Vigil Neuroscience Presents VGL101 Complete Phase 1 Data and Phase 2 IGNITE Trial Design at the 2023 American Neurological Association Annual Meeting

Sep 11, 2023

- Complete Phase 1 data analysis demonstrated that VGL101 continued to have a favorable safety and tolerability profile and proof-of-target engagement in SAD/MAD cohorts up to 60 mg/kg

- On track to report 6-month interim data from IGNITE trial in Q4 2023 from first 6 patients who have received 20 mg/kg of VGL101

WATERTOWN, Mass., Sept. 11, 2023 (GLOBE NEWSWIRE) -- Vigil Neuroscience, Inc. (Nasdaq: VGL), a clinical-stage biotechnology company committed to harnessing the power of microglia for the treatment of neurodegenerative diseases, today announced the complete data analysis from its VGL101 Phase 1 single and multiple ascending dose (SAD and MAD) healthy volunteer trial in a poster presentation at the 2023 American Neurological Association (ANA) Annual Meeting. In addition, the Company presented a poster highlighting the study design for its ongoing IGNITE Phase 2 clinical trial.

“The dataset from the VGL101 Phase 1 healthy volunteer trial is very encouraging and further validates our development strategy for the ongoing IGNITE Phase 2 trial in ALSP. VGL101 continued to demonstrate a favorable safety and tolerability profile and remains the first antibody to show durability of TREM2 engagement in a clinical setting,” said Ivana Magovčević-Liebisch, Ph.D., J.D., President and Chief Executive Officer of Vigil. “We are committed to achieving further milestones for VGL101, including the interim data readout from IGNITE in the fourth quarter of 2023. The IGNITE interim analysis will be the first ever clinical data provided from an interventional study in ALSP.”

The Phase 1 SAD and MAD trial was designed to assess the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of VGL101 in healthy volunteers. The trial enrolled 136 healthy volunteers who received either VGL101 (n=113) at fixed single doses ranging from 1 to 60 mg/kg or three ascending doses ranging from 20 to 60 mg/kg, or placebo (n=23). An interim safety analysis of VGL101 for the 1 mg/kg to 40 mg/kg SAD cohorts and data for the 20 mg/kg MAD cohort were previously disclosed in November 2022.

Highlights from the VGL101 Phase 1 healthy volunteer trial presented at the ANA Annual Meeting include:

- VGL101 demonstrated a favorable safety and tolerability profile in SAD and MAD cohorts at doses up to 60 mg/kg.
- VGL101 showed linear and predictable pharmacokinetic characteristics and an observed half-life that supports monthly dosing.
- The Phase 1 cerebrospinal fluid (CSF) biomarker data demonstrated pharmacologic activity across multiple measures:
  - Demonstrated proof-of-target engagement based on dose-dependent, robust and durable reductions in soluble TREM2 (sTREM2) following repeat dosing.
  - Increased soluble CSF1R (sCSF1R) and osteopontin levels were durable following repeat dosing indicating that VGL101 impacted microglial activity downstream of TREM2 target engagement.
- Target engagement and downstream pharmacodynamic responses of VGL101 at 20 mg/kg and 40 mg/kg support evaluating these doses in the ongoing IGNITE Phase 2 trial in ALSP patients.

In a separate poster at the ANA Annual Meeting, the Company presented the trial design for its ongoing Phase 2 IGNITE trial. IGNITE is a global, open-label clinical trial evaluating VGL101 in approximately 15 patients with symptomatic ALSP who have a confirmed CSF1R gene mutation. As part of the protocol, patients will receive an intravenous (IV) infusion of VGL101 at 20 mg/kg or 40 mg/kg approximately every four weeks, for a treatment duration of one year. The primary objective of the IGNITE trial is to evaluate the safety and tolerability of VGL101. Secondary objectives include evaluating the impact of VGL101 on magnetic resonance imaging (MRI) and its pharmacodynamic effect on fluid markers in patients with symptomatic ALSP. Clinical efficacy outcome measures are also being collected as exploratory endpoints. In the fourth quarter of 2023, the Company expects to report interim 6-month data from the IGNITE trial in the first 6 patients who have received 20 mg/kg of VGL101.

The posters can be accessed on the Publications page of the Company’s website.

About VGL101
VGL101, Vigil's lead product candidate, is a fully human monoclonal antibody 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 rare microgliopathies, such as 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 ALSP
ALSP is a rare, inherited, autosomal dominant neurological disease with high penetrance. It is caused by a mutation to the CSF1R gene and affects an estimated 10,000 people in the US, with similar prevalence in Europe and Japan. The disease generally presents in adults in their forties, is diagnosed through genetic testing and established clinical/radiologic criteria and is characterized by cognitive dysfunction, neuropsychiatric symptoms, and motor impairment. These symptoms typically exhibit rapid progression with a life expectancy of approximately six to seven years on average after diagnosis, causing significant patient and caregiver burden. There are currently no approved therapies for the treatment of ALSP, underlining the high unmet need in this rare indication.
About Vigil Neuroscience
Vigil Neuroscience is a clinical-stage biotechnology 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. VGL101, our lead clinical candidate, is a fully human monoclonal antibody agonist targeting human triggering receptor expressed on myeloid
cells 2 (TREM2) in people with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), a rare and fatal
neurodegenerative disease. We are also developing VG-3927, a novel small molecule TREM2 agonist, to treat common neurodegenerative diseases
associated with microglial dysfunction, with an initial focus on Alzheimer's disease (AD) in genetically defined subpopulations.

Forward-Looking Statements
This press release includes certain disclosures that contain “forward-looking statements” of Vigil Neuroscience, Inc.’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:
the progress and timing of the clinical development of Vigil’s programs, including the availability of data and expected timing for reporting interim data
from IGNITE; and the ability and timing to achieve future developmental, clinical and regulatory milestones for 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 uncertainties as to the availability and timing of results and data from clinical studies; as well as the risks and uncertainties identified in
the Company’s filings with the Securities and Exchange Commission (SEC), including Vigil’s Quarterly Report on Form 10-Q for the quarter ended
June 30, 2023 and in any subsequent filings it may make with the SEC. Forward-looking statements contained in this announcement are made as of
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The company encourages investors and potential investors to consult our website regularly for important information about Vigil Neuroscience.

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