*The following slides were presented by Robert J. DeLuccia, Executive Chairman of Acurx, who was an invited speaker at the Pipeline Corners Session at ECCMID 2023 Chaired by Dr. Ursula Theuresbacher. He was asked to gear his talk to address the following: An introduction to the Company, the concept of the scientific program and what it can do for patients and society; the greatest challenges regarding science and pursuit of such a program, what would be needed to support the program (In addition to money) and what would be the outlook for the Company in the next 5 years.*

ACURX PHARMACEUTICALS, INC.

# First of a New Class of Antibiotics Targeting "Priority Pathogens"

## Preparing for the Next Pandemic: Antimicrobial Resistance

Robert J. DeLuccia
Executive Chairman

**ECCMID 2023: Pipeline Corner**
April 15,2023

# Disclosure

Acurx

## Forward-Looking Statements

This presentation contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, development plans, regulatory activities, anticipated milestones, product candidate benefits, competitive position, business strategies, objectives of management, potential growth opportunities, potential market size, possible or assumed future results of operations, projected costs and use of proceeds. In some cases, forward-looking statements can be identified by terms such as “may,” “will,” “should,” “expect,” “plan,” “aim,” “anticipate,” “could,” “intent,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions. All statements other than statements of historical facts contained in this presentation are forward-looking statements. Acurx Pharmaceuticals, Inc. (the “ Company”) may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of the Company’s product candidates, including adverse results in our clinical development processes; whether results from one clinical trial will be predictive of the results of future trials and whether preliminary data from our clinical trials will be predictive of final results from such trials; decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our products; availability of funding sufficient for the Company’s foreseeable and unforeseeable operating expenses and capital expenditure requirements; our ability to obtain, maintain and enforce intellectual property and other proprietary rights for our product candidates; our ability to implement our strategic plans; and other factors discussed in the “Risk Factors” section of the Company’s filings with the Securities and Exchange Commission (“SEC”) in the future. The forward-looking statements included in this presentation represent the Company’s views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company’s views as of any date subsequent to the date of this presentation. This presentation may not be reproduced, forwarded to any person or published, in whole or in part.



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# AMR: GLOBAL CHALLENGE

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**Valeria Gigante, Ph.D.** (Geneva Switzerland)
Team Lead, AMR Division, WHO
*Co-Chair: WHO AMR Impact Initiatives and Research Coordination: WHO 2022 Bacterial Priority Pathogens List (BPPL); 17 April*

Not enough new antibiotics in the pipeline; Most are not new drug classes but evolution of existing classes; R&D process challenging and poorly funded; last novel class discovered in the 1980s*


**Rochelle Walensky, MD, MPH**; Director, U.S. Centers for Disease Control and Prevention

We must prepare our public health systems to fight multiple threats, simultaneously. Because antimicrobial resistance will not stop, we must meet the challenge. **Now is the time to address our current antimicrobial-resistant threats, while simultaneously preparing for unknown emerging threats in the future.****

## RE-EMPHASIZED PRIORITY PATHOGENS

**Because of pandemic impacts, 2020 data are delayed or unavailable for 9 of the 18 antimicrobial resistance threats.**

- *Clostridioides difficile (C. diff)*
- Drug-resistant *Neisseria gonorrhoeae*
- Drug-resistant *Campylobacter*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Drug-resistant *Streptococcus pneumoniae*
- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

**Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.**

- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

*C. diff* remains one of the most common healthcare-associated infections, affecting thousands of people every year



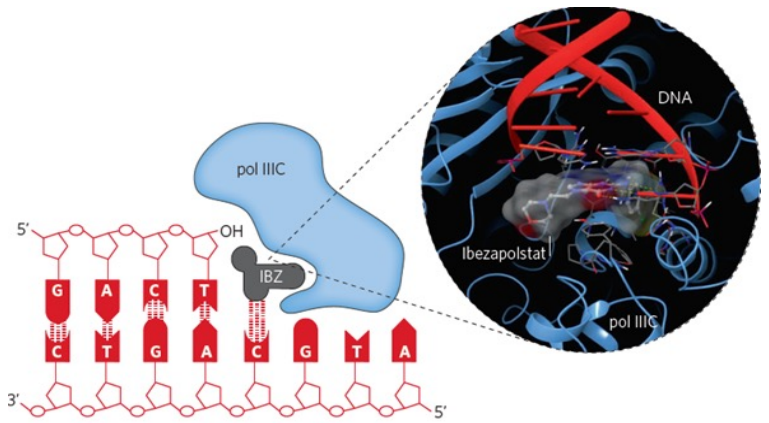
*ECCMID 2023, Copenhagen, 15-18 April, 2023, New Release 15 March 2023 **Excerpted from: CDC. COVID-19: U.S. Impact on Antimicrobial Resistance, Special Report 2022. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/drugresistance/covid19.html

