JP Morgan Healthcare Conference

January 15, 2025

Rĕclūdo (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-4Rα 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

Seagen GSK

Adcetris®, Tukysa®, Padcev®, Tivdak®

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

Lilly AMGEN biogen idec MERCK

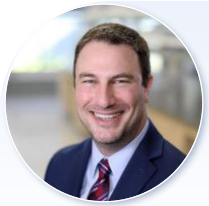
Rituxan®, Tecfidera®, Siliq®, Taltz®, Olumiant®, Omvoh®, Ebglyss®

Matt Caldemeyer, MBA
CBO

EVEREST MEDICINES AMBRX ARRAY BIOPHARMA
AMGEN Lilly

Catherine Bovenizer, C.P.A
SVP, Finance

RENOVA THERAPEUTICS APRICUS BIOSCIENCES ambit BIOSCIENCES
senomyx LIGAND PHARMACEUTICALS GeneFormatics



Brian Hodous, Ph.D.
SVP, Chemistry

ACCENT THERAPEUTICS blueprint MEDICINES MERCK SERONO AMGEN MIT

Ayvakit™

Daniel Treiber, Ph.D.
SVP, Discovery Technology

eurofins Discoverx ambit BIOSCIENCES MIT

Vanflyta®

Paul Smith, Ph.D.
SVP, Biology

CONNECT BIOPHARMA Incyte MERCK SERONO NOVARTIS

Opzelura™, Gilenya ®, Kesimpta®

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

blueprint MEDICINES AnaptysBio ambit BIOSCIENCES AMGEN
Kinetix Novartis/CIBA-GEIGY

Gleevec®
Lasker-DeBakey Award, Japan Prize

$102M Series A

NEA ACCESS BIOTECHNOLOGY Westlake BioPartners **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

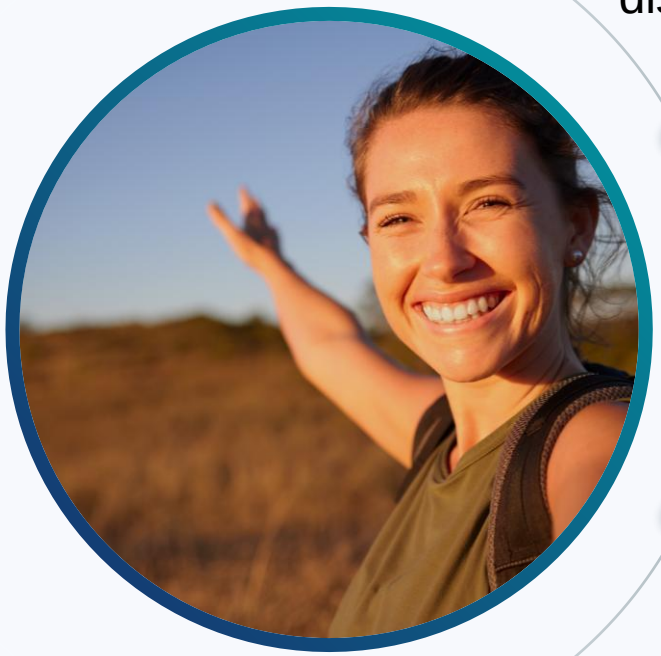
Recludix Pharma

- 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

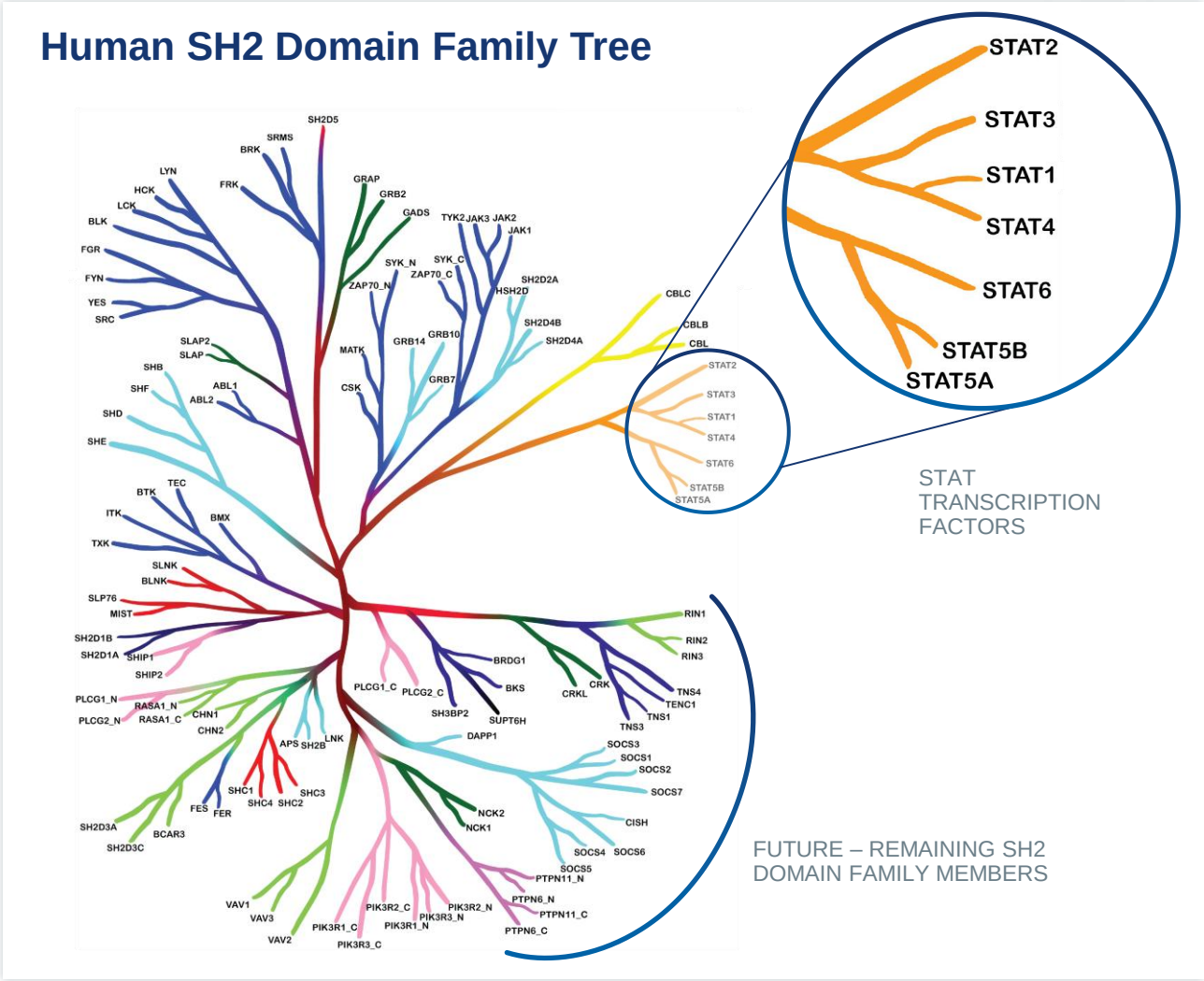
Source: GBD IMID Collaborators. eClinicalMedicine, The Lancet Discovery Science. 2023. ClearView HealthCare Partners

SH2 Domains Have Previously Been Deemed “Undruggable”

