



Corporate Presentation

September 2023

Rēclūdo (Latin)

transitive verb III conjugation

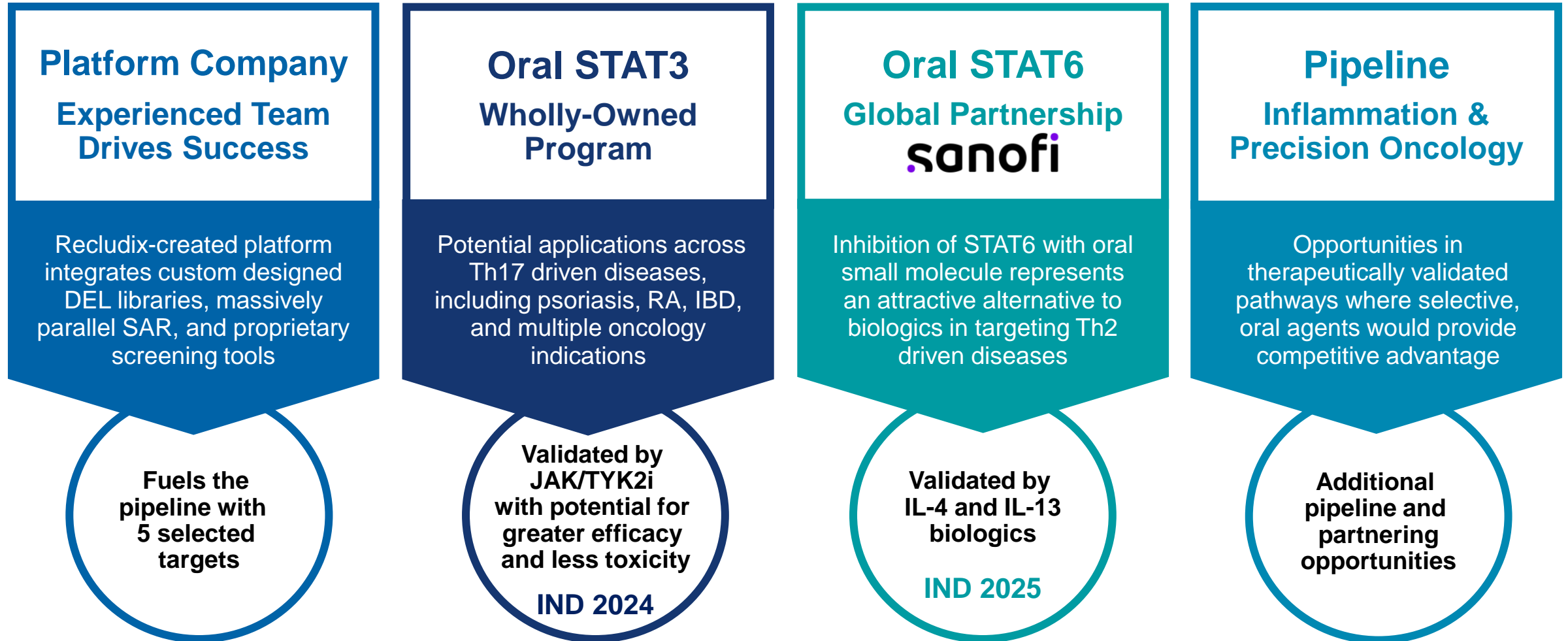
1 to open

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 and Cancer



Experienced Leadership and Top Tier Investors



Nancy Whiting, Pharm.D.

CEO

Seagen, GSK
Adcetris®, Tukysa®, Padcev®, Tivdak®



Patrick Zarrinkar, Ph.D.

CSO

Wellspring, Pfizer, Blueprint, Ambit, GNF, MIT



Catherine Bovenizer, C.P.A.

SVP, Finance

Renova, Apricus, Ambit, Senomyx, Ligand, GeneFormatics



Matt Caldemeyer, MBA

CBO

Everest Medicines, Ambrx, Array, Amgen, Lilly



Brian Hodous, Ph.D.

SVP, Chemistry

Accent, Blueprint, Merck-Serono, Amgen, MIT
Ayvakit™



Daniel Treiber, Ph.D. SVP, Discovery Technology

Eurofins, Discoverx, Ambit, MIT



Paul Smith, Ph.D.

SVP, Biology

Connect Biopharm, Incyte, Merck Serono, Novartis
Opzelura™



Nick Lydon, Ph.D.

Co-Founder, Board Member

Blueprint, AnaptysBio, Ambit, Amgen, Kinetix,
Novartis/CIBA-GEIGY
Gleevec®, Lasker-DeBakey Award, Japan Prize

\$102M Series A



Nick Lydon

Broad Oncology and Immunology Pipeline



Target	Program	Discovery	Lead Optimization	IND-Enabling	Partner
STAT3 SH2 domain	Inflammatory Diseases	<div></div>			Wholly-owned
	Cancer	<div></div>			
STAT6 SH2 domain	Inflammatory Diseases	<div></div>			sanofi ¹
	Cancer	<div></div>			
Undisclosed SH2 domain	Inflammatory Diseases	<div></div>			Wholly-owned
	Cancer	<div></div>			
Undisclosed SH2 domain	Cancer	<div></div>			Wholly-owned
Undisclosed Non-SH2 domain	Cancer	<div></div>			Wholly-owned

¹Option to participate in an equal profit-sharing arrangement in the US, which includes certain co-promotion activities

Strategic Collaboration with Sanofi for STAT6 Inhibitor

Strategic Collaboration to Advance Novel Oral STAT6 SH2 Domain Inhibitor

- Recludix will conduct preclinical research and early clinical development
- Sanofi will assume worldwide clinical development and commercialization from Phase 2 onwards
- Up to double-digit royalties on future sales
- Recludix has certain US co-promotion activities