# Acurx Snapshot



**Novel Mechanism of Action:**

- Previously unexploited scientific target
- Lead pol IIIC Inhibitor discovered by Wright/Brown Professors Emeriti, UMass; Acurx acquired in 2018[1]
- Innovation criteria[2]:
  - ✓ New chemical class
  - ✓ New target (Gram+; now clinically validated)
  - ✓ New MOA (Unique)
  - ✓ No cross-resistance
- Ibezapolstat (oral) potential for first-line treatment for *C. difficile* Infection (CDI)- FDA QIDP/Fast Track
- Gram-Positive Selective Spectrum (GPSS™) oral and IV antibiotics target all low G + C bacterial pathogens (including MRSA, VRE, DRSP) - QIDP/Fast Track eligible




Acurx compounds block the active site of the Gram+ specific bacterial enzyme DNA polymerase IIIC (pol IIIC), inhibiting DNA replication

**Unmet Medical Need**: CDC classifies CDI as an ***urgent threat*** requiring new antibiotic development; CDC classifies MRSA, VRE, PRSP as ***serious threats***

**Ibezapolstat Phase 2a Success/Phase 2b Enrolling:** Ph2a *demonstrated 100% cure rate and 100% sustained clinical cure 30 days after EOT. Microbiome restoration/sparing and bile acid ratio may inhibit recurrence.*[3]

- *Unexpected finding* of novel pharmacologic property of ibezapolstat likely related to its unique mechanism of action; **ECCMID 2023 Poster Session; #P2144**; Novel pharmacology and susceptibility of ibezapolstat against *Clostridioides difficile* isolates with reduced susceptibility to *C. difficile*-directed antibiotics; Dr. Kevin Garey, University of Houston



[1]Patented to May 2032 with 10 years regulatory exclusivity from FDA approval (QIDP and NCE); [2]*Theuretzbacher, WHO, 2017;* [3] *Garey ,CID, 2022*

# Systemic GPSS™ Antibiotic: Program Highlights

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**Systemic Pol IIIC Inhibitor Program**: Oral and IV formulations to target systemic treatment of *Staphylococcus, Streptococcus and Enterococcal* infections, including MRSA, VRE, and other resistant G+ bacterial infections; WHO/CDC Priority Pathogen Lists[1]

- Novel mechanism of action, inhibiting DNA pol IIIC, present in G+ and not G- bacteria or mammals[2]
- Bacteria resistant to current antibiotics, including daptomycin, telavancin, ceftaroline, new tetracyclines & linezolid-resistant bacteria
- In hospitalized patients in the United States, MRSA accounted for 52% of all infections, almost twice as many as MDR Gram-negative infections[3]
- VRE hospital infections exceeded carbapenem-resistant (CR) Acinetobacter, MDR *Pseudomonas aeruginosa* and CR Enterobacteriaceae infections combined[3]

**Potential Clinical Indications**: ABSSSI (MRSA + other G+). Follow-on: community-acquired bacterial pneumonia, hospital and/or ventilator-associated bacterial pneumonia; bacteremia with or w/o infectious endocarditis, bone/joint infections & diabetic foot infections



[1] CDC Antibiotic Resistance Threats in the U.S., 2019, Atlanta, U.S. Department of Health and Human Services, CDC, Nov. 2019; [2] Xu, et al., Bioorganic & Medicinal Chemistry https://doi.org/10.1016/j.bmc.2019.06.017; [3]Jernigan, et al., Multidrug-Resistant Bacterial Infections in U.S. Hospitalized Patients, 2012–2017, *N Engl J Med* 382:1309-19; (2020)

# Systemic GPSS™ Antibiotic: Program Goal / Progress

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- **Hit-to-Lead testing of >500 novel compounds** resulted in significant improvements in:
  - Cytotoxicity, solubility, plasma protein binding
  - In vitro & in vivo safety
  - Oral and IV efficacy in mouse infection models including in neutropenic mice (MRSA systemic & thigh, VRE thigh, and PRSP lung)

