

**ADIAL
PHARMACEUTICALS
RECEIVES THE 2023
TECHNOLOGY INNOVATION
LEADERSHIP AWARD**

*Identified as best in class in the North American
precision medicine for addiction disorders industry*

Best Practices Criteria for World-Class Performance

Frost & Sullivan applies a rigorous analytical process to evaluate multiple nominees for each award category before determining the final award recipient. The process involves a detailed evaluation of best practices criteria across two dimensions for each nominated company. Adial Pharmaceuticals excels in many of the criteria in the precision medicine for addiction disorders space.

AWARD CRITERIA	
<i>Technology Leverage</i>	<i>Business Impact</i>
Commitment to Innovation	Financial Performance
Commitment to Creativity	Customer Acquisition
Stage Gate Efficiency	Operational Efficiency
Commercialization Success	Growth Potential
Application Diversity	Human Capital

Challenges in Formulating Addiction-related Treatments

Alcohol use disorder (AUD) is a threat to the health of both the individual and society because it can result in the risk of developing heart disease, cancer, weakened immune system, and more and can result in loss of employment and family disruptions, which can disturb overall mental wellbeing.

Several drugs have been approved for alcohol addiction but require abstinence, wherein patients must give up alcohol before taking the drugs, which can be difficult to do. For patients who can abstain from drinking, maintaining this habit can be difficult, making the medication ineffective. Furthermore, some medicines cause side effects or are difficult to tolerate, and not all drugs are effective for everyone. Some drugs must be taken on an as-needed basis, leading to the lack of will to take the drug during the urge to consume alcohol.

Adial Pharmaceuticals is a biopharmaceutical company that develops drugs for addiction disorders. The company was established in 2010 based on the work of Dr. Johnson, who researched the genetic variations related to AUD. The companion genetic test and drug, therefore, can only treat patients with the target genotypes that are responsible for alcohol addiction. The drug can initially treat approximately 20% of alcohol addicts, which is a large market with an unmet need for precise treatment.

Adial Pharmaceuticals has limited competition in this space because few companies have developed precision medicine for general addictions. The use of a companion genetic diagnostic test is unique in the

market and has good potential to treat AUD, which can be fatal when left untreated or undiagnosed.

By using a novel mechanism of action, Adial Pharmaceuticals developed the lead candidate AD04 for AUD, blocking serotonin 3 receptors and thus reducing the release of dopamine, which in turn reduces the craving for alcohol. The drug is known to reduce alcohol cravings in heavy drinkers, with only a small dose of 0.33 mg/tablet of the active ingredient ondansetron, making it safe to take once or twice a day.

Currently, the company is trying to address this existing challenge in the treatment of AUD because it can identify the patient population that will benefit from the treatment and does not require abstinence from alcohol, making it more appealing to patients. The company's drug, however, must be taken every day and has a good safety profile.

Genetic Biomarker Test and Novel Mechanism of Action of the Drug Make It an Innovative Product in the Market

The AD04 drug blocks serotonin-3 receptors and is effective only if the patient has target genotypes, with the patient population identified through a unique genetic test. During the clinical trial conducted by the company, a panel for genetic markers was identified in early research up until phase three. Researchers investigated deeper into the specific genetic markers and found AD04 is effective for two of the markers: specific modulators of the serotonin 3 receptors A and B subunit genotypes. The drug works well for alcoholics who consume less than 10 drinks per day before enrollment. After combining the clinical trial

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***- Lonita Lawrence Lobo
Senior Research Analyst***

results of phases 2 and 3, the drug was validated to work well for the two specific genotypes and meets the US Food and Drug Administration's (FDA) prespecified, recommended, and confirmed end points of attaining and maintaining no heavy drinking days in the last two months of the six-month study period. The company, therefore, is pursuing a narrower label with those two primary genetic markers and is currently reviewing the data going forward with the next series of studies.

If a patient has those biomarkers, the drug will be effective and is considered precision medicine for AUD, which is rarely seen in drug development for

addiction disorders. The drug has been confirmed to be effective in a subgroup of patients who test positive for the genetic test, providing hope for patients who are undiagnosed and untreated because of a lack of confidence in such treatment efforts. The therapy, therefore, is innovative, unique, and effective in treating addiction disorders and thus provides Adial Pharmaceuticals with a competitive edge in the market.

