Soquelitinib Phase 1 Trial in Atopic Dermatitis

Initial results from Cohorts 1 and 2

December 18, 2024

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Forward-Looking Statements / Safe Harbor

This presentation and the accompanying oral presentation contain “forward-looking” statements, including statements related to the potential safety and efficacy of soquelitinib, ciforadenant and mupadolimab; the Company’s ability and Angel Pharmaceutical’s ability to develop and advance product candidates into and successfully complete preclinical studies and clinical trials, the timing of the availability and announcement of clinical data and certain other product development milestones, including the timing of results in the Phase 1/1b clinical trial of soquelitinib in PTCL, the Phase 1 trial in atopic dermatitis, the Phase 1b/2 clinical trial of ciforadenant and the Phase 3 trial of soquelitinib in PTCL. All statements other than statements of historical fact contained in this press release are forward-looking statements. These statements often include words such as “believe,” “expect,” “anticipate,” “intend,” “plan,” “estimate,” “seek,” “will,” “may” or similar expressions. Forward-looking statements are subject to a number of risks and uncertainties, many of which involve factors or circumstances that are beyond the Company’s control. The Company’s actual results could differ materially from those stated or implied in forward-looking statements due to a number of factors, including but not limited to, risks detailed in the Company’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, filed with the Securities and Exchange Commission (the “SEC”) on or about November 12, 2024, as well as other documents that may be filed by the Company from time to time with the SEC. In particular, the following factors, among others, could cause results to differ materially from those expressed or implied by such forward-looking statements: the Company’s ability to demonstrate sufficient evidence of efficacy and safety in its clinical trials of soquelitinib, ciforadenant or mupadolimab; the accuracy of the Company’s estimates relating to its ability to initiate and/or complete preclinical studies and clinical trials; delays in the clinical trial process; our ability to enroll subjects in our planned clinical trials; the results of preclinical studies not being predictive of future results; the unpredictability of the regulatory process; regulatory developments in the United States and other foreign countries; the costs of clinical trials exceeding expectations; and the Company’s ability to raise additional capital. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the events and circumstances reflected in the forward-looking statements will be achieved or occur, and the timing of events and circumstances and actual results could differ materially from those projected in the forward-looking statements. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and the Company undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise. This presentation concerns products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. Such products are currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

Key Highlights from Soquelitinib Early Phase 1 Data

1. Favorable safety and efficacy results
2. Attractive and competitive product profile
3. Proof-of-concept for broad immune disease opportunity

Soquelitinib Combines Favorable Drug Properties

A unique target effecting multiple immune functions

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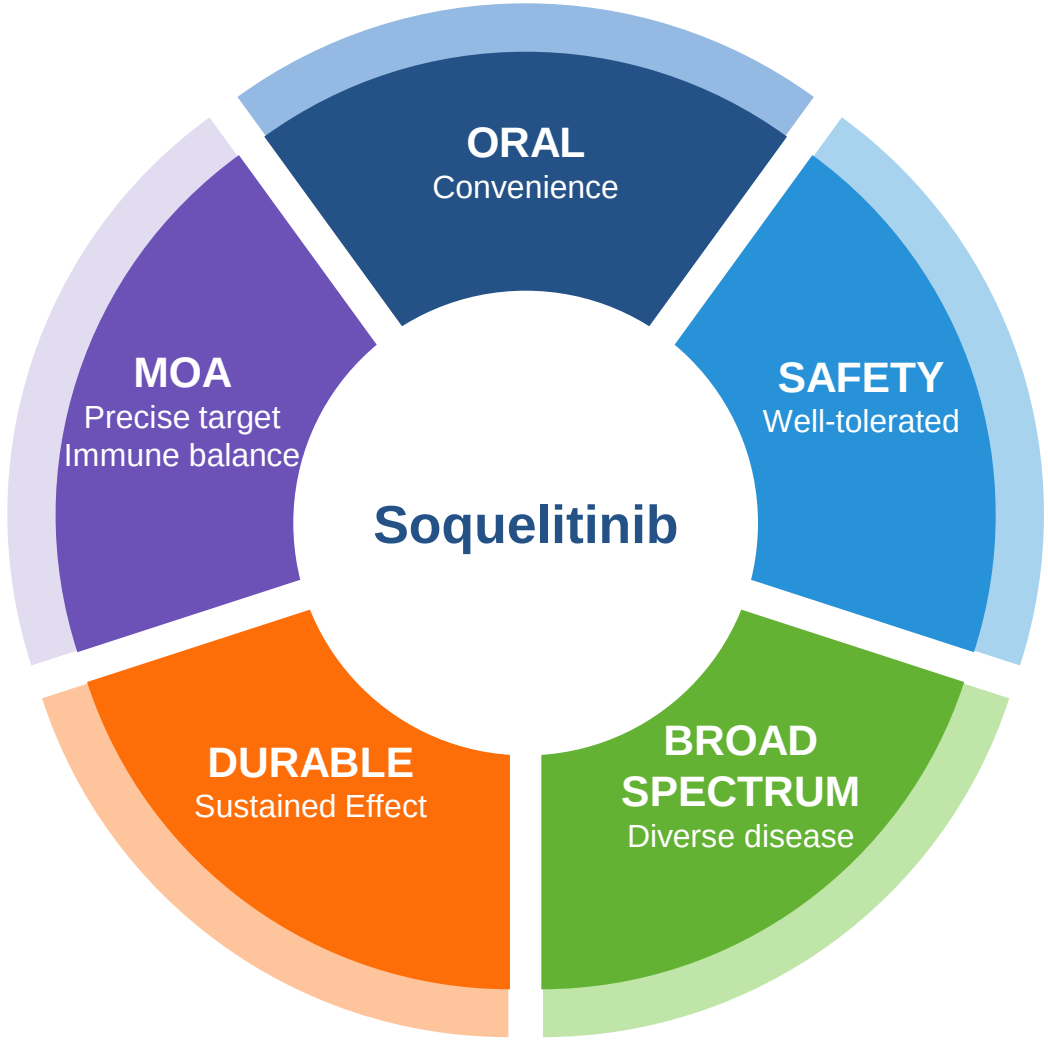
Bridge between topicals and injectables

- Convenient oral medication
- Potential for biologics-like efficacy with favorable safety and tolerability profile

Novel MOA to effect multiple parallel signaling pathways in immune cells provides features of:

