Corporate Presentation

September 2024

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 and Cancer

Recludix Pharma

Platform Company

Experienced Team Drives Success

Recludix-created platform integrates custom designed DEL libraries, massively parallel SAR, and proprietary screening tools

Fuels the pipeline with 5 selected targets

Oral STAT6

Global Partnership

sanofi

Inhibition of STAT6 with oral small molecule represents an attractive alternative to biologics in targeting Th2 driven diseases

Validated by IL-4 and IL-13 Biologics

IND 2025

Oral STAT3

Wholly-Owned Program

Potential applications across Th17 driven diseases, including psoriasis, RA, IBD, and multiple oncology indications

Validated by JAK/TYK2i with potential for greater efficacy and less toxicity

IND 2025

Pipeline

Inflammation & Precision Oncology

Opportunities in therapeutically validated pathways where selective, oral agents would provide competitive advantage

Additional pipeline and partnering opportunities

Expanded Leadership Team

Nancy Whiting, Pharm.D. — 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, Apricus, Ambit, Senomyx, Ligand, GeneFormatics

Brian Hodous, Ph.D. — SVP, Chemistry

Accent, Blueprint, Merck-Serono, Amgen, MIT

Ayvakit™

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

Eurofins, Discoverx, Ambit, MIT

Vanflyta®

Paul Smith, Ph.D. — SVP, Biology

Connect Biopharma, Incyte, Merck Serono, Novartis

Opelurza™

Nick Lydon, Ph.D. — Co-Founder, Board Member

Blueprint, AnaptysBio, Ambit, Amgen, Kinetix, Novartis/CIBA-GEIGY

Gleevec® (imatinib), Lasker-DeBakey Award, Japan Prize

$102M Series A

NEA

Access Industries

Westlake Village BioPartners

Nick Lydon

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 U.S. co-promotion activities

$125M	Near-term payments
50%	Option to participate in 50% U.S. Profit Share
>$1.2B	Potential future development and sales milestones

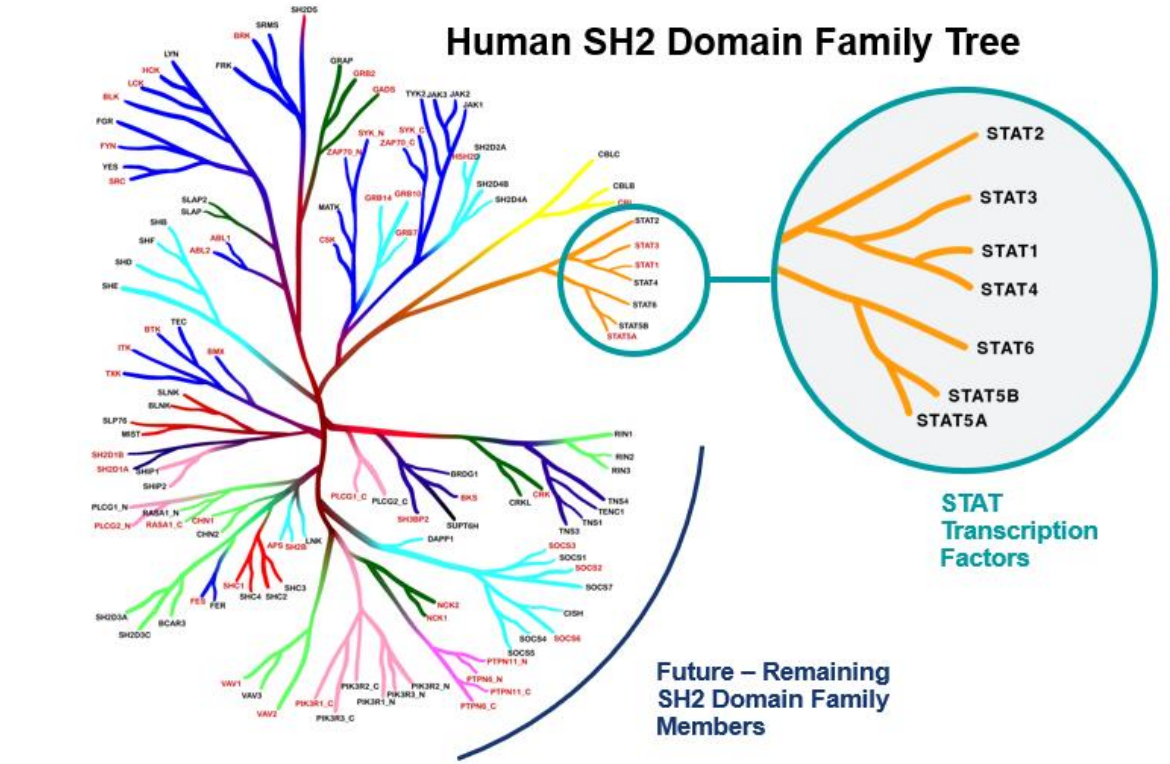
Validates Recludix Approach to Developing Selective Oral STAT SH2 Domain Inhibitors

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

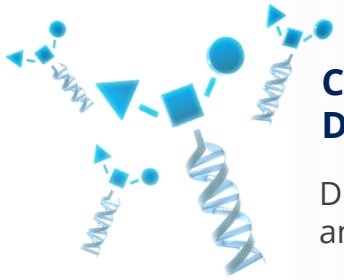
- Small protein modules made up of ~100 amino acids
- 120 human SH2 domains
- Play a key role in mediating protein-protein interactions
- The SH2 domain of STAT proteins is required for
  - Binding to cytokine receptors via the SH2 domain and phospho-tyrosine motifs on the receptor
  - Dimerization of STAT proteins occurs by reciprocal interactions with each monomer's SH2 domain; STAT DNA binding and transcriptional activity requires dimerization



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

Recludix Platform: Integrated Proprietary Technologies & New Chemical Approaches

Recludix Pharma



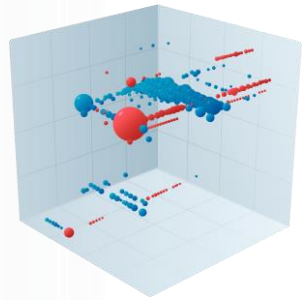
Custom SH2 Domain Targeting DNA-Encoded Libraries

