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Ivana Magovčević-Liebisch, PhD, JD
President & Chief Executive Officer

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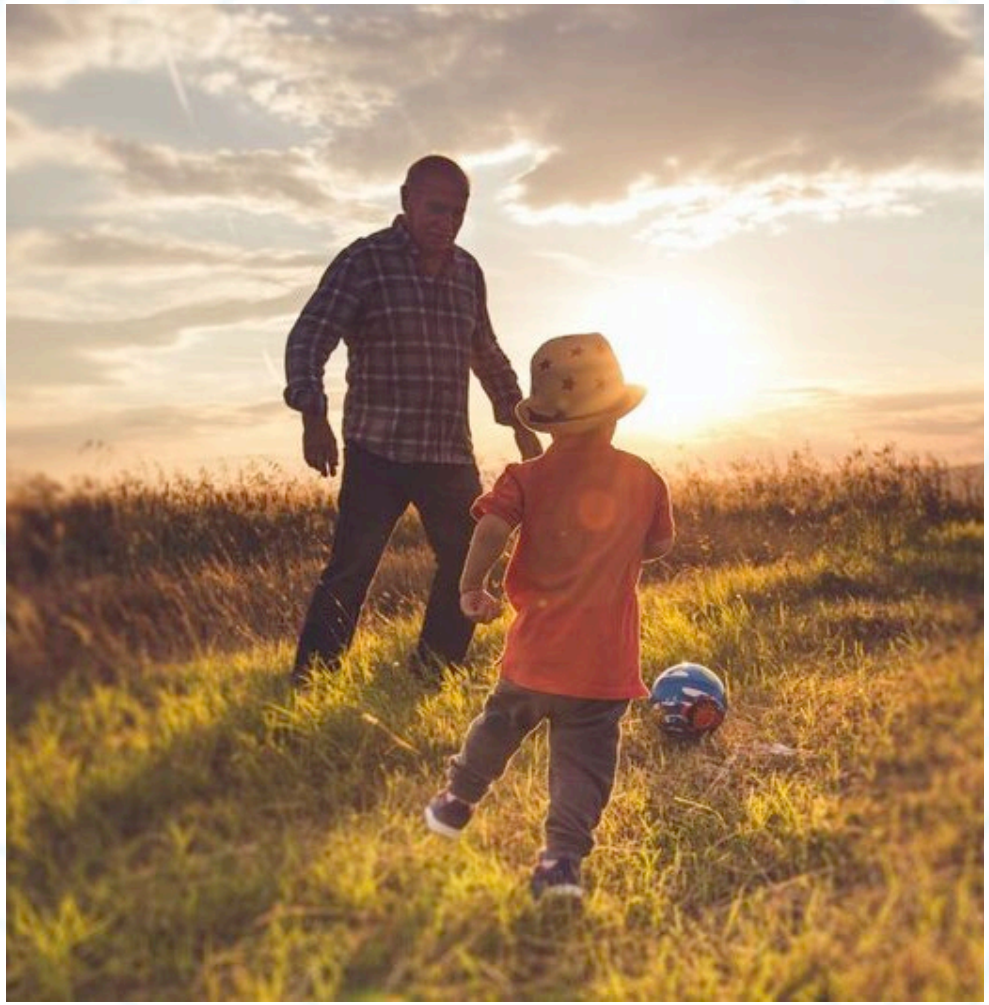
FORWARD-LOOKING STATEMENTS

This presentation contains "forward-looking statements," which are made pursuant to the safe harbor provisions of the federal securities laws, including the Private Securities Litigation Reform Act of 1995. Any statements that are not statements of historical fact may be deemed to be forward-looking statements. Such statements may contain words such as "may," "might," "will," "could," "should," "would," "expect," "intend," "plan," "prepare," "look," "seek," "anticipate," "believe," "estimate," "predict," "potential," "possible," "continue," "ongoing" or the negative of these terms, or other comparable words. These forward-looking statements include, among others, statements relating to: our plans to deliver precision-based therapies to improve the lives of patients and their families and to target a broad range of neurodegenerative diseases; plans to discover and develop novel therapeutics to leverage microglial biology, such as iluzanebart (VGL101), VG-3927 and current or future product candidates, identify additional indications for our current product candidates, and to enable success in clinical development; beliefs about TREM2 agonism's importance in ALSP & Alzheimer's disease; beliefs about the profiles and potential, including the commercial potential, of our pipeline and the strength of our intellectual property position; our analyses and beliefs about data, including pathology and disease biomarkers and the signaling, engagement and potency as an agonism of TREM2 in microglia; plans and upcoming milestones, including estimated timelines, for our pipeline program development activities and pipeline expansion opportunities; expected timing and next steps regarding data announcement, clinical trial activities and regulatory filings and potential approvals; expectations regarding our ability to develop and advance our current and future product candidates and discovery programs; and the belief that we are well-positioned to execute on our mission.

These forward-looking statements, which are only predictions, involve risks and uncertainties, many of which are beyond our control and are based on our current beliefs, expectations and assumptions regarding our business. As such, you should not place undue reliance on any forward-looking statements because such risks and uncertainties could cause actual results, performance or achievement to differ materially and adversely from those anticipated or implied in the forward-looking statements. Factors that could cause actual results to differ from those predicted in our forward-looking statements include, among others, risks and uncertainties related to product development, including delays or challenges that may arise in the development and regulatory approval of our current and future product candidates or programs; uncertainties as to the availability and timing of results and data from preclinical and clinical studies; the timing of our ability to submit and obtain regulatory clearance for investigational new drug applications and initiate additional clinical trials; our ability to initiate and complete our current and expected clinical trials; our ability to establish and maintain collaborations, strategic relationships and supply arrangements, or that we will not realize the intended benefits from such relationships or arrangements; whether our cash resources will be sufficient to fund our foreseeable and unforeseeable operating expenses and capital expenditure requirements; our ability to raise additional funding on favorable terms, or at all; the rate and degree of market acceptance and clinical utility of our product candidates; the ability and willingness of our third-party collaborators to continue research and, development and manufacturing activities relating to our product candidates; the accuracy of our data analyses or estimates for the potential and market for our products; our ability, and the ability of our collaborators, to protect our intellectual property and to conduct activities for the development and commercialization of our candidates in view of third party intellectual property positions; our financial performance; our ability to retain and recruit key personnel, as well as the potential contribution of our employees and board to our growth and success as a Company; developments and projections relating to our competitors or our industry; our ability to work with the FDA to successfully remove the partial clinical hold on VG-3927; changes in general economic conditions and global instability, in particular economic conditions in the markets on which we or our suppliers operate; changes in laws and regulations; and those risks and uncertainties identified in our filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in our most-recently filed Annual Report on Form 10-K or Quarterly Report on Form 10-Q, and such other risks and uncertainties that may be described in subsequent filings we may make with the SEC.

You should not rely upon forward-looking statements as predictions of future events or performance, or as a representation or warranty (express or implied) by us or any other person that we will achieve our objectives and plans in any specified time frame, on such specified terms, or at all. Although our management believes that the expectations reflected in our statements are reasonable, we cannot guarantee that the future results, performance or events and circumstances described in the forward-looking statements will be achieved or occur. These forward-looking statements speak only as of the date such statements are made. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Vigil Neuroscience: A Clinical-Stage Microglia-Focused Therapeutics Company



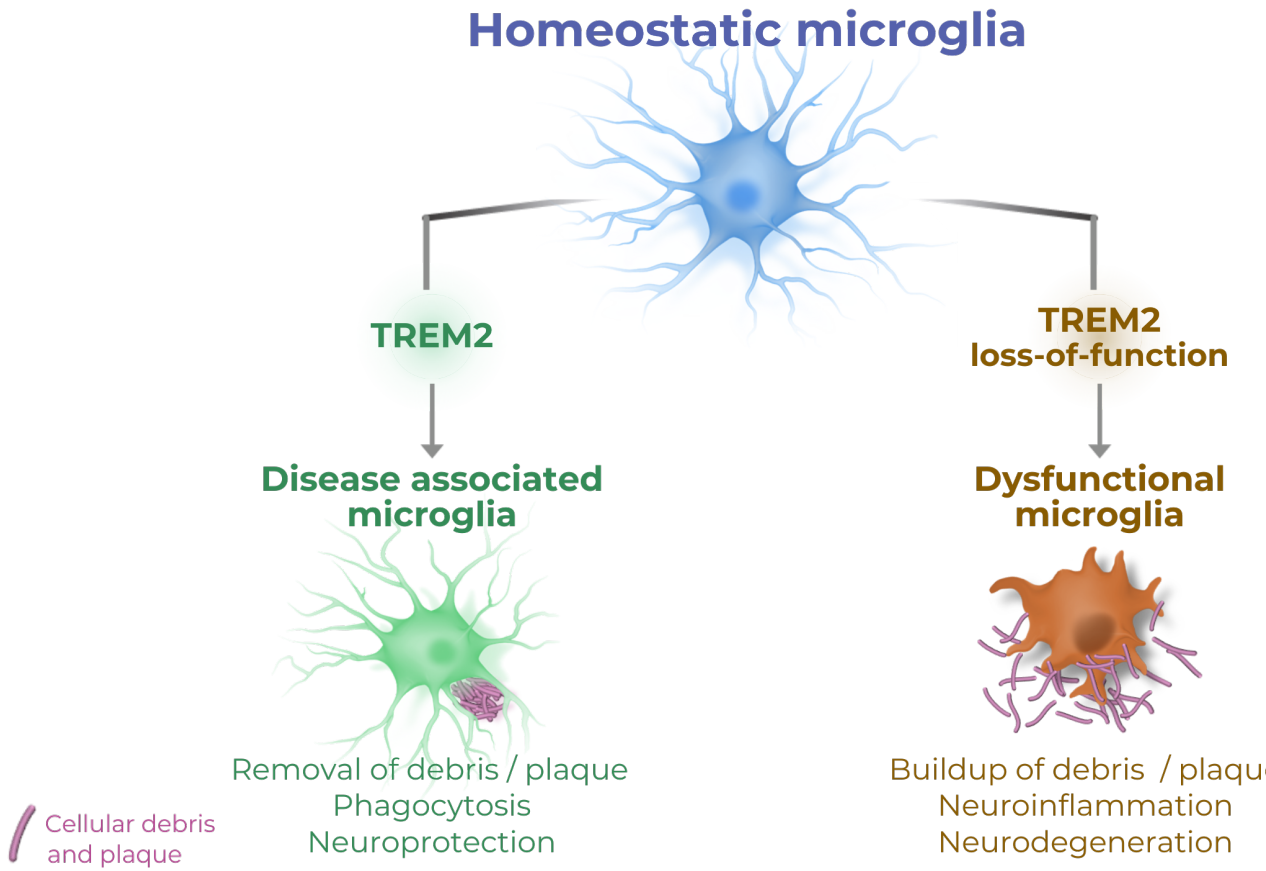
- Focused on treating rare and common neurodegenerative diseases by restoring vigilance of microglia, the brain's sentinel immune cells
- Precision-based strategy for developing microglia therapeutics
- Only company known to have 2 modalities for TREM2 agonism – monoclonal antibody and oral small molecule
- Multiple value-driving clinical milestones for lead development programs in 2024

