SAPHARY Phase 2a study to investigate the safety, efficacy, and pharmacokinetics of GAL-101 salt as oral treatment for patients with mild to moderate Alzheimer's disease

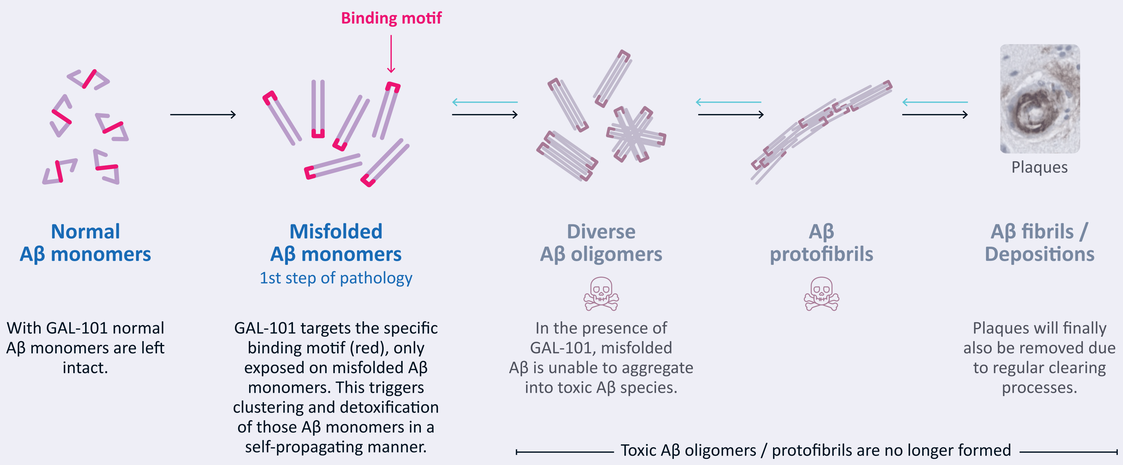
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BACKGROUND

GAL-101 Mechanism of action



GAL-101 is a small molecule that selectively binds β-sheet Aβ monomers and induces a conformational change into non-β-sheet structures, while leaving physiological Aβ intact.

Through a self-propagating, prion-like mechanism, these modified Aβ species recruit further misfolded Aβ and redirect aggregation toward non-toxic, non-β-sheet agglomerates that can be cleared from the body.

GAL-101 thereby prevents the formation of new toxic aggregates and progressively eliminates existing toxic Aβ species. Preclinical studies accordingly indicate neuroprotective and cognitive improvement in Alzheimer's disease models.

Successful Phase 1 trial in healthy volunteers completed:

In NCT07780604, GAL-101 was safe and well tolerated at all investigated doses, with no dose-limiting toxicity, accumulation, or relevant food effect. Elderly participants tolerated treatment equally well. CSF exposure confirmed CNS penetration, while changes in plasma and CSF Aβ levels provided initial evidence of target engagement.

SAPHARY PHASE 2A CLINICAL TRIAL

Given the advanced age, comorbidity burden, and disease-specific vulnerability of Alzheimer's patients, this Phase 2a study aims to further characterize the safety and tolerability profile of GAL-101, as well as gather preliminary efficacy data, prior to long-term clinical studies (NCT07789873).

Study Design & Objectives

This is a phase 2a, double-blind, randomized, multicenter, parallel group, placebo-controlled study to investigate the safety, efficacy and pharmacokinetics of GAL-101 salt tablets as oral treatment for 28 days in patients with mild to moderate AD.

Screening	Sample size	Double-blind treatment period 28 days	Follow up
-4 weeks	N = 100 R 1:1	**Two tablets daily** (within 5 min interval) **of GAL-101** (1200 mg total) Placebo	+4 weeks, safety follow-up

Key Eligibility criteria

Inclusion:

- ✓ Proven AD pathology as shown by Aβ-PET-Scan or pTAU217-CSF levels indicative for AD
- ✓ Immediate Word Recall Test indicative for mild to moderate clinical stage of AD
- ✓ Male or female patients aged 50 to 85 years
- ✓ Concomitant treatment with stable dose of AChEIs or memantine allowed

Exclusion:

- ✗ Prior use of anti-amyloid-β immunotherapy
- ✗ Medications affecting cognitive assessments
- ✗ Neurodegenerative diseases of different etiology as e.g. Lewy-Body Disease

Study Objectives & Endpoints

1. To demonstrate safety in AD patients
2. To determine efficacy readouts which reflect best the unique MoA of GAL-101

- **Primary Endpoint:** Safety and tolerability of GAL-101 in AD compared to placebo
- **Secondary Endpoints:** Evaluation of cognition, EEG, fluid biomarkers, assessment of plasma and CSF PK
- **Safety (primary):** Incidence of SAEs, AEs with severity ≥ 3 according to CTCAE, discontinuations due to AEs
- **Pharmacodynamics (exploratory):**
  → qEEG: global alpha-band AEC-c, global relative theta power and further EEG parameters
  → Fluid biomarkers in CSF: Neurogranin, VAMP2, SNAP-25, GFAP, $A\beta_{1-40}$, $A\beta_{1-42}$, $A\beta_{1-42}/A\beta_{1-40}$-ratio, pTau181, total Tau
  → Cognition tests involving memory, attention, visual and verbal learning, psychomotor function
- Others:
  → PK: concentrations of GAL-101 in plasma and CSF

RESULTS: **Study initiation is ongoing, clinical data are not yet available.**

CONCLUSIONS: **This study will provide important information on the safety and biological short-term effects of GAL-101 in the target Alzheimer's patient population and is intended to support the further clinical development of GAL-101 as an oral disease-modifying treatment of AD.**

BROADER DEVELOPMENT: **Galimedix recognizes for the oral Aβ aggregation inhibitor GAL-101 not only treatment potential in sporadic Alzheimer's disease but also in other forms of this disease with clearly amyloid β-driven pathology like Alzheimer' disease in Down Syndrome and Dominantly Inherited Alzheimer's disease (DIAD).**

Clinical Trial Page

SAEs: Serious Adverse Events; **AEs:** Adverse Effects; **CSF:** Cerebrospinal Fluid; **qEEG:** Quantitative Electroencephalography (or Quantitative EEG).

Galimedix THERAPEUTICS