FIRST-IN-CLASS ORAL PEPTIDE SYSTEMICALLY TARGETING THE IL-23 PATHWAY

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BACKGROUND/OBJECTIVE

- Human genetic associations and the efficacy of anti-IL-23 mAbs clearly define IL-23 pathway relevance in PsO, PsA, CD, and UC
- Currently, there are no orally delivered therapeutics selectively targeting this pathway
- To provide additional treatment options for patients, we developed an oral therapeutic peptide, JNJ-77242113, selectively targeting IL-23 to block IL-23 signaling

RESULTS

Figure 1. In Vitro Pharmacology
- JNJ-77242113 is a competitive peptide antagonist that binds with high affinity to IL-23R and selectively inhibits IL-23 proximal signaling and downstream cytokine production with high potency

Figure 2. Orally Dosed JNJ-77242113 Attenuates Weight Loss and Colon Inflammation in the Rat TNBS-induced Colitis Model
- Body weight change (%)
- Colon edema/microstructure

Figure 3. Orally Dosed JNJ-77242113 Shows Systemic Pharmacodynamic Activity in Rat Blood
- Oral dose vehicle or JNJ-77242113
- Draw blood and stimulate with IL-23

Figure 4. Oral JNJ-77242113 Achieves Inhibition of IL-23-induced Rat Skin Inflammation Equivalent to Anti-IL-23 Antibody

Figure 5. JNJ-77242113 Phase 1 Study: Safety, Pharmacokinetics, Systemic Pharmacodynamics
- Single and multiple oral doses were safe and generally well tolerated with no safety signal of concern

CONCLUSIONS

- Oral therapeutics selectively targeting the IL-23 pathway will provide additional options for patients
- JNJ-77242113 is a peptide antagonist, that binds with picomolar affinity to IL-23R, and potently blocks IL-23 signaling and downstream cytokine production
- Due to exquisite potency, GI stability and effective tissue distribution, orally dosed JNJ-77242113 in rats showed inhibition of
  - colon tissue inflammation
  - ex vivo IL-23-induced IL-17A production in blood
  - skin inflammation, achieving similar efficacy to an anti-IL-23 antibody
- Preclinical findings successfully translated to a Phase 1 human study, where systemic inhibition of ex vivo IL-23-induced IFN-γ production in blood was observed
- Accelerated development to Phase 2b in PsO

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Disclosures


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