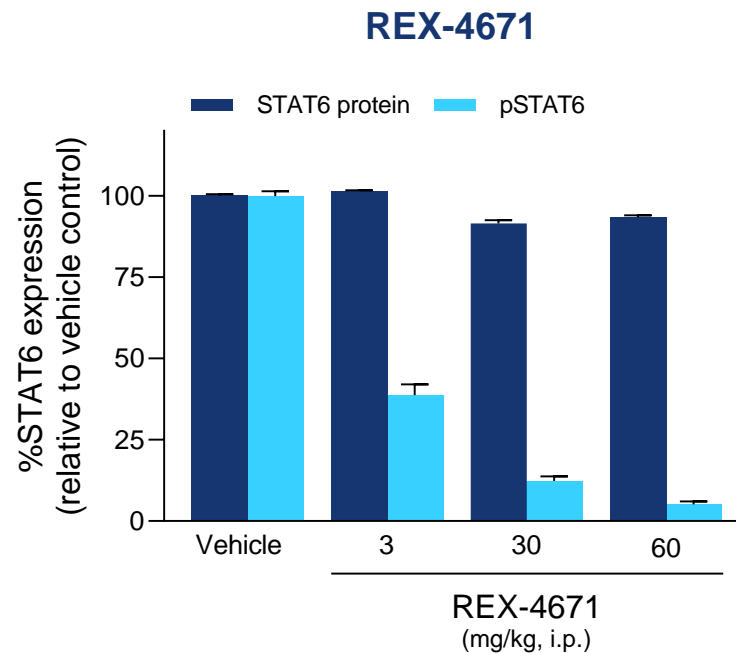
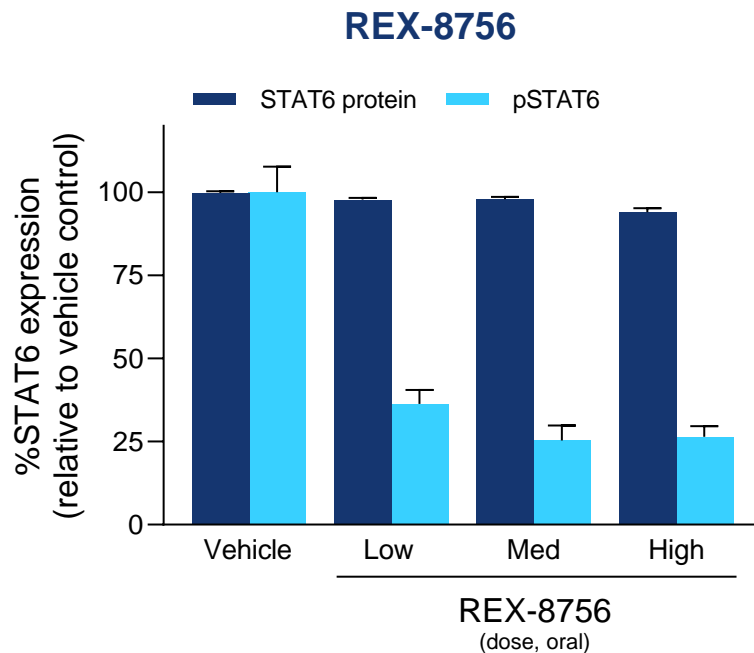
- Highly selective pSTAT6 inhibition, no off-target pSTAT1 or pSTAT3 impact observed
- Well tolerated at all dose levels

