Issuer Free Writing Prospectus
Filed Pursuant to Rule 433
Registration No. 333-256516

# Acurx Pharmaceuticals

**Potentially, we believe, to be First in a New Class of Antibiotics Since the 1980s[1,2]**

**World Health Organization & U.S. Centers for Disease Control and Prevention Priority Pathogens[1,3]**

**Readiness for the next Infectious Disease Pandemic: Antibiotic Resistance**

**June 2021**

[1]Centers for Disease Control, November 2019; [2]Wei-Chu Xu, et al., Bioorganic & Medicinal Chemistry, June 2018; [3]World Health Organization, December 2019

# Disclosure

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**DISCLAIMER**

The Company has filed a registration statement, including a preliminary prospectus, with the SEC (File No. 333-256156) in connection with the offering to which this presentation relates. Sales of the securities of the Company offered pursuant to the registration statement may not be made or offers for such securities accepted prior to the registration statement becoming effective. Before you invest, you should read the registration statement, the preliminary prospectus included within the registration statement and other documents the Company has filed with the SEC for more complete information about the Company and this offering. You can obtain a copy of the preliminary prospectus for free by visiting EDGAR on the SEC website at www.sec.gov. Alternatively, the Company will arrange to send you the preliminary prospectus, which you may request by emailing davidluci@acurxpharma.com.

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# Offering Summary and Use of Proceeds

| OFFERING TERMS SUMMARY | |
|---|---|
| Issuer: | **Acurx Pharmaceuticals** |
| Ticker/Exchange: | **ACXP/Nasdaq** |
| Base Offering size: | **$15,000,000** |
| Shares offered: | **2,500,000 Shares of Common Stock** |
| Filing range: | **$5.00 to $7.00 (Midpoint of $6.00 per share)** |
| Over-allotment option: | **15%** |
| Expected pricing date: | **06-24-21** |
| Underwriters: | **Alexander Capital, L.P. & Network 1 Financial Securities, Inc.** |

## USE OF PROCEEDS

- Complete Phase 2b clinical trial of ibezapolstat
- Complete pre-clinical development of ACX-375C
- General corporate purposes

# Executive Summary

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**Corporate:** Co-Founded July 2017 to develop a new class of antibiotics to address global crisis of antimicrobial resistance in Gram-positive bacteria; initial target - CDI

**Novel Mechanism of Action:** DNA polymerase IIIC inhibitor

- Previously unexploited scientific target
- Positioned, we believe, to be first-line treatment for CDI

**Unmet medical need**: CDC classifies CDI as an urgent threat requiring new antibiotic development. Existing antibiotics used to treat CDI marketed for decades have recurrent infection of 20% to 40%[1] and antibiotic resistance (metronidazole) necessitating development of new antibiotics to treat CDI

**Phase 2a Success/Phase 2b Ready:** Ibezapolstat recently completed Ph2a clinical trial in patients with CDI – *100% cure rate and 100% sustained clinical cure 30 days after EOT*

COVID-19 brings infectious disease threats into worldwide spotlight as policy makers look to bring antibiotics' development back to the U.S.

[1]Johnson,et al: Sustained Clinical Response as an Endpoint in Treatment Trials of *Clostridium difficile-Associated Diarrhea, Antimicrobial Agents and Chemotherapy, August 2012*

# Antimicrobial Resistance

- Antimicrobial resistance occurs when microorganisms (bacteria, fungi, viruses, and parasites) change when exposed to antimicrobial drugs.
- WHO Director-General recently warned that growing antimicrobial resistance is as dangerous as the ongoing COVID-19 pandemic threatens to unwind a century of medical progress and leave us defenceless against infections that today can be treated easily.*
- Acurx believes that the high level of awareness of COVID-19 viral pandemic sets the stage for higher awareness, interest and importance of our readiness for an antimicrobial resistance pandemic.

