October 19, 2023 Acurx Pharmaceuticals

Acurx Announces Ibezapolstat Scientific Posters and Presentations at ClostPath 2023 and IDWeek 2023 Scientific Conferences

- Three scientific posters highlighting novel anti-virulence pharmacologic properties of oral ibezapolstat for *C. difficile* Infection; effects on toxin production, biofilm and the gut microbiome
- A podium presentation entitled *First of a New Class of Antibiotics (pol IIIC Inhibitors) Targeting CDC/FDA/WHO Priority Pathogens; Preparing for the Next Pandemic: Antimicrobial Resistance in Gram-positive Bacterial Infections*
- Ibezapolstat has previously received FDA QIDP and Fast-Track Designation

STATEN ISLAND, N.Y., Oct. 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 three scientific posters were presented during the 13th International Conference on Molecular Biology and Pathogenesis of Clostridia (ClostPath) held in Banff, Canada from September 19 to 23, 2023. Additionally, two podium presentations were made at the Infectious Disease Society of America (IDSA) IDWeek™ 2023 Conference held October 11-15, 2023 in Boston, MA. Highlights of each are shown below.

Robert J. DeLuccia, Executive Chairman of Acurx, stated: "In light of our recent decision to discontinue the Phase 2b ibezapolstat clinical trial earlier than planned and prepare for Phase 3 clinical trials, the new information contained in these scientific posters and presentations at these conferences will add to our evidence-based briefing package for an End of Phase 2 FDA meeting planned for in the first half of next year." He also added: "We are currently compiling and verifying all data from the Phase 2b trial and we will report topline clinical efficacy for the primary clinical endpoint and safety data in the coming weeks, with other outcome data available later this year".

ClostPath:

- *Ibezapolstat modulates Clostridioides difficile virulence factors in vitro*
  - Presented by Eugenie Basseres, et al; University of Houston College of Pharmacy
  - Ibezapolstat reduces toxin production by *C. difficile*
- *C. difficile In Vitro Biofilm Studies of Ibezapolstat And Comparator Antibiotics*
  - Presented by M. Jahangir Alam et al; University of Houston College of Pharmacy
  - Ibezapolstat was as effective as the currently-used anti-*C. difficile agents* fidaxomicin, vancomycin and metronidazole to reduce biofilm-embedded *C. difficile* quantity and biofilm biomass
- *Metagenomic Evaluation of Ibezapolstat Compared to Other Anti-Clostridioides difficile*

Agents
- Presented by Jinhee Jo, University of Houston College of Pharmacy
- Ibezapolstat and fidaxomicin caused proportional increases in Bacteroidetes distinct from vancomycin and metronidazole, which caused proportional increases in Proteobacteria

IDWeek:

- *First of a New Class of Antibiotics (pol IIIC Inhibitors) Targeting CDC/FDA/WHO Priority Pathogens*
  - Presented by Michael Silverman, MD, FACP, Acurx's Medical Director; at the New Antimicrobials in the Pipeline session
  - Among the promising data for ibezapolstat in the treatment of *C. difficile* are in vitro potency, anti-virulence activities, high human fecal concentrations, 100% Clinical Cure rate in a 10-patient open-label trial, favorable safety profile to date, and potentially beneficial effects on the gut microbiome
- *Elucidating the Gram-Positive Selective Spectrum Activity of Ibezapolstat; Secondary Analysis from the Phase 2a trial*; Presented by Kevin Garey, PharmD, MS, Professor& Chair, University of Houston, School of Pharmacy
  - Ibezapolstat showed variable selectivity against Firmicutes helping to elucidate its narrow spectrum of activity against certain pathogenic Firmicutes including *C. difficile*

The posters and presentations 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.

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 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 Phase 2b clinical trial segment has been 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. 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, an Independent Data Monitoring Committee will not be required to perform an interim analysis of this Phase 2b trial data as originally planned. 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.

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.

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 noninferiority 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 ClostPath

The ClostPath conferences, which began in 1995, have been a leading venue to bring together top scientists and clinicians studying the molecular biology of clostridia and their role in health and disease. The scientific program of **ClostPath 13** included lectures by internationally recognized leaders in clostridial research and clinical practice. In addition to state-of-the-art invited talks on the most recent and exciting discoveries in the field, short oral contributions were selected from submitted abstracts. Poster presentations gave

attendees the opportunity to discuss their ongoing work with a broad audience in line with the goal to bring together basic science with clinical and translational research issues.

About the IDSA and IDWeek
The Infectious Diseases Society of America (IDSA) is a community of over 12,000 physicians, scientists and public health experts who specialize in infectious diseases. Our mission is to improve the health of individuals, communities, and society by promoting excellence in patient care, education, research, public health, and prevention relating to infectious diseases. IDWeek is the joint annual meeting of the Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), the HIV Medicine Association (HIVMA), the Pediatric Infectious Diseases Society (PIDS), and the Society of Infectious Diseases Pharmacists (SIDP). Over 9,500 participants attended this conference in October 2022.

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 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.

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