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

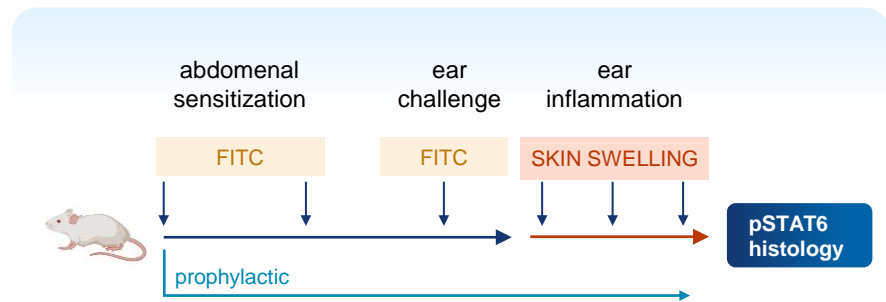


Single dose PK/PD study

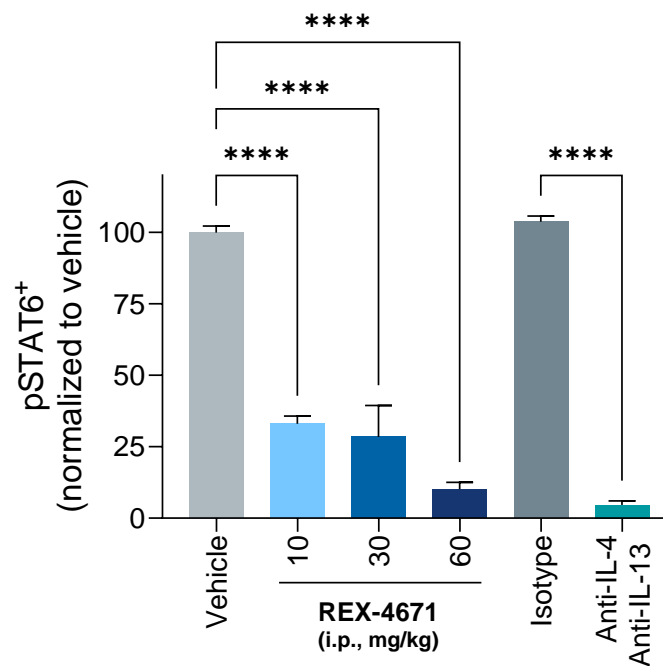
- Samples collected 4hr post single dose
- Whole blood and splenocytes ex vivo stimulated with IL-4 to induce STAT6 pathway activation
- Total STAT6 and pSTAT6 quantified by flow cytometry

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

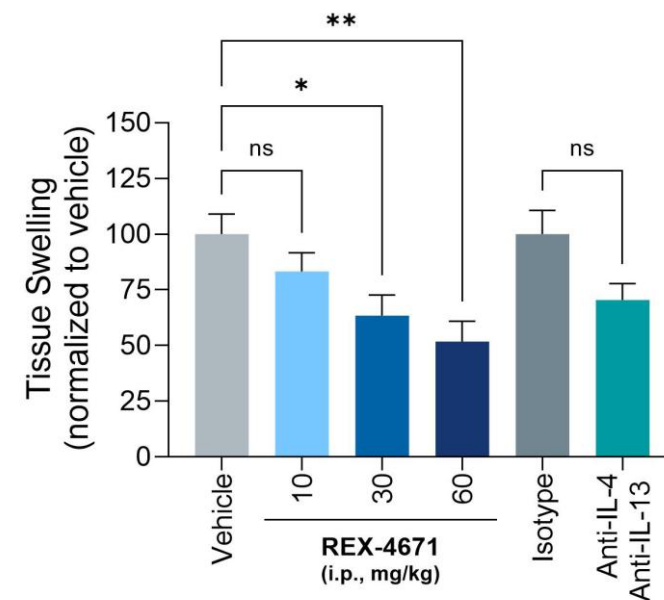
- REX-4671 dose dependently inhibits pSTAT6 and significantly reduced skin inflammation in chemical-induced dermatitis model
- Comparable in vivo efficacy to the combination of anti-IL-4/13 surrogate antibodies



