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.

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.

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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.

Status: Phase 2

We reported data from a randomized, double-blind, placebo-controlled Phase 2a clinical trial of vixarelimab in subjects with PN.

- In the Phase 2a trial, 49 patients with moderate-to-severe PN experiencing moderate-to-severe pruritus were randomized 1:1 and received a loading dose of vixarelimab 720 mg or placebo subcutaneously followed by vixarelimab 360 mg or placebo subcutaneously weekly. The primary efficacy endpoint was percent change versus baseline in weekly average WI-NRS at Week 8 (using a last observation carried forward analysis).
  - LS-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 -33.7% 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 ≥ 4-point reduction in weekly average WI-NRS at Week 8 compared to 30.8% of placebo recipients (*P*=0.1093).
  - 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.

We reported data from an exploratory Phase 2 clinical trial of vixarelimab in diseases characterized by chronic pruritus. The trial was designed to identify chronic pruritic conditions where signaling through OSMR may be playing a role and to investigate the efficacy, safety, and tolerability of vixarelimab in reducing the moderate-to-severe pruritus experienced by these subjects.

- In the Phase 2 trial, 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 an independently randomized sub-study. Patients were randomized and received a loading dose of vixarelimab 720 mg or placebo subcutaneously followed by vixarelimab 360 mg or placebo subcutaneously weekly for 8 weeks. The primary efficacy endpoint was percent change from baseline in weekly average WI-NRS at Week 8.
  - 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 treatment effect 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.