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**Media Release**

# Ferring Presents Complete Data across Five RBX2660 Trials Demonstrating Consistent and Durable Efficacy in Recurrent C. Difficile Infection, as Well as Multiple Analyses Demonstrating Positive Shifts in Microbiome Properties

- Data from award-winning presentation at IDWeek 2021 represents the first time Ferring is showcasing the RBX2660 clinical development program as a whole, comprising the largest, most robust program ever conducted in the field of microbiome-based therapeutics for recurrent C. difficile infection (rCDI)
- Only gut microbiome research program with five clinical studies demonstrating consistent safety, efficacy and durability
- New analysis of Phase 3 data also showed among treatment responders, RBX2660 significantly increased gut bacteria associated with health and decreased gut bacteria associated with CDI pathology
- Analysis of Phase 3 data showed bile acid compositions shifted significantly from primary to secondary bile acid predominance after treatment

**Parsippany, NJ, USA – September 29, 2021** – Ferring Pharmaceuticals and Rebiotix, a Ferring Company, today announced final results of an analysis from five prospective trials of its investigational microbiota-based live biotherapeutic, RBX2660, for the reduction of recurrent *C. difficile* infection (rCDI). The abstract, presented at IDWeek 2021, represents the first time these data are showcased together, and is one of only four abstracts to receive the Program Committee Choice award for outstanding scientific research.

*"For years, people with recurrent C. difficile infection haven't had an available, standardized treatment option to break the cycle of recurrence or clinically address the health of their gut microbiome composition that puts them at risk for this highly communicable disease, and they still do not,"* said Teena Chopra, MD, MPH, Professor of Medicine, Division of Infectious Disease, Wayne State University School of Medicine. *"The important data from the Ferring microbiome-based biotherapeutic trials provide a significant milestone for the C. difficile community to hopefully one day have an improved treatment option for patients suffering from this disease."*

Across the five prospective trials, which included 723 actively-treated participants, RBX2660 consistently reduced the recurrence of CDI, with up to 78.9% remaining recurrence-free for eight weeks post treatment (defined as treatment success). Among participants who did not respond to initial treatment, an optional additional treatment course was administered, resulting in overall rates of treatment success of up to 84.4%. Notably, most primary responders remained CDI-free for six months and up to two years, with a sustained clinical response success rate of up to 92.1% in the Phase 3 program.

*"These data provide the totality of evidence culminating in over a decade's worth of work that demonstrates a consistent efficacy profile for RBX2660, and importantly, a consistent safety profile across five prospective trials,"* said Lindy L. Bancke, PharmD, Head of Clinical Development at Rebiotix, who presented the research. *"They reinforce the enormous potential of microbiome-based therapeutics to transform the care of people suffering from rCDI."*

This analysis included three Phase 2 (PUNCH CD, PUNCH CD2, PUNCH CD Open Label) and two Phase 3 trials (PUNCH CD3, PUNCH CD3-OLS ad hoc analysis). All participants were ages 18 or older who had at least one recurrence after a primary episode of CDI and had completed at least one round of standard-of-care oral antibiotic therapy. According to a separate presentation on safety, RBX2660 demonstrated a consistent safety profile across all five clinical studies. The percentage of participants reporting a treatment-emergent adverse event (TEAE) in the RBX2660 group was similar to the group receiving the standard-of-care plus placebo. Most TEAEs were mild or moderate in severity, and no potentially life-threatening TEAEs were considered related to RBX2660.

A third abstract showed that, among treatment responders in the PUNCH CD3 trial, RBX2660 significantly increased gut bacteria associated with health and decreased gut bacteria associated with CDI pathology within seven days, maintaining that effect for up to six months following treatment. Specifically, RBX2660 demonstrated an increase in the relative abundance of two important classes of beneficial bacteria – Bacteroidia and Clostridia – and reduced relative abundance of classes that could be considered harmful, Gammaproteobacteria and Bacilli.

*"C. difficile infection often is marked by a vicious cycle of recurrence, wherein patients' infection may return within days after antibiotic treatment. This can significantly impact a person's health and well-being, and burden the healthcare system*," said Ken Blount, PhD, Chief Scientific Officer at Rebiotix and a study presenter. *"The shift of the microbiome observed in our study provides the first evidence linking Phase 3 efficacy data of RBX2660 with improved microbiota composition of the gut. This finding is important, as this is during a time when a person recovering from CDI is most vulnerable for reinfection, and these changes were durable for at least six months."*