\$125M

Near-term payments

50%

Option to participate in 50% US Profit Share

>\$1.2B

Potential future development and sales milestones

Validates Recludix Approach to Developing Selective Oral STAT SH2 Domain Inhibitors

Key Accomplishments in Drugging Previously Undruggable SH2 Domains

- Built a novel, chemistry-focused platform to drug undruggable SH2 domains
- Discovered and generated potent, selective, reversible and orally bioavailable STAT SH2 domain inhibitors
- For STAT3 and STAT6 demonstrated
 - Potent and selective activity in cell-based tumor and inflammatory disease models
 - Favorable differentiation from JAK and TYK2 inhibitors
 - Deep and durable target modulation in dogs
 - In vivo efficacy in inflammation disease models
- Identified inhibitors of additional undisclosed targets

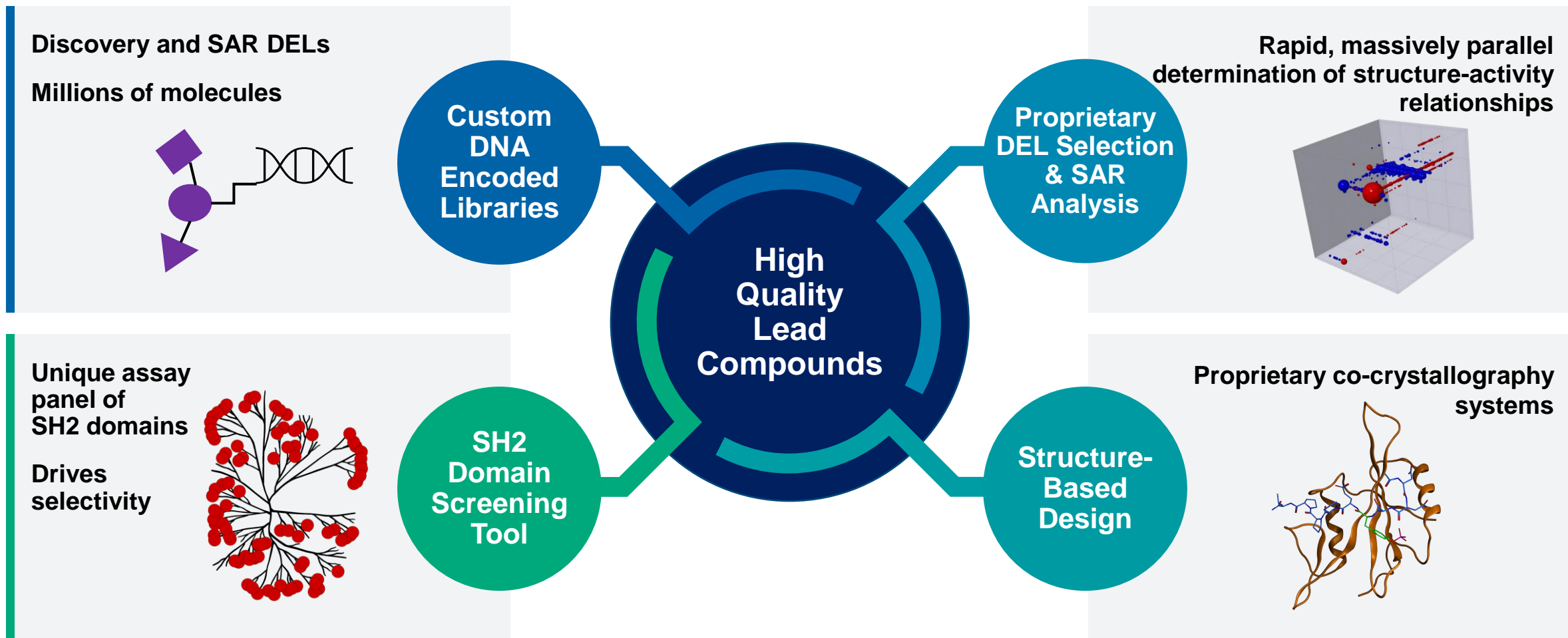
SH2 Domains Have Previously Been Deemed “Undruggable”

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 regulating the location and activity of proteins and in cellular signal transduction
- Mediate protein-protein interactions by binding to phospho-tyrosine containing motifs

