COGNITION™ Therapeutics

Developing disease-modifying medicines for degenerative disorders

August 2022

Forward-looking Statement

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MARKET & INDUSTRY DATA

Projections, estimates, industry data and information contained in this presentation, including the size of and growth in key end markets, are based on information from third-party sources and management estimates. Although we believe that these third party-sources are reliable, we cannot guarantee the accuracy or completeness of these sources. Our management's estimates are derived from third-party sources, publicly available information, our knowledge of our industry and assumptions based on such information and knowledge. Our management's estimates have not been verified by any independent source. All of the projections, estimates, market data and industry information used in this presentation involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such information. In addition, projections, estimates and assumptions relating to us and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including, but not limited to, those described above, that could cause future performance to differ materially from our expressed projections, estimates and assumptions or those provided by third parties.

Who We Are

Targeting unmet needs in age-related degenerative disorders of the central nervous system and retina such as Alzheimer's disease, dementia with Lewy bodies (DLB), dry age-related macular degeneration (dry AMD), and Parkinson's disease

Functionally distinct therapeutic approach focused on the sigma-2 (σ-2) receptor complex, backed by decades of expertise in the biology of synaptic function and plasticity

Received over $160 million in non-dilutive grant funding through key collaborations with the National Institute of Aging and other thought-leading institutions

- *Approximately 50% of ongoing R&D expenses covered by grants*

Multiple Phase 2 programs expected to provide significant value-creating milestones and data readouts over the next 12 to 24 months

Expanding pipeline through our proprietary NICE screening platform, strategic alliances and acquisitions

Seasoned management team with broad scientific, drug development and commercial expertise; experienced board and advisors

Pipeline

Product Candidate	Target Indication	Preclinical	Phase 1	Phase 2	Phase 3	Funding
CT1812	**SEQUEL** Mild-moderate AD					$3.3M NIH NIA
CT1812	**SHINE** Mild-moderate AD					$30M NIH NIA
CT1812	**SHIMMER** DLB					$30M NIH NIA
CT1812	**START** Early-stage AD					$81M NIH NIA
CT1812	**Dry AMD**					
CT2168	**Synucleinopathies** †	*IND enabling studies*				THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH
CT2074	**Dry AMD**	*IND enabling studies*				

† *including Parkinson's disease and DLB*

Please note: CT1812 and other pipeline candidates are not approved for use in the US or other jurisdictions

Grants Continue to Provide Funding

Approximately 50% of R&D Funded by Grants

Clinical Study	Total Awarded	Remaining (yet to be drawn down)
START (early AD)	$ 81 Million	$ 65.1 Million
SHINE (mild/mod AD)	$ 30.5 Million	$ 11 Million
SHIMMER (DLB)	$ 29.5 Million	$ 20.5 Million
SEQUEL (qEEG in AD)	$ 3.3 Million	$ 0.4 Million
	$ 144.3 Million	**$ 97 Million**

NOTE: figures are approximate dollar amounts as June 30, 2022

Key Upcoming Milestones & Expected Timing

2021

Completed

- ✓ SNAP
- ✓ SPARC
- ✓ SHINE (cohort 1)

2022

Completing

- PK
- Human AME
- SEQUEL

Conducting

- SHINE (cohort 2)
- Phase 2 in DLB
- Phase 2 with ACTC
- Phase 2 in dry AMD
- IND-enabling studies for research compounds

2023

Completing

- SHINE (cohort 2)

Ongoing Studies

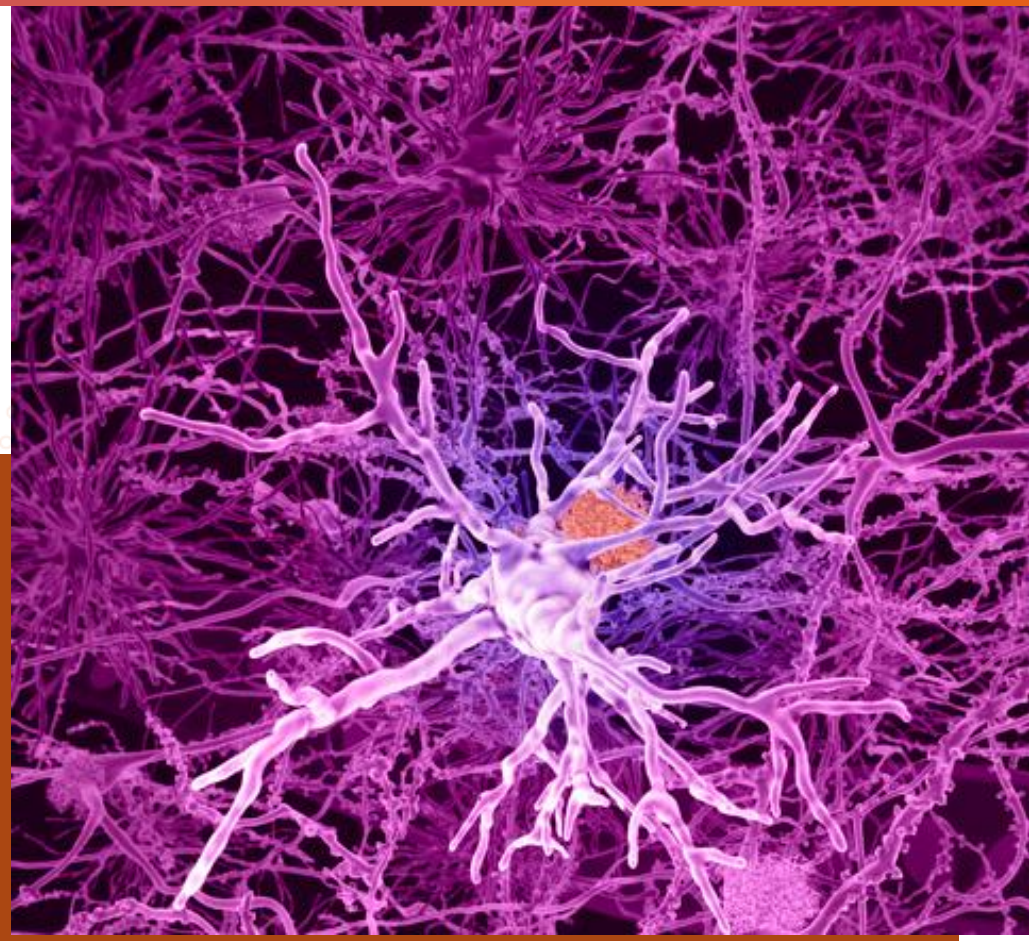
- Phase 2 in DLB
- Phase 2 with ACTC
- Phase 2 in dry AMD

Regulatory Actions

- IND filings for pipeline compounds

Cognition Lead Program:

Review of CT1812 for the Treatment of Alzheimer's Disease



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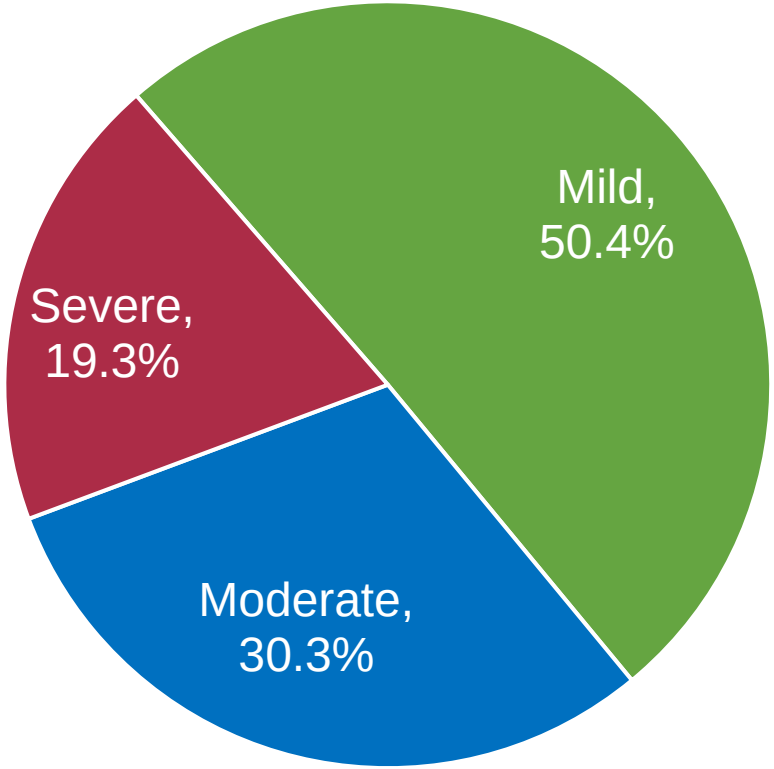
Alzheimer's Disease Market Overview

