



Vigil Neuroscience Reports Positive Interim Data from Phase 2 IGNITE Proof-of-Concept Clinical Trial Evaluating Iluzanebart (VGL101) as a Treatment for ALSP and from Ongoing Natural History Study ILLUMINATE

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- Iluzanebart demonstrated favorable safety and tolerability, including no hematologic adverse events -

- Clear CNS target engagement and downstream pharmacological activity at 20 mg/kg consistent with Phase 1 data; Directionally supportive changes in individual patients at 6 months on MRI and NfL biomarkers -

- Natural History Study continued to provide critical insights on MRI and NfL biomarkers; sCSF1R emerging as key biomarker of ALSP disease pathology -

- Company expects to report Phase 2 IGNITE results from all patients in 20 mg/kg and 40 mg/kg cohorts at 6 months in third quarter of 2024 -

- Company to host webinar today at 4:30 p.m. ET -

WATERTOWN, Mass., Nov. 16, 2023 (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 positive interim data from the Company's Phase 2 IGNITE proof-of-concept clinical trial in patients with adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP). The interim data, representing the first six patients following six months of treatment with 20 mg/kg of iluzanebart (formerly referred to as VGL101), further support the favorable safety and tolerability profile as was previously seen in healthy volunteers. In addition, these data demonstrated clear target engagement and downstream pharmacological activity at 20 mg/kg consistent with the Company's previously reported Phase 1 data in healthy volunteers. Directionally supportive changes at 6 months on magnetic resonance imaging (MRI) and neurofilament light (NfL) biomarkers of disease progression in individual patients with ALSP were also observed.

The Company also reported findings from its ongoing natural history study, ILLUMINATE, which continued to provide critical insights on MRI and NfL biomarkers and supports soluble colony stimulating factor 1 receptor (sCSF1R) as a potential key biomarker of ALSP disease pathology.

"The positive interim results from our Phase 2 IGNITE trial represent the first clinical data reported from an interventional study in patients with ALSP and reaffirm our belief in the potential of iluzanebart as a novel treatment option. Importantly, we are the first company to show clinical data on TREM2 agonism as a potential therapeutic approach in patients with a neurodegenerative disease," said Ivana Magovčević-Liebisch, Ph.D., J.D., President and Chief Executive Officer of Vigil. "In the 6 patients observed in the interim analysis, iluzanebart demonstrated a favorable safety and tolerability profile, compelling pharmacological activity, and positive quantifiable trends in NfL and MRI biomarkers in individual patients."

"In addition, our ongoing natural history study ILLUMINATE continues to provide critical insights into ALSP and biomarkers that we believe correlate with disease progression," continued Dr. Magovčević-Liebisch. "We expect to use the promising findings from IGNITE and ILLUMINATE to engage with the FDA to initiate discussions regarding a potential accelerated development pathway. We look forward to further executing on our precision medicine strategy in neurodegenerative diseases – because patients cannot wait."

Key Highlights from Phase 2 IGNITE Interim Data:

- Favorable safety and tolerability profile, including no hematologic adverse events.
- Predictable pharmacokinetic and brain penetration profile consistent with Phase 1 data in healthy volunteers.
- Clear target engagement, based on sTREM2 levels, and downstream pharmacological activity, based on sCSF1R and osteopontin levels, at 20 mg/kg, consistent with Phase 1 data in healthy volunteers.
- Directionally supportive changes in both NfL and MRI measurements on ventricular volume and gray matter volume in individual patients.
- We believe the quality and consistency of the interim data further support the continuation of IGNITE without modification.

Key Updates from Natural History Study ILLUMINATE:

- sCSF1R and NfL levels are remarkably altered in ALSP, supporting our hypothesis that these are key biomarkers of disease pathology.
- Totality of the data, including longitudinal progression observed on selected MRI measures and clinical endpoints, support engagement with regulatory authorities.
- We believe the quality and consistency of data in this interim analysis support chosen biomarkers for pharmacological activity.
- MRI measurements on ventricular volume and gray matter volume are emerging as key indicators of disease progression.
- Interim Montreal Cognitive Assessment (MoCA) and Cortical Basal Ganglia Functional Scale data support use as clinical endpoints in ALSP at 12 months.