Significant opportunity in targeting SH2 domain proteins

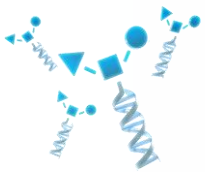
Src Homology 2 (SH2) domains are highly conserved protein domains that have long been recognized as attractive drug targets

- 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



Molecular Cell (2006) vol. 22, p.851

Recludix Platform: Integrated Proprietary Technologies & New Chemical Approaches

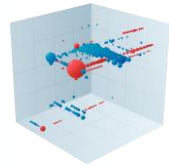


Custom SH2 Domain Targeting DNA-Encoded Libraries

Discovery and SAR DELs | Hundreds of millions of molecules

Proprietary DEL Selection & SAR Analysis

Rapid massively parallel determination of structure-activity relationships



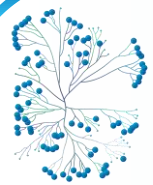
High Quality Lead Compounds

Prodrug Modality Expertise

Drives enhanced target coverage

Structure-Based Design

Proprietary co-crystallography systems

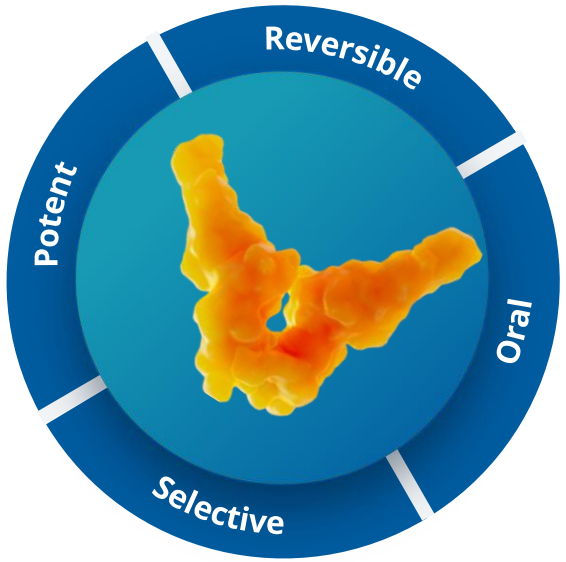


SH2 Domain Screening Tool

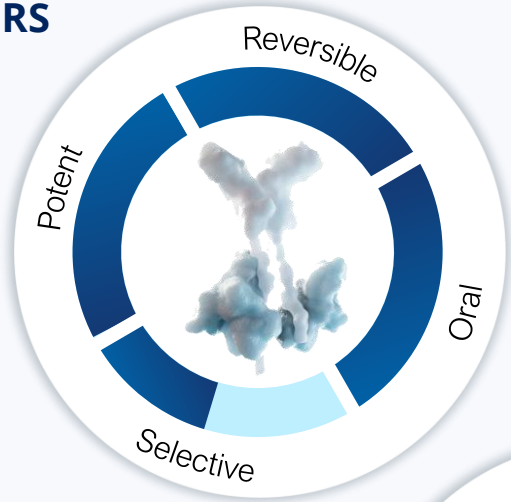
Unique panel of SH2 domain assays | Drives selectivity

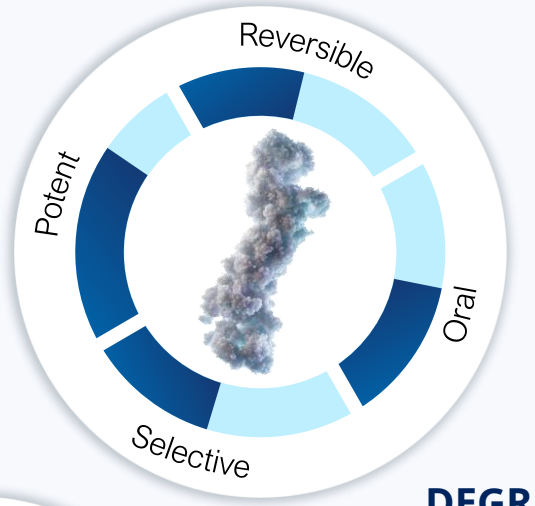
STAT SH2 Domain Inhibition Enables a Best-in-Class Product Profile

