SHIP-1 Activation Provides Significant Benefit in Interstitial Cystitis/Bladder Pain Syndrome: Results of a Phase 2 Randomized Placebo Controlled Trial

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INTRODUCTION AND OBJECTIVES: Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) is a chronic condition associated with inflammation of the bladder epithelium. We conducted a 6-week randomized, double-blind, placebo-controlled Phase 2 trial in North America with AQX-1125 (a novel SH2-containing inositol-5'-phosphatase 1 (SHIP1) activator) previously demonstrated to modulate inflammation to assess its safety and efficacy in addition to existing therapy.

METHODS: 69 women with moderate to severe IC/BPS, having had cystoscopy to exclude other disease within 3 years and a baseline mean pain score of ≥5, urinary frequency, urgency and nocturia were randomized to daily 200 mg AQX-1125 or placebo for 6 weeks. Daily average and maximal pain scores and urinary frequency were recorded by e-diary and in the clinic. The O'Leary-Sant Interstitial Cystitis Symptom and Problem Indexes (ICSI/PI), Bladder Pain IC Symptom Score (BPIC-SS) and Short Form 12 Health Survey (SF-12v2) questionnaires were administered. Safety data was collected through 6 weeks treatment and 4 weeks follow up.

RESULTS: At six weeks, the mean average e-diary pain score (primary efficacy outcome) and clinic average pain as well as maximum pain (e-diary and clinic recorded) and percent change in mean average pain score had decreased more in the 37 patients treated with AQX-1125 than placebo (see Table). Significant statistical differences at 6 weeks in the AQX-1125 group compared to placebo group for change from baseline were noted for the mean ICSI, ICPI and BPIC-SS (see Table). Urinary voiding frequency and SF-12v2 scores also improved. No safety issues were noted in either group.

CONCLUSIONS: AQX-1125 provided greater reduction in bladder pain and symptoms at 6 weeks, compared to placebo in women with moderate to severe IC/BPS and was well tolerated. Further clinical studies with AQX-1125 for IC/BPS are planned in 2016.

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TABLE: Clinical results (Change from baseline to 6 weeks)

	Placebo (N=32)	AQX-1125 (N=37)	Total (N=69)	
			LS Mean Difference	p value
Average pain (e-diary) (mean ± SE)	-1.4 (0.3)	-2.4 (0.4)	1.0 (0.5)	0.061
Average pain (clinic) (mean ± SE)	-1.1 (0.4)	-2.6 (0.5)	1.6 (0.6)	**0.008**
Percent change from baseline (mean ± SE)	-21.1 (4.8)	-38.1 (5.8)	16.5 (7.8)	**0.039**
Maximum pain (e-diary) (mean ± SE)	-1.4 (0.4)	-2.6 (0.4)	1.3 (0.6)	**0.030**
Maximum pain (clinic) (mean ± SE)	-1.1 (0.5)	-2.8 (0.6)	1.6 (0.7)	**0.028**
O'Leary-Sant ICSI (mean ± SE)	-1.4 (0.6)	-3.8 (0.6)	2.7 (0.9)	**0.005**
O'Leary-Sant ICPI (mean ± SE)	-1.6 (0.5)	-3.6 (0.7)	2.5 (1.0)	**0.014**
BPIC-SS (mean ± SE)	-4.0 (1.2)	-8.8 (1.4)	5.4 (2.1)	**0.011**

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