at a glance™

Key Takeaways: ***A Phase 2a trial of Acurx's lead antibiotic candidate was stopped early for success after 10 of 10 patients with clostridium difficile (C. diff) infection were clinically cured within 2 days of end of treatment and, importantly, had no recurrence at the 28-Day follow-up visit, outperforming the current standard of care (vancomycin) in both measures based on historical data. A Phase 2b trial is currently under way and could have a similar outcome, analysts say, with topline results potentially available in 2Q23. Analysts put the addressable market at $1+ billion.***

Key Considerations

- **Acurx is developing a portfolio of first-in-class antibiotics to treat major, life-threatening bacterial infections that lack adequate treatment options.**
- **Its lead candidate, ibezapolstat, is being developed as a potential first-line treatment for C. diff, a transmissible, life-threatening infection suffered by roughly 600,000 people in the US.**
- **An open-label Phase 2a trial completed in 2020 was stopped for success halfway through on the recommendation of the Scientific Advisory Board after 100 percent of the first 10 (of 20) patients were clinically cured of C. diff with no recurrence of infection within the 28-day period after the end of treatment.**
- **The results stand in positive contrast to vancomycin's average clinical cure rate of 80 percent, and a 30 percent recurrence within 28 days after treatment, confirming vancomycin's undesirable impact on the microbiome.**
- **Ibezapolstat is currently being studied in a Phase 2b double-blind, active-controlled trial. It was initiated in December 2021 with a target enrollment of 64 C. diff patients with mild to moderate disease.**
- **The goal is to establish noninferiority to vancomycin (vanco) in timed measures of clinical cure and infection recurrence with exploratory endpoints for superiority over oral vancomycin.**
- **The company recently activated eight additional clinical sites, bringing the total number currently to 28 (all in the US).**

Acurx Pharmaceuticals, Inc.
(Nasdaq: ACXP)

52-Wk Range:	**$2.33-4.85**
Recent Price:	**$3.49**
Shares O/S:	**11.6 Million**
Approx. Mkt Cap:	**$40.5 Million**
Fiscal Year Ends:	**Dec. 31**

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- **Acurx's ibezapolstat has been accorded Fast Track designation by the FDA and has been registered as a Qualified Infectious Disease Product (QIDP) by the FDA under the Generating Antibiotic Incentives Now (GAIN) Act.**
- **The Gain Act incentivizes the development of novel antibiotics for treating serious and life-threatening infections, and provides for priority review to shorten the approval process and a 5-year market exclusivity period.**
- **The company's pipeline includes several programs to develop other novel, first-in-class antibiotics, including one aimed at infections caused by MRSA.**

Overview

C. diff is a transmissible gram-positive bacterial infection of the colon.

It is caused when the gut's good bacteria, weakened by disease or off-target drugs, are overtaken by bad bacteria, allowing C. diff to colonize in the colon.

Symptoms associated with it include cramping and tenderness, watery diarrhea, and in more severe cases, rapid heartbeat and kidney failure, among other conditions.

According to the CDC, C. diff afflicts approximately 600,000 people annually in the US and causes about 55 deaths per day, or 20,000 yearly. Its cost to the US health care system is put at $4.5 billion annually.

Analysts predict the current $1.2 billion market for C. diff treatments will grow to $1.7 billion in the next three years, due to the continuing use of broad-spectrum antibiotics and the aging of the population. A 20 percent slice of the market in 2026 would equate to roughly $350 million in revenue; half the market would be worth $850 million.

The current go-to drug for treatment is 65-year-old vancomycin, the standard of care for C. diff and several other serious pathogenic infections. It is considered safe and efficacious, but over the years its effectiveness, like that of many broad-spectrum antibiotics, has been waning, especially when it comes to preventing recurrent C. diff.

Anticipated Milestones

Ph 2b C. diff

-1Q23- Complete enrollment
-2Q23- Topline results
-3Q23- Final results

Ph 3 C. diff

-4Q23- Protocol design

ACX-375C

-2H23- File for QIDP
-2H24- File for Fast Track

That's because C. diff and other bad bacteria have learned to outsmart or become resistant to old drugs like vanco, and also because the older drugs lack specificity, and often kill good bacteria as they are trying to kill bad bacteria.

A healthy gut has both good and bad bacteria, with the good usually keeping the

C. diff Scorecard

Acurx

Status	Product	*C. difficile Infection* – mITT population		
		Percent		
		Initial Cure	Sustained Cure	Recurrence*
Marketed (Ph3 Results US/CAN)[1]	vancomycin (n-309)	86	61	25
	fidaxomicin (n=287)	88	73	15
In Development (Ph2 Results)[2]	vancomycin (n=33)	70	42	39
	ridinilazole (n=36)	78	67	14
In Development (Ph3 Results)**	vancomycin (n=375)	92	71	17
	ridinilazole (n= 370)	87	73	8
In Development (Ph2a ITT results)[3]	Ibezapolstat (n=10) (Acurx)	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] Ibezapolstat Phase 2a, CID 2022;
*Calculated percent of patients with Initial Cure who experienced recurrence **IDWeek2022

bad in reasonable check. The elimination of beneficial bacteria allows bad bacteria to bloom more aggressively, creating ideal conditions for the onset of many diseases, some fatal.