- Durability of action
- Diverse indications



Soquelitinib Blocks Th2 and Th17 and Induces Th1 Skewing

Target for cancer, autoimmune and inflammatory diseases

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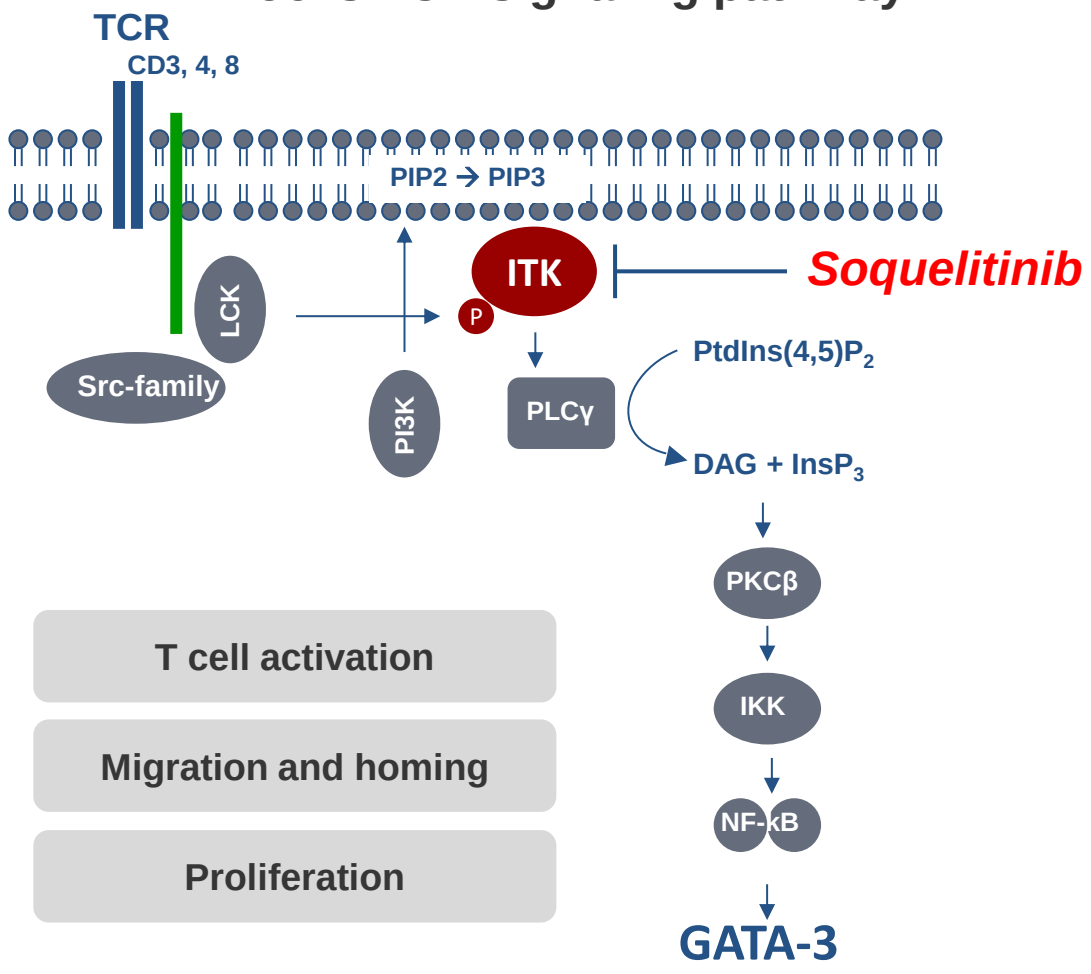
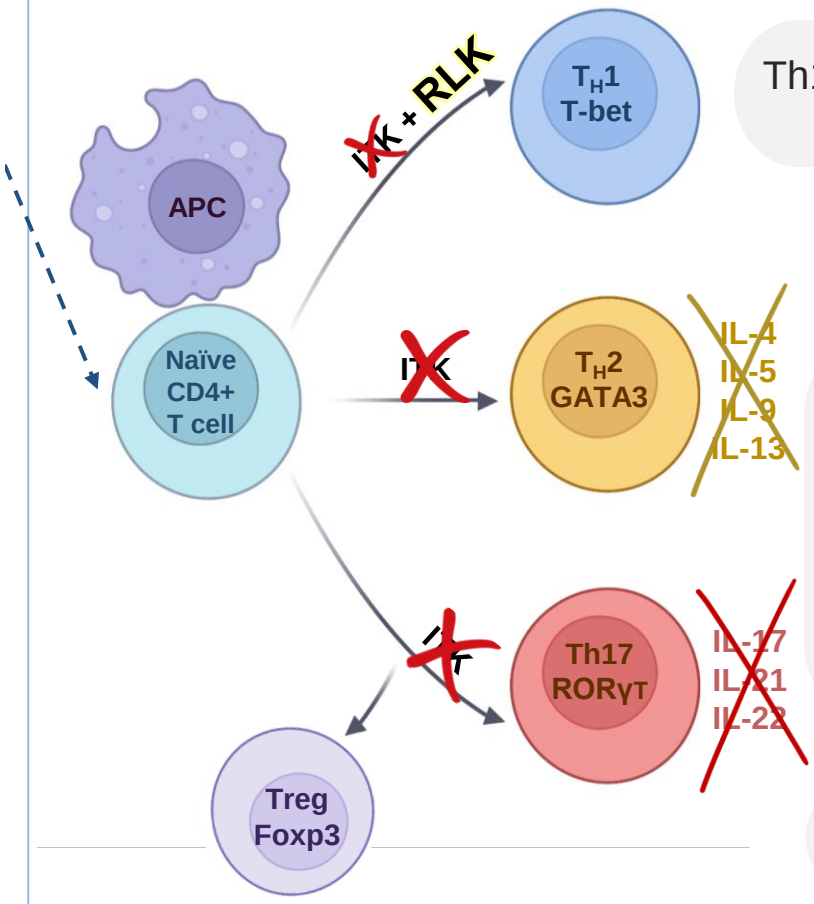
Blocks TCR signaling pathway



- T cell activation
- Migration and homing
- Proliferation

ITK blockade leads to increase in Th1 and reduction in Th2, Th17 "Th1 skewing"



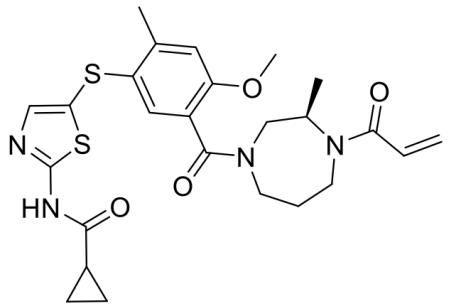
Th1 cells play a role in cancer cell and viral elimination

Th2 and Th17 cells are involved in autoimmune, inflammatory, fibrotic and allergic diseases

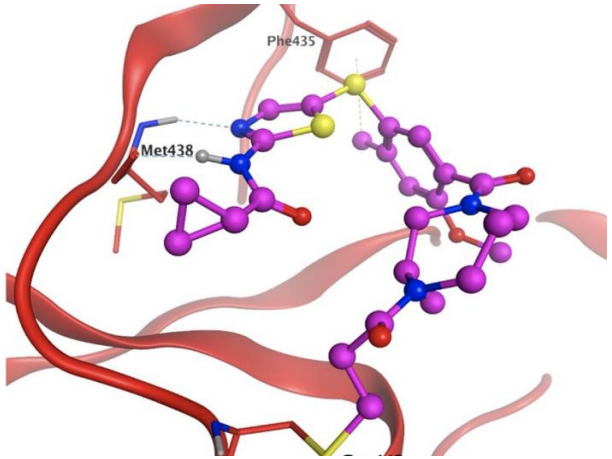
Treg suppresses inflammation

Chemistry Discovery Efforts Focused on Covalency and ITK Selectivity To Create Highly Differentiated and Unique Drug Properties

