January 2021

Disease-modifying medicines for neurodegenerative disorders

COGNITION™ Therapeutics

The “New” Cognition: CNS Disease Expertise with Compelling Neurodegenerative and Neuro-Ophthalmology Opportunities

The science of σ-2 biology led us to first pursue Alzheimer's disease and now dry AMD/GA - indications with significant unmet need and large market potential. Other indications to follow

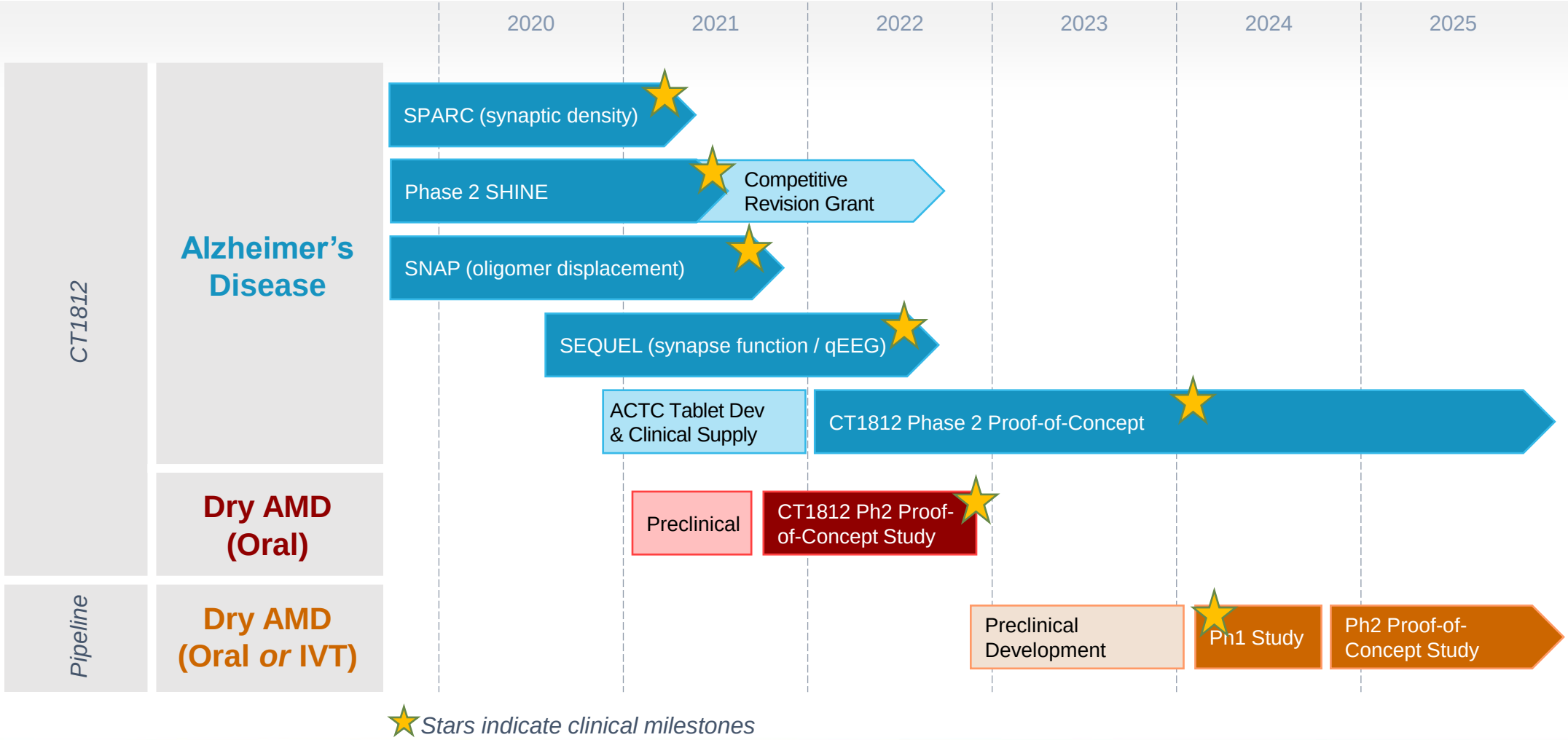
Neurodegenerative Diseases

- Alzheimer’s disease
- Parkinson’s disease
- Multiple system atrophy
- Huntington’s disease

