Vigil Neuroscience

VGL101 Phase 1 Interim Topline Data Results in Healthy Volunteers

November 2, 2022

vigil™ NEURO

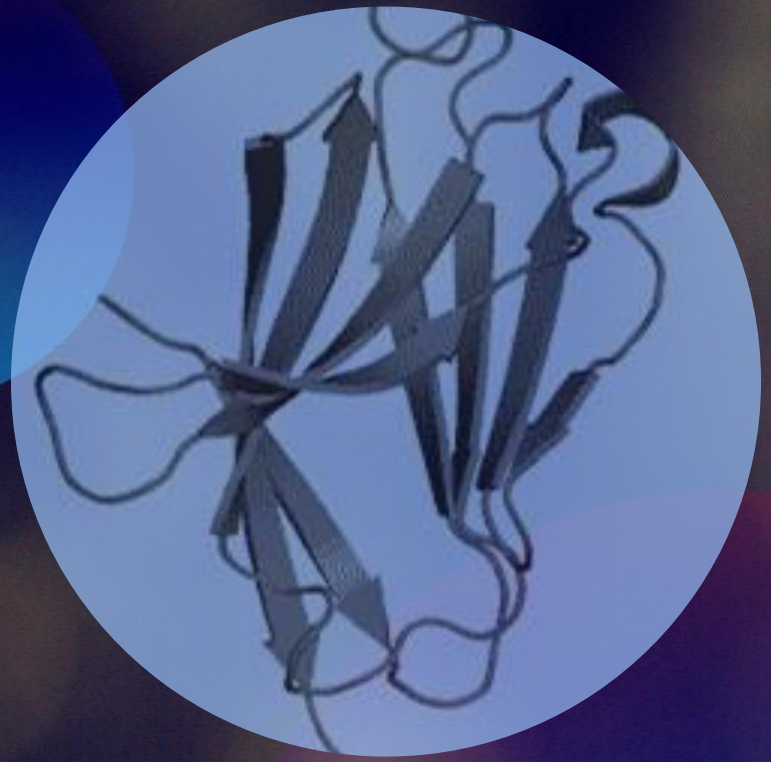
vigilant for you®

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 VGL101 and small molecules active against TREM2, and to enable success in ALSP in clinical development; our analyses and beliefs about data, including the VGL101 interim data and that it supports further dose escalation and Phase 2 initiation; plans and upcoming milestones, including estimated timelines, for our pipeline program development activities; and expected timing and next steps regarding clinical trial activities and regulatory filings and approvals.

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 conducting and reporting data analyses; 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, analyses and timing of results and data from preclinical and clinical studies and whether results from preclinical studies and early interim data will be predictive of the results of later preclinical studies and data readouts, and other clinical trials; 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 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; the effect of the COVID-19 pandemic, including mitigation efforts and economic impacts, on any of the foregoing or other aspects of our business operations, including our preclinical studies and clinical trials; 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 and in any subsequently filed Quarterly Reports on Form 10-Q, and such other risks and uncertainties that may be described in other filings we 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.

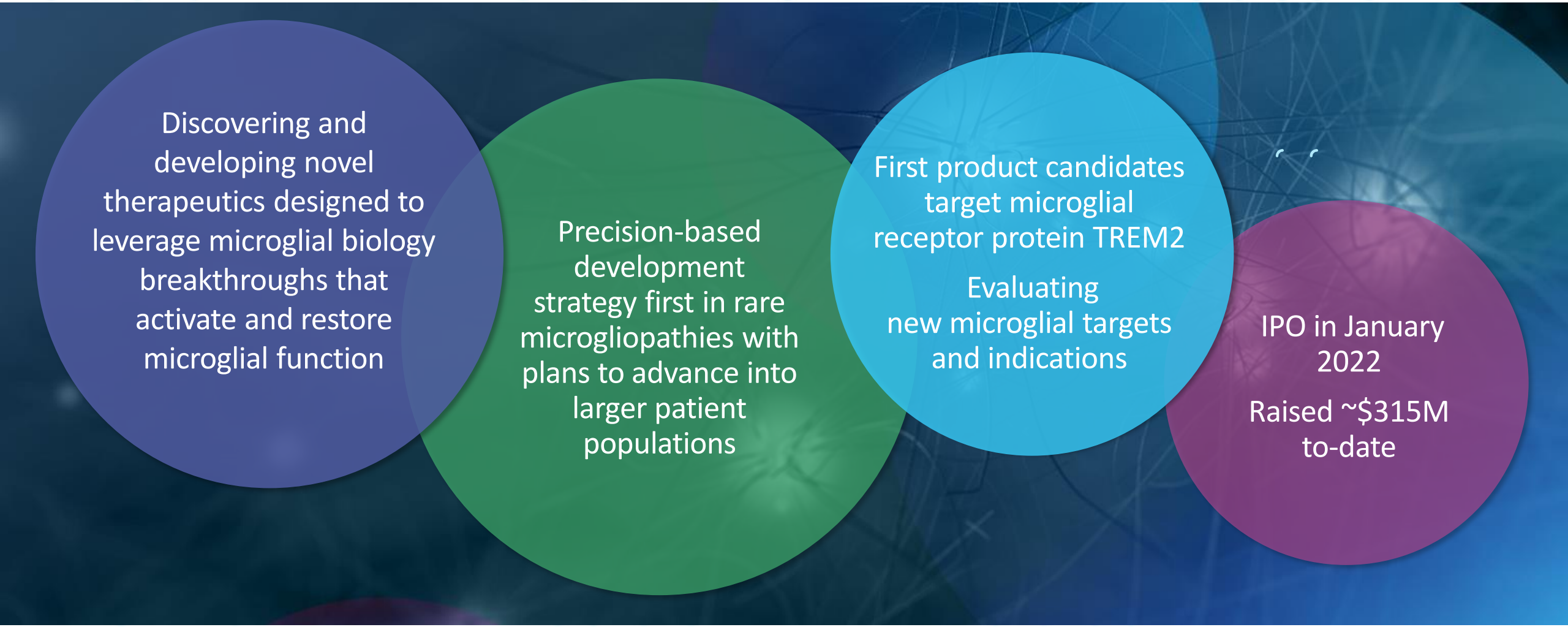


Opening Remarks

Ivana Magovcevic-Liebisch, President & CEO

vigilant for you®

Vigil's Mission: Restoring Microglial Vigilance to Create Disease-Modifying Treatments for Neurodegenerative Diseases