Chemical Structure



Covalently Bound to ITK (Model)

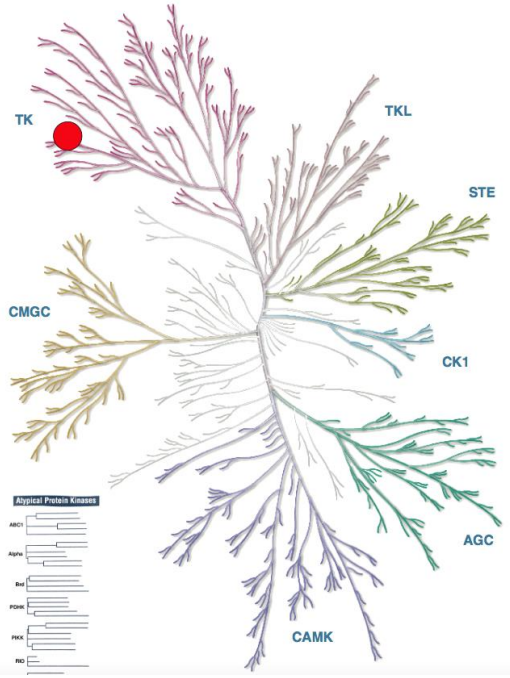


Kinase Binding Comparison to Ibrutinib

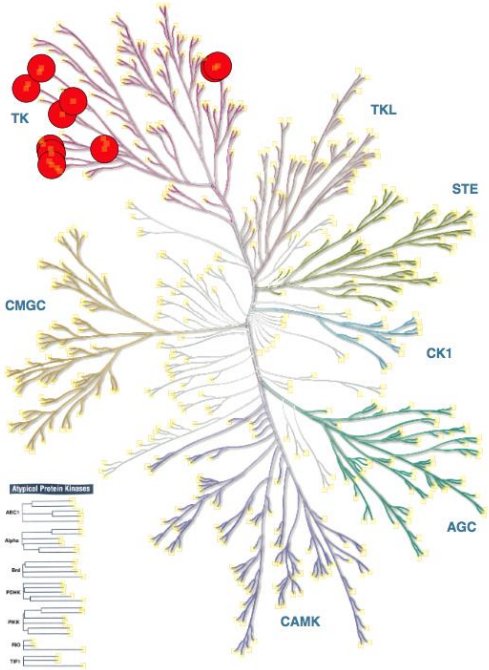
Specificity of Binding

Kinase	Ibrutinib Kd (nM)	Soquelitinib Kd (nM)
ITK	29.2	6.5
BLK	0.19	4700
BMX	0.72	9100
BTK	0.42	1200
EGFR	2.5	>10000
ERBB2	ND	>10000
ERBB4	ND	>10000
JAK3	13	2800
MKK7	ND	>10000
TEC	0.45	540
RLK	0.52	2700

Soquelitinib

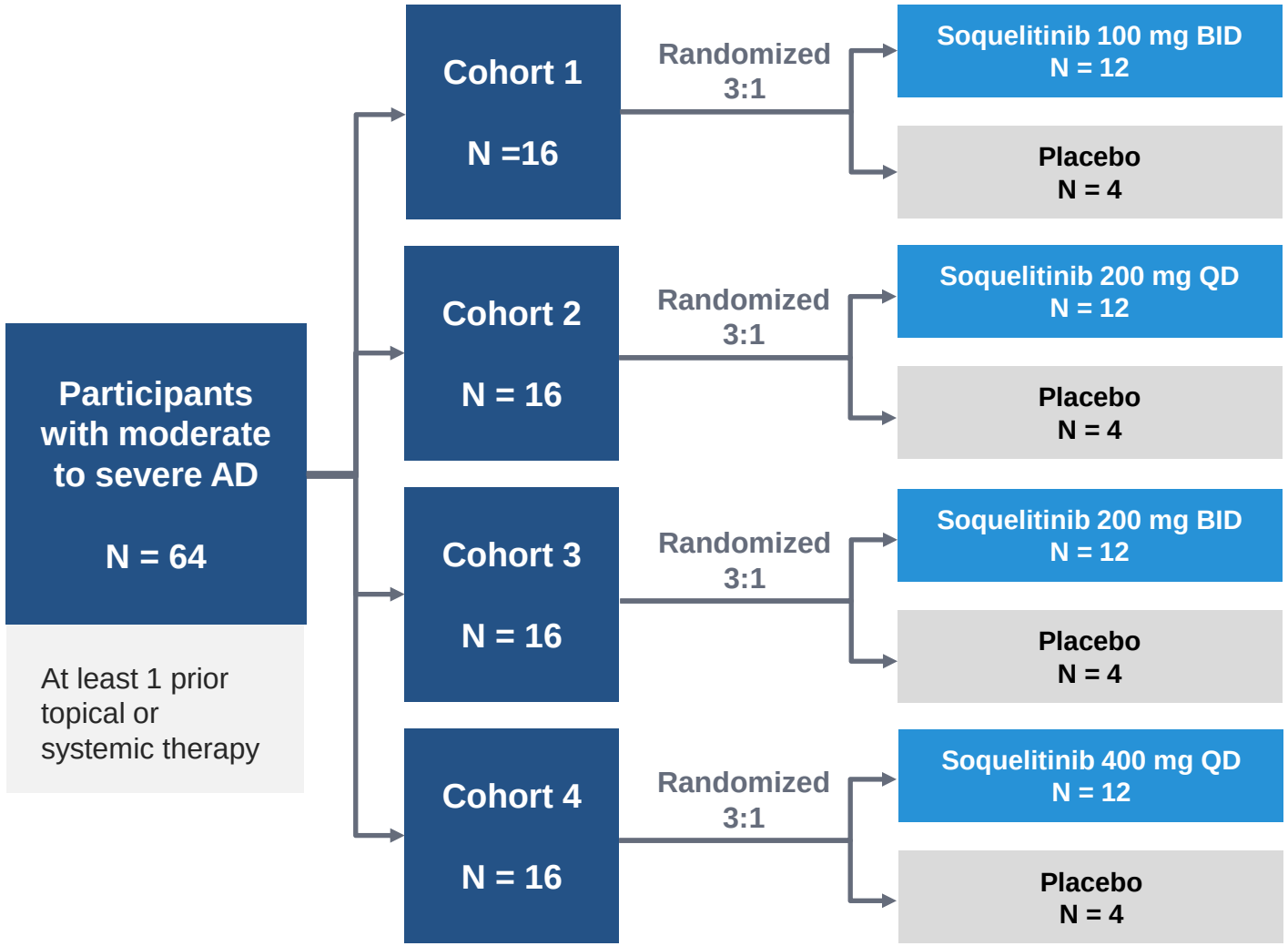


Ibrutinib



Clinical Trial Design

Randomized placebo controlled



Key Details

Rationale: ITK inhibition will block Th2, Th17

Design: Randomized, placebo-controlled, blinded study in moderate to severe AD

- 4 dose cohorts vs placebo **treat for 28 days; 30 day follow-up**
- **Primary endpoint:** Safety and tolerability
- **Secondary endpoints:** Efficacy – based on EASI, IGA
    - PROs – Patient reported improvement in disease symptoms
    - Biomarker – Serum cytokines

