Efficacy of Investigational Microbiota-Based Live Biotherapeutic RBX2660 in Patients With Recurrent *Clostridioides difficile* Infection: Data From Five Prospective Clinical Studies

Lindy Bancke PharmD[1], Xin Su MD[1]

Presented by:
Lindy L Bancke, PharmD
Head of Clinical Development,
Rebiotix, a Ferring Company

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[1]Rebiotix, Inc., a Ferring Company, Roseville, MN, USA

Track: Antimicrobial Agents and Resistance (AAR)
Subtrack: A6 New Drug Development

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A Standardized Microbiome-Based Therapeutic Is Needed to Break the Vicious Cycle of rCDI

- According to the CDC, *Clostridioides difficile* infection (CDI) remains **an urgent public health threat** that requires immediate and aggressive action

- Microbiome-based therapeutics are **increasingly accepted as a promising treatment option** for recurrent CDI (rCDI)
  - However, challenges remain (eg, lower efficacy rates observed in randomized studies compared to open-label studies, and standardization of products and procedures)

- A need exists for FDA approval of an **effective microbiome-based therapeutic standardized for quality and safety** to break the rCDI vicious cycle

CDC, Centers for Disease Control and Prevention; World Health Organization. Global observatory on health R&D. https://www.who.int/research-observatory/monitoring/processes/antibacterial_products_October_2018/en/, Accessed on September 24, 2021; Tariq *Clin Infect Dis* 2019 Apr 8;68(8):1351-1358.

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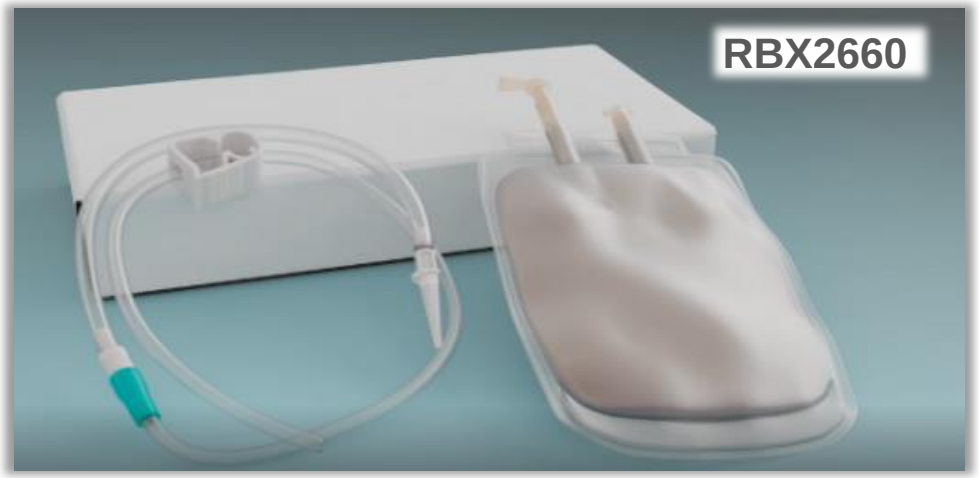
Investigational RBX2660: A Potential First-in-Class Microbiota-Based Live Biotherapeutic

- Designed with the goal of delivering a broad consortium of diverse microbes to the gut to reduce rCDI
- Manufactured using the same processes since the beginning of the development program, including rigorous screening to help ensure patient safety
- Granted Fast Track, Orphan, and Breakthrough Therapy designations by FDA



Robust RBX2660 Clinical Program in rCDI – Designed to Yield Consistent and Reliable Evidence

Study Design Criteria	PUNCH™ CD[1]	PUNCH™ CD2[2,3]	PUNCH™ CD Open Label[4,5]	PUNCH™ CD3[6,7]	PUNCH™ CD3-OLS*[8,9]
Phase	2	2b	2	3	3
Consistent Patient Population: Recurrent CDI	✓	✓	✓	✓	✓+
Consistent Efficacy Endpoint: Reducing Recurrent CDI	✓	✓	✓	✓	✓
Consistent Product: Same Manufacturing Process	✓	✓	✓	✓	✓
Placebo-Controlled Study	Open-label	Yes	Open-label	Yes	Open-label
Total Subjects Enrolled (Active + Control)	40	150	272	320	293*
Primary Efficacy Population (N=723)	32	133	142	262	154*
Follow-up Duration	6 months	24 months	24 months	6 months	6 months

*Expanded rCDI patient population (eg, IBD, IBS, and immunocompromised). Ad hoc data; enrollment is ongoing.