Neuro-ophthalmic Diseases

- Dry age-related macular degeneration
- Geography atrophy

Pipeline:
Near-term Milestones

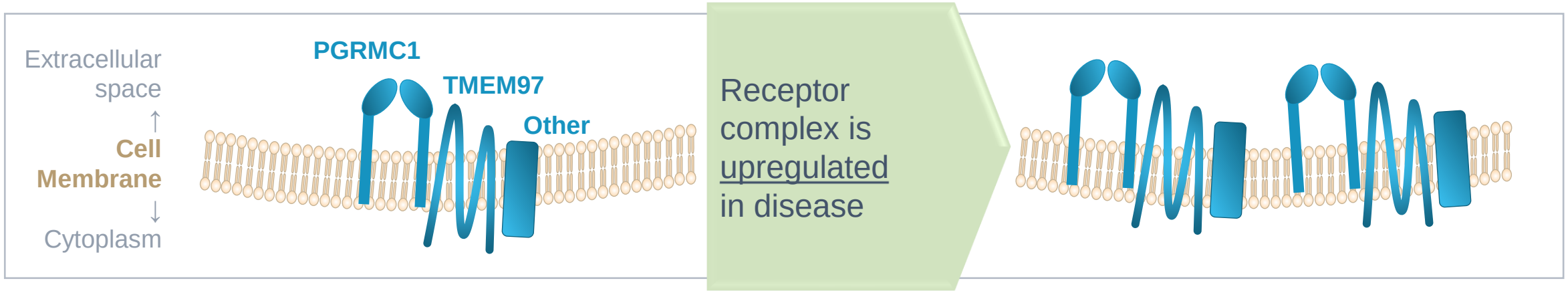


σ-2 Receptor Complex:
Cellular Damage Response Regulator

PGRMC1 is involved in vesicle trafficking, cell cycle regulation, autophagy

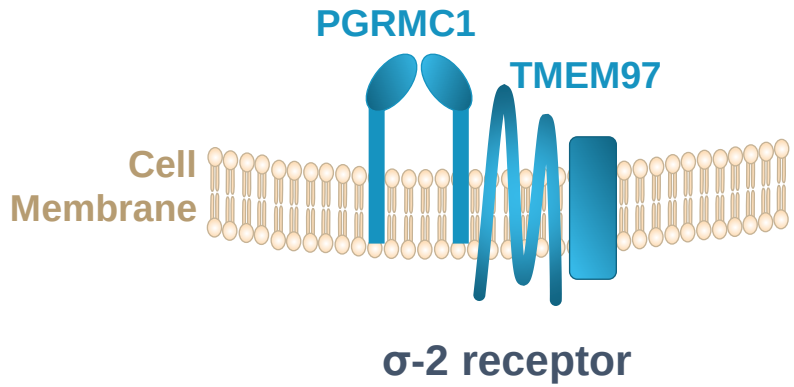
TMEM97 is involved in cholesterol transport

σ-2 receptor regulates cellular stress response



Cellular Damage Response Disrupted in Multiple Conditions

- PGRMC1 and TMEM97 (σ-2 proteins) regulate damage response processes:
  - Autophagy
  - Cholesterol synthesis
  - Lipid membrane-bound protein trafficking
- These pathways are impaired by the build-up of age-related stressors such as:
  - **Aβ oligomers** in Alzheimer's disease
  - **Protein aggregates, oxidative stress** and **inflammation** in dry AMD/GA
  - **α-synuclein oligomers** in Parkinson's disease, DLB and MSA
  - **Oxidative stress** and **inflammation** in ALS and other neurodegenerative diseases
- Cognition's candidates target PGRMC1 and TMEM97 proteins with aim to return pathways to normal function
- Expected to be synergistic with other therapies



Cognition Pipeline:
Preclinical & Clinical Data in Neurodegenerative Diseases

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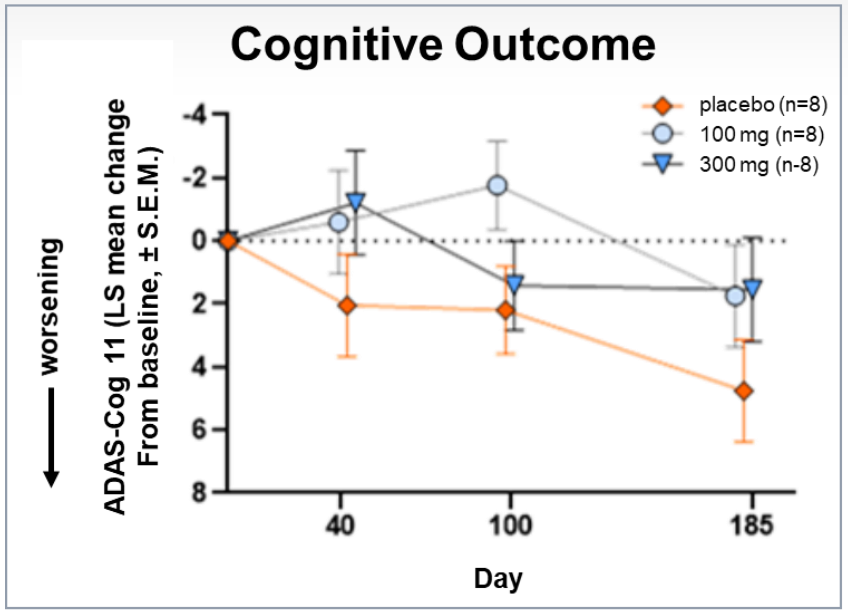
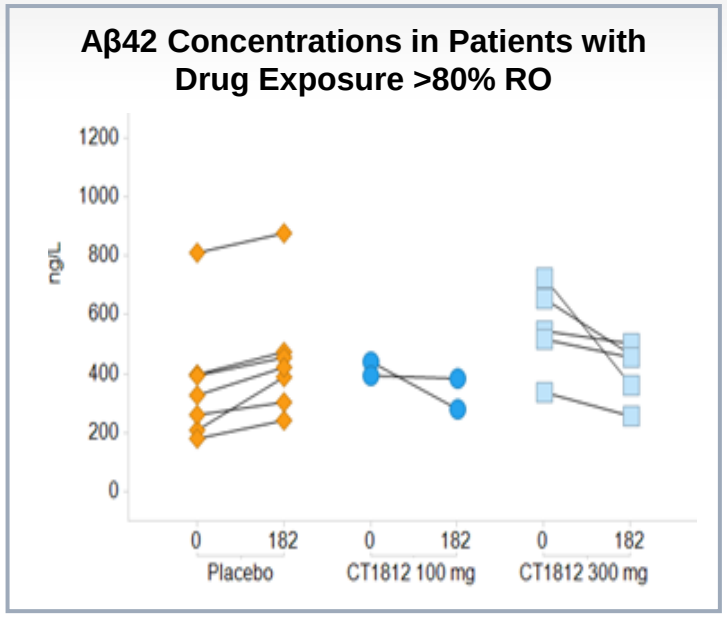
Alzheimer's Clinical Program
What We've Learned