- Approx. 6.2 million individuals in United States are afflicted with Alzheimer's disease[1]
  - Approximately 35 million people worldwide[2]
  - Prevalence expected to double by 2050[1]
- Direct healthcare costs for patients with Alzheimer's and other dementias is estimated to exceed $300 billion in the United States alone[1]
  - Projected to increase to $1+ trillion by 2050[1]

Stages of Disease Afflicting Current Population of Alzheimer's Patients



1) Economic Burden of Alzheimer Disease and Managed Care Considerations. Am J Manag Care. 2020;26:S177-S183
2) World Health Organization Key Facts: Dementia

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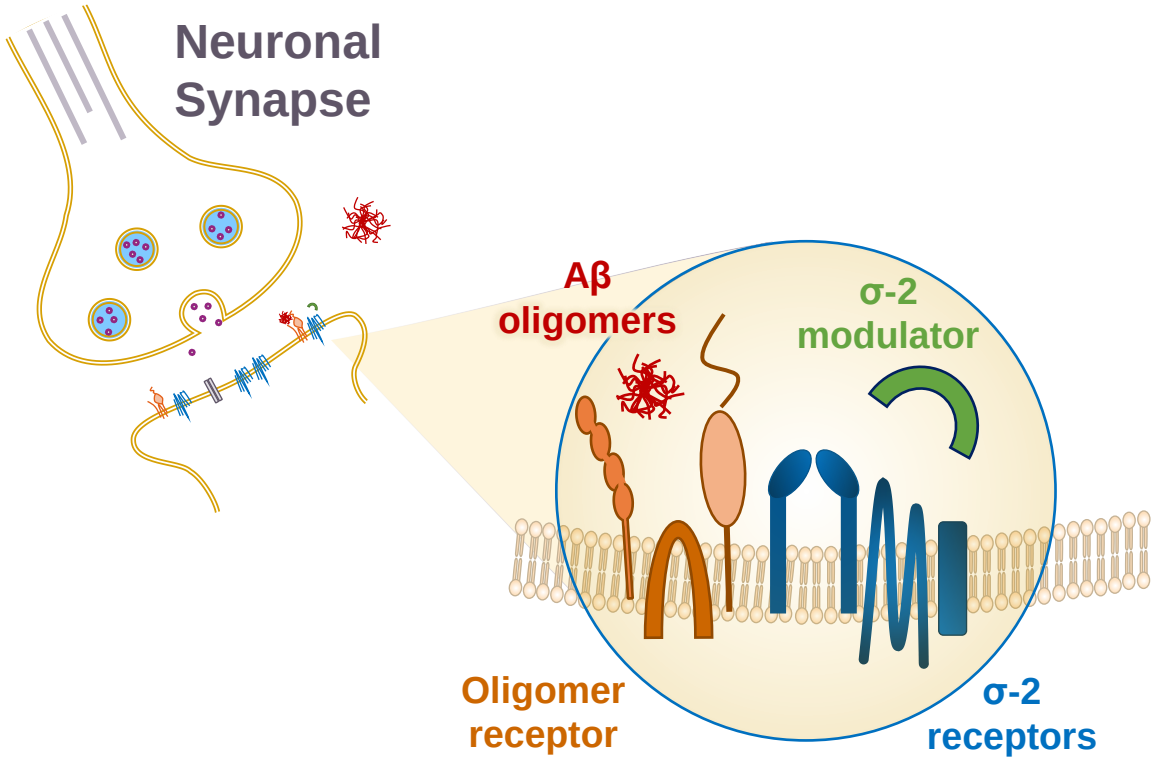
CT1812: A Synaptoprotective Approach to Alzheimer's Disease



- CT1812 penetrates the blood-brain barrier (BBB) and binds selectively to the σ-2 receptor
- By modulating σ-2, CT1812 displaces and prevents oligomers from binding to neurons and clears them into CSF
- Prevents synaptotoxicity and facilitates restoration of neuronal function
- CT1812 mimics the protective effects of the A673T-APP "Icelandic" mutation

- *Izzo NJ, et al. Preclinical and clinical biomarker studies of CT1812: A novel approach to Alzheimer's disease modification. Alzheimer's Dement. 2021;1–18*
- *Izzo NJ, et al. Alzheimer's therapeutics targeting amyloid beta 1-42 oligomers II: Sigma-2/PGRMC1 receptors mediate Abeta 42 oligomer binding and synaptotoxicity PLoS One. 2014 Nov 12; 9(11):e111899*
- *Izzo NJ, et al. Alzheimer's therapeutics targeting amyloid beta 1-42 oligomers I: Abeta 42 oligomer binding to specific neuronal receptors is displaced by drug candidates that improve cognitive deficits PLoS One. 2014 Nov 12; 9(11):e111898*
- *Limegrover, CS, et al. Alzheimer's Protection Effect of A673T Mutation May Be Driven by Lower Aβ Oligomer Binding Affinity. J Neurochem. 2020; 00: 1– 15. doi:10.1111/jnc.15212*

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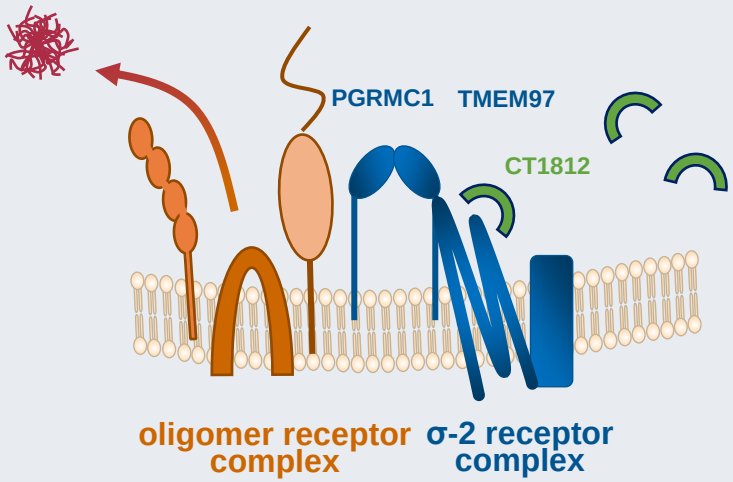
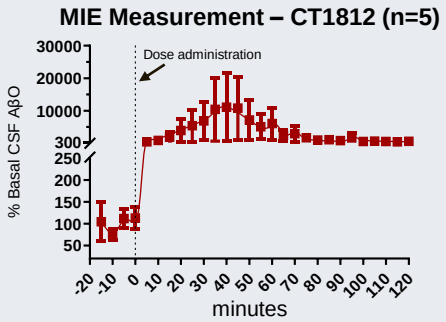
Evidence of Target Engagement: *SNAP (COG0104)*

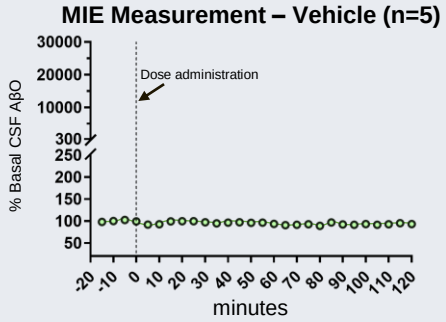
First evidence of target engagement in humans, mirrors preclinical findings, corroborating our mechanism of action

CT1812 mechanism of action: By binding to the σ-2 receptor, CT1812 displaces Aβ oligomers from synapses, thus preventing synaptic toxicity