World Health Organization

- Clinical pipeline remains insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance[3]

CDC

- Antibiotic resistance not only a U.S. problem—it is a global crisis[2]
- New antibiotics are an important piece of the fight against antibiotic resistance

[1]Prestinaci, et al, Antimicrobial Resistance: a Global Multifaceted Phenomenon, Pathog Gob Health, October 2015; [2]CDC Antibiotic Resistance Threats in the U.S., 2019, Atlanta, U.S. Department of Health and Human Services, CDC, 2019; [3]WHO, 2019 Antibacterial Agents in Clinical Development; *CTV News, 23Nov2020

# Unmet Medical Need

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**No new antibiotics in clinical development have shown improvement in either ICR or SCR in comparison to currently marketed antibiotics**

| | Product | *C. difficile* - mITT population | | |
|---|---|---|---|---|
| | | % Initial Cure | % Sustained Cure | % Recurrence* |
| Marketed (Ph 3 results US/CAN)[1] | vancomycin (n=309) | 86 | 61 | 25 |
| | fidaxomicin (n=287) | 88 | 73 | 15 |
| In Development (Ph 2 results)[2] | ridinilazole (n=36) | 78 | 67 | 14 |
| | vancomycin (n=33) | 70 | 42 | 39 |
| **In Development (Ph 2a ITT results)[3]** | **ibezapolstat (n=10)** | **100** | **100** | **0** |

*[1] Louie et al, Fidaxomicin vs Vancomycin, Phase 3 study, NEJM, Feb 2011; [2] Vickers et al, Efficacy and Safety of Ridinilazole Compared with Vancomycin for treatment of C. difficile Infection; Ph2 Randomized, Double-blind, Active-controlled, Non-inferiority Study; Lancet, July, 2017; [3] Garey, Late-Breaker Presentation, Ibezapolstat Clinical Update, 8th Annual International C.diff. Virtual Conference, Nov 18, 2020*

** Calculated percent of patients with Initial Cure who experienced recurrence*

# Antibiotics: Gold Standards to Treat CDI

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## Antibiotics

- Current standard of care first-line and first recurrence treatment with established marketed antibiotics (vancomycin, fidaxomicin) recommended by IDSA*
- Currently marketed antibiotics achieve relatively high initial cure rate but leave high burden of C. difficile in the gut; This, together with a pronounced detrimental effect on the gut microbiome, leads to recurrence in over 25% of CDI patients after their therapy stops
- Significant unmet need remains for antibiotics that can meaningfully reduce recurrence
- **We believe that the bactericidal effect / low incidence of recurrence positions ibezapolstat for first-line treatment of CDI**

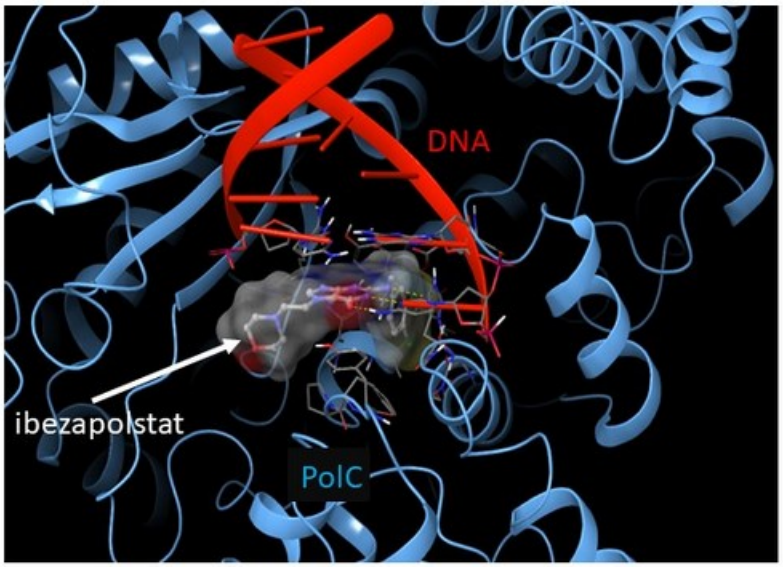
| Antibodies | FMT / Microbiologics | Vaccines |
|---|---|---|
| ▪ Generally, only administered in combination with antibiotic<br>▪ Only 1 approved<br>▪ Safety issues<br>▪ High costs and inability to use as a first-line-treatment have limited commercial attraction | ▪ Two treatments in late-stage development (SER 109, RBX2660) with clinical data forthcoming; nothing approved<br>▪ Safety, impact on microbiome are concerns; recommended only for patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments; **FDA SAFETY ALERT.** | ▪ Several vaccines in late-stage development, none currently approved<br>▪ Likely only commercially viable as a prevention of recurrent disease in high-risk patients, if these can be identified<br>▪ Large numbers of patients required for trials |