Restoring Microglia with TREM2 as a Therapeutic Target

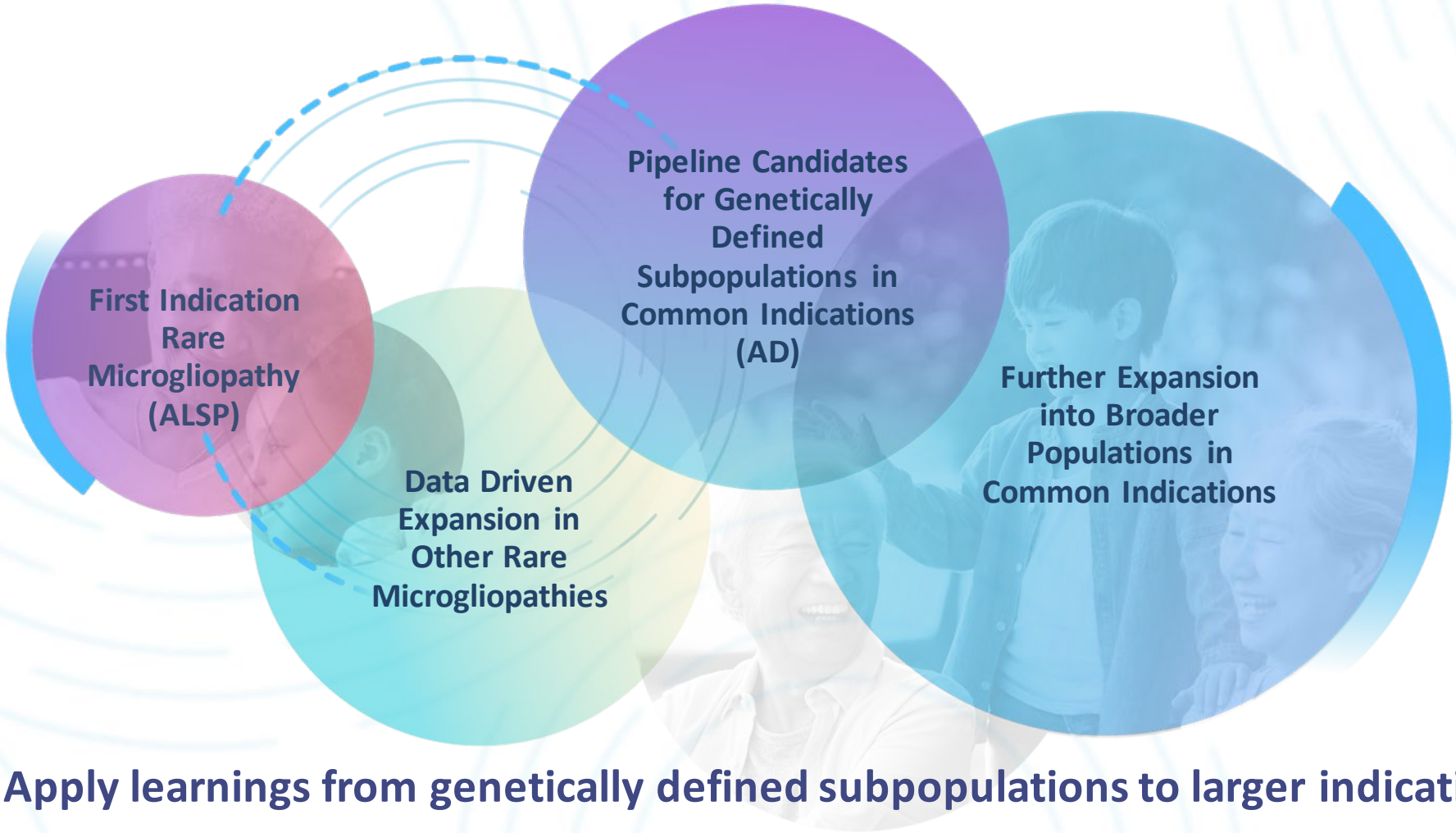
Sentinel for CNS Health

- Microglia sense and respond to damage signals and coordinate signal-specific downstream responses
- Microglial dysfunction is associated with rare and common neurodegenerative diseases

TREM2 is Essential for Microglial Function



Vigil's Precision Medicine Strategy to Target Broad Range of Neurodegenerative Diseases



Apply learnings from genetically defined subpopulations to larger indications

ALSP: Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia; AD: Alzheimer's Disease

Vigil TREM2 Agonists: Differentiated Strategy & Multiple Modalities

Iluzanebart (VGL101):
TREM2 mAb in development for ALSP

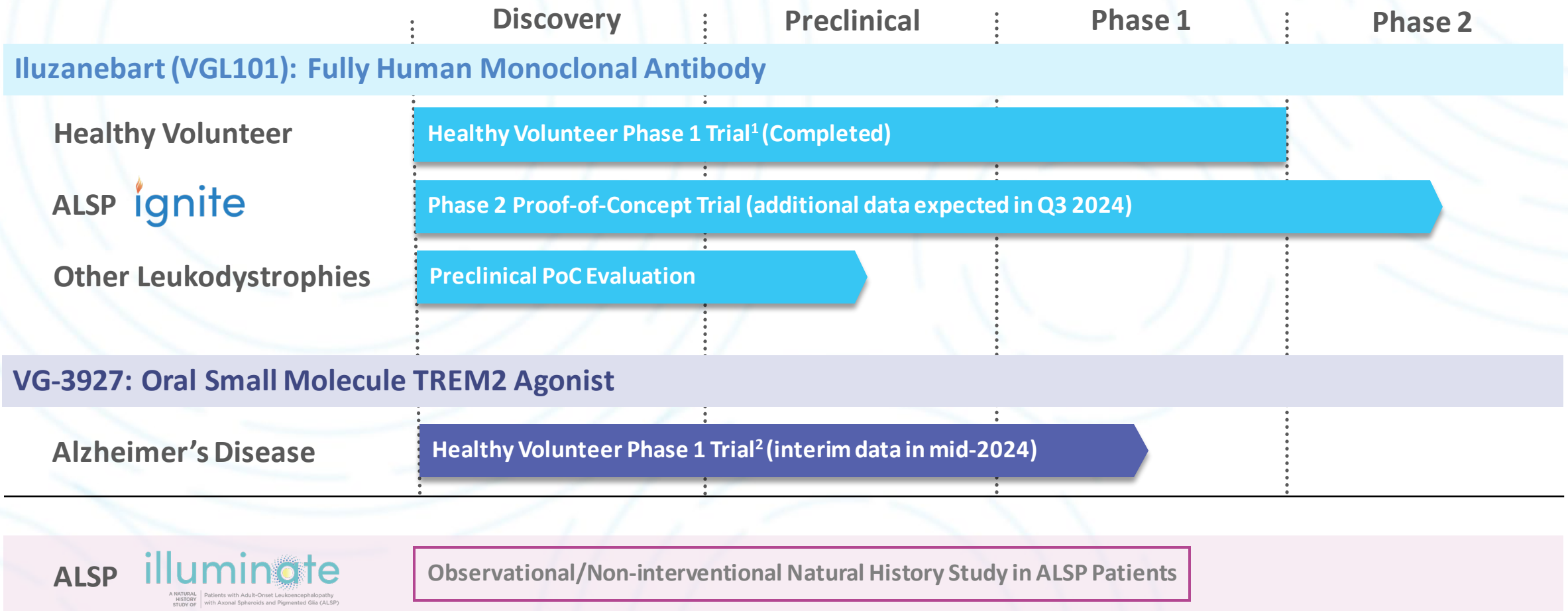
ONLY targeted drug candidate in clinical development for ALSP

VG-3927:
Small Molecule TREM2 Agonist in development for AD

1st & ONLY TREM2 small molecule agonist in clinical development

Building a Robust Pipeline in Rare & Common Neurodegenerative Diseases

Vigil has exclusive rights to all programs



1) *Complete Phase 1 data presented at ANA 2023 (please see Meier et al. ANA 2023 Poster M151 on Vigil's Publications webpage (https://www.vigilneuro.com/press-releases-publications)*
2) *IND for VG-3927 open; Phase 1 clinical trial in healthy volunteers allowed to proceed with partial clinical hold related to maximum exposure limit*

Iluzanebart (VGL101) Antibody TREM2 Agonist for Treatment of ALSP

Iluzanebart (VGL101) is an investigational therapy and has not been reviewed or approved by any regulatory authority