Discovery and SAR DELs

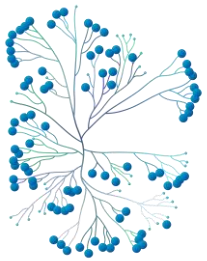
Hundreds of millions of molecules

Proprietary DEL Selection & SAR Analysis

Rapid massively parallel determination of structure-activity relationships



High Quality Lead Compounds



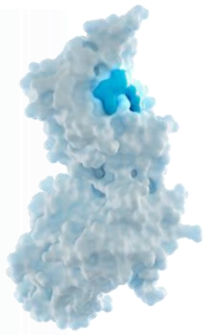
SH2 Domain Screening Tool

Unique panel of SH2 domain assays

Drives selectivity

Structure-Based Design

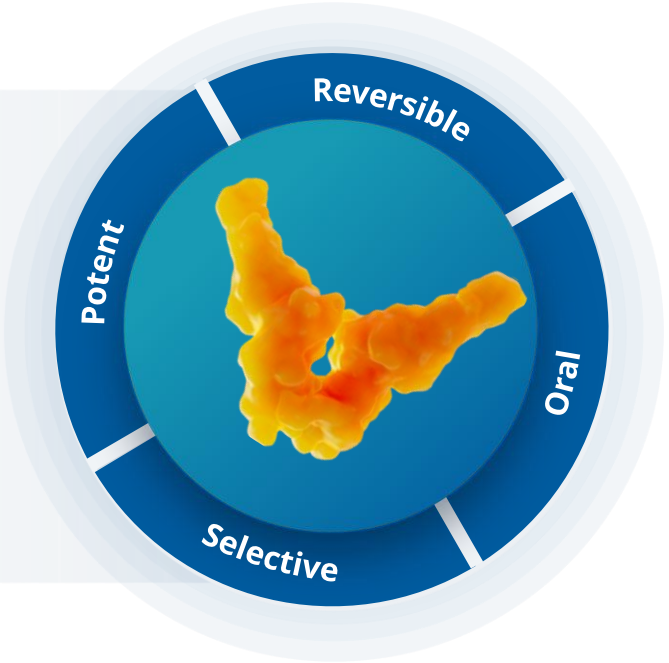
Proprietary co-crystallography systems



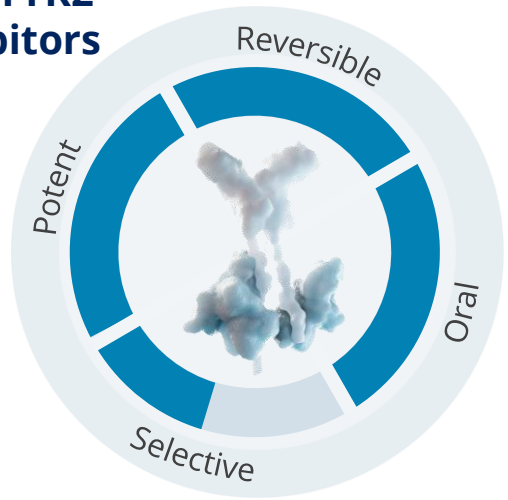
STAT SH2 Domain Inhibition Enables a Best-in-Class Product Profile

Differentiated Product Profile

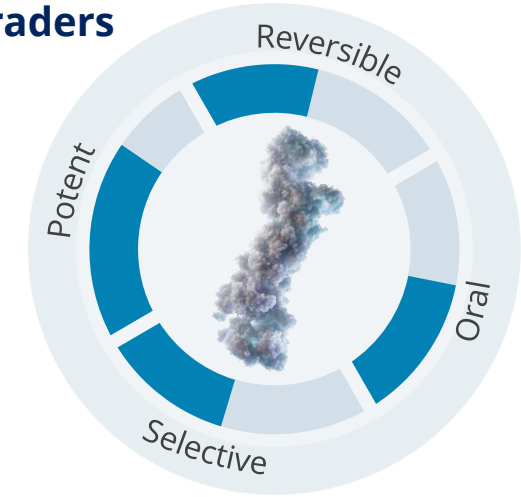
Recludix Pharma



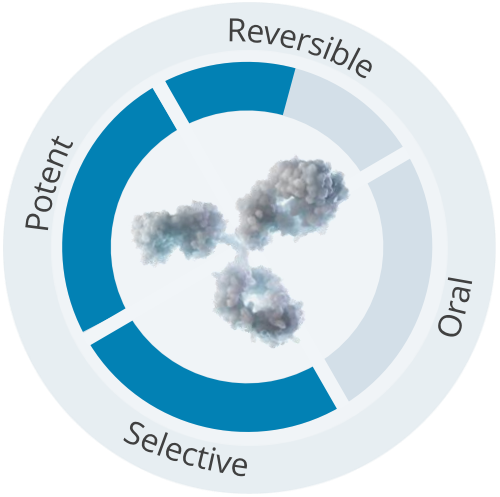
JAK/TYK2 Inhibitors



Degraders



Biologics

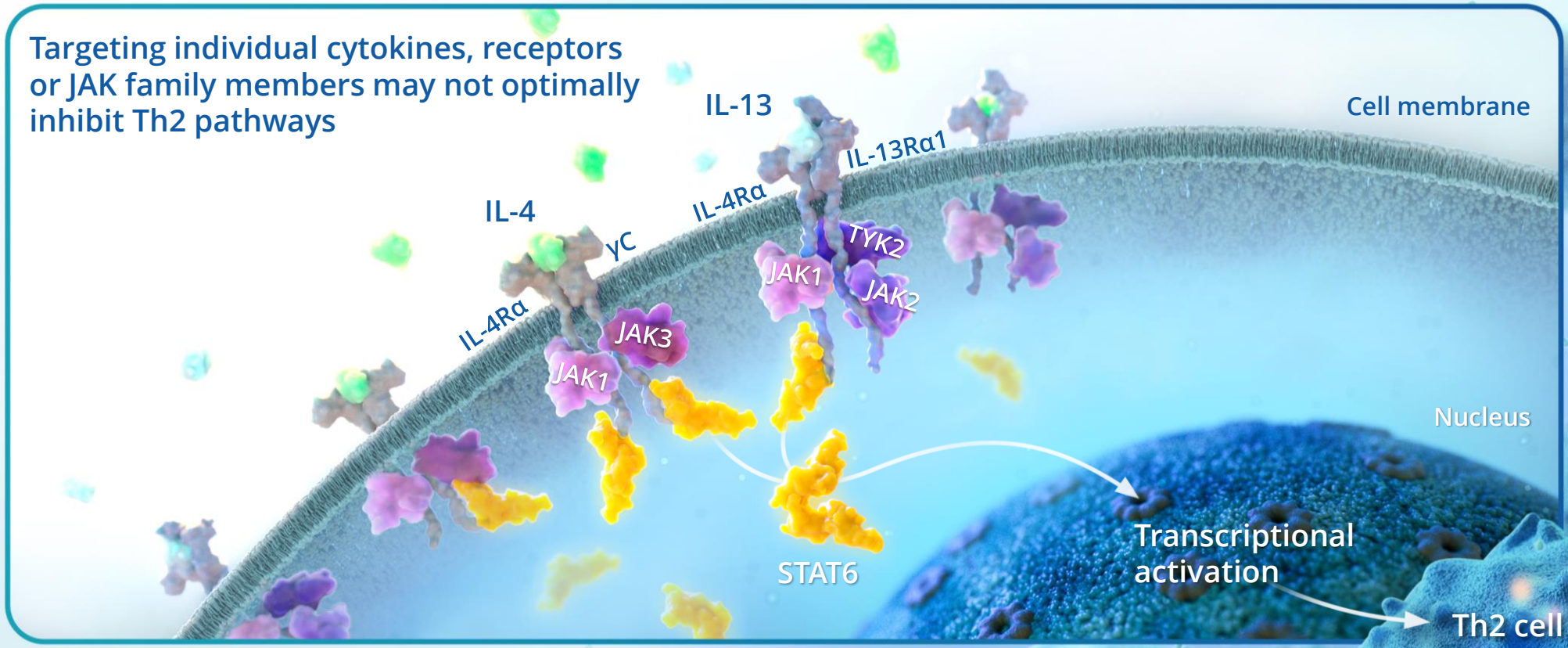


STAT6

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

Recludix Pharma

STAT6 mediates IL-4 and IL-13 signaling, two key inflammatory drivers of atopic dermatitis, asthma & COPD

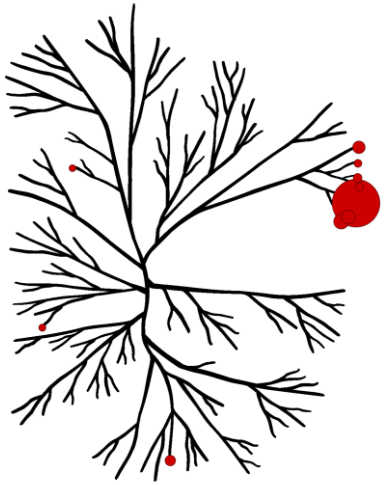


STAT6 Early Lead Compound REX-4671 is Potent and Selective in Biochemical and Cellular Assays