# R&D Pipeline

| Program | Target Pathogen | Discovery | Pre-Clinical | PH I | PH II | PH III |
|---|---|---|---|---|---|---|
| Ibezapolstat | C. *difficile* | Phase 2A successful completion; terminated early | | | | |
| ACX-375C | Gram-positive Infections | Lead Optimization | | | | |
| CCP[1] | Multiple product candidates; Gram-positive infections | | | | | |

[1]**Computational Chemistry Project:** Currently "mining" 2 to 4 additional DNA Polymerase IIIC new chemical entities in a computational chemistry modeling program in scientific collaboration with WuXi AppTec to expand pipeline of DNA Pol IIIC inhibitors.

# Mechanism of Action




- **Ibezapolstat:** We believe this is the only compound currently in clinical trials known to target *C. difficile* by acting specifically on pol IIIC[1]
- **Vancomycin**: Cell wall biosynthesis inhibitor[2]; selective RNA Inhibitor
- **Fidaxomicin**: RNA synthesis inhibitor[3]
- **Ridinilazole**: Unknown (Ph3)[4]

**Ibezapolstat:** DNA polymerase IIIC inhibitor occupies active site in bacterial cell enzyme (Same MOA for other Gram+ organisms)[1]

1. Wei-Chu Xu, et al., Bioorganic & Medicinal Chemistry https://doi.org/10.1016/j.bmc.2019.06.017. 2. Vancomycin Full Prescribing Information 3. Dificid Full Prescribing Information; [4]Bassères *et al*: Understanding the Mechanism of Action of Ridinilazole (SMT19969), a Novel Treatment for Clostridium difficile, 26th ECCMID, Amsterdam, 9-12 April 2016

# Market Opportunity

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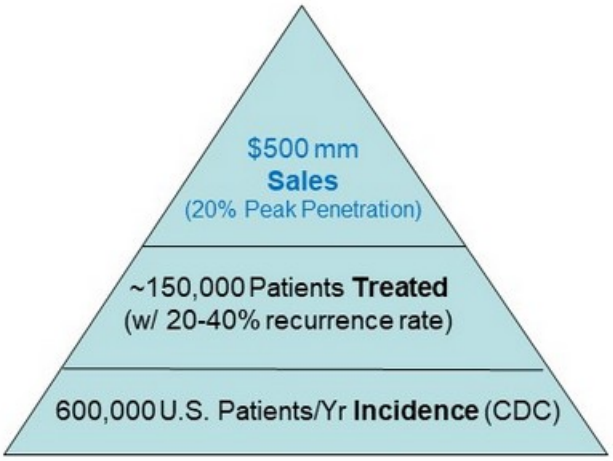
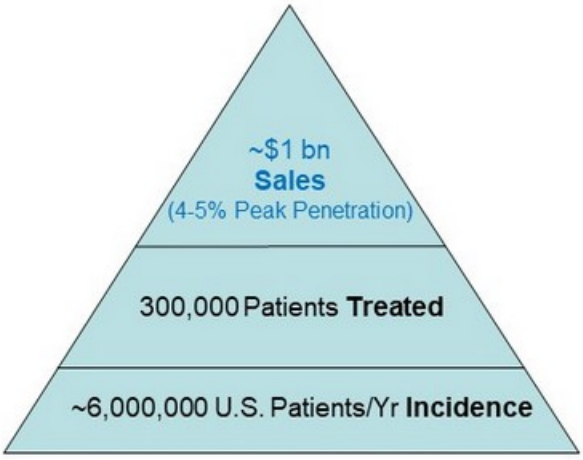
**Patients with *C. difficile* Infection (CDI)**
(ibezapolstat)