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ALSP: A Genetically-linked Microgliopathy with Significant Unmet Need

Epidemiology

- 10% adult-onset leukodystrophies:
  - Including ~10K patients in U.S. & ~15K patients in EU27+UK

Monogenic Disease

- Autosomal dominant *CSF1R* gene mutations

Clinical Phenotype

- Average age of onset in mid-40s
- Cognitive, neuropsychiatric and motor symptoms
  - Commonly misdiagnosed

Rapid Progression

- Incapacitated in 3-4 years; average time to death: 6-7 years

No Treatment

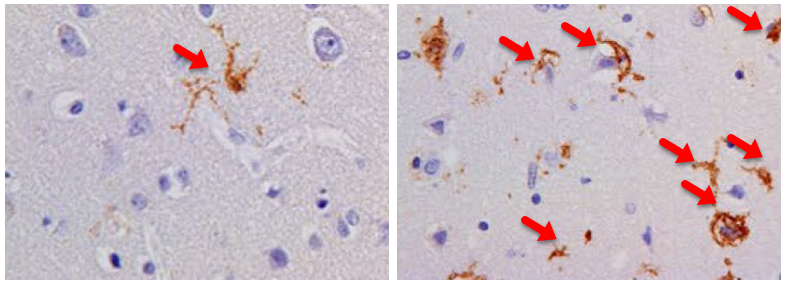
- No approved therapies or experimental treatments

Partnering with the ALSP Community

Lakshmanan et al, Neurol Genet 2017; Hayer et al, Neurology 2018; Lynch et al. J Neurol Neurosurg Psychiatry 2016; Konno et al. Neurol 2018; Ahmed et al. J Neurol Neurosurg Psych 2014; Papapetropoulos et al. Front. Neurol. 2022

Iluzanebart Rescues Microglial Deficiency Caused by CSF1R Mutations

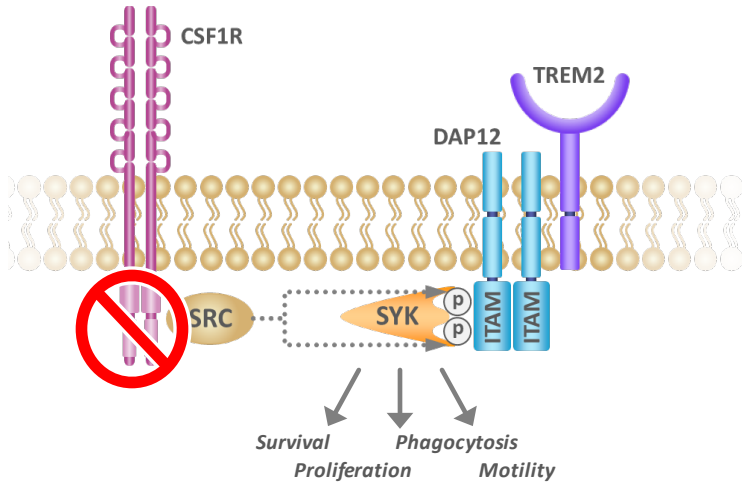
ALSP Disease Hallmark: Microglial Loss in CNS



ALSP Gray Matter | Control Gray Matter

IBA-staining; red arrows denote microglia - Berdowski et al. Acta Neuropath 2022

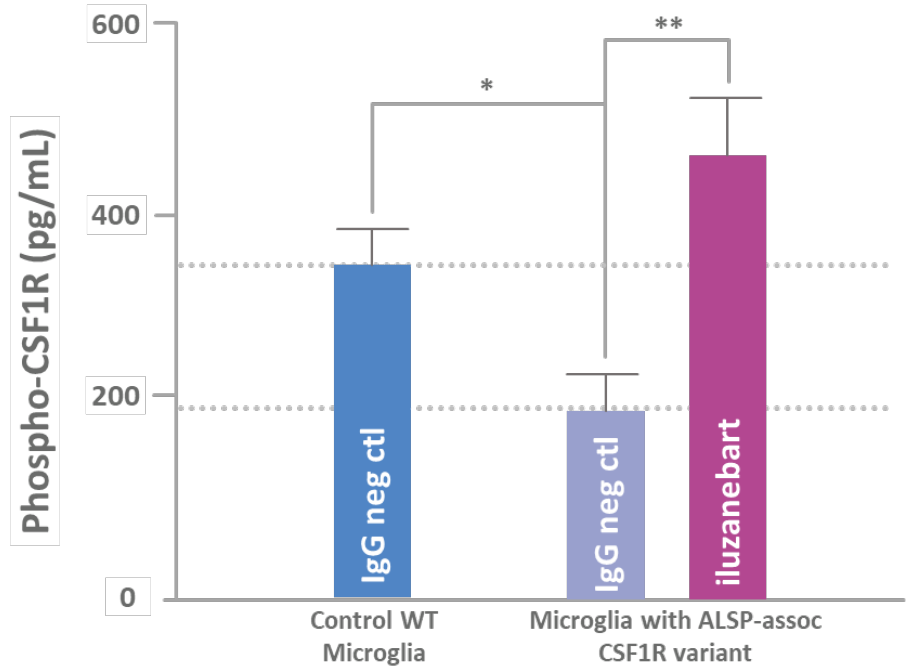
Hypothesis: TREM2 Activation Compensates for CSF1R LoF in ALSP



TREM2 Agonism via Iluzanebart

Pharmacological Rescue of ALSP-associated CSF1R Signaling & Human Microglia Dysfunction *In Vitro*

Validation: Iluzanebart Compensation of CSF1R Signaling Defect



** p < 0.05; ** p < 0.01*

Summary of Iluzanebart Phase 1 Data in Healthy Volunteers

Phase 1 SAD/MAD trial exploring safety, tolerability, PK & PD

- ☑ Favorable safety & tolerability profile demonstrated
- ☑ Human PK linearity/predictability & long half-life supports monthly dosing
- ☑ Proof of target engagement and pharmacological activity in healthy volunteers
- ☑ 1st antibody to report durable effect on microglial activity biomarkers in clinical setting

Phase 1 data support iluzanebart 20 and 40 mg/kg as pharmacologically active doses

Phase 2 IGNITE PoC trial in ALSP ongoing

SAD: single ascending dose; MAD: multiple ascending dose; PK: pharmacokinetics; PD pharmacodynamics

ILLUMINATE: First Natural History Study in ALSP

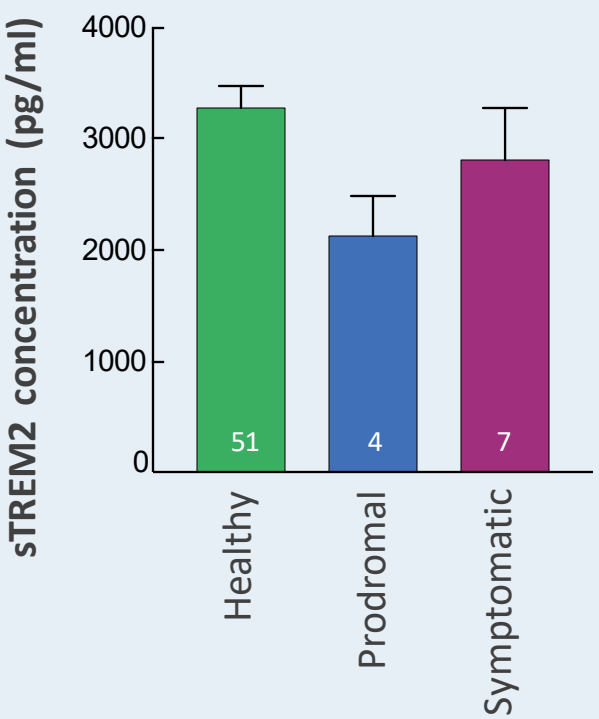
Setting up for clinical success in ALSP

- Ongoing natural history study of ALSP patients with *CSF1R* gene mutation
- Enrolling up to 50 subjects globally
- Observation period: 24 months
- To characterize MRI & CSF biomarkers, and clinical measures of disease progression in ALSP
- Potential to serve as synthetic control for interventional trial(s) & support disease modeling

ILLUMINATE: NCT05020743

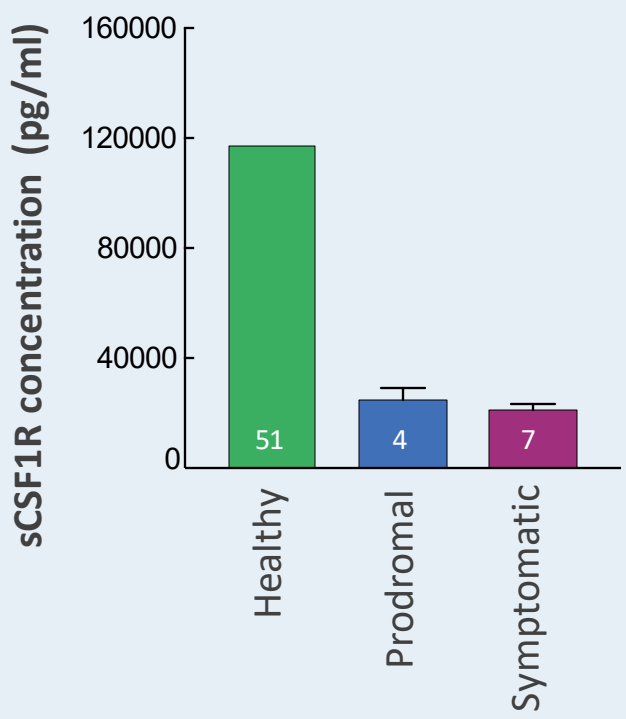
Baseline Fluid Biomarker Levels Altered in ALSP

