

# Medicines for Addiction

Investor Presentation  
January 2025



## Forward Looking Statements

This presentation includes statements that are, or may be deemed, “forward-looking statements.” In some cases, these forward-looking statements can be identified by the use of forward-looking terminology, including the terms “believes,” “might,” “estimates,” “approximately,” “expects,” “anticipates,” “intends,” “estimates,” “plans,” “seeks,” “may,” “should,” “could,” “would,” “will,” “future,” “likely,” “goal,” “continue,” “appears,” “suggests,” “ongoing,” or, in each case, their negative or other variations thereon or comparable terminology, although not all forward-looking statements contain these words. Forward looking statements appear in a number of places throughout this presentation and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned discovery and development of drugs targeting alcohol addiction, the strength and breadth of our intellectual property, our planned clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for our product candidates, our ability to partner our product development, the degree of clinical utility of our products, particularly in specific patient populations, expectations regarding clinical trial data, our results of operations, financial condition, liquidity, prospects, growth and strategies, the length of time that we will be able to continue to fund our operating expenses and capital expenditures, our expected financing needs and sources of financing, the industry in which we operate and the trends that may affect the industry or us.

By their nature, forward-looking statements involve risks and uncertainties because they relate to events, competitive dynamics, and healthcare, regulatory and scientific developments and depend on the economic circumstances that may or may not occur in the future or may occur on longer or shorter timelines than anticipated. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this presentation. In addition, even if our results of operations, financial condition and liquidity, and the development of the industry in which we operate are consistent with the forward-looking statements contained in this presentation, they may not be predictive of results or developments in future periods. Any forward-looking statements that we make in this presentation speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation, except as required by law.

You should read carefully our “Cautionary Note Regarding Forward-Looking Statements” and the factors described in the “Risk Factors” sections of our Annual Report on Form 10-K for the year ended December 31, 2023, and any subsequent reports that have been filed with the Securities and Exchange Commission (the “SEC”) to better understand the risks and uncertainties inherent in our business.

# Vision

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Adial is a clinical-stage biopharmaceutical company focused on the treatment and prevention of addictions and other unmet medical needs.



# Alcohol Use Disorder is a Major Public Health Problem in the U.S.

Failure to help people with AUD is a major health, social and financial problem



In the U.S. alone, an estimated **30 MILLION** people **SUFFER FROM AUD**, resulting in significant health, social and financial costs

## Excessive Alcohol Use:

- Leading risk factor for death ages 15–49 (Globally)
- 31% of driving fatalities due to alcohol use
- Contributes to over 200 different diseases
- Costs U.S. economy approximately \$250 billion annually
- 50% increase in prevalence from 2002 to 2013

***Despite these enormous costs, just over 7% seek help, but less than 5% AUD cases are treated by a health care practitioner***

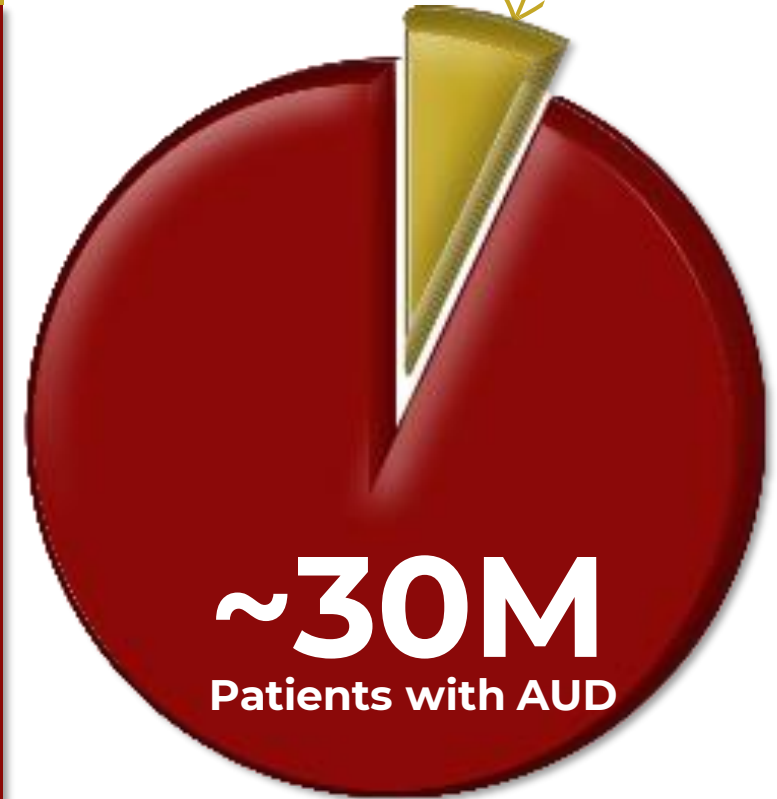
Sources: SAMHSA, Center for Behavioral Health Statistics and Quality. 2021 National Survey on Drug Use and Health. Tables [5.6A](#) & [5.6B](#).

