LAT8881 was well tolerated in healthy volunteers and peptide PK levels were comparable to those that reduce pain in rodent neuropathic pain models. Treatment of lumbar radicular neuropathy subjects is expected to complete by June 2023

Poster 37

A PROOF-OF-CONCEPT CLINICAL TRIAL OF LAT8881 AS A NON-OPIOID TREATMENT FOR LUMBAR RADICULAR NEUROPATHY

BACKGROUND & AIMS

- LAT8881 is a therapeutic candidate for neuropathic pain, acting via a novel target, lanthionine synthetase C-like protein (LanCL)
- Aims of this two-part clinical trial include:
  1. Characterize the pharmacokinetic (PK) profile of LAT8881,
  2. Confirm the safety of higher intravenous (IV) doses, and
  3. Demonstrate analgesia in subjects with chronic lumbar radicular neuropathy.

METHODS

Two-part study - IV LAT8881 vs placebo:

- **Part A**: a double-blind, randomized, placebo-controlled, single-ascending dose study in 8 healthy volunteers.
  - ➢ Outcome measures: safety and PK, identify dose for Part B
- **Part B**: randomized double-blind cross-over study in up to 20 patients with chronic lumbar radicular pain
  - ➢ Outcome measures: change in baseline pain, PK, pharmacodynamics and safety

RESULTS – Part A

- LAT8881 and its active metabolite were detected in the plasma of all subjects, evidence of a dose-proportional relationship to exposure, and a terminal half-life of less than 30 minutes.
- 1.8 mg/kg dose: the C_{max} and AUC_{0-t} of the active metabolite was 177-462 ng/ml and 16.5-35.5 ng/ml*h, respectively, t_{max} 5 minutes.
- No dose-limiting toxicities were reported

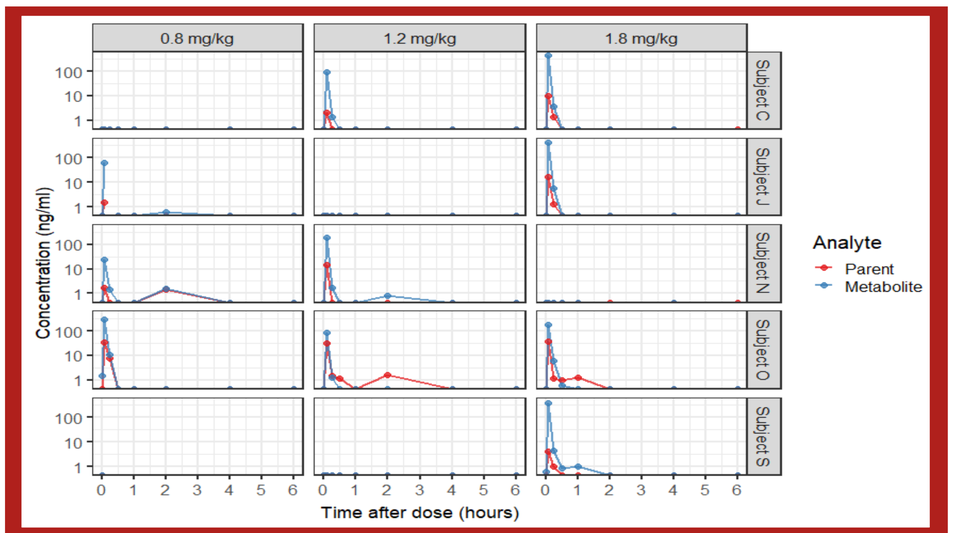

Figure 1: LAT8881 (Parent) and LAT9991F (metabolite) in the first 5 subjects as measured by LC-MSMS. The validated lower limit of quantitation was 1 ng/mL and 0.6 ng/mL for LAT8881 and LAT9991F, respectively.

CONCLUSIONS

- In **Part A**, LAT8881 was well tolerated and the PK profile comparable to what is efficacious in nonclinical models of neuropathic pain.
- Treatment of subjects in **Part B** is expected to complete in the first half of 2023.

WHAT ARE LAT8881 and LanCL?

- LAT8881 is a naturally-derived C-terminal peptide fragment of human Growth hormone (hGH), that has no hGH activity
- LAT8881 is the prototype of a family of peptide motifs with analgesic properties in rodent models of neuropathic pain which appear to act via intracellular LanCL proteins.
- LanCl proteins are highly conserved over evolution. They are widely expressed, including in neurons, acting as hub proteins that promote cellular homeostasis in response to cell stress or damage

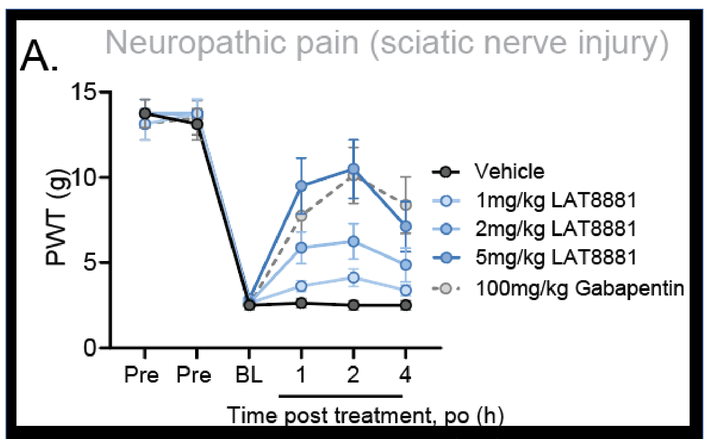

Figure 2: LAT8881, dosed orally (po), reversed mechanical allodynia in Chung models of neuropathic pain in a dose-dependent manner (Wei *et al* 2022).

PART B STUDY DESIGN:

- Male or female, ≥18 years, BMI ≥19 kg/m^2, and MRI/CT documented lumbar disc herniation
- History of persistent pain of ≥3 months radiating into a lower limb, with average daily leg pain at rest of ≥4/10 and ≤9/10 with a minimum of >3/10 on any day
- Randomly assigned: (1) LAT8881 (maximum tolerated dose (MTD) from Part A) then placebo, or (2) placebo then LAT8881
- Outcome measures: change in baseline pain from start of infusion up to 6 hours post-infusion measured on a 0-10 VAS; impact of a leg raise on pain; Patient General Impression of Change; PK; and safety of LAT8881.

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Take a picture to download the full abstract and poster

Reference: Wei *et al*, 2022, PWD221, IASP World Pain Congress 2022