Baseline Soluble TREM2 Levels in CSF



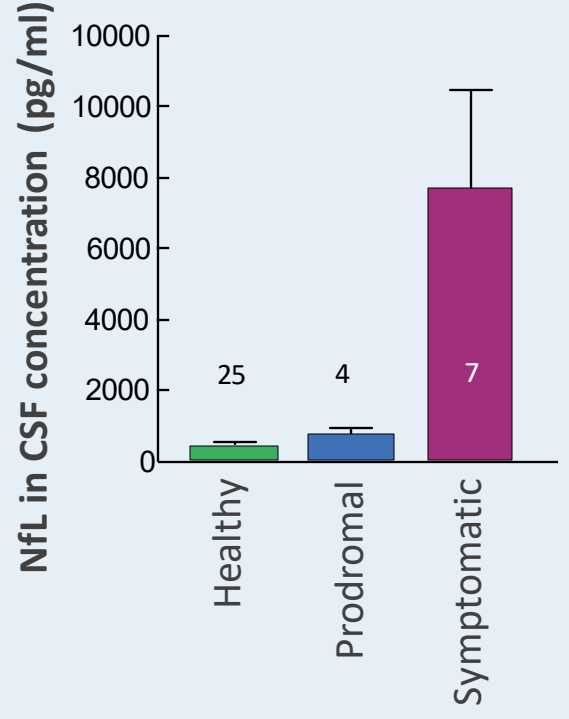
sTREM2 levels similar across all populations

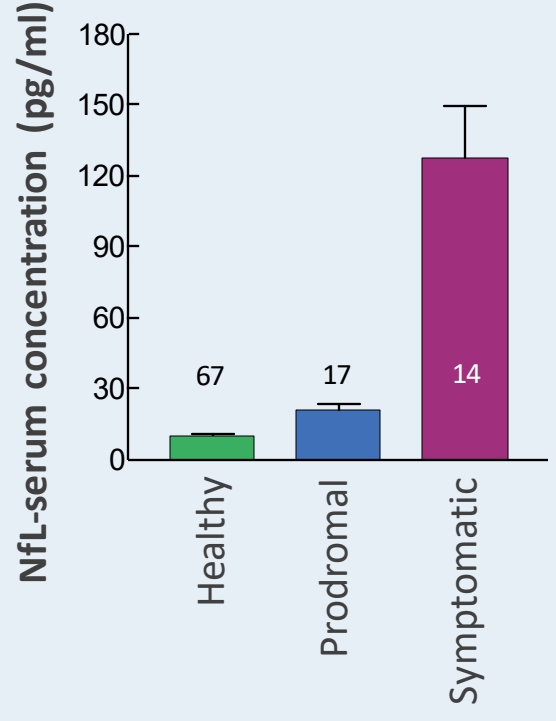
Baseline Soluble CSF1R Levels in CSF



sCSF1R levels significantly reduced in prodromal and symptomatic

Baseline NfL Levels in CSF (Left) & Serum (Right)





NfL levels highly elevated in symptomatic

Healthy: healthy volunteers from Vigil's VGL101 Phase 1 trial; Prodromal: participants with confirmed CSF1R mutation and MRI findings with <3 ALSP-related clinical signs or symptoms in Vigil's Natural History Study ILLUMINATE (NCT05020743); Symptomatic: subjects with CSF1R mutations and ≥3 ALSP-related clinical signs or symptoms in ILLUMINATE; CSF1R: Colony Stimulating Factor 1 Receptor; CSF: cerebrospinal fluid; NfL: neurofilament light chain

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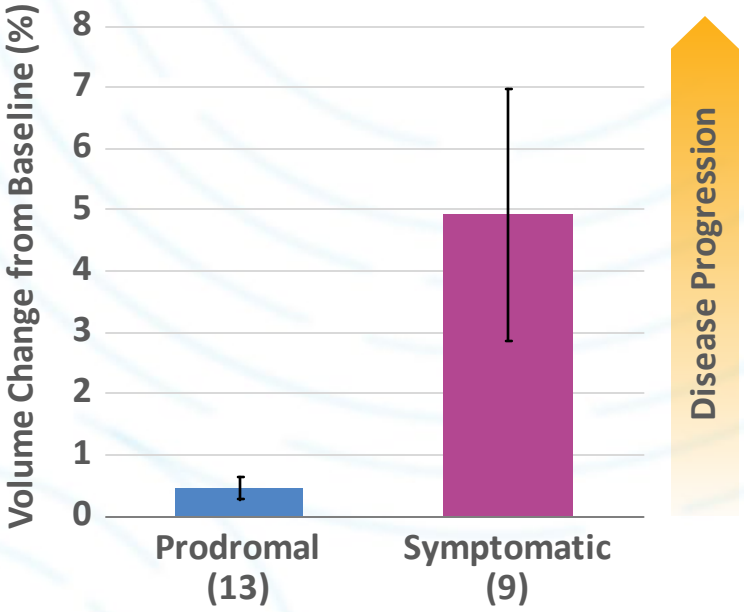
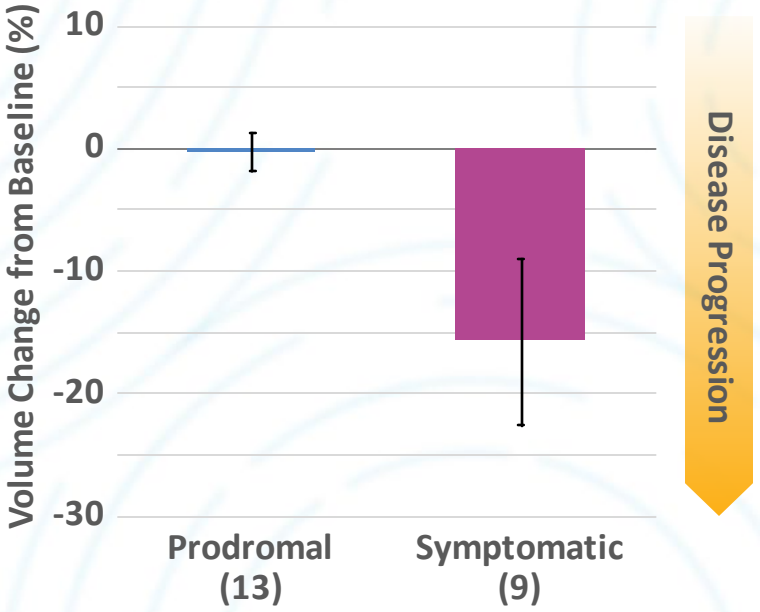
MRI Biomarkers of Disease Progression Precede Cognitive Decline

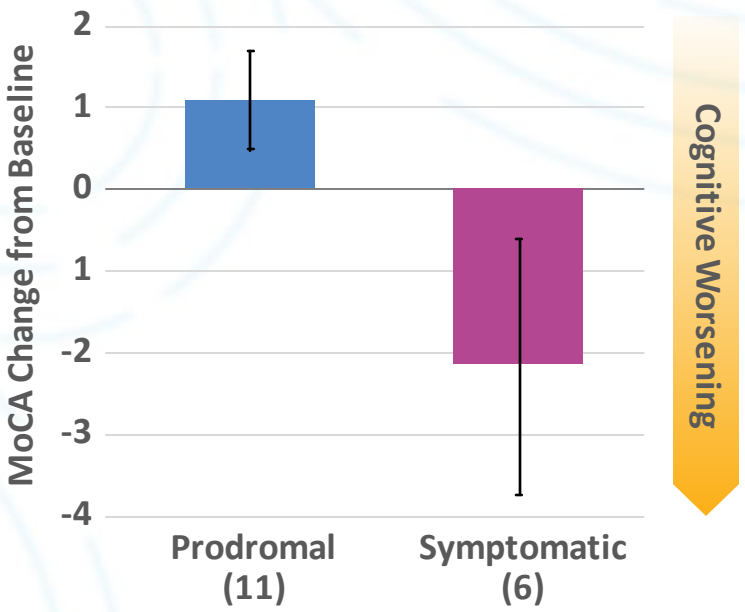
Greater ventricular expansion, gray matter atrophy & cognitive impairment (MoCA) in symptomatic vs. prodromal patients

Ventricular Volume | **Gray Matter Volume** | **Montreal Cognitive Assessment (MoCA)***

Change from Baseline at Month 6 | **Change from Baseline at Month 12**







Plots are Mean ± SE

** Montreal Cognitive Assessment: 30-point assessment on multiple cognitive domains including executive function, memory, visuospatial ability, language, and attention*

