Results of the Phase 2 PUNCH CD Safety Study of RBX2660 (microbiota suspension) for Recurrent *C. difficile* Infection

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Objectives: Perturbation of the intestinal microbiota has been linked to *C. difficile* infection (CDI). There is increasing recognition that restoration of a healthy gut microbiota is necessary to limit *Clostridium difficile* colonization. The aim of the study was to assess the safety and effectiveness of RBX2660 (microbiota suspension), a next-generation faecal transplant manufactured using standardized processes and available in a ready-to-use format.

Methods: Patients with recurrent CDI, defined as at least 3 CDI episodes or at least 2 severe episodes resulting in hospitalization, were enrolled. RBX2660 was administered to all patients via enema. A second dose was permitted if CDI recurred <8 weeks after the first dose. Follow-up was at 7, 30 and 60 days and 3 and 6 months after the last dose. The primary objective was product-related adverse events (AEs). A secondary objective was CDI resolution. Adverse events were rigorously solicited via a patient diary during the first week after treatment with RBX2660 and systematically recorded throughout the study. Descriptive statistics were used for data analysis.

Results: Forty patients were enrolled at 11 centres in the U.S. between August 15 and December 13, 2013. Thirty-four patients (mean age 66.8 years, 67.6% female) received at least one dose of RBX2660. A total of 31 patients completed 6-month follow-up and are included in this analysis. A total of 188 adverse events were reported in 28 patients. Of these, 56.9% (n=107) were solicited from baseline to day 7 days. Subsequently, 16.0% (n=30) were reported from days 8-30; 11.7% (n=22) from days 31-60; 4.3% (n=8) from day 61 to 3 months and 11.2% (n=21) between 3 and 6 months. The most common AEs were predominately mild to moderate flatulence, abdominal pain/cramping, constipation and diarrhoea and were self-limiting. The incidence and severity of solicited AEs declined over time. The proportion of patients reporting AEs at day 7 was lower after dose 2 than after dose 1. Twenty serious AEs were reported in 7 patients, including 3 cases of recurrent CDI ≤ 8 weeks post-treatment, all of which required hospitalization. Twelve serious AEs occurred in 2 patients presenting with multiple comorbidities. One unrelated patient death was due to respiratory failure. None of the serious AEs was judged related to RBX2660 or its administration. Efficacy of RBX2660, defined as the absence of CDI at 8 weeks after the last treatment, was 87.1% (27/31) with 16 successes after the first dose and 11 after the second dose.

Conclusions: RBX2660 demonstrated a satisfactory safety profile in a Phase 2 study targeted at recurrent CDI which included very rigorous documentation of AEs. The overall 87.1% efficacy is in line with previously reported results. Administration by enema should decrease costs and risks compared with nasoduodenal tube or colonoscopic administration.