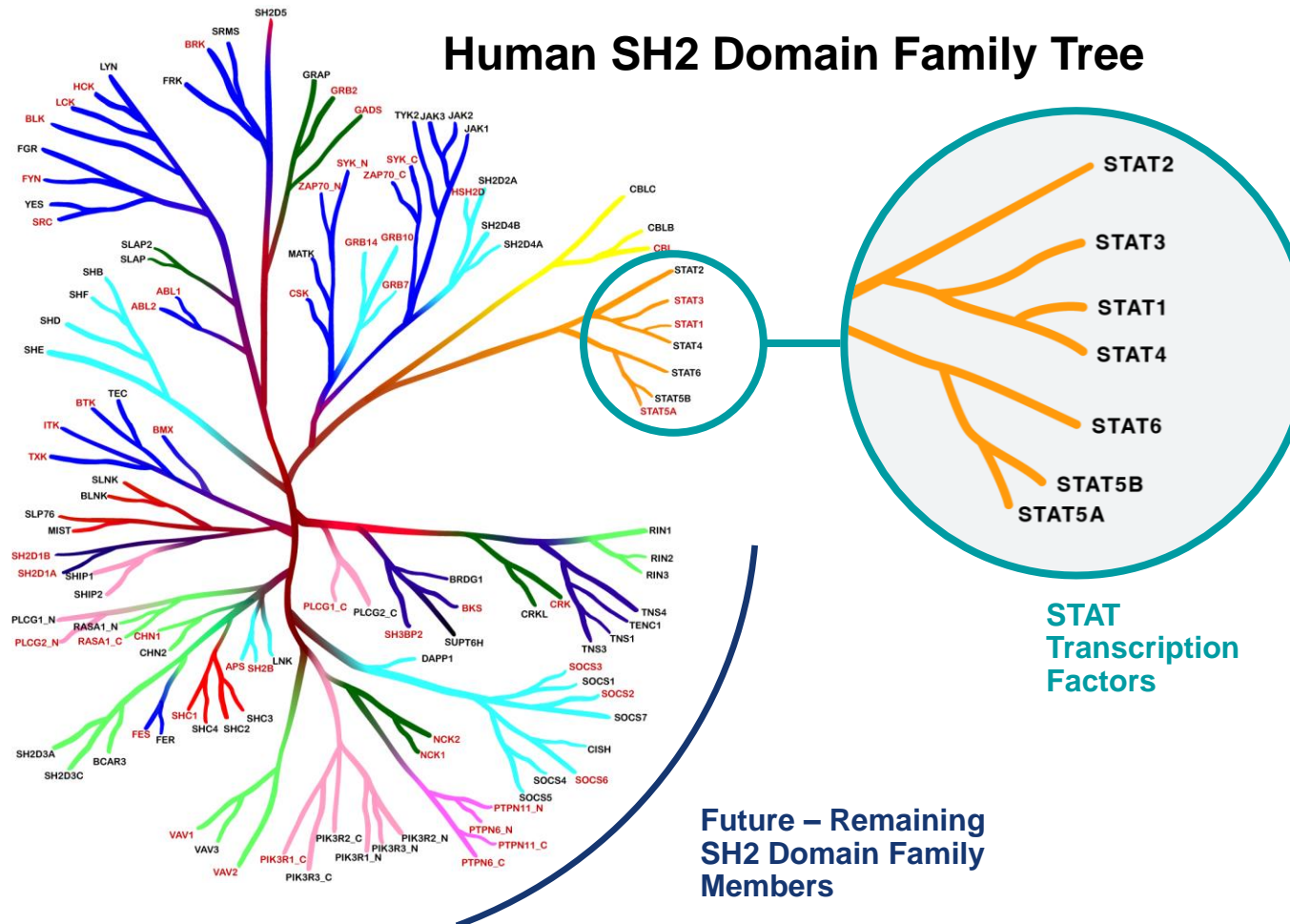


Recludix Platform: Integrated Proprietary Technologies & New Chemical Approaches



Significant Opportunity in Targeting SH2 Domain Proteins

Initially Focused on STAT3, STAT6 and 3 Additional Targets



1. STAT Transcription Factors

- Strong biological validation for STAT3 and STAT6
- Downstream in the JAK/STAT pathway; selective STAT inhibitors likely to be more targeted with fewer side effects

2. Undisclosed

- Plays a central role in both cancer and autoimmune diseases

3. Future - Remaining SH2 Domain Family Members

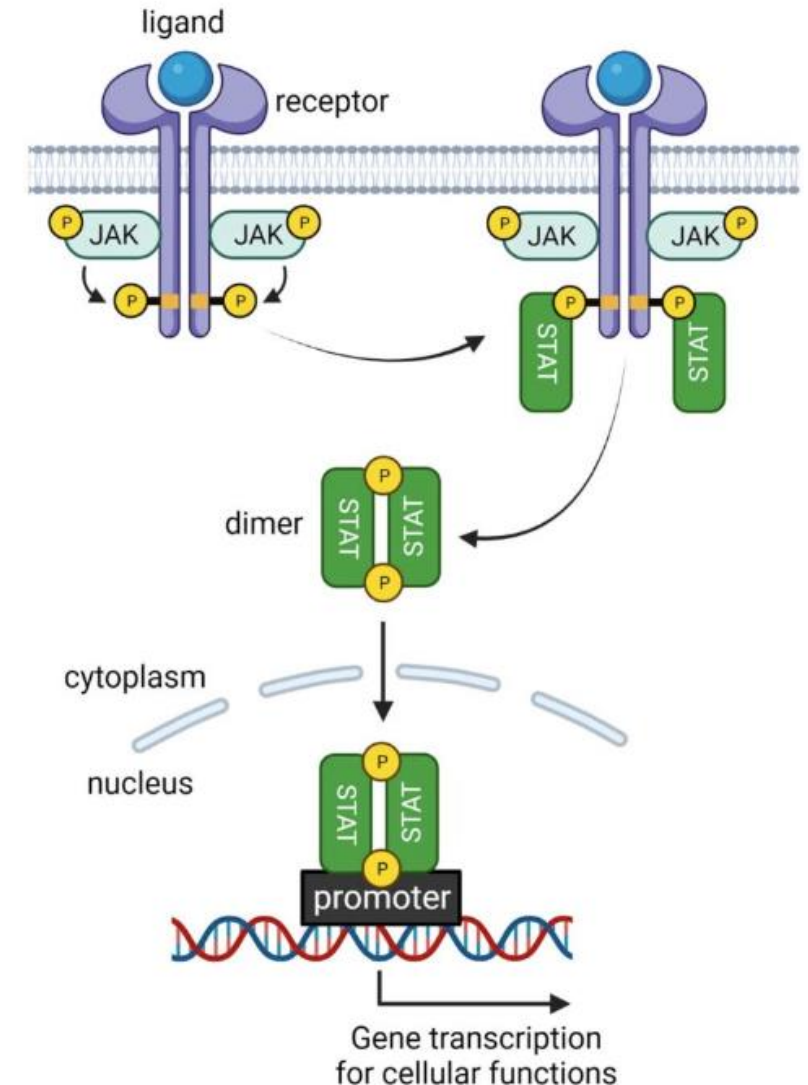
- Additional compelling targets enable a sustainable pipeline

STAT Transcription Factors Drive Immune System and Oncogenic Signaling

STAT proteins have been challenging to drug over the past 20 years but are yielding to Recludix's approach