Spleen pSTAT6 inhibition



Skin inflammation

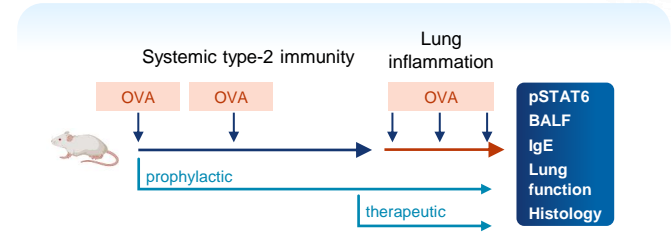


*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

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



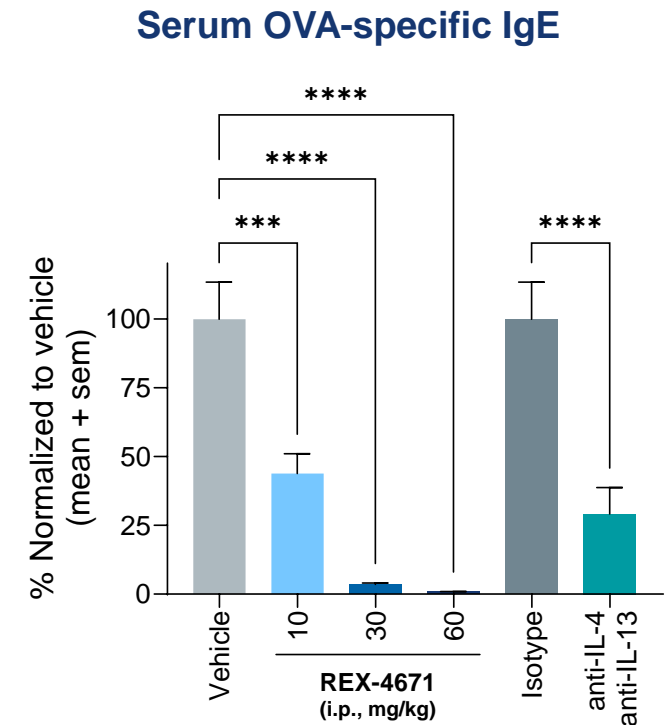
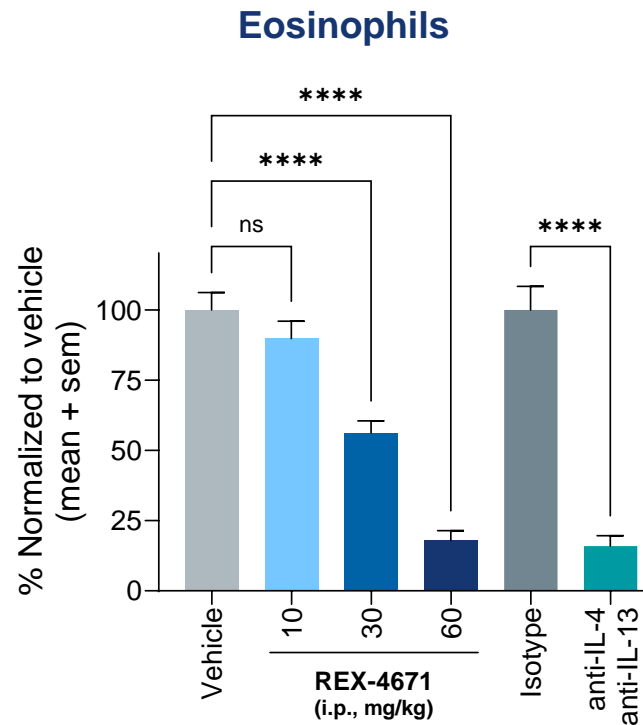
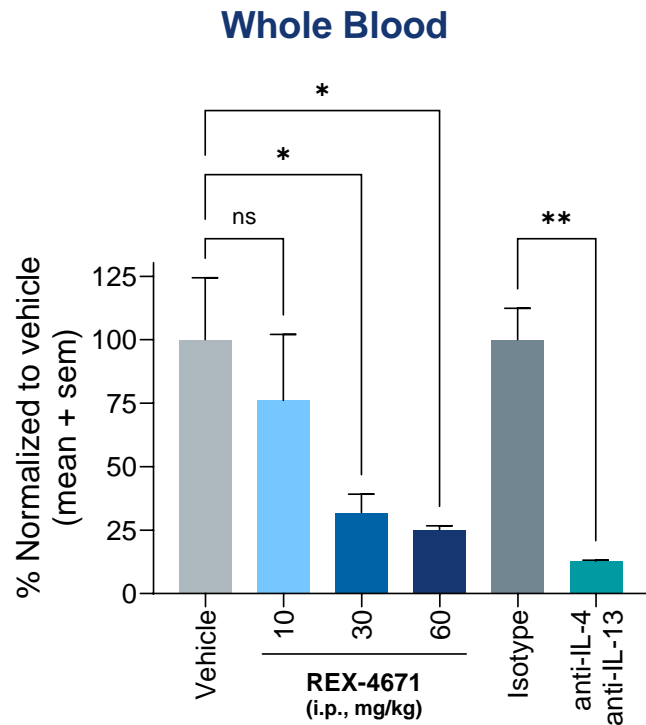
- REX-4671 demonstrates comparable efficacy to combined anti-IL-4/13 rodent surrogate antibodies



