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Summary

# TARGET ENGAGEMENT AND PHARMACODYNAMIC MOLECULAR MECHANISM EVALUATION IN A PHASE 1B STUDY OF THE NUCLEOTIDE-BINDING OLIGOMERIZATION DOMAIN, LEUCINE RICH REPEAT CONTAINING X1 (NLRX1) AGONIST NX-13 IN ULCERATIVE COLITIS

Silvio Danese

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**A phase 1B trial in 36 patients with active ulcerative colitis demonstrated that NX-13, a gut-selective NLRX1 agonist, achieved target engagement and induced downstream immunometabolic changes consistent with its preclinical mechanism of action, with changes correlating with clinical response.**

KEY POINTS

- NX-13 treatment for 4 weeks increased NLRX1 protein expression in all treated groups versus placebo, with more pronounced upregulation in responding patients compared to non-responders
- Gene expression analysis showed upregulation of the mitochondrial metabolism gene MT-ND3 and downstream reductions in HIF1α and NLRP3 in the immediate-release NX-13 groups but not placebo
- The 250mg immediate-release dose showed downstream decreases in IL-17α and IL-1β gene expression, while the 500mg immediate-release dose showed IL-1β reduction
- Changes in NLRX1 expression and immunometabolic markers were numerically greater in responding immediate-release-dosed patients compared to non-responding patients, suggesting target engagement parallels clinical benefit
- The novel mechanism targeting mitochondrial function through NLRX1 agonism is being further evaluated in a phase 2 proof-of-concept study

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