Recludix Pharma

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

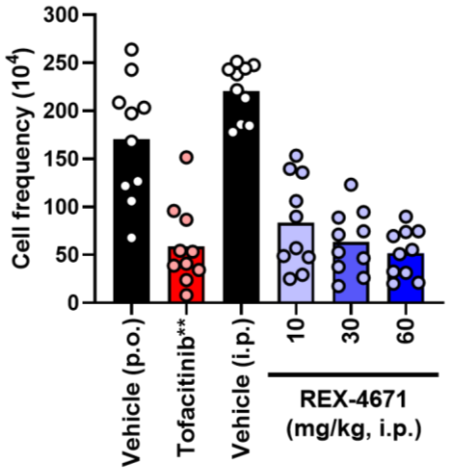
		T cell function				Hematologic homeostasis	
		General Adaptive Immune response	Defense against viruses and bacteria	Defense against extracellular pathogens	Defense against parasites and mediation of antibody responses	Erythropoiesis	Thrombopoiesis
		T Cell Activation (CD25)	Th1 Cell Function (IFNγ)	Th17 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

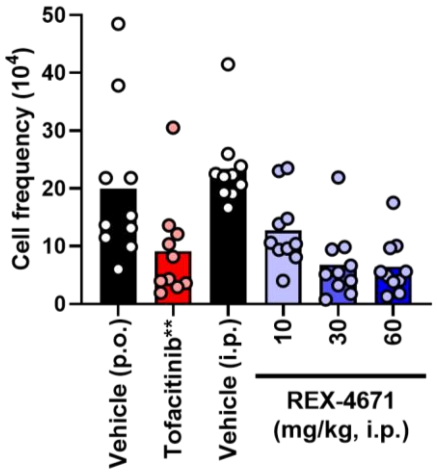
Reduction of Lung Inflammation in Ovalbumin Asthma Model

Lung immune cell infiltration

BALF: Eosinophils

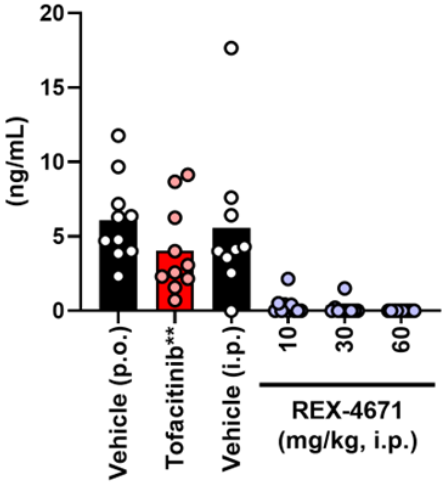


BALF: Lymphocytes



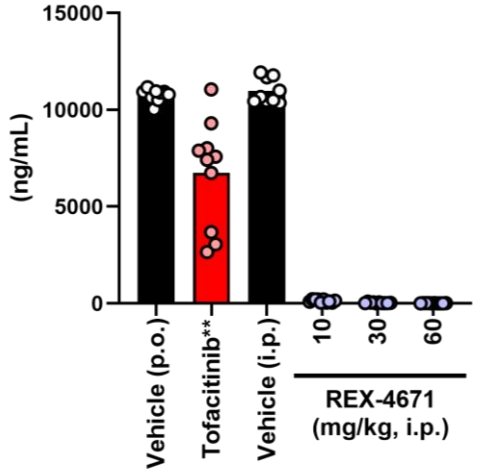
Lung IgE immunity

BALF: OVA-specific IgE



Systemic IgE immunity

Serum: OVA-specific IgE



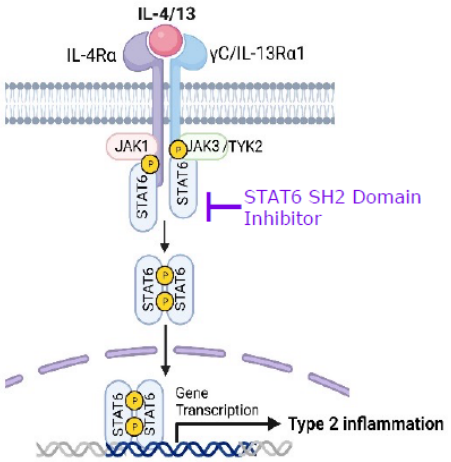
**Tofacitinib 30 mg/kg p.o.

- 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

Oral STAT6 Compounds Characterized by Selective and Sustained Target Inhibition

Program partnered with Sanofi

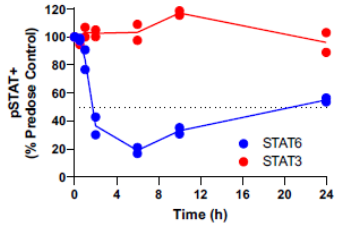
STAT6 pathway inhibitor: an *oral* small molecule that blocks type 2 IL-4 and IL-13 pathways



STAT6 SH2 domain inhibitors selectively target type 2 cellular responses and differentiate from JAK inhibitors

	STAT6 inhibitor	IL-4/13 antagonist[1]	JAK inhibitor[1]
T Cell Function (IC50)			
Th2	26nM	26nM	4nM
Th17	>100X	>35X (highest tested)	2X
Th1	>100X	>35X	9X
Hematological homeostasis			
EPO-STAT5	>300X	>35X	17X
TPO-STAT5	>300X	>35X	5X

Durable and selective pSTAT6 inhibition following single oral dose of STAT6 SH2 domain inhibitor in preclinical model



STAT6 inhibitor offers potential for *antibody-like efficacy* with oral convenience in type 2 diseases

Strong human *genetic evidence* for critical role of STAT6 with associated GWAS and gain of function mutations driving allergic disease[2,3,4,5]

Entered strategic collaboration with Recludix Pharma to advance novel oral STAT6 SH2 domain inhibitors with *IND projected in 2025*

1. Corporate presentation, Recludix Pharma, JPM HealthCare Conference, Jan 2023. 2. Baris et al., JACI 152, 2023. 3. Sharma et al., J Exp Med 220, 2023. 4. Takeuchi et al., JACI 151, 2023. 5. Suratannon et al., JACI 151, 2023.

108 R&D Day 2023

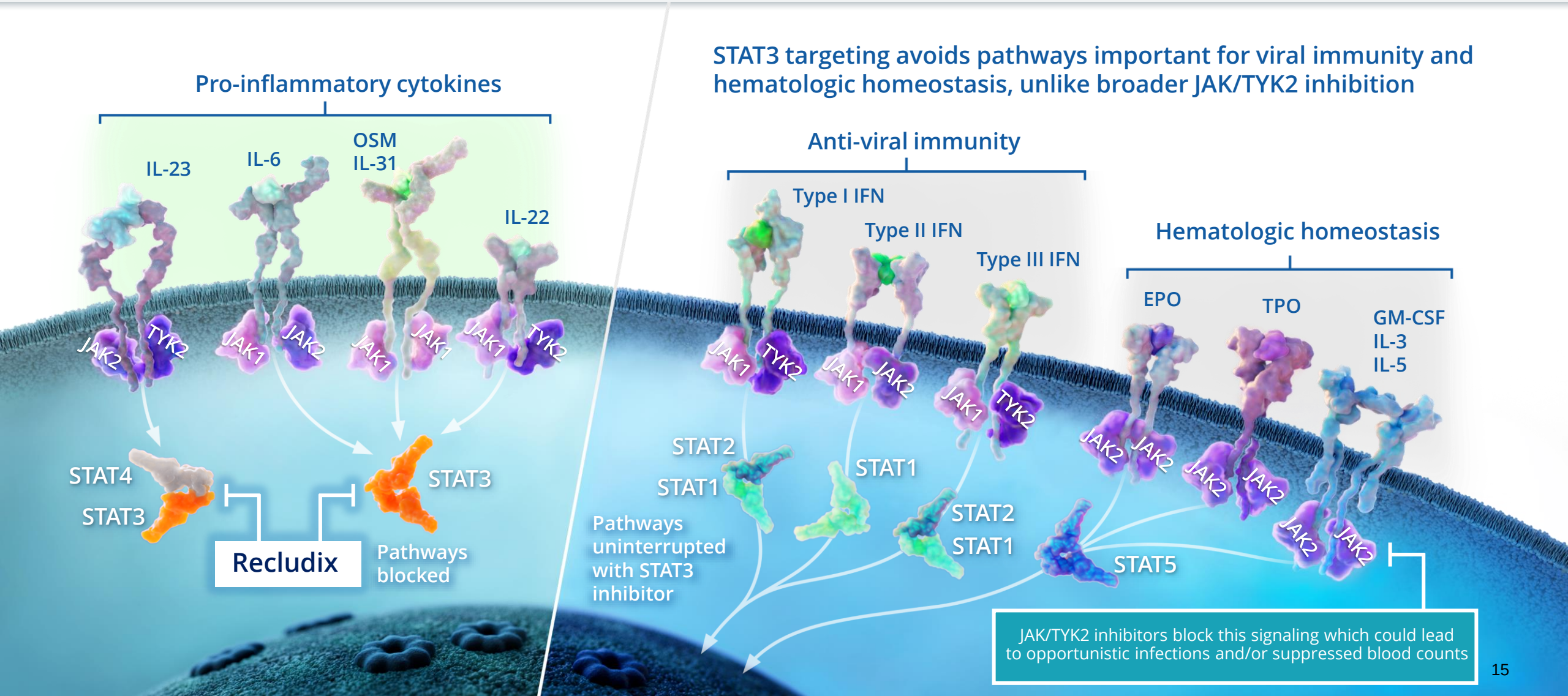
Corporate presentation, Sanofi, Sanofi R&D Day, Dec 2023

