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FERRING PHARMACEUTICALS

Microbiome Therapeutics Development

Media Release

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Ferring and Rebiotix Present Positive Interim Phase 3 Results from Open-Label Study of Investigational Microbiota-based Live Biotherapeutic RBX2660 at Digestive Disease Week® (DDW)

- *Interim analysis of the Phase 3 PUNCH™ CD3-Open-Label Study (OLS) showed positive efficacy and consistent safety with RBX2660 for up to six months in patients with recurrent Clostridioides difficile (C. difficile) infection, adding to robust evidence of largest clinical development program in microbiome-based therapeutics*

- *Expanded inclusion criteria allowed for enrollment of patients with C. difficile infection typically seen in clinical practice, including those with a co-diagnosis of inflammatory bowel disease (IBD) or irritable bowel syndrome (IBS)*

- *An additional data presentation demonstrating the devastating impact of sepsis – a potential complication of C. difficile infection – through an analysis of nearly 500,000 U.S. Medicare claims was also highlighted at DDW*

Saint-Prex, Switzerland, and Roseville, MN, USA – May 22, 2021 – Ferring Pharmaceuticals and Rebiotix, a Ferring Company, announced today the first presentation of interim data from a Phase 3 open-label study showing strong trends in efficacy and safety for investigational microbiota-based live biotherapeutic RBX2660 in reducing recurrent *Clostridioides difficile* (*C. difficile*) infection over six months, consistent with previous findings in the comprehensive RBX2660 clinical development program. The study also enrolled patients diagnosed with co-morbid conditions such as inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS). The patients enrolled closely reflect the recurrent *C. difficile* infection patients who healthcare providers treat every day. The results were presented at Digestive Disease Week® (DDW) 2021, taking place virtually this year from May 21-23.

"These data are significant because eligibility criteria for such studies are often rigid and exclude patients with potentially confounding co-morbid conditions. In contrast, eligibility criteria for the PUNCH CD3 open-label study were less restrictive, mimicking real clinical practice," said Colleen Kraft, MD, MSc, Associate Professor, Division of Infectious Diseases, Emory University School of Medicine, Atlanta, Ga., and presenting author. *"This interim analysis supports the safety and efficacy of RBX2660 in reducing CDI recurrence in a patient population representative of standard clinical practice, including those with a co-diagnosis of IBD and/or IBS. The observed efficacy and safety are also consistent with*

other trials of RBX2660, with the sustained efficacy at six months suggesting a potential long-term benefit."

At the time of the interim analysis, 75% of participants whose treatment outcomes could be analysed (n=60) were free of *C. difficile* infection at 8 weeks. Among patients with treatment successes who also reached six-month follow-up (n=27), 74% remained symptom-free. About half (49%) of patients reported treatment-emergent adverse events (TEAEs). The most common TEAEs were gastrointestinal, and mild to moderate in nature. These preliminary findings build on, and are supportive of, the data from the Phase 3 PUNCH™ CD3 randomized, placebo-controlled trial, which were presented at DDW on May 21.

The RBX2660 program is the largest and most robust clinical program ever conducted in the field of microbiome-based therapeutics, including six trials involving more than 1,000 patients. In addition to the interim six-month efficacy and safety seen in the PUNCH CD3-OLS, the Phase 2b double-blind, randomized, placebo-controlled trial (PUNCH CD2) and the Phase 2 open-label study (PUNCH Open Label) showed clinical response for up to two years post treatment.

"Our clinical program is the only one to capture consistent evidence over six clinical trials, repeatedly demonstrating the efficacy and safety of RBX2660," said Ken Blount, Chief Scientific Officer, Rebiotix and Vice President of Microbiome Research, Ferring Pharmaceuticals. *"The interim results of the PUNCH CD3-OLS, which encompasses rCDI patients that clinicians see in their daily practice, confirm the consistent safety we've seen with RBX2660 over the course of this development program. We believe RBX2660 could help tens of thousands of people who experience recurrent C. difficile infection every year – these data are a crucial demonstration of RBX2660's potential."*

Retrospective Study Shows Devastating Health, Financial Impact of Sepsis in CDI Patients

In addition to the PUNCH CD3-OLS results, Ferring presented a second poster comparing the rate of death, healthcare resource utilization (HRU), and cost among U.S. Medicare beneficiaries with primary CDI (pCDI) and rCDI with and without sepsis – sepsis is a life-threatening medical emergency caused by the body's extreme response to an infection and a common complication in patients with *C. difficile* infection. Overall, 41 percent of all patients had sepsis, which was more common in patients with rCDI than those with pCDI (45.1% vs. 39.2%, respectively). Patients with sepsis were more likely to die than those without sepsis (57.7% vs. 32.4%, respectively).

