UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): November 2, 2022

VIGIL NEUROSCIENCE, INC.
(Exact name of registrant as specified in its charter)

Delaware	001-41200	85-1880494
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)

Vigil Neuroscience, Inc.
1 Broadway, 7th Floor, Suite 07-300
Cambridge, Massachusetts , 02142
(Address of principal executive offices, including zip code)

(857) 254-4445
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trade Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**VIGL**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On November 2, 2022, Vigil Neuroscience, Inc. (the "Company") issued a press release and held a webcast announcing certain interim topline results from its ongoing Phase 1 clinical trial of VGL101. A copy of the press release and the presentation that accompanied the webcast are furnished as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K, respectively, and are incorporated herein by reference.

The information under this Item 7.01, including Exhibits 99.1 and 99.2 hereto, is being furnished herewith and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated November 2, 2022 (furnished herewith)
99.2	Slide Presentation, dated November 2, 2022 (furnished herewith)
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Vigil Neuroscience, Inc.

Date: November 2, 2022

By: /s/ Ivana Magovčević-Liebisch
Ivana Magovčević-Liebisch
President and Chief Executive Officer

Exhibit 99.1

Vigil Neuroscience Announces Interim Topline Results from its Ongoing Phase 1 Clinical Trial Evaluating VGL101 in Healthy Volunteers Supporting Phase 2 Initiation in ALSP

– VGL101 demonstrated favorable safety, tolerability and PK profiles in single ascending dose and multiple ascending dose cohorts -

– VGL101 achieved dose dependent, robust and durable decreases in CSF sTREM2 demonstrating proof of target engagement further validating its mechanism of action –

– On track to initiate Phase 2 trial with a 20 mg/kg dose of VGL101 in ALSP patients this quarter–

– Company to host conference call today at 8:00 a.m. ET–

CAMBRIDGE, Mass., November 2, 2022 (GLOBE NEWSWIRE) — Vigil Neuroscience, Inc. (Nasdaq: VIGL), a clinical-stage biotechnology company committed to harnessing the power of microglia for the treatment of neurodegenerative diseases, today announced interim topline results from its ongoing Phase 1 clinical trial of VGL101, its lead product candidate, in healthy volunteers. These interim data support the initiation of a Phase 2 proof-of-concept trial in patients with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP) with a 20 mg/kg dose.

“We are very excited by the overall clinical profile of VGL101 seen to date and the progress our team has made in advancing this important program in less than one year’s time,” said Ivana Magovčević-Liebisch, Ph.D., J.D., President and Chief Executive Officer of Vigil. “These interim data, alongside the anticipated initiation of the Phase 2 proof-of-concept trial in ALSP patients this quarter, are key milestones in the development of VGL101 for which we expect important data readouts in 2023.”

“Initiation of the Phase 2 trial will mark an important milestone for the ALSP community as it will be the first ever interventional trial in this underserved patient population. With this interim Phase 1 dataset, we demonstrated that VGL101 is safe, well tolerated, brain penetrant, and produces robust and durable reductions in sTREM2, validating its mechanism of action,” said Spyros Papapetropoulos, M.D., Ph.D., Chief Medical Officer of Vigil. “This interim Phase 1 dataset, combined with VGL101’s ability to rescue ALSP-like phenotypes in human microglia in our preclinical studies, gives us increased confidence in the therapeutic potential of VGL101 as we move toward Phase 2 clinical evaluation in patients.”

This ongoing trial is a Phase 1 single and multiple ascending dose trial to assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of VGL101. As of October 7, 2022, the trial had enrolled 82 healthy volunteers who received either VGL101 (n=68) at doses of 1, 3, 10, 20, 30 or 40 mg/kg or placebo (n=14). VGL101 was found to be safe and well-tolerated across both the SAD and MAD cohorts dosed.

Interim topline results from the ongoing Phase 1 trial of VGL101 include the following:

- All adverse events (AEs) were mild in severity with the exception of one moderate AE of dizziness, and all AEs resolved without intervention. No serious adverse events have been reported to date.
- VGL101 showed dose proportional PK with a favorable half-life and brain penetration.
- VGL101 achieved dose dependent, durable decreases in levels of sTREM2 in the cerebrospinal fluid (CSF) demonstrating proof of target engagement. VGL101 20 mg/kg repeat dosing was associated with robust reduction in sTREM2 levels and decreases were still observed 28 days after the third and final dose. VGL101 is the first antibody reported to demonstrate durability of TREM2 engagement in a clinical setting.
- VGL101 shows durable increases in sCSF1R levels in the CSF after repeat dosing.
- The Company continues to dose escalate in its Phase 1 trial in healthy volunteers and has been cleared to initiate a 60 mg/kg cohort in Australia. The Company expects to provide the final data analysis at a future medical conference.
- Vigil is on track to initiate the VGL101 Phase 2 trial in ALSP patients with a 20 mg/kg dose this quarter.