Recludix Pharma



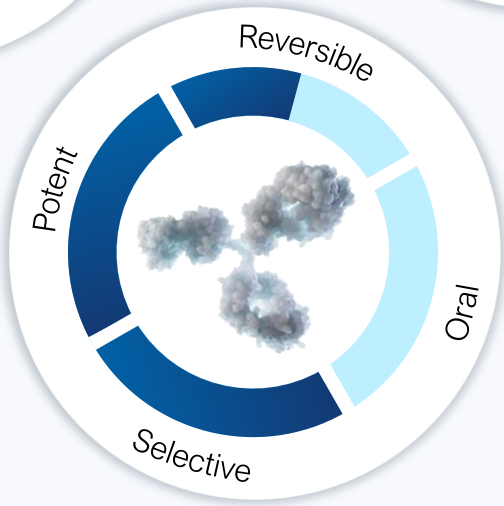
JAK/TYK2 INHIBITORS





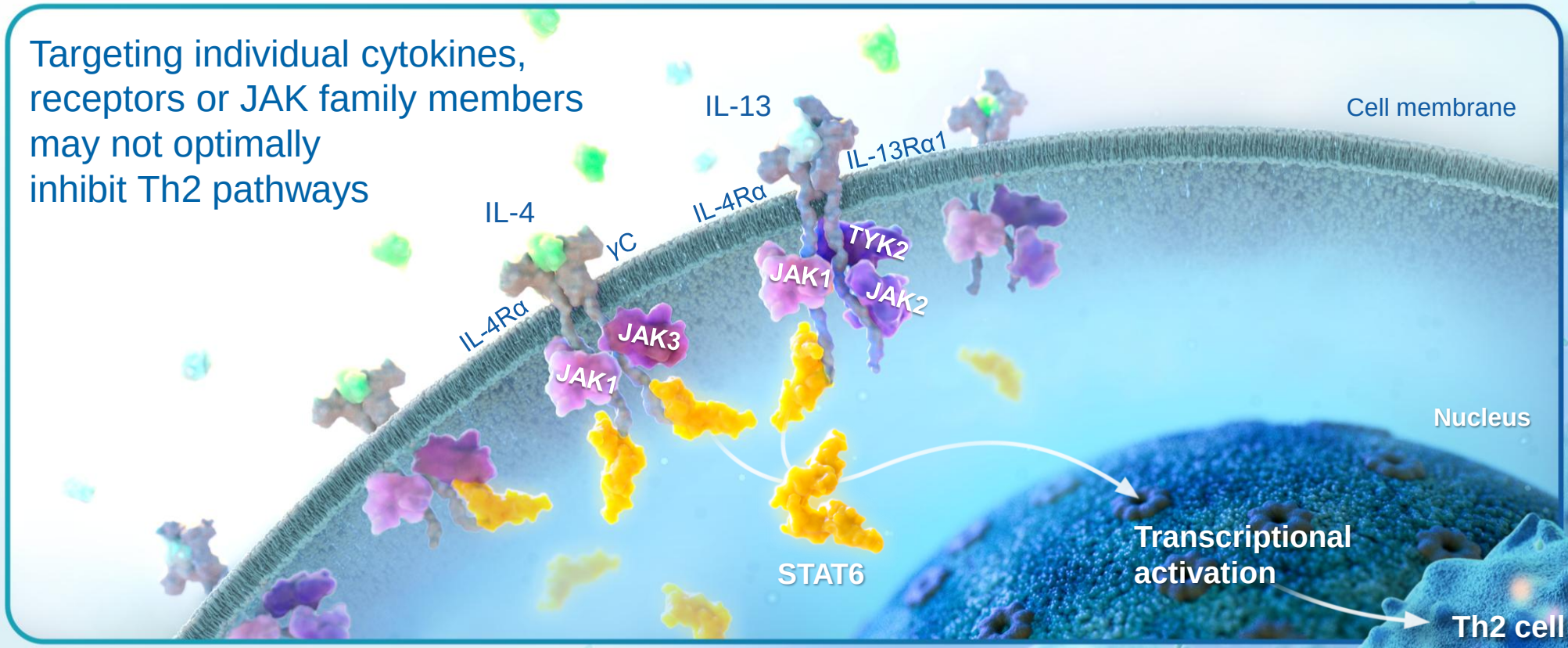
DEGRADERS

BIOLOGICS

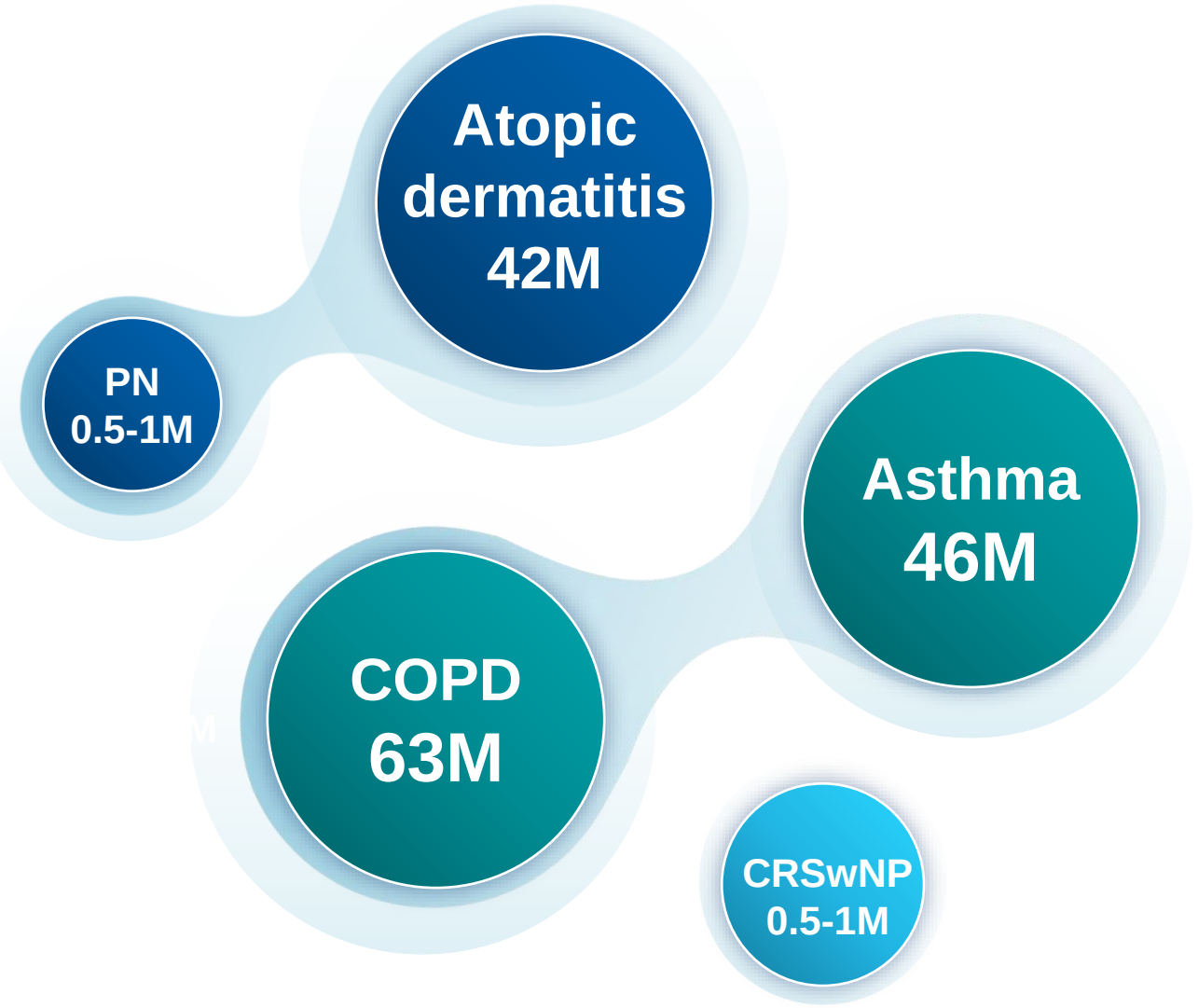


STAT6

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



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



>150M

TOTAL PATIENT IMPACT

LARGE POPULATIONS

Targeting broad, established patient populations with persistent unmet needs

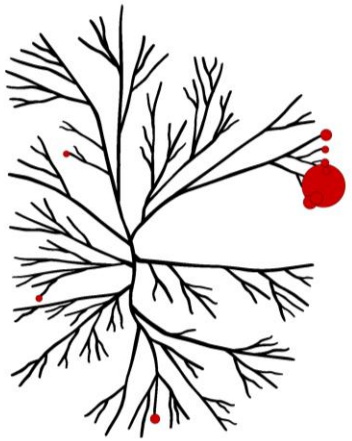
DIFFERENTIATED PRODUCT

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

Source: GlobalData 2023, ClearView HealthCare Partners

COPD: Chronic obstructive pulmonary disease, PN: Prurigo nodularis, CRSwNP: Chronic rhinosinusitis with nasal polyps

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

	Biochemical potency (SH2scan K_D)	Cellular potency (pSTAT6 IC_{50} in human PBMCs)	Biochemical STAT family selectivity	Cellular selectivity (PBMCs)	SH2 domain selectivity
REX-8756	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