Vigil TREM2 Agonists: Differentiated Strategy & Multiple Modalities

Vigil Neuroscience

TREM2 mAb in Development for ALSP: VGL101

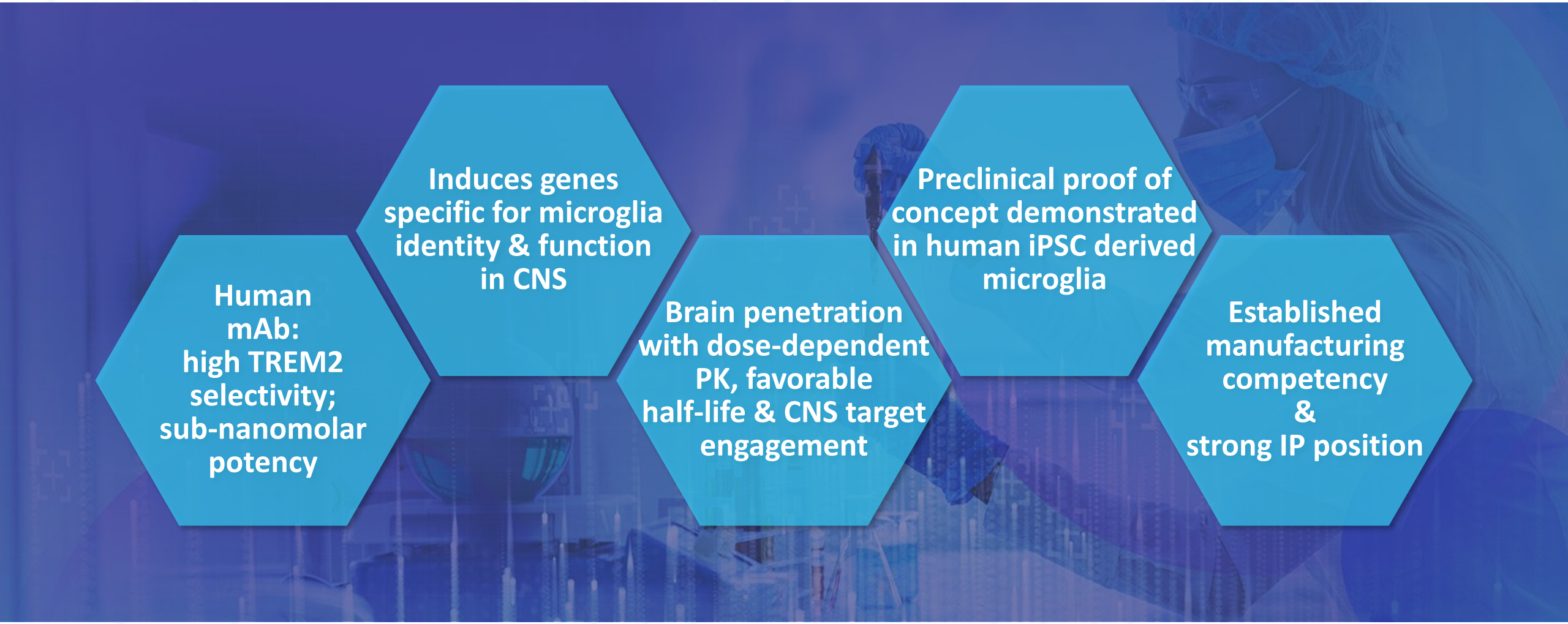
*The **ONLY** targeted drug candidate in development for ALSP*

Small Molecule TREM2 Agonist in Development for Larger Indications

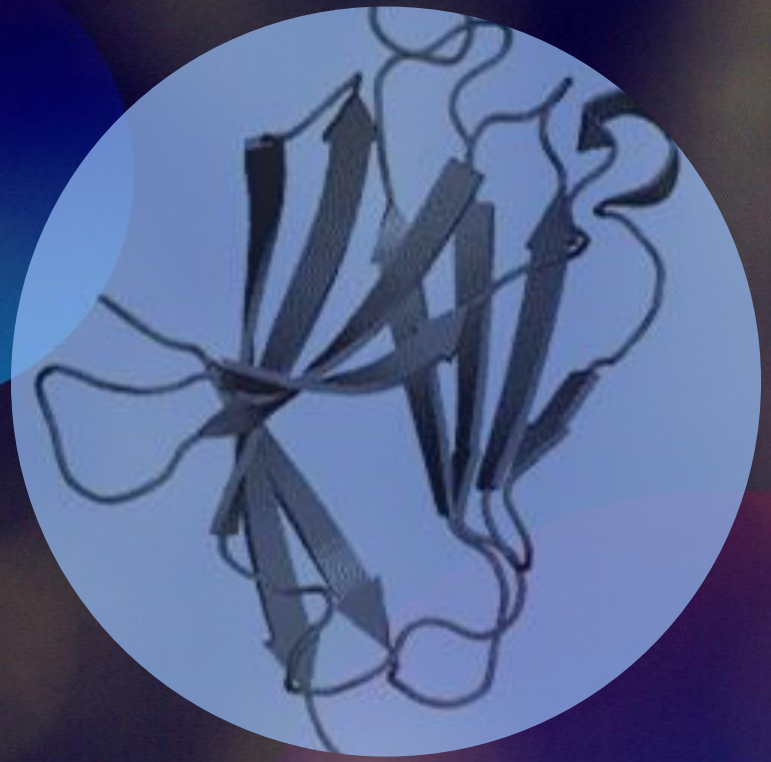
*The **ONLY** TREM2 small molecule agonist in development*