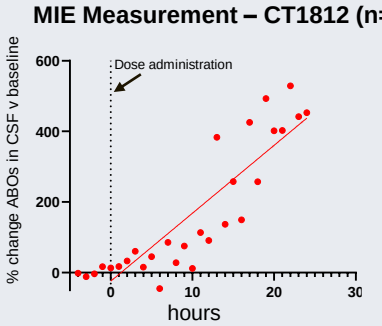
This displacement can be measured in the CSF in Alzheimer's mice treated with CT1812

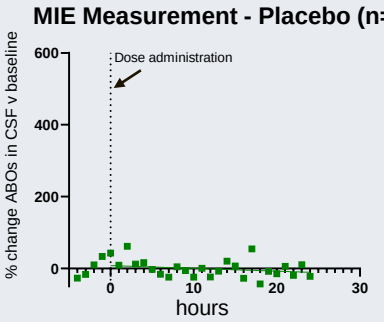




Izzo, NJ et al. Alzheimer's Dement. 2021; 17: 1365-1382. https://doi.org/10.1002/alz.12302

…and now in people with Alzheimer's disease





SNAP COG0104 study (NCT03522129) funded by NIA grant 1RF1AG057780

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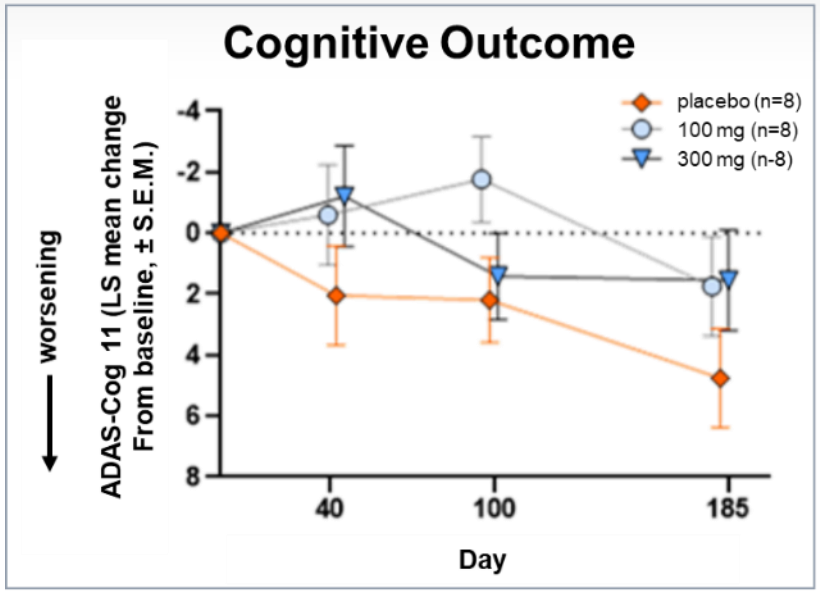
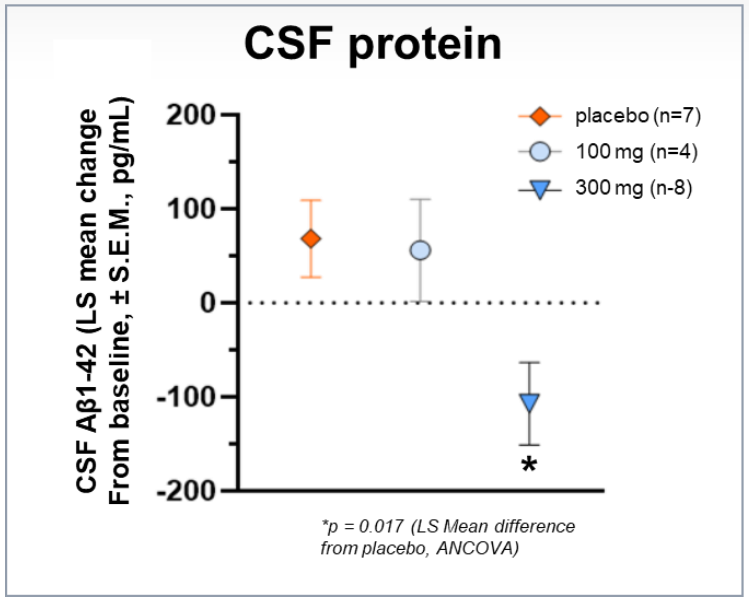
Cognitive & Biological Outcomes

SHINE interim analysis (n=24) yields promising evidence

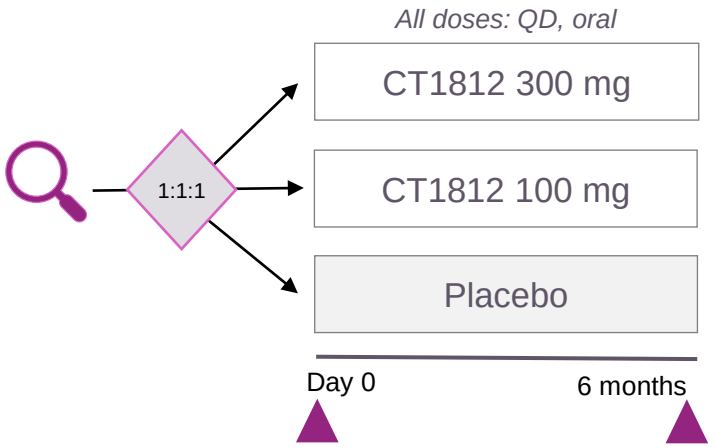


- Trend towards slower cognitive decline in CT1812-treated vs placebo-treated participants as measured by ADAS-Cog 11



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

Study Design (n=144)



SHINE COG0201 study (NCT03507790)
funded by NIA grant R01AG058660

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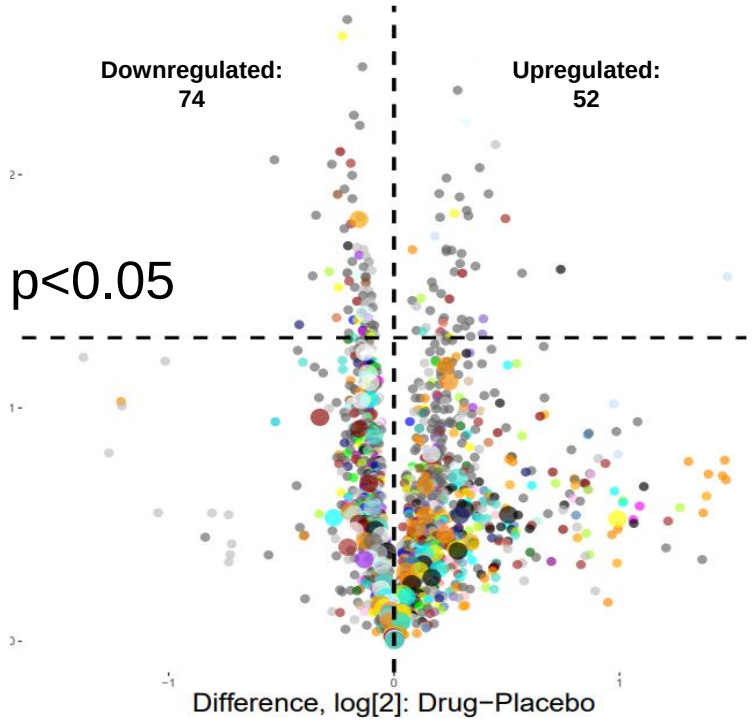
Biomarkers Associated with Alzheimer's Pathology Normalized by CT1812