Conference Call Information

Vigil will host a conference call and webcast today, November 2, at 8:00 a.m. ET to discuss the interim topline results from its Phase 1 trial of VGL101 in healthy volunteers. The live webcast and accompanying slides can be accessed on the Investors section of the Vigil Neuroscience website at https://investors.vigilneuro.com/news-events/events-presentations. To access the call by phone, participants should visit this registration link to receive dial-in details. A replay of the webcast will be available in the same section of the Company's website for approximately 90 days.

About VGL101

VGL101, Vigil's lead product candidate, is a fully human monoclonal antibody agonist targeting human triggering receptor expressed on myeloid cells 2 (TREM2), which is responsible for maintaining microglial cell function. TREM2 deficiency is believed to be a driver of certain neurodegenerative diseases. VGL101 is in development for the treatment of rare microgliopathies, such as adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), as well as other neurodegenerative diseases for which TREM2 and/or microglia deficiency is believed to be a key driver of disease pathway.

About Vigil Neuroscience

Vigil Neuroscience is a clinical-stage, microglia-focused therapeutics company focused on developing treatments for both rare and common neurodegenerative diseases by restoring the vigilance of microglia, the sentinel immune cells of the brain. We are utilizing the tools of modern neuroscience drug development across multiple therapeutic modalities in our efforts to develop precision-based therapies to improve the lives of patients and their families.

Forward-Looking Statements

This press release includes certain disclosures that contain "forward-looking statements" of Vigil Neuroscience's ("Vigil" or the "Company") that are made pursuant to the safe harbor provisions of the federal securities laws, including, without limitation, express or implied statements regarding: beliefs

about the interim data for VGL101 and plans, timing and dosing for initiation of the Phase 2 trial; expectations for data readouts in 2023; the impact of such developments on the ALSP community and beliefs about the patient population; and beliefs about the therapeutic potential of VGL101. Forward-looking statements are based on Vigil's current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties related to uncertainties inherent in conducting and reporting data analyses; the identification and development of product candidates, including the conduct of research activities and the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results and data from preclinical and clinical studies; the timing of the Company's ability to submit and obtain regulatory clearance for investigational new drug applications and initiate additional clinical trials; 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 Company's ability to initiate and complete its current and expected clinical trials and its ability to work with the FDA to successfully remove the partial clinical hold; whether Vigil's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; uncertainties associated with the impact of the COVID-19 pandemic on its business and operations; as well as the risks and uncertainties identified in the Company's filings with the Securities and Exchange Commission (SEC), including Vigil's IPO registration statement, its Annual Report on Form 10-K for the year ended December 31, 2021, its Quarterly Report on Form 10-Q for the quarter ended June 30, 2022 and in any subsequent filings it may make with the SEC, including its Quarterly Report on Form 10-Q for the quarter ended June 30, 2022. Forward-looking statements contained in this announcement are made as of this date, and Vigil undertakes no duty to update such information except as required under applicable law. Readers should not rely upon the information on this page as current or accurate after its publication date.

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Vigil Neuroscience
VGL101 Phase 1 Interim Topline Data Results in Healthy Volunteers
November 2, 2022
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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 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.

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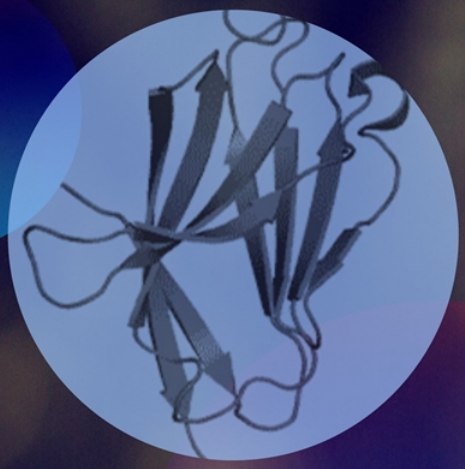