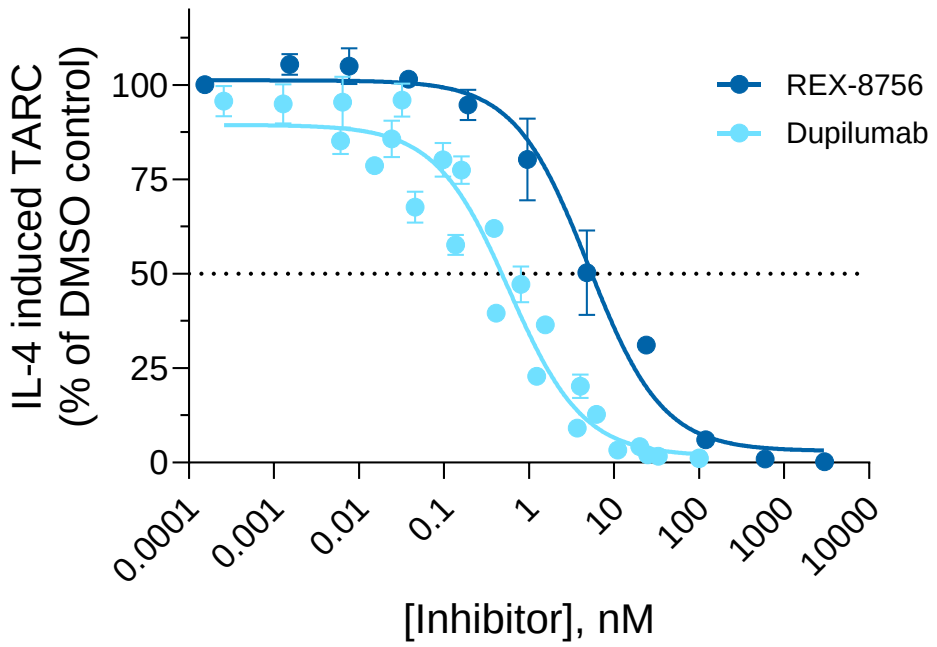
		T CELL FUNCTION				HEMATOLOGIC HOMEOSTASIS	
		General adaptive immune response	**Defense against viruses and bacteria**	**Defense against extracellular pathogens**	**Defense against parasites and mediation of antibody responses**	**Erythropoiesis**	**Thrombopoiesis**
		T Cell Activation (CD25)	Th1 Cell Function (IFNγ)	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**

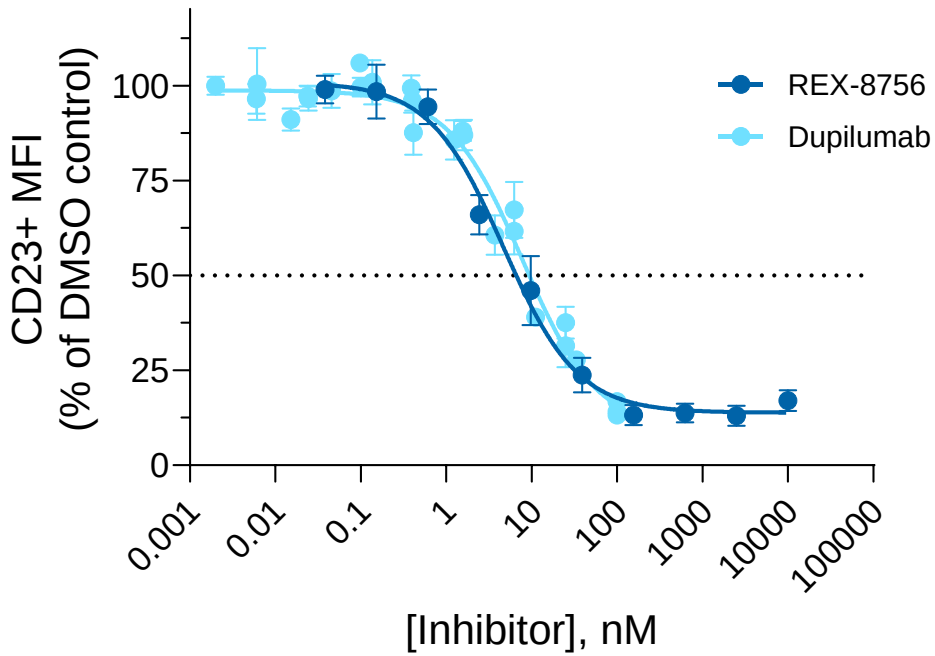
STAT6 Inhibitor Fully Inhibits IL-4/13 Stimulated STAT6-Driven Biomarkers in Human PMBCs

IL-4 induced TARC



	REX-8756	Dupilumab
IC_{50}	6.3 nM	0.8 nM

IL-4 induced CD23 activation



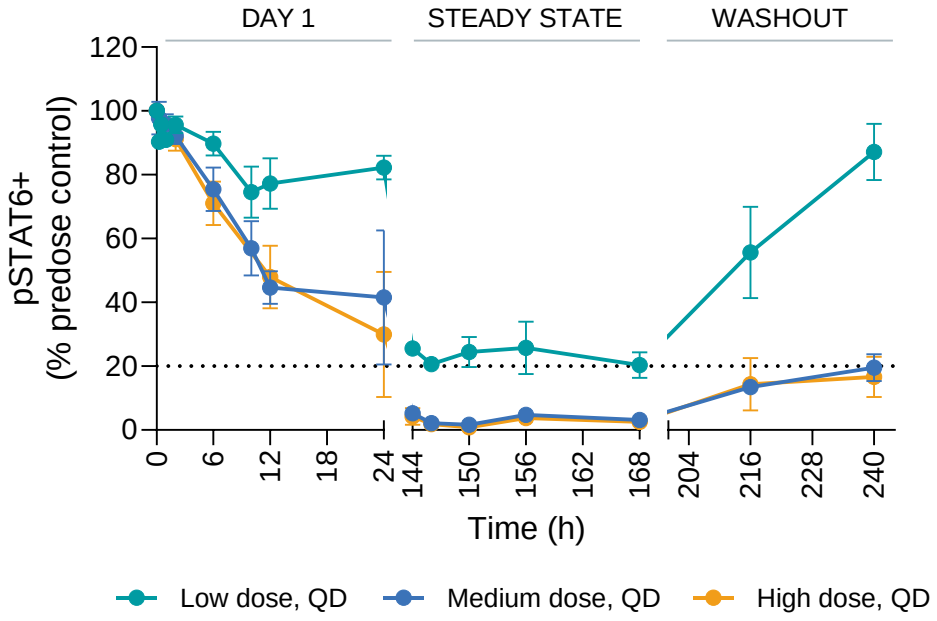
	REX-8756	Dupilumab
IC_{50}	5.1 nM	11 nM

Recludix Pharma data on file, April 2022

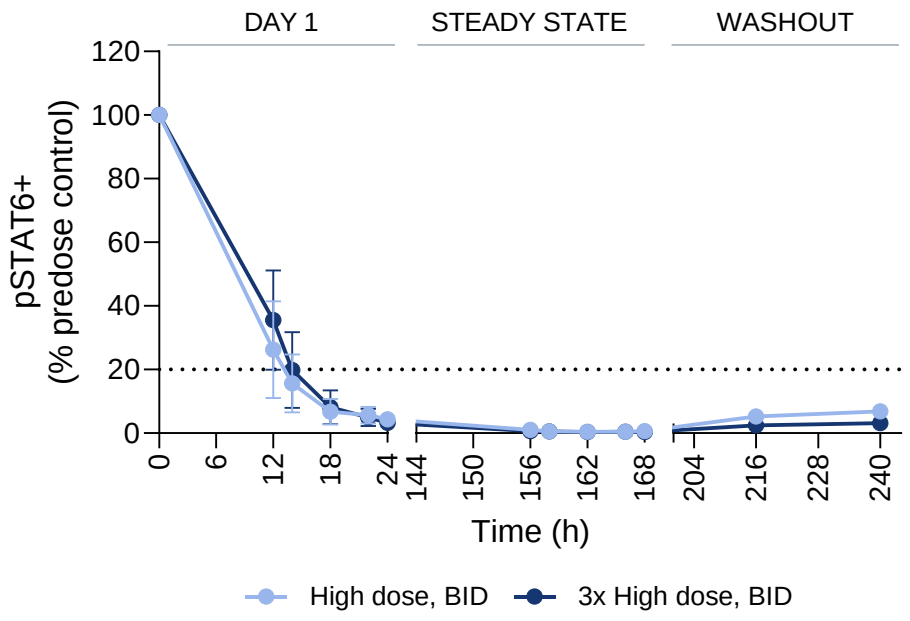
REX-8756 Achieves Complete pSTAT6 Inhibition with Once Daily Dosing and is Well Tolerated in Dog 7-Day Study