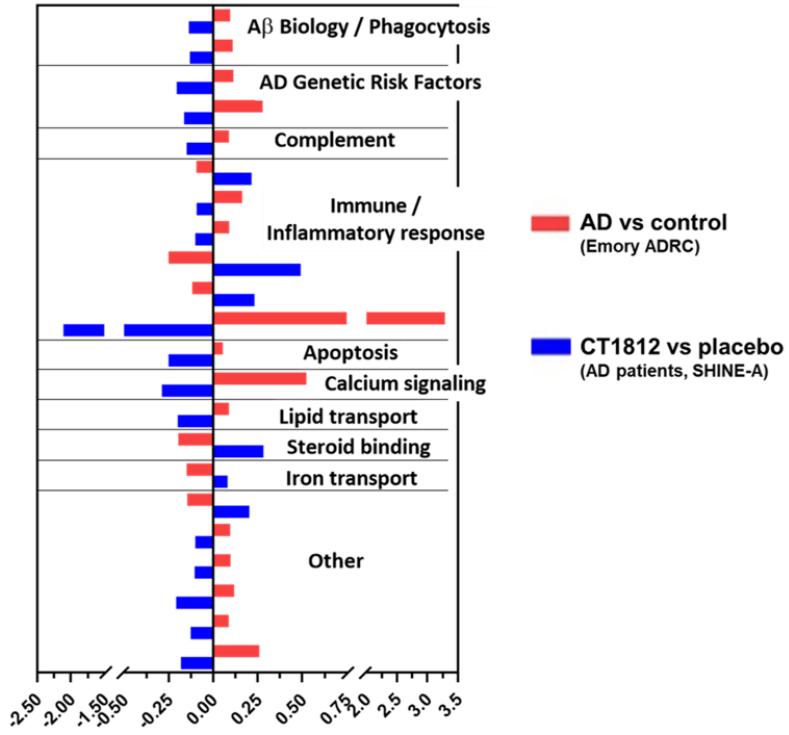
Pharmacodynamic Biomarkers of CT1812 Discovered



Most Highly Represented Pathways

- M4 Synapse/Neuron
- M3 Oligo/Myelination
- M1 Synapse/Neuron
- M21 MHC Complex/Immune
- M42 Matrisome
- M17 Transcription
- M11 Cell-ECM Interaction
- M29 Glycosylation/ER
- M7 MAPK/Metabolism
- M13 RNA Splicing
- M2 Mitochondria
- M16 RNA Binding

Biomarkers normalized by CT1812



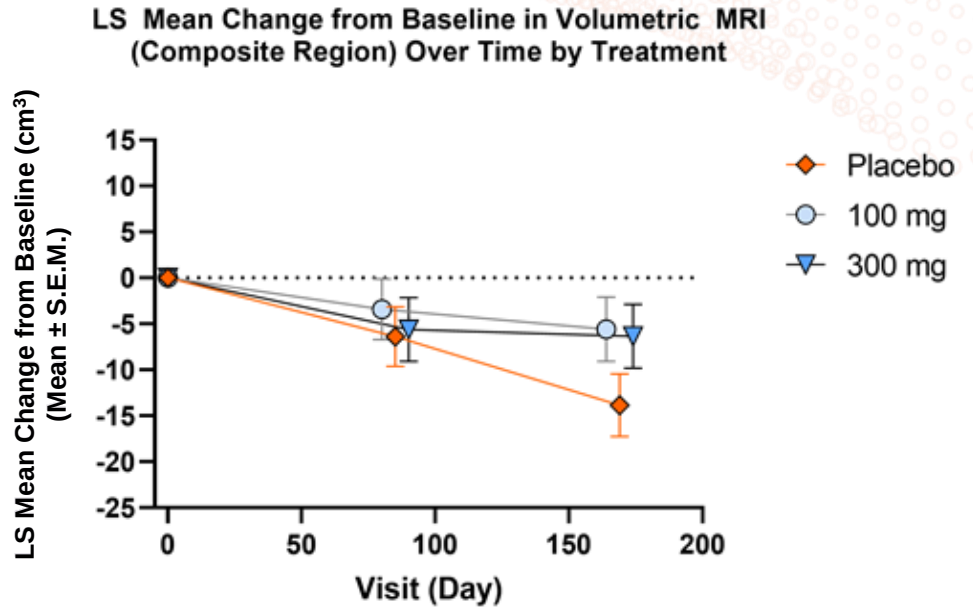
SPARC (COG0105) Results

1° Endpoints:

- Impact of CT1812 on synaptic density as measured by SV2A; safety and tolerability

Results:

- No difference in synaptic density in CT1812- or placebo-treated vs baseline
- Trend towards preservation of brain volume (composite) in CT1812- vs placebo-treated
  - Statistically significant ($p<0.05$) improvement in volume in three regions (bottom right)
- Adverse event profile consistent with prior studies
  - Elevated liver enzymes resolved upon discontinuation of study drug
  - No serious TEAEs were reported



MRI Brain Volume (cm^3)
6-mo change from baseline

	CT1812 (Pooled)	Placebo	P-value vs placebo
Hippocampus	-0.09 (0.08)	-0.40 (0.11)	0.0412
Prefrontal Cortex	-0.41 (0.95)	-4.80 (1.37)	0.0125
Pericentral Cortex	0.07 (0.53)	-2.90 (0.77)	0.0032

SPARC COG0105 study (NCT03493282) funded by NIA grant RF1AG057553

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Proteomic Data from SPARC Shows Effect of CT1812 on Disrupted Alzheimer's Disease Processes

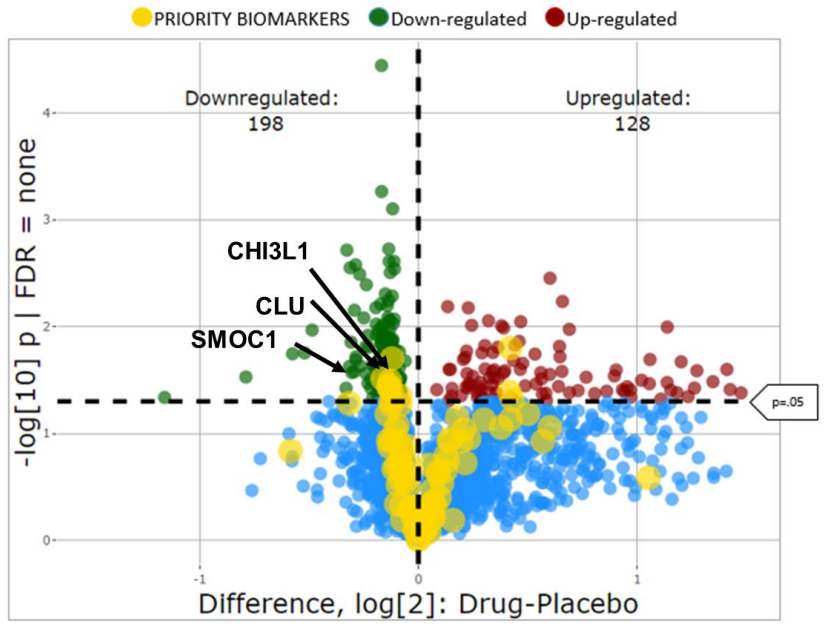
- 37 proteins in CSF were significantly ($p<0.05$) normalized towards control with CT1812 compared to placebo
- These proteins are involved in key pathways disrupted in Alzheimer's: autophagy, inflammation, synaptic function
  - Include previously well-characterized biomarkers of Alzheimer's disease, such as YKL-40 and genetic risk factors for Alzheimer's disease such as clusterin
- Analyses support targeting σ-2 receptor with CT1812

NOTE: proteomic analyses conducted on 18 SPARC participants for whom there were CSF samples at baseline and at end of study

ALZHEIMER'S ASSOCIATION AAIC 22 NEW

Biomarkers of CT1812 Identified, Several of Which May Reflect Disease Modification