Study	COG0101 SAD/MAD (n=74)	COG0102 (n = 19)	COG0103 DDI (n=15)	COG0104 SNAP (n=18)	COG0105 SPARC (n = 21)	COG0201 SHINE (n = 62)	COG0202 SEQUEL (n = 16)	COG0203 (n=540)
Indication	Healthy Volunteers	Mild-Moderate Alzheimer's	Healthy Volunteers	Mild-Moderate Alzheimer's	Mild-Moderate Alzheimer's	Mild-Moderate Alzheimer's	Mild-Moderate Alzheimer's	Early Alzheimer's
Phase	Phase 1	Phase 1b/2a	Phase 1	Phase 1	Phase 1	Phase 2	Phase 2	Phase 2
Objective	Safety & drug-food interaction	Safety & biomarker evidence of target engagement	Safety & drug-drug interaction	Aβ oligomers in CSF would be evidence of target engagement	Improvement in synapse numbers would be evidence of disease modification	Safety & biomarker evidence of disease modification	Changes in synapse function would be evidence of disease modification	Improvement in cognition
Status	Completed 2015	Completed 2018	Completed 2016	Ongoing	Ongoing	Cohort A Complete Cohort B Ongoing	Commencing enrollment in 2020	Funded / Enrollment Expected to commence in 2021
Results	Safe & well tolerated	Safe & well tolerated Evidence of target engagement	No clinically significant DDI	**Topline YE2021**	**Topline 1H2021**	SHINE A: trend for cognitive improvement **SHINE B: 1H 2021**	**Topline ~2H 2022**	**~2026**

Phase 2 SHINE Interim Analysis: Promising Evidence of CT1812 Impact on Cognitive and Biological Outcomes in First 24 pts





- Three-point difference (ADAS-COG) between treated and untreated patients at day 185
- Clinically meaningful magnitude of change
- Compares favorably with aducanumab results

- Statistically significantly lower Aβ protein (p=0.017) in treated versus placebo patients
- Additional therapeutic impact on p-tau, synaptic and AD-related proteins

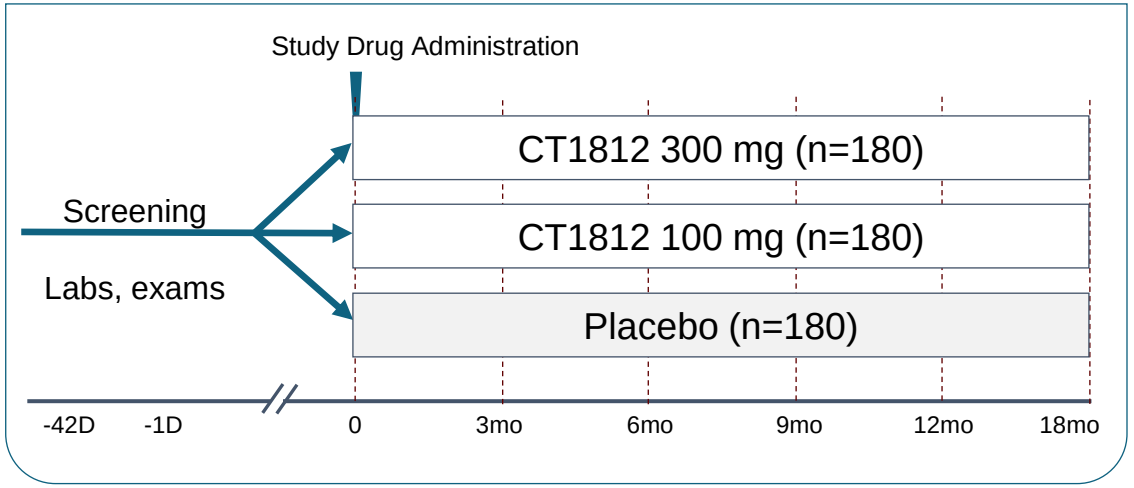
ACTC $80M Grant Drives Program Through Phase 2

- COG0203: Phase 2 efficacy study, powered to show change in cognition: slowing or halting cognitive decline
- Enrollment: 540 individuals with early Alzheimer's disease
- Conducted in collaboration with premier NIA-funded Alzheimer's clinical trial organization
- 35 U.S. sites with potential for expansion and acceleration

