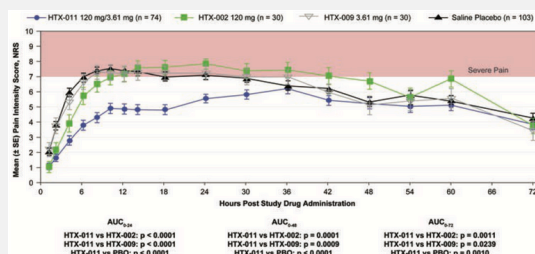
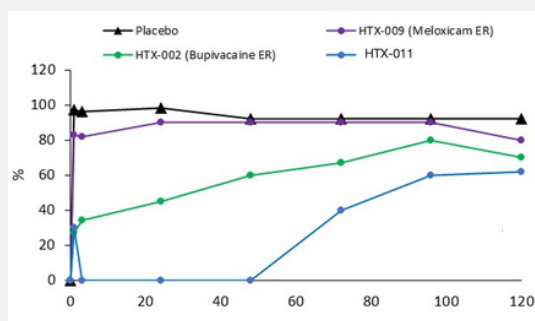


# MECHANISM OF ACTION OF HTX-011: A NOVEL, EXTENDED-RELEASE, DUAL-ACTING LOCAL ANESTHETIC FORMULATION FOR POSTOPERATIVE PAIN

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## RESULTS



**Synergistic Activity of HTX-011 in Pigs and Humans.** The top panel illustrates the combined effect of Meloxicam and Bupivacaine (HTX-011) in pigs, demonstrating their synergistic activity. The bottom panel presents the corresponding synergistic effect of HTX-011 in humans.

## OBJECTIVES

Obtaining consistent efficacy beyond 12–24 hours with local anesthetics, including extended-release formulations, has been a challenging goal. Inflammation resulting from surgery lowers the pH of affected tissues, reducing neuronal penetration of local anesthetics. HTX-011, an investigational, nonopioid, extended-release dual-acting local anesthetic combining bupivacaine and low-dose meloxicam, was developed to reduce postsurgical pain through 72 hours using novel extended-release polymer technology. Preclinical studies and a phase II clinical trial were conducted to confirm the mechanism of action of HTX-011.

## PRECLINICAL MODEL

**Postoperative Pain Pig Model:** an incision was made on the flank, simulating surgical pain. The treatment drug was then administered subcutaneously around the incision site. Pain was measured using von Frey filament testing, distress behavior scoring, and the approaching test. Pharmacokinetics and histological analysis were also performed.

## CONCLUSIONS

Preclinical animal and clinical results confirm that the low-dose meloxicam in HTX-011 normalizes the local pH in the incision, resulting in superior and synergistic analgesic activity compared with extended-release bupivacaine. HTX-011 represents an extended-release local anesthetic with a dual-acting mechanism of action that may provide an important advancement in the treatment of postoperative pain.

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