Sources: NIAAA Alcohol Facts & Statistics. [www.cdc.gov/features/costsofdrinking/index.html](http://www.cdc.gov/features/costsofdrinking/index.html) accessed Sep. 10. 2017. NIH study finds alcohol use disorder on the increase, June 3, 2015.

# Significant Segment of Market Not Being Addressed in U.S.



~2.6M patients seeking treatment AUD



***Due to limitations of existing therapies, over 95% of people with AUD do not receive medical treatment***

- The **vast majority** of patients that have AUD remain *undiagnosed* and *untreated*, creating a large market opportunity for a product that can address patient needs
- AUD is a potentially **multi-billion dollar** market with limited competition & unmet need. Excessive Alcohol Use accounts for ~5.3% of deaths worldwide and ~5.1% of disease worldwide
- The Lancet reports that alcohol is the **number one risk factor for death** globally among both men and women ages 15 to 49 years

Sources: SAMHSA, Center for Behavioral Health Statistics and Quality. 2022 National Survey on Drug Use and Health. Tables [5.9A](#).

Sources: NIAAA Alcohol Facts & Statistics. [www.cdc.gov/features/costsofdrinking/index.html](http://www.cdc.gov/features/costsofdrinking/index.html) accessed June 3, 2020. The Lancet Sep. 2018., WHO Fact Sheets [www.who.int/news-room/fact-sheets/detail/alcohol](http://www.who.int/news-room/fact-sheets/detail/alcohol)

# Current Market Solutions are Failing



Current therapeutic approaches are significant barriers to patient adoption

## Abstinence Barrier

Abstinence is often the only goal, and **current therapies require abstinence prior** to initiating therapy

- Causes a **mismatch between problem and solution**
- Abstinence requires dramatic changes and often **serious work and social consequences**

## Efficacy Barrier

Data show that **current therapeutic solutions are ineffective**

- **90% of patients do not achieve long-term abstinence**
- **AUD largely goes untreated** ... fears of stigmatization and beliefs that treatment is ineffective may explain the lack of AUD treatment in the U.S.

## Side Effect Barrier

Significant side effects of current therapies

- **Mental**—Nausea, dizziness, psychiatric disorders and depressive symptoms
- **Physical**—Vomiting, abdominal pain, arthritis and joint stiffness

## Ease of Use & Stigmatization Barriers

Patients face extreme solutions

- Require significant lifestyle changes
  - e.g., **Abstinence**
  - e.g., Vivitrol is **injectable by physician**
- Need to avoid friends, family and social events
- Social & professional damage for admitting problem

Sources: JAMA Psychiatry, Epidemiology of DSM-5 AUD, 2015. Dodes, et. al., The Sober Truth: Debunking the Bad Science Behind 12-Step Programs and the Rehab Industry, 2014

# Patients are Not Satisfied with Current Options



Adial's market research indicates that patients are not satisfied with current options

## They Do Not Want

- Side effects
- Painful injections
- Public humiliation by admission of problem
- Numerous visits to a doctor or other therapies
- Self help group sessions

## They Want Their Life Improved

- Stick to their drinking plan
- Not fight with friends and family
- Not embarrass themselves
- Not feel bad the next day
- Not miss work and other events in their life
- Avoid other negative consequences (e.g., auto accidents, relationship or financial problems, job loss, etc.)
- Reduce the monetary costs
- Attend events where there is alcohol

***Patients want to live their current life but with control and dignity; they do not want a life make-over.***

# AD04 is Designed to Meet the Market Need



## Management of Heavy Drinking

### New Mechanism Action: Treatment of Alcohol Use Disorder (AUD)

## AD04 Effectively Curbs Alcohol Intake by Reducing Craving

#### **AD04 is a Near Micro-Dose (0.33 mg/tablet) Formulation of Ondansetron.**

Ondansetron (brand name: Zofran), widely used for nausea since 1991, is well-characterized, has a good safety profile at high doses (from 4 mg oral to 16 mg i.v.). AD04 is a genetically targeted precision medication intended to reduce drinking in patients with specific genotypes.