STAT3

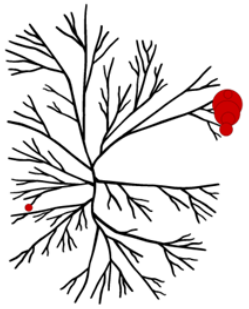
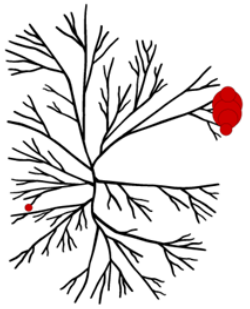
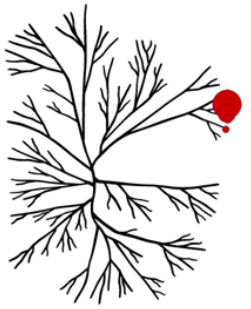
STAT3 is a First- and Best-In-Class Opportunity to Inhibit Clinically Validated Inflammatory Disease Pathways

Recludix Pharma

STAT3 dependent cytokines are key inflammatory drivers of psoriasis, inflammatory bowel disease & rheumatoid arthritis



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

	REX-4019	REX-5376	REX-7117
Biochemical Potency (SH2scan K_D)	0.28 nM	0.15 nM	0.16 nM
Cellular Potency (pSTAT3 IC_{50} in human PBMCs)	5.1 nM	0.72 nM	1.2 nM
Biochemical STAT Family Selectivity	~15X vs. STAT1 >300X vs. STAT2/4/5/6	~2X vs. STAT1 >150X vs. STAT2/4/5/6	~20X vs. STAT1 >500X vs. STAT2/4/5/6
Cellular Selectivity (PBMCs)	>10X vs. STAT1 >100X vs. STAT2/4/5/6	~2X vs. STAT1 ~20X vs. STAT2 >300X vs. STAT4/5/6	~20X vs. STAT1 >500X vs. STAT2/4/5/6
SH2 Domain Selectivity			

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

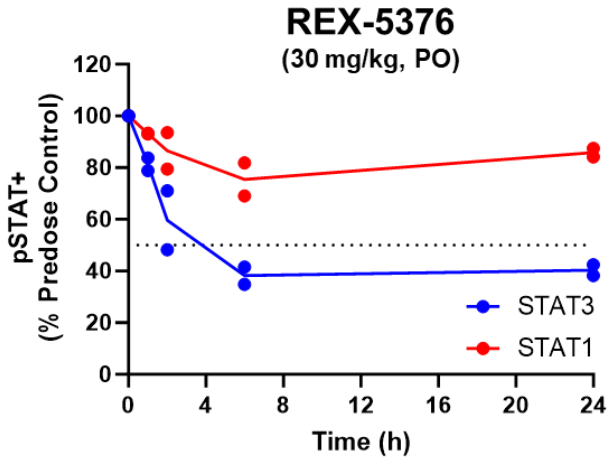
Recludix Pharma

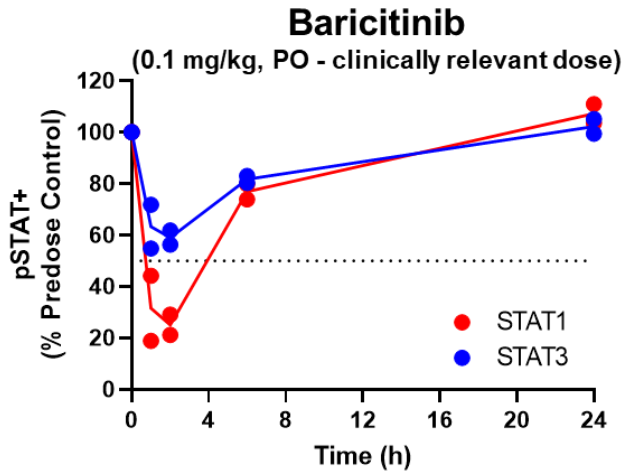
		T cell function				Hematologic homeostasis	
		General Adaptive Immune response	Defense against viruses and bacteria	Defense against extracellular pathogens	Defense against parasites and mediation of antibody responses	Erythropoiesis	Thrombopoiesis
		T Cell Activation (CD25)	Th1 Cell Function (IFNγ)	Th17 Cell Function (IL-17A)	Th2 Cell Function (IL-5)	EPO-Induced STAT5-Driven Transcription	TPO-Induced STAT5-Driven Transcription
STAT3 Inhibitors	**REX-4019**	**>10,000 nM**	**>2,000 nM**	**48 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**
	REX-7117	**>10,000 nM**	**>2,000 nM**	**14 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

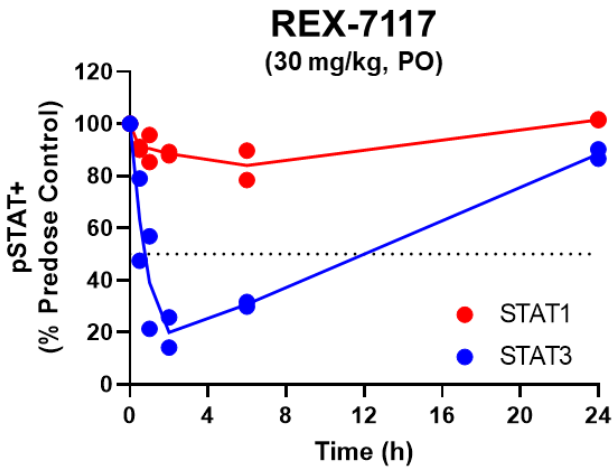
Selectivity relative to Th17 inhibition: >30X 10-30X <10X

