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**Vixarelimab (KPL-716) Phase 2 Data**

*May 2020*



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## Vixarelimab Phase 2a Study in Prurigo Nodularis

# Summary of Vixarelimab Phase 2a Study in Prurigo Nodularis

**Enrolled and treated 49 patients with moderate-to-severe prurigo nodularis (mean PN- IGA of 3.4) experiencing moderate-to-severe pruritus (mean WI-NRS score of 8.3)**

- Randomized 1:1 to receive a loading dose of vixarelimab 720 mg (n=23) or placebo (n=26) subcutaneous (SC) followed by vixarelimab 360 mg or placebo SC weekly
- Data includes 49 subjects through the 8-week treatment period

**Primary Efficacy Endpoint:** percent change versus baseline in weekly-average WI-NRS at Week 8 (using the last observation carried forward analysis)

## **Topline Observations:**

- Least squares-mean change from baseline in weekly-average WI-NRS at Week 8 was -50.6% in vixarelimab recipients compared to -29.4% in placebo recipients (mean difference 21.1%; p=0.035)
- Median change from baseline in weekly-average WI-NRS at Week 8 was -69.8% in vixarelimab recipients compared to -36.1% in placebo recipients
- 30.4% of vixarelimab recipients achieved a PN-IGA score of 0/1 at Week 8 compared to 7.7% of placebo recipients (p=0.032)
- 52.2% of vixarelimab recipients demonstrated a  $\geq 4$ -point reduction in weekly-average WI-NRS at Week 8 compared to 30.8% of placebo recipients (p=0.109)
- In this Phase 2a trial, vixarelimab was well-tolerated by all subjects and no dose-limiting adverse experiences were observed. There were no serious adverse events or atopic dermatitis flares

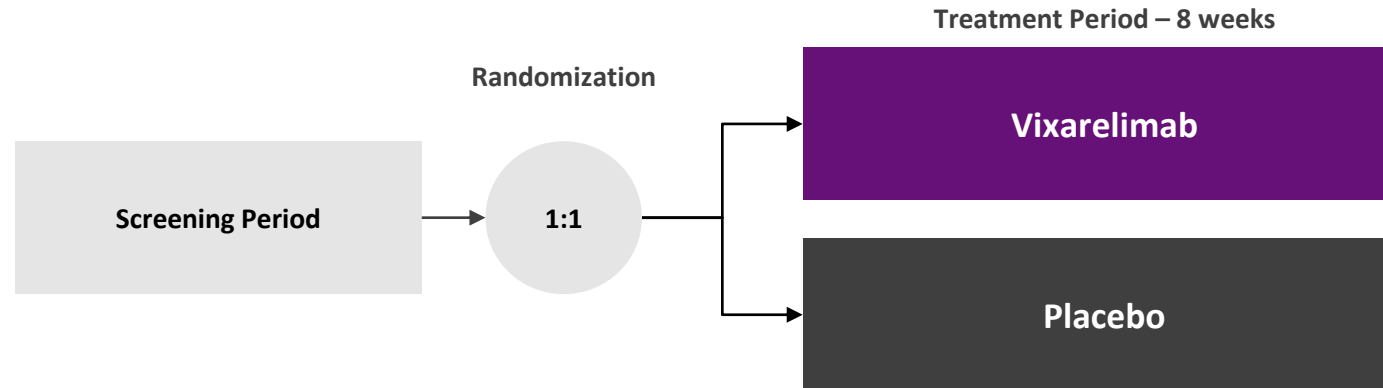
# Vixarelimab Phase 2a Trial in Prurigo Nodularis

## Phase 2a Proof-of-Concept

**Objective:** Assess pruritus reduction

**Dose:** 720 mg SC loading dose --> 360 mg single SC QW thereafter

**Primary Efficacy Endpoint :** % change from baseline in weekly average Worst Itch-Numeric Rating Scale (WI-NRS)



### Inclusion Criteria

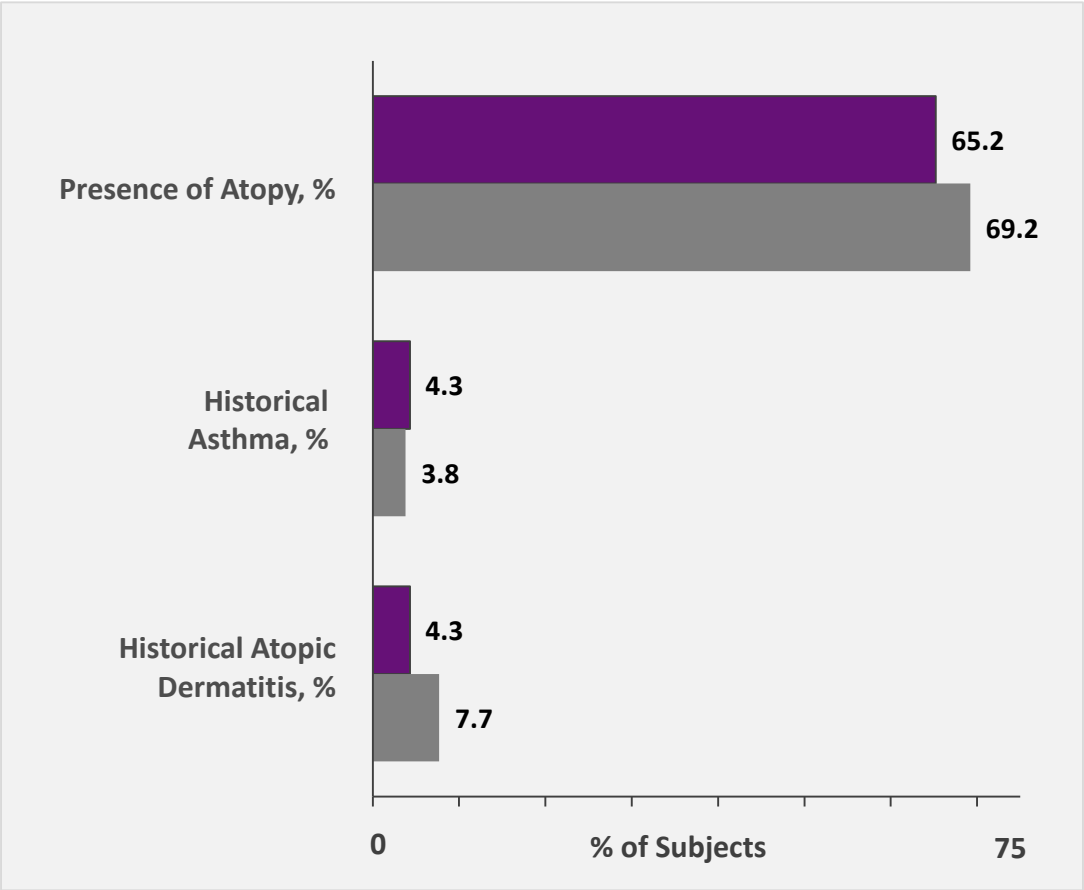
- Male or female aged 18 to 75 years, inclusive, at the time of consent
  - Have a physician-documented diagnosis of prurigo nodularis that is confirmed by review of medical photography during the Screening Period. Duration of prurigo nodularis (since the time of first PN nodule) must be at least 6 months from the time of first PN nodule to Day 1, as affirmed by the subject
  - Have at least 10 nodules of approximately 0.5 to 2 cm at the Screening Visit and Day 1. The nodules must be pruritic and present on at least 2 different anatomical locations (not be localized), involve the extremities, with extensor extremity involvement greater than the flexor extremity involvement. Nodules on the head (face and scalp) are not counted as an anatomical location for eligibility criteria. There must be normal appearing skin present in between nodules with the exception of atopic dermatitis. Each arm, each leg, and trunk are considered different anatomical locations
  - Subject has moderate to severe pruritus, defined as WI-NRS  $\geq 7$  at the Screening Visit and a mean weekly WI-NRS  $\geq 5$  for each of the 2 consecutive weeks immediately prior to randomization
- 4
- Patients were required to stop antihistamines and topical treatments, including corticosteroids, for at least two weeks prior to dosing
  - Prurigo nodularis treatments, other than study drug, were not allowed except for rescue