pSTAT6 inhibition

Lung immune cell infiltration

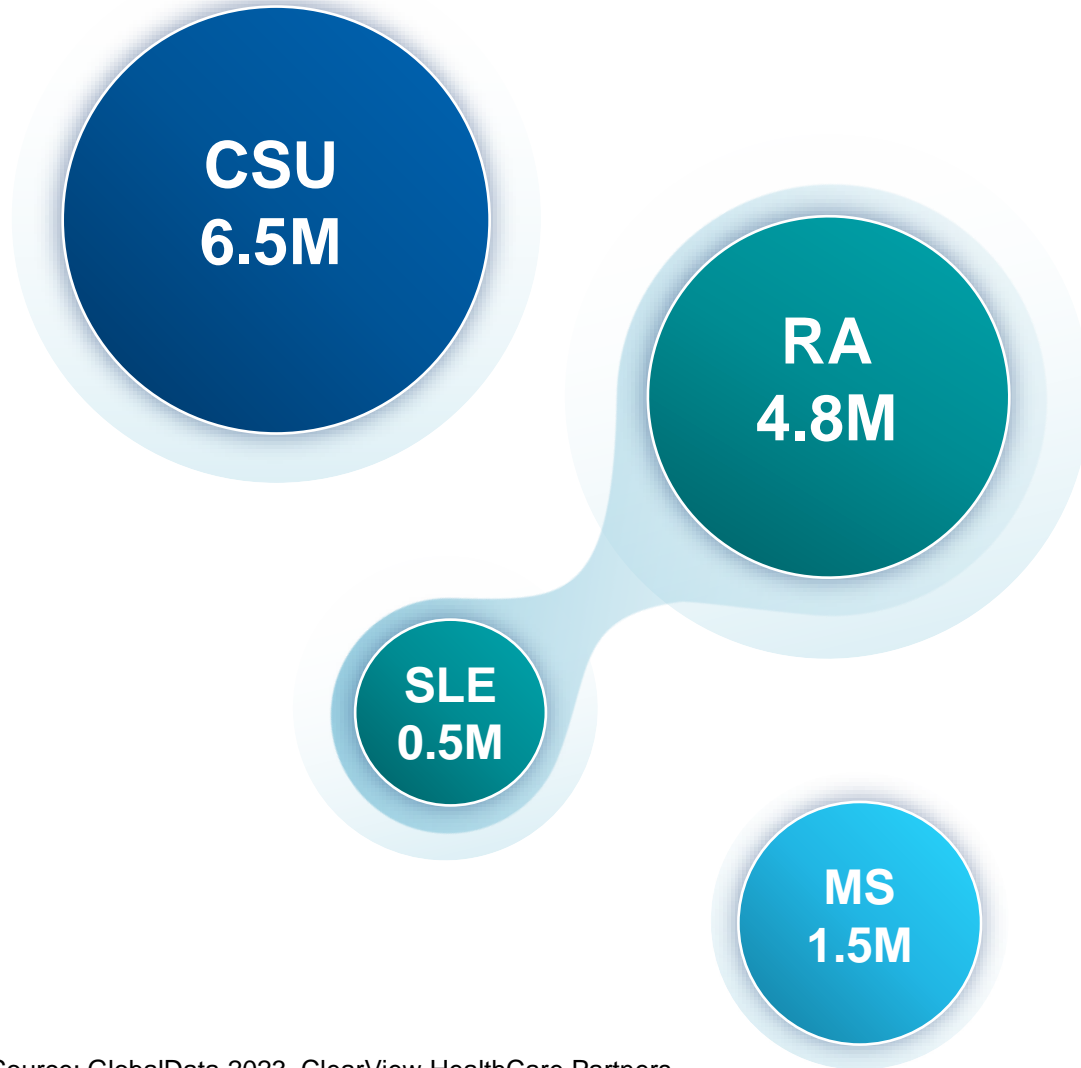
Humoral immunity



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