Additional evidence from the PUNCH CD3 trial, presented in two separate abstracts, demonstrated important potential benefits that may contribute to the therapeutic efficacy seen in the clinical program. In the trial, RBX2660 appeared to remove potentially deadly antimicrobial resistant (AMR) bacteria from the gut microbiota, as researchers found that the total number of AMR genes in participants receiving RBX2660 decreased significantly after treatment and remained low for at least six months. Colonization of AMR pathogens in the gut is a known risk factor for infection and common among people with recurrent CDI. The PUNCH CD3 analysis also showed that RBX2660 treatment responders exhibited reduction in primary bile acids, known to trigger CDI spore germination, and increase secondary bile acids, known to inhibit spore germination and growth.[1]

**About the gut microbiome and *C. difficile* infection**

*C. difficile* infection (CDI) is a serious and potentially deadly disease that impacts people across the globe. The *C. difficile* bacterium causes debilitating symptoms such as severe diarrhea, fever, stomach tenderness or pain, loss of appetite, nausea and colitis (an inflammation of the colon).[2] Declared a public health threat by the U.S. Centers for Disease Control and Prevention (CDC) requiring urgent and immediate action, CDI causes an estimated half a million illnesses and tens of thousands of deaths in the U.S. alone each year.[2,3,4]

*C. difficile* infection often is the start of a vicious cycle of recurrence, causing a significant burden for patients and the healthcare system.[5,6] Up to 35% of CDI cases recur after initial diagnosis[7,8] and people who have had a recurrence are at significantly higher risk of further infections.[9,10,11,12] After the first recurrence, it has been estimated that up to 60% of patients may develop a subsequent recurrence.[13]

Recurrent *C. difficile* infection (rCDI) is associated with disruptions to the gut microbiome, or "dysbiosis". The gut microbiome is a highly-diverse microbial community that plays an essential role in human health. There is a growing body of evidence that shows when there is a disruption of the composition and/or diversity of the gut microbiome, there may be an associated risk for serious illnesses, including CDI. The current standard of care treatment for rCDI is antibiotics, which does

not address the underlying dysbiosis or restore the gut microbiome.[14] The use of antibiotics has been shown to disrupt the ecology of the gut microbiome and are a predominant risk factor for rCDI.[7,8,14]

Restoring the gut microbiome is increasingly accepted as a promising treatment option for recurrent *C. difficile* infection.[15]

**About RBX2660**
RBX2660 is a potential first-in-class microbiota-based live biotherapeutic being studied to deliver a broad consortium of diverse microbes to the gut to reduce recurrent *C. difficile* infection. RBX2660 has been granted Fast Track, Orphan, and Breakthrough Therapy designations from the U.S. Food and Drug Administration (FDA). The pivotal Phase 3 program builds on nearly a decade of research with robust clinical and microbiome data collected over six controlled clinical trials with more than 1,000 participants.

**About Ferring Pharmaceuticals**
Ferring Pharmaceuticals is a research-driven, specialty biopharmaceutical group committed to helping people around the world build families and live better lives. Headquartered in Saint-Prex, Switzerland, Ferring is a leader in reproductive medicine and maternal health, and in specialty areas within gastroenterology and urology. Ferring has been developing treatments for mothers and babies for over 50 years and has a portfolio covering treatments from conception to birth. Founded in 1950, privately-owned Ferring now employs approximately 6,500 people worldwide, has its own operating subsidiaries in nearly 60 countries and markets its products in 110 countries. The Ferring Research Institute Inc. (FRI), based in San Diego, USA, is part of the Global Drug Discovery & External Innovation unit, which is the research and ideas engine of Ferring Pharmaceuticals. FRI is an integral part of Ferring's R&D organization, focusing on early drug discovery and development. Learn more at www.ferring.com, or connect with us on Twitter, Facebook, Instagram, LinkedIn and YouTube.

Ferring is committed to exploring the crucial link between the microbiome and human health, beginning with the threat of recurrent *C. difficile* infection. With the 2018 acquisition of Rebiotix and several other alliances, Ferring is a world leader in microbiome research, developing novel microbiome-based therapeutics to address significant unmet needs and help people live better lives. Connect with us on our dedicated microbiome therapeutics development channels on Twitter and LinkedIn.

**About Rebiotix**
Rebiotix Inc, a Ferring Company, is a late-stage clinical microbiome company focused on harnessing the power of the human microbiome to revolutionize the treatment of challenging diseases. Rebiotix has a diverse pipeline of investigational drug products built on its pioneering microbiota-based MRT™ drug platform. The platform consists of investigational drug technologies designed to potentially rehabilitate the human microbiome by delivering a broad consortium of live microbes into a patient's intestinal tract. For more information on Rebiotix and its pipeline of human microbiome-directed therapies for diverse disease states, visit www.rebiotix.com, or connect with us on Twitter, Facebook, LinkedIn and YouTube.

**About IDWeek**
IDWeek is the joint annual meeting of the Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), the HIV Medical Association (HIVMA), the Pediatric Infectious Diseases Society (PIDS), and the Society of Infectious Diseases Pharmacists (SIDP). More information can be found at www.idweek.org.

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