Vaxxinity Announces UB-312 Successfully Met Primary Objectives of Phase 1 Clinical Trial in Parkinson's Disease

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UB-312 was generally safe and well-tolerated.

Results are consistent with conclusions from Phase 1 Part A and preclinical studies, and support advancement of UB-312 into further clinical development.

CAPE CANAVERAL, Fla., June 22, 2023 (GLOBE NEWSWIRE) -- Vaxxinity, Inc. (Nasdaq: VAXX), a U.S. company pioneering the development of a new class of medicines today announced positive results from Part B of its Phase 1 clinical trial of UB-312, an investigational vaccine for Parkinson's disease (PD), demonstrating UB-312 was well-tolerated and induced anti-alpha-synuclein (aSyn) antibody responses in participants with early PD, meeting the primary objectives of the trial.

"These positive Phase 1 results demonstrate several important features necessary for an immunotherapy against Parkinson's disease and other synucleinopathies to be successful, and represent a further proof-of-principle for Vaxxinity's platform in chronic disease," said Mei Mei Hu, CEO of Vaxxinity. "UB-312 was observed to safely break immune tolerance, inducing antibodies against toxic aggregated forms of alpha-synuclein. Importantly, these antibodies crossed the blood brain barrier, and the data also suggest potential target engagement in the periphery, where pathological alpha-synuclein is known to be concentrated. Together these results support the further development of UB-312 in a Phase 2 clinical trial. We continue to view UB-312 as a promising candidate for the prevention or disease modification of Parkinson's disease globally."

UB-312 is an investigational synthetic peptide vaccine that targets toxic forms of aggregated aSyn to address PD and other synucleinopathies. Alpha-synuclein plays a central role in synaptic functions and regulation of neurotransmitter release. The accumulation and aggregation of misfolded aSyn in the brain is considered to be a key factor in the development and progression of PD.

The Phase 1 placebo-controlled, double-blind clinical trial of UB-312 consisted of two parts: Part A tested escalating doses of UB-312 versus placebo in 50 healthy volunteers aged 40 to 85 years, and Part B tested two doses of UB-312 versus placebo in 20 age-matched subjects with early PD (Hoehn & Yahr stage ≤ III), both conducted at the Centre for Human Drug Research (CHDR), an independent institute in the Netherlands. Results from Part A, published in *Movement Disorders* in 2022, suggested that UB-312 is highly immunogenic, with all individuals in the target dose group showing detectable anti-aSyn antibodies in both serum and cerebrospinal fluid (CSF).

Geert Jan Groeneveld, MD, PhD, Professor of Clinical Neuropharmacology at Leiden University Medical Center, CMO/CSO of CHDR, and principal investigator of the Phase 1 trial, said, "A vaccine against alpha-synuclein is a revolutionary concept that can be of immense impact in treating neurodegenerative diseases such as Parkinson's disease and synucleinopathies."

Part B consisted of a 20-week treatment period followed by 24 weeks of observation. This study was conducted to evaluate the safety, tolerability and immunogenicity of UB-312 in patients with PD. Part B end-of-study results are as follows:

- The primary objectives were met.
- 92% of patients (12 out of 13) who completed dosing with UB-312 developed anti-aSyn antibodies.
- UB-312 was generally safe and well-tolerated with overall adverse event profile similar across UB-312 and placebo groups. Two patients experienced serious adverse events (SAEs). Only one event was deemed possibly related to the trial, and all SAEs were resolved.
- Antibodies were also detectable in the CSF.

The trial included exploratory measures of Parkinson's disease progression, including UPDRS Parts II and III, and the Montréal Cognitive Assessment; however, the trial was not designed or powered to detect differences between UB-312 and placebo on these measures.

Additionally, The Michael J. Fox Foundation ("MJFF") is funding a 2-year collaborative project between Vaxxinity, the Mayo Clinic, and the University of Texas Houston using CSF collected from patients who participated in Part B of the trial. This work is evaluating the potential of protein misfolding cyclic amplification ("PMCA") to assess target engagement and will also aim to characterize the anti-aSyn antibodies produced after UB-312 administration.

More information about the Phase 1 trial is available at https://clinicaltrials.gov/ct2/show/NCT04075318.

About Parkinson's Disease

Parkinson's disease (PD) affects approximately one million people in the United States and more than 10 million people worldwide. PD is a chronic and progressive neurodegenerative disorder that affects predominately dopamine-producing ("dopaminergic") neurons in the substantia nigra area of the brain. While today's approved products are aimed at providing symptomatic relief, they often produce significant side effects and lose their beneficial effects over time. There are no currently approved disease-modifying therapeutics for PD. Alpha-synuclein (aSyn) is a protein highly expressed in neurons, mostly at presynaptic terminals, suggesting a role in synaptic vesicle trafficking, synaptic functions and in regulation of

neurotransmitter release at the synapse. Mutations in the gene encoding aSyn are known to cause or increase the risk of developing PD or dementia with Lewy bodies (DLB) and have been shown to alter the secondary structure of aSyn, resulting in misfolded and aggregated forms of the protein (i.e., pathological forms). While mutations in the aSyn gene are rare, aggregates of aSyn in the form of Lewy bodies (LB) and Lewy neurites are common neuropathological hallmarks of both familial and sporadic PD, suggesting a key role of aSyn in PD neuropathogenesis. Immunotherapy approaches targeting aSyn have been shown to ameliorate aSyn pathology as well as functional deficits in mouse models of PD and are now being investigated in the clinic.