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

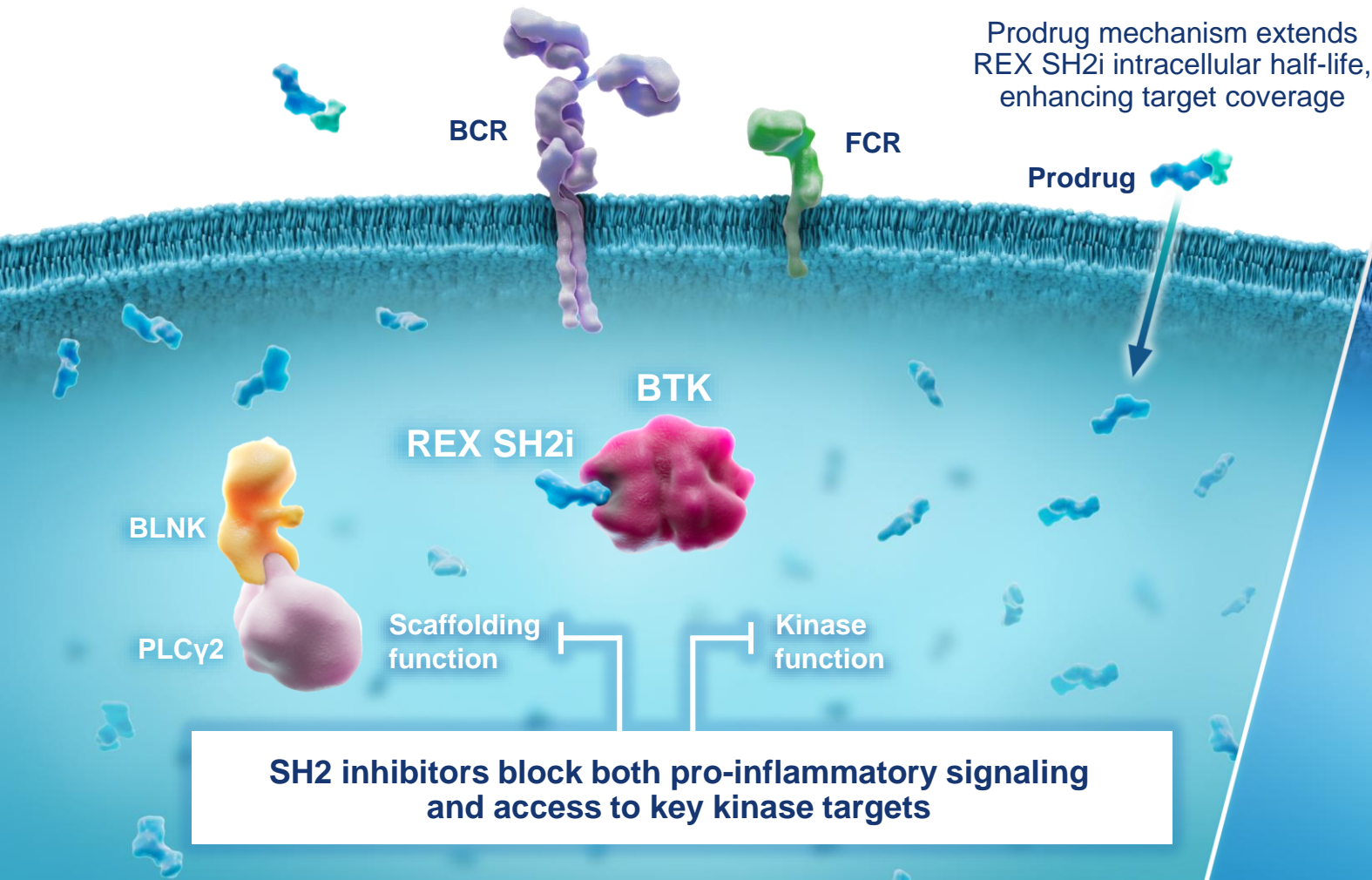
Source: GlobalData 2023, ClearView HealthCare Partners