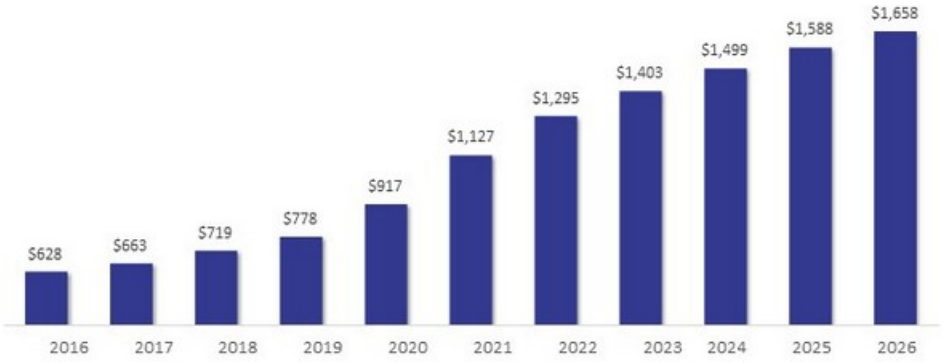

**Patients w/other Gram+ infections**
(*Staphylococcus, Streptococcus or Enterococcal* Infections, including MRSA, VRE & PRSP)
(ACX-375C Oral and I.V.)




***Combined Peak Sales Estimate > $1.5B per year for both Acurx products***

# C. *difficile* Market Maintaining Strong Growth

- ***C. difficile is*** **one of most common pathogens in healthcare associated infections (HAI) in North America**
- **20% to 40% of cases recurrent**
- **Mortality rate 9.3%**




**$1.7 bn**
***2026 C. difficile Market***

**>10%**
***2016-2026 CAGR***

**>485,000**
***Courses of Therapy (U.S.)***

Sources: Lessa et al. NEJM (2015), Louie et al. NEJM (2011), Johnson et al. Clin Inf Dis. (2014), GlobalData (2017)

**Ibezapolstat is positioned, we believe, to become first-line treatment for CDI**

# Ibezapolstat: Phase 2a Success

- Patients with mild to moderate CDI treated with orally administered ibezapolstat given 450mg twice daily for 10 days
- All 10 patients (100%) met the study's primary and secondary efficacy endpoints of Initial Cure and Sustained Cure
- Ibezapolstat very well tolerated; no treatment-related SAEs
- Meeting the treatment goals of eliminating the infection with an acceptable adverse event profile allowed early termination of the Phase 2a trial and advancement to the Phase 2b trial
- Phase 2b clinical trial: 64 patients in 2 arms treated for 10 days;
- 32 patients will receive ibezapolstat; 32 patients will receive vancomycin, which is the current standard of care
- US Exclusivity: Patented to September 2030; Potential Regulatory Exclusivity: 10 years from FDA marketing approval (QIDP and Fast Track)

# Ibezapolstat Enhances Actinobacteria

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Ibezapolstat enhances Actinobacteria in the Microbiome and Suppresses regrowth of Proteobacteria; potentially lessening the likelihood of recurrence[1]

| PHYLUM | ANTIBIOTIC ACTIVITY | |
|---|---|---|
| | ibezapolstat | vancomycin (oral) |
| Actinobacteria | No | Yes |
| Bacteroidetes | No | Yes |
| Firmicutes | Yes | Yes |
| Fusobacteria | No | No |
| Proteobacteria | No | No |

[1] Garey, Late-Breaker Presentation, Ibezapolstat Clinical Update, 8th Annual International C.diff. Virtual Conference, Nov 18, 2020

# ACX-375C Highlights

**Second DNA Pol IIIC Inhibitor ACX-375C**: Oral and I.V. formulation targets treatment of *Staphylococcus, Streptococcus and Enterococcal* infections, including vancomycin-resistant enterococcus (VRE), Methicillin-resistant staph (MRSA) and other resistant G+ bacterial infections; WHO/CDC Priority Pathogen List[1]

- In hospitalized patients, MRSA accounted for 52% of all infections, almost twice as many as MDR Gram-negative infections[2]

**Potential Clinical Indications**: Urinary tract, hospital acquired catheter/blood stream, intra-abdominal, skin/soft tissue, bone/joint, pneumonia, ear/sinus infections

**Unmet Medical Need**: Antibiotic resistance to currently used antibiotics; including daptomycin and linezolid-resistant bacteria[3]

**IP and Regulatory**: 2 patents covering composition-of-matter, formulation and method-of-use expire December 2039. QIDP, Fast Track and NCE eligible (potential regulatory exclusivity 10 years from FDA approval).

