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Acurx Pharmaceuticals

Acurx Announces Ibezapolstat Scientific Poster and Update on its Pol IIIC Pipeline Presented at ECCMID 2023 Scientific Conference

- A scientific poster highlighting a novel pharmacologic property of oral ibezapolstat for *C. difficile* Infection likely related to its unique mechanism of action was presented at ECCMID 2023
- An update on the Company's pre-clinical antibiotic program in Lead Optimization stage for systemic gram-positive bacterial infections was also presented
- Ibezapolstat has previously received FDA QIDP and Fast-Track Designation

STATEN ISLAND, N.Y., April 19, 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, today announced two presentations were given at the 33rd Annual European Congress of Clinical Microbiology and Infectious Disease (ECCMID) in Copenhagen. The scientific poster entitled "Novel Pharmacology and Susceptibility of Ibezapolstat Against *C. difficile* Isolates with Reduced Susceptibility to *C. difficile*-directed Antibiotics" was co-presented on April 17 by Dr. Kevin Garey, Professor and Chair, University of Houston College of Pharmacy, and the Principal Investigator for microbiome aspects of our ibezapolstat clinical trial program, and by Dr. Eugénie Bassères, Research Scientist Faculty at the University of Houston. According to Dr. Garey: "Our work is based on the hypothesis that ibezapolstat's mechanism of action is not only bactericidal to *C. difficile* but also could inhibit some of its virulence mechanisms.*C. difficile* strains with reduced susceptibility to metronidazole, vancomycin, or fidaxomicin were susceptible to ibezapolstat, confirming its unique mechanism of action. To study anti-virulence effect, our group investigated an under-studied virulence property of *C difficile*, namely, flagellar movement of the organism. Using sub-MIC concentrations of ibezapolstat, we demonstrated decreased movement of *C. difficile* through a semi-solid agar in concert with reduced expression of the primary genes used to synthesize flagella. All of these positive and unexpected findings reflect the unique mode of action in inhibiting DNA pol IIIC and support the continued development of ibezapolstat to treat *C. difficile* infection."

Also, Acurx Executive Chairman, Robert J. DeLuccia, presented an update on April 15 on the Company's preclinical, systemic oral and IV program for treatment of other gram-positive infections caused by MRSA, VRE and DRSP at the "Pipeline Corner" featured session at ECCMID, organized by Dr. Ursula Theuretzbacher, a world-renowned microbiology expert involved in antibacterial drug research, discovery and development strategies and policies for clinical and public health needs. Mr. DeLuccia summarized the progress of the company's GPSS™ (Gram Positive Selective Spectrum) program stating: "Our potential lead compound meets Dr. Theurezbacher's criteria for innovation in that it is a new chemical class, has novel mechanism and bacterial target, and has not shown cross-resistance in early in vitro microbiology studies. He further stated: "Following clinical validation of the pol

IIIC bacterial target in a Ph2a proof-of-principal trial showing 100% cure of *C. difficile* Infection, with no recurrence after 30 days' follow up, we have made substantial progress toward lead compound selection of our pan-active, gram-positive IV and oral compounds. We've made significant improvements in cytotoxicity, solubility and protein binding, in vitro and in vivo safety and have demonstrated oral and IV efficacy in a number of mouse infection models."

The poster and presentation are available on the Company's website www.acurxpharma.com.

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.

The Company currently is enrolling patients in a Ph2b clinical trial of ibezapolstat to treat patients with *C. difficile* infection (CDI). The Company successfully completed Phase 1 and Phase 2a clinical trials of ibezapolstat. The Phase 2a trial demonstrated 100% clinical cure and 100% sustained clinical cure in patients with CDI, along with beneficial microbiome changes during treatment including overgrowth of Actinobacteria and Firmicutes phylum species while on therapy and new findings which demonstrate potentially beneficial effects on bile acid metabolism. The Ph2b clinical trial is designed to enroll 64 patients and is a randomized (1:1), non-inferiority, double-blind trial of oral ibezapolstat compared to oral vancomycin, a standard of care to treat CDI.

The FDA has accepted the Company's plan to have an Independent Data Monitoring Committee (IDMC) conduct an interim review of clinical outcome from the ongoing Ph2b clinical trial of patients with *C. difficile* Infection (CDI). The interim review will be conducted upon reaching enrollment of 36 patients in total. FDA's acceptance was based on the Company's filing of a protocol amendment to its Investigational New Drug Application (IND) with FDA in January 2023. The Company's filing and intention for the IDMC to conduct an interim review of data was based on the observed blinded data to date from the ongoing Ph2b clinical trial at that time. Upon conducting the interim review, the IDMC will determine and recommend to the Company whether the most appropriate course of action is to terminate the Ph2b clinical trial early due to success, as the Company had done with the Ph2a clinical trial, or to continue patient enrollment. The Company intends to report available data promptly after the IDMC conducts this interim review. The IDMC initial organizational meeting was conducted in March 2023 and it has completed all organizational matters required to ensure readiness for data review.

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 ECCMID
ECCMID (European Congress of Clinical Microbiology and Infectious Diseases) is recognized as the largest international forum for presentations and discussions of research in the fields of clinical microbiology and infection for experts from academia, the clinical setting and the industry. ESCMID's (European Society of Clinical Microbiology and Infectious Diseases) yearly congress attracts over 14,000 participants. ECCMID offers a wide range of sessions including: keynotes, symposia, poster sessions, educational workshops, meet-the-expert sessions and more. The society's executive power is vested in ESCMID in Executive Committee elected by the ESCMID members. The administrative ESCMID office is in Basel, Switzerland.

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 of two of the three 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 *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. 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 the Ibezapolstat Phase 2 Clinical Trial
The multicenter, open-label single-arm segment of this study (Phase 2a) is to be followed by

a double- blind, randomized, active-controlled segment (Phase 2b) which, together, comprise the Phase 2 clinical trial. The Phase 2 clinical trial is designed to evaluate ibezapolstat in the treatment of CDI. Phase 2a of this trial is completed and 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, the Trial Oversight Committee assessed the safety and tolerability and made its recommendation regarding early termination of the Phase 2a study. Based on the recommendation of Acurx's Scientific Advisory Board (SAB) and Trial Oversight Committee, we terminated enrollment in Phase 2a early and are now advancing to Phase 2b. The SAB unanimously supported the early termination of the Phase 2a trial after 10 patients were enrolled in the trial instead of 20 patients as originally planned. The early termination was based on the evidence of meeting the primary and secondary endpoints of eliminating the infection (100%), with no recurrences of infection (100%), and with an acceptable adverse event profile. In the upcoming Phase 2b, approximately 64 additional patients with CDI will be enrolled and randomized in a 1:1 ratio to either ibezapolstat 450 mg every 12 hours or vancomycin 125mg 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 will be identical in appearance, dosing times, and number of capsules administered to maintain the blind. This Phase 2 clinical trial also will evaluate pharmacokinetics (PK) and microbiome changes and continue to 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.

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 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.

Investor Contact:
Acurx Pharmaceuticals, Inc.
David P. Luci, President & CEO
Tel: 917-533-1469
Email: davidluci@acurxpharma.com

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