ALSP: Adult-onset leukoencephalopathy with axonal spheroids and pigmented glia

VGL101 – Antibody Agonist of TREM2 with a Compelling Profile



mAb: monoclonal antibody
iPSC: induced pluripotent stem cells



VGL101 Interim Topline Phase 1 Results in Healthy Volunteers

Spyros Papapetropoulos, Chief Medical Officer

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

vigilant for you®

Trial Design: VGL101 Phase 1 SAD/MAD in Healthy Volunteers

Single Ascending Doses (SAD) of VGL101; 1 Infusion Total

Double-blind Randomized Cohorts

- 1 mg/kg n = 8 (6:2)
- 3 mg/kg n = 8 (6:2)
- 10 mg/kg n = 7 (5:2)
- 20 mg/kg n = 9 (6:3)
- 30 mg/kg n = 7 (6:1)
- 40 mg/kg n = 8 (6:2)
- 60 mg/kg n = 8 (6:2)[1]

Open-Label Cohorts for CSF Collection

- 3, 10, 20 mg/kg n = 19
- 40[2], 60 mg/kg

Multiple Ascending Doses (MAD) of VGL101, Every 28 Days, 3 Infusions Total

Double-blind Randomized Cohorts

- 20 mg/kg n = 8 (6:2)
- 40 mg/kg n = 8 (6:2)[1,2]
- 60 mg/kg n = 8 (6:2)[1]

Open-Label Cohorts for CSF Collection

- 20 mg/kg n = 8
- 40, 60 mg/kg

Completed cohort included for PD
Completed cohort included for PK
Completed cohort included for safety

[1]Targeted enrollment and randomization
[2] Ongoing cohorts

VGL101 Demonstrated Favorable Safety & Tolerability Profile at Doses up to 40 mg/kg SAD and 20 mg/kg MAD*

No reports of Serious Adverse Events (SAEs) or Adverse Events (AEs) of special interest to date*

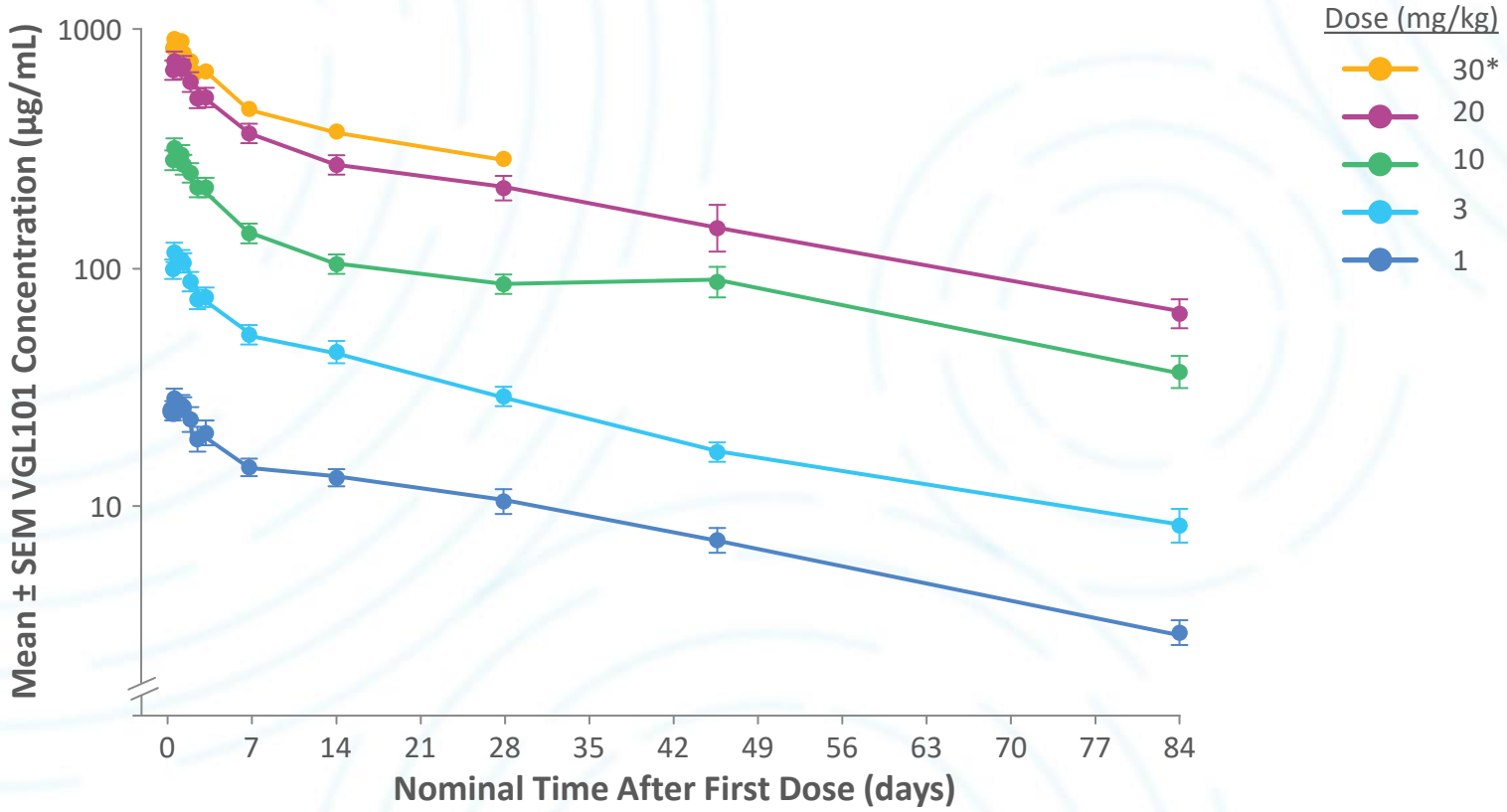
- 82 healthy volunteers have been dosed in the ongoing first-in-human Phase 1 SAD/MAD trial
  - 68 subjects received VGL101
  - 14 subjects received placebo
- In blinded interim safety review of completed cohorts VGL101 was generally safe and well tolerated
  - Across cohorts, all AEs were mild with the exception of one moderate AE of dizziness and all AEs resolved without intervention
  - No report of serious adverse events
  - No clinically meaningful abnormalities in
    - Vital signs
    - Electrocardiograms
    - Laboratory parameters
- Protocol-specified stopping criteria were not met

VGL101 Safety & Tolerability to Date Supports Further Dose Escalation and Phase 2 Initiation in ALSP Patients

* As of October 7, 2022

VGL101 Has Well-Characterized Linear & Dose Proportional PK

Single Ascending Dose Pharmacokinetics (PK)