The JAK/STAT pathway drives inflammatory diseases and cancer:

- In inflammatory diseases:
 - Required for function of disease-driving T cell populations
- In cancer:
 - Gain-of-function mutations
 - Aberrant upstream activation of the pathway
 - Mediates immunosuppressive tumor microenvironment



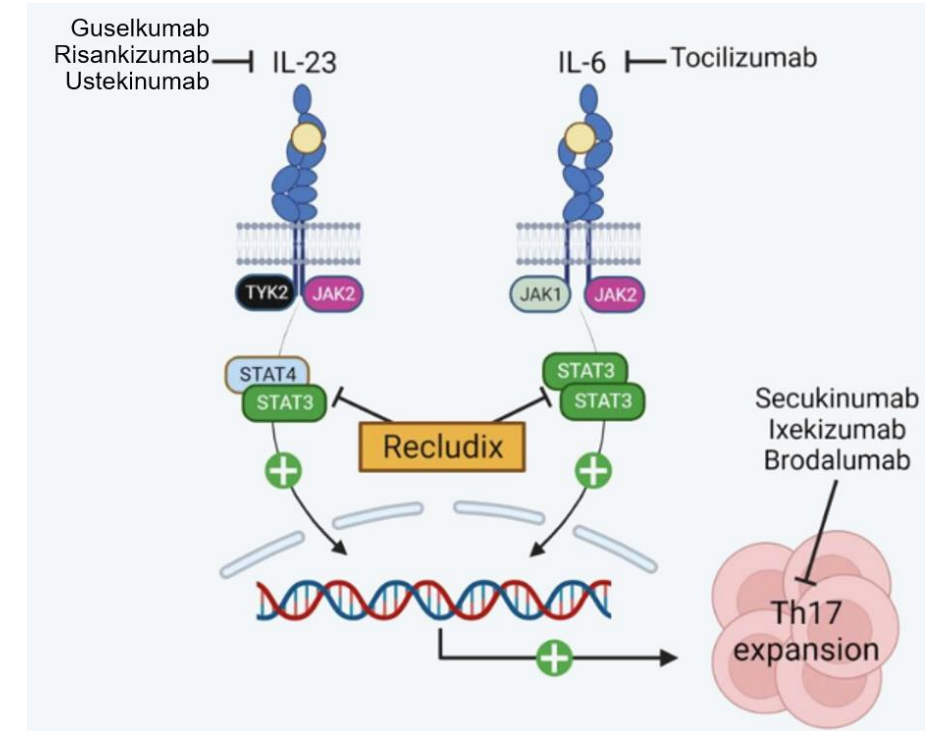
Recludix's Reversible, Oral, Small Molecule STAT Inhibitors are Differentiated from Competitors

	Recludix's STAT Inhibitors	TYK2 Inhibitors	JAK Inhibitors	Biologics	Degraders
Potent	++++	+++	+++	++++	+++
Selective	+++++	++	+	++++	+++
Reversible	+++++	++++	++++	+	+
Oral	+++++	++++	++++	-	+/-
Indication Expansion Potential	+++++	++	++++	++++	++

STAT3

STAT3 – First and Best-In-Class Opportunity to Selectively Inhibit Th17 Inflammatory Disease Pathways

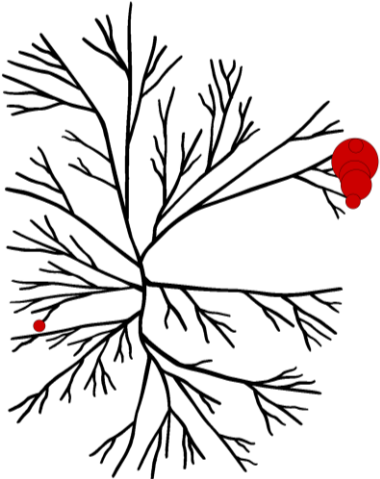
- STAT3 is a key driver of Th17 inflammatory cells which cause multiple inflammatory diseases such as psoriasis, rheumatoid arthritis, ulcerative colitis and Crohn's disease
- Increased selectivity by targeting STAT3 has the potential to provide both greater efficacy and less toxicity than JAK and TYK2 inhibitors
- A selective, oral STAT3 inhibitor has potential to replace JAK/TYK2 inhibitors and biologics for multiple inflammatory diseases with large market opportunities
 - JAK inhibitor global sales >\$4.7B annually, despite Black Box safety warnings
 - STELARA®, an injectable IL-12/23 inhibitor, annual sales >\$9.7B in 2022
- STAT3 inhibitors also have significant opportunity in cancer settings as STAT3 is activated in >70% of human cancers



	Efficacy Mechanisms		Anti-Viral Immunity		Hematol. Homeostasis	
	IL-6	IL-23	INFα/β	IFNγ	EPO	TPO
Tocilizumab	+					
Risankizumab Guselkumab		+				
JAK1/2 inhibitor	+	+	+	+	+	+
TYK2 inhibitor		+	+			
STAT3 inhibitor	+	+				

STAT3 Early Lead Compound REX-2317 is Potent and Selective in Biochemical and Cellular Assays

REX-2317

Biochemical Potency (SH2scan K_D)	Cellular Potency (pSTAT3 IC_{50} in human PBMCs)	Biochemical STAT Family Selectivity	Cellular Selectivity (PBMCs)	SH2 Domain Selectivity
0.83 nM	4.8 nM	>20X vs. STAT1/4 >1,000X vs. STAT2/5/6	12X vs. STAT1 40X to >2,000X vs. STAT4/5/6	

Selective STAT3 Inhibitors are Differentiated From JAK Inhibitors in Functional Assays

