September 29, 2026 Acurx Pharmaceuticals

Acurx Pharmaceuticals Announces First Patient Enrolled in PATHFINDER Clinical Trial of Ibezapolstat in Multiply-Recurrent C. difficile Infection

- PATHFINDER is a ground-breaking Phase 2 clinical trial with ibezapolstat (IBZ) in patients with multiply-recurrent CDI (*C. difficile* Infection) (rCDI) that, together with results from the planned ASPIRE Phase 3 trial in the broader patient population for the treatment of acute CDI, has potential to shift the paradigm of treatment and prevention of rCDI from two agents to one
- PATHFINDER by itself in patients with multiply-recurrent CDI will inform elements of a planned active-controlled, Phase 3 registration trial in rCDI. Upon subsequent successful completion of PATHFINDER, Acurx plans to request FDA approval for treatment and prevention of rCDI under the FDA's Limited Population Pathway for Antibacterial and Antifungal Drugs*
- Acurx is well positioned to commence its international pivotal Phase 3 ASPIRE trial, subject to funding availability, having both FDA and EMA alignment on the Phase 3 clinical program and pathway to U.S. NDA and MAA in the EU
- 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., Sept. 29, 2026 /PRNewswire/ -- Acurx Pharmaceuticals, Inc. (NASDAQ: ACXP) ("Acurx" or the "Company"), a late-stage biopharmaceutical company developing a new class of antibiotics for difficult-to-treat bacterial infections, today announced that the first patient has been enrolled in its new clinical trial (PATHFINDER) in patients with multiply recurrent *C. difficile* Infection (rCDI). This new, fully funded,PATHFINDER clinical trial is a pilot trial in approximately 20 patients with multiply-recurrent CDI (at least three episodes over the past 12 months), and will support filing of a U.S. NDA (New Drug Application) based on a single Phase 3 trial.

ThePATHFINDER Phase 2 multicenter, open-label, single-arm study evaluates the efficacy and safety of ibezapolstat in the treatment and reduction of recurrence of CDI in patients who have experienced at least 3 episodes of CDI within the past 12 months. Participants will be treated with IBZ for 14 days and assessed for Clinical Cure (Day 16), Sustained Clinical Cure (Day 42), rate of CDI recurrence (to Week 24), and Extended Clinical Cure (to Week 24).
https://clinicaltrials.gov/study/NCT07513285?term=acurx&viewType=Card&rank=2

Separately, the planned ASPIRE trial is of non-inferiority design with the primary efficacy analysis in the Modified Intent-To-Treat (mITT) population and will result in approximately 550 subjects in the mITT population, randomized in a 1:1 ratio to either ibezapolstat or standard-of-care vancomycin. The ASPIRE trial will be conducted when the Company has sufficient resources from public or private partnership(s) to fund this trial.

Acurx's Executive Chairman, Bob DeLuccia, stated: "We're very excited about our current momentum in moving ibezapolstat a few steps closer toward commercialization having a clearly defined regulatory and clinical pathway." He added: "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, potentially shifting 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., resulting in approximately 30,000 deaths, and generating a related public health cost burden of approximately $5 billion, of which $2.8 billion is related to rCDI."

*https://www.fda.gov/regulatory-information/search-fda-guidance-documents/limited-population-pathway-antibacterial-and-antifungal-drugs-guidance-industry

Acurx previously announced the successful outcome of a Type C Meeting conducted with FDA on July 13, 2026 to discuss ibezapolstat's Phase 3 clinical program and scope of its planned NDA. The Agency stated that it is open to further discussion at a Pre-NDA Meeting regarding the possibility of submitting an NDA with only a single Phase 3 trial, depending on the totality of the clinical data plus any other supportive data that Acurx may generate by that milestone. The Agency noted that determination of acceptability of one Phase 3 clinical trial for an NDA is made on a case-by-case basis, taking into consideration such factors as the magnitude, consistency, and overall robustness of the efficacy results; generalizability of the results to the US population; relevance of the results to US patient care and clinical practice guidelines; Phase 2 data; and an adequate safety database. The Agency acknowledged Acurx's planned clinical trial in recurrent CDI (rCDI) and noted the data from this rCDI trial, if successful, would support an NDA submission. If the IBZ-ASPIRE trial does not meet these criteria, then a second trial consistent with the agreement reached at the end of Phase 2 (EOP2) meeting on April 27, 2024, is recommended.

The currently planned IBZ-ASPIRE trial is of non-inferiority design with the primary efficacy analysis in the Modified Intent-To-Treat (mITT) population. This will result in approximately 550 subjects in the mITT population, randomized in a 1:1 ratio to either ibezapolstat or standard-of-care vancomycin. The Agency also agreed with the overall trial design and evaluation criteria and further agreed that the trial testing criteria, if successful, could support indications for both the acute treatment and the reduction of recurrence of CDI. In the event non-inferiority of ibezapolstat to vancomycin for Clinical Cure of CDI is demonstrated, further analyses will be conducted to test for superiority for reduction of recurrence and for clinical cure of CDI.

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 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. (see https://clinicaltrials.gov/ct2/show/NCT04247542). 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 and continue to test for anti-recurrence microbiome properties seen in the Phase 2a trial, including the treatment-related changes in alpha diversity and bacterial abundance and effects on bile acid metabolism. (Data published in Lancet, August 2025 https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(25)00054-0/fulltext).

About Clostridioides difficile Infection (CDI) and Recurrent CDI (rCDI)
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 30,000 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%.

In recent studies, rCDI incidence 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.

About the Microbiome in *C. difficile* Infection (CDI) 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, 8, 200; doi:10.3390/microorganisms8020200.) 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 (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+ 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 (CDI) is Phase 3 ready to advance to international clinical trials subject to obtaining appropriate financing. Acurx has received FDA guidance in meeting minutes from a July 13, 2026 Type C Meeting to discuss ibezapolstat's (IBZ) Phase 3 clinical program, including the potential to submit an NDA (New Drug Application) based on a single Phase 3 trial and a clinical trial design intended to support indications for both treatment and reduction of recurrence of Clostridioides difficile infection (CDI). FDA stated that it is open to further discussion on the totality of evidence from the clinical development program at a pre-NDA meeting after completion of a single Phase 3 trial and any other clinical trials conducted prior to the pre-NDA meeting, particularly if the clinical efficacy results are robust. Additionally, the Agency agreed that a successful clinical outcome from a single IBZ-ASPIRE Phase 3 trial, supported by the open-label IBZ-PATHFINDER Phase 2 trial in multiply-recurrent CDI (rCDI) will allow an NDA filing for both the acute treatment and the reduction of recurrence of CDI. The IBZ-PATHFINDER trial is currently enrolling. https://clinicaltrials.gov/study/NCT07513285?term=acurx&viewType=Card&rank=2

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 prophylaxis 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 described in the Company's annual report on Form 10-K for the year ended December 31, 2025 as filed with the Securities and Exchange Commission on March 12 2026, 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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