1. Orenstein R, et al. Clin Infect Dis. 2016;62(5):596-602; 2. Dubberke ER, et al. Clin Infect Dis. 2018;67(8):1198-1204; 3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02299570?term=NCT02299570&draw=2&rank=1. Accessed September 20, 2021; 4. Mische S. Presented at 2018 Digestive Disease Week; Washington, DC; June 2-5, 2018; 5. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02589847?term=NCT02589847&draw=2&rank=1. Accessed September 20, 2021; 6. Lee C. Presented at 2021 Digestive Disease Week Online; May 21-23, 2021; 7. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03244644?term=rbx2660&draw=2&rank=4. Accessed September 20, 2021; 8. Kraft C. Presented at 2021 Digestive Disease Week Online; May 21-23, 2021; 9. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03931941?term=rbx2660&draw=2&rank=1. Accessed September 20, 2021.

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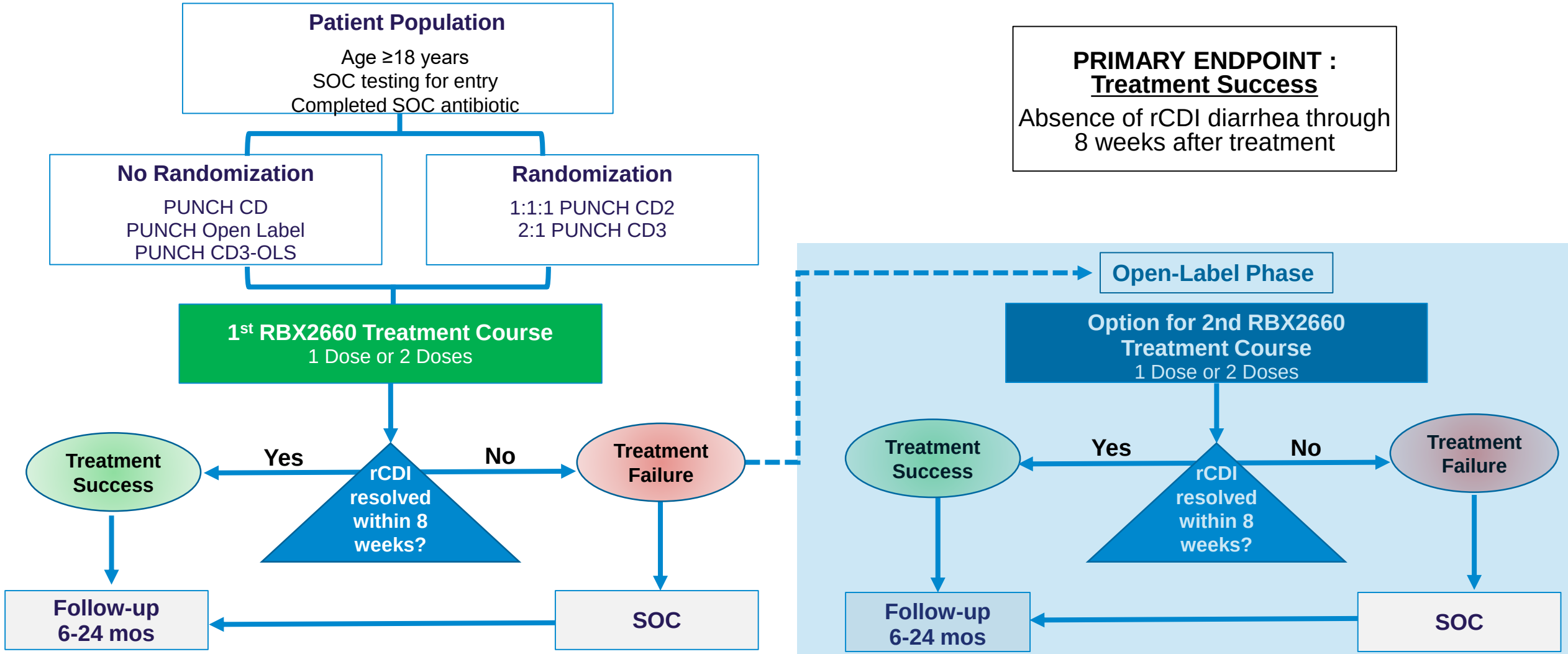
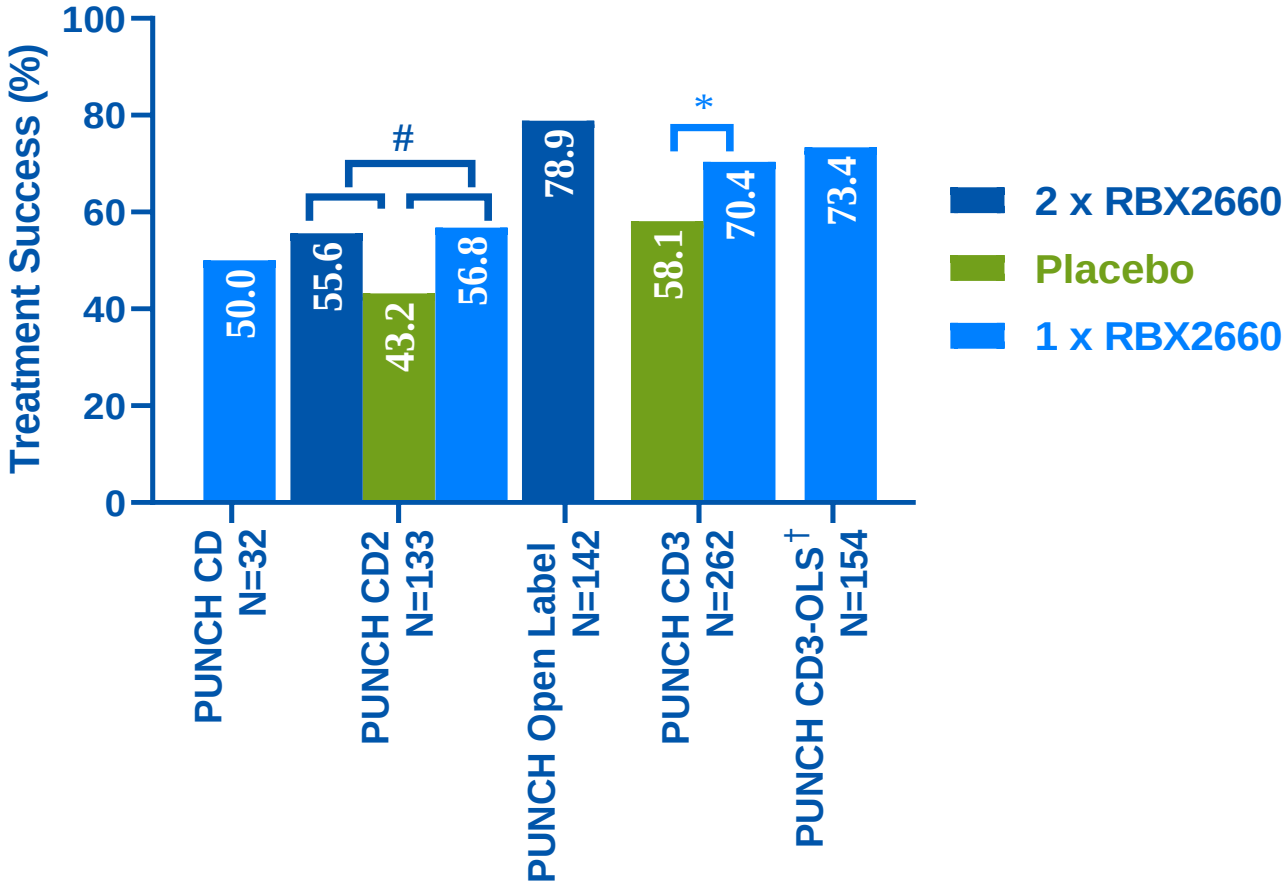
Consistent Study Design Across RBX2660 Clinical Program