Pharmacodynamic Biomarkers of CT1812 Discovered

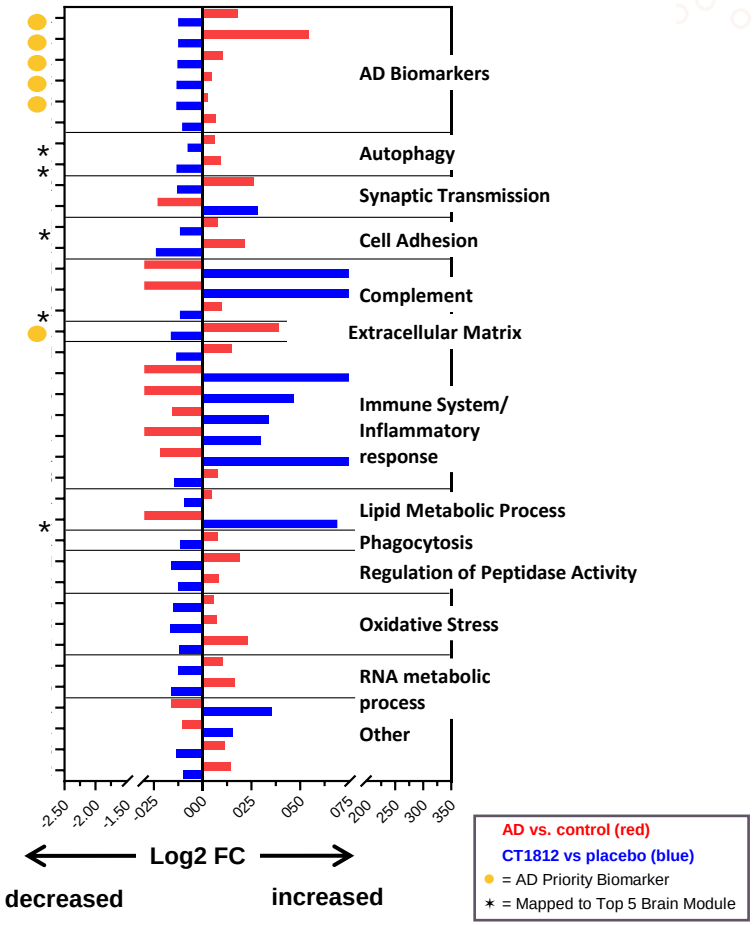


CHI3L1 (YKL-40) = inflammatory protein ↑ in Alzheimer's disease
SMOC1 = Aβ plaque-associated protein ↑ in Alzheimer's disease
CLU = Alzheimer's disease genetic risk factor (clusterin; APOJ)

Most Highly Represented Pathways

M3	Oligo / Myelination
M26	Complement / Acute Phase
M7	MAPK / Metabolism
M4	Synapse / Neuron
M1	Synapse / Neuron
M14	Protein Folding
M21	MHC Complex / Immune
M27	Extracellular Matrix

Biomarkers normalized by CT1812



NOTE: proteomic analyses conducted on 18 SPARC participants for whom there were CSF samples at baseline and at end of study

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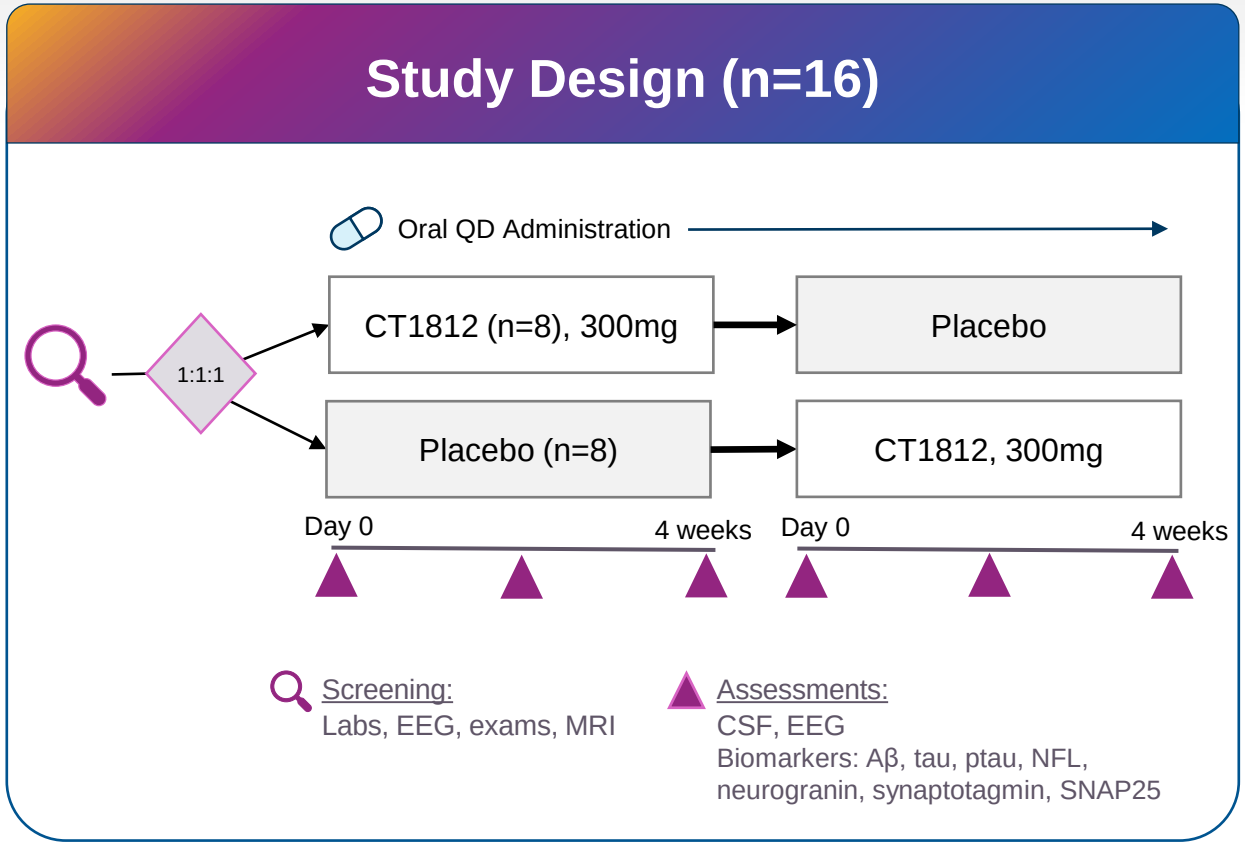
SEQUEL (COG0202)

Assessment of brain wave activity via quantitative EEG

- Principal investigator: E. Vijverberg, MD, PhD; neurologist at Vumc Alzheimer's Center

  Amsterdam UMC
  Universitair Medische Centra

- Single-site quantitative EEG study in patients with mild-to-moderate AD
- Two group cross over design
- Objective: evaluate the efficacy of CT1812 in restoring synaptic function through quantitative EEG, as reflected by relative theta power



SEQUEL COG0202 study (NCT04735536) funded by NIA grant RF1AG058710

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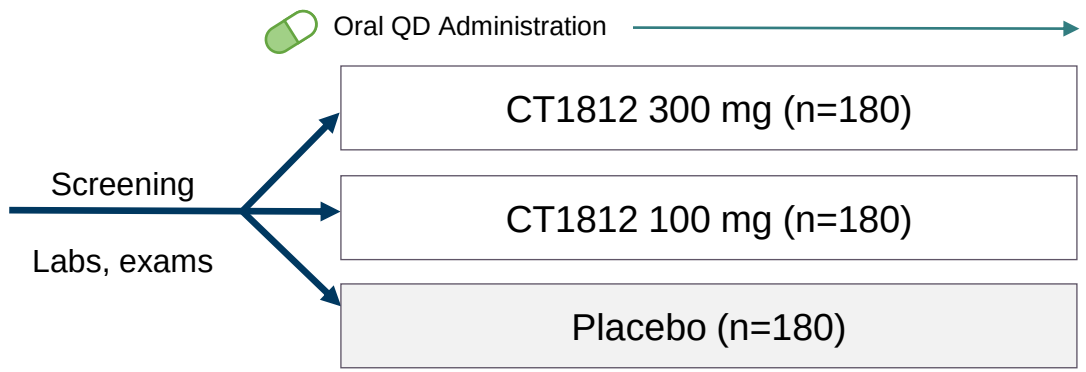
Patient Population: Early AD

Substantial grant award of $81M funds program

- Phase 2 efficacy study, powered to show change in cognition: slowing or halting cognitive decline
- Enrollment expected to commence 2H 2022
- Enrolling 540 participants with early Alzheimer's disease at 50-60 U.S. sites
- Supported by $81M Grant from NIA
  - Grant awarded in collaboration with ACTC: premier Alzheimer's clinical trial group