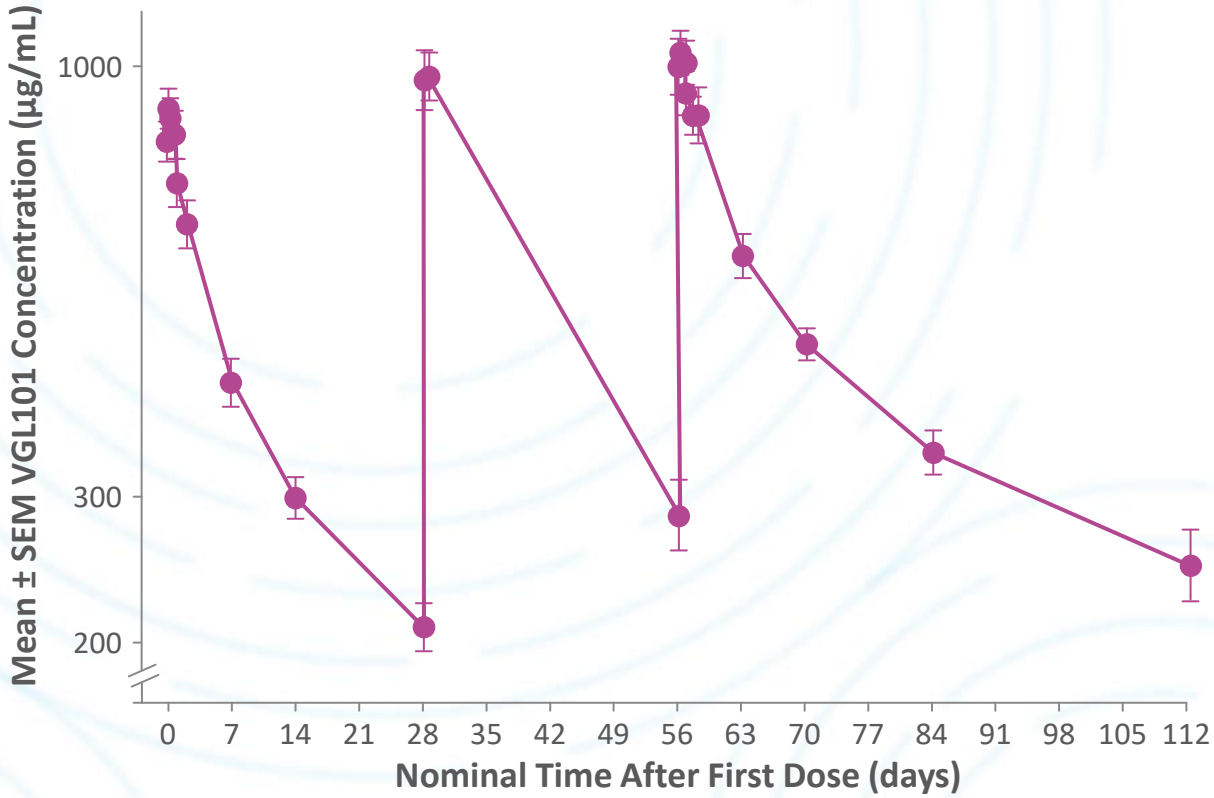


As of October 7, 2022

*Data on 30 mg/kg dose available for up to 28 days post-dose. Terminal data not yet available.

VGL101 Has Predictable PK with Repeat Dosing

20 mg/kg Multiple Dose PK
(3 doses at 28-day intervals; n=12)



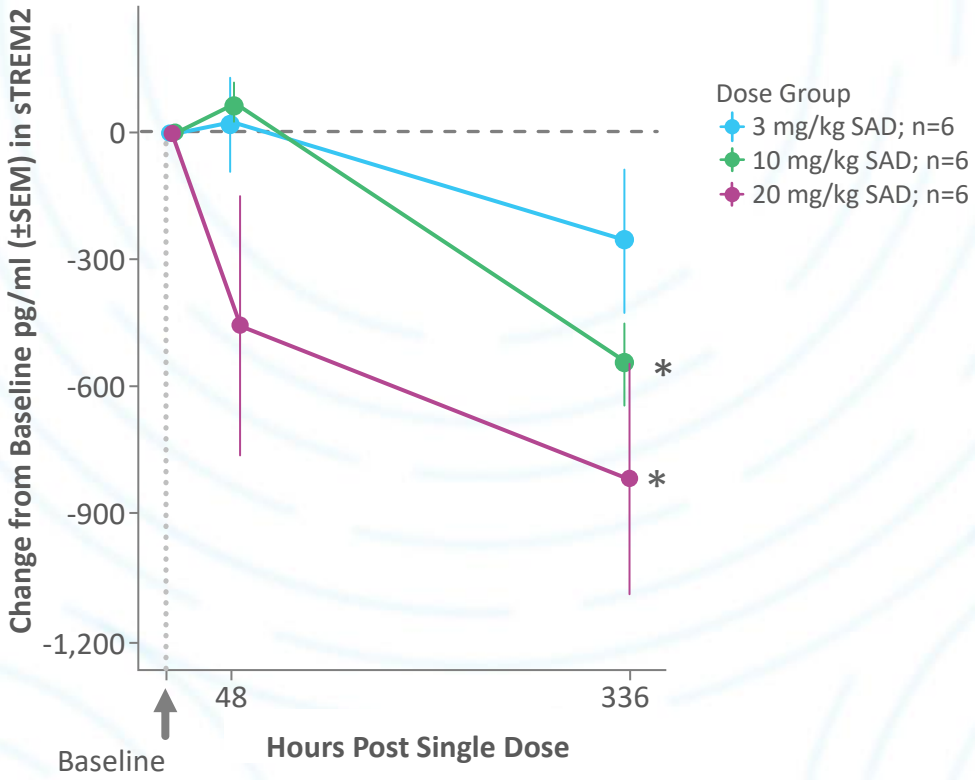
- ~27 days half-life supporting monthly dosing interval
- Brain penetration and achieving projected CSF therapeutic exposures
  - 0.1 – 0.2% CSF-to-serum ratio