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

# Microbiome: Ibezapolstat vs. Vancomycin

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## Head-to-Head Comparison In Phase 1 clinical trial[1]:

**Vancomycin**

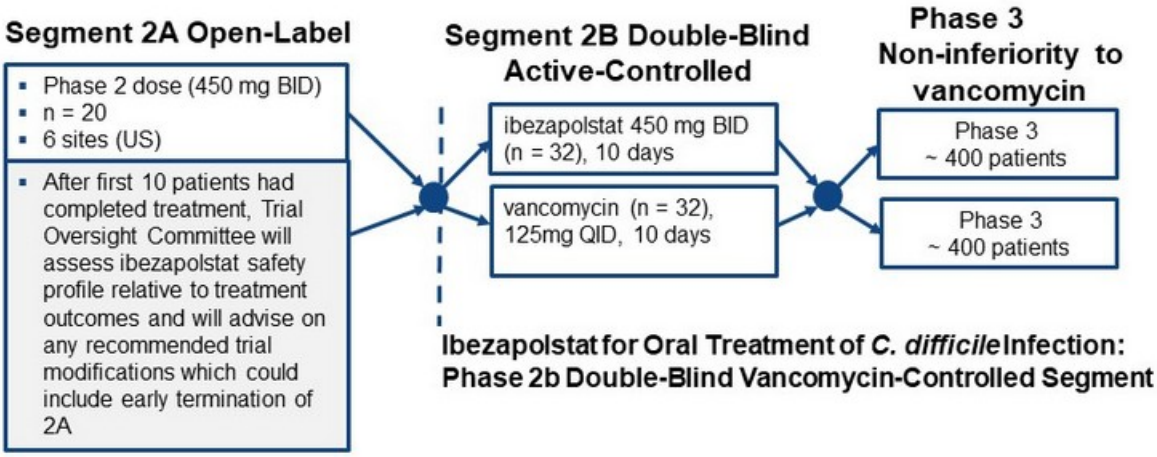
- 2 to 3 log reduction in healthy bacteria

**Ibezapolstat**

- No appreciable reduction
- Poorly soluble in the gut
- Free concentrations of ibezapolstat high enough, we believe, to kill *C. difficile* but too low, we believe, to kill healthy bacteria like Bacteroides & Firmicutes which constitute ~ 90% of the healthy microbiome

1. Press Release. Acurx's Novel Lead Antibiotic Candidate Presented at Two Prominent International Scientific Conferences. Oct 2019.

# Ibezapolstat Phase 2 Clinical Trial Design




- Management will continue to pursue non-dilutive grants for late-stage clinical trials.


1. BioSpace. Summit Announces BARDA Increases Award for Ridinilazole Clinical and Regulatory Development to up to $63.7 Million and Exercises Next Contract Option. June 2019.
2. Seeking Alpha. Summit nabs $4.5M grant to support development of new antibiotics; shares up 11% premarket. July 2018.
3. Seeking Alpha. Specialty Report On Infectious Disease: Unlocking The Upcoming Binary Event Of Achaogen And Value Of Melinta. April 2018.
4. Genetic Engineering and Biotech News. Gates Foundation Supports Achaogen's Antibacterial Platform with $20.5M. May 2017.
5. Investors Observers. Large investor in Achaogen Inc. buys $6 million in additional shares. April 2018.

# Expectation of Success in Phase 2b

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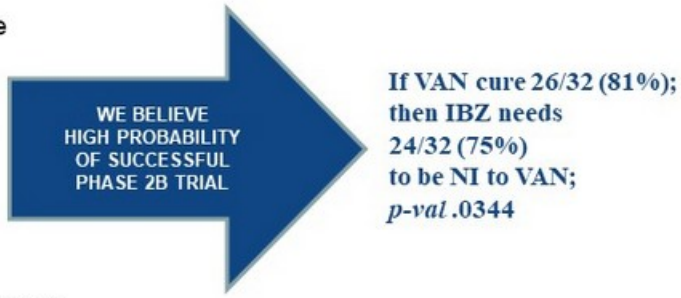
## 10 Factors that will provide confidence in successful outcomes of future clinical trials:

- In Vitro potency vs *C. difficile*
- In Vivo efficacy hamster model (industry standard)
- Excellent human safety profile to date
- High human fecal concentrations (>100-fold above $MIC_{50}$ in patient samples)
- Favorable microbiome effects (healthy volunteers and patients; ⇩ recurrence)
  - Ph2A patients: Data to come
- 100% efficacy clinical cure (10 Ph2a patients)
- 100% efficacy (sustained clinical cure/28day post EOT); (10 Ph2a patients)
- Rapid eradication (by Day 3) of *C. difficile* in patients
- Does not trigger sporulation or toxin release (Data to come)
- Favorable effect on bile acids (Data to come)




**If VAN cure 26/32 (81%); then IBZ needs 24/32 (75%) to be NI to VAN; *p-val* .0344**

# External Positive Drivers in 2020

## External positive drivers in 2020 encouraging for sector

### PASTEUR Act

- Provide critical 'pull' incentive in US
- HHS to pay subscription payment for eligible products
- **$750m - $3bn subscription payments over 10 years**
- **Transitional support available for Ph3 trials and manufacturing**

### AMR Action Fund

- Cross-industry collaborative investment initiative
- Provide $1bn support for clinical activities
- Currently in formation and ready for first investments in 2021
- **Acurx eligible for support and is engaged with the fund**

### DISARM ACT

- Removes financial disincentive to prescribe novel agents
- Provides clinicians greater opportunity to treat infectious diseases with most effective agents
- Allows novel agents to be reimbursed in the hospital setting outside constraint of the DRG

### EU Pull Incentives

- New Pharmaceutical Strategy for Europe specifically discusses antibiotics
- New European pull-incentives under discussion
- New European "BARDA-like" body (Health Emergency Response Authority) to be created

# Experienced Management

- **David P. Luci, CPA, Esq.,** Former CEO Dipexium Pharmaceuticals (Nasdaq:DPRX); Abeona Therapeutics, MacroChem, Bioenvision. Raised capital in several public offerings and private placements; sold 3 public companies from "C" suite

- **Robert J. DeLuccia,** Former Chairman Dipexium Pharmaceuticals (Nasdaq: DPRX); Former President Sanofi U.S.and Pfizer, Sr. Executive; Former CEO Immunomedics (Nasdaq: IMMU) and MacroChem Corporation (OTC BB: MACM); Lead Director BOD, IBEX Pharmaceuticals (IBT-TSX)

# Management Team

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- **Michael Silverman**, MD, FACP, Medical Director

  KPMG Health Care Consulting, Biopure Corp, Sandoz, Sterling-Winthrop (Kodak-Sanofi) and clinical practice of medicine

- **Les Johnson**, Manufacturing Director

  Clear Path Development, Salamandra, Celsis, Cambrex, Biosynexus, Baxter Bioscience, Protein Polymer Technologies, Bayer Biologics, Cetus/Codon/Berlex

- **Xiang Yu**, Ph.D., Director of Pre-Clinical Development

  Cubist Pharmaceuticals, Accellient Partners, Ironwood Pharmaceuticals, Epix Pharmaceuticals

- **Larry Mortin**, Ph.D., Director of Pharmacology

  Cubist Pharmaceuticals

# Timeline

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| 2H 2020 | 1H 2021 | 2H 2021-1H 2022 |
|---|---|---|
| ▪ Completed Ph2a trial of ibezapolstat in CDI<br>▪ Complete "crossover" financing<br>▪ Obtained 2 new patents on ACX-375C (17 claims including composition of matter and formulation) | ▪ IPO<br>▪ File for AMR financing<br>▪ Business development | ▪ Start and complete ibezapolstat Ph2b trial in CDI<br>▪ File for QIDP/ACX-375C<br>▪ Start Pre-IND Pharm/Tox studies for ACX-375C<br>▪ File IND / start ACX-375C<br>▪ Phase 1 (oral & I.V.)<br>▪ File FDA Fast Track for ACX-375C |

# Acurx Pharmaceuticals

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