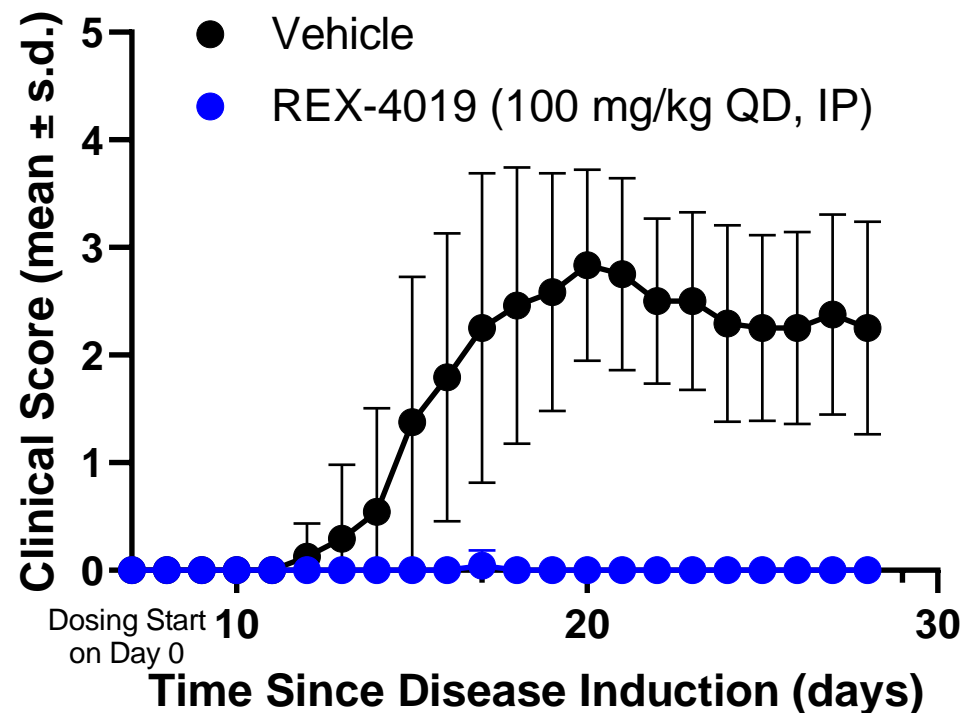
Direct selective STAT3 inhibition provides greater selectivity than currently approved JAK inhibitors

		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
STAT3 Inhibitors	REX-2317	>10,000 nM	>2,000 nM	13 nM	>3,000 nM	>10,000 nM	>10,000 nM
	REX-5376	>10,000 nM	>2,000 nM	11 nM	>3,000 nM	>10,000 nM	>10,000 nM
IL-6 Antagonist	Tocilizumab	>1,000 nM	>1,000 nM	In progress	>1,000 nM	>1,000 nM	>1,000 nM
IL-23 Antagonist	Risankizumab	>1,000 nM	>1,000 nM	In progress	>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

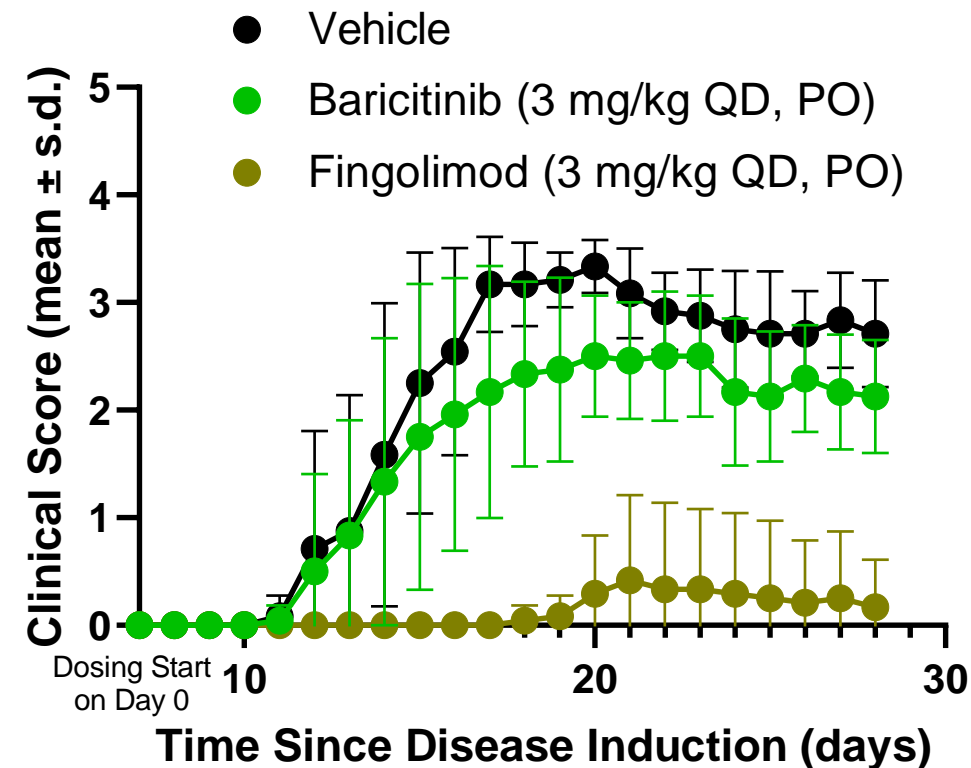
Selectivity relative to Th17 inhibition: >30X 10-30X <10X