Opening Remarks

Ivana Magovcevic-Liebisch, President & CEO

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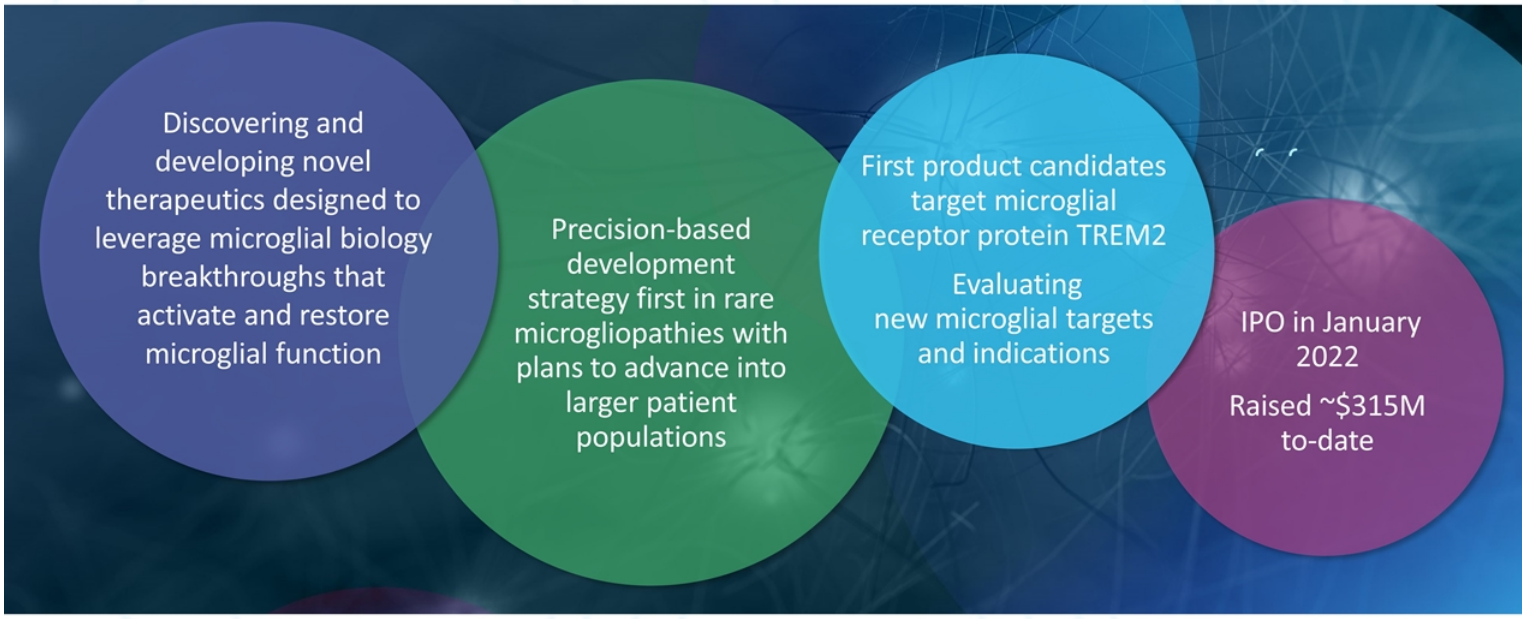
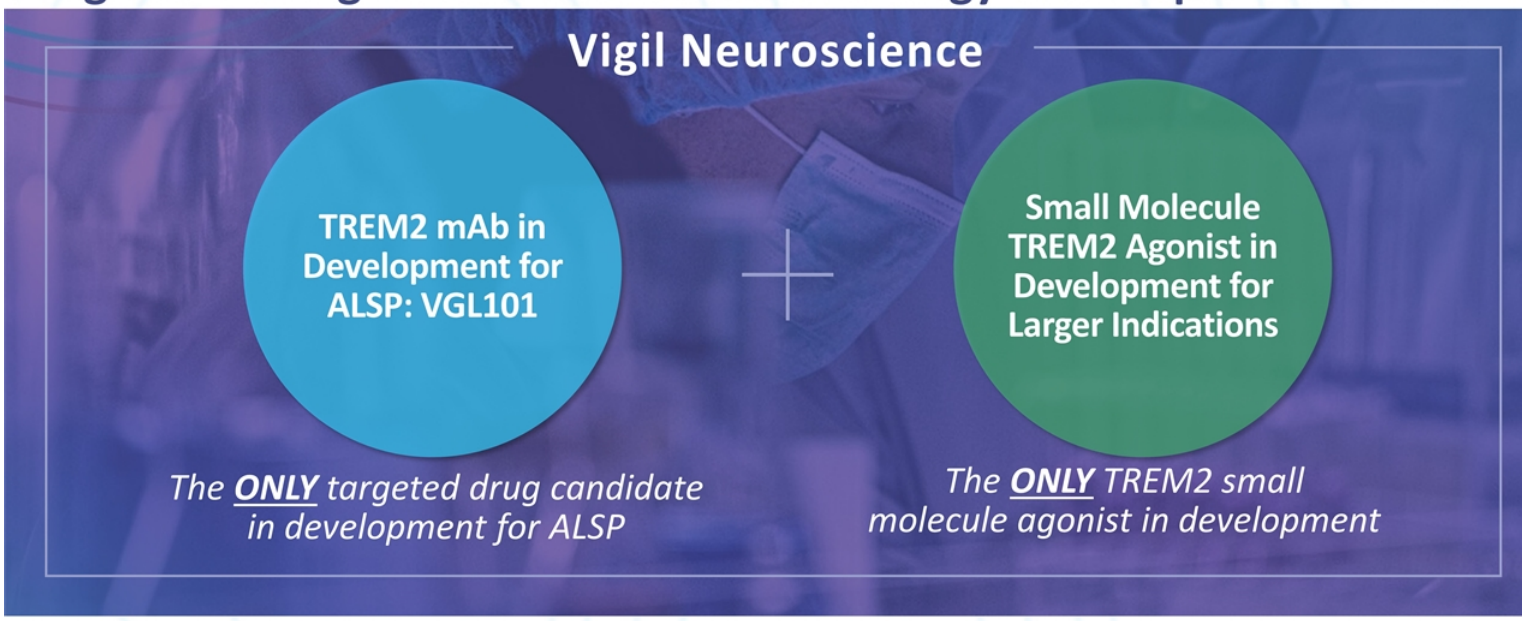
Vigil's Mission: Restoring Microglial Vigilance to Create Disease-Modifying Treatments for Neurodegenerative Diseases

