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Acurx Pharmaceuticals

Acurx Announces Positive Extended Clinical Cure Data for Ibezapolstat from Phase 2b Clinical Trial in CDI Patients

- 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
- Further analyses will be forthcoming as data become available regarding effects on bile acid metabolism and pharmacokinetic data
- Preparation is underway for meetings with FDA, European Medicines Agency and other global regulatory agencies and advancement to international Phase 3 clinical trials
- Ibezapolstat has previously received FDA QIDP and Fast-Track Designation

STATEN ISLAND, N.Y., Jan. 29, 2024 /PRNewswire/ -- Acurx Pharmaceuticals, Inc. (NASDAQ: ACXP) ("Acurx" or the "Company"), a late-stage biopharmaceutical company developing a new class of small molecule antibiotics for difficult-to-treat bacterial infections, today announced 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.

According to Dr. Garey: "CDI has long-term consequences including poor quality of life for the patient. It's exciting to see that the ibezapolstat Phase 2b study followed patients for an extended time period to assure that the ibezapolstat cure and anti-recurrence effects are long-lasting and durable. This adds to the exciting microbiome data showing replenishment of healthy microbiota that we have seen in our prior studies."

Robert J. DeLuccia, Executive Chairman of Acurx, stated: "This Extended Clinical Cure data showing that no ibezapolstat-treated patient who achieved Clinical Cure and consented to three months of post-treatment observation experienced a recurrence of CDI during this period further strengthens the ibezapolstat lineage of clinical success building on our previously reported Phase 2 results of 96% Clinical Cure and 100% Sustained Clinical Cure along with favorable preservation of the microbiome and no safety signals." He further stated: "We look forward to advancing to Phase 3 clinical trials and are optimistic about achieving non-inferiority versus vancomycin which is the regulatory clinical development hurdle for marketing registration".

David P. Luci, President & CEO of Acurx, stated: "Ibezapolstat continues to demonstrate

success compared to a standard of care, oral vancomycin, to treat patients with CDI. We anticipate continued favorable differentiation between the two therapeutic options in 2024. We expect to leverage this success in a $1 billion plus US CDI global market as we move forward with an international Phase 3 clinical trial mandate." He added: "The Company also anticipates its price point for ibezapolstat, if approved, could meet or beat other antibiotics recommended for use in treating patients with CDI, thereby providing the whole package of clinical comparability with microbiome health, safety and cost for patients with this life-threatening disease."

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.

The completed Phase 2a segment of this trial was an open label cohort of up to 20 subjects from study centers in the United States. In this cohort, 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), the Trial Oversight Committee assessed the safety and tolerability and made its recommendation regarding early termination of the Phase 2a study and advancement to the Ph2b segment. The Company's Scientific Advisory Board concurred with this recommendation.

In the now completed 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. 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).

The Phase 2b clinical trial segment was discontinued due to success. The Company made this decision in consultation with its medical and scientific advisors and statisticians based on observed aggregate blinded data and other factors, including the cost to maintain clinical trial sites and slow enrollment due to COVID-19 and its aftermath. The Company had determined that the trial performed as anticipated for both treatments, ibezapolstat and the control antibiotic vancomycin (a standard of care to treat patients with CDI), with high rates of clinical cure observed across the trial without any emerging safety concerns. Accordingly, an Independent Data Monitoring Committee was not required to perform an interim analysis of this Phase 2b trial data as originally planned. The Company anticipated that this decision would allow the Company to advance this first-in-class, FDA QIDP/Fast Track-designated antibiotic product candidate to Phase 3 clinical trials more expeditiously.

The Phase 2b trial was originally designed to be a non-inferiority (NI) trial and later amended to include an interim efficacy analysis with review by an Independent Data Monitoring Committee (IDMC). The decision to end the trial early based on blinded clinical observations obviated the need for an interim analysis, IDMC review, and NI assessment. The Company determined, in consultation with its clinical and statistical experts, that presenting clinical cure rates for the primary efficacy endpoint is the most appropriate representation for the clinical activity of ibezapolstat in treating CDI.

In the Phase 2 clinical trial, the Company will also evaluate 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.

About Ibezapolstat
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 January 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 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, 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).

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) and drug-resistant Streptococcus pneumoniae (DRSP).

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, 2022, 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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