**Clinical Trial Results and Post-Hoc Analysis Demonstrated that AD04 Reduces Craving in Heavy Drinkers.** AD04 reduced heavy drinking days (HDDs) by 86% among heavy drinkers<sup>1</sup> and eliminated HDDs in 48% of subjects who possessed the AG+ genotype.<sup>2</sup> These results are thought to be due to AD04's suppression of the craving and pleasure derived from alcohol by affecting the 5HT3 system (serotonin signaling and dopamine release).

**Parallels Can be Drawn Between Semaglutide and AD04 Mechanisms of Action.** There has been significant adoption of Semaglutide for weight loss, which interacts with the parts of the brain that suppress appetite. Interestingly, Semaglutide and AD04 share a feature in common, which may promote a better understanding of AD04's Mechanism of Action on drinking, as they both impact parts of the brain that curb craving.



# AD04 is Designed to Meet the Market Need



## Management of Heavy Drinking

***A new approach for patients who desire to control drinking but cannot or will not undertake existing treatment options.***

### **Good Safety Profile, High Tolerability**

Brings 20+ year record of acute clinical use with positive safety and tolerability profile

### **Oral Daily Dosing (twice-a-day now, once-a-day expected)**

Patient compliance, ease of use & increased effect

### **Reduction of Heavy Drinking Target Indication**

Ends need for abstinence, a major hurdle in starting & continuing pharmacologic therapy

### **Lowers the Stigma of AUD and Empowers the Patient**

Takes treatment from detox clinics & group therapy -  
- realizes patients' desire of reduced drinking

### **Genetic Tests for Precision Medicine**

Genetic biomarker test identifies the patients likely to benefit from AD04

# AD04/Ondansetron



Well-Characterized, Widely Used

## Limited Threat of Off-Label Use

- **Lack of Efficacy** – Efficacy not seen at Zofran doses in clinical testing for AUD
- **Safety Concerns** – Warning for cardiovascular side effects at higher doses

## Phase 2b Trial of AD04 in AUD Completed

- Trial met primary and secondary endpoints

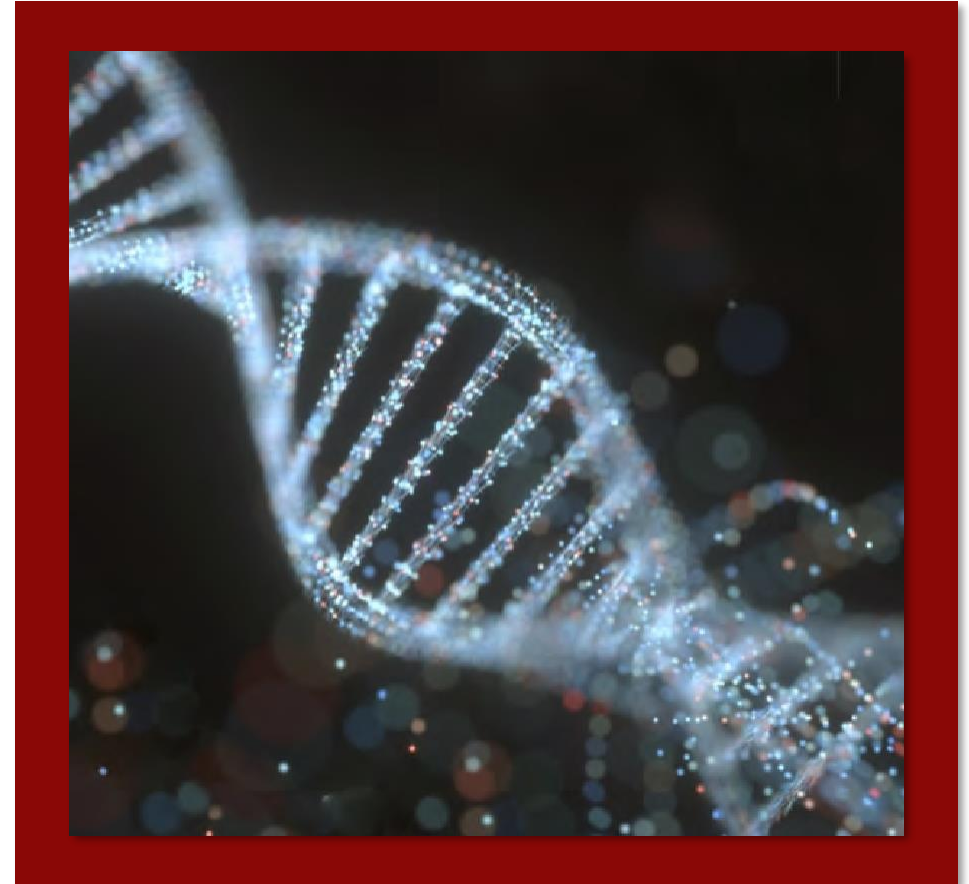
## ONWARD Phase 3 Trial of AD04 in AUD Completed