# Baseline Characteristics

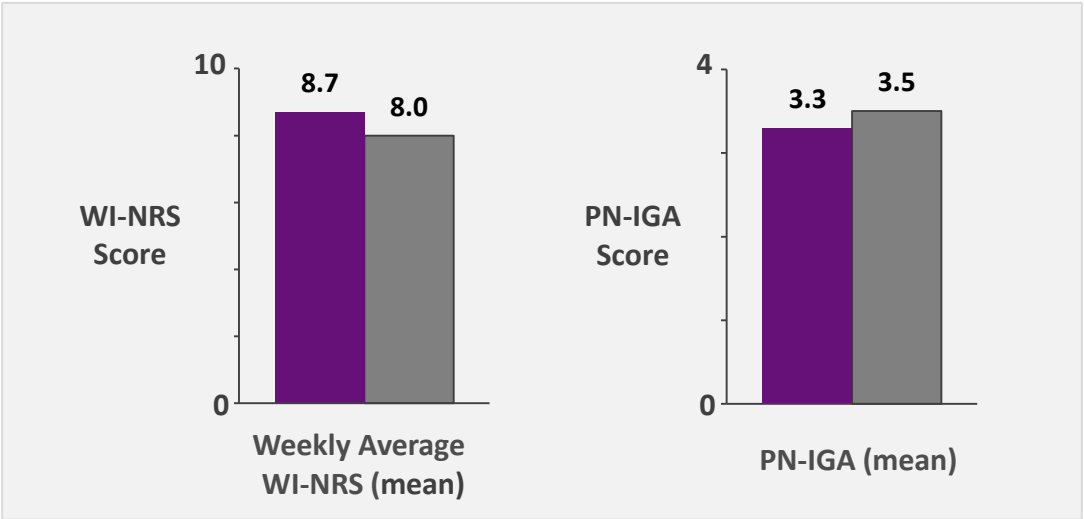
General Characteristics*	Vixarelimab (n=23)	Placebo (n=26)	Total (n=49)
Age (Mean Years)	52	64	58
Sex (Male/Female)	10/13	10/16	20/29
Race			
White (n)	65.2% (15)	80.8% (21)	73.5% (36)
Black or African American (n)	21.7% (5)	11.5% (3)	16.3% (8)
Asian (n)	8.7% (2)	0	4.1% (2)
American Indian or Alaska Native (n)	0	3.8% (1)	2.0% (1)
Multiple (n)	4.3% (1)	0	2.0% (1)
Other (n)	0	3.8% (1)	2.0% (1)

