



Advancing a New Class of Antibiotics to Phase 3 Trials

Targeting “Priority Pathogens”
– WHO and CDC

April 2024

Disclosure



FREE WRITING PROSPECTUS

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A registration statement on Form S-1 (File No. 333- 278028), as amended, including a preliminary prospectus, relating to the offering of securities has been filed by the Company with the SEC. The registration statement has not yet become effective. Before you invest, you should read the preliminary prospectus in the registration statement and, when available, the final prospectus relating to the offering. An electronic copy of the preliminary prospectus relating to the offering is available, and a copy of the final prospectus relating to the offering will be available, on the website of the SEC at www.sec.gov. Copies of the preliminary prospectus and final prospectus relating to the offering, when available, may be obtained by contacting Titan Partners Group, LLC, a division of American Capital Partners, LLC, 4 World Trade Center, 29th Floor, New York, New York 10007, by phone at (929) 833-1246 or by email at info@titanpartnersgroup.com.



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Executive Summary



Corporate (Nasdaq: ACPX)

Acquired ibezapolstat (lead antibiotic) – Feb 2018



Novel Mechanism of Action

Pipeline (2) of DNA polymerase III inhibitors

- Previously unexploited scientific target
- Ibezapolstat potential first-line treatment for C. difficile infection (CDI)
- ACX-375 targets all known gram-positive bacterial infections (MRSA, VRE, PRSP)



Unmet Medical Need

CDC classifies CDI as an **urgent threat** requiring new antibiotic development. 2 of 3 current antibiotics used to treat CDI have recurrent infection of 20% to 40% and antibiotic resistance¹ necessitating development of new antibiotics to treat CDI



Phase 3 Ready

Successful Phase 1 and Phase 2 COMPLETED

Ibezapolstat demonstrated overall 96% cure rate in Ph2 trials (2a and 2b) at EOT. FDA meeting is April 2024



CMC

Robust with low COGS targeted at \$300 or less for full course of treatment



Cash On Hand

~\$7.5 mm cash at 12/31/23

¹Anne J. Gonzales-Luna, University of Houston College of Pharmacy, ECCMID 2023, Scientific Poster, April 6-20m 2023



No new antibiotics in clinical development showing improvement in either IC or SCC

	Product	C. difficile Infection – mITT population		
		% Initial Cure	% without recurrence	% Sustained Clinical Cure*
Marketed (Ph3 Results US/CAN) ¹	vancomycin (n=309)	86	75	61
	fidaxomicin (n=287)	88	85	73
In Development (Ph2 Results) ²	vancomycin (n=33)	70	61	42
	ridinilazole (n=36)	78	86	67
In Development Ph3 Results**	vancomycin (n=375)	92	83	71
	ridinilazole (n= 370)	87	92	73
In Development (Ph2 PPP results) ³	ibezapolstat (n=26)	96%	100%	100%
	Vancomycin (n=14)	100%	86%	86%

¹Louie et al, Fidaxomicin vs Vancomycin, Phase 3 study, NEJM, Feb 2011; ²Vickers 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; ³Ibezapolstat Phase 2a, CID 2022 and Ph2b data on File Acuro; *Calculated percent of patients with Initial Cure who SCC; **IDWeek2022

Antibiotics: Global Standard to Treat CDI



Antibiotics

- Existing standard of care first-line and first recurrence treatment with established marketed antibiotics (vancomycin, fidaxomicin) recommended by IDSA¹
- 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 approximately 20%-40%² of CDI patients after therapy ends
- Significant unmet need remains for antibiotics that can meaningfully reduce recurrence
- Fast bactericidal effect noted in trials / low incidence of recurrence -- positions ibezapolstat for first-line treatment if approved**



Antibodies

- Generally, only administered in combination with antibiotic
- Only 1 approved
- Safety issues; Mild success
- High costs and inability to use as a first-line treatment have limited commercial traction**



FMT / Microbiotics

- Two treatments approved for recurrent CDI (VOWST and Rebiotix)
- Safety & impact on microbiome are concerns; recommended only for patients with multiple recurrences of CDI who failed appropriate antibiotic treatments; **FDA box warning in labelling**
- High costs and inability to use as first-line treatment have limited commercial appeal



Vaccines

- Pfizer vaccine failed in Ph3 (March 2022)
- Sanofi vaccine failed in 2017
- None approved; publicly available data all negative
- Large numbers of patients required for trials

¹Clinical Practice Guidelines for Clostridium difficile in Adults and Children: 2017 Update by the Infectious Diseases Society of IDSA and SHEA

²Johnson et al: Sustained Clinical Response as an Endpoint in Treatment Trials of Clostridium difficile-Associated Diarrhea, Antimicrobial Agents and Chemotherapy, August 2012



Program	Target Pathogen	Discovery	Pre-Clinical	Ph 1	Ph 2	Ph 3	
Ibezapolstat	<i>C. Difficile</i>						
ACX-375C	Gram-positive Infections						
CCP ¹	Multiple product candidates; Gram-positive infections						

¹Computational Chemistry Project
Currently "mining" 2 to 4 additional DNA Polymerase IIIIC new chemical entities in a computational chemistry modeling program in scientific collaboration with WuXi AppTec, and Leiden University Medical Center.