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

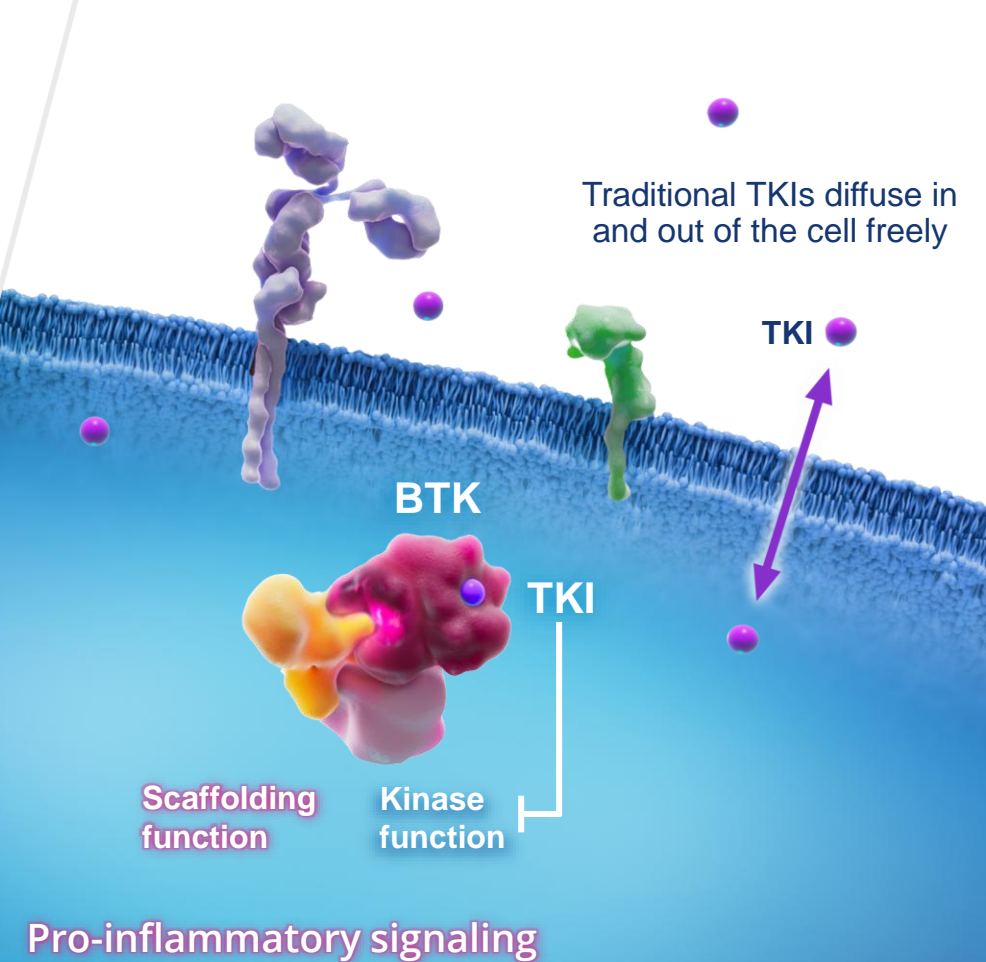
BTK SH2 Inhibitor is First-In-Class with Differentiated Profile Relative to Traditional TKIs