# Baseline Characteristics

### Clinical Findings at Baseline: History of Atopy



### Clinical Findings at Baseline: WI-NRS & PN-IGA



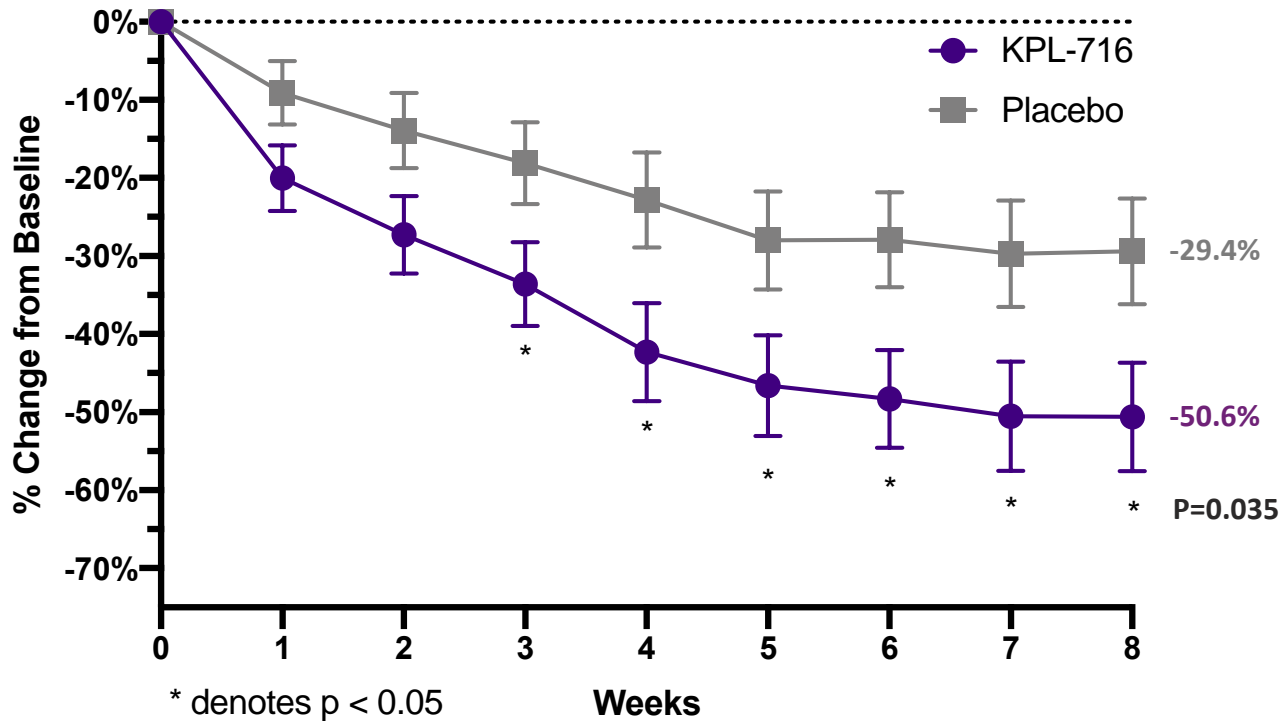
Vixarelimab  
Placebo



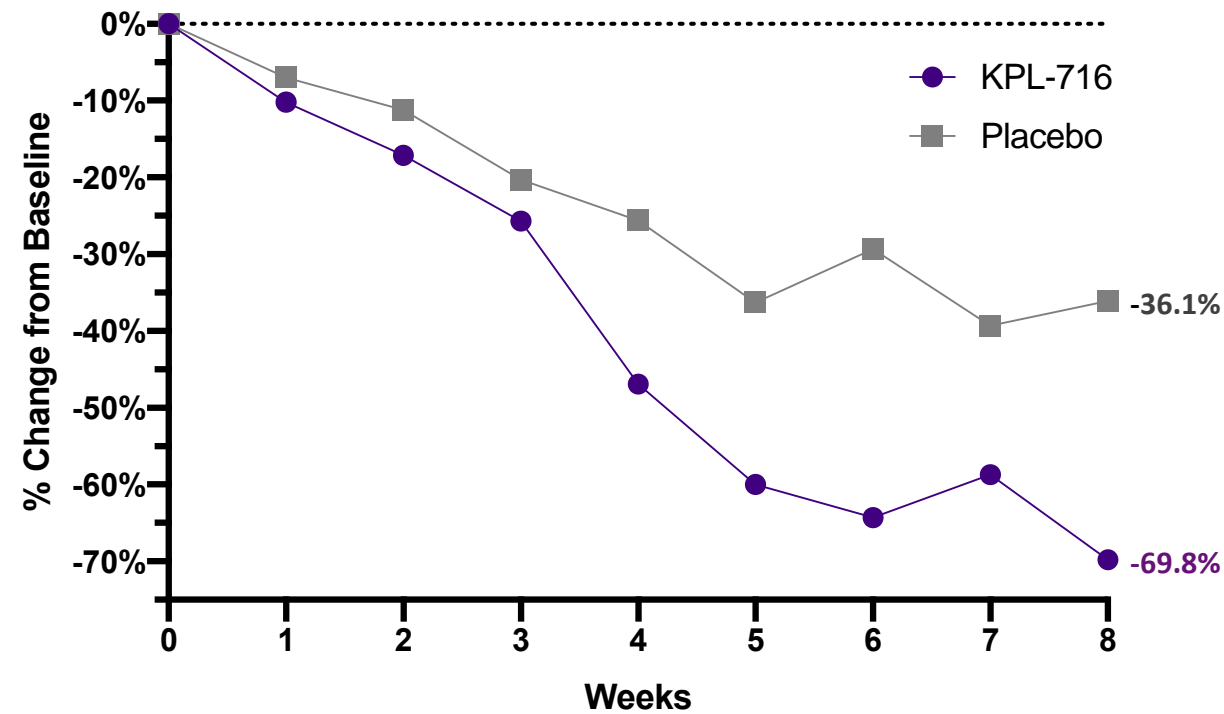
# Vixarelimab (KPL-716) Phase 2 Study Showed a Statistically Significant Reduction in Mean Weekly-Average WI-NRS Versus Placebo