REX-4019 Is Active In Mouse Encephalomyelitis (EAE) Model

Recludix Compound



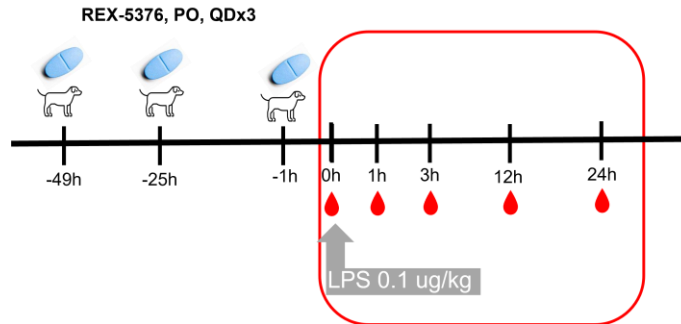
Benchmark Compounds



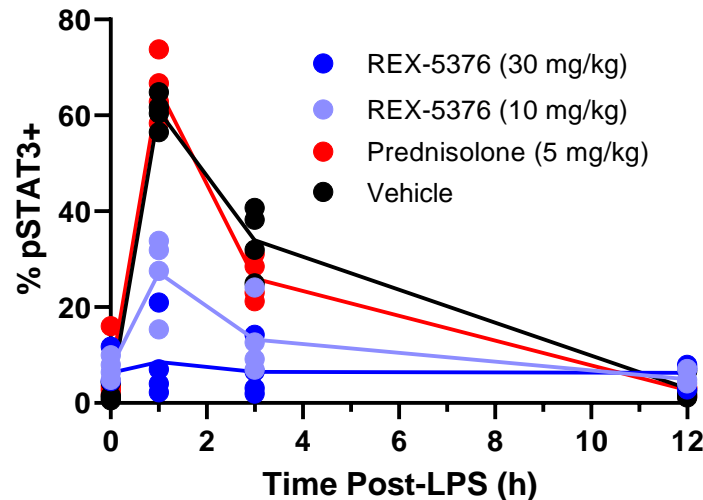
- First demonstration of efficacy in a disease model for Recludix STAT3 inhibitor
- Proof-of-Concept that reversible small molecule STAT3 inhibition modulates disease

Orally Administered STAT3 Inhibitor REX-5376 Inhibits LPS-induced Inflammation in Dogs

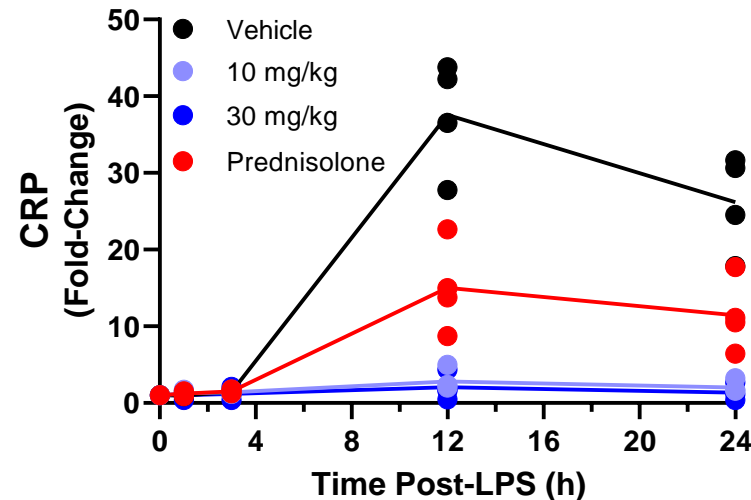
Study Design:



pSTAT3 Inhibition



CRP Inhibition

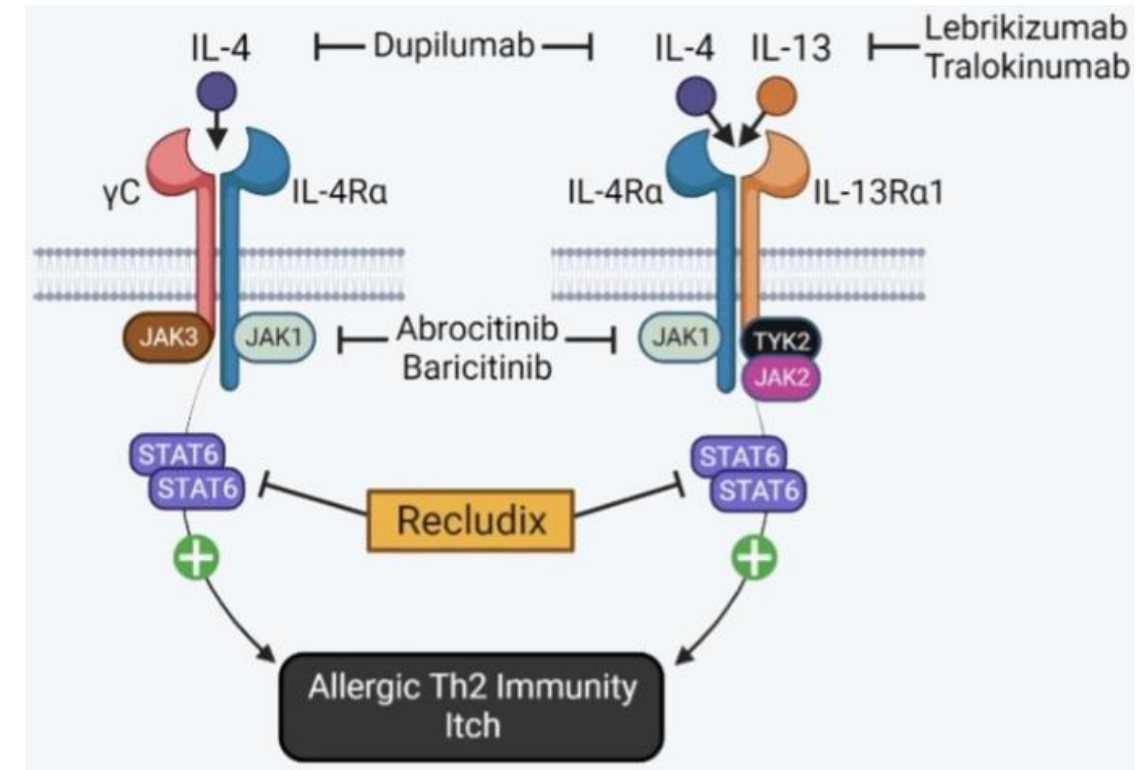


- REX-5376 inhibits LPS-induced pSTAT3 activation and CRP expression after oral administration
- Prednisolone inhibits CRP, but not STAT3 activation, demonstrating a differentiated mechanism