ACTC ALZHEIMER'S CLINICAL TRIALS CONSORTIUM

NIH NIA

Trial Schematic



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Cognition Study of A673T “Icelandic” Mutation Supports CT1812 MoA

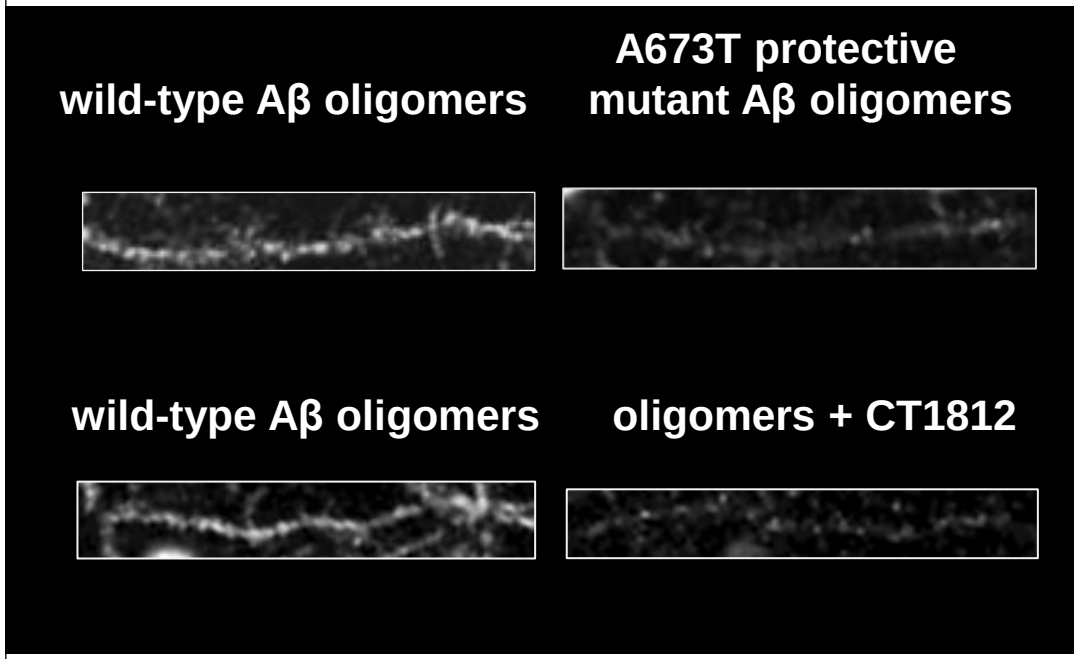
- Carriers of the A673T “Icelandic” mutation of the Aβ protein are 4 times less likely to get Alzheimer’s disease than non-carriers
- Cognition study demonstrates that mutant Aβ oligomers bind with 4-fold lower affinity to brain cell synapses than normal protein
- CT1812 is the only drug that mimics the effects of this protective mutation

Journal of Neurochemistry JNC The Official Journal of the International Society for Neurochemistry

Alzheimer’s Protection Effect of A673T Mutation May Be Driven by Lower Aβ Oligomer Binding Affinity*

Colleen S. Limegrover, Harry LeVine III, Nicholas J. Izzo, Raymond Yurko, Kelsie Mozzoni, Courtney Rehak, Kelsey Sadlek, Hank Safferstein, Susan M. Catalano

