Donors are Universal in the Fight Against *Clostridium difficile*: Results from Two Trials Investigating the Safety and Efficacy of RBX2660, a Microbiota-based Drug

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### Background
- Live microbial therapies are becoming an increasingly accepted treatment for recurrent *Clostridium difficile* infection (CDI).
- Questions remain regarding factors contributing to therapeutic success, including donor influence on patient outcome.
- RBX2660 is a microbiota-based drug derived from healthy human donors.
- The impact of donor on clinical outcome following RBX2660 treatment was evaluated in two clinical trials: PUNCH CD, an open label clinical trial, and the blinded phase of PUNCH CD 2, a randomized, double-blind, placebo-controlled trial.

### RBX2660
- Each dose of RBX2660 is 150 mL of microbial suspension packaged in a ready-to-use enema format.
- Manufactured using standardized, quality-controlled processes with guaranteed minimum quantity of microbes.
- In both studies, donor batches were randomized to the patient, and randomized again for the second dose. Patients could receive product from the same or different donors.

### Clinical Studies
- Patients in the PUNCH CD (Phase 2) - an open label study where patients received 1 dose of RBX2660, with opportunity to receive a second dose.
- Patients in the PUNCH CD 2 (Phase 2B) trial were randomized to receive either: 2 doses of RBX2660, 2 doses of placebo; or 1 dose of RBX2660 followed by 1 dose of placebo. Therapies were administered via enema with doses 7 days apart.
- Success was defined as the absence of *C. difficile*-associated diarrhea at 8 weeks following completion of the last treatment.

### Mathematical Model
- For each clinical study, a mixed model was used to predict treatment success taking into account donors and dose number.
- Repeated measures data was included to account for patients who received 2 doses of RBX2660. A patient was classified as either a success or failure for each dose.
- P<0.05 indicates statistical significance; all analyses were done using the R statistical package.

### Results
#### Results from PUNCH CD<sup>1</sup>
- A total of 34 patients enrolled in the PUNCH CD Phase 2 trial (mean age 68.8 years, 67.6% female) were treated with at least one dose of RBX2660. Fifteen patients received a second dose.
- Success was not impacted by the donor or the dose order.

#### Results from PUNCH CD 2<sup>2</sup>
- A total of 83 patients enrolled in the PUNCH CD 2 Phase 2B trial (mean age 62 years, 59% female) received at least one dose of RBX2660 in the blinded arm of the study. Forty-one patients received 2 doses of RBX2660.
- Success was not impacted by the donor or the dose order.

### Methods
#### Donor Sourcing and Traceability
- Donors underwent pre-enrollment blood and stool pathogen screening as well as extensive health history reviews prior to acceptance into the program.
- All drug product associated with that donor during a cycle process with guaranteed minimum quantity of microbes.
- Donations were not pooled allowing for direct donor to patient traceability.
- Donors were randomized to patients for both the first and second doses.

### References

### Conclusions
- RBX2660 success in preventing recurrent CDI is not determined by specific donor.
- Data from two separate clinical studies demonstrate that preparation of RBX2660 from a universal group of screened donors does not impact patient outcomes.
- A super donor was not identified.
- The role of donor in RBX2660 success for treatment of other clinical indications requires further study.