June 16, 2026

Acurx Pharmaceuticals

Acurx Pharmaceuticals Announces Presentation of Results from Leiden University Medical Center Public-Private Partnership for Its DNA pol IIIC Inhibitors at the Leiden Early Drug Discovery & Development (LED3) Scientific Conference

- Results are from Acurx's ongoing scientific collaboration with Leiden University Medical Center (LUMC) partially under a grant from Health Holland to further study the mechanism of action of DNA pol IIIC inhibitors
- LUMC highlighted Acurx's new class of promising antimicrobials, ibezapolstat and related analogues specifically target Gram-positive bacteria
- High-resolution cryo-electron microscopy resolved the structure of ibezapolstat in relationship to the binding pocket of a Gram-positive DNA pol IIIC to the level of 3.2Å
- The Company's preclinical pipeline includes development of an oral product candidate for treatment of ABSSSI (Acute Bacterial Skin and Skin Structure Infections), with a development program for post-exposure prophylaxis of inhalation anthrax being planned in parallel
- Ibezapolstat has previously been granted FDA QIDP and Fast-Track Designations and has received SME (Small and Medium-sized Enterprise) designation by the EMA

STATEN ISLAND, N.Y., June 16, 2026 /PRNewswire/ -- Acurx Pharmaceuticals, Inc. (NASDAQ: ACXP) ("Acurx" or the "Company") is a late-stage biopharmaceutical company developing a new class of small molecule antibiotics for difficult-to-treat bacterial infections. Its lead antibiotic candidate, ibezapolstat (IBZ), is ready to advance to international pivotal Phase 3 clinical trials for treatment of patients with *C. difficile* infection (CDI).

The Company today announced that a presentation was given by Mia Urem, PhD, from Leiden University Medical Center in the Netherlands entitled: "A unique inhibitor conformation selectively targets Gram+ Bacterial DNA Replication" at the Leiden Early Drug Discovery & Development (LED3) Scientific Conference on June 11, 2026. Attendees of this symposium were PhDs, post-doctoral researchers and faculty from Leiden University and the LUMC. The event focused on drug discovery and development with topics including antibiotics, antivirals, central nervous system and cancer. Additional focus included the use of AI and computer sciences, quantitative pharmacology, microbiology and medical biology.

Dr. Urem's group utilized high-resolution cryo-electron microscopy to resolve the structure of ibezapolstat in relationship to the binding pocket of a Gram-positive DNA pol IIIC to the level of 3.2Å. The active site of the polymerase is conserved in >220 Gram-positive species, indicating potential for broad clinical utility of this bactericidal inhibitory mechanism of action of Acurx compounds. The distinctive non-planar conformation of IBZ and chemically related

molecules, together with high conservation of the binding pocket in DNA pol IIIC, suggests that this is a general mechanism for this class of inhibitor and that a wide range of Gram-positive infections, including those caused by high-priority pathogenic Gram-positive bacteria, may be susceptible to treatment with Acurx pipeline antibiotics.

According to Dr. Wiep Klaas Smits, Associate Professor/Principal Investigator, Leiden University Medical Center: "Our findings with regard to the structural biology of DNA pol IIIC in complex with inhibitors have important implications for the development of this novel class of antibiotics to treat high priority, multi-drug resistant, Gram-positive infections".

Acurx's Executive Chairman, Bob DeLuccia, stated: "This research outcome provides a deeper understanding of the mechanism of action and selectivity of ibezapolstat with respect to the gut microbiota. These data will guide the rational design of new compounds with improved inhibitory activity and drug-like characteristics that will be crucial in addressing the pandemic of antimicrobial resistance".

Acurx's 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). 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.

THE PRESENTATION IS POSTED ON THE ACURX WEBSITE www.acurxpharma.com

About the Leiden Early Drug Discovery & Development (LED3) Multidisciplinary Research Network

Leiden Early Drug Discovery & Development (LED3) is a multidisciplinary research network at Leiden University dedicated to advancing innovative approaches in early drug discovery and development. The initiative brings together 58 principal investigators from four institutes —the Institute of Biology Leiden (IBL), Leiden Academic Centre for Drug Research (LACDR), Leiden Institute of Advanced Computer Science (LIACS), and Leiden Institute of Chemistry (LIC), supported by the university's technology transfer office LURIS. Together, the network represents more than 250 researchers and staff with expertise spanning artificial intelligence, medicinal chemistry, molecular biology, pharmacology, metabolomics, structural biology, toxicology, and many other fields essential for modern drug discovery.