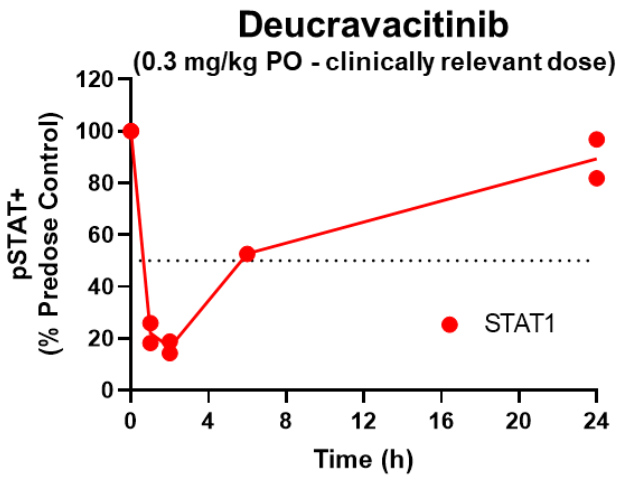
Recludix Oral STAT3 Compounds Characterized by Selective and Sustained Target Inhibition

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





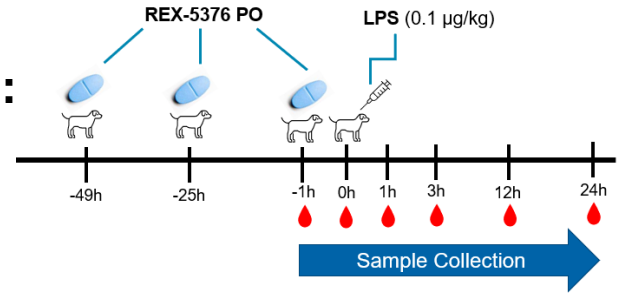




Oral STAT3 Inhibition Significantly Reduces an IL-6 Dependent LPS-Induced Inflammation in Dogs

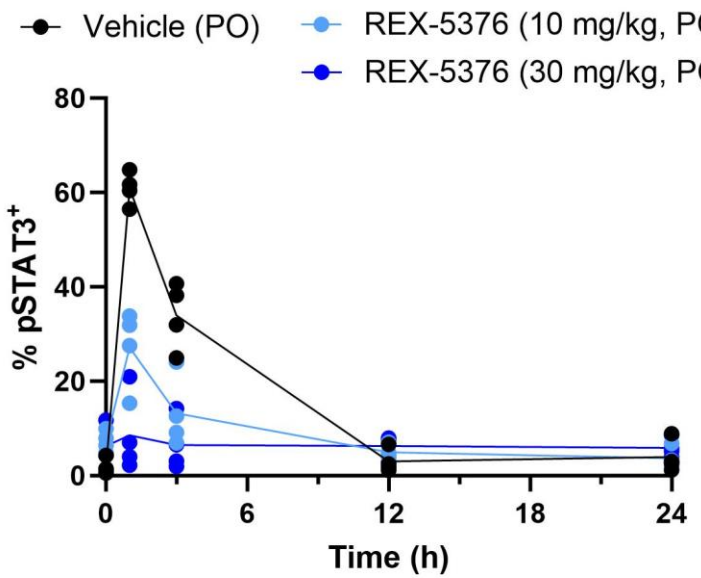
Oral STAT3 inhibition effectively impairs IL-6 mediated inflammatory responses

Study Design:

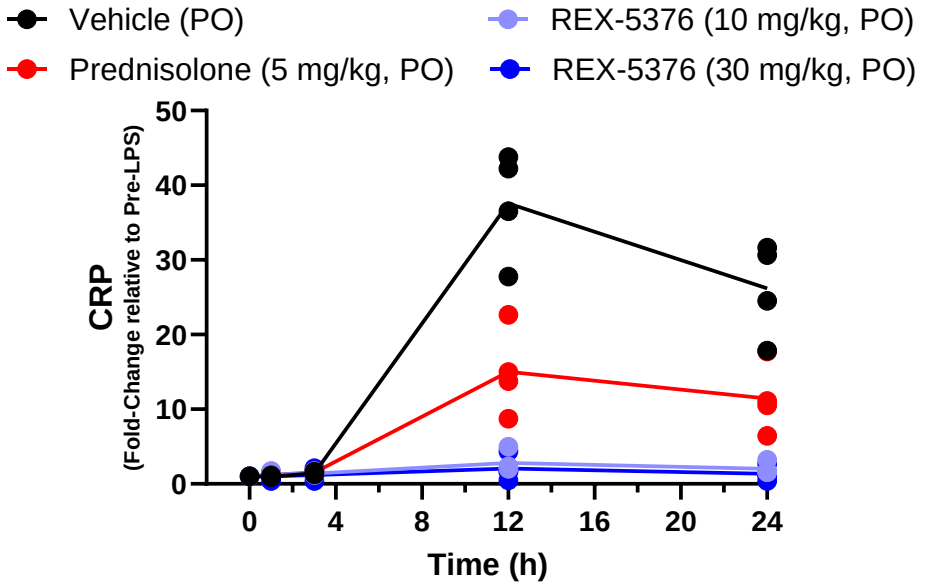


- LPS challenge drives pSTAT3 activation, immune activation, and IL-6 dependent CRP production
- Oral REX-5376 inhibits endogenous pSTAT3 signaling and abrogates CRP induction

PBMC pSTAT Activity



Serum CRP

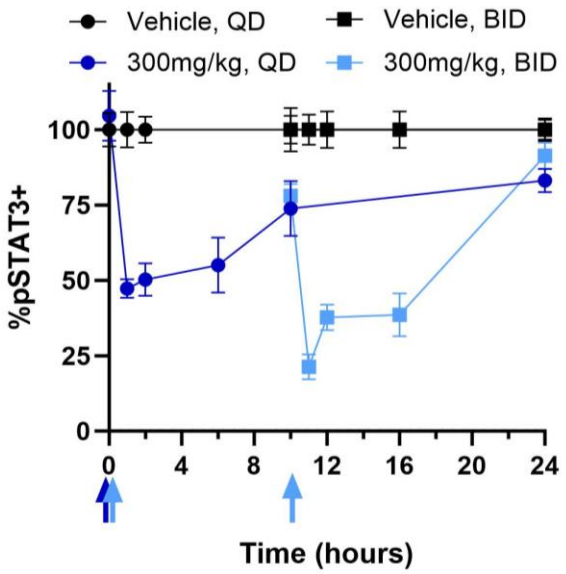


REX-7117 Demonstrates Efficacy After Oral Dosing in a Murine IL-23-Induced Th17 Model of Psoriasis

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

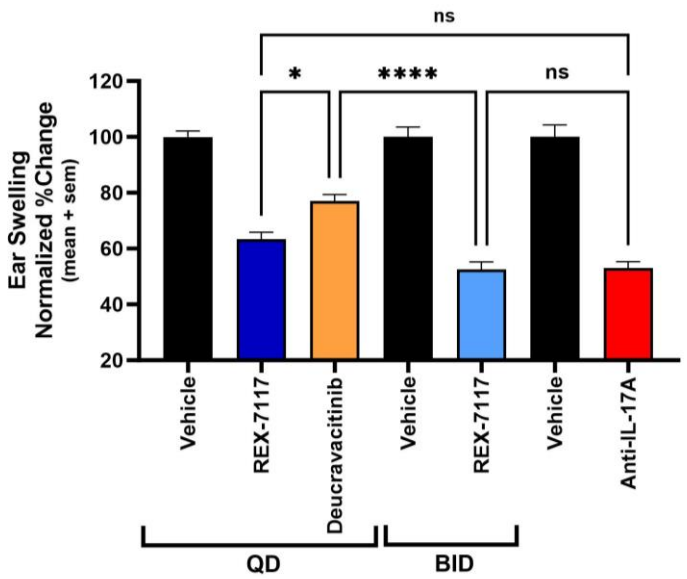
- Preclinical model used in the development of anti-IL-17 and anti-IL-23 biologics therapies
- REX-7117 dose was selected to match PD profile to that observed in dog at 15 mg/kg QD
- Deucravacitinib clinically relevant dose determined from regulatory filings and publications