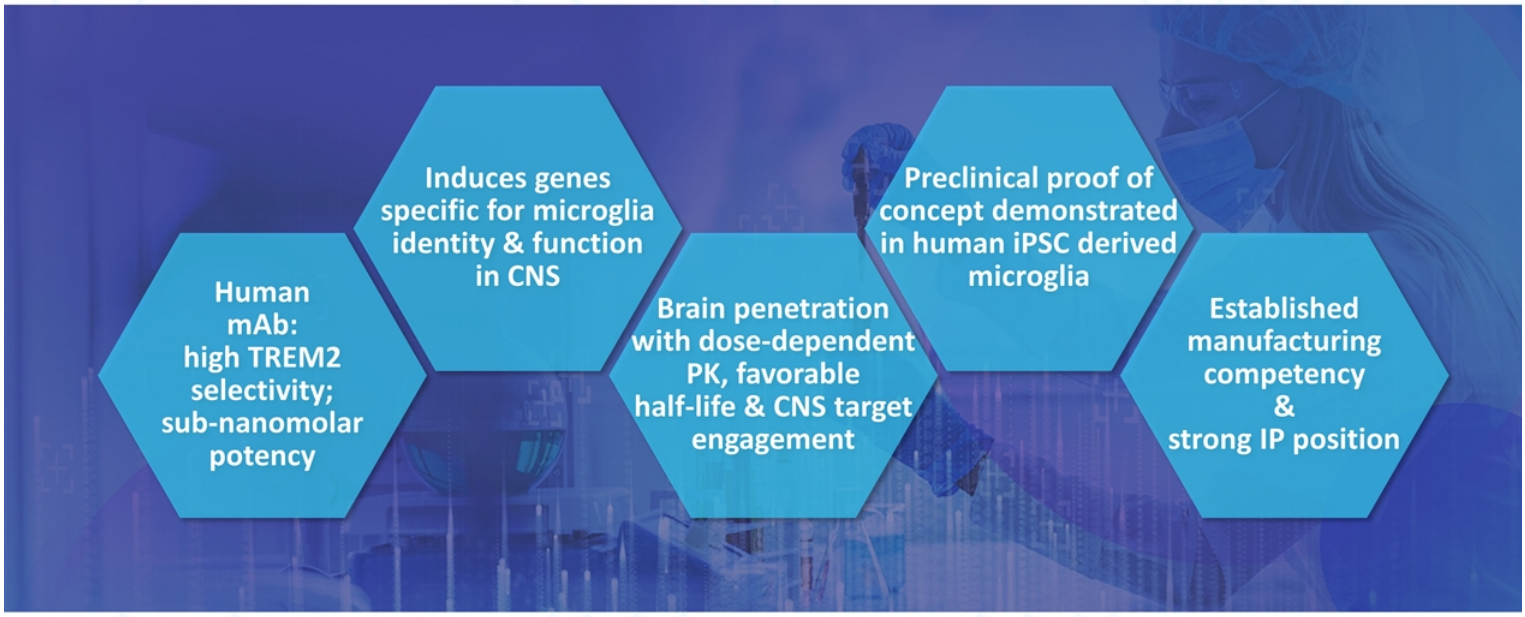


Vigil TREM2 Agonists: Differentiated Strategy & Multiple Modalities



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

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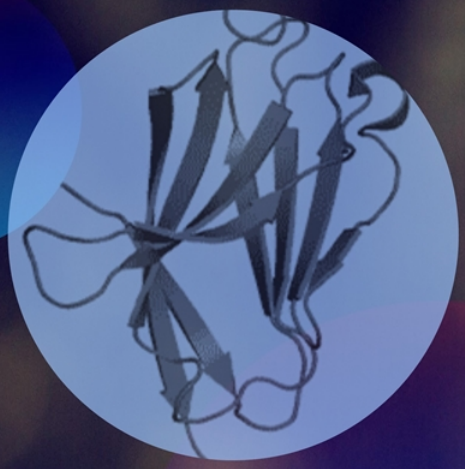