About Leiden University Medical Center

Leiden University was the first university to be established in the Netherlands. Its motto is praesidium libertatis – bastion of freedom. The University wishes to create an increasingly attractive and challenging working climate for top academics and young researchers that is guided by quality and excellence. Leiden University Medical Center (LUMC) research aims to meet the highest international standards of quality and academic integrity. LUMC promotes excellent research through greater collaboration, both disciplinary and interdisciplinary; stronger positioning and greater scope for top talent; and better supervision and more support for young researchers.

Antimicrobial resistant microorganisms are a major threat to global health and pose a significant economic burden. Increasing resistance to multiple agents and resistance to so called last-resort antibiotics underscore the necessity to develop therapeutics that have a novel mode of action. DNA replication is a process that can be successfully targeted by small molecules. Ibezapolstat, an inhibitor of the replicative DNA polymerase pol IIIC from Gram-positive bacteria identified by screening library of dGTP analogues, has shown promising results for the treatment of *Clostridioides difficile* Infection in a recent Phase 2a clinical trial, but the molecular basis of selective inhibition is not fully characterized as no structural information is available on pol IIIC proteins from pathogens. Ongoing research project will determine the structure of pol IIIC from the multidrug-resistant organisms methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant Enterococci (VRE) and/or penicillin resistant *Streptococcus pneumoniae* (PRSP) in the absence and presence of lead compounds. These results will reveal the structural space of inhibitor-binding and guide the rational design of inhibitors with optimal pharmacological properties and organism-specificity that will be demonstrated by *in vitro* polymerase inhibition assays and *in vivo* minimal inhibitory concentration determination.

The presented research was performed in part as a public-private partnership that includes the Dutch Top Sector Life Sciences and Health ('Topconsortium voor Kennis en Innovatie' or 'TKI' Life Sciences and Health) and is represented by Stichting Life Sciences Health – TKI (aka, Health~Holland). This foundation is tasked by the Dutch government to promote and stimulate public-private partnerships (PPPs) to undertake R&D projects in the life sciences. To promote such partnerships, the Minister of Economic Affairs and Climate Policy has allocated certain funds to Stichting LSH-TKI, to grant allowances to projects under the TKI-programme Life Sciences & Health. Stichting LSH-TKI has designated the Board of Directors of LUMC as delegated grantor for the PPP allowance allocated to the LUMC.

Together with Acurx Pharmaceuticals the PPP has led to the research project entitled "Bad bugs, new drugs: elucidation of the structure of DNA polymerase C of multidrug resistant bacteria in complex with novel classes of antimicrobials." The collaboration project was co-funded by the PPS Allowance made available by Health~Holland, Top Sector Life Sciences & Health, to stimulate public-private partnerships.

Acurx previously announced that it had received positive regulatory guidance from the EMA during its Scientific Advice Procedure which confirmed that the clinical, non-clinical and CMC (Chemistry Manufacturing and Controls) information package submitted to EMA supports advancement of the ibezapolstat Phase 3 program and if the Phase 3 program is successful, supports the submission of a Marketing Authorization Application (MAA) for regulatory approval in Europe. The information package submitted to EMA by the Company to which agreement has been reached with EMA included details on Acurx's two planned international Phase 3 clinical trials, 1:1 randomized (designed as non-inferiority vs vancomycin), primary and secondary endpoints, sample size, statistical analysis plan and the overall registration safety database. With mutually consistent feedback from both EMA and FDA, Acurx is well positioned to commence our international Phase 3 registration program.

The primary efficacy analysis will be performed using a Modified Intent-To-Treat (mITT) population. 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 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. 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 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) and Recurrent C. difficile Infection (rCDI)

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, 2015, NEJM). Recent estimates suggest C. difficile approaches 500,000 infections annually in the U.S. and is associated with approximately 30,000 deaths annually. (Guh, 2020, NEJM. 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%.

In recent studies, rCDI ranges from 4 to 19.5% following treatment with fidaxomicin and 17 to 27% following treatment with vancomycin. In patients with multiple prior episodes of CDI, rCDI following treatment with vancomycin is even more problematic, with an incidence of up to 40%. Consequently, the principal unmet medical need in this disease is the prevention of recurrence. The estimated annual public health cost burden in the U.S. annually is ~$5 billion annually with ~$2.8 billion due to recurrent CDI.

About the Microbiome in C. difficile Infection 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.) 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 (Garey, 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 post-exposure prophylaxis of inhalation 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 quarterlyreport on Form 10-Q filed with the Securities and Exchange Commission on for the quarter ended March 31, 2026, 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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