Median change from baseline in weekly-average WI-NRS at Week 8 was -69.8%

### LS-Mean % Change in Weekly Average WI-NRS

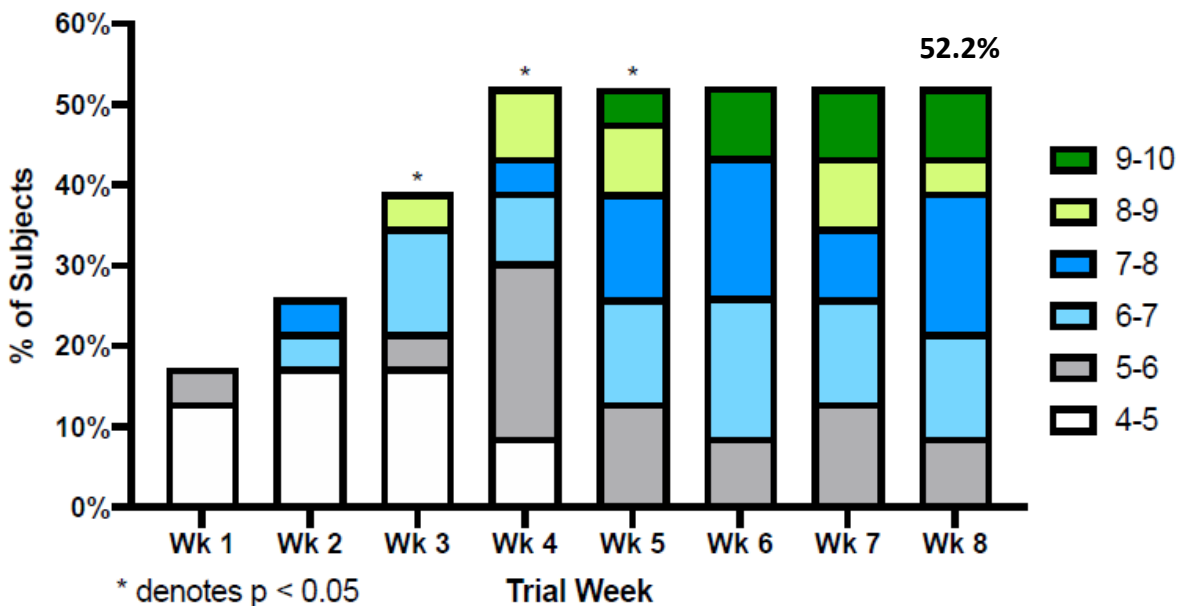


### Median % Change in Weekly Average WI-NRS

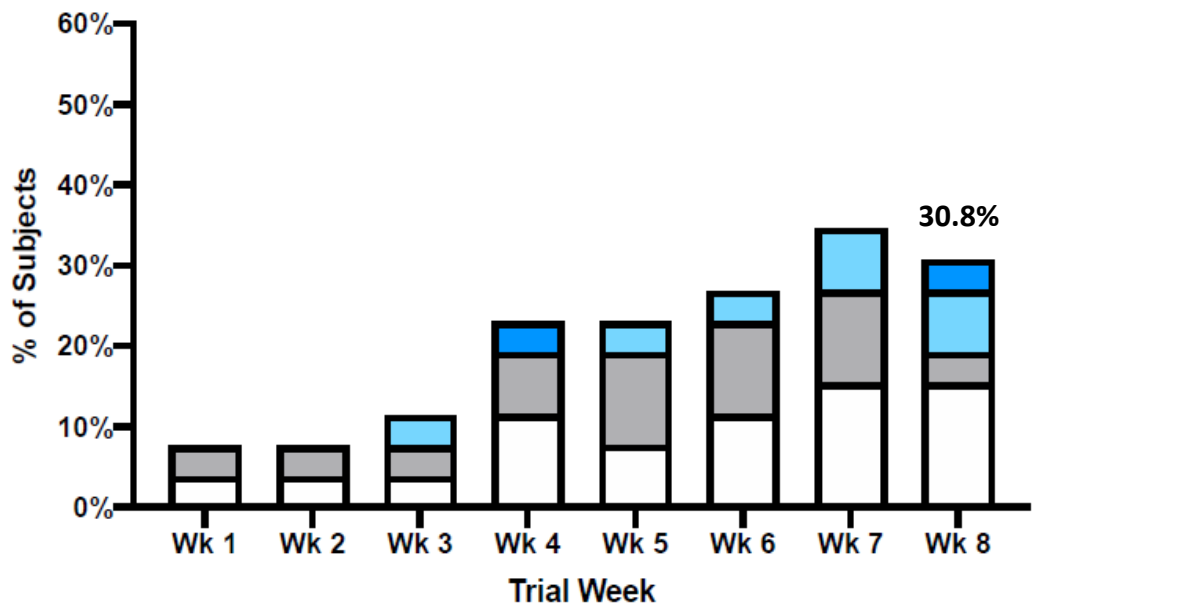


# The Majority of Vixarelimab (KPL-716) Recipients Showed a Clinically Meaningful $\geq 4$ -Point WI-NRS Reduction

% of KPL-716 Subjects with a Clinically Meaningful Response in WI-NRS



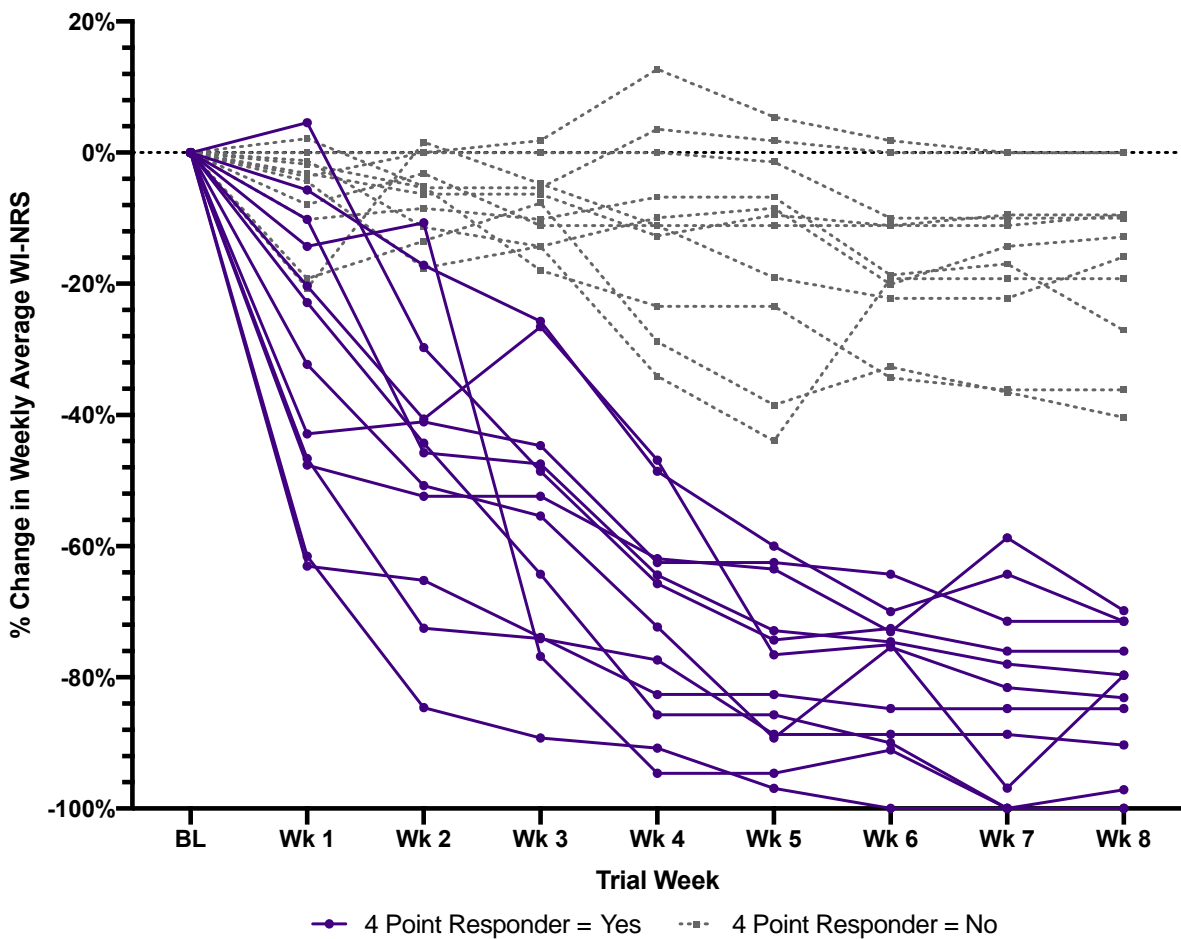
% of Placebo Subjects with a Clinically Meaningful Response in WI-NRS