VGL101 Interim Topline Phase 1 Results in Healthy Volunteers

Spyros Papapetropoulos, Chief Medical Officer

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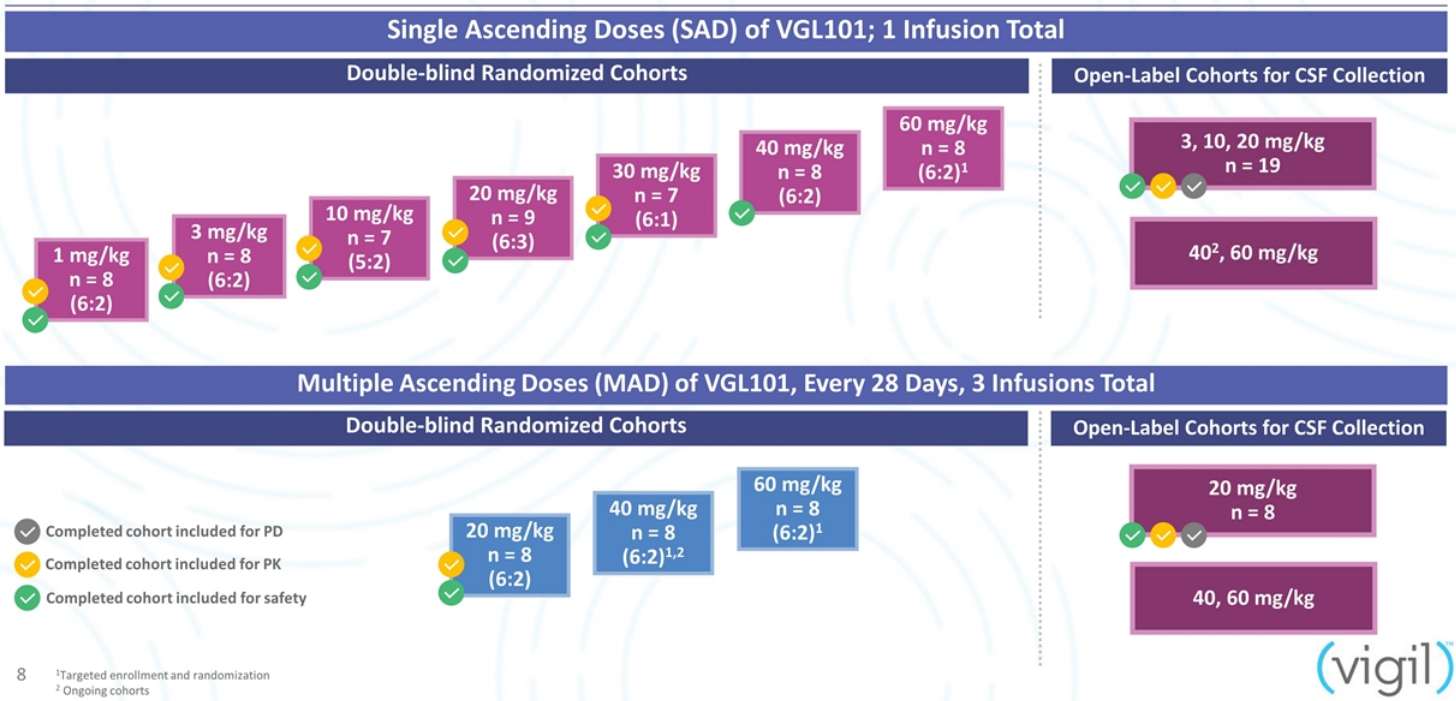
Trial Design: VGL101 Phase 1 SAD/MAD in Healthy Volunteers