- 302-patient randomized double-blind, placebo-controlled study
- Limited side effects observed
- Missed Primary endpoint for overall patient population
- Pre-specified patient sub-groups responded extraordinarily well to AD04

# Genetic Test Expected to Drive Market Uptake

## Precision Medicine Enables:

- Physician conversation with patient
- First step of a test vs. a drug
- Patient buy-in to treatment after positive test
- Potential of increased compliance resulting in effective therapeutic



***The genetic test is expected to increase prescription fill rate and compliance.***

# AD04 Expected Unique Profile Compared to Currently Approved Products



Key anticipated unique selling points drive AD04 differentiation – expected to meet patient needs

	ADO4*	EU only Selincro**	Vivitrol	Campral	Revia	Antabuse
Novel Mechanism of Action	✓	✗	✗	✗	✗	✗
Oral Dosing	✓	✓	✗	✓	✓	✓
Designed to reduce Heavy Drinking	✓	✓	✓	✗	✗	✗
No Abstinence Requirement	✓	✓	✗	✗	✗	✗
Genetic Targeting	✓	✗	✗	✗	✗	✗

***AD04 addresses key unmet medical needs in AUD market.***

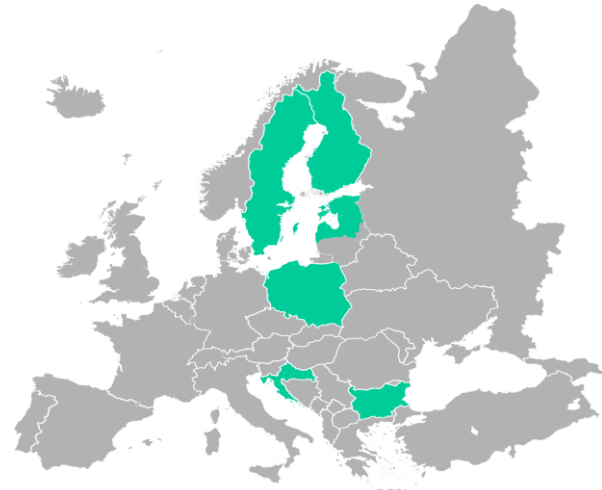
\*AD04 is not yet approved for marketing and product characteristics shown as those expected based on currently available data and current plans. In all cases, the characteristics shown are fully qualified based on future data and regulatory approval.

\*\* Taken as needed; all others are on a time regiment of at least daily or are a monthly injection (i.e., Vivitrol)..

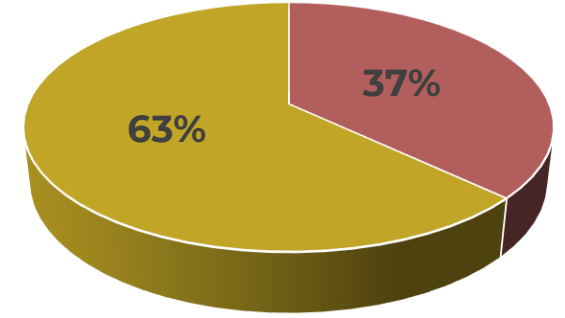
# ONWARD Phase 3 Study Conducted in Europe