Efficacious dose at >80% pSTAT6 PD modulation

Oral, QD dosing



Oral, BID dosing



Multi-day PK/PD & Hazard ID study

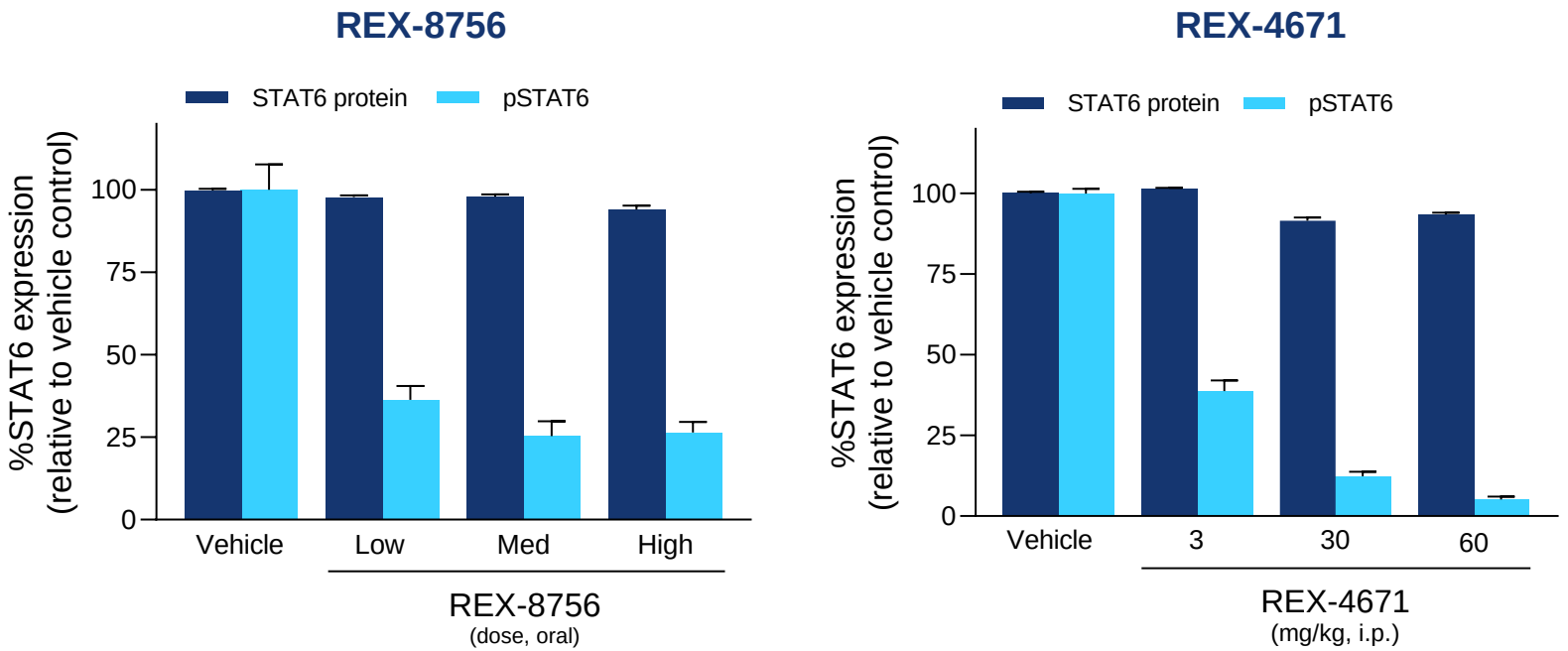
- Once or twice daily oral administration
  - Day 1
  - Day 7: Steady State
  - Day 9-10: Washout
- Clinical observations, hematology, serum chemistry, coagulation

- 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

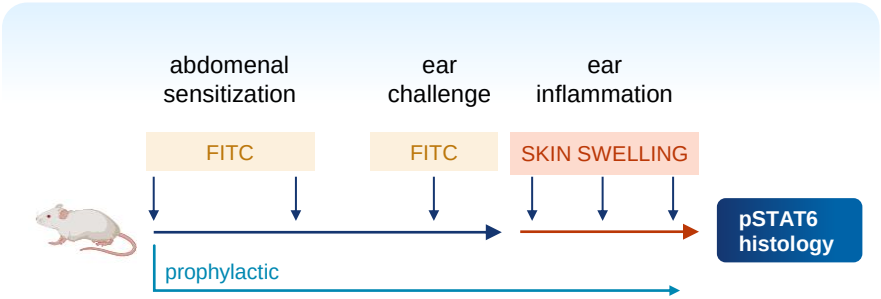


Single dose PK/PD study

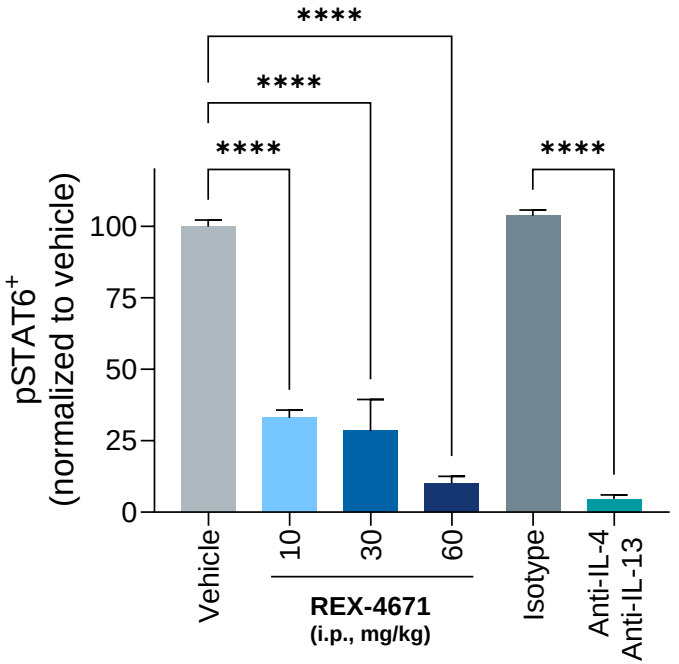
- Samples collected 4hr post single dose
- Whole blood and splenocytes ex vivo stimulated with IL-4 to induce STAT6 pathway activation
- Total STAT6 and pSTAT6 quantified by flow cytometry

