A Phase 2 Randomized, Double-blind, Placebo-controlled Study to Evaluate the Effectiveness and Safety of Single, Oral Doses of SYM-1219, a Granule Formulation Containing 1 and 2 Gram Doses of Secnidazole, for the Treatment of Women with Bacterial Vaginosis

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Objectives: SYM-1219, a granule formulation of secnidazole, a 5-nitroimidazole with a longer half-life (~17 hr) than metronidazole (~8 hr), is being developed to treat bacterial vaginosis (BV). Secnidazole has been used outside the US to treat protozoal and anaerobic infections. The objectives of this study were to compare the efficacy and safety of SYM-1219 granules containing 1 or 2 grams of secnidazole to placebo for the treatment of women with BV.

Methods: 215 women who met the 4 Amsel criteria for BV (discharge, pH ≥ 4.7, ≥ 20% clue cells, positive whiff test) were randomized 1:1:1 at 24 US sites to single oral doses of 1 or 2 g of secnidazole as SYM-1219 granules or placebo. A baseline vaginal smear was evaluated in a central laboratory for Nugent scoring (a score ≥ 4 was required for the study), and tests for sexually transmitted pathogens were obtained. Safety data included assessment of AEs, physical exam findings and laboratory results. Patients were evaluated for efficacy between days 21-30. The primary endpoint was clinical cure defined as a normal discharge, negative whiff test and clue cells < 20%. Microbiological cure was a Nugent score of 0-3 and therapeutic cure was both clinical and microbiological cure. The modified Intention-to-Treat (mITT) population was used for the efficacy analyses. All statistical comparisons used a stratified Cochran-Mantel-Haenszel (CMH) test performed at a 0.05 level of significance (2-sided).

Results: The mITT population included 188 women (exclusions: baseline STI (n=13), Nugent score 0-3 (n=13), other (n=1)). The median age was 33 years (range 19-54), 68% reported ≤ 3 BV episodes in the previous year, and 54% self-identified as black or African American race. Clinical cure was higher in the 2 g group (42/62; 67.7%) and the 1 g group (35/64; 51.6%) compared to placebo (11/62; 17.7%, $p<0.001$ for both comparisons). Microbiological cure in the 2 g group (25/62; 40.3%) and the 1 g group (15/64; 23.4%) was superior to placebo (4/62; 6.5%) ($p<0.01$ for both comparisons). Therapeutic cure was 40.3%, 21.9% and 6.5% for the 2 g, 1 g and placebo groups ($p<0.05$ for both comparisons). The overall rate of AEs was low; both study doses were well tolerated.

Conclusions: Both the 1 and 2 g secnidazole doses of SYM-1219 granules were statistically superior to placebo and the 2 g dose was numerically better than the 1 g dose. These data support the continued development of the 2 g dose of SYM-1219 granules for the treatment of BV.

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Learning Objective: At the end of this presentation, participants will be able to describe the efficacy of SYM-1219 for the treatment of women with BV.