DRC & Corvus will be unblinded – DRC and Corvus will monitor clinical data

Soquelitinib Target Occupancy In Peripheral Blood T cells

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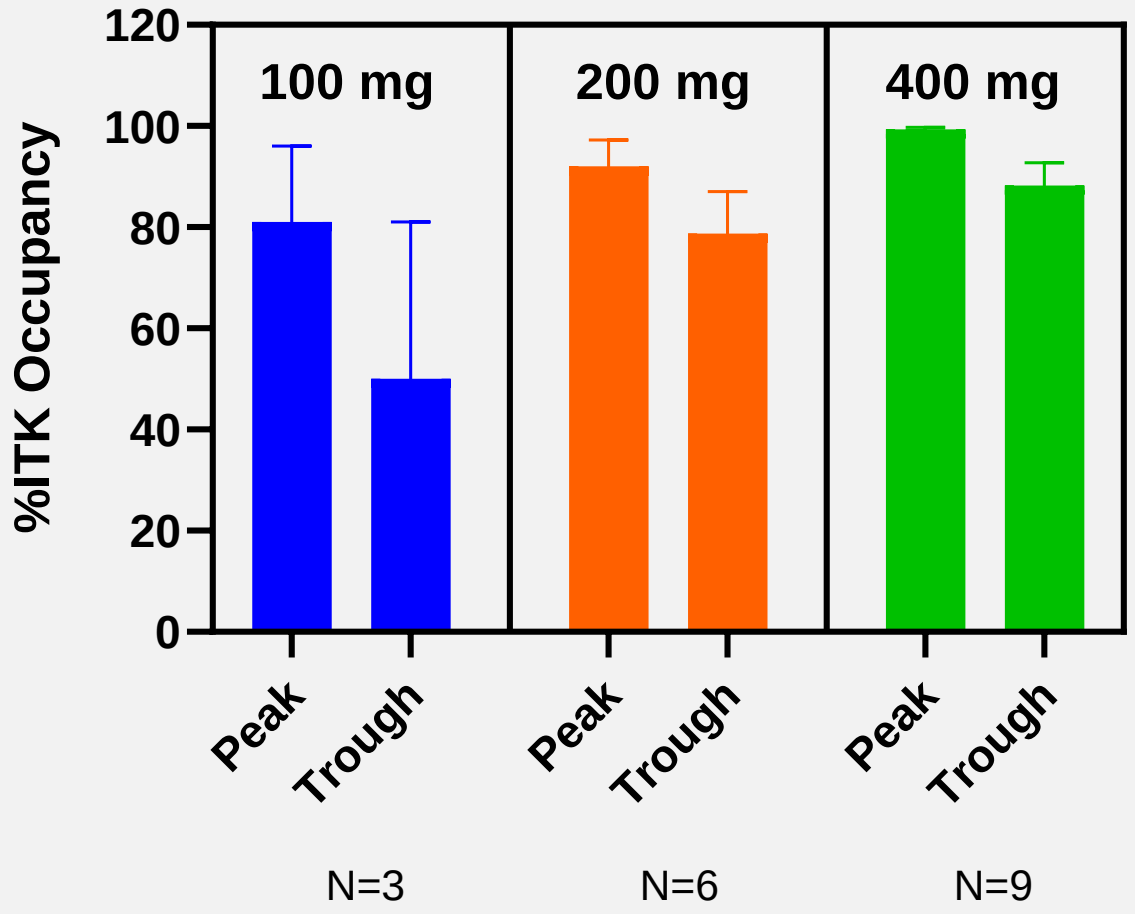
Doses of 200mg and higher provide maximal target occupancy



Soquelitinib Atopic Dermatitis Clinical Trial

Patient Characteristics: Cohort 1

	Soquelitinib (N=12)	Placebo (N=4)
Age, mean (range), yrs	46.3 (30–66)	50.5 (32–62)
Gender, male n (%)	7 (58.3)	4 (100)
Race/ethnicity, n (%)		
Asian	2 (16.7)	0 (0)
Black or African American	6 (50)	4 (100)
White	3 (25)	0 (0)
Hispanic or Latino	1 (8.3)	0 (0)
Baseline EASI, mean (range)	20.4 (15.0–46.6)	18.5 (14.9–24.8)
Baseline IGA, mean (range)	3.0 (2-4)	3.3 (3–4)
Prior AD therapies, n (%)		
Topical Corticosteroids	11 (91.7)	4 (100)
Systemic therapies	3 (25)	2 (50)
Concomitant topical steroids	0 (0)	1 (25)

Soquelitinib Efficacy Results

Treatment for 4 weeks with Day 58 follow-up

	Soquelitinib (Cohort 1)			
	Phase 1			
	4 week		8 week (Day 58)	
	Placebo (N=4)	Active *Cohort 1* (N=12)	Placebo (N=4)	Active *Cohort 1* (N=10)
Change EASI Mean % Reduction	27.0	55.9	19.1	69.1
EASI 50 (%pts)	50	75	25	90
EASI 75 (%pts)	0	25	0	40
EASI 90 (%pts)	0	8	0	10
IGA 0 or 1 (%pts)	0	25	0	30