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

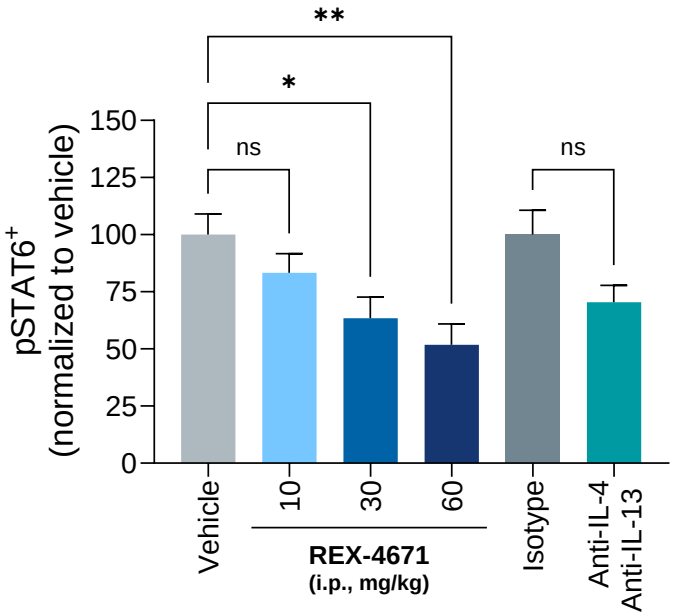
- REX-4671 dose dependently inhibits pSTAT6 and significantly reduced skin inflammation in chemical-induced dermatitis model
- Comparable in vivo efficacy to the combination of anti-IL-4/13 surrogate antibodies



Spleen pSTAT6 inhibition



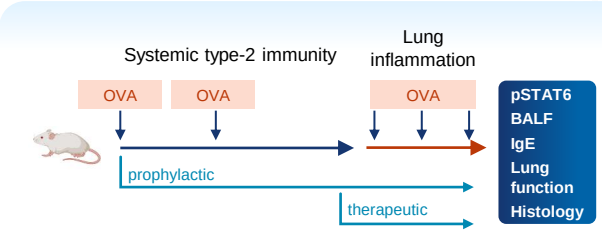
Skin inflammation



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

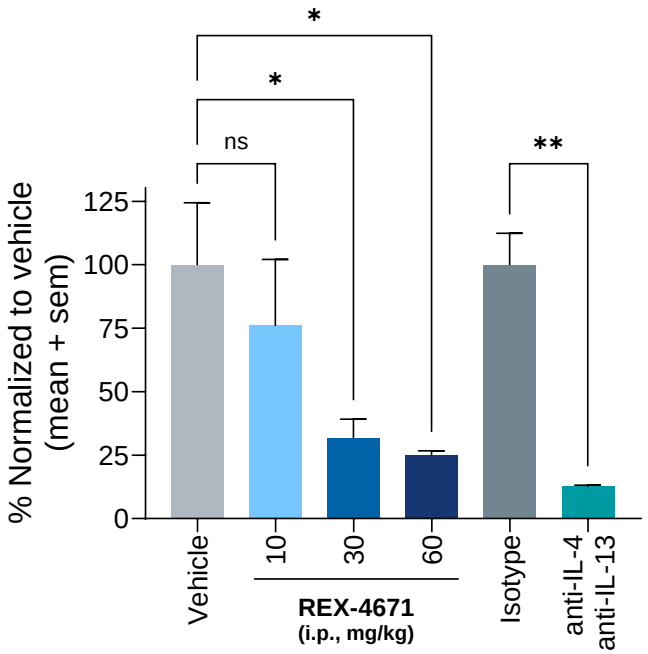
Prophylactic REX-4671 Demonstrates Comparable Efficacy to Combined Anti-IL-4/13 Biologics in OVA-Asthma Model