"ALSP is a rare, devastating and fast-progressing disease with no approved treatments that target the underlying cause of the disease or slow its progression," said Zbigniew Wszolek, M.D., Neurologist at Mayo Clinic. "These interim results are a great step forward for patients and caregivers impacted by ALSP and I am encouraged by the progress the Vigil team has made developing a potential novel treatment option for this autosomal dominant disease. To date, iluzanebart has been well-tolerated, and the data seem to suggest that we are seeing directional changes in CSF1R and positive trends in NfL and MRI measurements. This is an important milestone for the underserved ALSP community of patients and caregivers."

"Today's results are a reflection of the dedication and expertise of our incredible team who brings an unwavering commitment to patients to their work," concluded Dr. Magovčević-Liebisch. "We extend a sincere thank you to all who have contributed to this progress, including our trial participants, their caregivers, and the clinical investigators. We look forward to sharing additional data from the IGNITE trial, including results from all patients in both the 20 mg/kg and 40 mg/kg cohorts at 6 months, in the third quarter of 2024."

The Company also announced that it will host a virtual webinar to discuss the Phase 2 IGNITE interim data today, Thursday, November 16, 2023, from 4:30 p.m. to 5:30 p.m. ET.

The event will include prepared remarks by the Vigil management team who will be joined by David S. Lynch, M.D., Ph.D., Consultant Neurologist National Hospital for Neurology & Neurosurgery, Queen Square & UCL Institute of Neurology, London & Clinical Lead, Adult Inherited White Matter Disorders Highly Specialist Service, NHS England.

To access the live webinar, please [register here](#) or visit "[Events & Presentations](#)" in the "Investors" section of the Vigil website at www.vigilneuro.com. An archived replay of the webinar will be available for approximately 90 days following the event.

About Phase 2 IGNITE Clinical Trial

IGNITE is a global Phase 2, open-label proof-of-concept trial evaluating iluzanebart in approximately 15 patients with symptomatic ALSP who have a confirmed *CSF1R* gene mutation. The primary objective of the IGNITE trial is to evaluate the safety and tolerability of iluzanebart. Secondary outcome measures include evaluating the effects of iluzanebart on target engagement and on MRI and NfL biomarkers of disease progression. Exploratory outcome assessments include the evaluation of clinical efficacy measures using standard cognitive, motor and functional assessments of iluzanebart in patients with ALSP. Patients enrolled in the trial will receive an intravenous (IV) infusion of iluzanebart at 20 mg/kg or 40 mg/kg approximately every four weeks for a treatment duration of one year.

About Iluzanebart (VGL101)

Iluzanebart, Vigil's lead clinical 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. Iluzanebart 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 United States, 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, underscoring 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. Vigil is utilizing the tools of modern neuroscience drug development across multiple therapeutic modalities in its efforts to develop precision-based therapies to improve the lives of patients and their families. Iluzanebart, Vigil's 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. Vigil is 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 ("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 potential of iluzanebart as a novel treatment option for patients with ALSP; Vigil's beliefs about TREM2 agonism's importance in Alzheimer's disease and ALSP; the progress and timing of the clinical development of Vigil's programs, including the availability of, and expected timing for reporting, interim and final data from both the IGNITE Phase 2 clinical trial; and the success and timing of the Company's interactions with regulatory authorities, including with the FDA regarding an accelerated development pathway. 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 the identification and development of product candidates, including the conduct of research activities and the conduct of clinical trials; uncertainties as to the availability and timing of results and data from clinical trials; whether results from preclinical studies and interim data from clinical trials will be predictive of the results of final data from clinical trials; the timing and content of additional regulatory information from the FDA; whether Vigil's cash resources will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; 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 September 30, 2023 and in any subsequent filings Vigil makes with the SEC. 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.

Internet Posting of Information

Vigil Neuroscience routinely posts information that may be important to investors in the "Investors" section of its website at <https://www.vigilneuro.com>. The company encourages investors and potential investors to consult our website regularly for important information about Vigil Neuroscience.

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