February 7, 2022 Acurx Pharmaceuticals

Acurx Announces Publication of Positive Phase 2a Clinical Trial Results of Ibezapolstat for CDI in Clinical Infectious Diseases

STATEN ISLAND, N.Y., Feb. 7, 2022 /PRNewswire/ --

- Publication of study presents:
  - Clinical results of 10 of 10 patients (100%) enrolled met the study's primary and secondary efficacy endpoints of Clinical Cure at end of treatment and Sustained Clinical Cure of no recurrence of CDI at the 28-day follow-up visit
  - PK data showing low plasma and high fecal concentrations of ibezapolstat
  - Favorable microbiome changes included regrowth of Actinobacteria and Firmicutes phylum species while on treatment
  - Potential beneficial effects on bile acid metabolism while on treatment
- Currently enrolling Ph2b trial in 12 U.S. sites will compare efficacy of ibezapolstat to vancomycin
- Ibezapolstat is FDA QIDP and Fast Track Designated for priority review

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 results of its positive Phase 2a clinical trial have been published in *Clinical Infectious Diseases*, the official publication of the Infectious Disease Society of America https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac096/6522822?login=true. The senior author of the publication is Dr. Kevin Garey, Professor and Chair, University of Houston College of Pharmacy and the Principal Investigator for the microbiome aspects of the trial.

Dr. Garey stated: "In this publication, we are particularly pleased to present the totality of the ibezapolstat Phase 2a clinical and microbiome data for this promising novel antibiotic which appears to possess key properties of an ideal oral antibiotic for CDI: highly potent against *C. difficile*; good tolerability; and limited gastrointestinal absorption, resulting in very high fecal concentrations which may reach three orders of magnitude above the MIC for *C. difficile.*" He also noted: "This first-in-class GPSS™ (Gram Positive Selective Spectrum) antimicrobial is a novel DNA polymerase IIIC inhibitor with a unique mechanism of action that targets low G+C content gram-positive bacteria. Ibezapolstat has potent activity as demonstrated by the eradication of *C. difficile* by day three of treatment. Our data also show it unexpectedly spares other Firmicutes along with the important Actinobacteria phylum necessary for maintaining a healthy microbiome. These characteristics, in conjunction with ibezapolstat's ability to favorably increase the ratio of secondary-to-primary bile acids in the colon, suggest that ibezapolstat may reduce the likelihood of CDI recurrence when compared to standard of care vancomycin."

Robert J. DeLuccia, Executive Chairman of Acurx, stated: "Considering the entirety of our preclinical, Phase 1 and Phase 2a clinical results and the favorable microbiome signature of ibezapolstat compared to vancomycin, we are confident of a high probability of successful Phase 2b trial outcome. In the event ibezapolstat demonstrates non-inferiority to vancomycin, further analysis will be conducted to test for superiority". He further stated: "Currently enrolling patients in our Phase 2b segment is a very important clinical development milestone for our company. We look forward to successfully completing trial enrollment in mid-2022, albeit in a challenging environment with Covid-19 and its variants interfering with operations at some investigator sites."

The *Clinical Infectious Diseases* publication can also be viewed on the company's website at www.acurxpharma.com, (Tab: Pipeline, Publications). Additionally, the company has filed multiple provisional patent applications relating to the use of ibezapolstat to treat C. *difficile* Infection while reducing the recurrence of the infection, as well as improving the health of the gut microbiome.

About Clinical Infectious Diseases. *Clinical Infectious Diseases (CID)* is a leading journal in the field of infectious disease with a broad international readership. The Journal publishes articles on a variety of subjects of interest to practitioners and researchers. Topics range from clinical descriptions of infections, public health, microbiology, and immunology to the prevention of infection, the evaluation of current and novel treatments, and the promotion of optimal practices for diagnosis and treatment. The Journal publishes original research (as Major Articles or Brief Reports), Review Articles, Viewpoints, Editorials, Invited Commentaries, Photo Quizzes, Practice Guidelines, Correspondence, and Supplements and is among the most highly cited journals in the field of infectious diseases. *Clinical Infectious Diseases* is an official publication of the Infectious Diseases Society of America.

About the Ibezapolstat Phase 2 Clinical Trial. The completed multicenter, open-label single-arm segment (Phase 2a) study is now followed by a double-blind, randomized, active-controlled, non-inferiority, segment (Phase 2b) at 12 US clinical trial sites which together comprise the Phase 2 clinical trial (see https://clinicaltrials.gov/ct2/show/NCT04247542). This Phase 2 clinical trial is 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, 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 currently enrolling Phase 2b, trial segment, 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 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 will be 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 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. 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 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 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.

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 United States 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 factors. In addition, the forward-looking statements included in this press release represent our views as of February 7, 2022. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we specifically disclaim any obligation to do so.

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View original content:https://www.prnewswire.com/news-releases/acurx-announces-publication-of-positive-phase-2a-clinical-trial-results-of-ibezapolstat-for-cdi-in-clinical-infectious-diseases-301476414.html

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