# Vixarelimab

## Phase 2

### Therapeutic Area

Prurigo nodularis (PN) is a chronic inflammatory skin condition characterized by severely pruritic skin nodules.

### Mechanism of Action

Monoclonal antibody inhibiting signaling through oncostatin M receptor beta (OSMRβ).

- Vixarelimab inhibits signaling of interleukin-31 (IL-31) and oncostatin M (OSM), 2 key cytokines implicated in inflammation, pruritus, and fibrosis.

### US Prevalence

We estimate that there are approximately 300,000 patients with PN in the US.

### Breakthrough Therapy designation

**Breakthrough Therapy designation granted by the US Food and Drug Administration (FDA) to vixarelimab for the treatment of pruritus associated with prurigo nodularis.**

## Rationale

Studies link many pruritic and inflammatory diseases to both IL-31 and OSM via signaling through OSMR. By targeting both pathways simultaneously, vixarelimab may disrupt the pathologic cycle in patients afflicted by a variety of pruritic diseases.

- Internal research shows that IL-31, OSM, and OSMR mRNA are all upregulated in lesional biopsies of subjects with PN with severe pruritus versus normal healthy controls.
- Our Phase 2a study of vixarelimab in PN met its primary efficacy endpoint: the reduction in weekly average Worst-Itch Numeric Rating Scale (WI-NRS) from baseline at Week 8 was statistically significantly greater in patients who received vixarelimab versus those who received placebo. Additionally, a statistically significant percentage of vixarelimab recipients achieved a PN-investigator's global assessment (PN-IGA) score of 0/1 at Week 8 compared to placebo recipients, and the majority of vixarelimab recipients showed a clinically meaningful weekly average reduction in WI-NRS of greater than 4 points.

## Unmet Need

We are not aware of any current therapies approved by the FDA for the treatment of PN.

- The treatment approach for PN ranges from topical corticosteroids and occlusive corticosteroid-containing bandages for patients who have milder forms of PN to systemic corticosteroids, ultraviolet phototherapy, and systemic therapies such as thalidomide, methotrexate, and cyclosporine for those patients whose conditions don't improve on initial treatments. Patients have reported using opioid pain medications to attempt to control PN in its most severe form.
- Based on market research, we believe ~25% to 30% of subjects are refractory to treatment.

## Status

We are conducting a dose-ranging Ph2b trial of vixarelimab in patients with prurigo nodularis.

- The Phase 2b trial is a randomized, double-blind, placebo-controlled study designed to investigate the efficacy, safety, and pharmacokinetics of vixarelimab in reducing pruritus in subjects with prurigo nodularis. The trial is expected to enroll approximately 180 patients with moderate-to-severe prurigo nodularis experiencing moderate-to-severe pruritus (WI-NRS ≥ 7 at the screening visit and a mean weekly WI-NRS of ≥ 7 for each of the two consecutive weeks immediately prior to randomization). Patients are required to stop antihistamines and topical treatments, including corticosteroids, for at least two weeks prior to dosing. Prurigo nodularis treatments, other than study drug, are not allowed except for rescue. Patients will be randomized 1:1:1:1 to receive vixarelimab 540 mg, 360 mg, 120 mg, or placebo subcutaneously monthly. The primary efficacy endpoint is the percent change from baseline in the weekly-average Worst-Itch Numeric Rating Scale (WI-NRS) at Week 16. Key secondary endpoints include the proportion of patients achieving greater-than-or-equal-to 4-point weekly-average WI-NRS reduction at Week 16 and the proportion of patients achieving a 0/1 score (clear/almost clear) on the prurigo nodularis-investigator's global assessment (PN-IGA) at Week 16.

In 2020, we reported data from a randomized, double-blind, placebo-controlled Phase 2a clinical trial of vixarelimab in patients with prurigo nodularis.

- The trial met its primary efficacy endpoint: the reduction in weekly-average WI-NRS from baseline at Week 8 was statistically significantly greater in patients who received vixarelimab versus those who received placebo. Additionally, a statistically significant percentage of vixarelimab recipients achieved a PN-IGA score of 0/1 at Week 8 compared to placebo recipients, and the majority of vixarelimab recipients showed a clinically meaningful greater-than-or-equal-to 4-point weekly-average WI-NRS reduction at Week 8. 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.

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