START Trial Schematic



COG0203 Study funded by NIA grant R01AG065248

Cognition Pipeline:

Synucleinopathies

Disorders such as DLB and Parkinson's disease that are characterized by deposits of α-synuclein aggregates (called Lewy bodies) that disrupt key cellular processes

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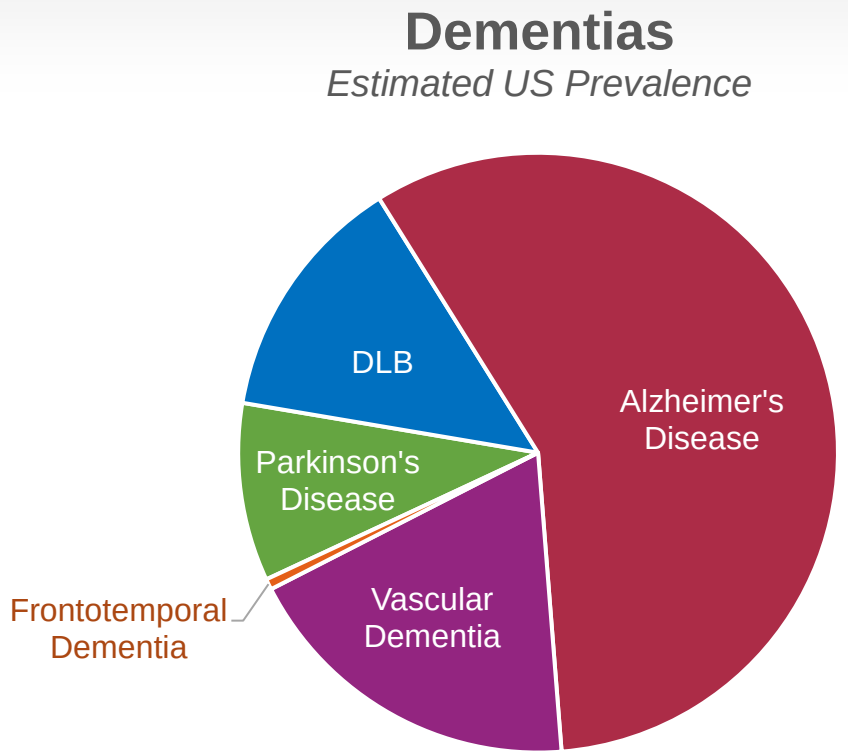
Synucleinopathies are 2nd only to AD in Prevalence

- In the U.S., approximately 13 million people have a form of dementia[1]
  - Dementia with Lewy bodies (DLB): 1.4 million
  - PD: 1 million
- Direct healthcare costs:
  - DLB: $31.5 billion[2]
  - PD: $25 billion[3]



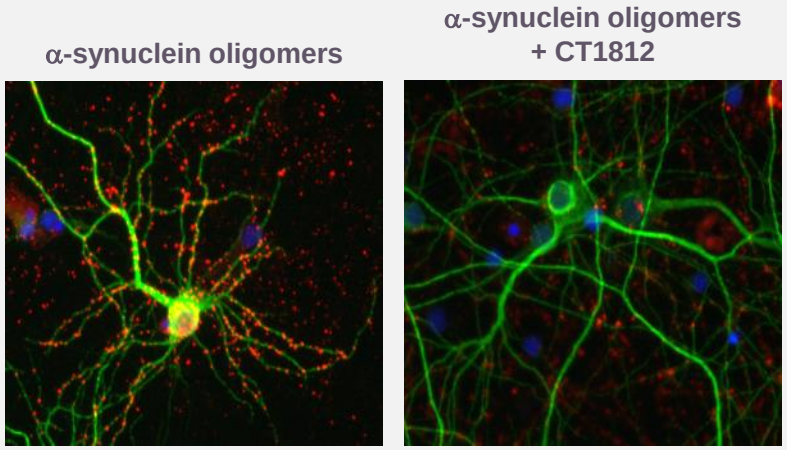
α-synuclein oligomers, which disrupt key cellular processes, are a hallmark of both disorders

1) Milken Institute report: (2019) Reducing the Cost and Risk of Dementia: Recommendations to Improve Brain Health and Decrease Disparities.
2) LBDA (extrapolated): LBD is the Most Expensive Dementia in America and Yingjia Chen et al Alzheimers Dement. 2019
3) MJFF and The Lewin Group: Economic Burden and Future Impact of Parkinson's Disease (2019)

σ-2 Modulators May be Disease Modifying in Synucleinopathies

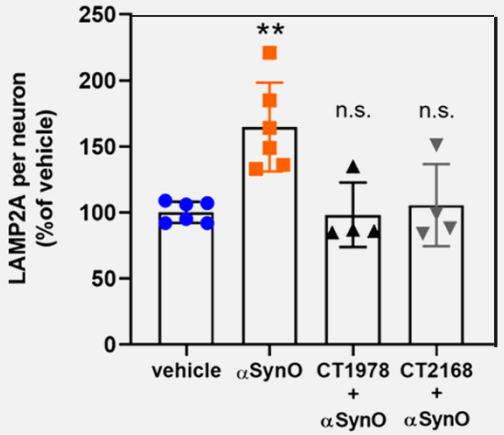
Cellular evidence that σ-2 modulators have a beneficial impact

Cognition antagonists block the binding / internalization of α-synuclein oligomers at synapses

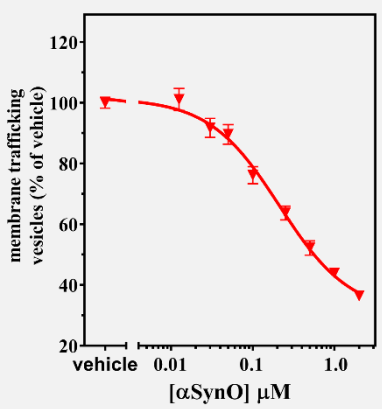


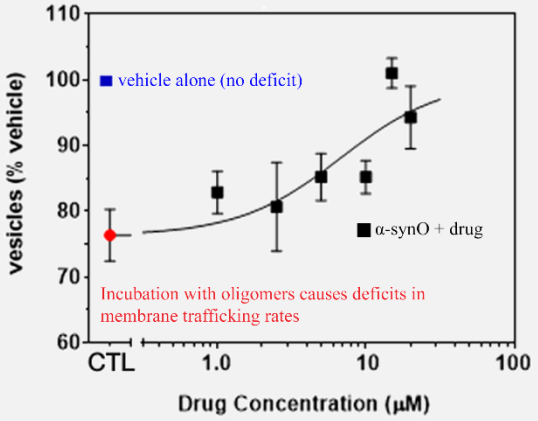
α-Synuclein oligomers in red

Cognition compounds (black and gray) reverse the effect of α-synuclein oligomers on LAMP2a (orange)



α-synuclein oligomer-induced trafficking deficits (red) are reversed by Cognition drug (black)