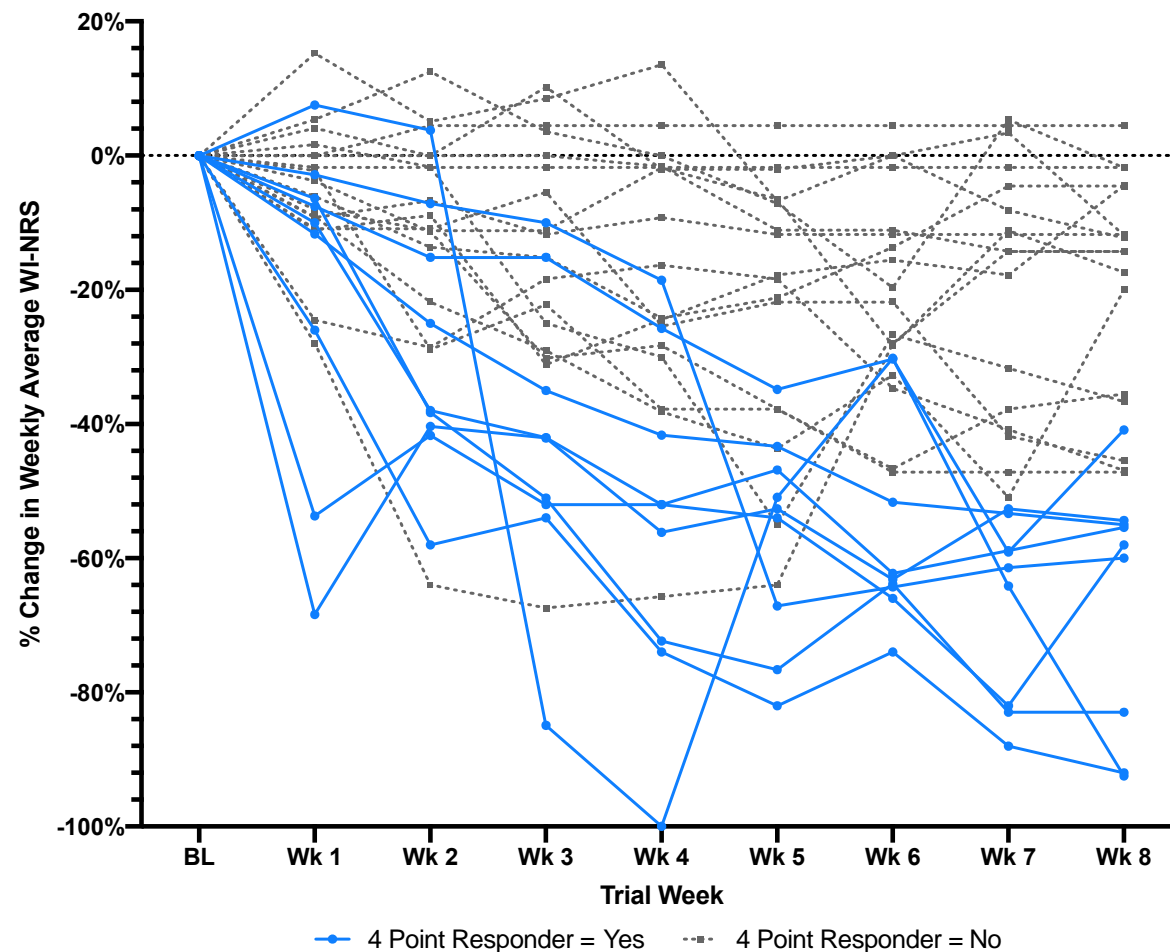


# The Majority of Vixarelimab (KPL-716) Recipients Showed a Clinically Meaningful $\geq 4$ -Point WI-NRS Reduction

KPL-716 Per Subject Plots

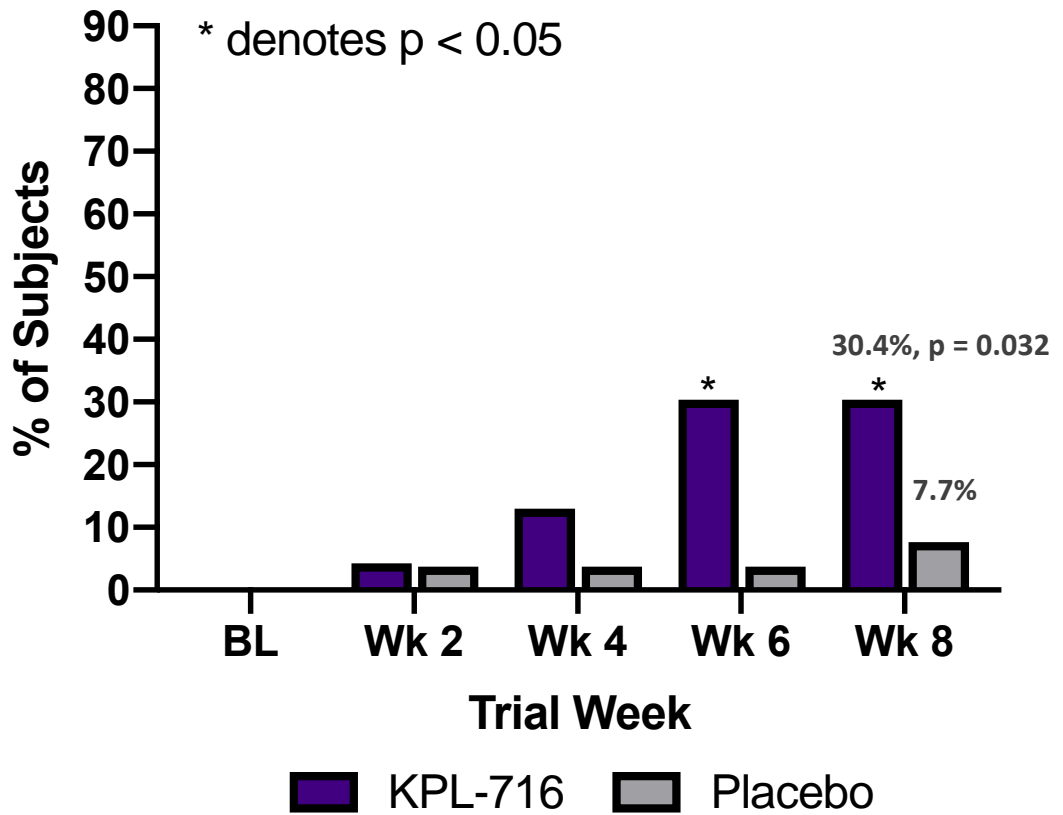


Placebo Per Subject Plots

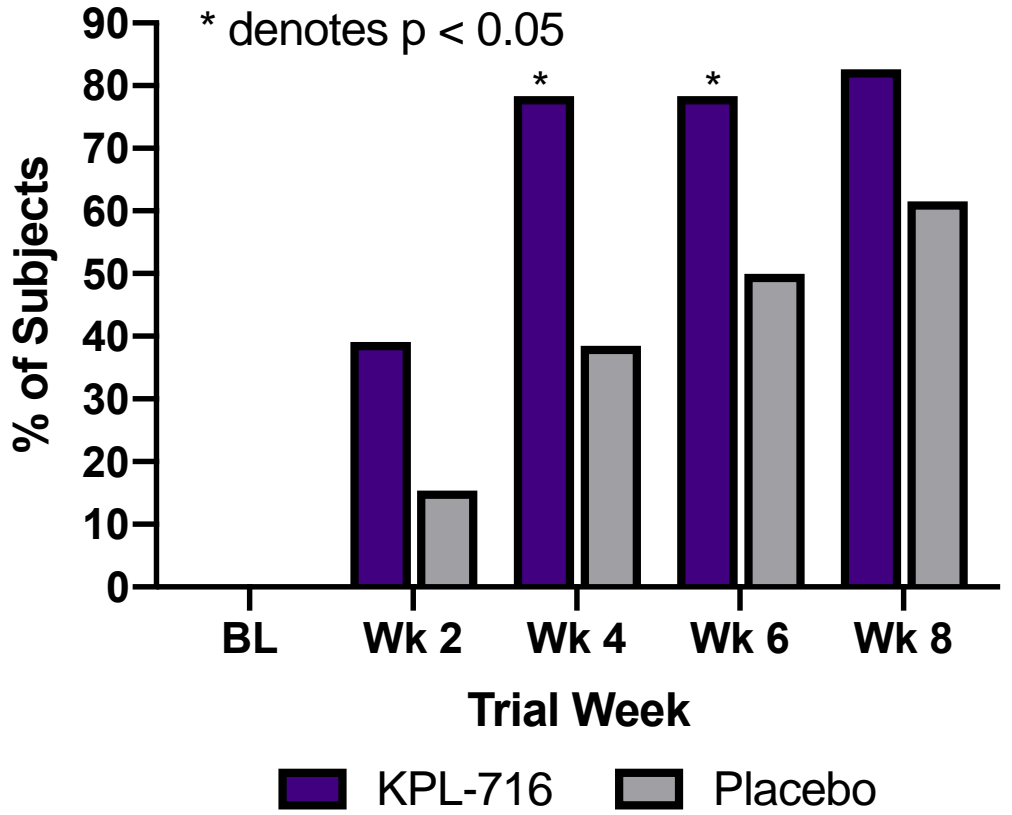


# Disease Severity Response: Significantly More Vixarelimab (KPL-716) Recipients Attained A Clear/Almost Clear Lesion Score by Week 8 Versus Placebo