rCDI, recurrent CDI; SOC, standard of care.

RBX2660 Treatment Consistently Reduced CDI Recurrence across Five Studies in Over 700 Treated Patients



Open-Label Studies

PUNCH CD, PUNCH CD Open Label, PUNCH CD3-OLS:

Treatment Success rates: 50.0% to 78.9%

Randomized, Placebo-Controlled Studies

PUNCH CD2:

2-dose RBX2660 group had a similar treatment success rate (55.6%) with 1-dose RBX2660 (56.8%)—higher than placebo (43.2%)

PUNCH CD3:

Treatment Success rate in RBX2660 arm (70.4%) was significantly superior vs placebo (58.1%)

Figure is updated compared to abstract

*Bayesian hierarchical model; 98.6% (0.986) probability of superiority, which exceeded the predefined 0.975 success threshold.
#Chi-square test; *P*>0.05.
†PUNCH CD3-OLS: enrolled subjects with IBD, IBS, immunocompromised conditions; ongoing, ad hoc analysis.

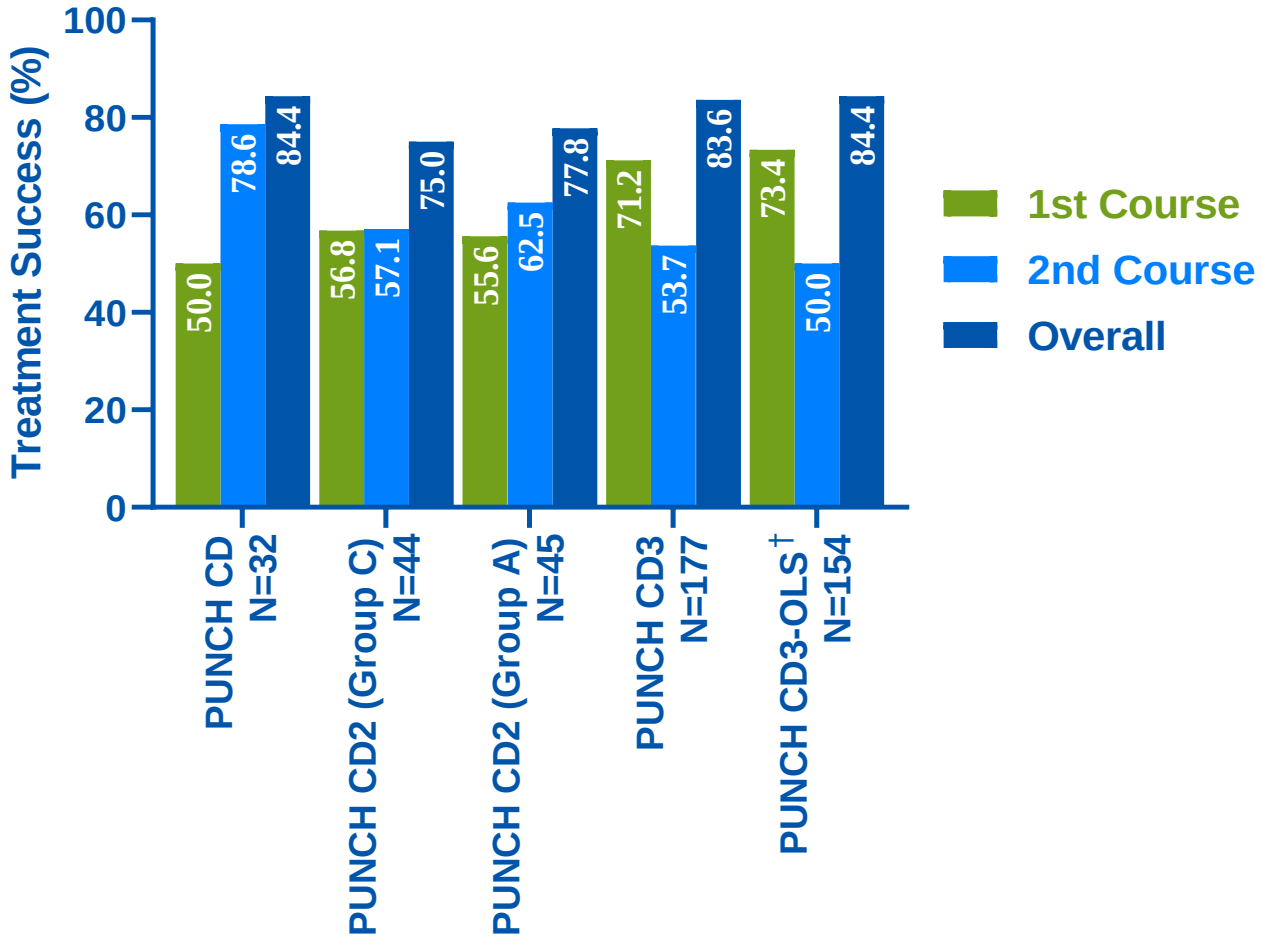
RBX2660 Demonstrated Superior Efficacy vs Placebo at 8 Weeks in Pivotal Study PUNCH CD3