Journal of Neurochemistry. doi: https://doi:10.1111/jnc.15212



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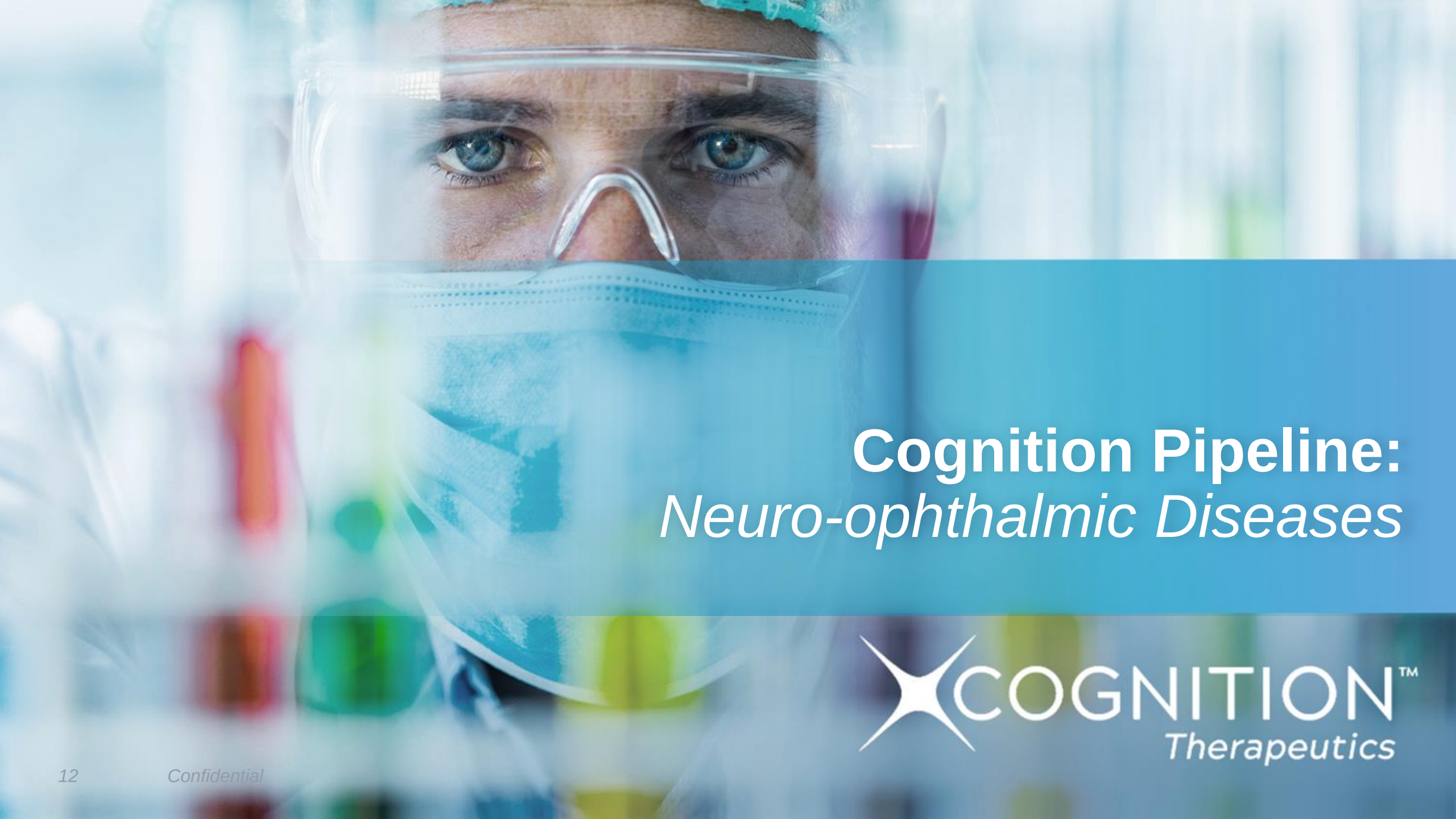

Cognition Pipeline:
Neuro-ophthalmic Diseases

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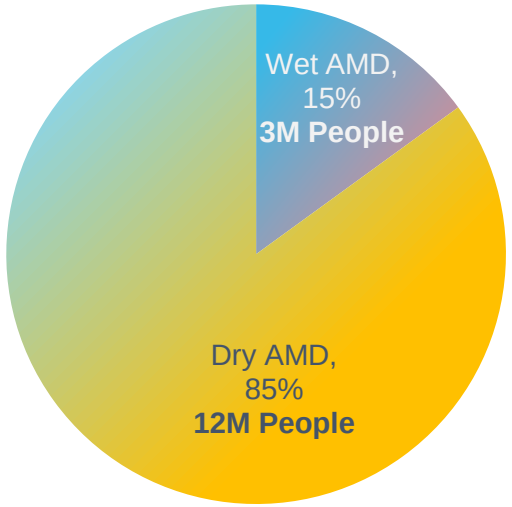
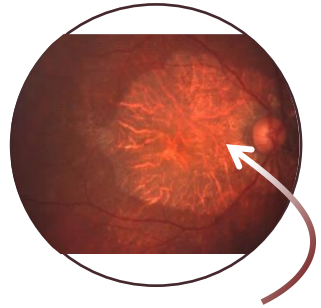
Dry AMD / Geographic Atrophy are Compelling Markets

*Leading Cause of Severe Vision Loss in People over 50 (AAO)**

15 million people in North America have AMD



- Unlike wet AMD, there are no approved drugs
  - Dietary supplements are current standard of care
- Disease progression is measured in part by magnitude of geographic atrophy (GA)
  - GA is a progressive degeneration of the macula
  - Regions of atrophy result in a blind spot in the visual field

