June 17, 2025

Acurx Pharmaceuticals

Acurx Announces Publication in Lancet Microbe of Phase 2b Clinical Trial Data for Ibezapolstat in CDI

- As previously reported, 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
- In contrast, 2 of 14 (14%) patients treated with the standard of care, oral vancomycin, experienced recurrent infection within one month after EOT
- When Phase 2b results are combined with Phase 2a results, 25 of 25 (100%) ibezapolstat-treated patients with CDI who had CC at EOT remained recurrence-free through 1 month after EOT; additionally, all 5 Phase 2b ibezapolstat-treated patients observed for up to 3 months following CC experienced no recurrence of infection
- Adding to this Lancet Microbe publication, two recent Journal of Antimicrobial Agents and Chemotherapeutics publications regarding, respectively, favorable gut microbiome effects which differentiate IBZ from other anti-CDI antibiotics and positive results from an in-silico study predicting the microbiome-restorative potential of IBZ
- The totality of ibezapolstat data-to-date further advances Acurx's robust data package and are reshaping the therapeutic landscape for future treatment of CDI with ibezapolstat's innovative and potentially transformative new class of antibiotics to treat gram-positive infections while preserving and restoring the protective gut microbiota
- 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., June 17, 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. Its lead antibiotic candidate, ibezapolstat (IBZ), is ready to advance to international Phase 3 clinical trials for treatment of patients with *C. difficile* infection (CDI). The Company today announced the publication of results in *Lancet Microbe* of its Phase 2b clinical study entitled: *Efficacy, safety, pharmacokinetics, and associated microbiome changes of ibezapolstat compared with vancomycin in adults with Clostridioides difficile infection: a phase 2b, randomized, double-blind, active-controlled, multicenter study.* The senior author is Kevin Garey, PharmD, MS, FIDSA, Professor and Chair, University of Houston College of Pharmacy, and Principal Investigator for microbiology and microbiome aspects of the IBZ clinical trial program, and a co-author of the IDSA (Infectious Diseases Society of America) *C. difficile* Treatment Guidelines.

Professor Garey noted that current US and European treatment guidelines for CDI recommend only two antibiotics for treatment of CDI: oral vancomycin (VAN) or fidaxomicin (FDX). VAN is most commonly used with a low CC rate of 70-92% and an SCC rate of 42-71%. FDX has fewer recurrences but low rates of CC (84%) and SCC (67%); furthermore,

both FDX and VAN are associated with emerging antimicrobial resistance. Dr. Garey also stated: "The clinical need for a new antibiotic, like IBZ, to treat CDI is underscored by a study recently published in Clinical Infectious Diseases conducted in a hospital setting, documenting that *C. difficile* isolates with clinically relevant reduced fidaxomicin susceptibility may emerge during therapy and spread to other patients. The medical community should be aware of this alarming finding."

Acurx's Executive Chairman, Bob DeLuccia, stated: "This Lancet Microbe article complements the body of our published data to date, the totality of which establishes a comprehensive and formidable dossier to support our optimism for a successful Phase 3 clinical program and, if successful, first choice of IBZ as a front-line treatment for CDI. Our publications include data on IBZ chemistry, mechanism of action, microbiological activity, in vivo efficacy in the hamster model, human efficacy and safety, and favorable effects on the gut microbiome and bile acid metabolism." He further stated: "Data from our Phase 3 pivotal trials, if successful, will form the foundation for our continually evolving and attractive value proposition including in-market competitive advantage compared to vancomycin and fidaxomicin. Additionally, continuing optimization of our 'home-grown and made-in-America" supply chain will ensure scalability and reliability to be accessible and affordable worldwide".

This most recent publication adds important scientific information to supplement a growing list of peer-reviewed publications, including a Phase 1 study showing IBZ to be well-tolerated, localized to the gastrointestinal tract, and associated with preservation and restoration of beneficial gut microbiota. These Phase 2b study findings were supported by a Phase 2a, open-label, non-comparative study and showed 10 of 10 subjects were cured of CDI with no recurrence of infection. Based on this evidence, the Phase 2b study was initiated to assess the efficacy, safety, and associated microbiome changes of IBZ versus standard of care vancomycin (VAN).

This Phase 2b multi-site study was conducted at US medical clinics and hospitals. In the publication, Professor Garey summarized results which included high rates of CC in IBZ-treated subjects treated with no recurrence; furthermore, IBZ was found to be safe, well-tolerated, and associated with the preservation and restoration of key health-promoting bacteria responsible for bile acid homeostasis, a key component in preventing recurrent CDI. The publication establishes that IBZ shows potential as a novel antibiotic treatment for CDI with high rates of CC and SCC while minimally disturbing the protective gut microbiota, thus further supporting its clinical development.

THE ABOVE-MENTIONED PUBLICATIONS ARE ON OUR WEBSITE:
www.acurxpharma.com

> **Lancet Microbe**: *Efficacy, safety, pharmacokinetics, and associated microbiome changes of ibezapolstat compared with vancomycin in adults with* Clostridioides difficile *infection: a phase 2b, randomized, double-blind, active-controlled, multicenter study*
> **Clinical Infectious Diseases:** *Emergence and Spread of* Clostridioides difficile *Isolates with Reduced Fidaxomicin Susceptibility in an Acute Care Hospital*

About the Lancet Microbe
The Lancet Microbe is the world-leading microbiology research journal and publishes clinically relevant content on microbes at all scales, from the nature of the microbe (eg,

antimicrobial resistance genes/plasmids, virulence factors) to the microbiome, to pathology (including immunology) to population level effects (eg, outbreaks, epidemiology). It also publishes early phase clinical trials and other interventional studies where the outcomes are focused on the pathogen. It is an internationally trusted source of clinical, public health, and global health knowledge.

About Clinical Infectious Diseases
Clinical Infectious Diseases (CID) is a leading journal in the field of infectious disease with a broad international readership. The Journal publishes articles on a variety of subjects of interest to practitioners and researchers. Topics range from clinical descriptions of infections, public health, microbiology, and immunology to the prevention of infection, the evaluation of current and novel treatments, and the promotion of optimal practices for diagnosis and treatment. The Journal publishes original research (as Major Articles or Brief Reports), Review Articles, Viewpoints, Editorials, Invited Commentaries, Photo Quizzes, Practice Guidelines, Correspondence, and Supplements and is among the most highly cited journals in the field of infectious diseases. *Clinical Infectious Diseases* is an official publication of the Infectious Diseases Society of America.

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 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, 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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