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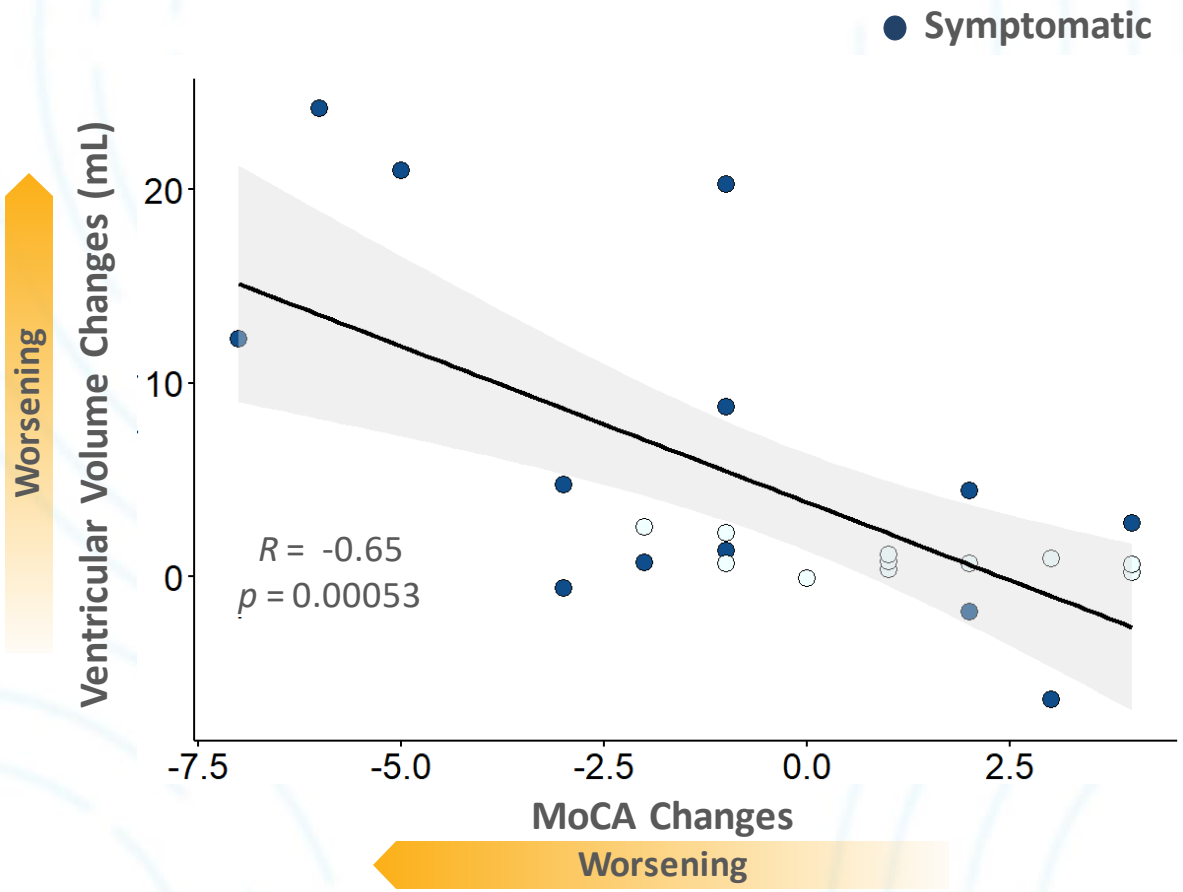
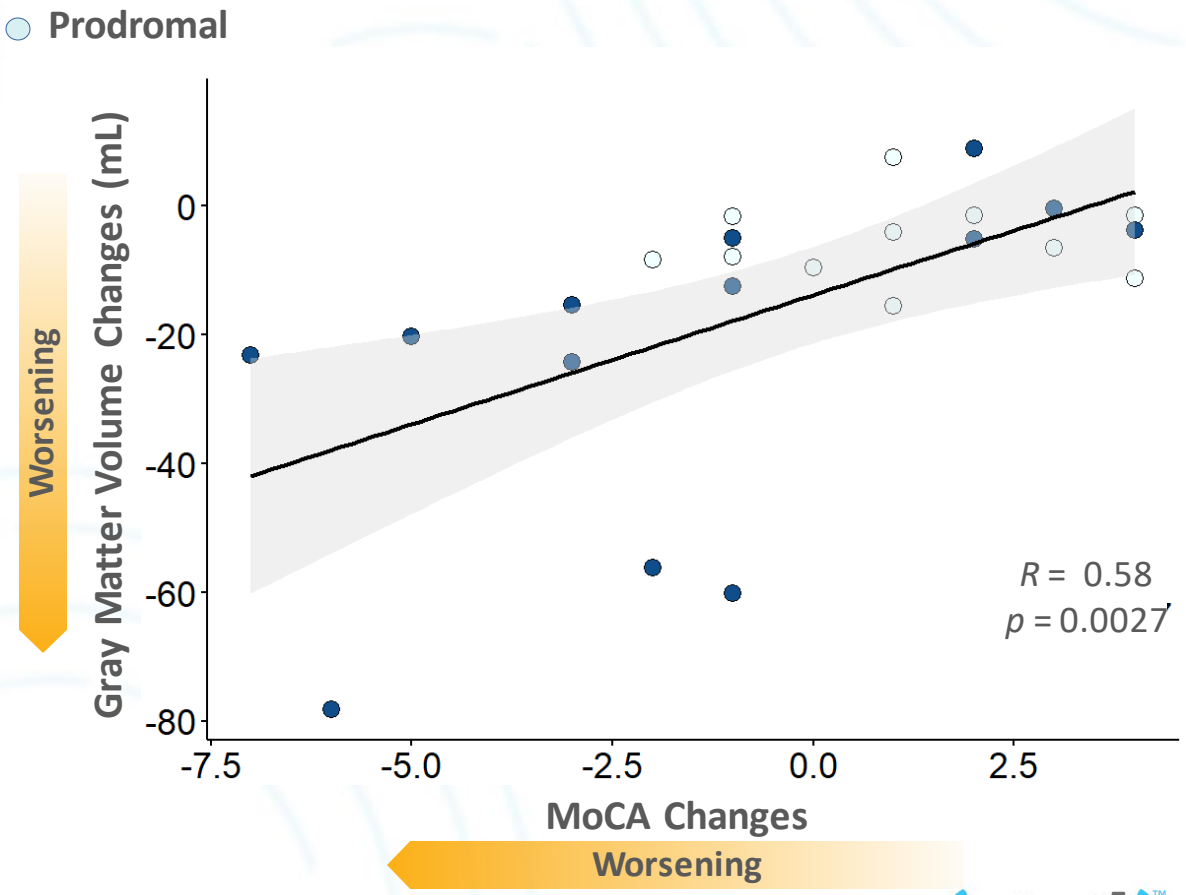
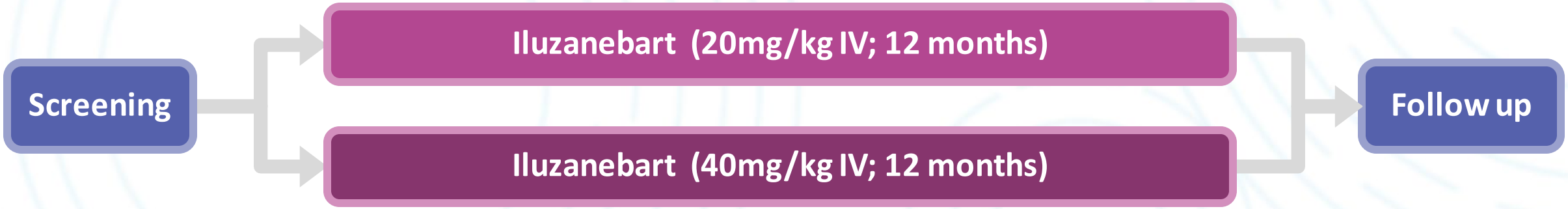
MRI Biomarkers of Disease Progression Correlate with Cognitive Decline

Ventricular/Gray matter volume changes correlate with MoCA changes at 12 Months





Evaluating Iluzanebart for ALSP in IGNITE Phase 2 Open-Label Proof-of-Concept Trial



Trial Population	▪ Patients with symptomatic ALSP related to *CSF1R* gene mutation
Trial Design	▪ Open-label, ~15 patients
Treatment Duration	▪ 12 months (with opportunity for further extension), monthly IV administration of iluzanebart
Outcome Assessments	▪ Safety and tolerability of Iluzanebart in ALSP patients ▪ MRI-based assessment of brain and ventricular volume, and white matter lesions ▪ CSF biomarkers for neurodegeneration and PD (NfL, sCSF1R, sTREM2, osteopontin) ▪ Clinical outcome measures (MoCA, CBFS, CDR+NACC+FTD) and PK
Interim Analysis	▪ 6 months (n=6: 20 mg/kg); Completed
Primary Analysis	▪ 6 months (all subjects: 20 mg/kg + 40 mg/kg)
Final Analysis	▪ 12 months (all subjects: 20 mg/kg + 40 mg/kg)

Clinicaltrials.gov identifier: NCT05677659

IGNITE Phase 2 Interim Readout: Favorable Safety & Tolerability Profile

Safety data summary

Summary of Safety Outcomes (N=6)[a]	
	Patients with TEAEs
Any AE, n (%)	4 (66.7)
Treatment-related AEs, n (%)[b]	2 (33.3)
Mild[c]	2 (33.3)
Moderate[c]	1 (16.7)
Severe	0
Treatment-related AEs occurring in ≥2 participants, n (%)	0
SAEs, n (%)	1 (16.7)
Treatment-related serious AEs, n (%)	0
Discontinuation of study drug due to AEs, n (%)	0

[a] IGNITE Ph2 interim data cut as of 22 September 2023

[b]Events determined by investigator to be "related" to study drug.

