



COGNIGENICS

**New Approaches For
Treating Alzheimer's Symptoms
Business Summary**

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Goals

- Assist our aging population in maintaining mental acuity
 - Treat symptoms of Alzheimer’s Disease (AD)
 - Defend against cognitive decline
- Improve mental performance in age-related cognitive disorders
 - Attention, executive function, processing speed
- Slow the progression of cognitive impairment
 - Alleviate stress, mitigate depression, relieve anxiety

Research Objectives

- Relieve Alzheimer's symptoms
 - Lucidity, clarity, focus, mental acuity, attention, memory (short/intermediate)
- Produce a safe and effective treatment with no known side effects
- Achieve proof of principle quickly at minimum cost
- Use state-of-the art technology

Market

- Worldwide cost of Alzheimer's care projected to reach \$1 trillion by 2020 ¹
- Mitigating symptoms will reduce cost
- Symptomatic relievers are a large opportunity

¹ Alzheimer's Association (James Hendrix)

Prior Art

- Industry has focused on drug discovery for cure
- \$3.5 billion R&D spent in 4 years
- 99.6% failure rate

Source: Alzheimer's Association (James Hendrix)

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New Approach

- Target symptomatic relief
 - Much simpler than cure
- Modify neuron performance to enhance cognition
- Directly target neurons with CRISPR
- Edit RNA to reduce gene expression
 - No changes to genome

Symptom Relief Strategy

- 1) Reduce stress
 - Promote alpha frequency brainwaves
 - Induce relaxation
- 2) Sharpen mental acuity
 - Increase theta frequency brainwaves
 - Enhance mental clarity
- 3) Raise conscious attention
 - Lower brainwave activity
 - Expand available cognitive resources

Project Timetable

Phase	Title	Description	Schedule
Preclinical	In vitro experiments	Demonstrate the treatment's neuron-level mechanism of action by modifying neuron excitability and activity with CRISPR.	2019 / 2020
	In vivo experiments	Establish the therapy's efficacy in mammals by using behavioral tests for measuring cognitive ability in edited laboratory animals.	2020
Phase 1	Safety	Determine safety and dosage in 20-50 healthy adult volunteers for an RNA version of the therapy with temporary effects.	2021
Phase 2	Efficacy	Measure the RNA therapy's efficacy in relieving Alzheimer's symptoms in a group of several hundred patients.	2022
Phase 3	Efficacy and adverse reactions	Measure the RNA therapy's efficacy in relieving Alzheimer's symptoms in a group of 300 to 3000 patients.	2023

Proof-of-Principle Experiment

Goal	Demonstrate CRISPR can lower neuron excitability
Strategy	Administer specially-designed CRISPR to neurons <i>in vitro</i> and measure change in excitability
Tactics	Reduce a neuron's excitability by genetically raising its electrical resistance
Success Criteria	Edited neurons display lower activity than control group neurons
Cost	\$250 K
Schedule	6 months

Experiment Success

- Validates foundational science
- Supports ongoing project discussions with pharmaceutical companies
- Paves way for animal studies and human trials
- Stimulates financial community
- Raises company's value

Success Factors

- **Straightforward design**
 - Single point of contact in cells
- **No known side effects**
 - Precise CRISPR targeting to neurons
- **Low R&D costs**
 - No custom drug development
 - Use industry-standard editing tools
- **Design approach supported by neuroscience experiments**
- **Leverage global CRISPR R&D**

Human Benefits

- Improve quality of life for AD patients and their families
- Lower society's cost for elder care

Business Benefits

- Radically new kind of treatment method
- Hedge bets on cure
- Technology transferable to secondary markets
 - Mild cognitive impairment (MCI)
 - Neurological disorders
 - General purpose cognitive enhancement

Risks

1. Unforeseen problems in preclinical or clinical trials
2. Unproven application (RNA editing)
3. Unintended long-term consequences
4. New technology
5. Cure breakthrough obviates symptomatic relief

Conclusions

- Opportunity to improve millions of lives
 - Lower society's cost for elder care
- Innovative, unique approach
 - No known competition
- Patents pending
- Large market
- Potentially fast results and significant rewards with manageable risks

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