September 30, 2025

Acurx Pharmaceuticals

Acurx Announces Positive Opinion from EMA on Pediatric Investigation Plan for Ibezapolstat Use in Children with C. difficile Infection

- The Paediatric Committee (PDCO) of the European Medicines Agency issued a positive opinion on Acurx's Pediatric Investigation Plan (PIP) for ibezapolstat use in children with *C. difficile* infection
- Receipt of this positive opinion caps off the EMA's requirement to have the PIP agreed to by the initiation of ibezapolstat Phase 3 clinical trials in the European Union
- Acurx previously announced that both the EMA and the FDA are aligned with its clinical trial program in the adult population along with clearly defined requirements for the regulatory pathway to an EU MAA and a U.S. NDA
- In addition to receiving this positive EMA opinion, Acurx will proceed with its integrated PIP submission to the FDA
- Acurx is well positioned to begin international Phase 3 clinical trials and 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., Sept. 30, 2025 /PRNewswire/ -- Acurx Pharmaceuticals, Inc. (NASDAQ: ACXP) ("Acurx" or the "Company") is a late-stage biopharmaceutical company developing a new class of small molecule antibiotics for difficult-to-treat bacterial infections announced receipt of a favorable opinion from the PDCO of the EMA on Acurx's Pediatric Investigation Plan (PIP) for ibezapolstat use in children with *C. difficile* infection (CDI).

C. difficile is the most important infectious cause of antibiotic-associated diarrhea worldwide and a leading cause of healthcare-associated infection in the United States. The incidence of CDI in children has increased, with 20,000 cases now reported annually. CDI in children is more commonly community-associated, accounting for three-quarters of all cases. A wide spectrum of disease severity ranging from asymptomatic carriage to severe diarrhea can occur, varying by age. Fulminant disease, although rare in children, is associated with high morbidity and even fatality. Similar to disease in adults, recurrence of CDI in children is common, affecting 20% to 30% of incident cases. Recent advancements in understanding of emerging epidemiologic trends and management of CDI unique to children are being realized. Despite encouraging therapeutic advancements, there remains a pressing need to optimize CDI therapy in children, particularly as it pertains to severe and recurrent disease.*

Acurx's Executive Chairman, Bob DeLuccia, stated: We're very pleased to have received this positive EMA opinion as part of our EMA regulatory pathway, since there is a significant unmet need for an innovative antibiotic to treat children suffering from CDI. Our pediatric clinical trial program is designed to demonstrate that ibezapolstat will be a safe and effective treatment that could represent a transformative advance to achieve CDI cure, reduce recurrences, and preserve the gut microbiome in this vulnerable patient population.

Importantly, this could lead to reduction of the overall antimicrobial exposure in children with CDI." He added: "Additionally, ibezapolstat would be eligible to apply for an additional one year of marketing exclusivity in Europe on top of the 10 years exclusivity period to be granted for a successful MAA for a new class of antibiotic."

** Adapted from: Shirley DA, Tornel W, Warren CA, Moonah S. Clostridioides difficile Infection in Children: Recent Updates on Epidemiology, Diagnosis, Therapy. Pediatrics. 2023 Sep 1;152(3):e2023062307. doi: 10.1542/peds.2023-062307. PMID: 37560802; PMCID: PMC10471512.*

About the Pediatric Committee (PDCO)
The Pediatric Committee (PDCO) is the European Medicines Agency's (EMA) scientific committee responsible for activities on medicines for children and to support the development of such medicines in the European Union by providing scientific expertise and defining pediatric needs. The PDCO issues an opinion on PIP as part of the regulatory process and the EMA adopts a final decision based on the PDCO's opinion.

About the Pediatric Investigation Plan (PIP)
A pediatric investigation plan (PIP) is a development plan aimed at ensuring that the necessary data are obtained through studies in children, to support the authorization of a medicine for children. As part of the regulatory process for the registration of new medicines in Europe, the EMA requires pharmaceutical companies to provide a PIP detailing their strategy for investigation of the new medicinal product in the pediatric population. An approved PIP is a prerequisite for filing a Marketing Authorization Application (MAA).

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 IIIC 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 or 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 IIIC (pol IIIC), 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.

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.

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