- **Lead Optimization**: Further improve drug-like properties through:
  - Streamlined chemical synthesis and testing paradigm
  - Advanced molecular modeling
  - Stepwise core modifications
  - Collaboration with LUMC (Leiden University Medical Center):
    - High-throughput measurement of pol IIIC inhibition
    - 3D structural determination of pol IIIC enzyme alone and bound to Acurx inhibitors
    - Design of new compounds based on 3D target binding site data
  - Prodrug approaches for IV and oral delivery (Preliminary prodrug approach confirmed)



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# Benefits and Challenges of Developing a New Class of Antibiotics

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## For Society and Patients

- Match up the societal challenge of AMR evolution to the opportunity and probability of success to commercialize a new therapeutic for serious and life-threatening infections
- Novel treatments for multi-drug resistance organisms contribute to a productive society by reducing absenteeism and contributing to a healthy work force:
  - A global economic model projected that over 35 years, AMR could lead to 300,000,000 premature deaths, loss of GDP growth of 2-3.5%, and loss of $60-100 trillion worth of economic output[1]
  - Pol IIIC inhibitor would support antibiotic stewardship by providing a new choice of drug class and new MOA for treatment of serious infections caused by MRSA and other Gram+ pathogens
  - Acurx clinical plan is for hospital based ABSSSI, a well-established development pathway
  - The IV to oral switch will provide an important hospital-based step-down therapeutic alternative
  - Acurx intends to support development of the pol IIIC inhibitors for use in LMICs



[1] *World Bank. 2017. "Drug-Resistant Infections: A Threat to Our Economic Future." Washington, DC*

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# Benefits and Challenges of Developing a New Class of Antibiotics

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## Scientific Challenges and Pursuit of Commercialization of a new antibiotic

- Need sophisticated scientific tools, talent and collaborations to enhance medicinal chemistry efforts
  - Novel analogs of pol IIIC inhibitors with improved binding will be tested in collaboration with LUMC under a Dutch government grant; the 3-D structure of pol IIIC from MRSA, VRE and PRSP alone and bound to Acurx inhibitors are being studied using cryo-EM/X-ray crystallography

## Requirements to support the program (beyond funding)

- Antibiotics not commercially attractive to warrant R&D investment vs other therapeutic areas; big pharma has abandoned the space
- *"Antibiotic-resistant infections could dwarf the COVID-19 pandemic. Antibiotics are being taken for granted and many bacteria have become resistant to them. Given enough time, bacterial evolution will render every antibiotic ineffective. We need to act."*
- PUSH Incentives
  - Renewed and sustained substantial investment (public and private) required to support R&D of new antibiotics from early stages of basic science through clinical trials, regardless of successful market access
- PULL Incentives to reward antibiotic developers/marketers <u>required to attract PUSH incentives</u>
  - Governments must fix the broken commercialization model, stimulate innovation, and at same time ensure physicians can prescribe the most effective antibiotics to patients in need
  - E.g., UK; first subscription model recently launched to pay for an antibiotic's value to society instead of its volume of sales
  - U.S. Congress currently considering **P**ioneering **A**ntimicrobial **S**ubscriptions **T**o **E**nd **U**p surging **R**esistance Act (similar model to UK) and how Medicare pays for the use of new antibiotics **D**eveloping an **I**nnovative **S**trategy for **A**ntimicrobial **R**esistant **M**icroorganisms
  - Every G7 country publicly committed to enacting market reforms to address AMR public health crisis



[1]Boston Globe: OPINION; Outterson, Skinner; July 18, 2022

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# Outlook / Vision: Next 5 years

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- AMR treatable with new classes of antibiotics with appropriate antibiotic stewardship
- Acurx market introduction of ibezapolstat for first-line treatment of CDI
- Acurx advances lead Oral and IV antibiotic candidate for pan-active Gram+ infections into Ph2 clinical trials
- Antimicrobials' business model and Medicare reimbursement (at least in U.S.) "fixed" by adoption of "pull incentives" like Pasteur Act and/or DISARM Act
- SMEs and large pharma companies continue pursuit of new modalities to address AMR with enhanced interest due to adoption of "pull incentives"
- Financial institution investment into AMR-related incubator companies reaches new highs as financial resources flow back into the newly "fixed" sector

# No new class of antibiotics discovered and approved in decades

ACURX PHARMACEUTICALS, INC.

*…Acting **NOW** to replenish the pipeline with novel antibiotics to treat infections caused by **Gram+** organisms*

Please visit our website: www.acurxpharma.com
ACXP: Nasdaq

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