

Acurx Receives Positive Regulatory Guidance from EMA for Ibezapolstat Phase 3 Program for C. Difficile Infection (CDI)

- *Acurx has now received positive written responses from the EMA (European Medicines Agency) under its Scientific Advice Procedure that the clinical, non-clinical and CMC (Chemistry Manufacturing and Controls) information package submitted supports advancement of the ibezapolstat Phase 3 program*
- *The responses also included guidance on ibezapolstat's regulatory pathway for a Marketing Authorization Application for ibezapolstat in CDI*
- *With mutually consistent feedback from both EMA and FDA, Acurx is well positioned to commence our international Phase 3 registration program*
- *Acurx is also preparing to request regulatory guidance to initiate clinical trials in Japan, Canada and the United Kingdom*
- *Ibezapolstat has previously been granted FDA QIDP and Fast-Track Designation from FDA and Acurx has received SME (Small and Medium-sized Enterprise) designation by the EMA to benefit from fee incentives and other support from the EMA for EU Marketing Authorization*

STATEN ISLAND, N.Y., Jan. 6, 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, with its lead antibiotic candidate, ibezapolstat, preparing to advance to international Phase 3 clinical trials to treat patients with *C. difficile* Infection (CDI). The Company today announced that it has received positive regulatory guidance from the EMA during its Scientific Advice Procedure that the clinical, non-clinical and CMC (Chemistry Manufacturing and Controls) information package submitted supports advancement of the ibezapolstat Phase 3 program. The information package supporting the Phase 3 program included details on Acurx's two planned Phase 3 clinical trials (designed as non-inferiority trials vs vancomycin), the patient population, primary endpoint of Clinical Cure, sample size, statistical analysis plan and the overall registration safety database.

Acurx's Executive Chairman, Bob DeLuccia, stated: "We are appreciative of the EMA's constructive suggestions, and we will proactively incorporate them into our global registration plan. He further stated: "We are very pleased with the latest favorable communications from both regulatory agencies which provide a straightforward international roadmap for conduct of our Phase 3 program and ultimate requirements for a US NDA (New Drug Application) submission and EU Marketing Authorization Application."

Written communications are used by both regulatory agencies in lieu of face-to-face or teleconference/video conferences when these agencies determine that a written response to the sponsor's questions would be the most appropriate means for providing feedback and advice to the sponsor. ([FDA Guidance on Formal Meetings](#), [EMA Guidance on Centralised Procedure](#))

Acurx previously announced it had a successful End of Phase 2 Meeting achieving agreement with FDA on non-clinical and clinical Phase 3-readiness, including written positive feedback regarding acceptability of its CMC (Chemistry Manufacturing and Controls) plan and data package proposed to support the Phase 3 clinical program. In addition, Acurx had initiated the Scientific Advice procedure with the EMA to discuss the readiness for initiation of the Phase 3 clinical program in the EU. Acurx is preparing to submit requests for regulatory guidance to initiate clinical trials in the European Union, to be followed by requests to be submitted in the United Kingdom, Japan and Canada.

Key elements for the two Phase 3, non-inferiority, pivotal trials were confirmed and included agreement on the protocol design, patient population, primary and secondary endpoints, and size of the registration safety database. 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. ([Link to Clinicaltrials.gov/NCT042447542](https://clinicaltrials.gov/NCT042447542)) 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).

In the Phase 2b trial segment, which was discontinued due to success, 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. The Company previously reported that the overall observed Clinical Cure rate in the combined Phase 2 trials 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. Ibezapolstat was well-tolerated, with three patients each experiencing one mild adverse event assessed by the blinded investigator to be drug-related. All three events were gastrointestinal in nature and resolved without treatment.

There were no drug-related treatment withdrawals or no drug-related serious adverse events, or other safety findings of concern. In the Phase 2b vancomycin control arm, 14 out of 14 patients experienced Clinical Cure. The Company is confident that based on the

pooled Phase 2 ibezapolstat Clinical Cure rate of 96% and the historical vancomycin cure rate of approximately 81% (Vancocin® Prescribing Information, January 2021), we will demonstrate non-inferiority of ibezapolstat to vancomycin in Phase 3 trials in accordance with the applicable FDA Guidance for Industry (October 2022).

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 recently 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 12 patients who agreed to be followed up to three months following Clinical Cure of their infection, 5 of 5 IBZ patients experienced no recurrence of infection. In the vancomycin control arm of the trial, 7 of 7 patients experienced no recurrence of infection. ECC success is defined as a clinical cure at the TOC visit (i.e., at least 48 hours post EOT) and no recurrence of CDI within the 56 ± 2 days post EOT (ECC56) and 84 ± 2 days post EOT (ECC84) in patients who consented to extended observation. In the Phase 2b trial, 100% (5 of 5) of ibezapolstat-treated patients who agreed to observation for up to three months following Clinical Cure of CDI 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 (CDI). 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 C 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 (CDI)

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, et al, 2015,

New England Journal of Medicine). 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, New England Journal of Medicine). 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 (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-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 next year. 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, 2023, 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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