

Plasma and Urinary Pharmacokinetics of a Novel, Oral SHIP1 Activator AQX-1125 in Female Patients with Interstitial Cystitis

J. Curtis Nickel, Kingston, Canada, Robert Evans, Winston Salem, NC, Patrick Tam, Judy Toews, Lloyd Mackenzie, Heidi Biagi, Stephen Shrewsbury, Vancouver, Canada*

INTRODUCTION AND OBJECTIVES: AQX-1125 is a novel SH2-containing inositol-5'-phosphatase 1 (SHIP1) activator previously demonstrated to modulate inflammation. Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a chronic condition of unknown etiology, associated with inflammation of the bladder epithelium. The LEADERSHIP trial was a multicenter, randomized, double-blind, placebo-controlled, Phase 2 clinical trial investigating the ability of 200 mg AQX-1125 to reduce pain in female patients with IC/BPS in North America. Here we assess the extent of bladder exposure to AQX-1125 over 6 weeks with trough drug levels in plasma and urine.

METHODS: Blood and urine was collected after 28 and 42 days. Samples were analyzed for concentrations of AQX-1125 via HPLC-MS/MS methods and trough levels calculated.

RESULTS: PK samples were collected from 35 patients randomized to AQX-1125. The mean/geometric mean plasma concentrations were 252/211 and 225/162 ng/mL for Days 28 and 42, respectively. The mean/geometric mean urine concentrations were 49,863/34,450 and 33,396/22,934 ng/mL for Days 28 and 42, respectively, at least 140-fold higher than the corresponding plasma levels. The trough plasma concentrations are similar to, or exceed, those anticipated for efficacy from earlier clinical trials and pre-clinical studies.

CONCLUSIONS: The novel SHIP1 activator, AQX-1125 reaches the bladder of IC/BPS patients via both the bloodstream and the urine. The urinary route of elimination of AQX-1125 as parent compound may be an attractive property of the drug for IC/BPS. If once daily oral AQX-1125 proves effective in ameliorating symptoms of IC/BPS, both systemic and direct exposure of drug to the bladder may contribute to that response. This pharmacokinetic data supports continued development of AQX-1125 as an oral, once-daily therapy for IC/BPS.

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Contacts:

Robert Evans III, Wake Forest University Health Sciences, Winston Salem, NC 27103
revans@wakehealth.edu

Pat Tam, Aquinox Pharmaceuticals, Vancouver, BC, V5T 4T5,
ptam@aqxpharma.com

Judy Toews, Aquinox Pharmaceuticals, Vancouver, BC, V5T 4T5,
jtoews@aqxpharma.com

Heidi Biagi, Aquinox Pharmaceuticals, Vancouver, BC, V5T 4T5,
hbiagi@aqxpharma.com

Lloyd Mackenzie, Aquinox Pharmaceuticals, Vancouver, BC, V5T 4T5,
lmackenzie@aqxpharma.com

Stephen B Shrewsbury, Aquinox Pharmaceuticals, Vancouver, BC V5T 4T5,
sshrewsbury@aqxpharma.com