Acurx's orally dosed ibezapolstat, on the other hand, is so targeted to C. diff that even in systemic circulation it doesn't affect the beneficial bacteria in the microbiome, reserving its payload only for colonized C. diff in the colon

This specificity was documented in Phase 1 clinical findings that showed ibezapolstat improves the healthiness of good bacteria in the gut, a second mechanistic feature that may be contributing to ibezapolstat's huge Phase 2a success in preventing recurrent C. diff.

Acrux's second lead compound is a novel, first-in-class antibiotic for MRSA, which could be eligible for substantial nondilutive funding under several NGO and government programs, including the anticipated Pasteur Act, which would reimburse for Phase 3 trial costs and guarantee the purchase of $750 million to $3 billion of product from the sponsor over 10 years for use in federal healthcare programs.

Defining Success in C. diff

Top-line results of the Phase 2a open-label trial were announced in November 2020 and showed that 10/10, or 100 percent, of the first 10 patients treated met the primary endpoint of clinical cure, defined as a resolution of diarrhea in the 24-hour period immediately before the end of the 10-day treatment period and for 48 hours after the end of treatment.

The secondary endpoint was also met: sustained clinical cure with no recurrence of infection at the 28-Day follow-up visit. One patient experienced treatment-related nausea, and no serious adverse events were reported.

Microbiome data from the trial showed that C. diff was eradicated by Day 3 of treatment on average, and growth of healthy gut bacteria occurred during treatment, suggesting that ibezapolstat targets pathogenic C. diff, and not healthy bacteria.

The Phase 2b trial currently underway is a double-blind, active-controlled study that calls for 32 patients to receive 450mgs of ibezapolstat twice daily and for 32 patients to receive 125mgs of vancomycin four-times daily, for a total of 10 consecutive days.

The goal is to establish noninferiority of ibezapolstat to vancomycin, defined as being considered equal to vancomycin in meeting both the primary endpoint (resolution of diarrhea in the 24-hour period immediately before the end of the 10-day treatment period and for 48 hours after the end of treatment), and the secondary endpoint (sustained clinical cure with no recurrence of infection at the 28-Day follow-up visit).

These are the same endpoints that were met by ibezapolstat with high success in the Phase 2a trial.

For the Phase 2b trial, Acrux included exploratory endpoints of recurrence rates at 60 and 90 days after treatment—measures that have not previously been included in any other clinical trial of C. diff.

The company is developing a protocol for a pivotal Phase 3 program for FDA review with the hope of launching the first of two required Phase 3 trials in early 2024, assuming a successful Phase 2b.

Pipeline Strategy

Acurx is developing a pipeline of antibiotics designed to block the replication of bacterial DNA by inhibiting a key enzyme, DNA polymerase IIIC, aka DNA Pol IIIC, which is vital to the replication process of prokaryotic cells, which includes bacterial cells. By inhibiting the enzyme, ibezapostat slows down DNA replication and eventually stops the bacterium's spread.

Acurx's C. diff candidate is the first to target DNA Pol IIIC for treating C. diff. Acurx believes DNA Pol IIIC blocking can be effective against other pathogens and is currently developing ACX-373C for other gram-positive infections, initially MRSA, which require systemic therapy.

Additional indications being explored in a computational chemistry program include vancomycin-resistant Enterococcus, penicillin-resistant Streptococcus pneumonia, septicemia, and acute bacterial skin and skin structure infections, or ABSSSI, a disease affecting more than three million in the US yearly, and for which vancomycin is the standard of care.

Summary

- **Acurx expects to report top-line results from a Phase 2b trial of its lead compound in C. diff in 2Q23 with the FDA's approval of an interim analysis.**
- **The earlier Phase 2a trial was stopped early for success after 100 percent of the first 10 patients treated achieved clinical cure and remained symptom free at the Day 28 visit, per protocol, which is better than historical cure data of vancomycin, the current standard of care, which has an average clinical cure rate of 80 percent, and a recurrence rate of 30 percent.**
- **Recurrence is the key cause of serious C. diff morbidity and C. diff mortality (approximately 55 deaths daily in the US), and the principal contributor to C. diff's roughly $4.5 billion annual cost to the US healthcare system.**
- **Ibezapolstat is fast-tracked at the FDA and has QIDP designation by FDA for priority review under the GAIN Act.**
- **Acurx is expanding its portfolio of anti-infectives with novel first-in-class technology designed for targeted treatment of life-threatening diseases - farthest along is a DNA Pol IIIC inhibitor for treating MRSA.**

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