[c]Mild to moderate AEs include 1 patient with mild hepatic enzyme increase and; 1 patient with both mild irritability, tremor and lethargy, and moderate pruritus, lethargy and amnestic disorder (memory loss)

AE: adverse event; SAE: serious adverse event; TEAE: treatment emergent adverse event

Overview of Safety & Tolerability:

- Iluzanebart was generally well tolerated
- Majority of patients did not report treatment-related AEs
- No treatment-related severe AE or SAE
- No discontinuations due to AE
- One patient was briefly hospitalized for non-treatment related SAEs of abdominal pain, asthenia, vomiting, and diarrhea
- No hematological AEs
- No imaging-related abnormalities

Emerging Patient Segments in IGNITE Phase 2 Interim Readout

Progressive Disease
at baseline

- NfL significantly higher than age-normal range
- MoCA <26
- Significant neurodegeneration with cognitive impairment as one of ALSP symptoms

Cognitively Normal
at baseline

- NfL within age-normal range
- MoCA ≥26
- Have other ALSP symptoms except cognitive

Potentially Converting
at baseline

- NfL higher than age-normal range
- MoCA ≥26
- Evidence of neurodegeneration
- Have other ALSP symptoms except cognitive

IGNITE Phase 2: Summary of Biomarker Changes

6-month interim analysis[1]

ALSP Patient Segment	Patient[1]	Baseline NfL (pg/mL)	Baseline MoCA	ΔMRI Venticular[2]	ΔMRI Gray Matter[2]	ΔsCSF1R CSF[3]	ΔNfL Serum[4]	VGL101 Impact Based on Biomarker Changes
Progressive Disease	A	80	17					Slowing progression
	B	159	21					Slowing progression
	F	54	25					Slowing progression
Cognitively Normal	D	10	28					Stabilization
	E	12	28					Stabilization
Potentially Converting	C	42	30					Variable impact

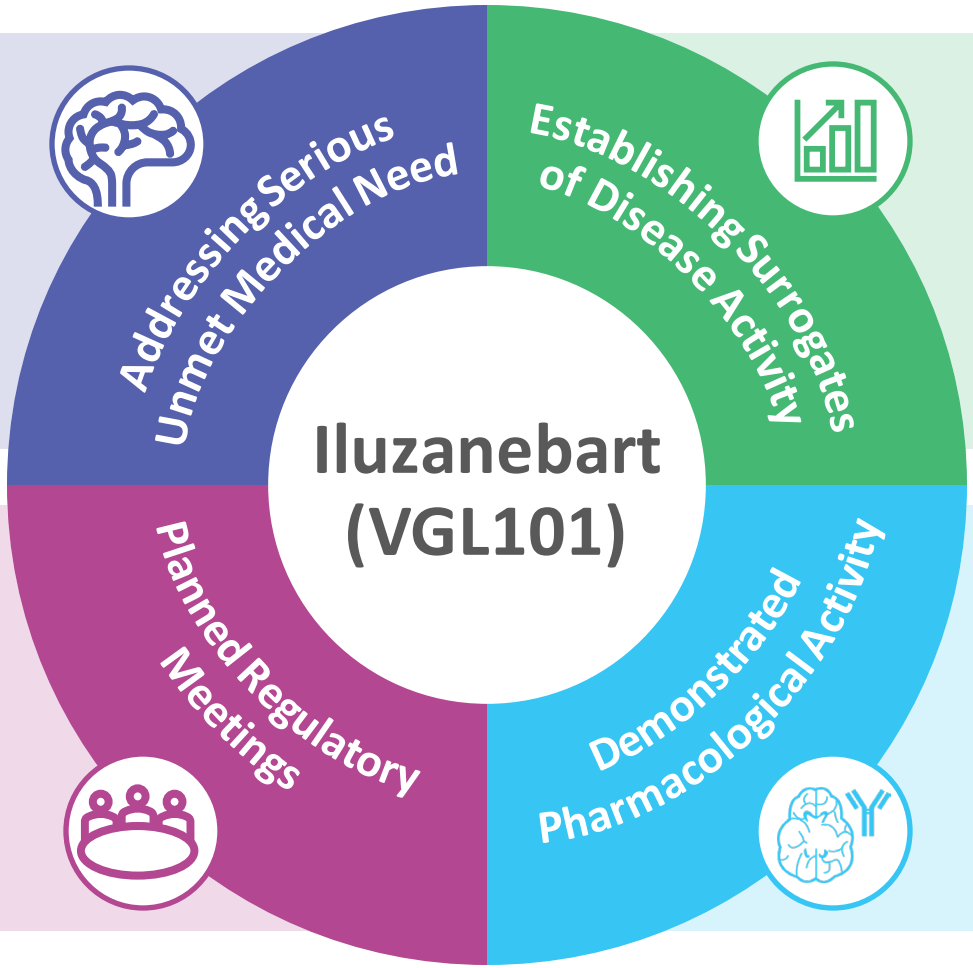
1. Please refer to presentation of interim Phase 2 IGNITE data (including individual patient data) on our corporate website (www.vigilneuro.com); 2. MRI trajectories for 0 to 6 mos in IGNITE vs pre-IGNITE run-in data (from ILLUMINATE) for each patient - ΔMRI Ventricular: change to ventricular MRI trajectory, ΔMRI Gray Matter: change to gray matter MRI trajectory; 3. sCSF1R levels in cerebrospinal fluid (CSF) at 6 mos vs 0 mos (IGNITE baseline); 4. NfL trajectories for 0 to 6 mos vs pre-IGNITE run-in data (from ILLUMINATE; for Patients B, D, E & F) or for 6 to 9 mos vs 0 to 6 mos in IGNITE (Patients A & C)

- Meaningful changes in a direction consistent with treatment benefit
- Meaningful changes in a direction not consistent with treatment benefit
- Limited changes in a direction consistent with treatment benefit
- Limited changes in a direction not consistent with treatment benefit

Positioning Iluzanebart for Potential Accelerated Development Pathway

Additional IGNITE Phase 2 data expected in Q3 2024

- Fatal, rare, rapidly progressing neurodegenerative disorder
- No approved therapy



- MRI biomarkers correlating with cognitive changes
- NfL levels indicative of disease severity

- Several regulatory engagements planned for 2024
  - Discuss NHS & interim Ph2 data for potential accelerated development

- Target engagement with mechanistic link - iluzanebart increased sCSF1R levels (very low in untreated patients)
- Directionally supportive changes on MRI & NfL for iluzanebart in Ph2

VG-3927
Small Molecule TREM2 Agonist for Treatment of Alzheimer's Disease

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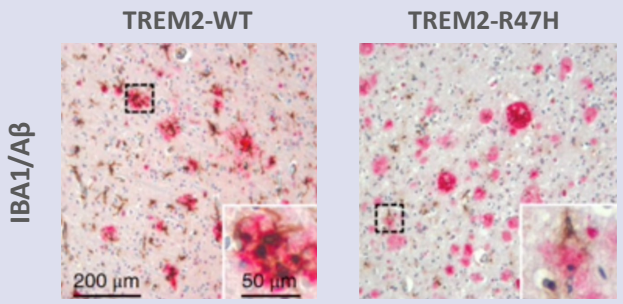
Importance of TREM2 Agonism in Alzheimer's Disease

Genetic Support

Human Microglia Play a Central Role in Alzheimer's Disease (AD)

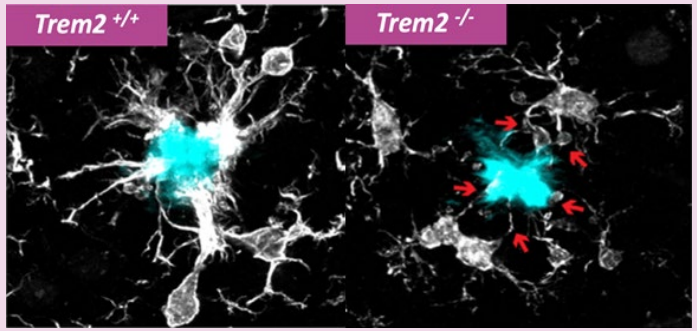
- AD risk variants impair microglia clustering around Aβ plaques



Microglia (IBA-1 staining) *Amyloid plaques (Aβ staining)*

Loss of TREM2 Function Worsens Neurodegeneration in AD Models

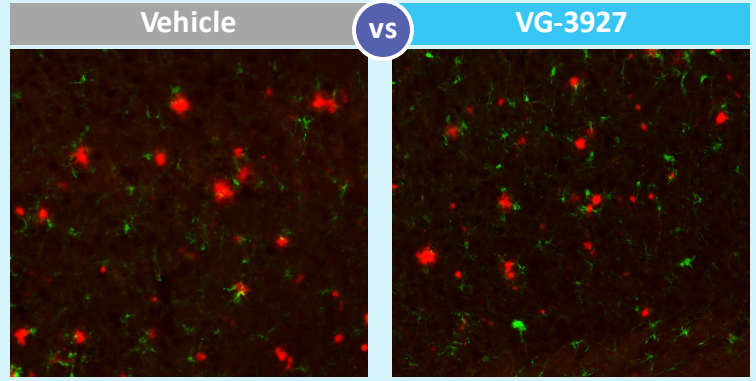
- TREM2 deficiency is associated with both Aβ and tau pathology in *in vivo* models



Microglia (IBA-1 staining) *Amyloid plaques*

TREM2 Small Molecule Agonist: Broad Potential to Reduce AD Pathology via Oral Dosing

- Preclinical evidence suggests TREM2 agonism has potential to reduce Aβ pathology



