December 9, 2024 Acurx Pharmaceuticals

Acurx Updates Phase 3 Readiness for Ibezapolstat in C. difficile Infection Based on Recent FDA and EMA Communications

- *Following the previously announced successful End of Phase 2 Meeting achieving agreement with FDA on non-clinical and clinical Phase 3-readiness, Acurx has now also received written positive feedback from FDA regarding acceptability of our CMC (Chemistry Manufacturing and Controls) plan and data package proposed to support the Phase 3 clinical program*
- *Acurx has initiated the Scientific Advice procedure with the European Medicines Agency (EMA) to discuss the readiness for initiation of the Phase 3 clinical program in the European Union (EU). Acurx has been notified that we should expect to receive the final written advice letter in the coming few weeks*
- *Acurx is also in the process of discussing the pediatric development plans for ibezapolstat in C. difficile* Infection *with FDA and EU health authorities, per regulatory requirements.*
- *Phase 3 international trial planning continues to advance, using AI and other state-of-the-art techniques to identify and qualify clinical trial sites with the highest potential for patient enrollment*
- *Acurx is also preparing to request regulatory guidance to initiate clinical trials in Japan, Canada and the United Kingdom*
- *Ibezapolstat has previously been granted FDA QIDP and Fast-Track Designation from FDA and Acurx has received SME (Small and Medium-sized Enterprise) designation by the EMA to benefit from fee incentives and other support from the EMA for EU Marketing Authorization*

STATEN ISLAND, N.Y., Dec. 9, 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, with its lead antibiotic candidate, ibezapolstat, preparing to advance to international Phase 3 clinical trials to treat patients with *C. difficile* Infection (CDI). The Company today announced updates on Phase 3 Readiness for Ibezapolstat in *C. difficile* Infection based on recent FDA and EMA Communications.

Written communications are used by both regulatory agencies in lieu of face-to-face or teleconference/video conferences when these agencies determine that a written response to the sponsor's questions would be the most appropriate means for providing feedback and advice to the sponsor. (FDA Guidance on Formal Meetings, EMA Guidance on Centralised Procedure)

Acurx's Executive Chairman, Bob DeLuccia, stated: "We are very pleased with these latest favorable communications from both regulatory agencies and in our opinion are a testament to the strength of our clinical data to date, our robust regulatory submissions, and adherence to current regulatory guidance." He further added: "We anticipate, and are confident, that

with final EMA advice for our ibezapolstat Phase 3 trials for adult patients with CDI and the pediatric development plans from both regulatory agencies, Acurx will have a clear international roadmap for conduct of our Phase 3 program and, if successful, requirements for US NDA submission and EU Marketing Authorization."

Acurx has previously announced that it had a successful FDA End-of-Phase 2 Meeting and Phase 3 Readiness for ibezapolstat for the Treatment of *C. difficile* Infection. Agreement with FDA was reached on key elements to move forward with its international Phase 3 clinical trial program. Agreement was also reached with FDA on the complete non-clinical and clinical development plan for filing of a New Drug Application (NDA) for marketing approval. Planning continues to advance ibezapolstat into international Phase 3 clinical trials for treatment of *C. difficile* Infection (CDI). Acurx is also preparing to submit requests for regulatory guidance to initiate clinical trials in the European Union, to be followed by requests to be submitted in the United Kingdom, Japan and Canada.

Key elements for the two Phase 3, non-inferiority, pivotal trials were confirmed and included agreement on the protocol design, patient population, primary and secondary endpoints, and size of the registration safety database. Based on FDA recommendations, and in anticipation of an EMA Scientific Advice Meeting, the primary efficacy analysis will be performed using a Modified Intent-To-reat (mITT) population consistent with EMA requirements. 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. (Link to Clinicaltrials.gov/NCT042447542) 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).

In the Phase 2b trial segment, which was discontinued due to success, 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).

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 recently 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 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. 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. 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 (CDI). 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: 0.3390/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). 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, 2023, 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

View original content:https://www.prnewswire.com/news-releases/acurx-updates-phase-3-readiness-for-ibezapolstat-in-c-difficile-infection-based-on-recent-fda-and-ema-communications-302325768.html

SOURCE Acurx Pharmaceuticals, Inc.