As of October 7, 2022
SEM: Standard Error of Mean

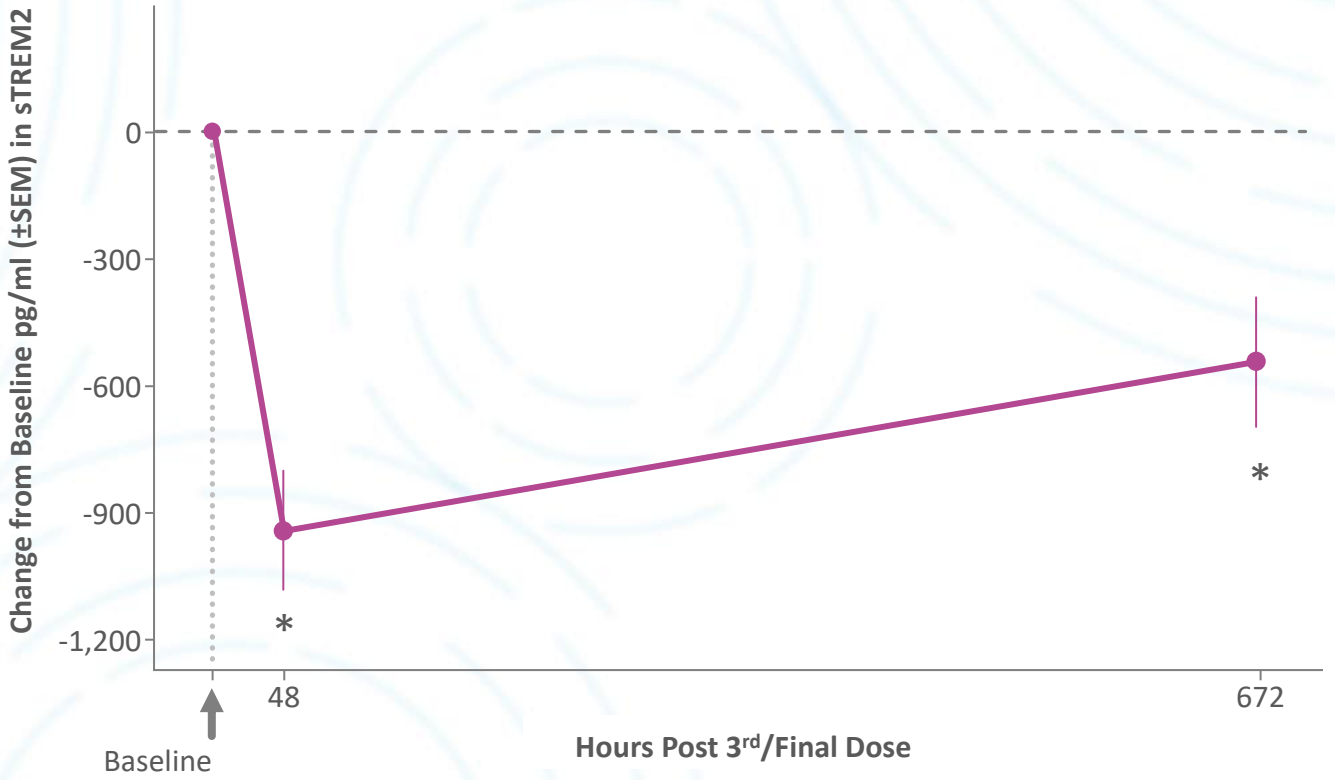
Proof of Target Engagement: VGL101 Has Dose Dependent, Robust & Durable sTREM2 Decreases

Absolute change in concentration of sTREM2 in cerebrospinal fluid (CSF)

Single Ascending Doses



20 mg/kg Multiple Dose
(3 doses at 28-day intervals; n=6)

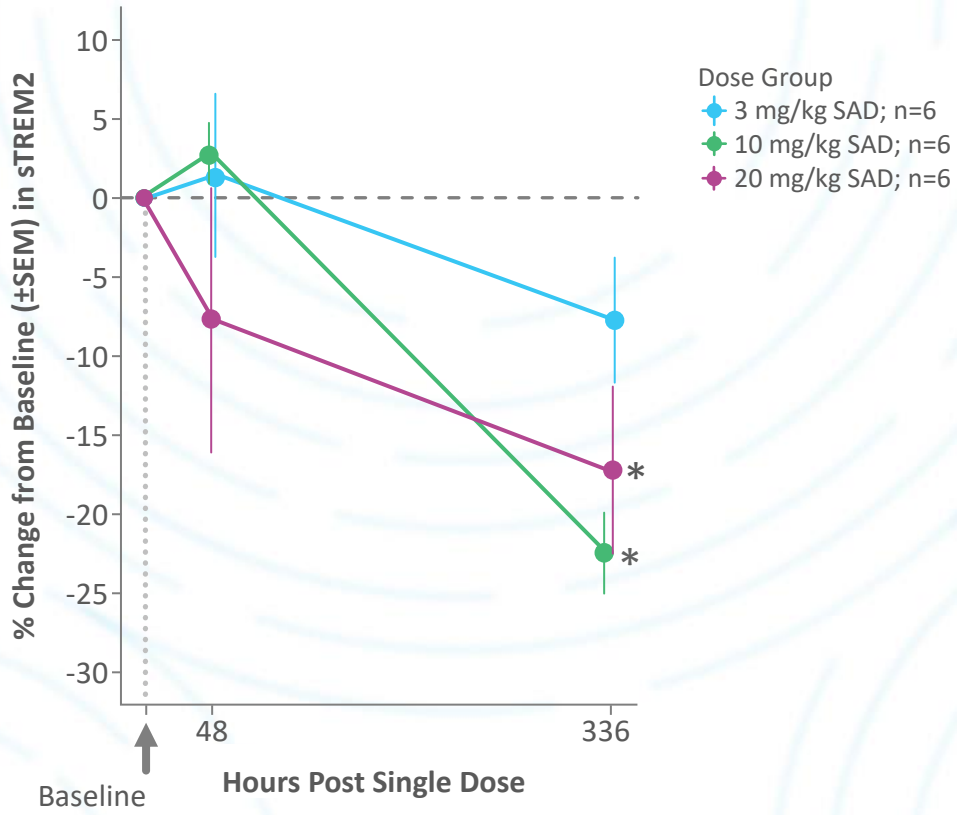


As of October 7, 2022
SEM: Standard Error of Mean; Baseline: Pre-dose Levels
*p-value < 0.05

