

# Acurx Announces New Ibezapolstat Clinical Trial Program in Patients with Recurrent CDI That Has the Potential to Shift the Paradigm of Treatment and Prevention of *C. difficile* Infection

## *Acurx's Program in the Broader CDI Patient Population is Ready to Advance to Phase 3 International Clinical Trials*

- Acurx is launching a ground-breaking clinical trial with ibezapolstat in patients with multiply-recurrent CDI (rCDI) that has the potential to shift the paradigm of treatment and prevention of rCDI from two agents to one
- When coupled with IBZ Phase 2 results of being highly effective (96% clinical cure of 26 patients) in treating acute CDI with no recurrence in patients while sparing the gut microbiome, this new trial will position IBZ as a candidate to be the first agent to demonstrate clinical success in both the treatment of CDI and the prevention of rCDI
- In a Phase 2 trial, all 25 patients treated with IBZ who experienced a clinical cure of CDI were free of recurrence 1 month after treatment and 5 of 5 (100%) of these patients who were observed for 3 months after treatment remained free of recurrence
- Recent unpublished data from Dr. Kevin Garey's laboratory at the University of Houston demonstrate that beneficial bacterial taxa persist in fecal samples from patients with rCDI despite multiple prior CDI treatments with the antibiotic standards of care, vancomycin and/or fidaxomicin, indicating that, following acute treatment with IBZ, these beneficial microorganisms will have the opportunity to repopulate the microbiome in a favorable way that may prevent recurrence
- Trial start-up activities for this new clinical trial in rCDI will initiate later this month with the first patient expected to enroll in the fourth quarter this year. This open-label trial will enroll up to 20 patients whose CDI has recurred at least twice following standard of care antibiotic treatment within the past 12 months.
- Acurx has previously been granted FDA QIDP and Fast-Track Designation and has received SME (Small and Medium-sized Enterprise) designation by the EMA

STATEN ISLAND, N.Y., March 9, 2026 /PRNewswire/ -- **Acurx Pharmaceuticals, Inc.** (Nasdaq: ACXP) ("Acurx" or the "Company"), a clinical stage biopharmaceutical company developing a new class of antibiotics for difficult-to-treat bacterial infections, today announced that it will conduct a new clinical trial in patients with recurrent *C. difficile* Infection (rCDI) while its program in the broader CDI patient population is ready to advance to Phase 3 international clinical trials, subject to receiving appropriate funding. This new clinical trial in rCDI begins with an open-label pilot trial to gain experience with IBZ in patients with multiply-recurrent CDI with at least 3 episodes of CDI within the past 12 months. This will inform elements of a planned active-controlled, Phase 3 registration trial in the rCDI indication to be implemented following favorable results from the open-label 20 patient trial. Upon

subsequent successful completion of the Ph3 pivotal rCDI trial, and per the operative FDA procedure, Acurx plans to request FDA approval for treatment and prevention of rCDI under the FDA's Limited Population Pathway for Antibacterial and Antifungal Drugs (Guidance for Industry, 2020).

Results of the above-mentioned experimental data from the University of Houston laboratory of Dr. Kevin Garey, has been submitted in abstract form to the Anaerobe Society of the Americas scientific conference July 7-10, 2026, at Columbia University in New York and will be publicly disclosed shortly thereafter.

More details about this new program will be discussed on the company's March 13, 2026 earnings call for full year and fourth quarter 2025 financial results on Friday, March 13, 2026 at 8:00 am ET (Toll-Free (U.S.): 877-790-1503 Access ID: 13758852). [Click here for participant International Toll-Free access numbers](#). Members of the Acurx R&D team will be available on the earnings call to answer questions from stockholders or other interested parties.

Robert J. DeLuccia, Executive Chairman of Acurx, stated "Ibezapolstat has been demonstrated in Phase 2 to be highly effective in both curing CDI and in preventing recurrence. We believe ibezapolstat has the potential to be the first agent to demonstrate clinical success in both the treatment of CDI and the prevention of rCDI, and such success would shift the paradigm of treatment and prevention of rCDI from two agents to one. This would be a game changer to the public health threat that affects approximately 500,000 patients with CDI each year in the U.S., results in approximately 30,000 deaths, and generates a related public health cost burden of approximately \$5 billion, of which \$2.8 billion is related to rCDI."