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Recent & Upcoming Milestones

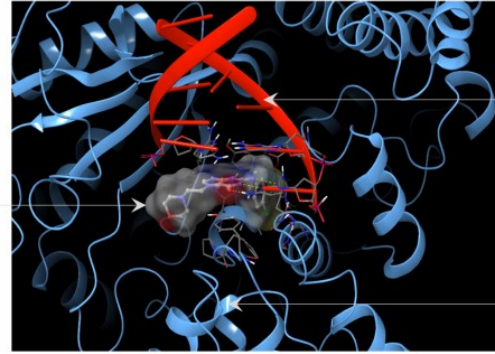


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Ibezapolstat kills *C. difficile* bacteria by blocking the pol IIIIC enzyme thereby not allowing DNA replication of the bacterial cell.¹

Same MOA applies to the ACX-375C series of compounds



DNA

PolC

Ibezapolstat

¹ Wei-Chu Xu, et al., Bioorganic & Medicinal Chemistry <https://doi.org/10.1016/j.bmc.2019.06.017>.

C. difficile Infection: Large Growing Market



Global Market Current and Forecast (2023-2032)



Ibezapolstat positioned to become first-line treatment for CDI if approved

* Clostridium Difficile Infection (CDI) -Market Outlook, Epidemiology, Competitive landscape, and Market Forecast; 2022 to 2032; TheLansis, June 2023

Ibezapolstat: Phase 2 Success



EOT (End of Treatment)

25/26 (96%) of evaluable patients were cured at EOT (10 of 10 in Ph2a and 15 of 16 in Ph2b). No drug related SAE's

SCC (Sustained Clinical Cures)

All 15 ibezapolstat-treated patients in Phase 2b who achieved Clinical Cure (CC) at end of treatment (EOT) remained free of CDI recurrence 30 days after EOT, for a Sustained Clinical Cure (SCC) rate of 100%

ECC (Extended Clinical Cures)

100% (5 of 5) of ibezapolstat-treated patients experienced no recurrence of infection



Regulatory/Patent Exclusivity

Rolling 10 years regulatory exclusivity from FDA approval (QIDP and NCE); similar regulatory exclusivity in EU and internationally; Patents expire September 2030

Clinical Comparability

Ph 2 clinical results* shows early-stage clinical comparability of a new class of antibiotics to treat CDI compared to oral vancomycin

Ibezapolstat outperformed vancomycin showing eradication of fecal *C. difficile* at Day 3 of treatment in 15 of 16 treated patients (94%), versus vancomycin which had eradication of *C. difficile* in 10 of 14 treated patients (71%)

Ibezapolstat microbiome head-to-head showed IBZ beat vancomycin at preservation and regrowth of key gut microbiota essential to avoid recurrent CDI

Ibezapolstat Preserves & Enhances the Microbiome



Ibezapolstat restores the microbiome by enhancing Actinobacteria in the microbiome while suppressing regrowth of Proteobacteria; reducing the likelihood of recurrence¹

PHYLUM	ANTIBIOTIC ACTIVITY	
	ibezapolstat	vancomycin (oral)
Actinobacteria	No	Yes
Bacteroidetes	No	Yes
Firmicutes	Selective	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



Segment 2A Open-Label

- Phase 2 dose (450 mg BID)
- n = 10
- 6 sites (US)

After first 10 patients completed treatment, Trial Oversight Committee assessed ibezapolstat safety profile relative to treatment outcomes and recommended early termination of Ph2A

Segment 2B Double-Blind Active-Controlled

ibezapolstat 450 mg BID (n = 16), 10 days

vancomycin (n = 14), 125mg QID, 10 days

28 sites (US); observed aggregate blinded data discontinued the Ph 2b due to success; trial performed as anticipated for ibezapolstat and VAN control with high rates of clinical cure observed across the trial without any emerging safety concerns

Ibezapolstat for Oral Treatment of *C. difficile* Infection

A Phase 3 Double-Blind Vancomycin-Controlled Trial (IBZ-ASPIRE-1 and IBZ-ASPIRE-2)

Ph 3 (US and Ex-US) ~ TBD patients

Ph 3 (US and Ex-US) ~ TBD patients

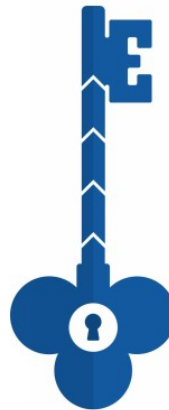
Rationale for the study objectives, endpoints, dose and regimen selection, study population, comparator, design features, sample size, and the statistical analysis plan TBD at EoP2 FDA meeting