PN-IGA Score of 0 or 1

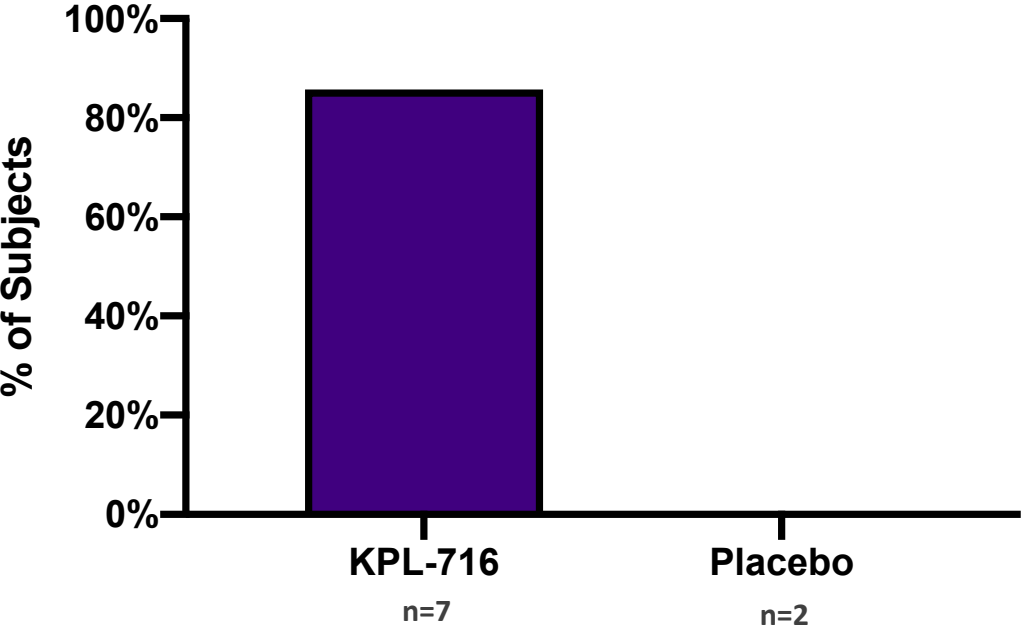


≥1 Point Change in PN-IGA



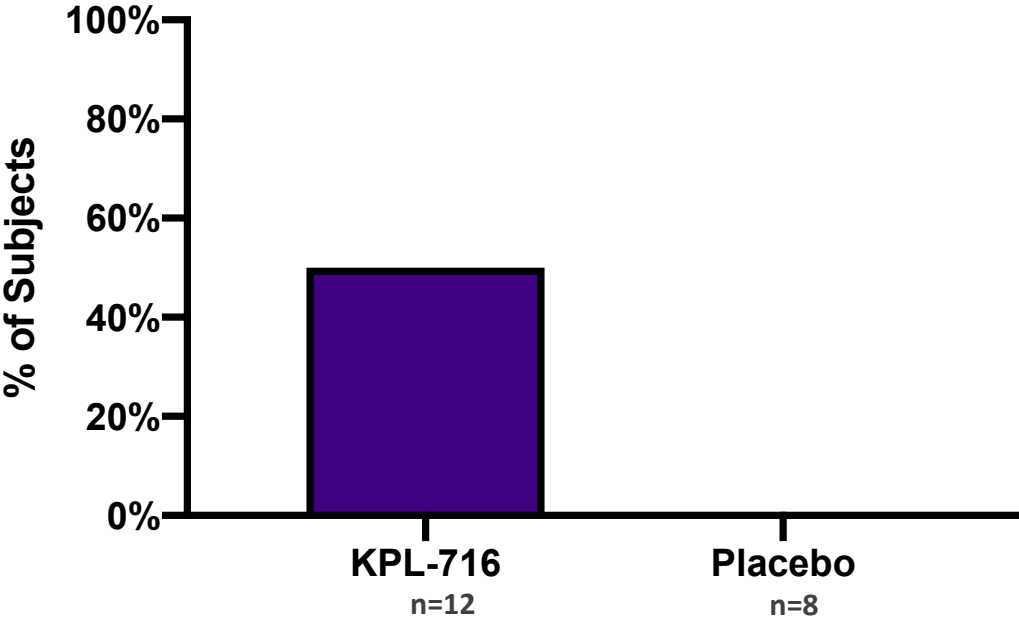
# Concordant Effect of Vixarelimab (KPL-716) on PN-IGA and Pruritus

% of IGA 0-1 Subjects with  $\geq 4$  Point Change in WI-NRS



*85.7% of the subjects who achieved 0-1 on the PN-IGA scale were also 4-point responders on WI-NRS vs. none for placebo*

% of Subjects with  $\geq 4$  Point Change in WI-NRS and an IGA of 0-1



*50% of the subjects who had a clinically meaningful reduction in itch by week 8 also had an PN-IGA score of 0-1 vs. none for placebo*



# Representative Images of Nodule Resolution at Week 8 in Two Vixarelimab-Treated Subjects

Day 1

Week 8

Subject 1



Subject 2



# Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

	Vixarelimab (n=23)	Placebo (n=26)
Any AE (n)	82.6% (19)	65.4% (17)
TEAE (n)	82.6% (19)	65.4% (17)
Drug-Related TEAE (n)	39.1% (9)	30.8% (8)
Serious TEAE	0	0
Drug-Related Serious TEAE	0	0
TEAE Leading to Treatment Discontinuation	0	0
Drug-Related TEAE Leading to Treatment Discontinuation	0	0
Serious TEAE Leading to Treatment Discontinuation	0	0
Drug-Related Serious TEAE Leading to Treatment Discontinuation	0	0
TEAE Leading to Death	0	0

# Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

System Organ Class Preferred Term	Vixarelimab (n=23)	Placebo (n=26)
Infections and Infestations (n)	30.4% (7)	46.2% (12)
Upper Respiratory Tract Infection (n)	17.4% (4)	3.8% (1)
Nasopharyngitis (n)	4.3% (1)	7.7% (2)
Gastroenteritis Viral (n)	4.3% (1)	0
Influenza (n)	4.3% (1)	0
Postoperative Wound Infection (n)	4.3% (1)	0
Subcutaneous Abscess (n)	4.3% (1)	0
Urinary Tract Infection (n)	0	11.5% (3)
Bronchitis (n)	0	3.8% (1)
Cellulitis (n)	0	3.8% (1)
Eczema Impetiginous (n)	0	3.8% (1)
Herpes Simplex (n)	0	3.8% (1)
Otis Media (n)	0	3.8% (1)
Skin Infection (n)	0	3.8% (1)
Tooth Abscess (n)	0	3.8% (1)

## Vixarelimab was Well-Tolerated in Prurigo Nodularis Phase 2a Study

System Organ Class Preferred Term	Vixarelimab (n=23)	Placebo (n=26)
Skin and Subcutaneous Tissue Disorders	26.1% (6)	15.4% (4)
Eczema Nummular	4.3% (1)	3.8% (1)
Pruritus	4.3% (1)	3.8% (1)
Dermatitis Allergic	4.3% (1)	0
Idiopathic Angioedema	4.3% (1)	0
Night Sweats	4.3% (1)	0
Urticaria	4.3% (1)	0
Skin Burning Sensation	0	7.7% (2)
Neurodermatitis	0	3.8% (1)



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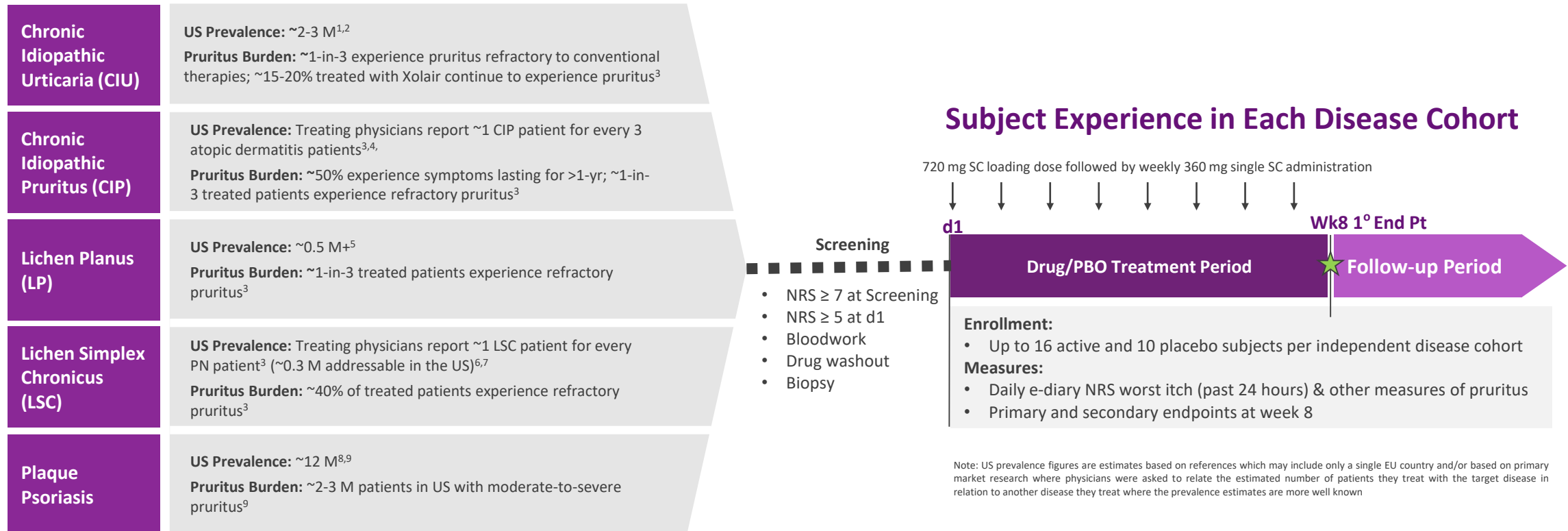
## Vixarelimab Phase 2 Study in Diseases Characterized by Chronic Pruritus



# Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus

## Pilot Study Rationale

- 1 Investigate presence of IL-31 & OSM signature in multiple diseases characterized by chronic pruritus
- 2 In diseases where IL-31 is present (based on post-hoc biopsy analysis) → link inhibition of IL-31 with vixarelimab to clinical response
- 3 Diseases where IL-31 is NOT present (based on post-hoc biopsy analysis) → Investigate whether blocking OSMRβ has any effect



# Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus

Plaque psoriasis cohort achieved statistically significant reduction in weekly-average WI-NRS at Week 8

**Enrolled patients experiencing moderate-to-severe pruritus and assigned them to one of the following cohorts based upon their diagnosis: plaque psoriasis, chronic idiopathic pruritus, lichen simplex chronicus, chronic idiopathic urticaria, or lichen planus**

- Each cohort was evaluated as an independently randomized sub-study. Patients were randomized and received a loading dose of vixarelimab 720 mg or placebo subcutaneous (SC) followed by vixarelimab 360 mg or placebo SC weekly for 8 weeks.