- **RBX2660 successfully met its primary endpoint**, demonstrating superior efficacy vs placebo (70.4% and 58.1%, respectively) at 8 weeks
  - Exceeded the predefined criteria for statistical significance with a 98.6% posterior probability of superiority*
- Efficacy was demonstrated **as early as first recurrence**
- **Subgroup analyses showed no statistically significant impact** on blinded treatment outcome for covariates including: age, sex, race, or prior number of CDI episodes

Treatment Success	mITT Population	
	RBX2660	Placebo
Treatment Success Mean (SD)	0.704 (0.034)	0.581 (0.051)
95% CI	0.637, 0.768	0.484, 0.682
Posterior Probability of Superiority*	0.986	

mITT, modified intent-to-treat; SD, standard deviation, CI, Confidence interval.
*Posterior probability of superiority threshold to declare success=0.975.

Second Treatment Course of RBX2660 Further Reduced Recurrence of rCDI



Second Treatment Course

Subjects deemed Treatment Failures post-1st treatment course were eligible for a 2nd course of treatment

Treatment Success rates post-2nd RBX2660 course ranged from 50.0% to 78.6%

Overall Treatment Success rates ranged from 75.0% to 84.4%

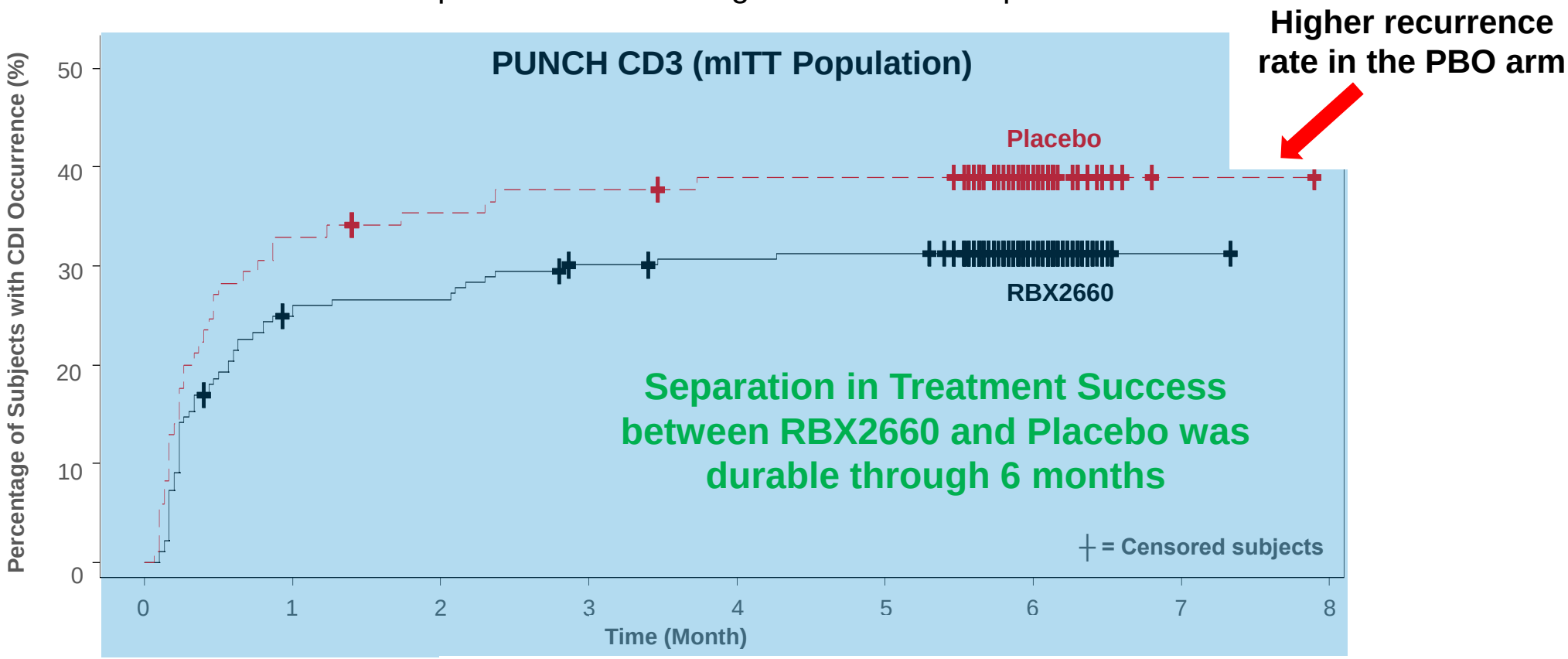
These data suggest that, following rCDI after the 1st course of RBX2660 treatment, a **second course of treatment with RBX2660 may improve the overall rate of Treatment Success**

Figure is updated compared to abstract

PUNCH CD2 Group C = 1 x RBX2660, Group A = 2 x RBX2660 in blinded phase.
