



## Enabling Rapid Identification of Potential Treatments in Alzheimer's Disease

The Discover study is a clinical trial to test the safety, tolerability, pharmacodynamics and pharmacokinetics in people with Early AD

# Alzheimer's Disease (AD)

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- In 2017, Alzheimer's disease remains an irreversible, progressive, brain disease that slowly destroys memory and thinking skills.
- **AD is not part of normal aging.** It is caused by a disease that affects the brain.



# Quick Review: Treating AD

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No treatment has been proven to arrest, reverse or prevent Alzheimer's disease.

- Current treatments only affect the symptoms of the disease – they do not stop the progression of AD.
- No new drug has been approved for treatment of AD in more than a decade.
- About 99% of all Alzheimer's disease drug trials fail drugs fail in Alzheimer's disease drug trials.



# AD-Related Public Health Issues

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Once considered a rare disorder, AD is now a major public health problem and sixth leading cause of death in US.

- Demographics tell the story - Over 10,000 people a day turn 65 in the US.
- The prevalence of AD in the population will increase through 2050
- The national cost of caring for people with AD is expected to exponentially increase by hundreds of billions of dollars.



# Identifying AD in People

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There are currently two ways to know for certain whether or not a person has AD:

- Through a combination of advanced imaging (MRI and PET) and cognitive testing.
- By looking at a person's cerebral spinal fluid for hallmark AD proteins coupled with cognitive testing.



# The Hallmarks of AD

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THE BRAINS OF PEOPLE WITH AD HAVE TOO MUCH “BETA AMYLOID” PLAQUE



THE BRAINS OF PEOPLE WITH AD HAVE TOO MANY “TAU” TANGLES



# Problems in Recent Late Stage AD Trials

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- Potential AD therapies advance into late stage clinical research before we know whether they work or not.
- Researchers often make a decision to move forward with a potential drug therapy without knowing whether the drug hits its target (aka “target engagement”).

# Discover is a Phase 1 Clinical Trial

## Preclinical

Studies in test-tube or animals required before testing in humans

## Phase 1

First step in humans, small number of patients or normal controls, usually designed to find highest tolerated dose

## Phase 2

Tests safety and possible effectiveness in a moderate number of patients, usually insufficient in itself to prove medication's value

## Phase 3

Large scale trials designed to test safety and effectiveness of a new treatment  
- adequate for final approval

## Phase 4

Post-approval studies done to obtain additional safety information, promote clinical experience or for marketing purposes





# AD Clinical Research Needs to Accelerate

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- In comparison to the public health need; the current drug pipeline for AD is small.
- It takes more than a decade for a drug to get “from the bench to the bedside”.  
(i.e. from the research lab through FDA-approval).



# We Can't Keep Doing the Research the Same Way

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Many of the problems with recent trials may stem from a lack of information including:

- Early clinical research confirming that a drug successfully engages a target.
- Aim for clinically meaningful results.
- Early clinical research confirming how much of a drug to use.



# Changing the Approach to AD Clinical Research

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- Generate robust clinical data regarding target engagement.
- Aim for clinically meaningful results.
- Develop early evidence outside of the lab.



# Finding Answers Early in the Discover Study

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The Discover clinical trial project is designed to identify a rapid and effective way to determine whether:

- A drug is tolerated and safe in humans.
- A drug is getting through to the brain and the specific target.
- A drug should move advance in the research pipeline.



# About the Discover Study

The Discover Study is two month, Phase I, randomized, double blind, placebo-controlled, study of Posiphen for the treatment of people mild Alzheimer's disease or MCI.

- The Discover clinical trial is funded through a grant from the US National Institute on Aging (NIA)
- This study drug was developed by QR pharma – our pharmaceutical partner in Discover.
- Discover will recruit 24 participants at three U.S. sites



# What is a Randomized, Double Blind, Placebo-Controlled Study?

Randomized: Patients are assigned to treatment or inactive placebo by chance methods, like the flip of a coin

Double Blind: Neither the doctor nor the patient knows whether the patient is receiving the study medication

Placebo-controlled: An inactive substance given to study participants for comparison purposes



# The Discover Study Drug

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- Posiphen is being developed as a drug to delay or slow the progression of AD.
- Posiphen is a small, orally active, compound with a high blood brain barrier permeability.



# Discover Study Eligibility

- Men and women 55-85
- Diagnosis of mild cognitive impairment or mild Alzheimer's disease.
- Able to undergo an MRI scan, and a lumbar puncture (spinal tap).
- Willing to undertake a 36 hour stay at a hospital-based clinical research unit.





# Eligibility Criteria

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- Participants need to have a study partner who has contact with you an average of 10 hours/week or more
- Participants need to be in good health (other than AD).



# The Discover Study Schedule for Participants

- Participants take the study drug (or placebo) 3x per day for 21 days.
- The study will last for up to two months and requires at least five study visits.
- The study requires overnighting in a hospital-based setting.
- Requires CSF collection



# Why CSF in AD Research?

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- CSF reflects, in real time, what is happening in the brain because the brain is bathed in CSF and proteins move in and out of this fluid depending on what is happening in the brain.
- CSF is much more accurate than imaging.
- CSF provides the ability to succinctly measure the response to drug.

# Discover Goals

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The goals of the Discover Study include:

- Testing the safety and tolerability of Posiphen
- Measuring the amount of Posiphen in the cerebrospinal fluid (surrounding the brain and spinal cord), and
- Measuring Posiphen's effect on certain AD- related protein levels in the blood.

# What's Great About Discover?

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- Truly cutting edge research.
- Short duration clinical trial in AD

We are allowed to provide modest compensation for participation in Discover.

# Questions?

For more information, please contact:  
(Site name and contact info)