**Primary Efficacy Endpoint:** percent change versus baseline in weekly-average WI-NRS at Week 8

## **Topline Observations:**

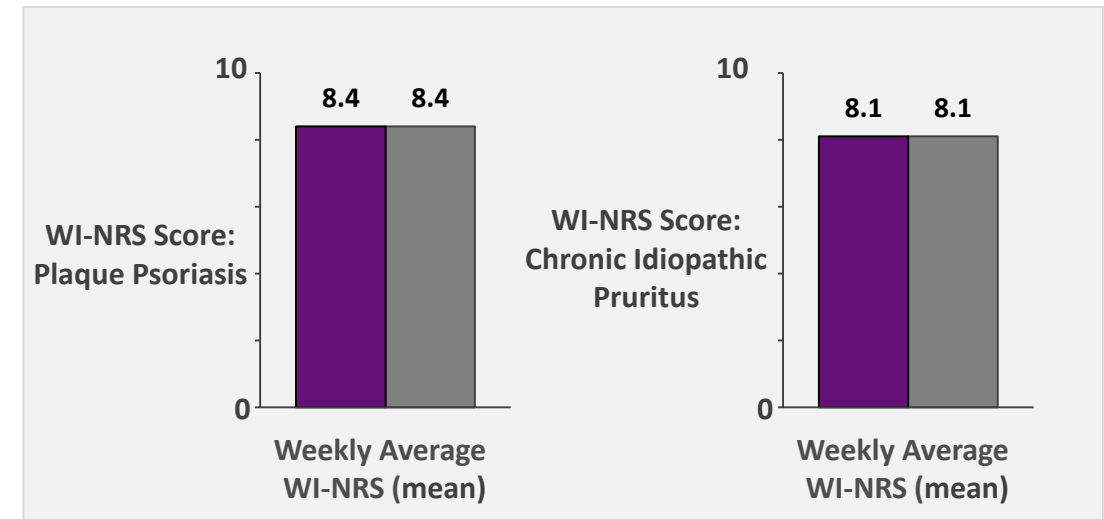
- The plaque psoriasis cohort achieved a statistically significant reduction in weekly-average WI-NRS at Week 8. Least squares (LS)-mean change from baseline (mean WI-NRS score of 8.4) in weekly-average WI-NRS at Week 8 was -66.5% (n=14) in vixarelimab recipients compared to -29.0% (n=7) in placebo recipients (LS-mean difference -37.5%; p=0.012).
- In the chronic idiopathic pruritus cohort, the LS-mean change from baseline (mean WI-NRS score of 8.1) in weekly-average WI-NRS at Week 8 was -52.4% (n=14) in vixarelimab recipients compared to -48.8% (n=9) in placebo recipients (LS-mean difference -3.6%; p=0.813).
- The lichen simplex chronicus (n=4), chronic idiopathic urticaria (n=4) and lichen planus (n=3) cohorts showed encouraging efficacy results as measured by percent change from baseline in weekly-average WI-NRS at Week 8. Comparative summary statistics were not performed due to the small number of patients enrolled in each cohort.
- Vixarelimab was well-tolerated, and no dose-limiting adverse events were recorded.

# Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: Baseline Characteristics

General Characteristics* Plaque Psoriasis	Vixarelimab (n=14)	Placebo (n=7)	Total (n=21)
Age (Mean Years)	49	53	50
Sex (Male/Female)	5/9	3/4	8/13
Race			
White (n)	92.9% (13)	85.7% (6)	90.5% (19)
Black or African American (n)	7.1% (1)	14.3% (1)	9.5% (2)

General Characteristics* Chronic Idiopathic Pruritus	Vixarelimab (n=14)	Placebo (n=9)	Total (n=23)
Age (Mean Years)	57	58	57
Sex (Male/Female)	4/10	1/8	5/18
Race			
White (n)	78.6% (11)	77.8% (7)	78.3% (18)
Black or African American (n)	14.3% (2)	22.2% (2)	17.4% (4)
Asian (n)	7.1% (1)	0	4.3% (1)

Clinical Findings at Baseline: WI-NRS

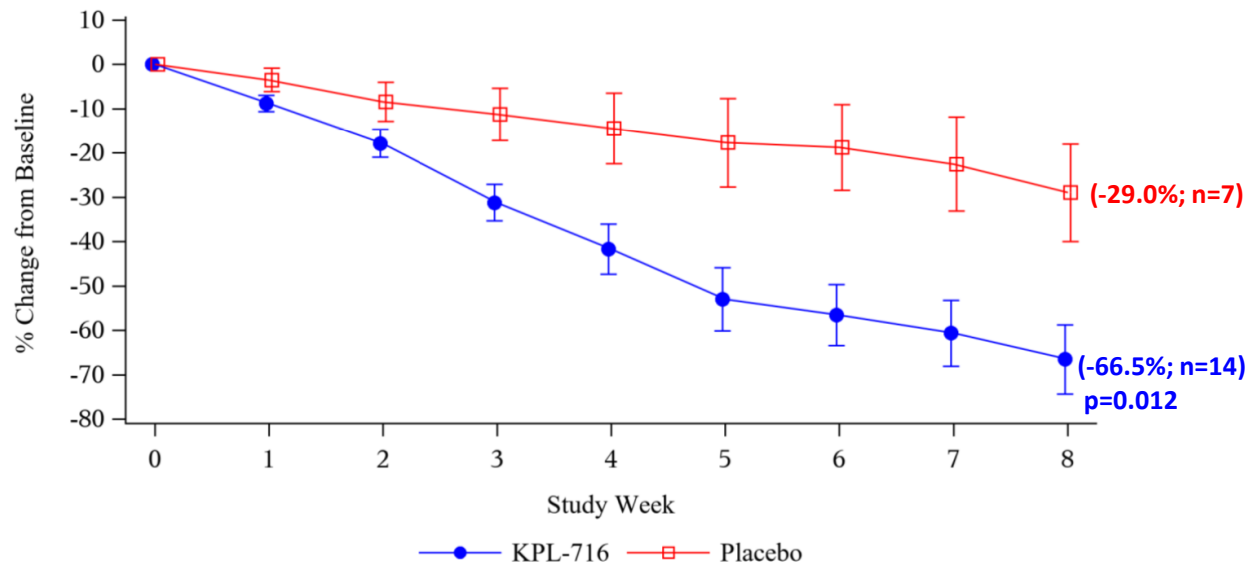


# Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: Reduction in Weekly-Average WI-NRS at Week 8

Plaque psoriasis cohort achieved statistically significant reduction in weekly-average WI-NRS at Week 8