Microglia (IBA-1 staining) *Amyloid plaques*

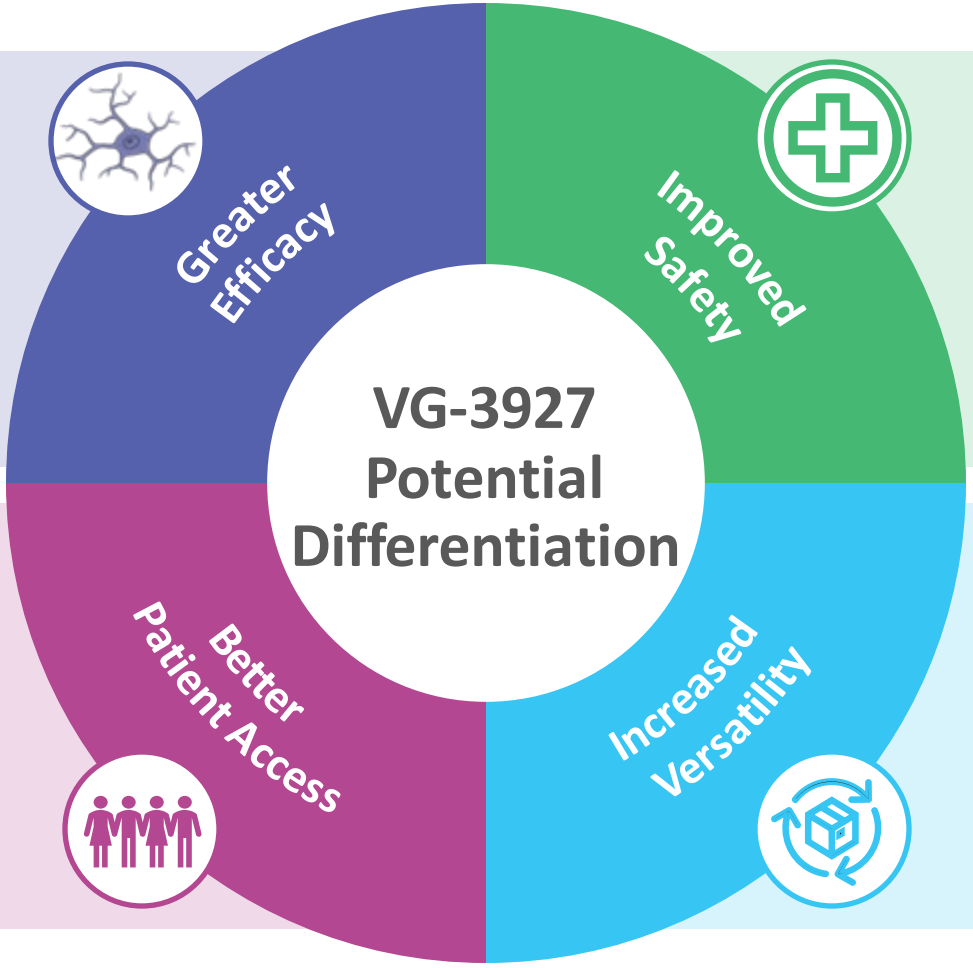
Parhizkar et al. Nat Neurosci. 2019; Yuan et al Neuron 2016

VG-3927: First & Only Clinical-stage Small Molecule TREM2 Agonist

Potential to become next-generation AD treatment

- Boosting microglial repair functions
- Impact broader disease pathophysiology

- Convenient & patient-friendly oral dosing

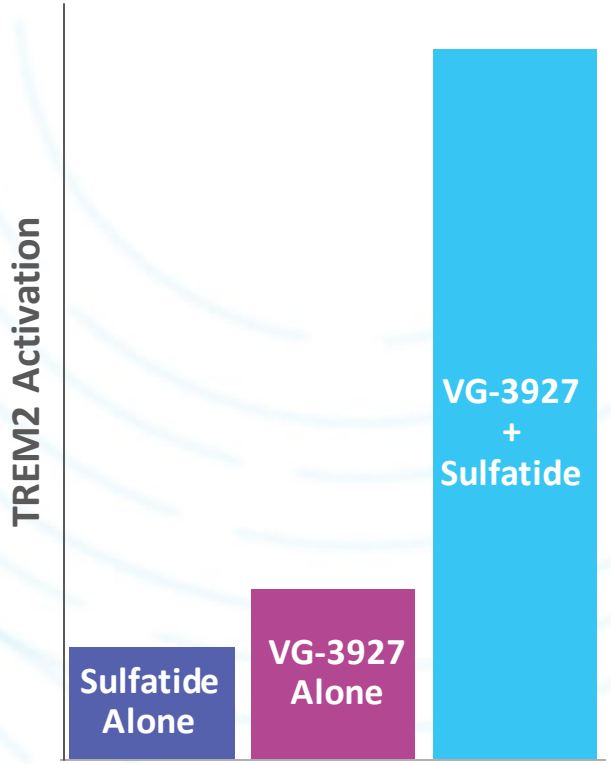


- Wider therapeutic window: synergy with natural damage ligands
- ARIA mitigation & management

- Small molecule optimal for future combination therapy & preventive paradigms

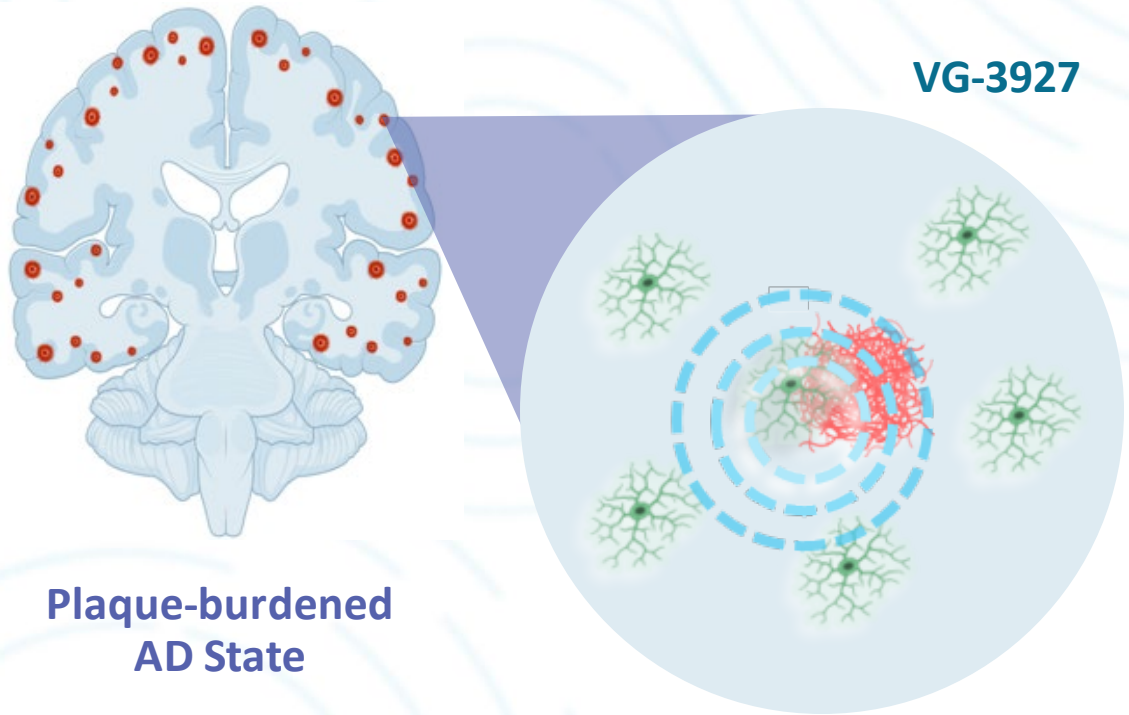
VG-3927 Potentiates Signaling of Damage-associated Ligands

Potentiation of TREM2 Activation



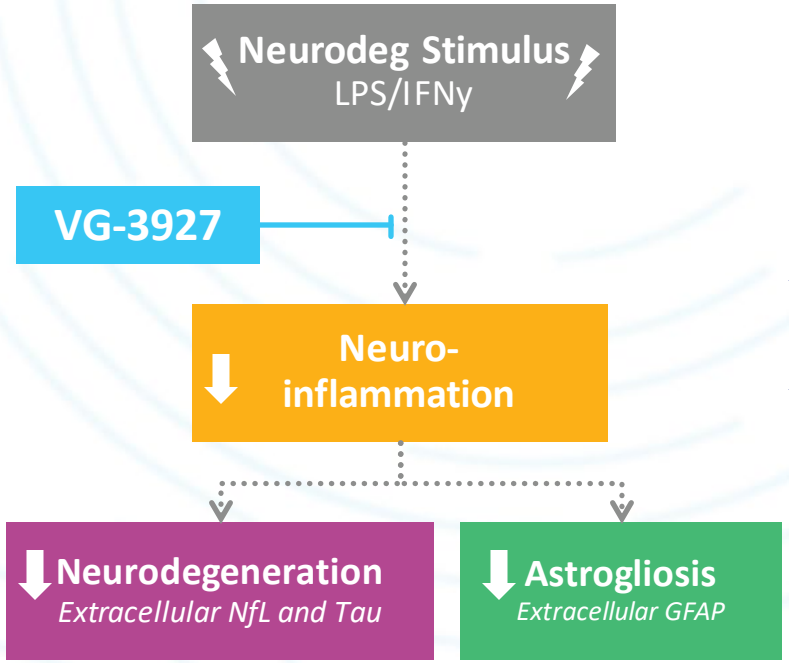
Sulfatide: natural damage ligand

Focusing Efficacy in Pathological Microenvironments



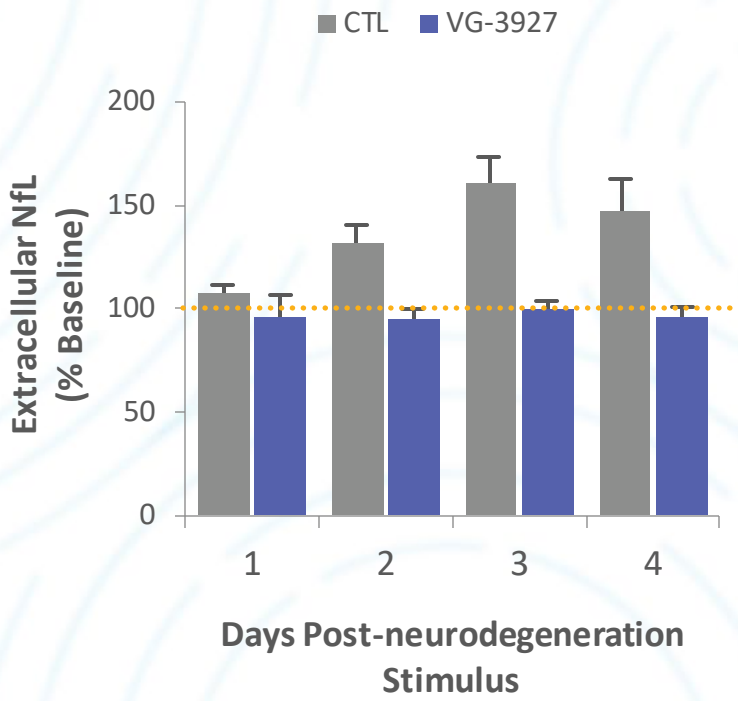
VG-3927 Protects Against Biomarkers of Inflammation-induced Neurodegeneration