Mouse pSTAT3 Inhibiton



n = 8-13 per timepoint

IL-23 Induced Psoriasis Model



Deucravacitinib 1mg/kg is the estimated clinically relevant dose
Anti-IL-17A = Mouse surrogates of Cosentyx®

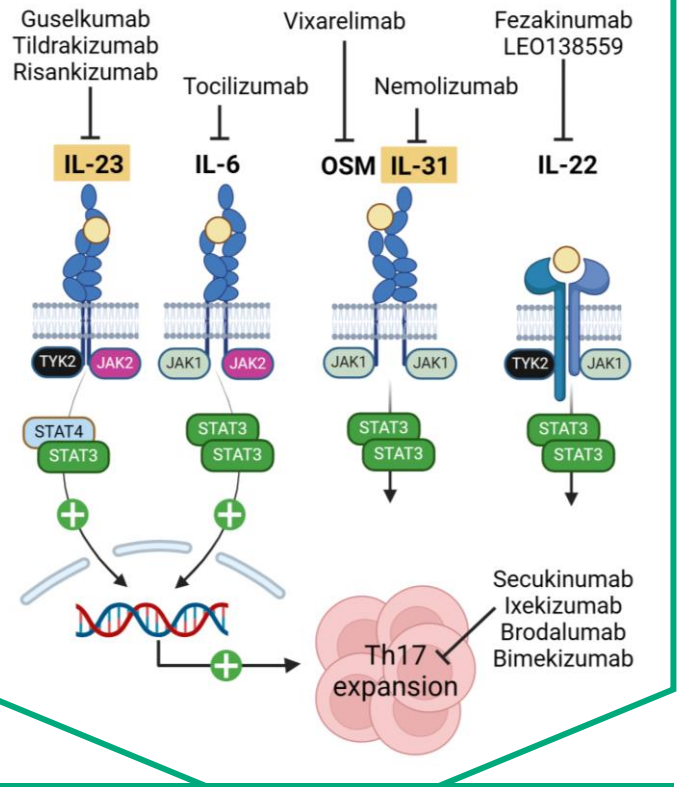
*P < 0.05
****P < 0.0001
ns – not significant

STAT3 Inhibition Selectively Targets Key Inflammatory Cytokines and Downstream Th17 Cell Pathogenesis

Recludix Pharma

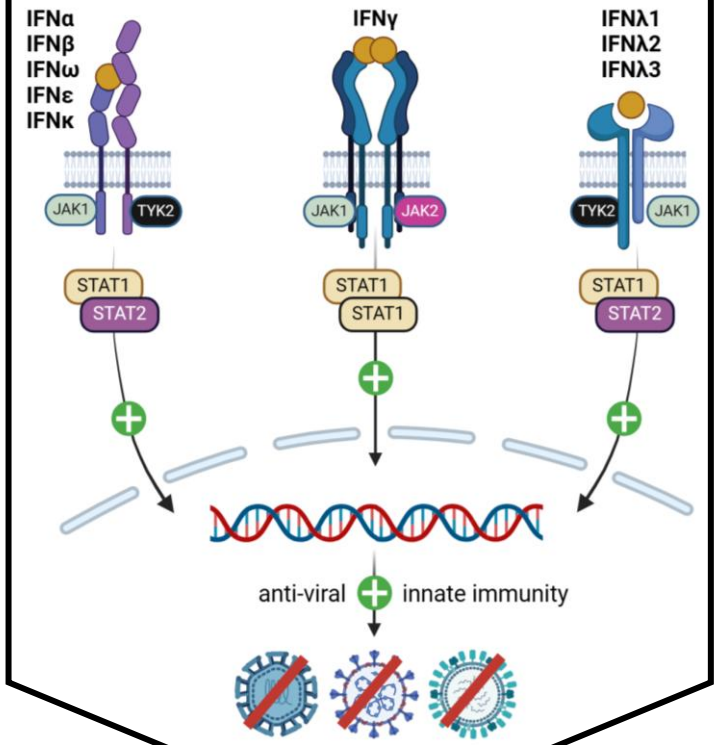
Selective STAT3 inhibitors have potential JAK/TYK2 safety differentiation advantages

Pro-inflammatory cytokines



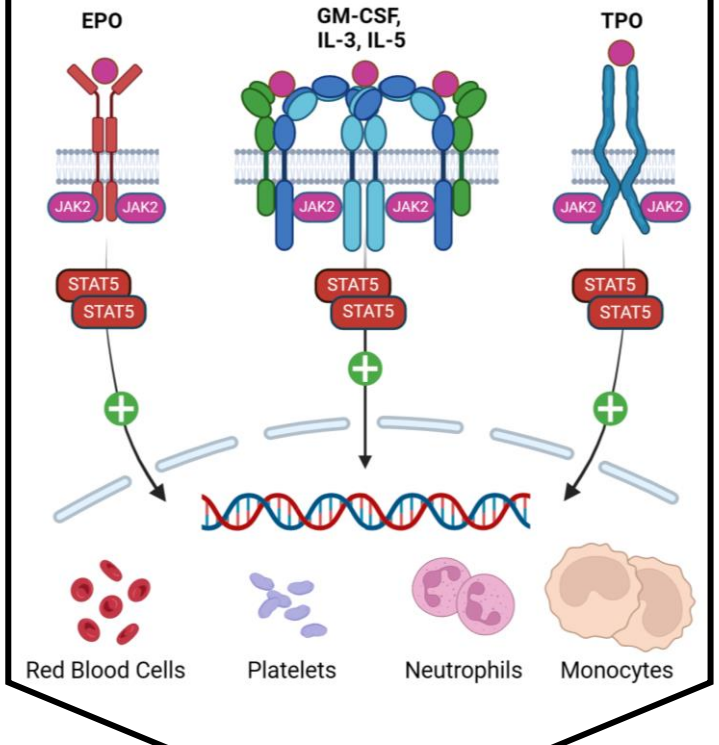
Clinical Efficacy

Anti-Viral Immunity



Opportunistic Infections

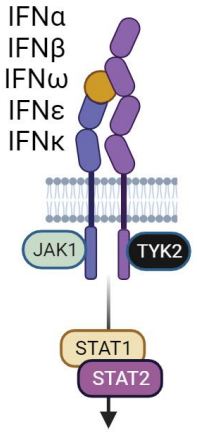
Hematologic Homeostasis

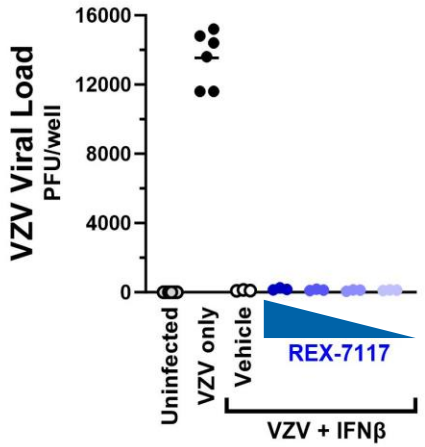


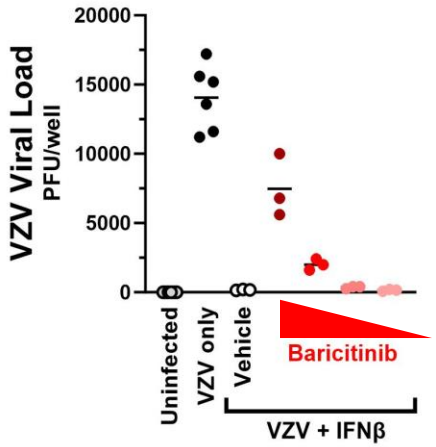
Anemia, Thrombocytopenia, Neutropenia

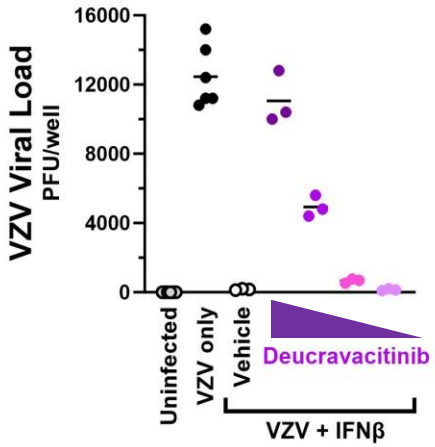
Selectively STAT3 Inhibitors Do Not Impair Interferon-Mediated Inhibition of Viral Replication Unlike JAK/TYK2 Inhibitors