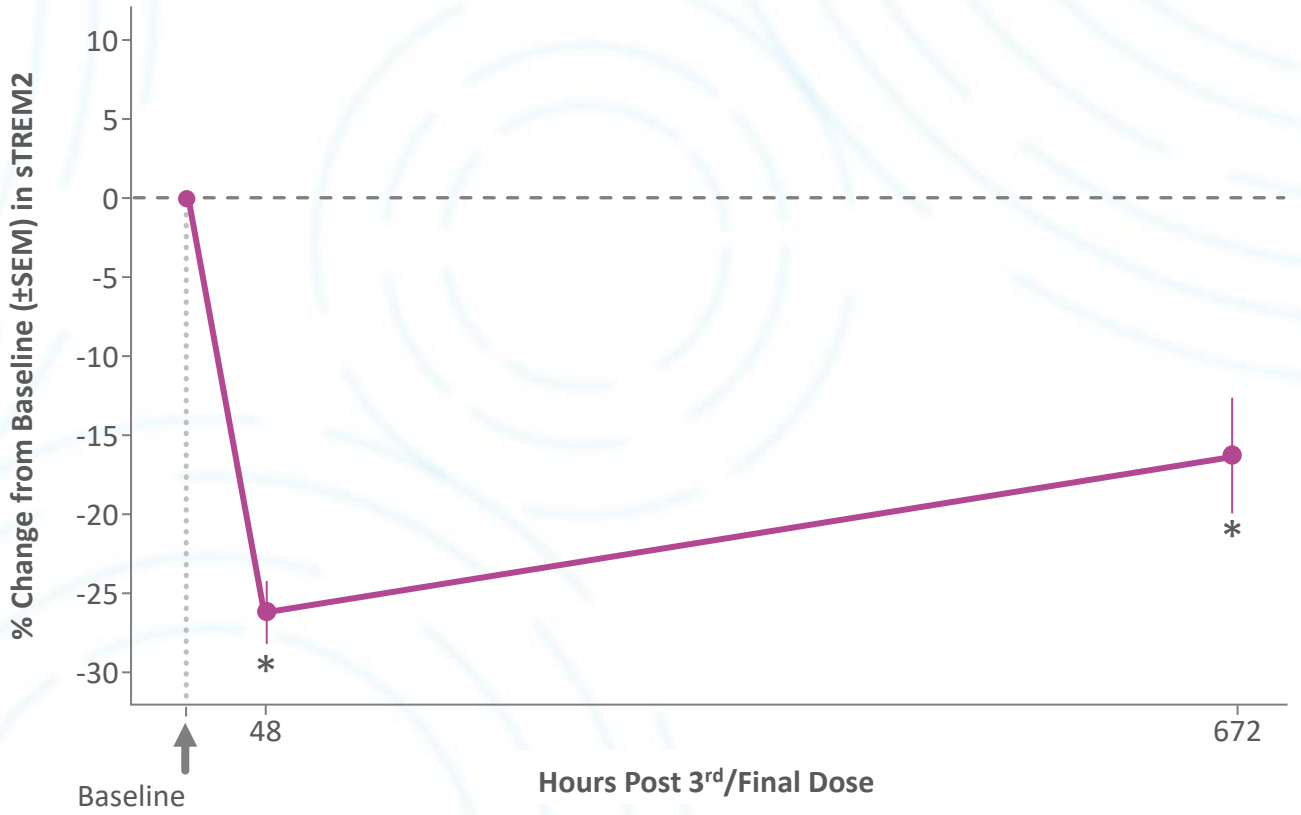
Proof of Target Engagement: VGL101 Has Dose Dependent, Robust & Durable sTREM2 Decreases

% change in sTREM2 concentration in cerebrospinal fluid (CSF) from pre-dosing baseline

Single Ascending Doses



20 mg/kg Multiple Dose
(3 doses at 28-day intervals; n=6)

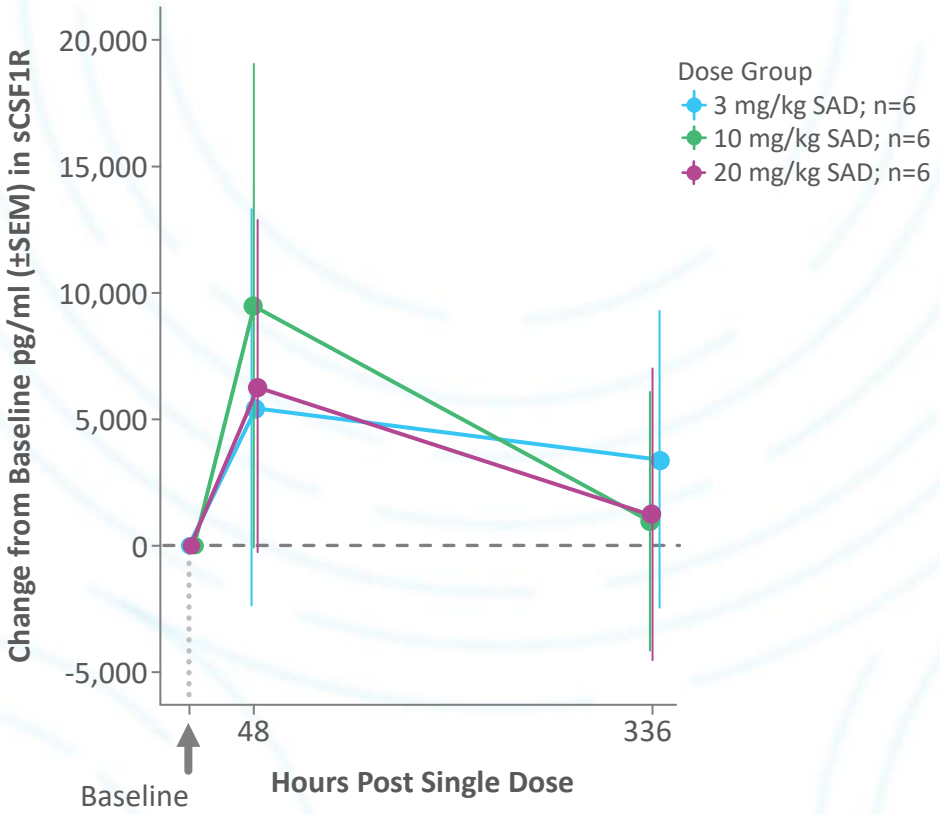


As of October 7, 2022
SEM: Standard Error of Mean; Baseline: Pre-dose Levels
*p-value < 0.05