Key Factors For Potential Phase 3 Success



Nonclinical

- Bactericidal potency vs *C. difficile*
- Effective against MDR strains including vanco resistant and Fidax resistant strains
- Does not trigger sporulation or toxin release
- Reduced flagellar movement
- Active in biofilms
- Preserves and restores microbiome unlike vancomycin



Clinical

- Clinical Cure Rate 96% (25 of 26 patients) in Ph2 trials
- Sustained Clinical Cure Rate of 100% 30 days after EOT (15 of 15)
- Extended Clinical Care Rate 100% (5 of 5 patients)
- High human fecal concentrations (>1000x MIC)
- Rapid eradication of *C. difficile* (by Day 3) in CDI patients
- Favorable microbiome effects by day 3 while on treatment
- Favorable effect on bile acids
- No drug related SAEs



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 List¹

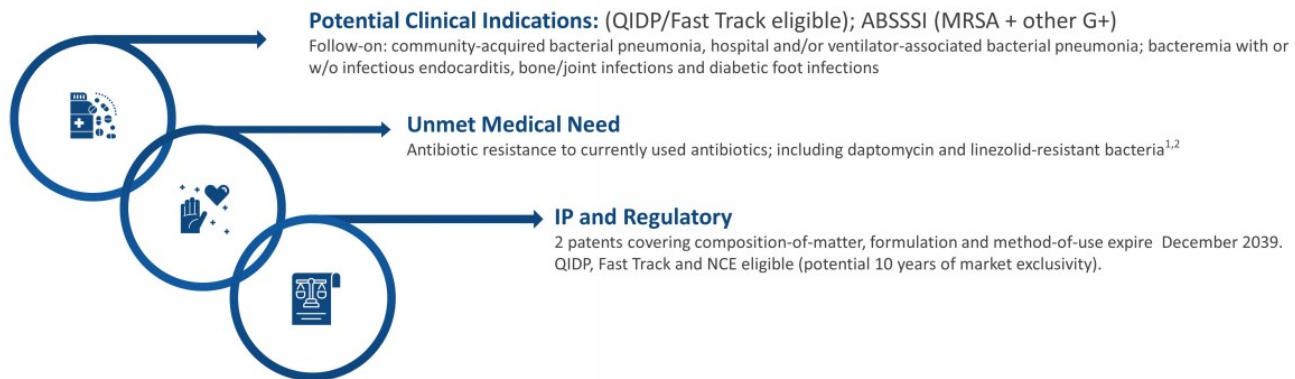
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In hospitalized patients, MRSA accounted for 52% of all infections, almost twice as many as MDR Gram-negative infections²

2

VRE hospital infections exceeded carbapenem-resistant (CR) *Acinetobacter*, MDR *Pseudomonas aeruginosa* and CR Enterobacteriaceae infections combined²

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)



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2. Wei-Chu Xu, et al., Bioorganic & Medicinal Chemistry <https://doi.org/10.1016/j.bmc.2019.06.017>

Capitalization Summary



Cap Table as of 12/31/23

Common Shares Outstanding	14,468,229
Warrants (WAEP: \$3.28)	6,195,456
Stock Options (WAEP: \$5.64)	2,985,000
Fully Diluted Shares Outstanding	23,648,685

Balance Sheet as of 12/31/23 (\$mm)

Cash & Cash Equivalents	\$7.5
Total Assets	\$7.7
Total Debt	\$0
Total Liabilities	\$3.0
Shareholders' Equity	\$4.7

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Experienced Senior Executive Management



David P. Luci, CPA, Esq
Co-Founder & CEO

Former CEO of Dipexium Pharmaceuticals (Nasdaq: DPRX), Abeona Therapeutics (Nasdaq: ABEO), MacroChem (OTC BB: MACM), and Bioenvision (Nasdaq: BIVN). Sold all 3 public companies he co-founded or joined in early stage. Orchestrated several in and out-licensing transactions prior to dispositions. M&A and corporate finance attorney (Paul Hastings NY) and CPA with Ernst & Young NY



Robert J. DeLuccia
Co-Founder & Executive Chairman

Former Chairman of 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)