About UB-312

UB-312 is a vaccine candidate targeting pathological forms of alpha-synuclein (aSyn) for the disease-modifying treatment and prevention of Parkinson's disease (PD) and other synucleinopathies. Preclinical data indicated that UB-312 elicits antibodies that preferentially recognize pathological forms of aSyn, and improve motor performance in mouse models of synucleinopathies. Clinical data from the Phase 1 trial indicate that UB-312 elicits antibody levels sufficient to cross the blood–brain barrier (i.e., detectable in cerebrospinal fluid). The European Medical Agency has granted UB-312 orphan designation for multiple system atrophy.

About Vaxxinity

Vaxxinity, Inc. is a purpose-driven biotechnology company committed to democratizing healthcare across the globe. The company is pioneering a new class of medicines aimed at disrupting the existing treatment paradigm for chronic disease, increasingly dominated by monoclonal antibodies, which suffer from prohibitive costs and cumbersome administration. The company's proprietary technology platform has enabled the innovation of novel synthetic peptide immunotherapy candidates designed to bring the efficiency of vaccines to the treatment of chronic diseases, including Alzheimer's disease, Parkinson's disease, migraine, and hypercholesterolemia. The technology is also implemented as part of a COVID-19 vaccine program. Vaxxinity has optimized its pipeline to achieve a potentially historic, global impact on human health.

For more information about Vaxxinity, Inc., visit http://www.vaxxinity.com and follow us on social media @vaxxinity.

About the Centre for Human Drug Research

The Centre for Human Drug Research (CHDR) is an independent institute that specializes in cutting edge early-stage clinical drug research. Combining innovative methods and technologies, state-of-the-art facilities, and talented, motivated researchers helps CHDR maximize its clients' success. In addition, CHDR places the highest priority on its subjects' comfort and safety, and plays an active role in helping to educate the medical and clinical research communities.

Forward-looking Statements

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. The use of certain words, including "believe," "may," "continue," "advancing," "will" and similar expressions, are intended to identify forward-looking statements. Forward-looking statements include statements, other than statements of historical fact, regarding, among other things: the plans for, or progress, scope, initiation, duration, enrollment, results or timing for availability of results of, development of any of Vaxxinity's product candidates or programs, including timing of the data readouts of UB-312 and subsequent clinical trials of UB-312; the target indication(s) for development or approval, the size, design, population, location, conduct, cost, objective, enrollment, duration or endpoints of any clinical trial, or the timing for initiation or completion of or availability or reporting of results from any clinical trial; the potential future regulatory authorization or approval and commercialization of Vaxxinity's product candidates; the potential benefits or competitive position of any Vaxxinity product candidate or program or the commercial opportunity in any target indication; and Vaxxinity's plans, expectations or future operations, financial position, revenues, costs or expenses. These forward-looking statements involve substantial risks and uncertainties, including statements that are based on the current expectations and assumptions of Vaxxinity's management about the development of a new class of immunotherapeutic vaccines and the innovation and efficacy of Vaxxinity's product candidates. Various important factors could cause actual results or events to differ materially from those that may be expressed or implied by our forward-looking statements, including, but not limited to: whether UB-312 or any other current or future product candidate of Vaxxinity will be approved or authorized by any regulatory agency for the indications that Vaxxinity targets; any potential negative impacts of the COVID-19 pandemic, including on manufacturing, supply, conduct or initiation of clinical trials, or other aspects of Vaxxinity's business; Vaxxinity's product candidates may not be successful or clinical development may take longer and be more costly than anticipated; product candidates that appeared promising in earlier research and clinical trials may not demonstrate safety or efficacy in larger-scale or later clinical trials or in clinical trials for other indications; the timing for initiation or completion of, or for availability of data from, clinical trials, and the outcomes of such trials; Vaxxinity's reliance on collaborative partners and other third parties for development of its product candidates; Vaxxinity's ability to obtain coverage, pricing or reimbursement for any approved products and acceptance from patients and physicians for any approved indications; delays or other challenges in the recruitment of patients for, or the conduct of, Vaxxinity's clinical trials; challenges associated with supply and manufacturing activities; and Vaxxinity's accounting policies. These and other important factors to be considered in connection with forward-looking statements are described in the "Risk Factors" section of Vaxxinity's Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission on March 27, 2023. The forward-looking statements are made as of this date and Vaxxinity does not undertake any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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