Soquelitinib Efficacy Response Kinetics Cohort 1

Treatment for 4 weeks with Day 58 follow-up

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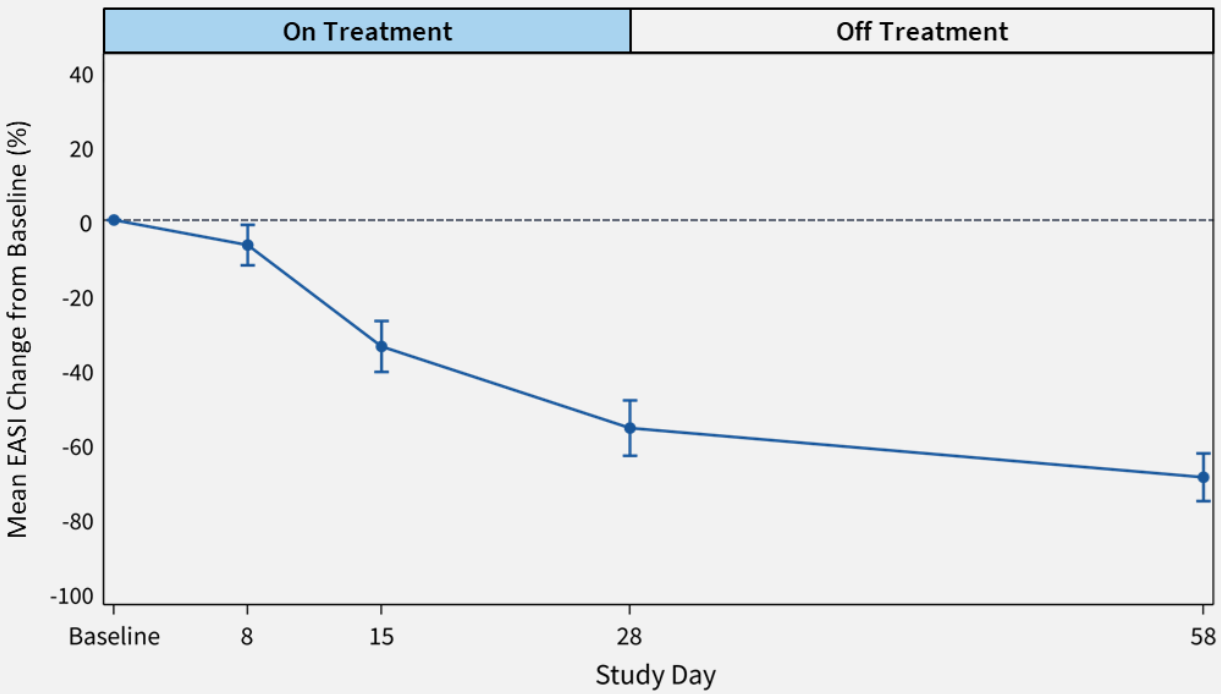
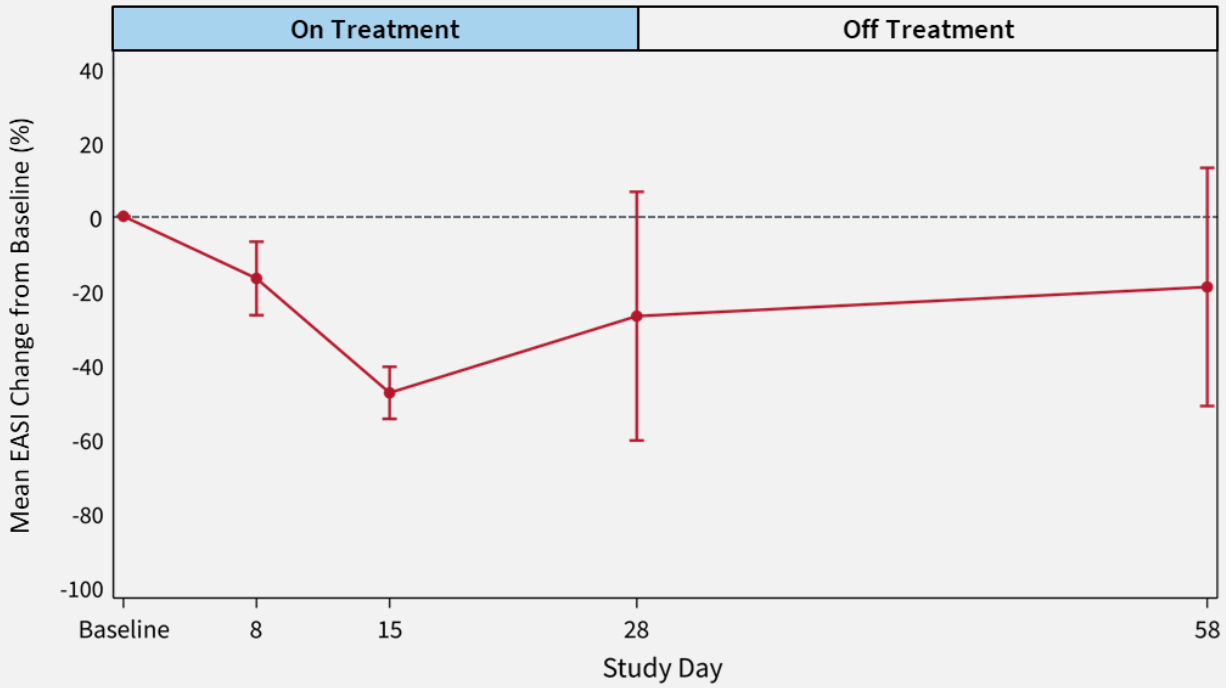
Soquelitinib



- Soquelitinib treated patients show continuous reduction in EASI score
- Continued improvement beyond treatment period

Placebo



- Placebo group demonstrates minimal change over the course of the study

Soquelitinib Efficacy Comparisons to Ph1 Dupixent Trial

Treatment results for 4 weeks in Cohort 1

	Soquelitinib (Cohort 1)		Dupixent	
	Phase 1		Phase 1 [a]	
	4 week		4 week	
	Placebo (N=4)	Active (N=12)	Placebo (N=16)	Active *300/150 mg QW* (N=51)
Change EASI Mean % Reduction	27.0	55.9	25.4	57.7
EASI 50 (%pts)	50	75	19	59
EASI 75 (%pts)	0	25	6	29
EASI 90 (%pts)	0	8	NR	NR
IGA 0 or 1 (%pts)	0	25	6	12

Dupixent 300mg or 150mg SC given weekly in Ph1.
NR = not reported

[a] NEJM 371:130, 2014

Soquelitinib Comparisons to Ph1 Dupixent Trial

Treatment results for 4 weeks with Day 58 follow-up

	Soquelitinib				Dupixent			
	Phase 1				Phase 1 [a]			
	4 week		8 week (Day 58)		4 week		12 week	
	Placebo (N=4)	Active *Cohort 1* (N=12)	Placebo (N=4)	Active *Cohort 1* (N=10)	Placebo (N=16)	Active (N=51)	Placebo (N=54)	Active (N=55)
Change EASI Mean % Reduction	27.0	55.9	19.1	69.1	25.4	57.7	23.3	74.0
EASI 50 (%pts)	50	75	25	90	19	59	35	85
EASI 75 (%pts)	0	25	0	40	6	29	15	62
EASI 90 (%pts)	0	8	0	10	NR	NR	NR	NR
IGA 0 or 1 (%pts)	0	25	0	30	6	12	7	40