Recludix BTK SH2i Prodrugs



Traditional BTK TKIs

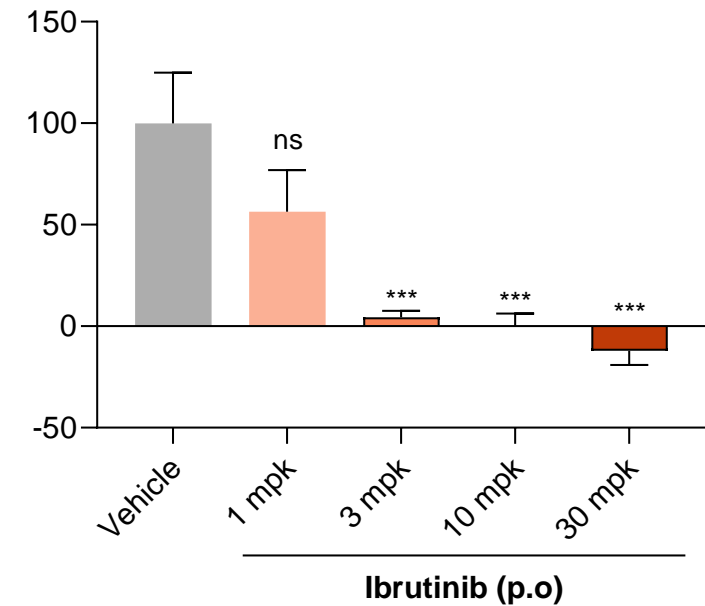
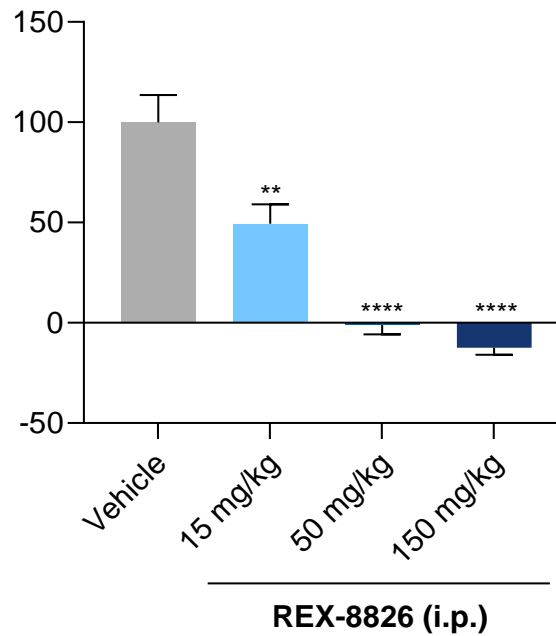
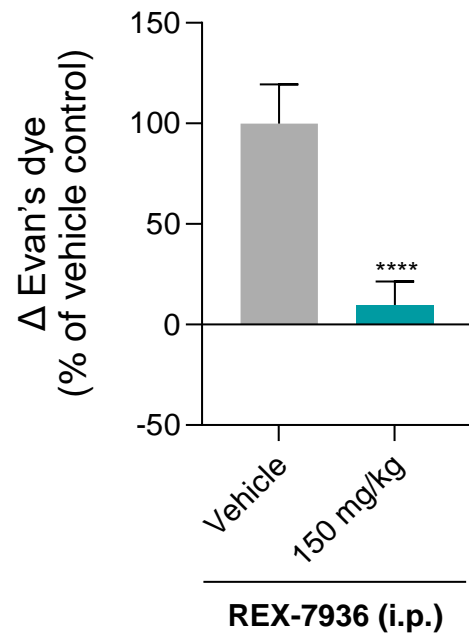
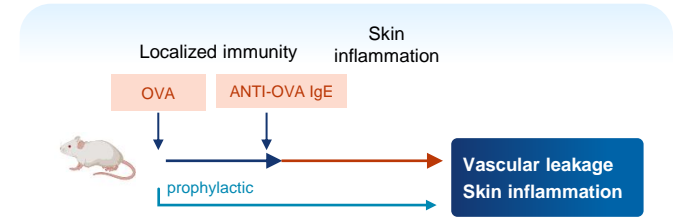


BTK SH2 Inhibitors Abrogate Mast Cell Activation in In Vivo Model of Chronic Urticaria

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

www.recludixpharma.com

info@recludix.com

bd@recludix.com

Unlocking New Therapeutic Possibilities