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

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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*

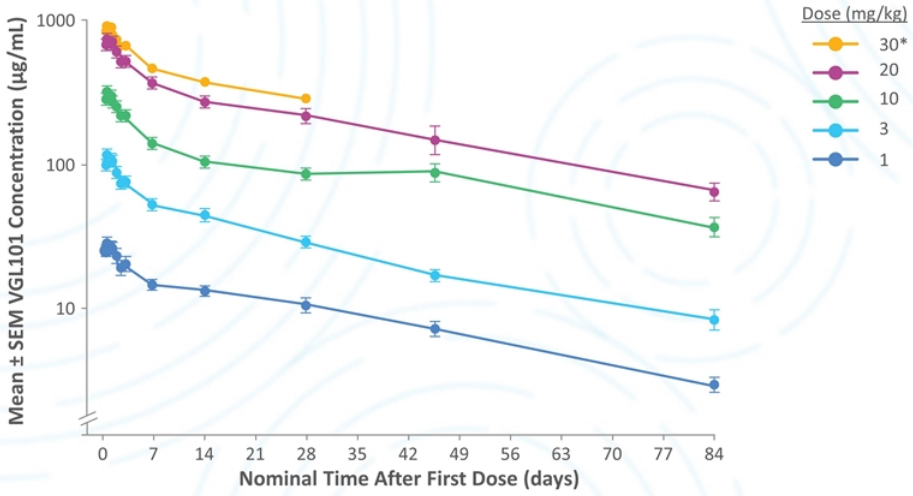
- 82 healthy volunteers have been dosed in the ongoing first-in-human Phase 1 SAD/MAD trial
  - 68 subjects received VGL101
  - 14 subjects received placebo
- In blinded interim safety review of completed cohorts VGL101 was generally safe and well tolerated
  - Across cohorts, all AEs were mild with 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)

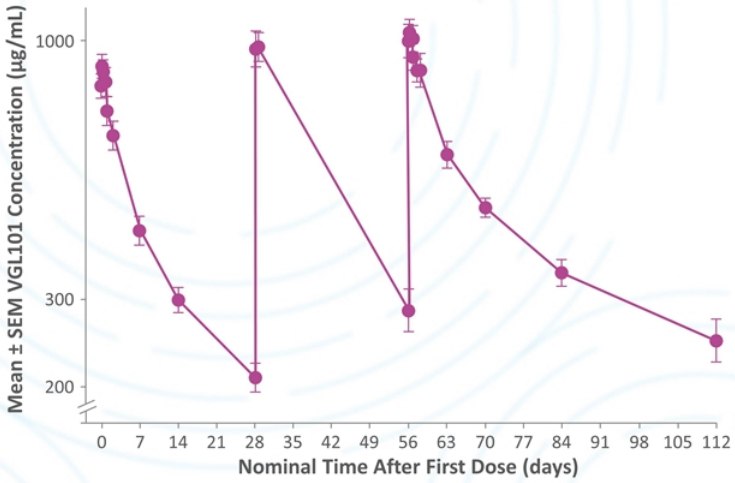


As of October 7, 2022

*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)



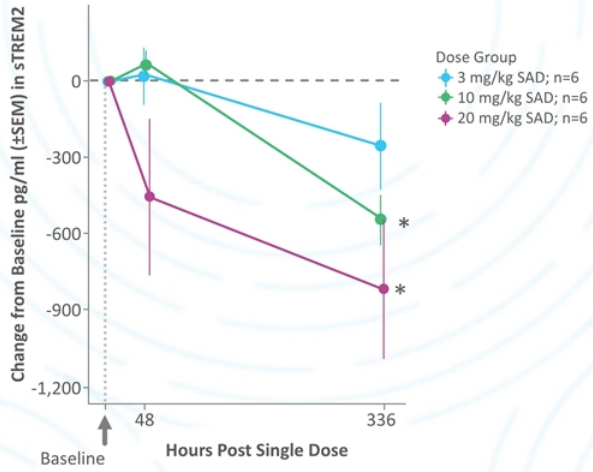
- ~27 days half-life supporting monthly dosing interval
- Brain penetration and achieving projected CSF therapeutic exposures
  - 0.1 – 0.2% CSF-to-serum ratio