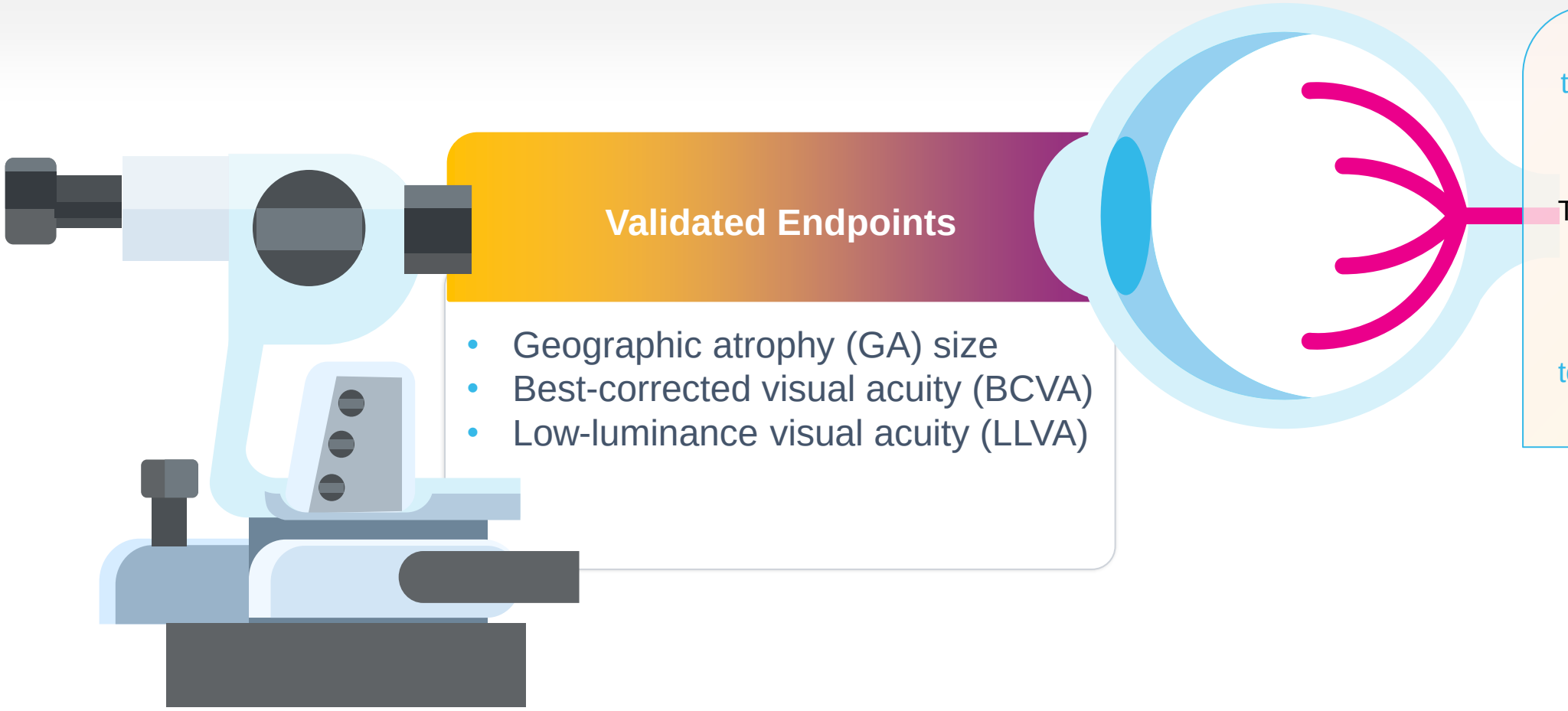


geographic atrophy

** American Academy of Ophthalmology*

Dry AMD / Geographic Atrophy:

Goal: Treat Biological Defects that Lead to Retinal Cell Degeneration



Validated Endpoints

- Geographic atrophy (GA) size
- Best-corrected visual acuity (BCVA)
- Low-luminance visual acuity (LLVA)

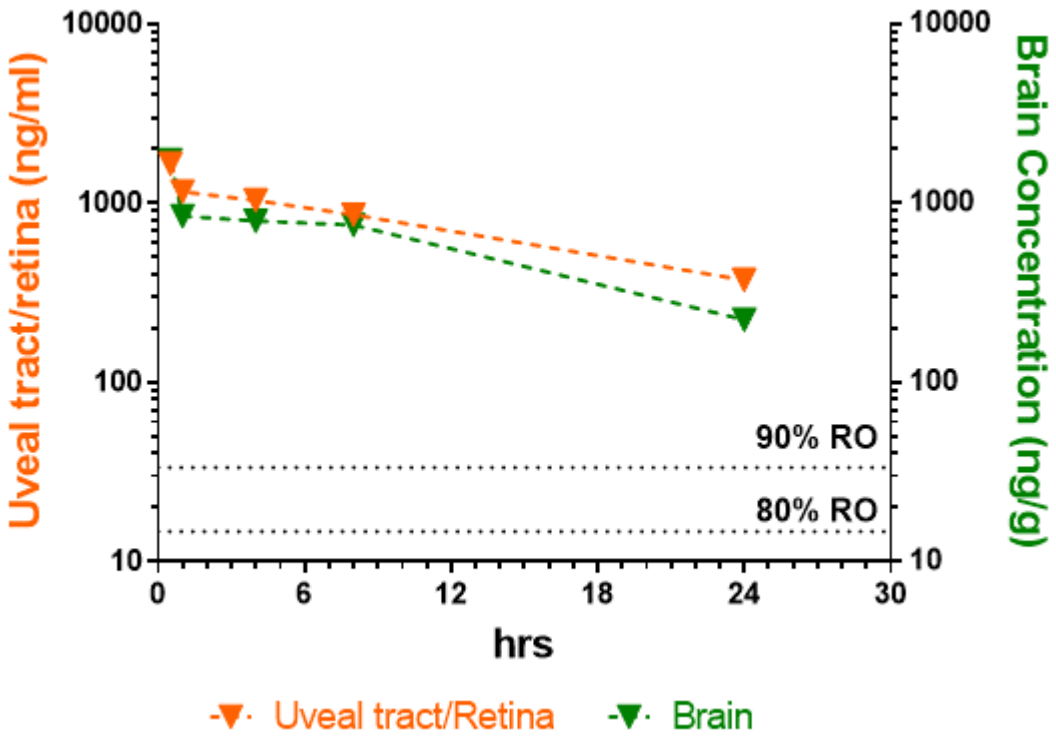
Autophagy, protein trafficking, lipid metabolism dysregulated in AMD[1,2,3]; regulated by σ-2[4,5,6]