STAT6

STAT6 – First and Best-In-Class Opportunity to Selectively Inhibit Th2 Inflammatory Disease Pathways

- STAT6 is a critical driver of Th2 inflammatory cells and is the only STAT utilized by IL-4 and IL-13 signaling
- IL-4/IL-13 biologics have demonstrated efficacy in Th2 diseases such as atopic dermatitis, asthma, and COPD
- While JAK inhibitors have utility in Th2 disease, increased selectivity gained by targeting STAT6 has the potential to provide both greater efficacy and less toxicity
- A selective, oral STAT6 inhibitor has potential to complement and/or replace biologics in multiple Th2 diseases with large market opportunities
 - DUPIXENT®, an injectable IL-4Ra inhibitor, annual sales >\$8B in 2022

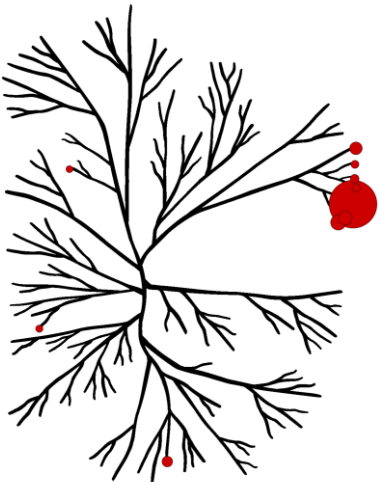


STAT6 Early Lead Compound REX-4671 is Potent and Selective in Biochemical and Cellular Assays

Current Lead Compounds Further Optimized

REX-4671

Biochemical Potency (SH2scan K_D)	Cellular Potency (pSTAT6 IC_{50} in human PBMCs)	Biochemical STAT Family Selectivity	Cellular Selectivity (PBMCs)	SH2 Domain Selectivity
0.025 nM	1.3 nM	>1,000X vs. STAT1/2/3/4/5	>1,000X vs. STAT1/2/3/4/5	



STAT6 Inhibitor Phenocopies Dupilumab In Functional Assays and Differentiates From JAK Inhibitors

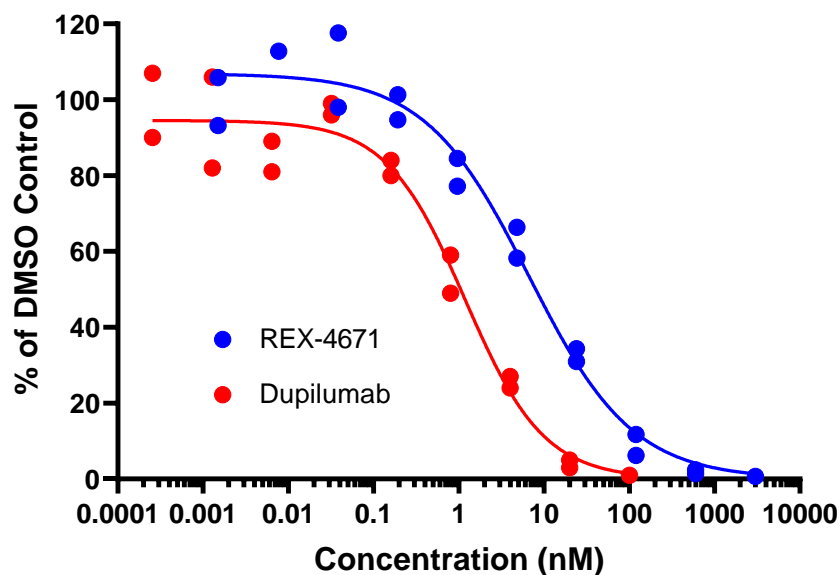
Direct selective STAT6 inhibition provides greater selectivity than currently approved JAK inhibitors

		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-4671	>10,000 nM	>3,000 nM	>10,000 nM	20 nM	>10,000 nM	>10,000 nM
IL-4/IL-13 Antagonist	Dupilumab	>10,000 nM	>1,000 nM	>1,000 nM	22 nM	>1,000 nM	>1,000 nM
JAK Inhibitors	Abrocitinib	1,300 nM	900 nM	81 nM	81 nM	3,200 nM	2,800 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	56 nM	42 nM

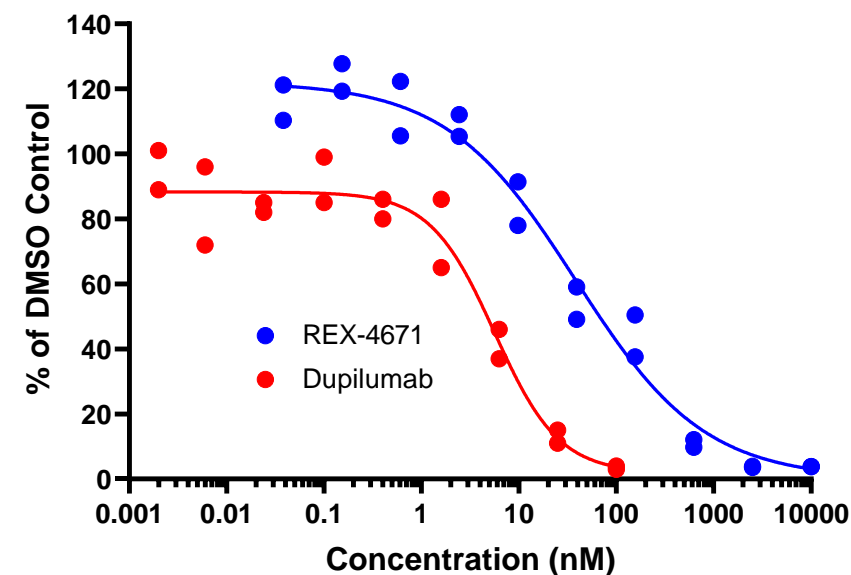
Selectivity relative to Th2 inhibition: >30X 10-30X <10X