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

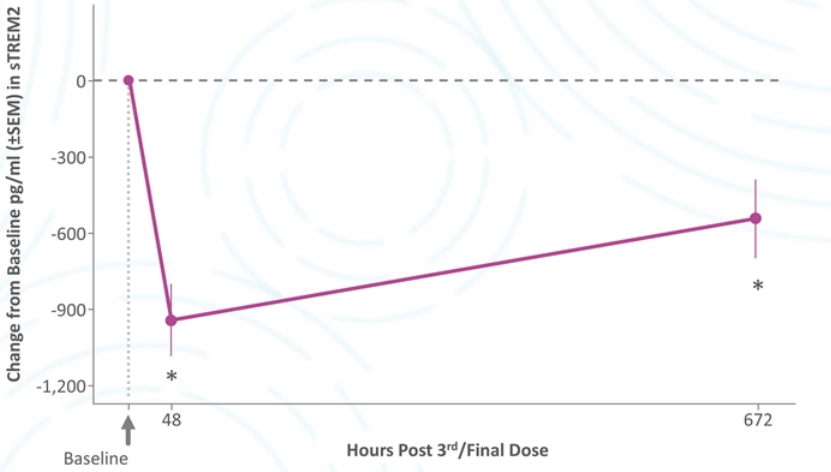
Proof of Target Engagement: VGL101 Has Dose Dependent, Robust & Durable sTREM2 Decreases

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)

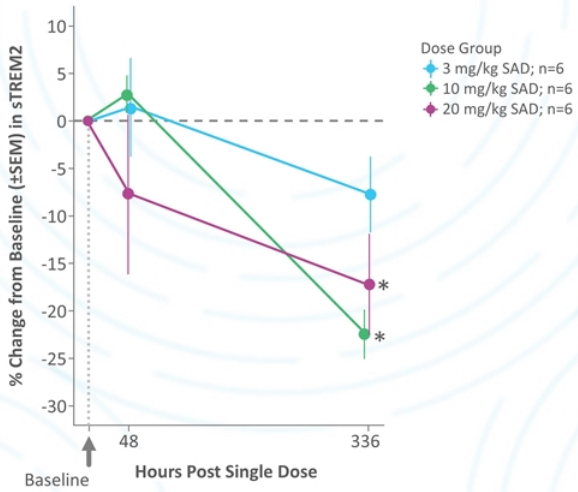


As of October 7, 2022
SEM: Standard Error of Mean; Baseline: Pre-dose Levels
*p-value < 0.05

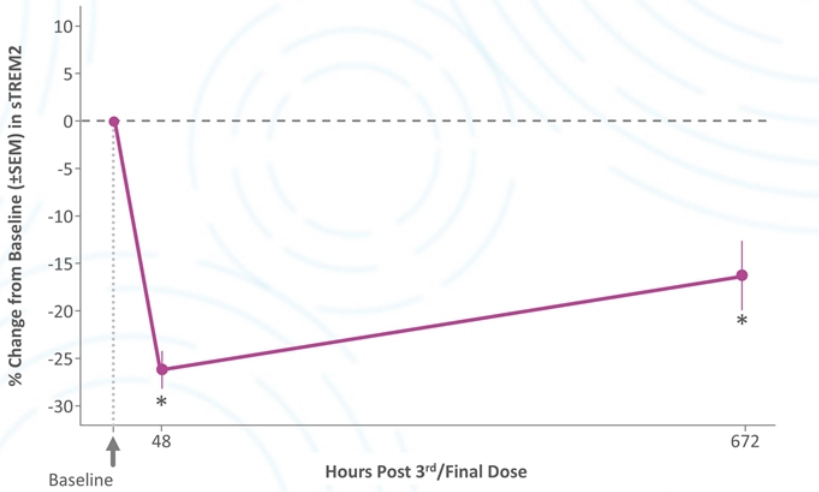
Proof of Target Engagement: VGL101 Has Dose Dependent, Robust & Durable sTREM2 Decreases

% 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)



