Vigil Presents Data on its Small Molecule TREM2 Agonist Program at 2024 Alzheimer's Association International Conference (AAIC)

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- First presentation of clinical data on sTREM2 from SAD cohorts in ongoing Phase 1 clinical trial of VG-3927 in healthy volunteers demonstrate proof-of-pharmacology -

- New in vitro and in vivo data demonstrate the Company's small molecule TREM2 agonists modulate AD pathophysiology -

WATERTOWN, Mass., July 30, 2024 (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 presented one oral and two poster presentations at the 2024 Alzheimer's Association International Conference (AAIC) being held July 28 - August 1, 2024 in Philadelphia, Pennsylvania and virtually.

"As the first company to advance a small molecule TREM2 agonist into clinical development, we are excited to present data from this important program at AAIC," said David Gray, Ph.D., Chief Science Officer at Vigil. "TREM2 has a strong causal link to Alzheimer's disease risk and the data shared today further support our growing body of both preclinical and clinical findings that VG-3927 is a potent molecule that functionally engages TREM2 receptors in the brain. According to the World Health Organization, AD is the most common type of dementia, and we believe VG-3927 has the potential to offer a differentiated approach to treating this devastating disease."

Oral presentation by Christian Mirescu, Ph.D., Vigil Neuroscience: *Orally Administered Small Molecule TREM2 Agonists for Modulating AD Pathophysiology*

The oral presentation highlighted new data from the Company's small molecule Triggering Receptor Expressed on Myeloid Cells 2 (TREM2) Agonist program, including:

- *In vivo* data showing that Vigil's small molecule TREM2 agonist selectively activates downstream function leading to microglial amyloid-beta (Aβ) phagocytosis.
- *In vivo* data from Vigil's small molecule TREM2 agonist program demonstrating acute modulation of AD pathophysiology, comparable to an approved therapeutic, without effector function liability.
- *In vitro* data from VG-3927 demonstrating preferential activity on cellular TREM2 establishing sTREM2 as a target engagement biomarker linked to TREM2 signaling.
- Clinical data from single ascending dose (SAD) cohorts in the ongoing Phase 1 trial evaluating VG-3927 showing a robust decrease of sTREM2 in the CSF demonstrating proof-of-pharmacology.

Poster presentation by Raj Rajagovindan, Ph.D., Vigil Neuroscience: *Design of a Phase 1, First-in-human, Randomized, Double-blind, Placebo-controlled, Single- and Multiple-Ascending Dose Study of a Novel Orally Administered TREM2 Agonist (VG-3927) in Healthy Volunteers*

Poster details include:

- The Phase 1 clinical trial is a randomized, double-blind, placebo-controlled, SAD/MAD study evaluating the safety, tolerability, PK, and PD following oral administration of VG-3927 in healthy volunteers.
- Cohorts are conducted sequentially in a dose-escalating manner, and dosing may be adjusted based on safety and tolerability assessments and emerging PK data.
    - For each cohort, 8 participants are randomized in a 6:2 allocation ratio to VG-3927 or placebo.
    - Blood samples are collected in all cohorts to characterize PK of VG-3927.
    - Cerebrospinal fluid samples are collected in select cohorts to investigate biomarkers of target engagement.

Poster presentation by Borislav Dejanovic, Ph.D., Vigil Neuroscience: *Pharmacological and Functional Characterization of the First Small Molecule TREM2 Agonist, VG-3927, for the Treatment of Alzheimer's Disease*

Poster details show that VG-3927:

- Is a TREM2 specific, highly potent molecule that potentiates signaling from lipid ligands.
- Induces functional agonism via unique clustering of TREM2 complexes in microglia.
- Activates protective gene signatures in mouse model of amyloidosis.
- Suppresses pro-inflammatory cytokines and protects against neurodegeneration in human CNS triculture model.

The presentation and posters are available on the Publications page of the Company's website.

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) patients, including some who carry TREM2 and other disease-associated variants.

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: Vigil's strategy, business plans and focus; the potential therapeutic benefit of our product candidates, including VG-3927, and the expected therapeutic benefits of such programs; VG-3927's potential as a TREM2 agonist and its ability to convert microglia into a neuroprotective state. 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 development of product candidates, including the conduct of research activities and the conduct of clinical trials; whether results from preclinical studies and clinical trials will be predictive of the results of later preclinical studies and clinical trials; the timing and content of additional regulatory interactions with the FDA – including the Company's discussions regarding the partial clinical hold on VG-3927; 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 March 31, 2024 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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