TMEM97 protective against cellular stress[7]

Aβ oligomer-induced toxicity posited in AMD[8,9]; toxicity blocked by σ-2 drug candidates[10]

In Vivo Pharmacokinetics Show Ample Distribution to Eye

Retinal and Brain Concentrations in Rats*
Following Oral CT1812 (40mg/kg)

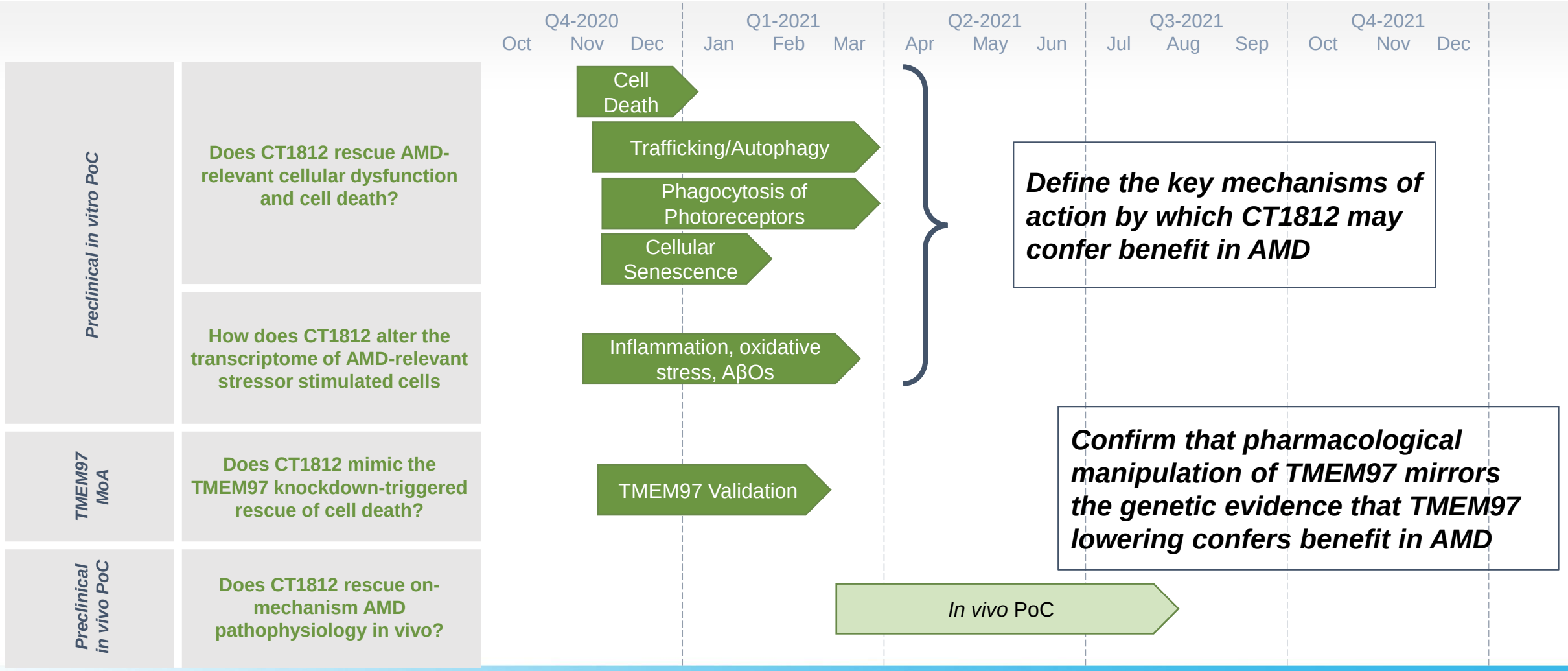


- *In vivo* study using ^{14}C-labeled CT1812 achieves levels† in the retina (orange) at least as great as those in the brain (green)

† *>80% occupancy is target dose associated with positive effects in animal models of Alzheimer's disease*