Recludix Compound Inhibits IL-4 Stimulated Production of STAT6-Driven Biomarkers

Secreted **TARC/CCL17** in culture media
(4 days)



Expression of **CD23** surface marker
(4 days)



IL-4-stimulated
human PBMCs

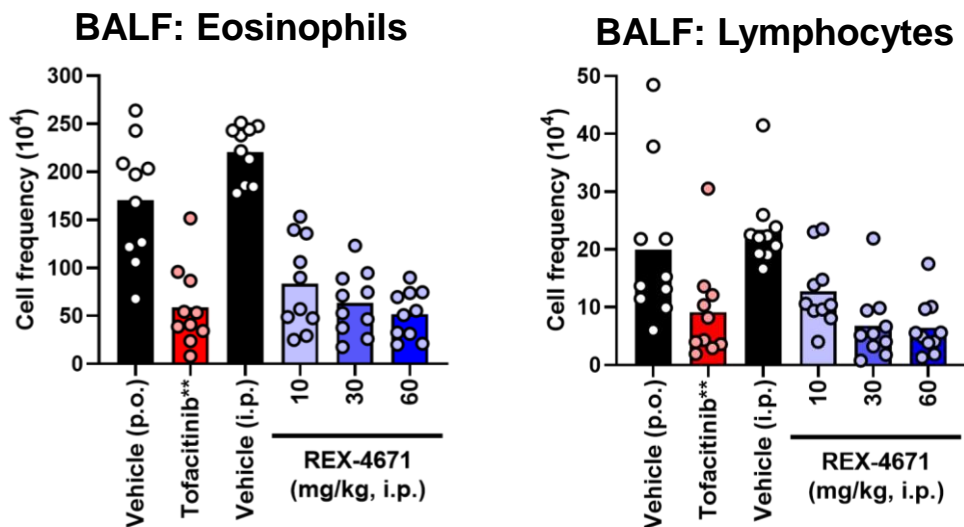
TARC is a clinical biomarker for atopic dermatitis

	TARC IC ₅₀ (Avg.)	CD23 IC ₅₀ (Avg.)
REX-4671	8.7 nM	33 nM
Dupilumab	0.79 nM	9.3 nM

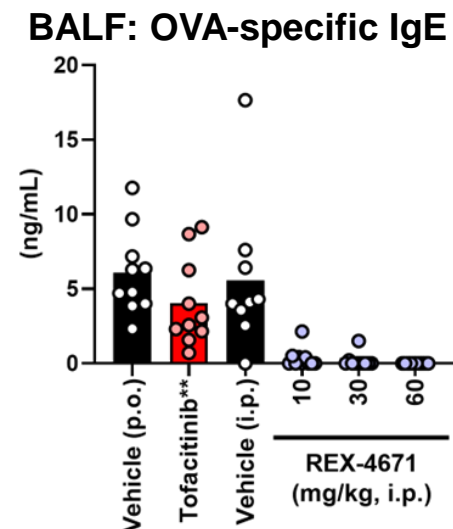
- Both biomarkers used in preclinical package of Dupixent BLA

Reduction of Lung Inflammation in Ovalbumin Asthma Model

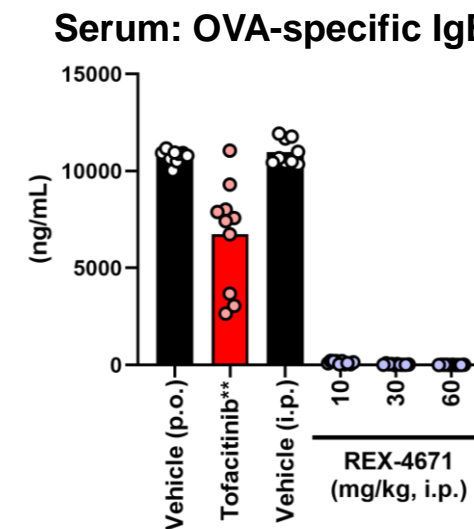
Lung immune cell infiltration



Lung IgE immunity



Systemic IgE immunity



**Tofacitinib 30 mg/kg p.o.

- Prophylactic REX-4671 treatment reduced pathogenic immune cell infiltration and IgE levels
- Improvements in lung function and histopathology in REX-4671 treated animals also observed
- REX-4671 abrogates serum IgE immunity, a clinical biomarker of treatment response in asthma and dermatitis

Strong Progress in Advancing STAT3 and STAT6 Inhibitors Towards the Clinic

Near Term Milestones

- Complete lead optimization
- Generate additional in vivo efficacy data in other models of inflammatory disease
- Conduct preliminary toxicology studies
- Nominate development candidates for STAT3 (2023) and STAT6 (2024)
- Initiate Phase 1 clinical trials for STAT3 (2024) and for STAT6 (2025)

Recludix is Well Positioned to be the Leader in SH2-Targeted Therapeutics



Foundational Platform with Experienced Team

Custom DNA-Encoded Libraries

Proprietary DEL Selection and SAR Analyses

Structure-Based Drug Design

Family-Wide Screening Tools



First Applications in SH2 Domain Inhibitors

Five high-interest targets in inflammatory diseases & cancer



Significant market opportunity in inflammatory diseases



Differentiated selectivity and oral administration



Validating strategic partnership with Sanofi



Pipeline Opportunities Beyond SH2 Domain



Thank you

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Unlocking New Therapeutic Possibilities

