October 2, 2023 Acurx Pharmaceuticals

Acurx Pharmaceuticals Announces Successful Completion and Early Discontinuation of the Ibezapolstat Phase 2b Trial for Treatment of C. difficile Infection

- *Based on observed aggregate blinded data the Company has determined that both treatments, ibezapolstat and the control antibiotic vancomycin, have performed as expected*
- *High rates of Clinical Cure were observed without any emerging safety concerns*
- *Data will be analyzed and topline efficacy results will be reported as soon as possible*
- *This successful milestone will allow advancement of this first-in-class,*FDA *QIDP/Fast Track-designated antibiotic candidate to Phase 3 clinical trials more expeditiously*

STATEN ISLAND, N.Y., Oct. 2, 2023 /PRNewswire/ -- Acurx Pharmaceuticals, Inc. (NASDAQ: ACXP) ("Acurx" or the "Company"), a clinical stage biopharmaceutical company developing a new class of antibiotics for difficult-to-treat bacterial infections, announced today that the Company has discontinued the Phase 2b clinical trial of its lead antibiotic candidate, ibezapolstat, for the treatment of patients with *Clostridioides difficile* infection (CDI) 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. The Company has 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, the Independent Data Monitoring Committee will not be required to perform an interim analysis of this Phase 2b trial data as originally planned and the Company has discontinued the trial. Acurx will analyze the data and report topline efficacy results promptly. The Company anticipates that this decision will allow the Company to advance this first-in-class, FDA QIDP/Fast Track-designated antibiotic product candidate to Phase 3 clinical trials more expeditiously.

Robert J. DeLuccia, Executive Chairman of Acurx, stated: "Considering the totality and weight of evidence of our preclinical, Phase 1 and Phase 2a clinical results and now with the observed aggregate blinded data, we determined it was in the best interests of the Company and its shareholders to discontinue the Phase 2b clinical trial early and prepare for Phase 3 clinical trials. Mr. DeLuccia stated further, "We look forward to compiling, analyzing the data and reporting topline results for the study's primary clinical endpoint and safety aspects as soon as possible". He further stated: "We thank the clinical trial investigators and patients across the country who participated in this study allowing advancement of this

promising new antibiotic into late-stage clinical trials for this serious and life-threating infection which is classified by FDA and CDC as an urgent priority for which new classes of antibiotics are needed."

David P. Luci, the Company's President and Chief Executive Officer, stated: "We also look forward to reporting the full ibezapolstat data which will include the most extensive data for any antibiotic on sustained clinical cure to date in patients with CDI, as well as a comparison of the effect on the microbiome between oral ibezapolstat and oral vancomycin. We believe that, if approved by FDA for marketing, these attributes will support the use of ibezapolstat for front-line treatment of 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.

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. In the now discontinued 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. This Phase 2 clinical trial 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. In the event non-inferiority of ibezapolstat to vancomycin is demonstrated, further analysis will be conducted to test for superiority.

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 the Microbiome in *Clostridioides 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.

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 for 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 of two of thethree antibiotics currently used to treat CDI is between 20% and 40% among approximately150,000 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 Acurx Pharmaceuticals, Inc.
Acurx Pharmaceuticals is a clinical stage biopharmaceutical company focused on developing new antibiotics for difficult to treat infections. The Company's approach is to develop antibiotic candidates that target the DNA polymerase IIIC enzyme, and its R&D pipeline includes early-stage 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 Qualified Infectious Disease Product 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 U.S. Food and Drug Administration 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 filings with the Securities and Exchange Commission ("SEC"), including the factors described in the section entitled "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2022, and in other filings that the Company has made and future filings the Company will make with the SEC. The Company expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations with regard thereto or any change in events, conditions, or circumstances on which any such statements are based.

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View original content:https://www.prnewswire.com/news-releases/acurx-pharmaceuticals-announces-successful-completion-and-early-discontinuation-of-the-ibezapolstat-phase-2b-trial-for-treatment-of-c-difficile-infection-301943990.html

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