He further stated: "We're also very excited about the FDA's recent announcement published in the New England Journal of Medicine '...that a one-trial requirement will be FDA's new default standard [for registration]. If formalized, this would end the long-standing two-trial dogma. We look forward to FDA's further clarification and the potentially favorable implications to our clinical development programs, such as the opportunity to seek marketing approval for the broader CDI population with one pivotal clinical trial. This would of course have favorable effects for our stockholders and, very importantly, CDI patients in need."

*For recent publications regarding above, please see our website:*[www.acurxpharma.com](http://www.acurxpharma.com)

*Makary, NEJM, Feb2026; WK Smits, Nature Communications, Nov2025; Lancet Microbe, June 2025*

### **About rCDI (Recurrent *C. difficile* Infection)**

In recent studies, rCDI ranges from 4 to 19.5% following treatment with fidaxomicin and 17 to 27% following treatment with vancomycin. In patients with multiple prior episodes of CDI, rCDI following treatment with vancomycin is even more problematic, with an incidence of up to 40%. Consequently, the principal unmet medical need in this disease is the prevention of recurrence. The estimated annual public health cost burden in the U.S. annually is ~\$5 billion annually with ~\$2.8 billion due to recurrent CDI.

Acurx previously announced that it had received positive regulatory guidance from the EMA during its Scientific Advice Procedure which confirmed that the clinical, non-clinical and CMC

(Chemistry Manufacturing and Controls) information package submitted to EMA supports advancement of the ibezapolstat Phase 3 program and if the Phase 3 program is successful, supports the submission of a Marketing Authorization Application (MAA) for regulatory approval in Europe. The information package submitted to EMA by the Company to which agreement has been reached with EMA included details on Acurx's two planned international Phase 3 clinical trials, 1:1 randomized (designed as non-inferiority vs vancomycin), primary and secondary endpoints, sample size, statistical analysis plan and the overall registration safety database. With mutually consistent feedback from both EMA and FDA, Acurx is well positioned to commence our international Phase 3 registration program.

The primary efficacy analysis will be performed using a Modified Intent-To-Treat (mITT) population. This will result in an estimated 450 subjects in the mITT population, randomized in a 1:1 ratio to either ibezapolstat or standard-of-care vancomycin, enrolled into the initial Phase 3 trial. The trial design not only allows determination of ibezapolstat's ability to achieve Clinical Cure of CDI as measured 2 days after 10 days of oral treatment but also includes assessment of ibezapolstat's potential effect on reduction of CDI recurrence in the target population. In the event non-inferiority of ibezapolstat to vancomycin is demonstrated, further analysis will be conducted to test for superiority.

### **About the Ibezapolstat Phase 2 Clinical Trial**

The completed multicenter, open-label single-arm segment (Phase 2a) study was followed by a double-blind, randomized, active-controlled, non-inferiority, segment (Phase 2b) at 28 US clinical trial sites which together comprise the Phase 2 clinical trial. This Phase 2 clinical trial was designed to evaluate the clinical efficacy of ibezapolstat in the treatment of CDI including pharmacokinetics and microbiome changes from baseline. from study centers in the United States. In the Phase 2a trial segment, 10 patients with diarrhea caused by *C. difficile* were treated with ibezapolstat 450 mg orally, twice daily for 10 days. All patients were followed for recurrence for 28 ± 2 days. Per protocol, after 10 patients of the projected 20 Phase 2a patients completed treatment (100% cured infection at End of Treatment (10 of 10).

In the Phase 2b trial segment, 32 patients with CDI were enrolled and randomized in a 1:1 ratio to either ibezapolstat 450 mg every 12 hours or vancomycin 125 mg orally every 6 hours, in each case, for 10 days and followed for 28 ± 2 days following the end of treatment for recurrence of CDI. The two treatments were identical in appearance, dosing times, and number of capsules administered to maintain the blind. In this Phase 2b trial segment, 15 out of 16 (94%) patients in Phase 2b in the Per Protocol Population experienced Clinical Cure (CC) and all 15 of 15 (100%) remained free of *C. difficile* infection (CDI) recurrence through one month after EOT.