Robert G. Shawah
CPA, Co-Founder & CFO

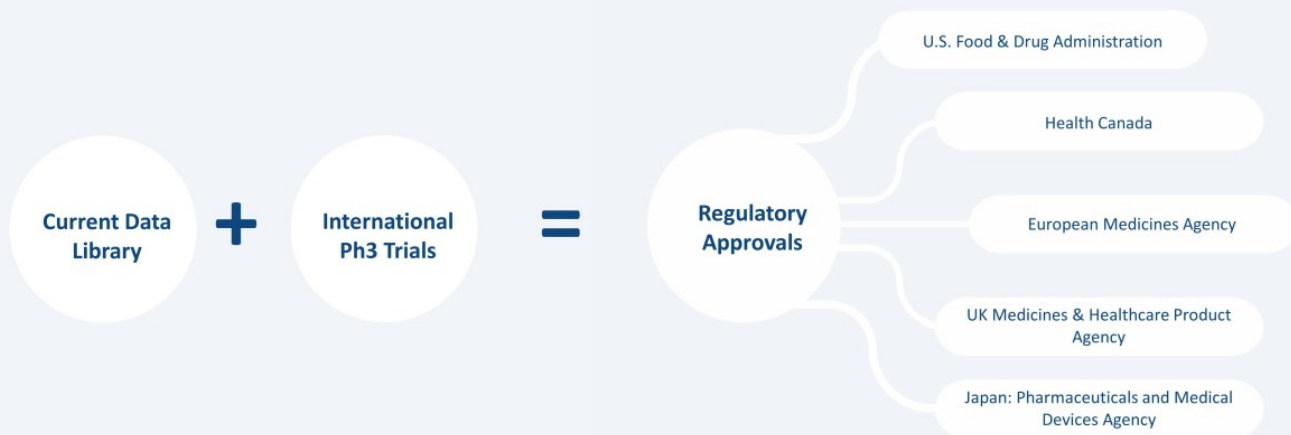
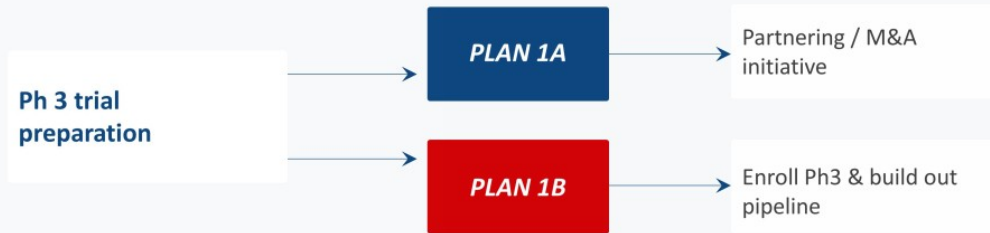
Former Chief Accounting Officer of Dipexium Pharmaceuticals (Nasdaq: DPRX); Former Vice President of Baldwin Pearson & Co., a commercial real estate firm

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OBJECTIVE

In parallel with Ph3 trial preparation, explore strategic alternatives



Recent M&A Transactions



June 2023

Shionogi buys Qpex Pharma, an early-stage developer of beta lactamase inhibitor for drug resistant gram-negative bacterial infections. Deal terms - \$100 million upfront and up to \$40 million in downstream milestones. **Lead antibiotic candidate is in Ph1b.**

March 2023

Sebela Pharmaceuticals acquires Destiny Pharmaceuticals, developer of a microbiome therapeutic to treat patients with recurrent C diff, in a structured deal valued at up to \$570 million plus tiered double-digit royalties.

May 2022

Innoviva buys Entasis, in a deal valued at \$113 mm for an antibiotic which succeeded in Phase 3 trials and was ready to apply for FDA approval. Clinical indication is quite small patient numbers – **Acinetobacter baumannii**. Deal was 50% premium over closing price day prior to announcement.

October 2021

Novartis' Sandoz acquires cephalosporin business from GSK acquiring revenue streams of \$140 million per year. Deal terms not announced but Sandoz confirmed antibiotics are the centerpiece of their product pipeline.

November 2020

Tillotts Pharma buys fidaxomicin rights in EU, Middle East and Africa from Astellas Pharma AG for **\$125 mm**. 2022 sales in Europe alone were **\$80 million** primarily as last-line therapy.

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Non-Executive Members of the Board of Directors



- **Jack H. Dean, Ph.D.**, Former Director, Worldwide Pre-Clinical Research at Sanofi; Research Professor, Univ of Arizona (Pharmacology & Toxicology)
- **James Donohue**, Vice President of Charles River Associates (Nasdaq: CRAI)
- **Thomas Harrison**, Chairman Emeritus of the Diversified Agency Services (“DAS”) division of Omicron Group Inc. (NYSE:OMC). Previous Chairman and Chief Executive Officer of Omicron Group Inc.
- **Carl Sailer**, VP Global Account Lead for Syneos Health (Nasdaq:SYNH). Previous VP of Sales and Marketing for Emisphere Technologies
- **Joseph C. Scodari**, Chairman of the Board of Directors of Optinose (Nasdaq:OPTN). Previous Worldwide Chairman, Pharmaceuticals Group, of Johnson & Johnson, and member of Executive Committee

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