TREM2 Agonism Activates Anti-inflammatory Benefit

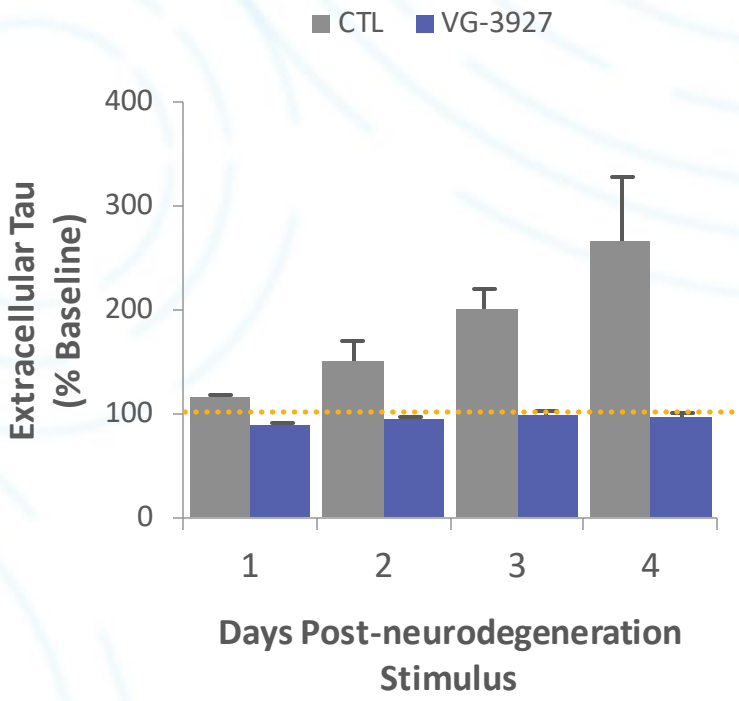


LPS: lipopolysaccharide; IFNY: interferon-gamma
GFAP: glial fibrillary acidic protein

VG-3927 Suppresses Extracellular NfL & Tau Accumulation in LPS Model



$ANOVA_{Treatment}$, $p<0.05$



$ANOVA_{Treatment}$, $p<0.05$

VG-3927 Reduces Aβ Pathology in Plaque-bearing Mice

Effects following 6 weeks of oral dosing

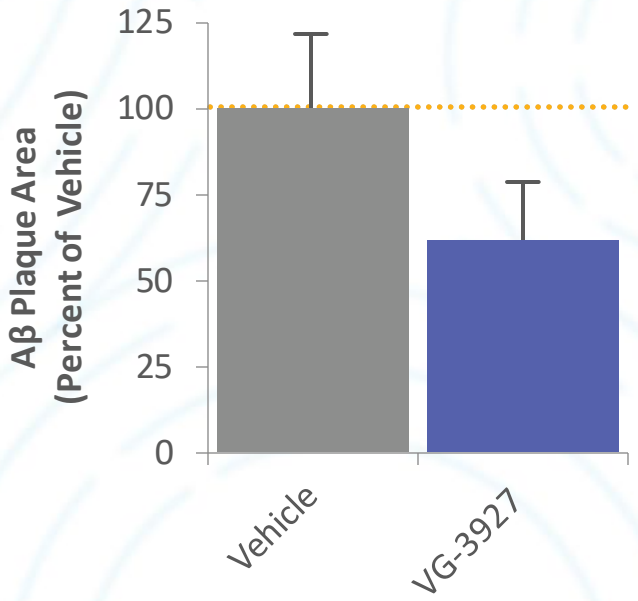
VG-3927 Effects in Humanized TREM2 AD Mouse Model

- VG-3927 dosing initiated at ~5 months (plaque deposition already ongoing)
- Trend toward reducing plaque area and insoluble Aβ

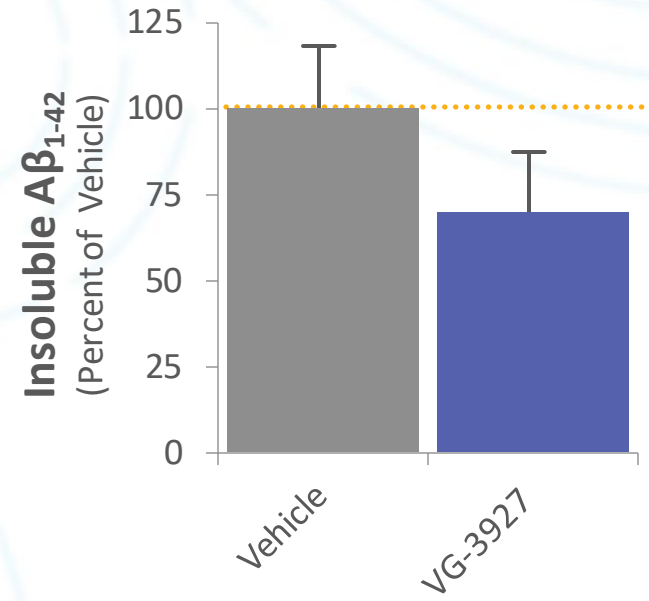
Daily Dosing for 6 Weeks

VG-3927
10mpk
QD

VG-3927 Effects on Aβ Plaque Area
Immunohistology from Brain Slices

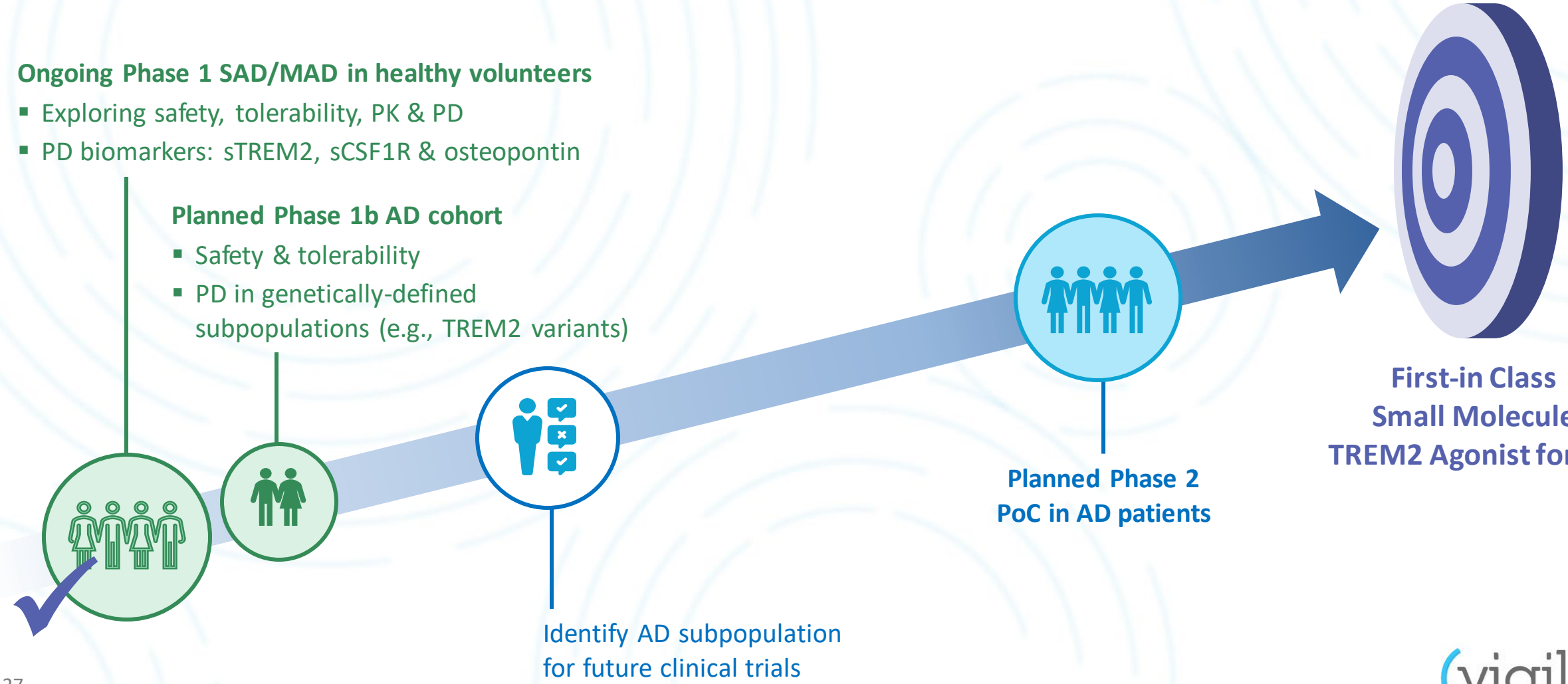


VG-3927 Effects on Insoluble $Aβ_{1-42}$
Biochemistry of Brain Homogenates



VG-3927: Early-Stage Clinical Strategy to De-Risk Development for AD

Leveraging precision-based approach to increase probability of success in AD drug development



Corporate Overview

vigilant for you®

Achieved & Anticipated Milestones

☑	Report full data analysis for Phase 1 trial with iluzanebart in healthy volunteers	**Q3 2023**
☑	Begin Phase 1 dosing of VG-3927 in healthy volunteers	**Oct 2023**
☑	Report iluzanebart six-month interim data on six patients from IGNITE Phase 2 trial in ALSP	**Q4 2023**
☐	Report VG-3927 interim Phase 1 data in healthy volunteers	**Mid-2024**
☐	Report iluzanebart IGNITE Phase 2 data on all patients at 6 months (20mg/kg & 40mg/kg doses)	**Q3 2024**

Vigil is Well-positioned to Execute on Our Mission