## Trial Design

- Randomized, double-blind, placebo-controlled, parallel-group multicenter study
- Patients were screened for the appropriate genotypes via an inexpensive, standard blood test to determine eligibility for treatment with AD04
- **Primary End Point: PHDD change from baseline (months 5 & 6)**
- **Eligibility Criteria (n=302)**
  - ≥6 HDDs in 4 weeks prior to Baseline Visit
  - ≥40g EtOH per day for males or ≥20g EtOH for females 4 weeks prior to Screening Visit
  - ≤14 consecutive abstinent days
  - DSM-V Moderate- or Severe- AUD
  - No withdrawal symptoms
  - No in nor out-patient treatment w/in 28 days prior to Baseline Visit



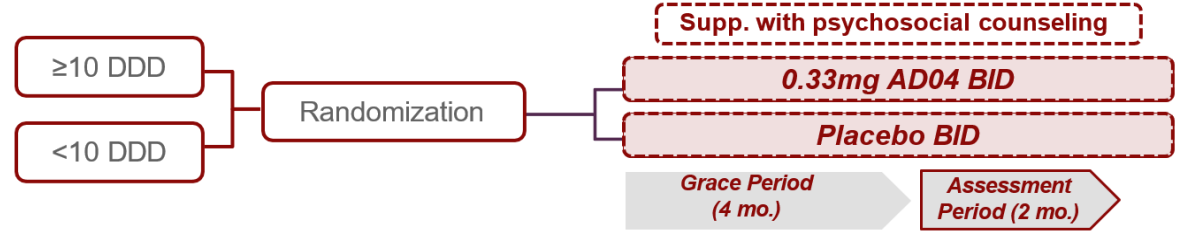
Conducted in **six countries** in Central/Eastern Europe



■ Very Heavy Drinker ■ Heavy Drinker

**Group 1:** Heavy drinker (< 10 drinks/drinking day): ~63% of Trial participants

**Group 2:** Very heavy drinker (> 10 drinks/drinking day): ~37% of Trial participants



Source: Company filings, presentations.  
 Note: DDD = Drinks per Drinking Day; HDD = Heavy Drinking Day; PHDD = Percentage of Heavy Drinking Days; EtOH = Alcohol. HDD is defined as >= 60g of EtOH for M and >=40g of EtOH for FM; ctrl = controlled.  
 (1) Adial ONWARD Phase 3 Trial results (publication pending).

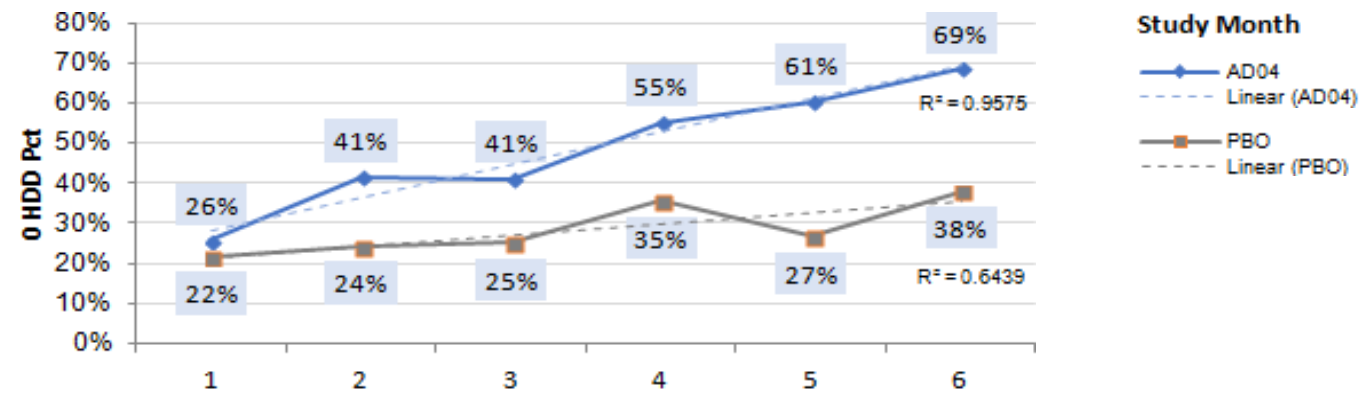
# Specific Patient Sub-Groups Responded Well Based on U.S. Endpoint



## Post Hoc Data Analysis Based on U.S. Endpoint

- **U.S. Primary End Point: Responder Analysis**, defined as the percentage of patients with 0 HDDs in the treatment arm versus placebo at a specific time point
- **AG+ subjects showed statistically significant separation from placebo (p=0.0210 in Months 5 & 6)**
- The percentage of 0 HDD patients in the treatment arm appears to increase linearly during the study period of 6 months
- Analysis of data from patients in **Group 1: Heavy drinker**