When Phase 2b results are combined with Phase 2a results, the Clinical Cure rate in patients with CDI was 96% (25 out of 26 patients), based on 10 out of 10 patients (100%) in Phase 2a in the Modified Intent to Treat Population, plus 15 out of 16 (94%) patients in Phase 2b in the Per Protocol Population, who experienced Clinical Cure during treatment with ibezapolstat. Notably, in the combined Phase 2 trial, 100% (25 of 25) ibezapolstat-treated patients) who had Clinical Cure at EOT (End of Treatment) remained cured through one month after EOT, as compared to 86% (12 of 14) for the vancomycin patient group.

Ibezapolstat was well-tolerated, with no serious adverse events assessed by the blinded investigator to be drug-related. The Company is confident that based on the pooled Phase 2

ibezapolstat Clinical Cure rate of 96%, Sustained Clinical Cure Rate of 100% and the historical vancomycin Clinical Cure Rate range of 70% to 92% and a Sustained Clinical Cure historical range of 42% to 74%, we will demonstrate non-inferiority of ibezapolstat to vancomycin in Phase 3 trials, in accordance with the applicable FDA Guidance for Industry (October 2022), with favorable differentiation in both Clinical Cure and Sustained Clinical Cure.

In the Phase 2 clinical trial (both trial segments), the Company also evaluated pharmacokinetics (PK) and microbiome changes and test for anti-recurrence microbiome properties, including the change from baseline in alpha diversity and bacterial abundance, especially overgrowth of healthy gut microbiota Actinobacteria and Firmicute phylum species during and after therapy. Phase 2a data demonstrated complete eradication of colonic *C. difficile* by day three of treatment with ibezapolstat as well as the observed overgrowth of healthy gut microbiota, Actinobacteria and Firmicute phyla species, during and after therapy. Very importantly, emerging data show an increased concentration of secondary bile acids during and following ibezapolstat therapy which is known to correlate with colonization resistance against *C. difficile*. A decrease in primary bile acids and the favorable increase in the ratio of secondary-to-primary bile acids suggest that ibezapolstat may reduce the likelihood of CDI recurrence when compared to vancomycin. The company also reported positive extended clinical cure (ECC) data for ibezapolstat (IBZ), its lead antibiotic candidate, from the Company's recently completed Phase 2b clinical trial in patients with CDI. This exploratory endpoint showed that 5 of 5 IBZ patients followed for up to three months following Clinical Cure experienced no recurrence of infection. Furthermore, ibezapolstat-treated patients showed lower concentrations of fecal primary bile acids, and higher beneficial ratio of secondary to primary bile acids than vancomycin-treated patients.

### **About Ibezapolstat**

Ibezapolstat is the Company's lead antibiotic candidate planning to advance to international Phase 3 clinical trials to treat patients with *C. difficile* infection. Ibezapolstat is a novel, orally administered antibiotic, being developed as a Gram-Positive Selective Spectrum (GPSS®) antibacterial. It is the first of a new class of DNA polymerase III inhibitors under development by Acurx to treat bacterial infections. Ibezapolstat's unique spectrum of activity, which includes *C. difficile* but spares other

Firmicutes and the important Actinobacteria phyla, appears to contribute to the maintenance of a healthy gut microbiome.

In June 2018, ibezapolstat was designated by the U.S. Food and Drug Administration (FDA) as a Qualified Infectious Disease Product (QIDP) for the treatment of patients with CDI and will be eligible to benefit from the incentives for the development of new antibiotics established under the Generating New Antibiotic Incentives Now (GAIN) Act. In 2019, FDA granted "Fast Track" designation to ibezapolstat for the treatment of patients with CDI. The CDC has designated *C. difficile* as an urgent threat highlighting the need for new antibiotics to treat CDI.

### **About *Clostridioides difficile* Infection**

According to the 2017 Update (published February 2018) of the Clinical Practice Guidelines for *C. difficile* Infection by the Infectious Diseases Society of America (IDSA) and Society of Healthcare Epidemiology of America (SHEA), CDI remains a significant medical problem in hospitals, in long-term care facilities and in the community. *C. difficile* is one of the most

common causes of health care-associated infections in U.S. hospitals (Lessa, 2015, NEJM). Recent estimates suggest *C. difficile* approaches 500,000 infections annually in the U.S. and is associated with approximately 20,000 deaths annually. (Guh, 2020, NEJM. Based on internal estimates, the recurrence rate for the antibiotics currently used to treat CDI is between 20% and 40% among approximately 150,000 patients treated. We believe the annual incidence of CDI in the U.S. approaches 600,000 infections and a mortality rate of approximately 9.3%.