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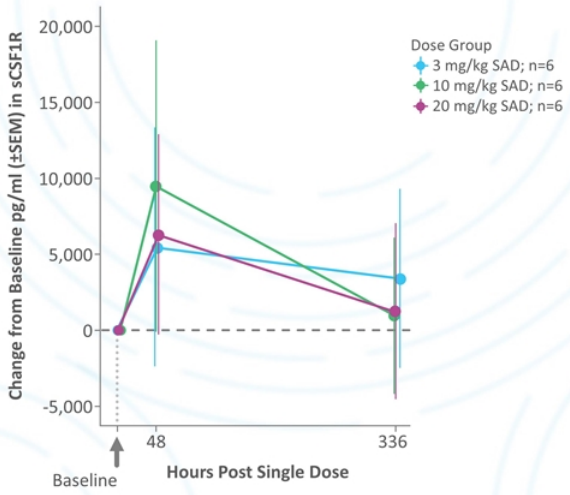
As of October 7, 2022
SEM: Standard Error of Mean; Baseline: Pre-dose Levels
*p-value < 0.05

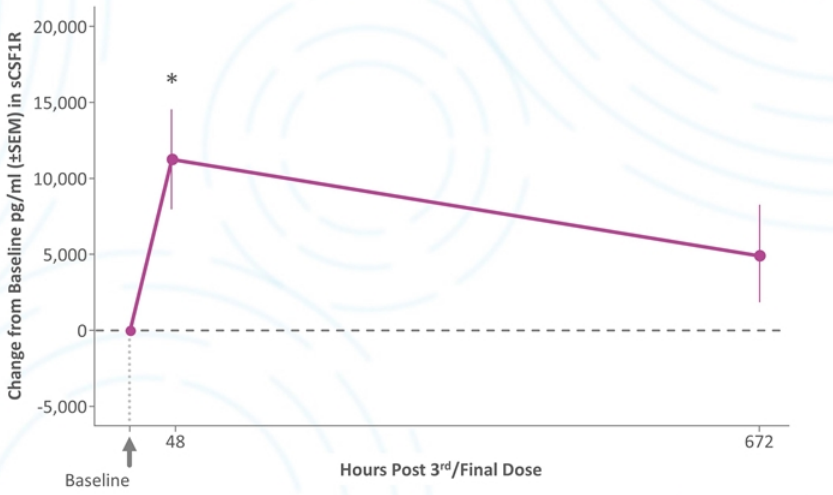
Proof of Pharmacology: VGL101 Shows Durable sCSF1R Increases

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)

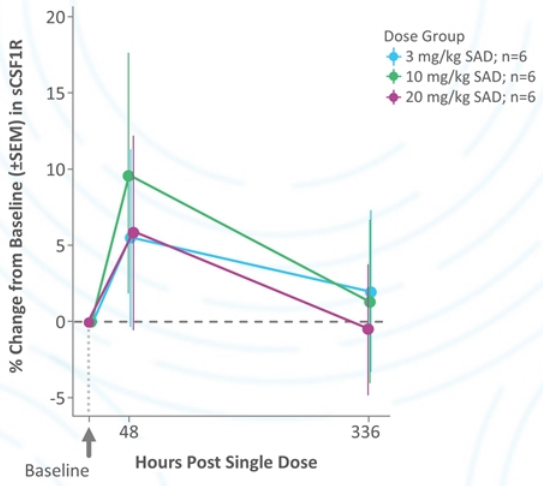


As of October 7, 2022
SEM: Standard Error of Mean; Baseline: Pre-dose Levels
*p-value < 0.05

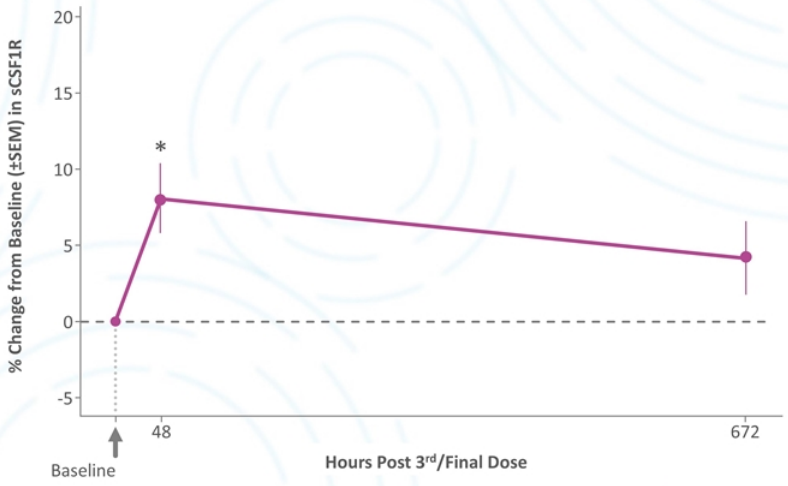
Proof of Pharmacology: VGL101 Shows Durable sCSF1R Increases

% 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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Closing Remarks
17
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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.*


Q&A
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