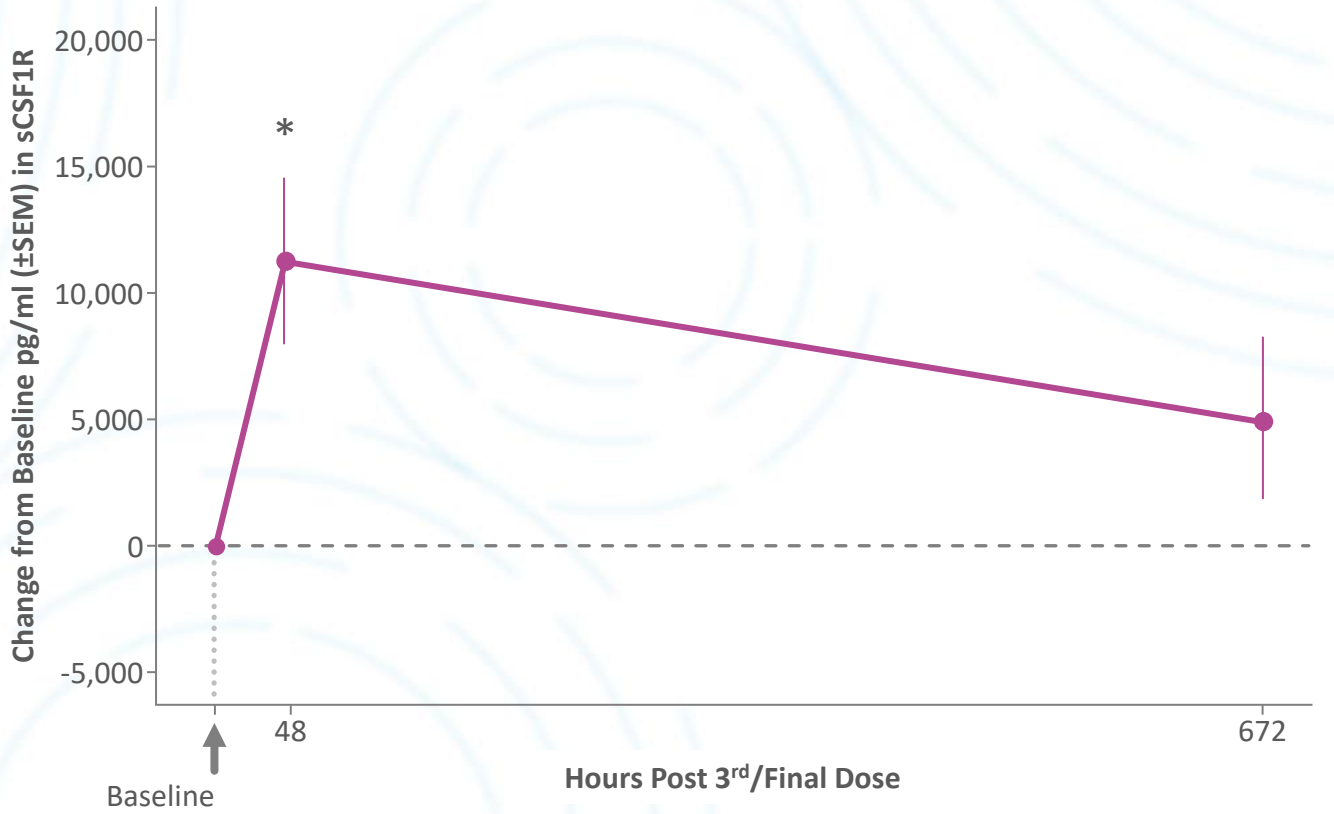
Proof of Pharmacology: VGL101 Shows Durable sCSF1R Increases

Absolute change in concentration of sCSF1R in cerebrospinal fluid (CSF)

Single Ascending Doses



20 mg/kg Multiple Dose
(3 doses at 28-day intervals; n=6)

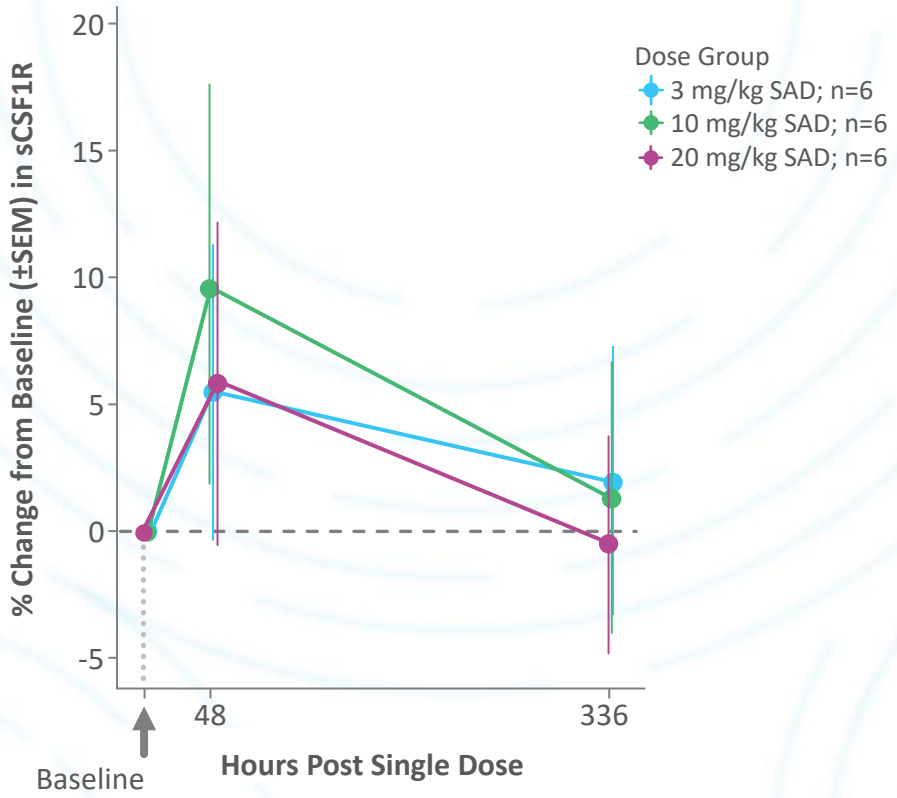


As of October 7, 2022
SEM: Standard Error of Mean; Baseline: Pre-dose Levels
*p-value < 0.05