Responder Analysis<sup>(1)</sup> (AG+ <10DDD)



Post Hoc Analysis of U.S. Endpoint					
Genotype	DDD Category	Treatment Arm <sup>(2)</sup>	Placebo Arm	Total	Responder Analysis (U.S. Endpoint) <sup>(3)</sup> P-Value at Months 5&6
<b>AG+</b>	<10	37	<b>30</b>	<b>67</b>	<b>0.0210</b>
<b>LL+/TT+</b>	<10	29	29	58	0.619
<b>AC+</b>	<10	25	25	50	0.329
<b>GG+</b>	<10	12	12	24	0.116

Source: Company filings, presentations.  
 Note: DDD = Drinks per Drinking Day; HDD = Heavy Drinking Day; PHDD = Percentage of Heavy Drinking Days; EtOH = Alcohol. HDD is defined as >= 60g of EtOH for M and >=40g of EtOH for FM; ctrl = controlled.  
 (1) Responder analysis is defined as the percentage of patients with 0 HDDs in the treatment arm versus placebo at a specific time point.  
 (2) The U.S. responder analysis excludes individuals who did not have recorded measurements during the assessment period which in turn results in lower sample sizes for some genotypes.  
 (3) Adial analysis of Phase 3 Trial results.

# Pharmacokinetics Study for AD04



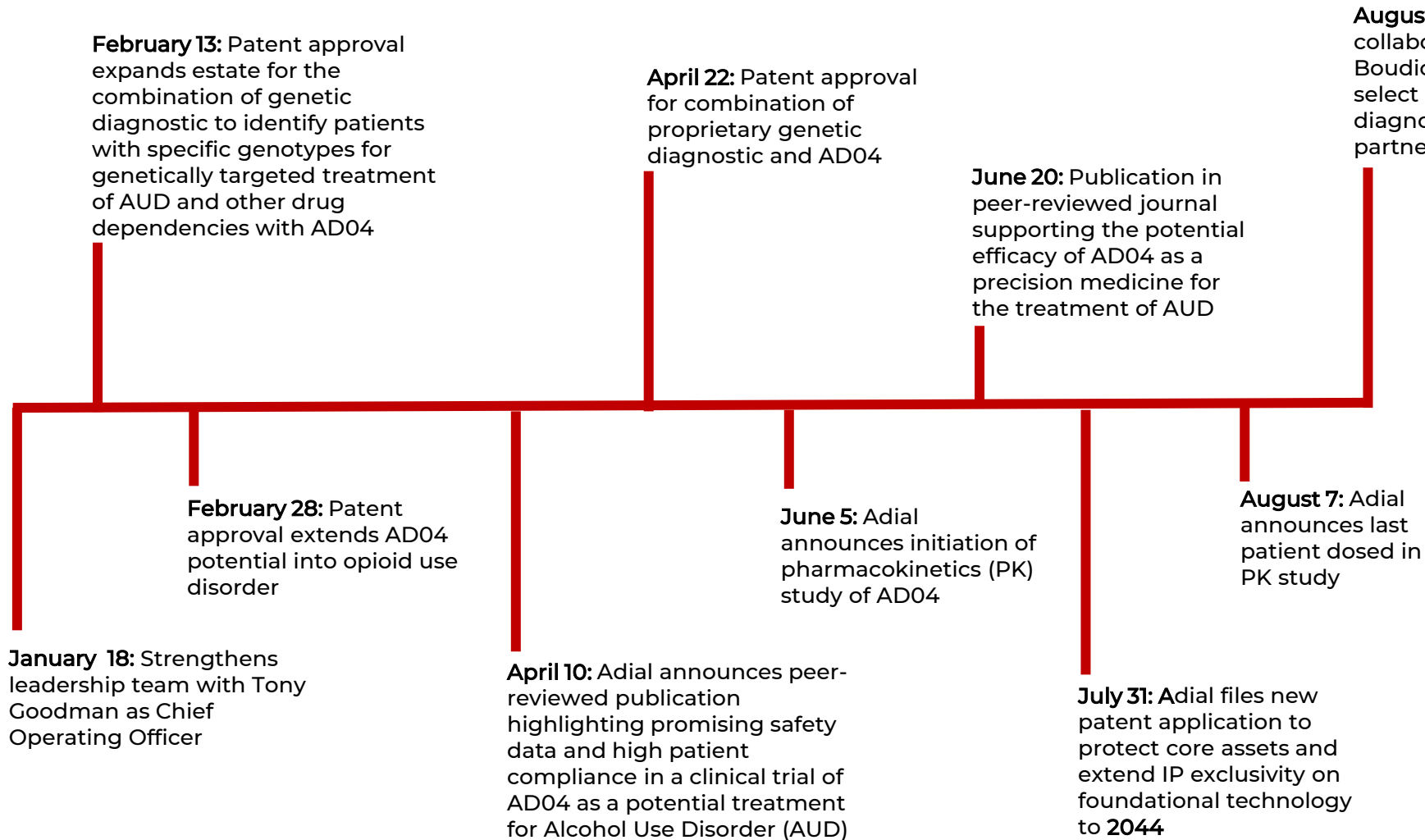
Objective defined by the FDA to design a precise and informed Phase 3 Trial