The drugs available in the market to treat AUD are disulfiram and opioid antagonist. While disulfiram changes the metabolism of alcohol, opioid antagonist blocks the release of endorphins after drinking. Adial Pharmaceuticals, therefore, chose the mechanism of action for its drug because it differs from competing solutions, making it targeted and more innovative.

Reducing the Stigma of AUD to Position the Drug in a Challenging Market

One of the challenges in targeting an addiction-related issue is that many patients do not voluntarily agree that they have a drinking problem and are often unwilling to take medication. For such situations, Adial Pharmaceuticals has made it easier for physicians to identify patients that may benefit from treatment with AD04 and initiate the necessary conversations about taking the genetic test that could help them reduce their habit without abstinence. When learning that their drinking habit could be based on a genetic condition, patients are more likely to take the test rather than denying they have a problem. Their condition, therefore, is labeled as a treatable genetic-based disease instead of a personal weakness. In addition, the genetic test is affordable, and physicians can explain to patients that it is effective only in a subgroup of people suffering from alcohol addiction.

The concept of precision medicine in a condition such as alcohol addiction is unique because few pharmaceutical companies are developing a companion diagnostic and drug for a condition where patients could be in the denial phase and may reject therapy. Adial Pharmaceuticals has creatively developed a solution to bridge a huge market gap in addiction-related diseases.

Addiction-related Disorders Beyond AUD Are the Future Targets for Therapy

Adial Pharmaceuticals focuses on the development of medicines for addiction because of the mechanism of action of AD04 to treat opioid use disorder and obesity. Even though the label is not yet expanded, and the current focus is on developing the drug for AUD, the company might disclose more details of a genetic test for each of these conditions and the drug's future ability to treat different addiction-related disorders.

Financial Performance

Adial Pharmaceuticals is focusing completely on the late-stage development of its drug candidate AD04 for AUD. In May 2023, the company entered into an agreement to sell its subsidiary company, Purnovate, to a new company called Adenomed that was established by the CEO of Purnovate, who is the former CEO of Adial Pharmaceuticals. As per the terms of the agreement, Adial Pharmaceuticals will receive \$450,000 and approximately \$11 million for each compound development and approval milestone, meaning the company is eligible to gain \$33 million for the first three compounds that are potentially developed. The company will gain an additional \$50 million for commercial milestones achieved and will receive a royalty when the compounds generate sales. Moreover, Adial Pharmaceuticals has a 19.9% equity stake in Adenomed and has raised \$750,000 in gross proceeds in its most recently announced financing.

All of this cashflow will contribute to the funding necessary to concentrate on the continued late-stage development and approval of its leading drug candidate AD04.

Strategic Partnerships and Promising Pipeline of Collaborations to Bolster Adial Pharmaceuticals' Growth

AD04 is Adial Pharmaceuticals' first drug candidate, and the company is targeting a unique space that is rarely explored by pharma companies, including precision medicine for addiction-related disorders. The company will need to partner with diagnostic providers to conduct the simple polymerase chain reaction

(PCR) blood test that will identify the patients who can benefit from the drug.

The company is in talks with health insurers in the United States to gauge the chance of AD04 and the genetic biomarker test of getting reimbursed and has received positive feedback on reimbursement possibilities because the biomarker test ensures efficacy. The company, therefore, has a good feeling about the access and adoption of the drug in the market.

Patents are issued in the United States and the European Union (EU), where the drug is going to be marketed post-launch and with the company maintaining exclusive license rights. The company,

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therefore, is preparing to launch its drug by 2026 or later, depending on the changes in studies discussed based on the results of the phase 3 trial. Assuming approval, the drug will be marketed in the United States and Europe.

Adial Pharmaceuticals has been partnering with Catalent since 2019 for the progress of AD04 clinical activities. In addition, the company partners with Tedor Pharma, a contract development and manufacturing organization (CDMO) company, which

will provide Current Good Manufacturing Practice (CGMP) services for the drug. The Keswick Group helps Adial Pharmaceuticals engage, manage, and develop strategic partnerships that will help the launch of the drug in large markets in a cost-effective way within appropriate timelines. Partnerships to advance the drug in clinical trials and manufacturing and to foster more strategic partnerships with other companies will help Adial Pharmaceuticals propel the success of its drug.

Once the drug is ready to be commercialized, the company’s strategy is to penetrate the market based on recommendations from general practitioners to their patients and will then gradually become a direct-to-consumer product provider in the United States and expand its presence to other countries. The company intends to forge partnerships with companies that have a commercial presence and with psychiatrists and addiction specialists.