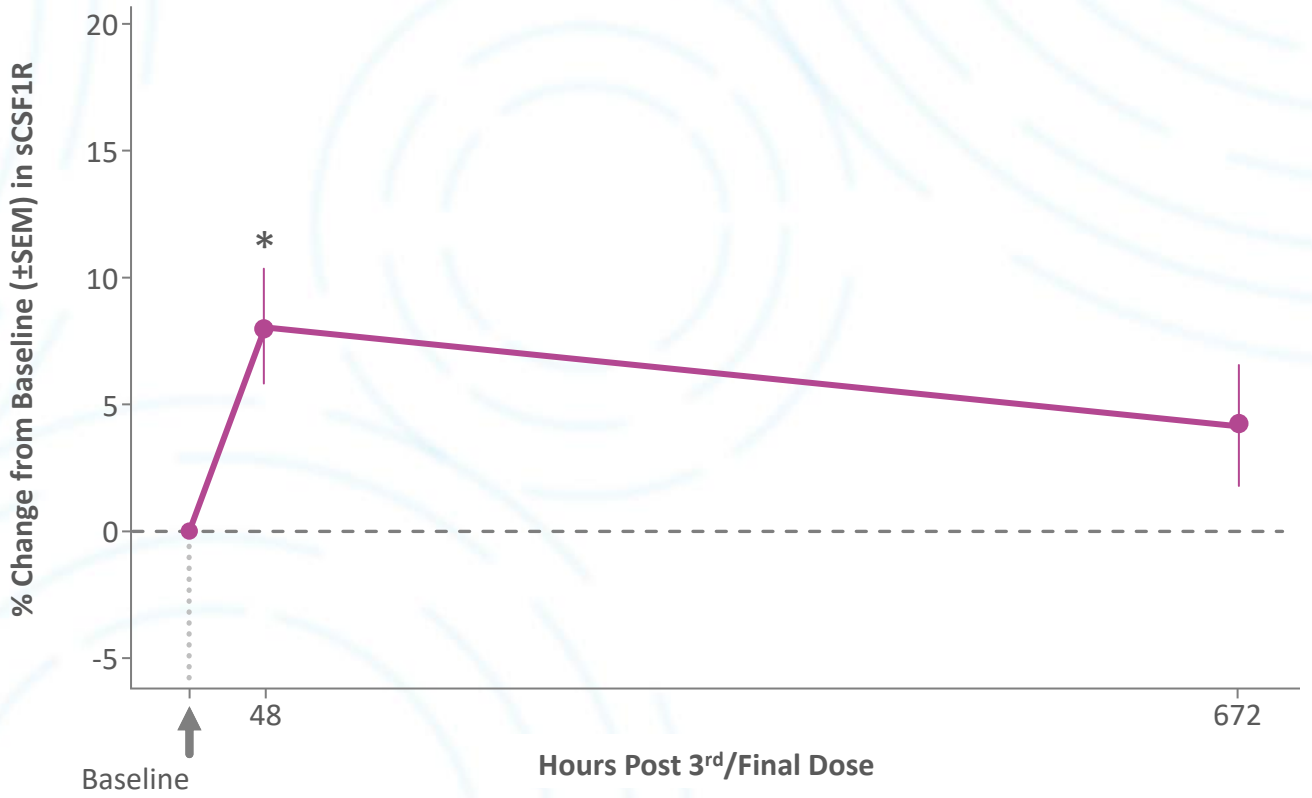
Proof of Pharmacology: VGL101 Shows Durable sCSF1R Increases

% change in sCSF1R concentration in cerebrospinal fluid (CSF) from pre-dosing baseline

Single Ascending Doses



20 mg/kg Multiple Dose
(3 doses at 28-day intervals; n=6)



As of October 7, 2022
SEM: Standard Error of Mean; Baseline: Pre-dose Levels
*p-value < 0.05

In Summary

- VGL101 was generally safe and well-tolerated at doses up to 40 mg/kg SAD and 20 mg/kg MAD
- VGL101 PK shows linear, predictable characteristics across doses and a half-life supports monthly dosing
- VGL101 demonstrated proof of target engagement and pharmacological activity based on dose dependent, robust and durable reductions in sTREM2 following repeat dosing; first antibody to report durability of TREM2 engagement in a clinical setting
- VGL101 showed increases in sCSF1R levels which were durable following repeat dosing
- Exploration of higher doses of VGL101 in Phase 1 healthy volunteer trial ongoing; Cleared to evaluate 60 mg/kg SAD dose cohort in Australia
- Safety, tolerability, PK and PD data from Phase 1 trial support 20mg/kg as a pharmacologically active dose for Phase 2 proof-of-concept trial in ALSP patients
- On-track for initiation of the Phase 2 trial in ALSP patients this quarter

* As of October 7, 2022

Closing Remarks

vigilant for you®

2022–2023 Anticipated Milestones

☑ Announce topline data for Phase 1 clinical trial with VGL101 in healthy volunteers*	**Q4 2022**
☐ Initiate Phase 2 portion of the Phase 2/3 clinical trial with VGL101 in ALSP	**Q4 2022**
☐ Establish Phase 2 proof of concept in ALSP	**2023**
☐ Submit IND and initiate clinical development for small molecule TREM2 agonist	**2023**

**The healthy volunteer single and multiple ascending dose trial is a first-in-human Phase 1 clinical trial, principally to evaluate VGL101's safety and tolerability. The trial, depending on the safety and tolerability results, is expected to provide a basis for conducting subsequent clinical trials in ALSP, AD and other rare CNS indications.*