* Sprague Dawley rats

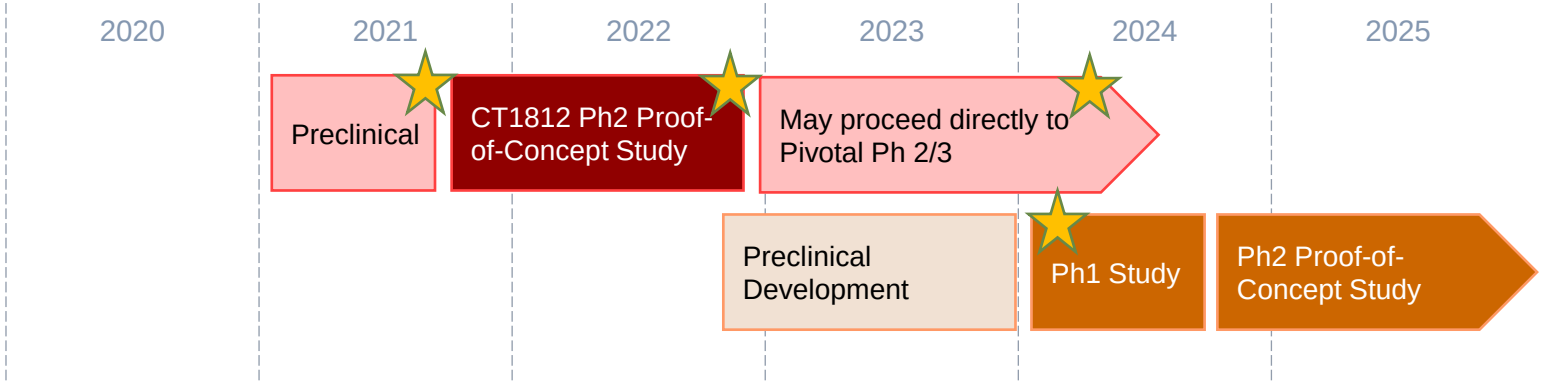
AMD – Evidence of Preclinical Proof of Concept of CT1812



CT1812 may Restore Downstream Processes

- CT1812 may remove toxic proteins from the sites where they damage retinal cells
- Objective is to restore downstream processes
- On track to complete proof-of-concept trial in 2022
- Pipeline molecules also being assessed as potential candidates for dry AMD

CT1812	**Dry AMD (Oral)**
Pipeline	**Dry AMD (Oral or IVT)**



$1.5M preclinical costs

★ *Stars indicate clinical milestones*

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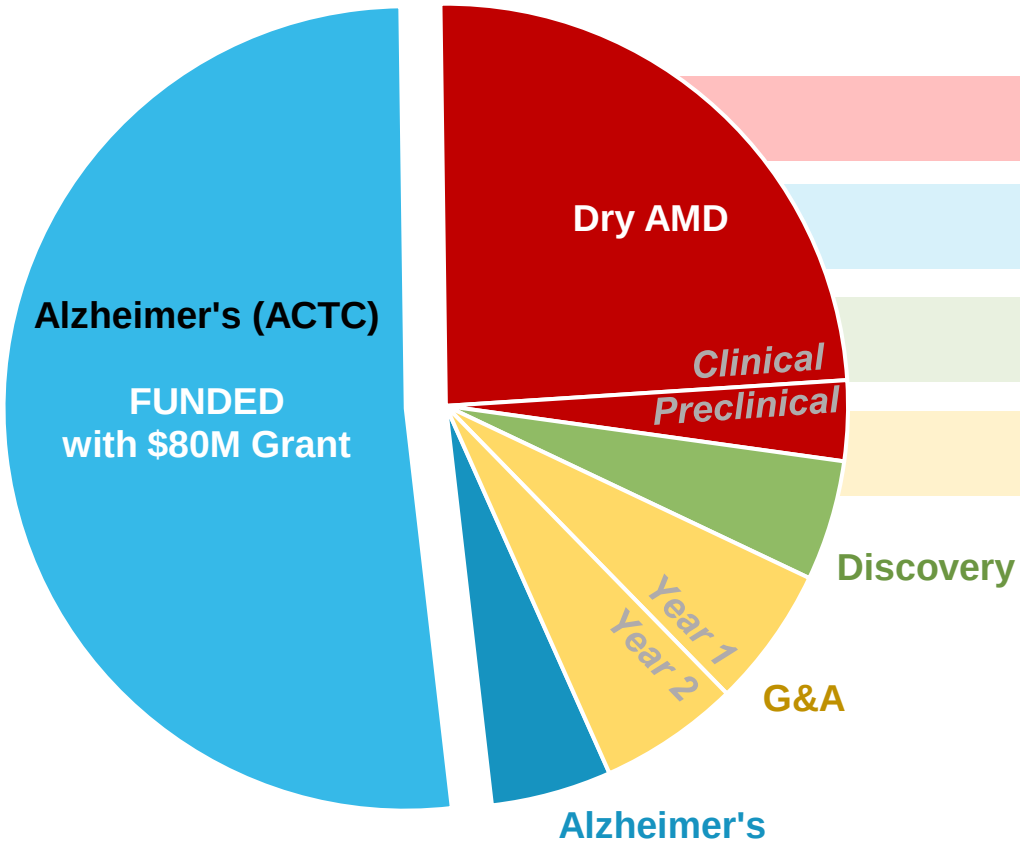
Financial Update

	Year ended December 31, 2019 (Audited)	Nine-month ended September 30, 2020 (Unaudited)
Cash	$2,889,670	$5,193,100
Convertible Notes Outstanding	$7,626,055	$13,000,000
Grant Revenue	$13,164,335	$10,958,200
Research & Development Expenses	$14,379,145	$13,434,700
Loss from Operations	$4,666,425	$6,562,600
Fully Diluted Shares Outstanding	56,171,147	58,270,700

Scored grant applications for DLB ($30M) and SHINE B ($13M) via NIA

Use of Proceeds 2021-2022



• Dry AMD - CT1812	$17M
• Alzheimer's disease - CT1812	$3 M
• Pipeline/Discovery	$3 M
• G&A Support	$7 M

Total: $30 M

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Thank You

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