

# Health Holland Awards Innovative Research Grant for DNA Pol III $\epsilon$ Inhibitors to Leiden University Medical Center and Acurx Pharmaceuticals

**-Health Holland has awarded a grant of approximately \$500,000 USD to Leiden University Medical Center to further study the mechanism of action of pol III $\epsilon$  inhibitors in scientific collaboration with Acurx Pharmaceuticals**

**-Innovative research will study 3-dimensional structures of DNA polymerases and their binding interactions with Acurx inhibitors**

**-The antibacterial molecular target of Acurx's pipeline of novel DNA pol III $\epsilon$  inhibitors has been clinically validated by ibezapolstat's recent completion of a Ph2a trial in *C. difficile* Infection (CDI)**

**-Research outcome intended to accelerate lead product candidate selection for Acurx's ACX-375 program and for other WHO, CDC and FDA high-priority, drug-resistant Gram-positive pathogens where new classes of antibiotics are needed**

STATEN ISLAND, N.Y., Aug. 2, 2021 /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, announced today that Health Holland has awarded a grant of approximately \$500,000 USD to Leiden University Medical Center (LUMC) and, through a three-party Consortium Agreement, Acurx Pharmaceuticals.

This grant will fund an innovative research project entitled: *Bad bugs, new drugs: structural elucidation of polymerase C\* from multidrug resistant organisms to guide optimization of a new class of therapeutics.*

Dr. Wiep Klaas Smits, Associate Professor, LUMC Department of Medical Microbiology will be the lead researcher in collaboration with Dr. Meindert Lamers, Associate Professor, LUMC Department of Cell and Chemical Biology.

Dr. Smits stated: "This collaborative grant opportunity will be a novel scientific accomplishment contributing to Acurx programs by enhancing knowledge of the structure of pol III $\epsilon$  from different pathogenic, multidrug-resistant organisms. Additionally, we will study the binding of Acurx drug candidates in complex with pol III $\epsilon$  enzymes to establish a detailed in vitro characterization of polymerase and inhibiting activity." He further stated: "This work will lead to important insights into differences between replicative polymerases of critical

drug-resistant Gram-positive pathogens and pave the way for rational design of novel inhibitors based on structure-activity relationships in the future."

Acurx is commencing a Ph2b clinical trial in patients with CDI during the second half of this year after having recently completed a Ph2a clinical trial which demonstrated that 10 of 10 patients with CDI (100%) met the study's primary and secondary efficacy endpoints of Clinical Cure at end of treatment and Sustained Clinical Cure with no recurrence of CDI at the 28-day follow-up visit. These results have validated the therapeutic effect of DNA pol III<sub>C</sub> as a bacterial target.

Robert J. DeLuccia, Executive Chairman of Acurx, stated "We believe this state-of-the-art structural biology research, which includes crystallography and cryo-electron microscopy, can be translated into chemical synthesis strategies to develop an innovative portfolio of novel inhibitors of DNA polymerases of target organisms with our GPSS™ (Gram-positive Selective Spectrum) antibiotic candidates". He further stated: "This could lead to identification of selective inhibitors for serious Gram-positive pathogens, particularly MRSA, VRE and PRSP, offering more opportunities to enhance our development pipeline and to expand the treatment options with new classes of antibiotics for multi-drug resistant bacterial infections."

*\*"pol C" is alternative nomenclature for "pol III<sub>C</sub>"*

### **About the Research Project, Leiden University Medical Center, the Research Consortium**

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 III<sub>C</sub> 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 III<sub>C</sub> proteins from pathogens. This research project will determine the structure of pol III<sub>C</sub> 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.

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.

The Research Consortium participants are 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) and is tasked by the Dutch government to promote and stimulate new 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 will initiate 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 is co-funded by the PPS Allowance made available by Health~Holland, Top Sector Life Sciences & Health, to stimulate public-private partnerships.

### **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 of 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%.

The U.S. Center for Diseases Control 2019 Update on Antimicrobial Resistance. <https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf> . CDC reported that more than 2.8 million antibiotic-resistant infections occur in the U.S. each year and more than 35,000 people die as a result, nearly twice as many annual deaths than previously reported by CDC in 2013. These deaths are attributed to antimicrobial-resistant pathogens including Enterococcus (including vancomycin-resistant strains or VRE), Staphylococcus (including methicillin-resistant strains or MRSA), and Streptococcus (including antibiotic-resistant strains), which are the bacterial targets of the Company's antibiotic pipeline with its GPSS™ (Gram-Positive Selective Spectrum) in preclinical development and also potentially eligible for QIDP and FDA-Fast-Track-Designation for priority review.

### **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 III C enzyme. 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 Penicillin-Resistant Streptococcus pneumoniae (PRSP). For more

information, please visit: [www.acurxpharma.com](http://www.acurxpharma.com).

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the potential of Ibezapolstat, Acurx's future expectations, plans and prospects, including without limitation, Acurx's expectations regarding its growth, strategy, progress and timing of its clinical trials, the potential of its antibiotics, and its intellectual property protection. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify such forward-looking statements. All such forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include the possibility that data from clinical trials will be inconsistent with the data observed in subsequent clinical trials, 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, competition from third parties that are developing products for similar uses, Acurx's ability to obtain, maintain and protect its intellectual property, Acurx's dependence on third parties for development and manufacture of product candidates including to supply any clinical trials, Acurx's ability to manage expenses and to obtain additional funding when needed to support its business activities and establish and maintain strategic business alliances and new business initiatives, and the impacts of public health pandemics such as COVID-19 on business operations including its clinical trials. Additional detailed information concerning a number of the important factors that could cause actual results to differ materially from the forward-looking information contained in this release is readily available in Acurx's publicly filed Registration Statement on Form S-1 and will also be included in quarterly, annual and other reports. Acurx disclaims any obligation to update developments of these risk factors or to announce publicly any revision to any of the forward-looking statements contained in this release, or to make corrections to reflect future events or developments.

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