Type I IFNβ: Varicella Zoster Virus (VZV)

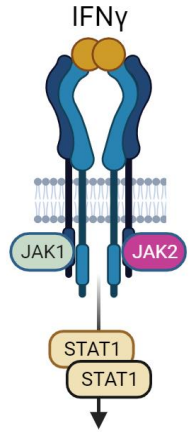


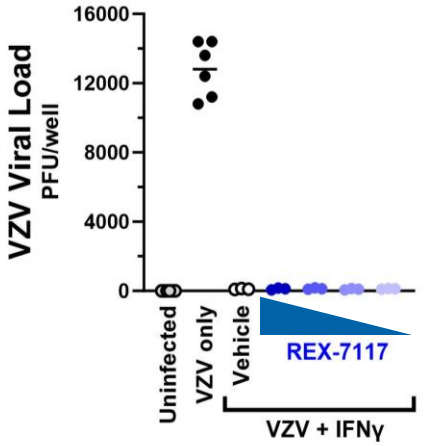


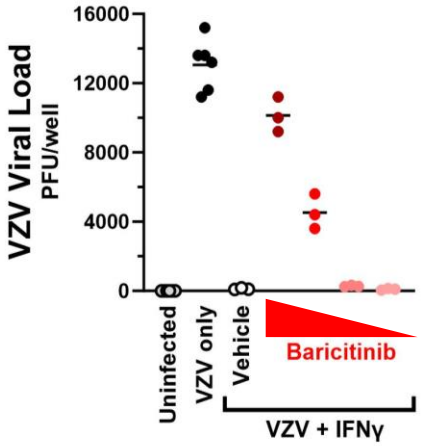


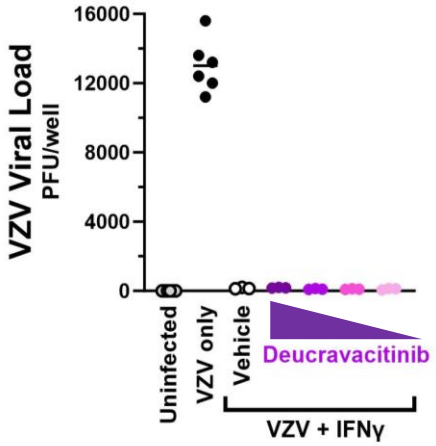


Type II IFNγ: Varicella Zoster Virus (VZV)







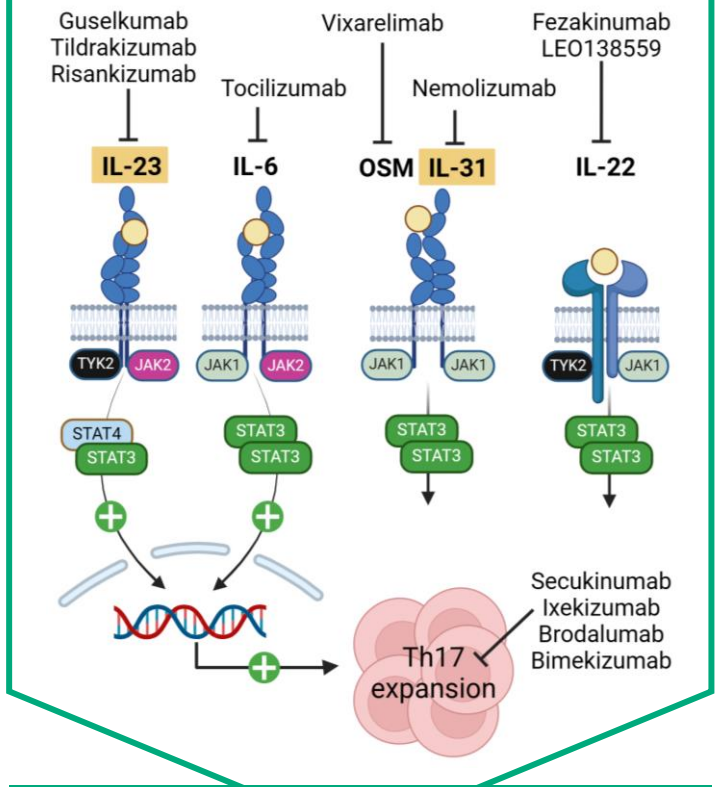


STAT3 Inhibition Selectively Targets Key Inflammatory Cytokines and Downstream Th17 Cell Pathogenesis

Recludix Pharma

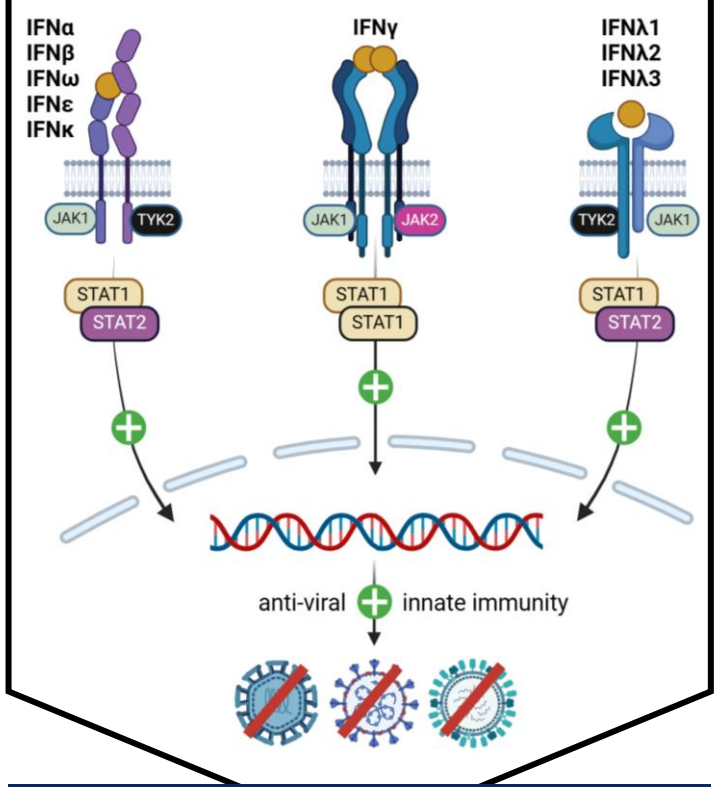
Selective STAT3 inhibitors have potential JAK/TYK2 safety differentiation advantages