NR = not reported

[a] NEJM 371:130, 2014

12 week regimen 300 mg SC weekly

Soquelitinib Comparisons to Ph1 and Ph 3 Dupixent Trials

Treatment results for 4 weeks with Day 58 follow-up

	Soquelitinib				Dupixent			
	Phase 1				Phase 1 [a]		Phase 3 [b]	
	4 week		8 week (Day 58)		12 week		SOLO 1 / 2 (16 weeks)	
	Placebo (N=4)	Active *Cohort 1* (N=12)	Placebo (N=4)	Active *Cohort 1* (N=10)	Placebo (N=54)	Active (N=55)	Placebo (N=224/236)	Active (N=224/233)
Change EASI Mean % Reduction	27.0	55.9	19.1	69.1	23.3	74.0	37.6/30.9	72.3/67.1
EASI 50 (%pts)	50	75	25	90	35	85	25/22	69/65
EASI 75 (%pts)	0	25	0	40	15	62	15/12	51/44
EASI 90 (%pts)	0	8	0	10	NR	NR	8/7	36/30
IGA 0 or 1 (%pts)	0	25	0	30	7	40	10/8	38/36

Dupixent given weekly in Ph1 and q1 or q2 weeks in SOLO for 16 weeks.
NR= not reported

[a] NEJM 371:130, 2014
[b] NEJM 375: 2335, 2016

Soquelitinib Cohort 1 Safety Summary

	Soquelitinib (N=12)	Placebo (N=4)
Subjects with AEs	2*	0
Serious AEs	0	0
AEs leading to study drug discontinuation	0	0
AEs leading to death	0	0
Treatment-related AEs		
Nausea (Grade 1)	1	0

**Reported AEs: Nausea (N=1) and Covid-19 (N=1); both resolved without any dose modification*

- No clinically significant laboratory abnormalities
- Safety observed in over 100 patients with lymphoma and atopic dermatitis
- Experience in approximately 9,000 patient-treatment days

Relationship of Serum Cytokine Changes to EASI-50 Response with Soquelitinib

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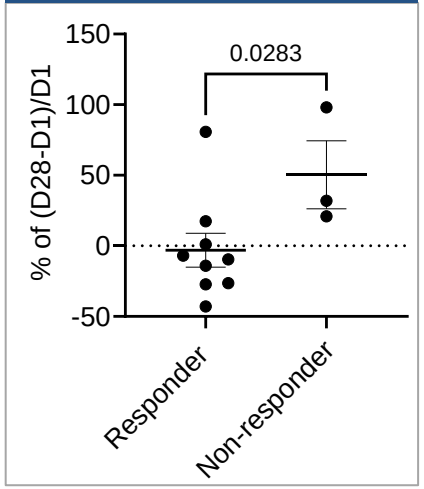
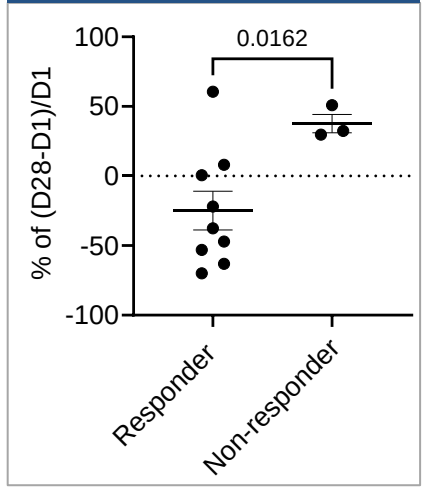
IL-5



TSLP



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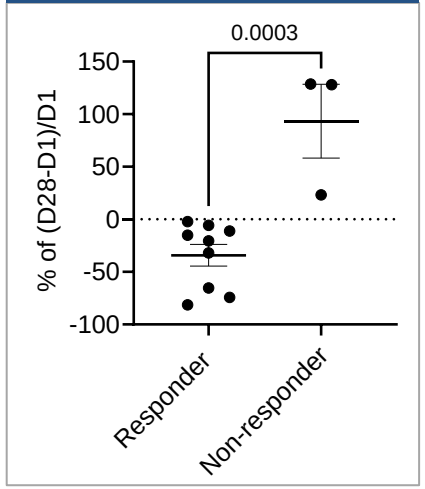

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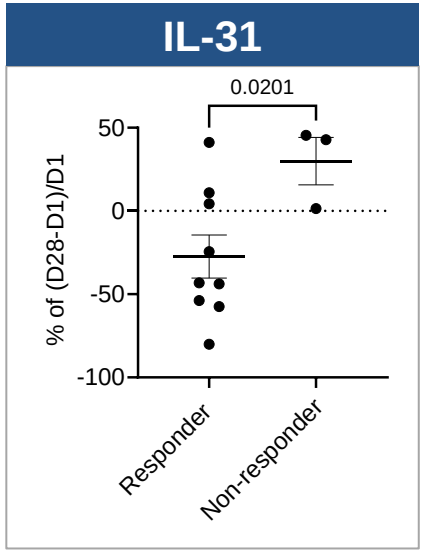

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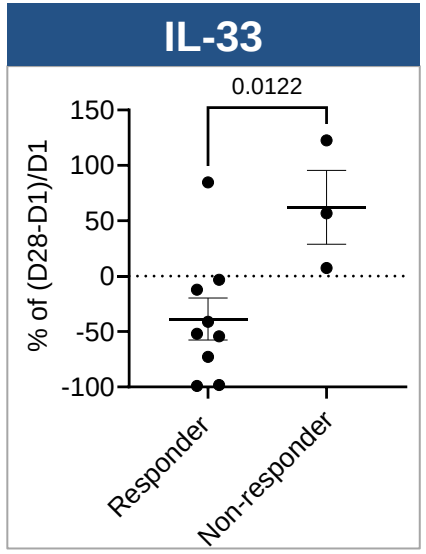
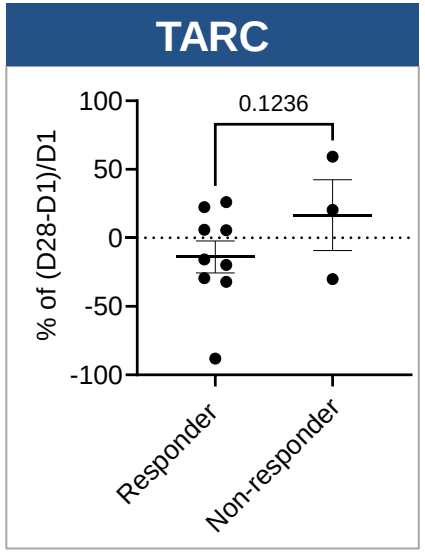


TARC



Overview

- Cytokine levels measured at baseline and after 28 days treatment
- Change in cytokine levels after 28 days compared to baseline (each dot represents a patient)
- Significant difference in EASI 50 responders (N=9) compared to non-responders (N=3); (TARC trend)
- Other cytokines may have short serum half-lives making measurements challenging

No Relationship of Serum Cytokine Changes to Response with Placebo

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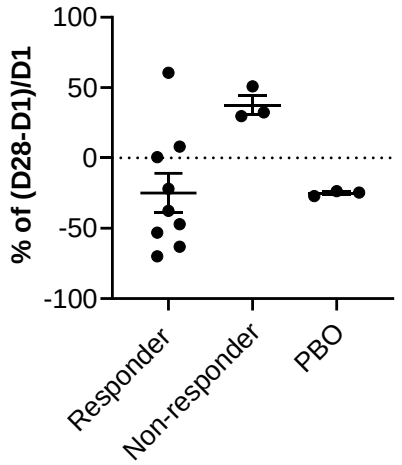