PUNCH CD3-OLS: enrolled subjects with IBD, IBS, Immunocompromised Conditions; Ad hoc data; enrollment is ongoing.

RBX2660 Treatment Response Is Durable Through 6 Months

Sustained clinical response: Treatment Success of presenting CDI recurrence and no new CDI episodes for >8 weeks post treatment during 6-month follow-up



Overall, the majority of primary **RBX2660 responders remained CDI-free to 6 months and up to 24 months** post-treatment, with success rates in the Phase 3 program ranging from 82.0% to 92.1%

Conclusions

- Across 5 trials with **consistent investigational product and clinical endpoints**, RBX2660 consistently reduced recurrent *Clostridioides difficile* infection (rCDI) within 8 weeks after treatment
- A majority of treatment responders had a sustained clinical response **after at least 6 months** and up to 24 months
- In patients with further CDI recurrence after RBX2660 treatment, a second treatment course **improved the overall clinical benefit of RBX2660** for rCDI
- Collectively, these data demonstrate **consistency and reliability** of the potential benefit of RBX2660 across an entire clinical program

RBX2660 is effective for the reduction of rCDI in adult patients, as early as first recurrence, after receiving standard-of-care antibiotic treatment

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Patients

Caregivers

We would like to thank all of the investigators and site staff that contributed to the RBX2660 PUNCH CD Clinical Program at ~100 study locations over the last decade, as well as the 1000+ patients, and their families and caregivers.