- Adial recently completed a **Pharmacokinetics Study**, a key component to progress AD04's clinical development as advised by the FDA.
- **Topline Results** indicate that AD04 displays proportional dose response pharmacokinetic properties and can be taken in fed or fasted states.
- The study evaluated:
  - Pharmacokinetic variability and dose proportionality between two doses of AD04 (0.33mg and 0.99mg)
  - Relative bioavailability of AD04 (0.33mg) compared to a marketed ondansetron tablet (4mg)
  - The effect of food on the bioavailability of AD04 (0.33mg)
- The study produced data which will help Adial **optimize study design elements needed for the upcoming Phase 3 Clinical Trial** of AD04.
- The study validates Adial's proprietary formulation of AD04 and the pharmacokinetic properties are being designed to meet FDA requirements.
- By completing this study, it fulfills a necessary component of Adial's partnering strategy.

# Significant Progress Made in 2024



## Laying the Groundwork to Advance AD04 to Phase 3



Completed \$8.6 million in total gross financings

Secured 4 patents issued/pending

Launched key PK Study



# Next Steps

Finalize plans to achieve potential commercial launch by 2027

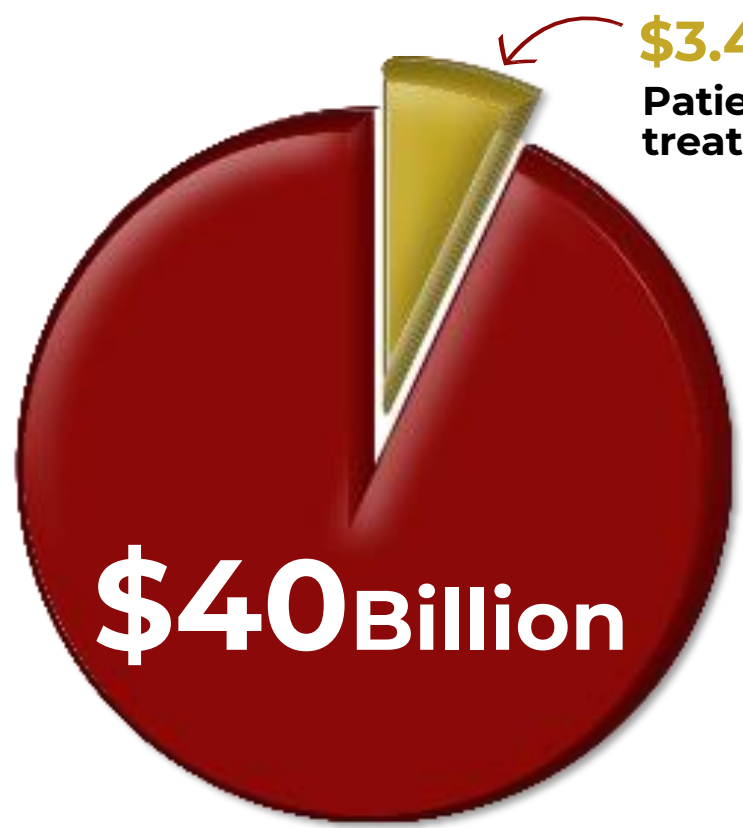
- **Complete Pharmacokinetics Study to Optimize Elements of Phase 3 Studies**
- **Finalize Clinical Development Plan**
  - Final decision on conducting one or two Trials
  - Finalize Trial design and Costs (current estimate \$8 - \$12 million per Trial pending final design and scope)
  - Timeline completion
- **Review Study Design, Protocol and Statistical Analysis Plan with FDA**
- **Advancing Discussions with Potential Strategic Partners:**
  - Phase 3 clinical program funding
  - Commercialization of AD04 assuming a successful regulatory outcome