Among those who died, *C. difficile* infection patients with sepsis, especially those with rCDI, had substantially higher rates of intensive care unit (ICU) use, longer hospital stays, and higher healthcare costs versus *C. difficile* infection without sepsis. Specifically:

- ICU use: (pCDI: 29% vs 15%; rCDI: 65% vs 34%)
- Hospital stays (pCDI: 12 vs 10 days; rCDI: 12 vs 9 days)
- Healthcare costs (pCDI: $34,841 vs $22,753; rCDI: $42,269 vs. $25,047)

Costs for patients with sepsis who survived were lower but had a similar pattern compared to those without sepsis (pCDI: $10,093 vs. $4,930; rCDI: $12,013 vs. $5,707).

"These data show that recurrent C. difficile infection and resulting complications such as sepsis have a devastating and potentially deadly impact on patients, and places a significant burden on the overall healthcare system," said James Tursi, MD, Chief Scientific Officer, Ferring Pharmaceuticals USA. *"Urgent action is needed to halt the unrelenting cycle of recurrence seen with this disease. We're committed to further research that helps generate a greater understanding of the magnitude of C. difficile infection in order to help patients live better lives."*

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 the microbiome and *C. difficile* infection

The 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, such as *C. difficile* infection.

C. difficile is a bacterium that causes debilitating symptoms such as severe diarrhea, fever, stomach tenderness or pain, loss of appetite, nausea and colitis (an inflammation of the colon).[1] Estimated to cause up to half a million illnesses and thousands of deaths annually in the US alone every year, *C. difficile* infection is considered an urgent threat to public health by the CDC and can lead to severe complications, including hospitalization, surgery, sepsis and death.[1,2] *C. difficile* infection is often the start of a vicious cycle of recurrence, causing a significant burden for patients and the healthcare system.[3,4] The use of antibiotics has been shown to disrupt the ecology of the gut microbiome, and are a predominant risk factor for *C. difficile* recurrence – occurring in up to 35% of patients after initial *C. difficile* infection diagnosis.[5,6,7] After the first recurrence, it has been estimated that up to 60% of patients may develop a subsequent recurrence.[8]

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. 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 DDW

Digestive Disease Week® (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW is a fully virtual meeting from May 21-23, 2021. The meeting showcases more than 2,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. More information can be found at www.ddw.org.

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References:

1. Centers for Disease Control and Prevention. What Is C. Diff? 17 Dec. 2018. Available at: https://www.cdc.gov/cdiff/what-is.html.
2. Centers for Disease Control and Prevention. Biggest Threats and Data, 14 Nov. 2019. Available at: https://www.cdc.gov/drugresistance/biggest-threats.html.
3. Centers for Disease Control and Prevention. 24 June 2020. Available at: https://www.cdc.gov/drugresistance/pdf/threats-report/clostridioides-difficile-508.pdf.
4. Feuerstadt P, et al. *J Med Econ.* 2020;23(6):603-609.
5. Lessa FC, Mu Y, Bamberg WM, et al. Burden of *Clostridium difficile* infection in the United States. *N Engl J Med.* 2015;372(9):825-834.
6. Cornely OA, et al. Treatment of First Recurrence of Clostridium difficile Infection: Fidaxomicin Versus Vancomycin. *Clinical Infectious Diseases*. 2012;55(S2):S154–61.
7. Langdon A, Crook N, Dantas G. The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation. *Genome Med.* 2016;8(1):39.
8. Leong C, Zelenitsky S. Treatment strategies for recurrent *Clostridium difficile* infection. *Can J Hosp Pharm.* 2013;66(6):361-368.