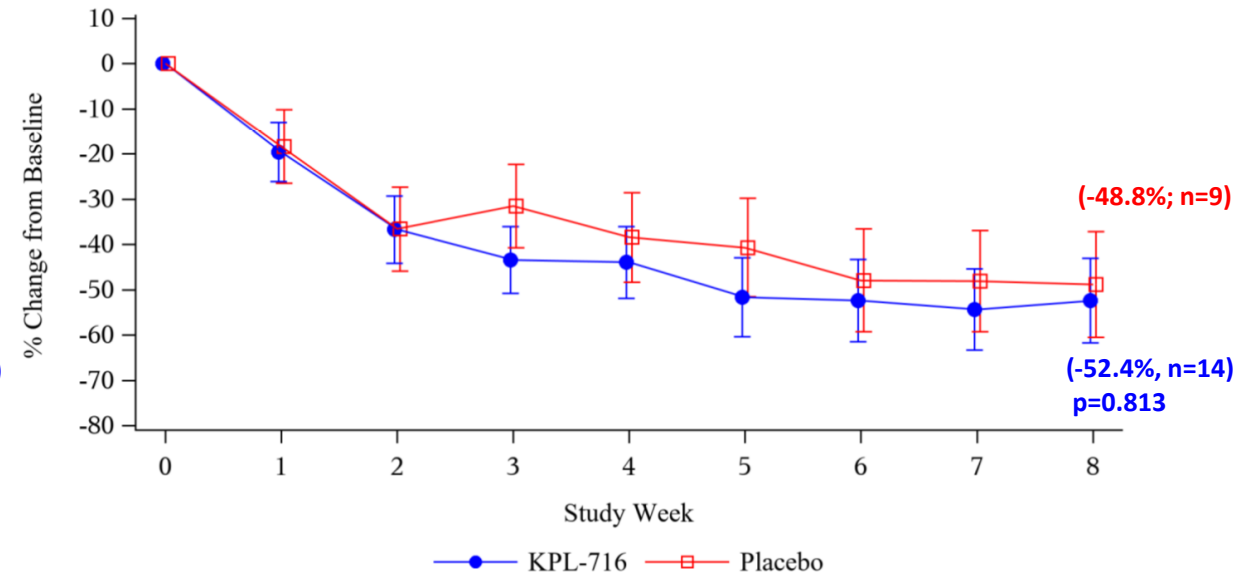
## Plaque Psoriasis

LS-Mean % Change in Weekly Average WI-NRS



## Chronic Idiopathic Pruritus

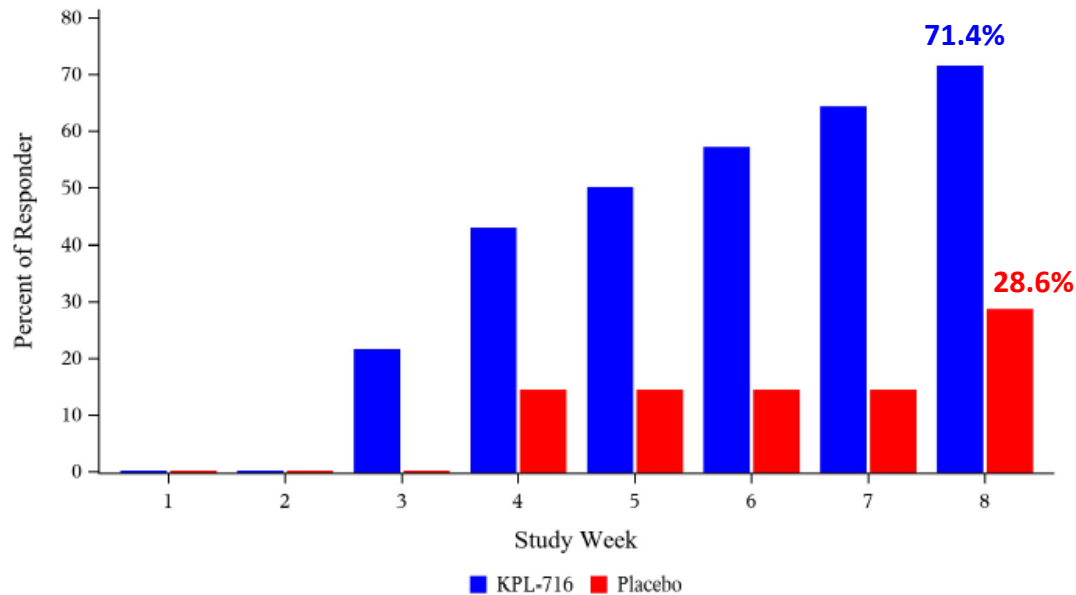
LS-Mean % Change in Weekly Average WI-NRS



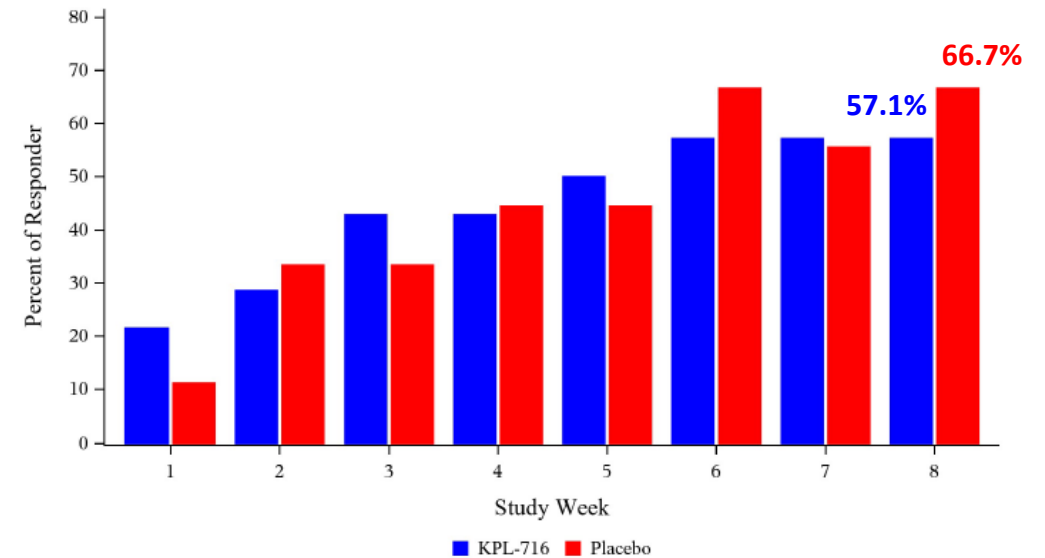
# Vixarelimab Exploratory Phase 2 Study in Diseases Characterized by Chronic Pruritus: ≥ 4-Point Weekly-Average WI-NRS Reduction at Week 8

71.4% of vixarelimab recipients in plaque psoriasis cohort showed a clinically meaningful ≥ 4-point reduction

## Plaque Psoriasis



## Chronic Idiopathic Pruritus



# Vixarelimab was Well-Tolerated in Exploratory Phase 2 Trial

	Plaque Psoriasis Cohort		Chronic Idiopathic Pruritus Cohort	
Summary of Adverse Events	Vixarelimab (n=14)	Placebo (n=7)	Vixarelimab (n=14)	Placebo (n=9)
Any AE (n)	42.9% (6)	14.3% (1)	28.6% (4)	22.2% (2)
TEAE (n)	42.9% (6)	14.3% (1)	28.6% (4)	22.2% (2)
Drug-Related TEAE (n)	7.1% (1)	0	7.1% (1)	11.1% (1)
Serious TEAE	0	0	7.1% (1)	0
Drug-Related Serious TEAE	0	0	7.1% (1)	0
TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
Drug-Related TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
Serious TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
Drug-Related Serious TEAE Leading to Treatment Discontinuation	0	0	7.1% (1)	0
TEAE Leading to Death	0	0	0	0



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