LX1606 (aka LX1032), a Novel Inhibitor of Serotonin Synthesis, Alleviates Development of Inflammatory Bowel Disease in a Preclinical Model

Tamas Oravec, Kanchan Jhaveri, Qi M. Yang, Alan G. Wilson, Alan J. Main, and Brian Zambrowicz
Lexicon Pharmaceuticals, Inc., The Woodlands, TX

**BACKGROUND**

Dysfunctional signaling by the immunoendocrine mediator serotonin (5-HT) may play an important role in the pathophysiology of gastrointestinal (GI) diseases, support the hypothesis that lowering 5-HT production could provide benefit for IBD patients. We have developed TPH inhibitors that decrease serotonin production in both peripheral and central nervous system (CNS).

**METHODS**

C57Bl/6brd x 129SvEv F1 hybrid mice were used in all experiments. The studies were carried out with protocols approved by the Institutional Animal Care and Use Committee of Lexicon Pharmaceuticals, Inc.

**RESULTS**

LX1606 reduces serotonin content in the periphery, but not in the brain.

**CONCLUSIONS**

• LX1606 is a novel, orally delivered inhibitor of tryptophan hydroxylase that reduces serotonin production:
  - Absorbed into peripheral circulation
  - Does not cross the blood-brain barrier

• LX1606 consistently reduced 5-HT levels in the periphery but not in the brain.

• Treatment with LX1606 showed a strong positive effect in ameliorating TNBS-induced BD in mice as assessed by various parameters of disease development:
  - These preclinical data demonstrate that inhibition of TPH activity by LX1606 may provide a new approach for the treatment of BD and its serotonin-mediated symptoms.

**REFERENCES**