Limegrover CS, et al. *J Neurosci Res*. 2021. doi: 10.1002/jnr.24782

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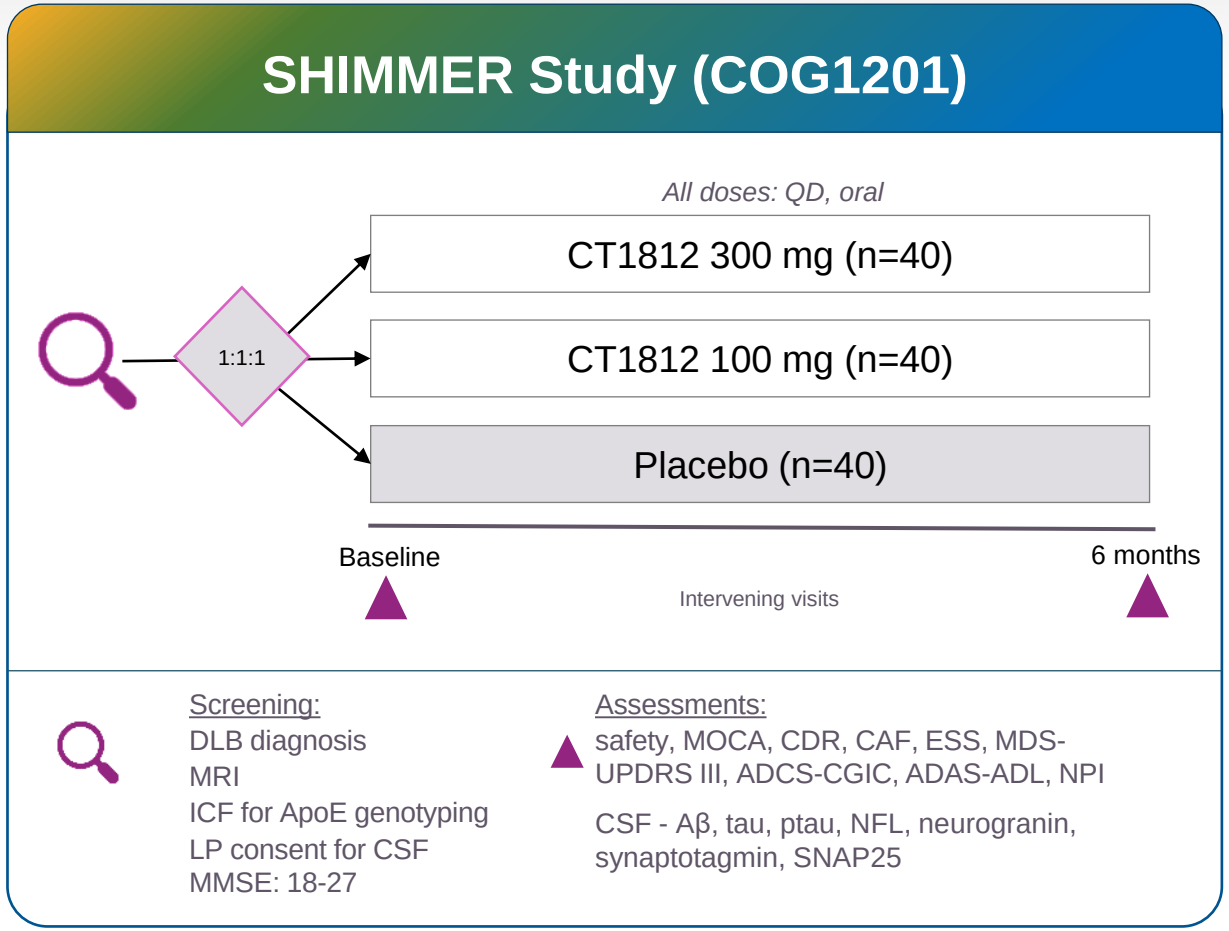
DLB Phase 2 Funded with ~$30M NIA Grant

- Principal investigator: James E. Galvin, MD, MPH, professor of neurology and director of the Comprehensive Center for Brain Health

MIAMI MILLER SCHOOL of MEDICINE

- Phase 2 SHIMMER trial ongoing
  - Participant dosing underway
- U Miami and 20+ academic sites
- *Archived DLB R&D educational symposium available: https://ir.cogrx.com*



COG1201 study partially funded by NIA grant R01AG071643

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Cognition Pipeline:

Dry Age-related Macular Degeneration

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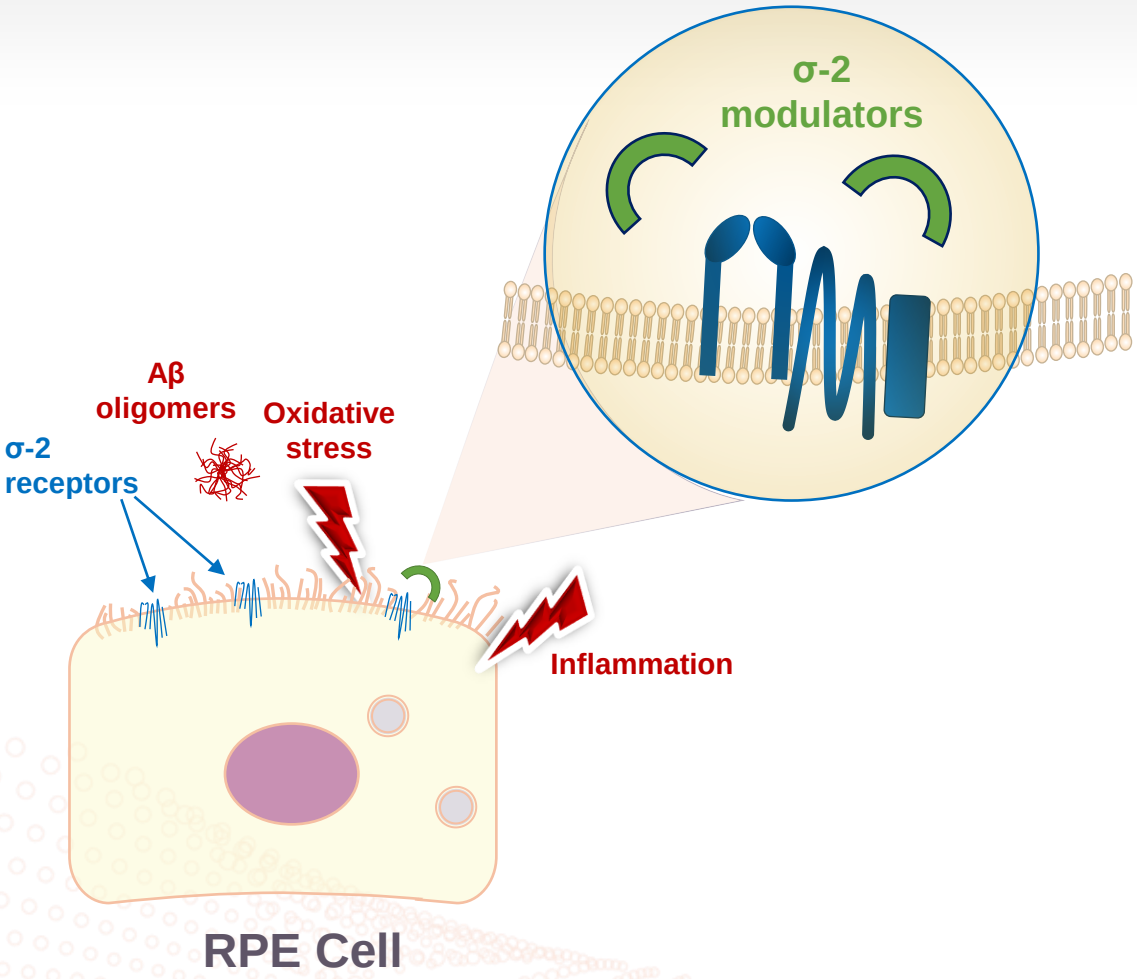
Rationale for σ-2 Modulators in Dry AMD

Goal: Protect RPE Cells From Disease-relevant Stressors



σ-2 receptors

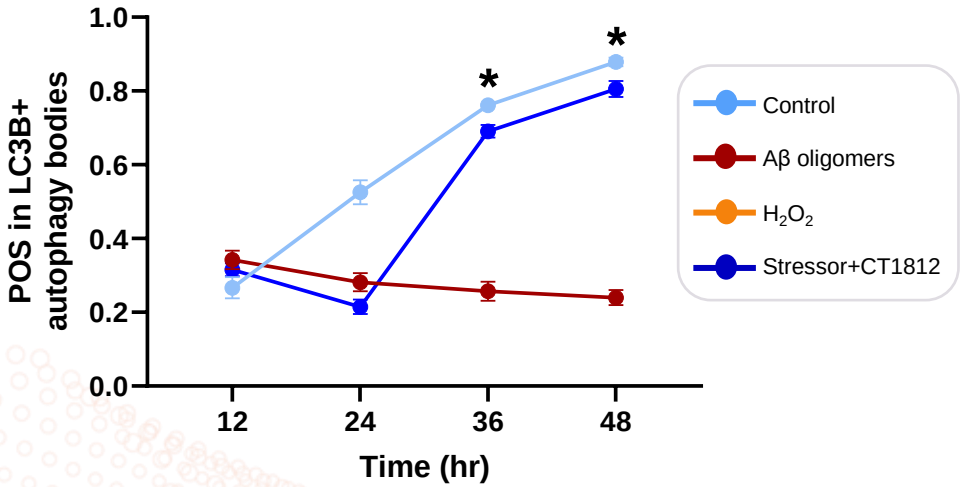
- **Expression:** in RPE cells, retinal ganglion cells, photoreceptors in retina
- **Biology**: Regulates autophagy, protein trafficking, lipid metabolism dysregulated in AMD
- **Target validation:** TMEM97 knockdown is protective
- **Human genetics:** Linked to dry AMD