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



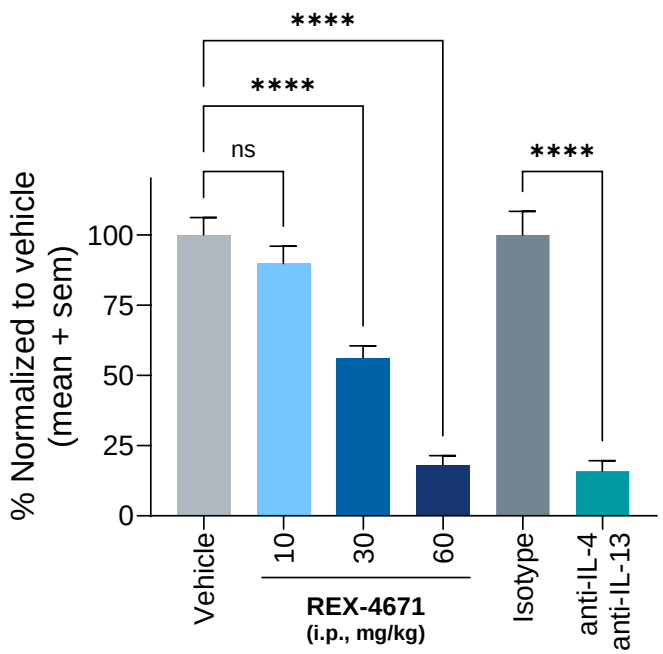
pSTAT6 inhibition

Whole Blood



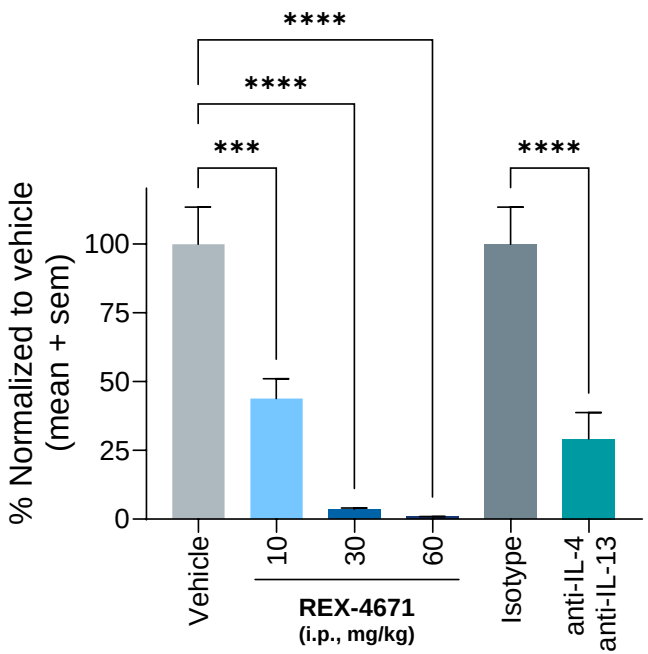
Lung immune cell infiltration

Eosinophils



Humoral immunity

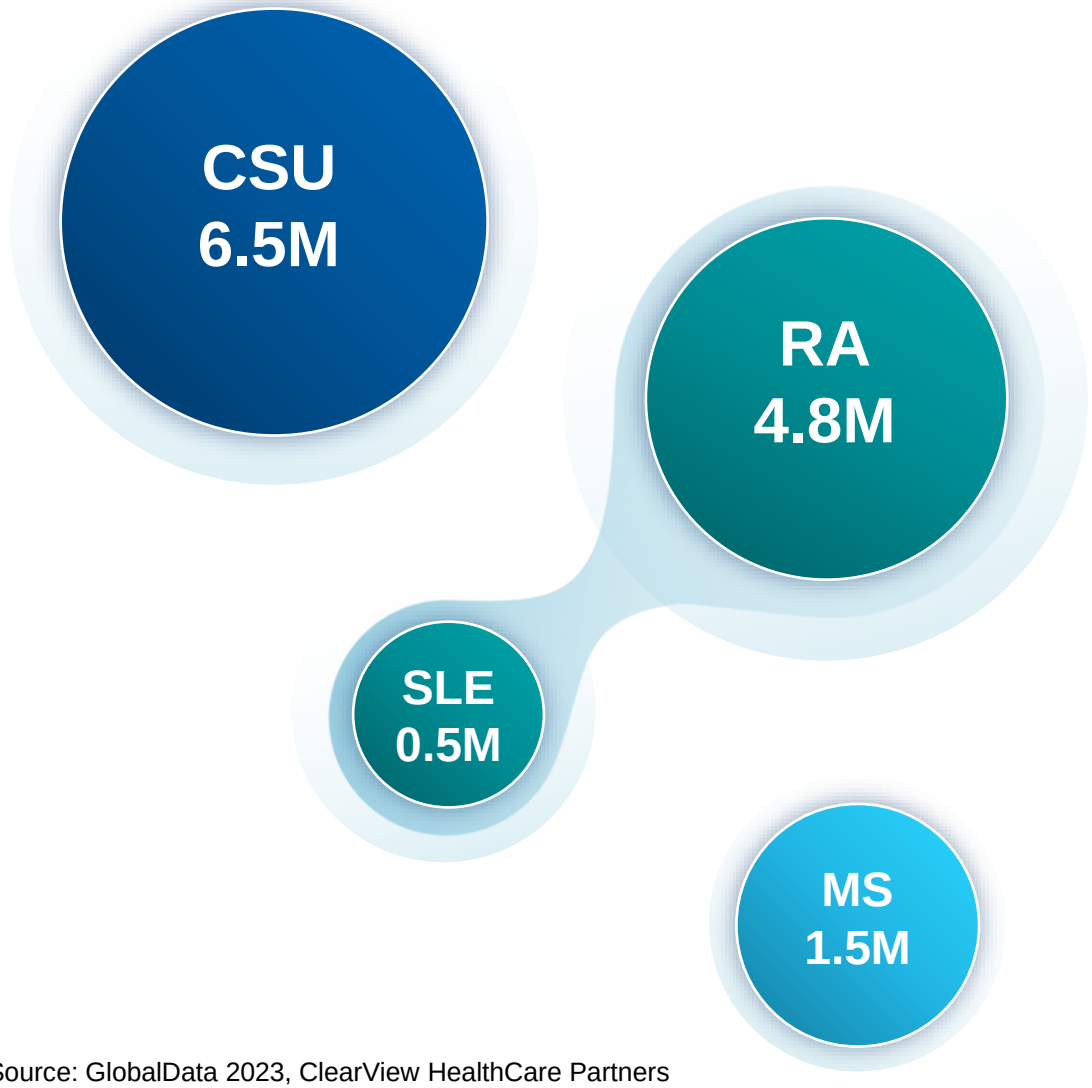
Serum OVA-specific IgE



*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

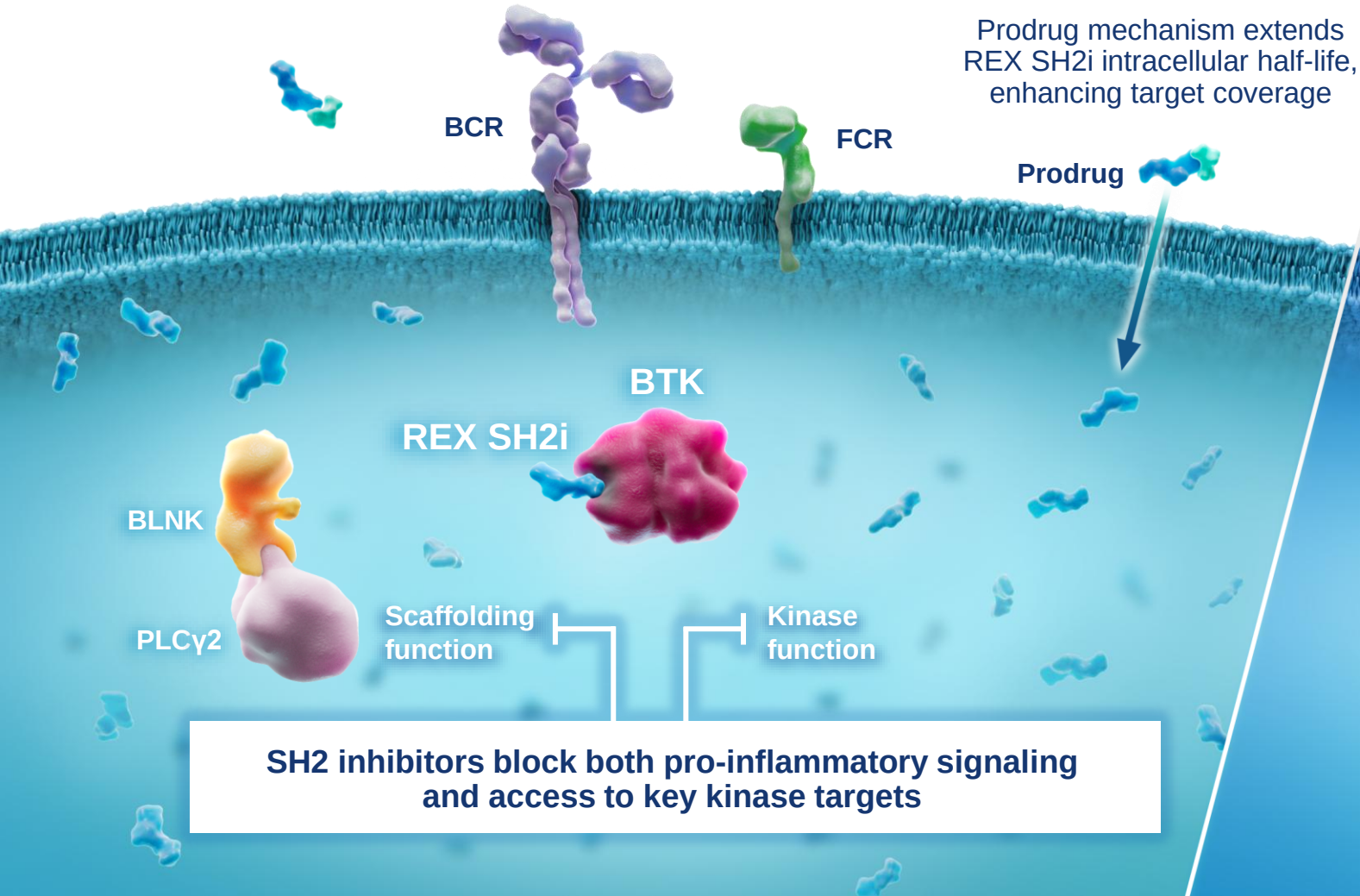
Prodrug mechanism enhances target coverage to drive improved efficacy

