**RESULTS**

MIP-1

**Figure 4. IL-33 Directly Induces Cytokine Production from Peritoneal Mast Cells in vitro**

- Mast cells are the only ST2L (IL-33 receptor) expressing cells in the peritoneal cavity
- IL-33 directly stimulates peritoneal mast cells and induces cytokine and chemokine production in vivo

Figure 2. Lirentelimab (AK002) Mechanism of Action

- Mast cells are the only ST2L (IL-33 receptor) expressing cells in the peritoneal cavity
- IL-33 directly stimulates peritoneal mast cells and induces cytokine and chemokine production in vivo

**Figure 5. Lirentelimab (AK002) Reduces IL-33-driven Neutrophil Infiltration**

- Administration of IL-33 (Figure 3) induces a rapid influx of neutrophils into the peritoneal cavity
- Treatment with lirentelimab (AK002) significantly reduces IL-33-driven neutrophil infiltration in the peritoneal cavity

**Figure 6. Lirentelimab (AK002) Decreases Monocyte and Eosinophil Infiltration Induced by IL-33**

- IL-33 administration also drives infiltration of monocytes and eosinophils into the peritoneal cavity that is reduced by lirentelimab (AK002)
- Consistent with previous findings, lirentelimab (AK002) does not reduce mast cell numbers, suggesting the reduction in IL-33-mediated leukocyte infiltration is most likely mast cell inhibition

**Figure 7. Lirentelimab (AK002) Decreases IL-33-induced Cytokines and Chemokines in vivo**

- IL-33 in vivo administration induces global changes in the transcriptome of peritoneal mast cells that is modulated by lirentelimab (AK002)
- These data strongly suggest that lirentelimab (AK002) globally inhibits IL-33-mediated mast cell activation at the transcriptome level

**Figure 8. Lirentelimab (AK002) Globally.Inhibits IL-33 Activated Mast Cells**

- IL-33 in vivo administration induces global changes in the transcriptome of peritoneal mast cells that is modulated by lirentelimab (AK002)
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**Figure 9. Lirentelimab (AK002) Inhibits Downstream Signaling Pathways of IL-33 Activation**

- Lirentelimab (AK002) significantly reduces IL-33-driven inflammation by directly inhibiting IL-33-mediated mast cell activation
- Targeting Siglec-8 may have the potential to treat diseases associated with mast cells and eosinophils, including those where IL-33 can exacerbate immune responses, such as eosinophilic gastrointestinal diseases, atopic dermatitis, asthma, and food allergy

**CONCLUSIONS/DISCUSSION**

- Lirentelimab (AK002) significantly reduces IL-33-driven inflammation by directly inhibiting IL-33-mediated mast cell activation
- Targeting Siglec-8 may have the potential to treat diseases associated with mast cells and eosinophils, including those where IL-33 can exacerbate immune responses, such as eosinophilic gastrointestinal diseases, atopic dermatitis, asthma, and food allergy