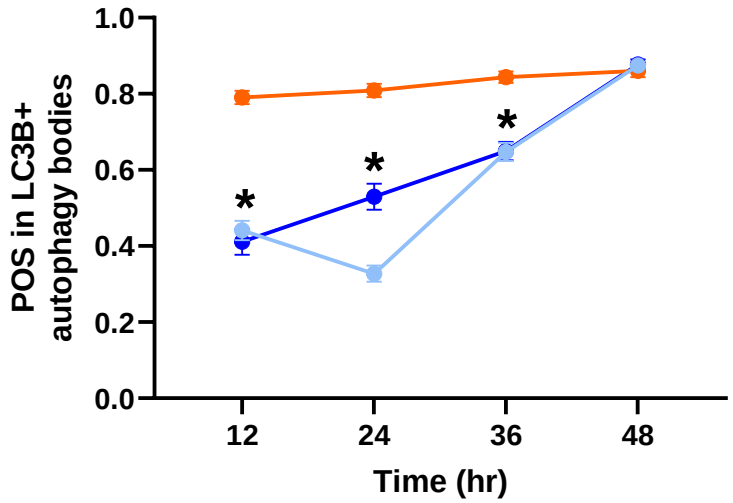
σ-2 receptor modulators

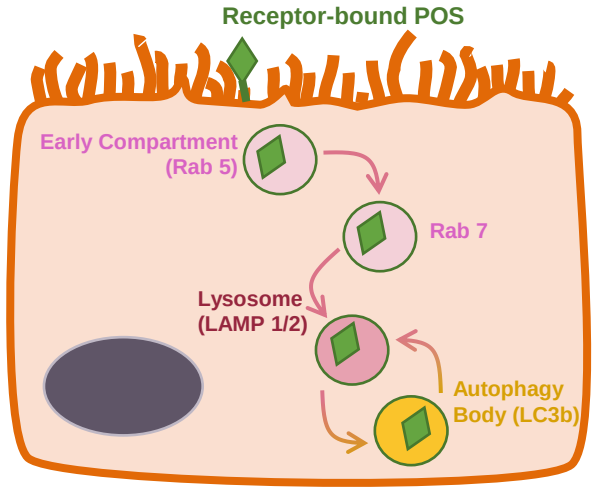
- **Non-invasive oral small molecule approach to reach retina**
- **Clinical biomarker support**: Proteomics analyses showed differential movement of proteins involved in dry AMD
- **Preclinical data:** regulates cell survival and inflammatory pathways, ameliorate trafficking deficits

Results: *σ-2 Receptor Modulators Prevent Deficits in Trafficking / Degradation of POS from 2 Insults*

- Aβ oligomers and oxidative stress cause lysosomal deficits in capacity to traffic & degrade photoreceptor outer segments (POS) cargos in RPE cells
- σ-2 receptor modulators from 3 chemically distinct series rescued these deficits

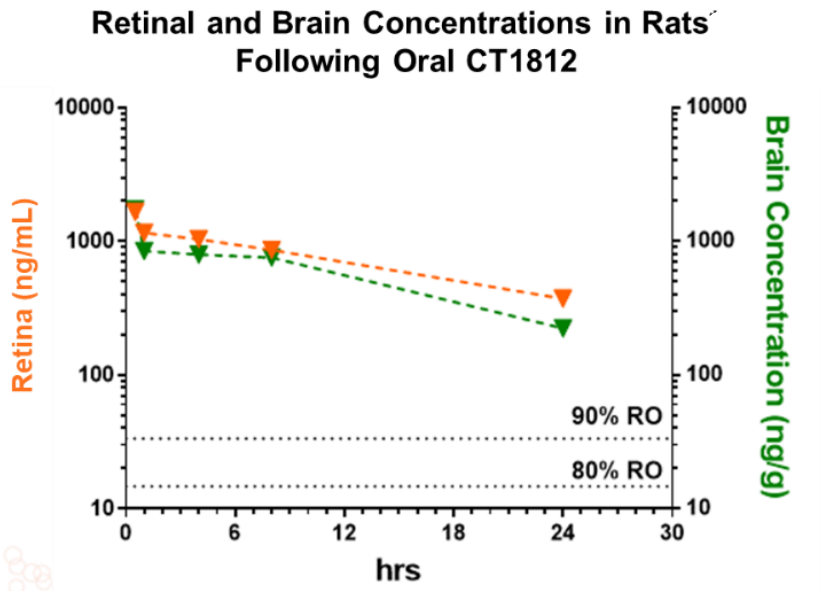




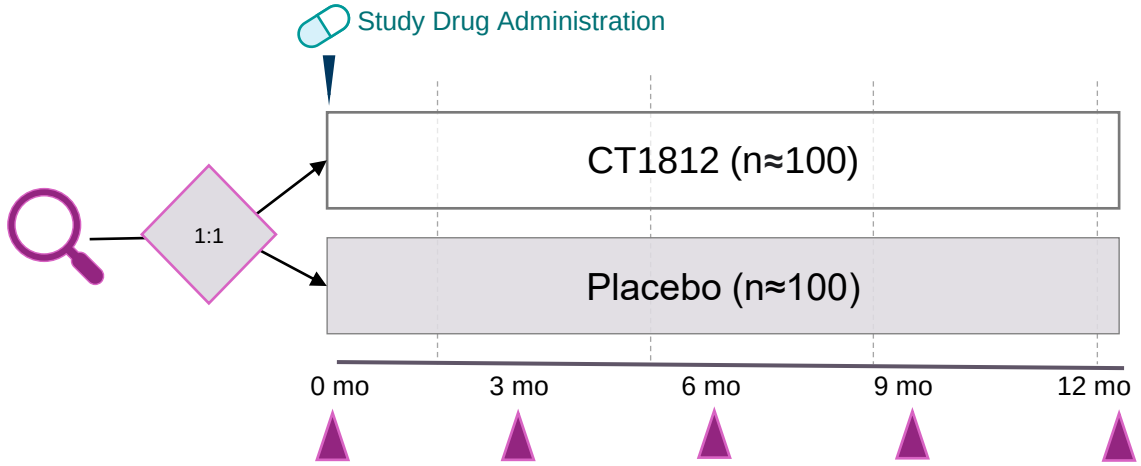


Genetic, Clinical Biomarker and Preclinical Data Support Moving Forward with CT1812 for dAMD

Orally administered CT1812 reaches the target tissue at >80% RO



Planned Phase 2 will assess CT1812 in patients with diagnosed dry AMD and measurable GA



Screening:
Age: ≥ 50
Diagnosis of dry AMD
BCVA ≥ 24 letters (ETDRS)
GA lesion ≥ 2.5 and ≤17.5mm^2

Assessments such as:
Change in GA lesion
Low luminance visual acuity (LLVA)
Best-corrected visual acuity (BCVA)

Financial Position

Financials as of June 30, 2022

- Cash and Cash Equivalents: $45.8 million
- Proceeds raised from IPO: $52.0 million
- Expected cash runway into 2H 2023

NIA funding for CT1812 studies as of June 30, 2022

- Preclinical through Phase 2 studies $168.4 million
- Approximate funding used ($70.4 million)
  - *Remaining NIA funding* **$98.0 million**

COGNITION™ Therapeutics

Thank You

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