Source: GlobalData 2023, ClearView HealthCare Partners

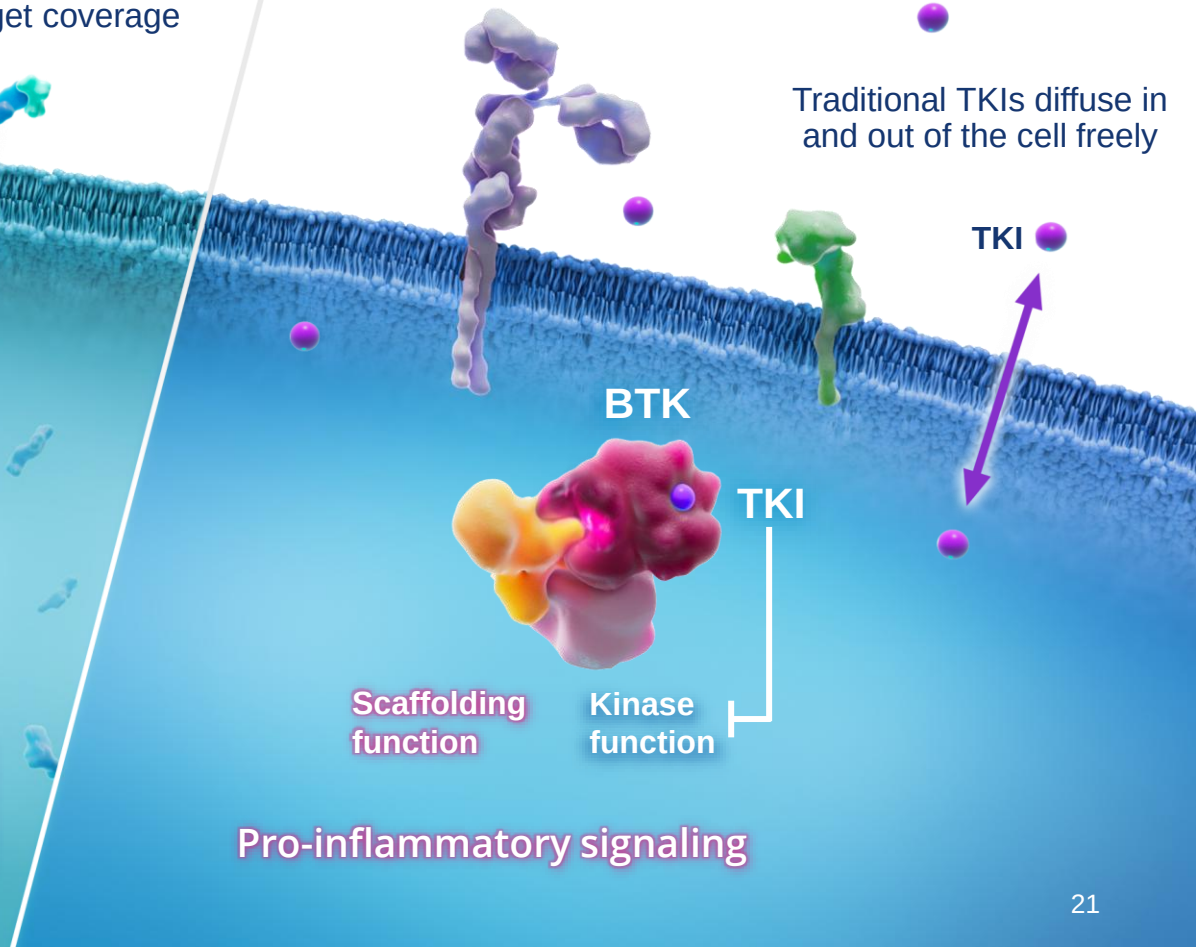
CSU: Chronic spontaneous urticaria, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, MS: Multiple sclerosis

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

Recludix BTK SH2i Prodrugs

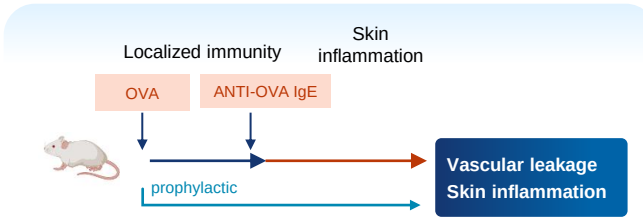


Traditional BTK TKIs

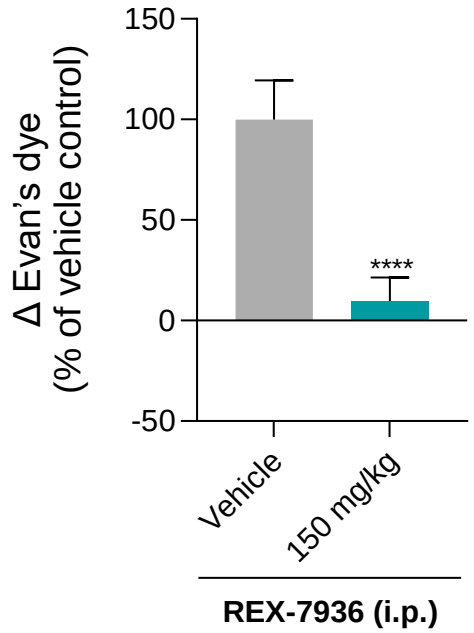


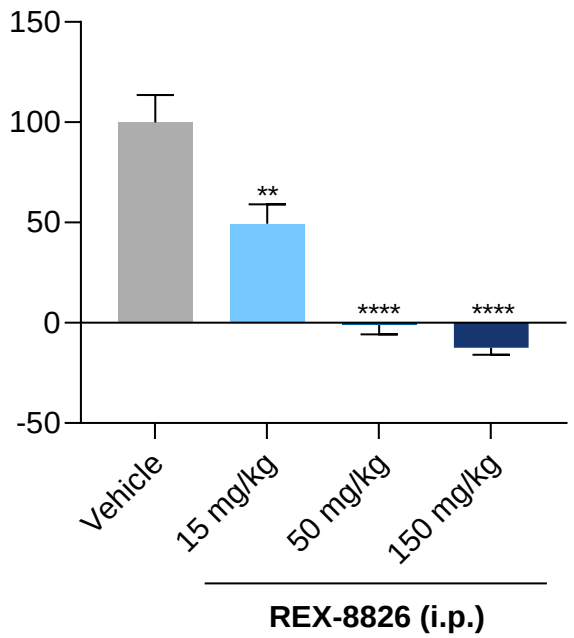
BTK SH2 Inhibitors Abrogate Mast Cell Activation in In Vivo Model of Chronic Urticaria

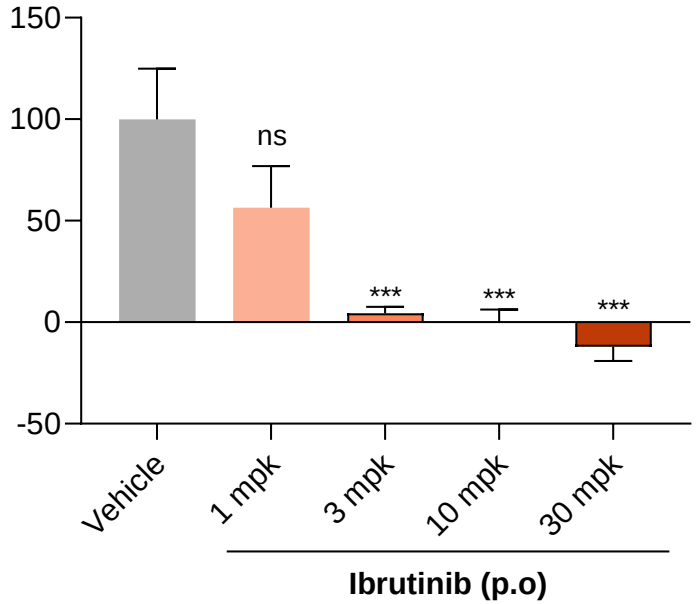
BTK SH2 inhibitors demonstrate strong dose-dependent efficacy



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

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Unlocking New Therapeutic Possibilities