### ***About the Microbiome in C. difficile Infection and Bile Acid Metabolism***

*C. difficile* can be a normal component of the healthy gut microbiome, but when the microbiome is thrown out of balance, the *C. difficile* can thrive and cause an infection. After colonization with *C. difficile*, the organism produces and releases the main virulence factors, the two large clostridial toxins A (TcdA) and B (TcdB). (Kachrimanidou, Microorganisms 2020.) TcdA and TcdB are exotoxins that bind to human intestinal epithelial cells and are responsible for inflammation, fluid and mucous secretion, as well as damage to the intestinal mucosa. Bile acids perform many functional roles in the GI tract, with one of the most important being maintenance of a healthy microbiome by inhibiting *C. difficile* growth. Primary bile acids, which are secreted by the liver into the intestines, promote germination of *C. difficile* spores and thereby increase the risk of recurrent CDI after successful treatment of an initial episode. On the other hand, secondary bile acids, which are produced by normal gut microbiota through metabolism of primary bile acids, do not induce *C. difficile* sporulation and therefore protect against recurrent disease. Since ibezapolstat treatment leads to minimal disruption of the gut microbiome, bacterial production of secondary bile acids continues which may contribute to an anti-recurrence effect. Beneficial effects of bile acids include a decrease in primary bile acids and an increase in secondary bile acids in patients with CDI, which was observed in the Company's Ph2a trial results and previously reported (Garey, CID, 2022). In the Ph2b trial, ibezapolstat-treated patients showed lower concentrations of fecal primary bile acids, and higher beneficial ratio of secondary to primary bile acids than vancomycin-treated patients.

### **About Acurx Pharmaceuticals, Inc.**

Acurx Pharmaceuticals is a late-stage biopharmaceutical company focused on developing a new class of small molecule antibiotics for difficult-to-treat bacterial infections. The Company's approach is to develop antibiotic candidates with a Gram-positive selective spectrum (GPSS®) that blocks the active site of the Gram-positive specific bacterial enzyme DNA polymerase III C (pol III C), inhibiting DNA replication and leading to Gram-positive bacterial cell death. Its R&D pipeline includes antibiotic product candidates that target Gram-positive bacteria, including *Clostridioides difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant Enterococcus (VRE), drug-resistant *Streptococcus pneumoniae* (DRSP) and *B. anthracis* (anthrax; a Bioterrorism Category A Threat-Level pathogen). Acurx's lead product candidate, ibezapolstat, for the treatment of *C. difficile* Infection is Phase 3 ready with plans in progress to begin international clinical trials. The Company's preclinical pipeline includes development of an oral product candidate for treatment of ABSSSI (Acute Bacterial Skin and Skin Structure Infections), upon which a development program for treatment of inhaled anthrax is being planned in parallel.

To learn more about Acurx Pharmaceuticals and its product pipeline, please visit [www.acurxpharma.com](http://www.acurxpharma.com).

## **Forward-Looking Statements**

Any statements in this press release about our future expectations, plans and prospects, including statements regarding our strategy, future operations, prospects, plans and objectives, and other statements containing the words "believes," "anticipates," "plans," "expects," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: whether ibezapolstat will benefit from the QIDP designation; whether ibezapolstat will advance through the clinical trial process on a timely basis; whether the results of the clinical trials of ibezapolstat will warrant the submission of applications for marketing approval, and if so, whether ibezapolstat will receive approval from the FDA or equivalent foreign regulatory agencies where approval is sought; whether, if ibezapolstat obtains approval, it will be successfully distributed and marketed; and other risks and uncertainties described in the Company's annual report filed with the Securities and Exchange Commission on Form 10-K for the year ended December 31, 2024, and in the Company's subsequent filings with the Securities and Exchange Commission. Such forward-looking statements speak only as of the date of this press release, and Acurx disclaims any intent or obligation to update these forward-looking statements to reflect events or circumstances after the date of such statements, except as may be required by law.

### **Investor Contact:**

Acurx Pharmaceuticals, Inc..

David P. Luci, President & CEO

Tel: 917-533-1469;

Email: [davidluci@acurxpharma.com](mailto:davidluci@acurxpharma.com)

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