Targeted Treatment for a Subtype of AUD Patients Has Good Potential for Growth

As previously mentioned, Adial Pharmaceuticals’ drug will be effective in approximately 20% of AUD patients; however, this percentage is a large population in the United States and in the EU, paving the way for huge market potential for the drug. The drug may become a direct-to-consumer treatment because it has a good safety profile, which will encourage more alcoholics to take the test and use the drug. The company will likely expand its presence beyond the United States and the EU at a later stage, enabling it to gain higher revenue potential.

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Some of the drugs for alcoholism are Disulfiram, Naltrexone, and Campral, but none of these can target a

specific population in AUD similar to the drug AD04, thus creating no direct competition. One competitive threat for the company is the repurposing of approved drugs for addiction disorders. The AD04 drug faced a few issues in the phase 3 trial because it did not meet its primary clinical endpoint of reducing alcohol addiction in very heavy and heavy drinkers combined; however, the company had encouraging evidence that it can reduce drinking in heavy drinkers, which is a significant amount of the population and a specific target group, making it a precise drug for AUD, which is not the case in any competing drug.

The company is looking for more strategic partnerships in the future to expand the reach of its drug because it is nearing the time for approval. In 2021, Purnovate (the former subsidiary of Adial Pharmaceuticals) signed a research collaboration with the University of Virginia to develop next-generation adenosine compounds for wound healing. The company has the potential to engage in research collaboration with universities and demonstrates a potential to be involved in more research and drug development in the space of addiction disorders, paving the way for more growth opportunities for the company.

Conclusion

Adial Pharmaceuticals has developed a precision therapy for alcohol addiction and, along with its genetic test, offers a personalized approach to address unmet clinical needs. The company has positioned its drug to address a treatable genetic disease rather than a personal weakness, thus meeting the challenge of patients' unwillingness to undergo treatment. Moreover, the safety profile of the drug makes it appealing to patients. The company is well positioned in the industry, in terms of obtaining regulatory approvals, and is in initial conversations with stakeholders, such as payers and physicians, for drug adoption. Adial Pharmaceuticals is looking forward to making strategic partnerships that will boost its overall growth.

For its strong overall performance, Adial Pharmaceuticals is recognized with Frost & Sullivan's 2023 North American Technology Innovation Leadership Award in the precision medicine for addiction disorders industry.

What You Need to Know about the Technology Innovation Leadership Recognition

Frost & Sullivan's Technology Innovation Leadership Award recognizes the company that has introduced the best underlying technology for achieving remarkable product and customer success while driving future business value.

Best Practices Award Analysis

For the Technology Innovation Leadership Award, Frost & Sullivan analysts independently evaluated the criteria listed below.

Technology Leverage

Commitment to Innovation: Continuous emerging technology adoption and creation enables new product development and enhances product performance.

Commitment to Creativity: Company leverages technology advancements to push the limits of form and function in the pursuit of white space innovation.

Stage Gate Efficiency: Technology adoption enhances the stage gate process for launching new products and solutions.

Commercialization Success: Company displays a proven track record of taking new technologies to market with a high success rate.

Application Diversity: Company develops and/or integrates technology that serves multiple applications and multiple environments.

Business Impact

Financial Performance: Strong overall financial performance is achieved in terms of revenues, revenue growth, operating margin, and other key financial metrics.

Customer Acquisition: Customer-facing processes support efficient and consistent new customer acquisition while enhancing customer retention.

Operational Efficiency: Company staff performs assigned tasks productively, quickly, and to a high-quality standard.

Growth Potential: Growth is fostered by a strong customer focus that strengthens the brand and reinforces customer loyalty.

Human Capital: Commitment to quality and to customers characterize the company culture, which in turn enhances employee morale and retention.

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Key Impacts:

- **Growth Pipeline:** Continuous Flow of Growth Opportunities
- **Growth Strategies:** Proven Best Practices
- **Innovation Culture:** Optimized Customer Experience
- **ROI & Margin:** Implementation Excellence
- **Transformational Growth:** Industry Leadership



The Innovation Generator™

Our 6 analytical perspectives are crucial in capturing the broadest range of innovative growth opportunities, most of which occur at the points of these perspectives.

Analytical Perspectives:

- **Mega Trend (MT)**
- **Business Model (BM)**
- **Technology (TE)**
- **Industries (IN)**
- **Customer (CU)**
- **Geographies (GE)**