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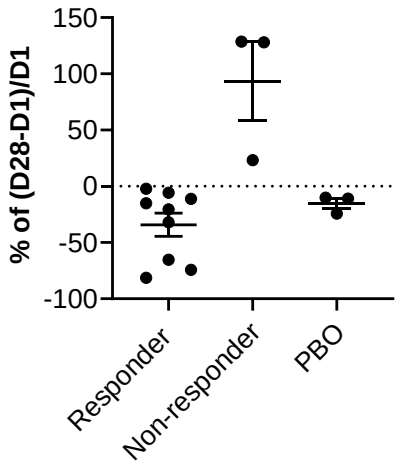

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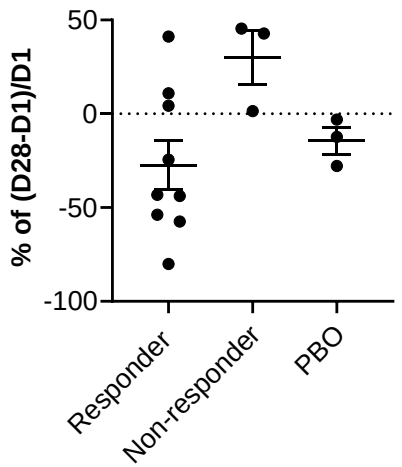

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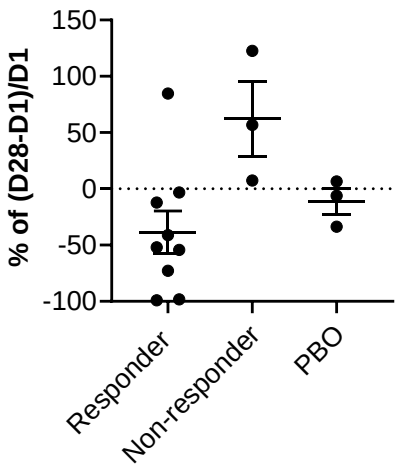


Overview

- Cytokine levels measured at baseline and after 28 days treatment
- Change in cytokine levels after 28 days compared to baseline (each dot represents a patient)
- Cytokine in placebo (PBO) patients show minimal changes

Soquelitinib Atopic Dermatitis Clinical Trial

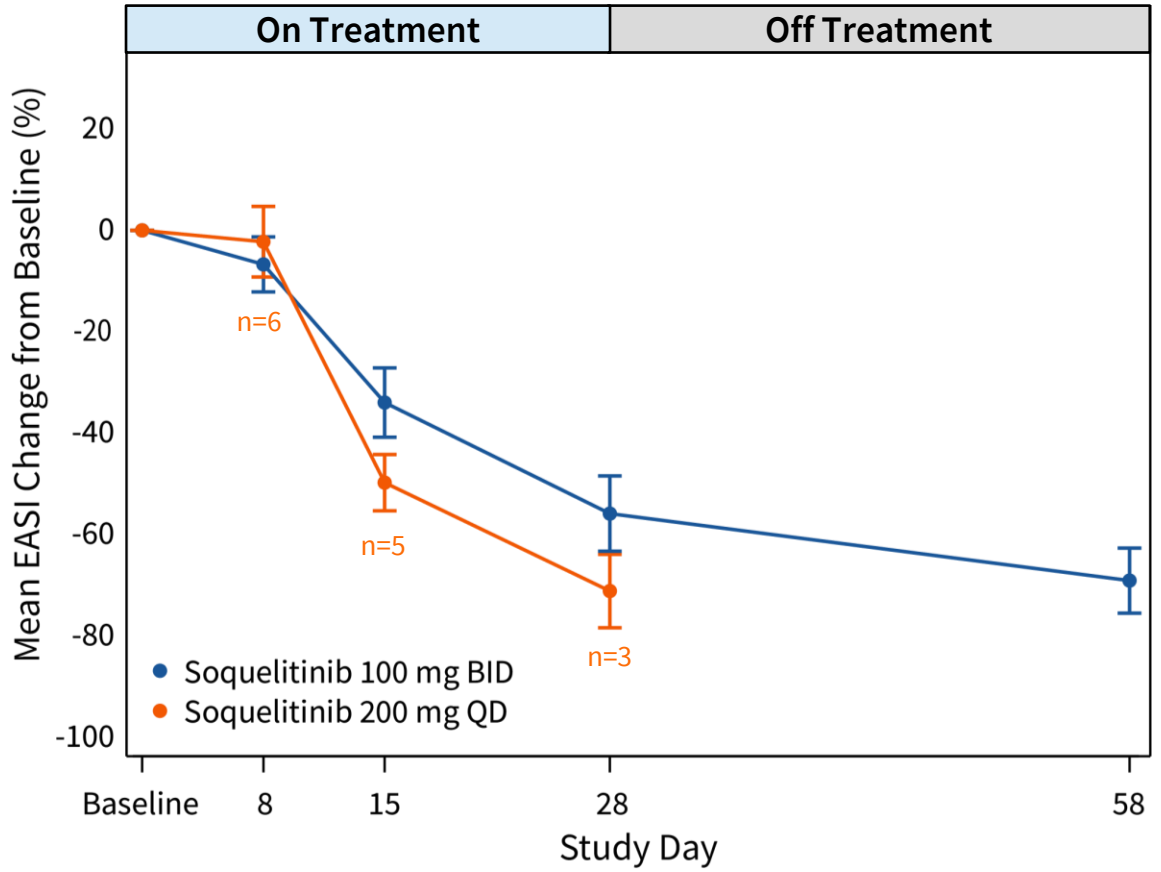
Preliminary Cohort 2 patient characteristics and EASI change

Cohort 2 Patient Characteristics

	Soquelitinib 200 mg QD (N=6)	Placebo (N=3)
Age, mean (range), yrs	48.8 (21–63)	40.0 (27–50)
Gender, male n (%)	4 (66.7)	0 (0)
Race/ethnicity, n (%)		
Asian	0 (0)	0 (0)
Black or African American	3 (50)	1 (33.3)
White	0 (0)	0 (0)
Hispanic or Latino	3 (50)	2 (66.7)
Baseline EASI, mean (range)	18.7 (14.7–27.9)	16.8 (14.4–19.1)
Baseline IGA, mean (range)	3.2 (3–4)	3.0 (3–3)
Prior AD therapies, n (%)		
Topical corticosteroids	3 (50)	2 (66.7)
Systemic therapies	1 (16.7)	0 (0)
Concomitant topical steroids	0 (0)	0 (0)

