Vigil Neuroscience Presents Preclinical Data on VGL101 for Adult-Onset Leukoencephalopathy with Axonal Spheroids and Pigmented Glia (ALSP) and Clinical Phenotype of ALSP at Alzheimer's Association International Conference 2022

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CAMBRIDGE, Mass., Aug. 01, 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 presented two posters at the Alzheimer's Association International Conference (AAIC) in San Diego.

“Findings from our preclinical studies evaluating TREM2 agonism continue to support the therapeutic potential of our lead clinical product candidate, VGL101 for the treatment of ALSP, an underdiagnosed, rapidly progressive, fatal autosomal dominant neurodegenerative disease caused by *CSF1R* gene mutations that results in microglial dysfunction,” said Spyros Papapetropoulos, M.D., Ph.D., Chief Medical Officer of Vigil. “In addition, we continue to make progress in increasing disease awareness by elucidating the disease progression of ALSP, including the onset and rapid advancement of symptoms, family history and the global presence of the disease, which will inform our ongoing clinical development efforts in this rare leukoencephalopathy. Importantly, ALSP is commonly misdiagnosed as a neurodegenerative dementia and in the presence of family history and radiological findings physicians should consider genetic testing for ALSP.”

The first poster titled “VGL101 Rescues CSF1R Dysfunction in Human Microglia and Macrophages: Evaluation of *In Vitro* TREM2 Agonism in Models of a CSF1R-dependent Leukodystrophy” demonstrates that TREM2 agonism by VGL101 was able to compensate for CSF1R dysfunction in *in vitro* ALSP models utilizing healthy, human monocyte derived macrophages (hMDM) and induced pluripotent stem cell derived human microglia (iMGL), providing a rational basis for developing VGL101 as a potential therapeutic for ALSP.

Key highlights from the presentation include:

- CSF1R inhibition by PLX5622 (known inhibitor of CSF1R) or CSF1R ligands withdrawal resulted in decreased viability, increased caspase 3/7 activation, and an altered morphology.
- VGL101 administration induced phosphorylation of SYK in both hMDM and iMGL models, demonstrating agonism of the TREM2 receptor.
- VGL101 rescued CSF1R inhibition-induced morphology and cell death in both hMDM and iMGL.
- Increases in soluble CSF1R and decreases in soluble TREM2 upon VGL101 administration in iMGLs may inform target engagement studies.

In a separate poster titled “Phenotypic Features of Adult-Onset Leukoencephalopathy with Axonal Spheroids and Pigmented Glia (ALSP): Presenting Symptoms and Clinical Course,” Vigil conducted a systematic literature review of published case studies on the clinical and genetic features of ALSP to better understand the phenotypic characteristics of ALSP, with data extracted from a cohort of 292 patients, representing the largest case series to date of ALSP. The findings of this study supported and expanded the previous, smaller case reports on the phenotypic characteristics of ALSP.

Key highlights from the presentation include:

- The mean (SD) age of onset (years) of symptoms was 43.2 (11.6), survival time (years) was 6.1 (4.7), age of death (years) was 52.2 (11.1) and the number of deaths was 118.
- Family history was considerably more frequent (58.9%) than absence of family history (26.4%), supporting that genetic testing for CSF1R mutations should be used as a key marker for early and accurate diagnosis of ALSP.
- The most common initial symptoms were cognitive impairment (45.9%), behavioral and psychiatric dysfunction (26.4%), extrapyramidal and pyramidal motor abnormalities (15.4%, 11.6%, respectively) and speech difficulty (11.3%).
    - The clinical symptoms at disease onset reinforced ALSP phenotypic heterogeneity, a significant contributor to frequent misdiagnosis of ALSP as Alzheimer’s disease or frontotemporal dementia.
- The clinical symptoms associated with progression of ALSP were more prevalent compared to the same initial symptoms and consisted of cognitive impairment (80.8%), behavioral and psychiatric dysfunction (72.9%), extrapyramidal and pyramidal motor abnormalities (65.1%, 49.0%, respectively), speech difficulty (41.1%) and seizures (25.3%).

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 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 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 the progress and timing of the preclinical and clinical development of Vigil’s programs and expectations regarding the development of VGL101 in ALSP and other indications, beliefs about findings and analyses of data from preclinical studies and support for the therapeutic potential of VGL101 for the treatment of ALSP and beliefs that progress in increasing disease awareness will inform ongoing clinical development efforts. 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 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 will be predictive of the results of later preclinical studies and 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 and in subsequent filings it may make with the SEC, including its Quarterly Report on Form 10-Q for the three months ended March 31, 2022 and its Annual Report on Form 10-K for the year ended December 31, 2021. 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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