Pro-inflammatory cytokines



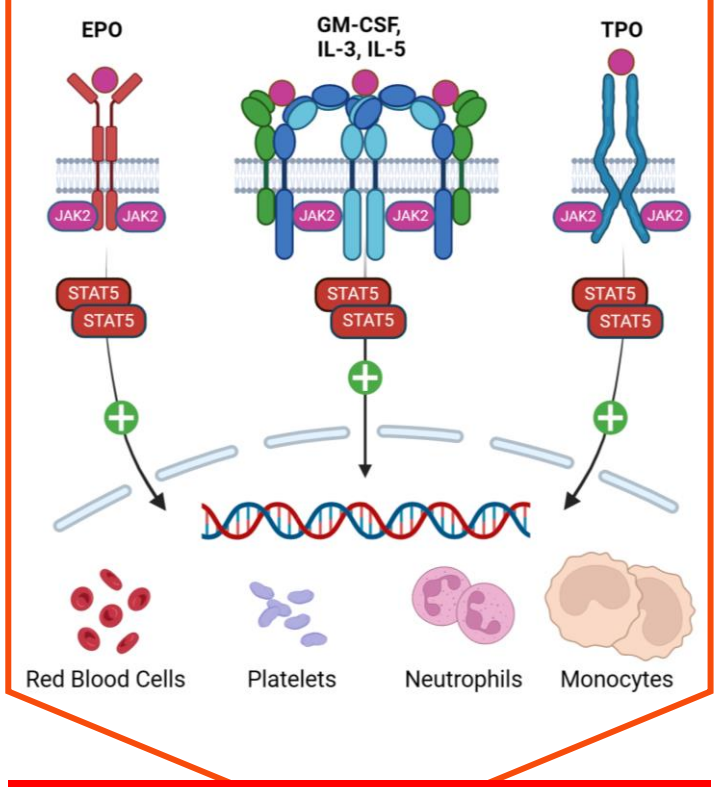
Clinical Efficacy

Anti-Viral Immunity



Opportunistic Infections

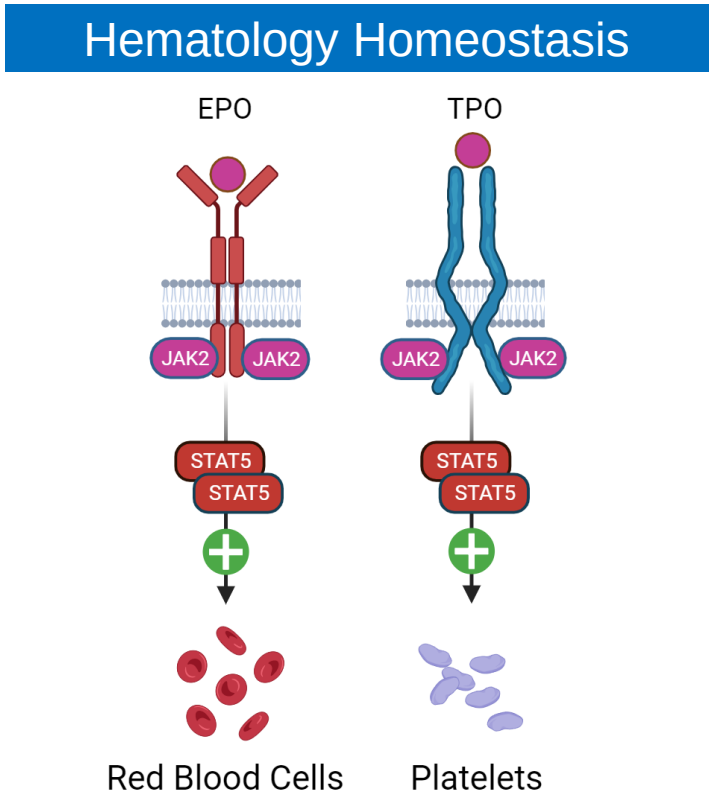
Hematologic Homeostasis



Anemia, Thrombocytopenia, Neutropenia

Targeting STAT3 Spares STAT5 Mediated Hematopoietic Signaling

JAK inhibitors impair hematopoietic signaling at equivalent concentrations to their anti-inflammatory mechanism of action



Erythropoietin (EPO) or Thrombopoietin (TPO) mediated pSTAT5 signaling in reporter cell lines		STAT3-driven Inflammation	Hematopoiesis	
			Erythropoiesis	Thrombopoiesis
		IL-6-Driven pSTAT3 Activation in PBMCs (IC_{50})	EPO-Induced STAT5-Driven Transcription (IC_{50})	TPO-Induced STAT5-Driven Transcription (IC_{50})
STAT3 Inhibitors	**REX-5376**	**6 nM**	**>10,000 nM**	**>10,000 nM**
	REX-7117	**1 nM**	**>10,000 nM**	**>10,000 nM**
TYK2 Inhibitors	Deucravacitinib	**140 nM**	3,200 nM	250 nM
	TAK-279	**>10,000 nM**	>10,000 nM	>10,000 nM
JAK Inhibitors	Tofacitinib	**110 nM**	340 nM	200 nM
	Upadacitinib	**48 nM**	69 nM	20 nM
	Baricitinib	**28 nM**	55 nM	46 nM

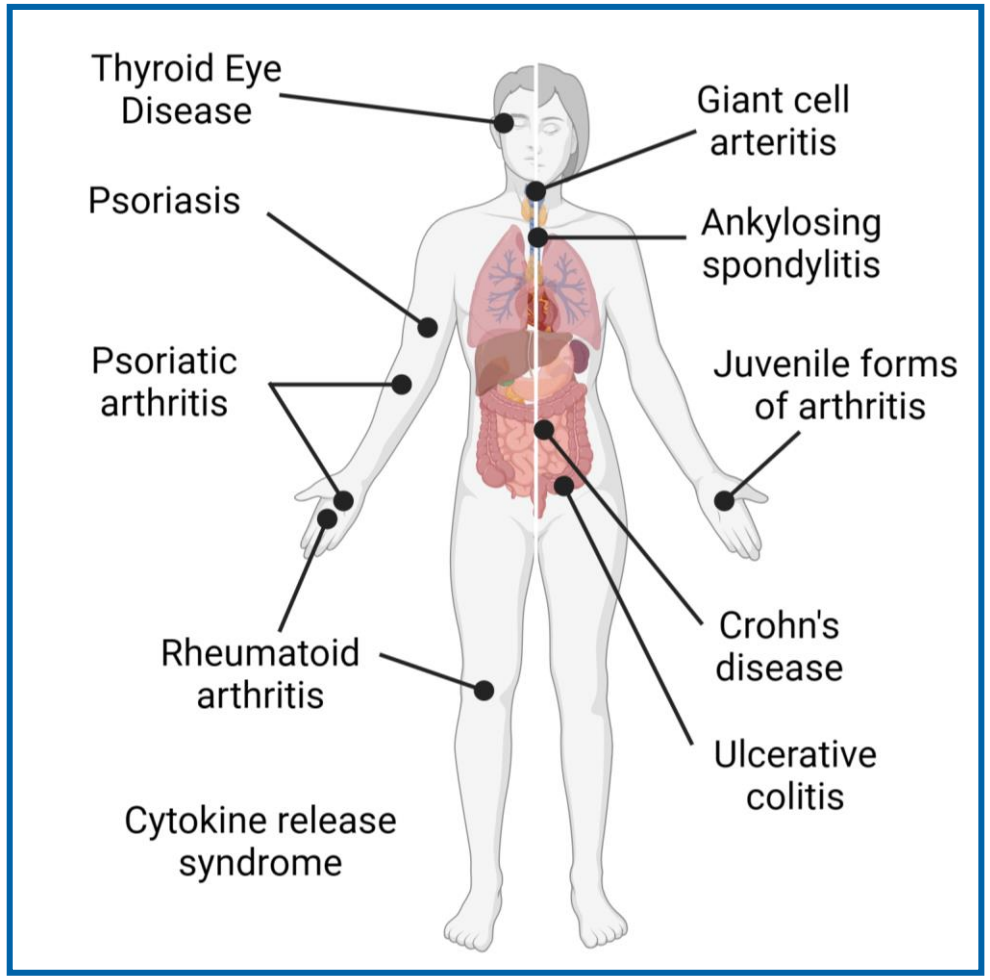
Selectivity relative to PBMC pSTAT3 inhibition: >30X 10-30X <10X

STAT3 Inhibition Has Potential Clinical Applications Across Multiple I&I Diseases

Leveraging clinically validated mechanisms with selective STAT3 inhibition

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 >$10.8B in 2023



Thank you

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Unlocking New Therapeutic Possibilities