# Target Market – Total Addressable Market (TAM) Potential



## U.S. Market

Assuming only 20% of patients are treatable with AD04, based on the genetic test, the total potential annual revenue for AD04 in the U.S. alone is **\$40 Billion<sup>1</sup>**



**\$3.4B**  
Patients seeking treatment for AUD

**Color Key:**

- AD04 Target Market**  
Patients with AUD & with AD04 Target Genetics
- Low Hanging Fruit**  
Patients seeking treatment for AUD & with AD04 Target Genetics

***A small percentage of the potential market would make AD04 a commercial success.***

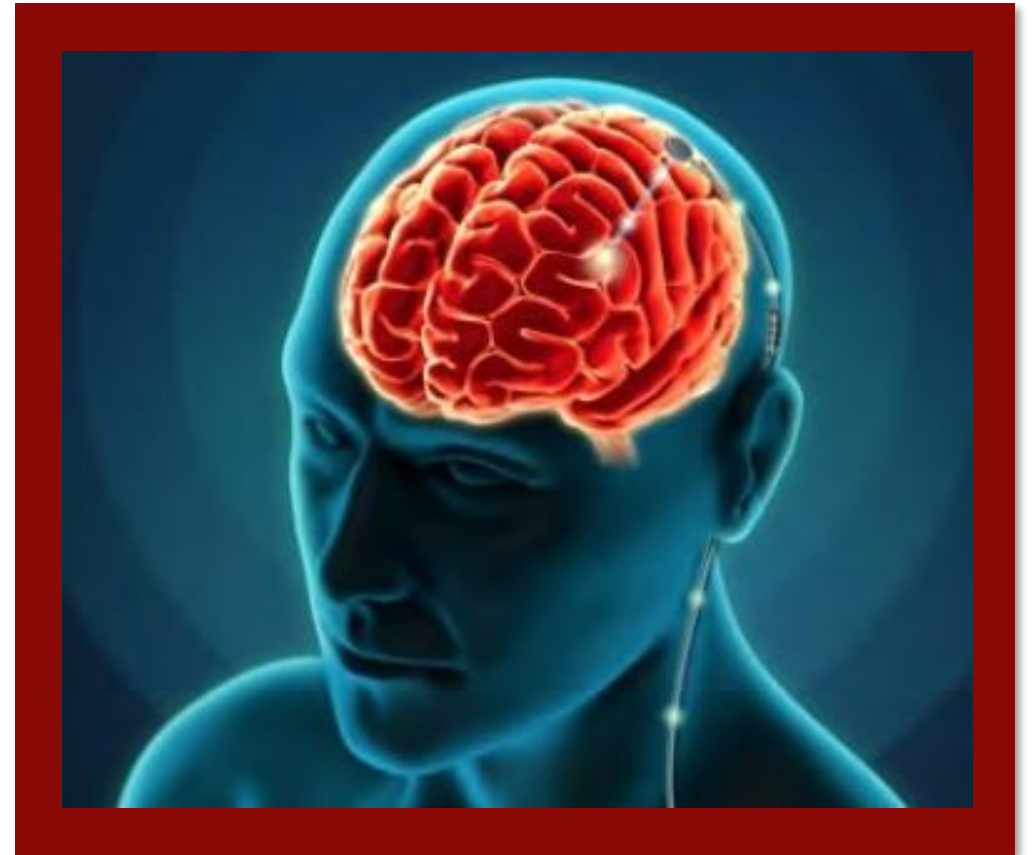
1. Note: Assumes 20% of patients genetically positive and treated; \$600 per month pricing  
ADIAL PHARMACEUTICALS INC. | MEDICINES FOR ADDICTION 20250108

## ✓ Lead Product for AUD

- Large market with unmet need
- Late-stage oral drug (Phase 3)
- Companion diagnostic designed to identify responders
- Seeking 505(B)(2) path to regulatory approval
- Low-cost manufacturing
- Licensed patent protection through 2031

## ✓ Potential Indication Expansion Opportunities for AD04 (opioid use disorder, obesity, others)

## ✓ Experienced and Qualified Management Team



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