Data cut: 07 Dec 2024

Cohorts 1 and 2 Mean EASI Change



Cohort 2 Adverse Events

- No AEs were reported in any patients

Soquelitinib Effects Multiple Inflammatory Pathways

Comparison to other agents

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	Th2				Th17			ILC2	Treg
	IL-4	IL-5	IL-13	IL-31	IL-17	IL-21	IL-22		
SOQUELITINIB®	✓	✓	✓	✓	✓	✓	✓	✓	↑
DUPIXENT®	✓		✓					✓	
EBGLYSS™			✓						
NEMLUVIO®				✓					
RINVOQ®	✓		✓	✓		✓			

SOQUELITINIB®

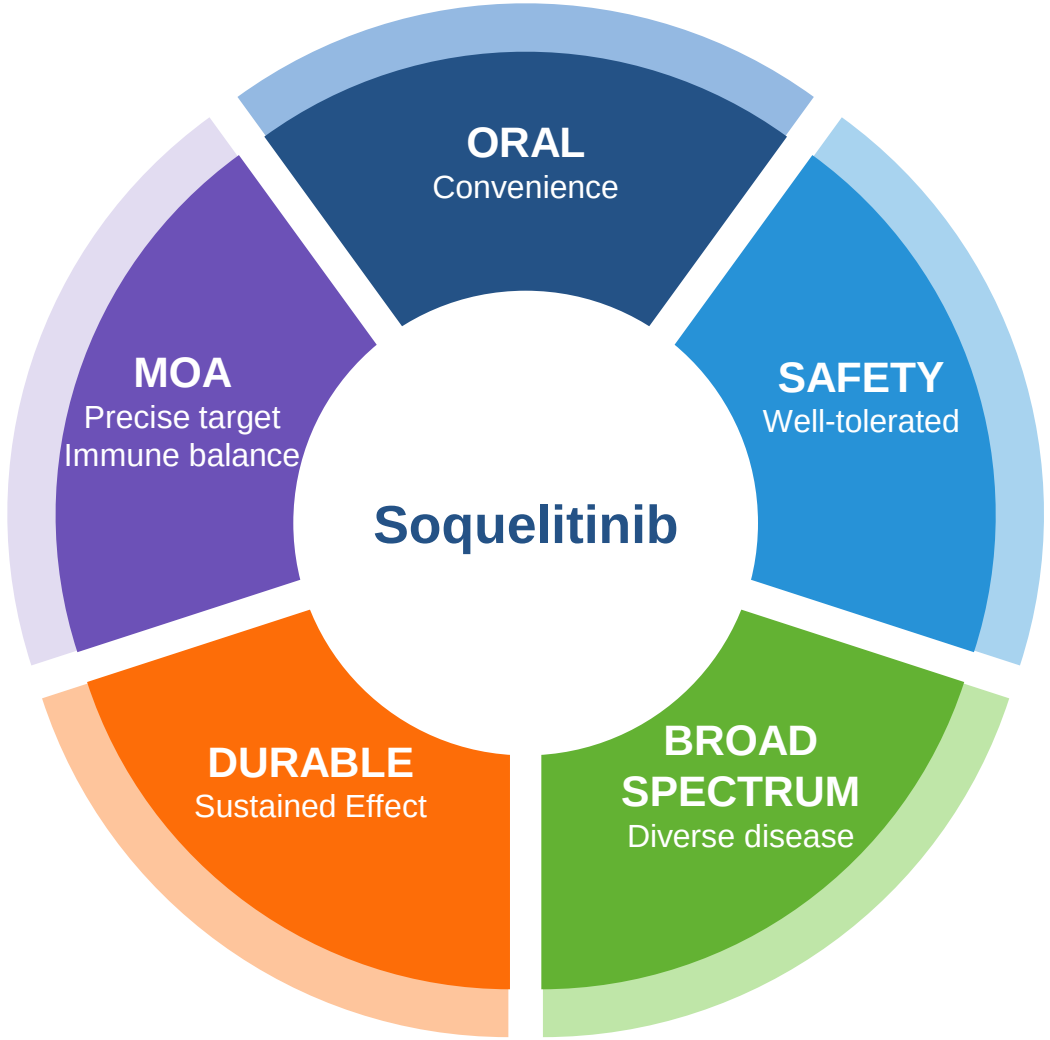
Inhibits cells responsible for production and control of many inflammatory cytokines

Restores immune balance by enhancing T regs

Promising Results from Initial Cohorts

Summary of early Phase 1 data

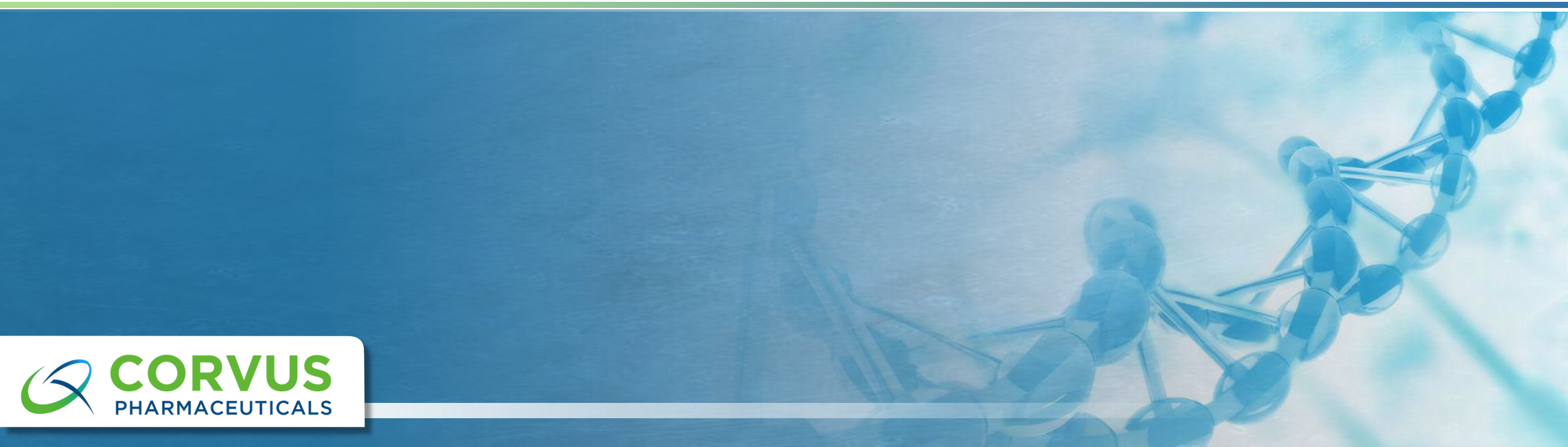
- Oral administration
- Novel MOA
- Safety seen in over 100 patients
  - Lymphoma
  - Phase 1 AD
- Preliminary efficacy seen in Phase 1 AD
- Cytokine changes related to EASI response
- Durable responses
- Potential for broad indications
- Dose optimization continues



Dr. Albert Chiou

Clinical Associate Professor, Dermatology and Director of Clinical Research in the Department of Dermatology at Stanford University Medical Center

Questions & Answers



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