Vaxxinity Demonstrates Target Engagement of Toxic Alpha-Synuclein in Parkinson's Patients

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Disease-modifying candidate UB-312 demonstrated target engagement of aggregated alpha-synuclein in cerebrospinal fluid of Parkinson's patients

Data provide validation of the Vaxxinity platform's ability to selectively target aggregated, toxic forms of neurodegenerative proteins

CAPE CANAVERAL, Fla., July 17, 2023 (GLOBE NEWSWIRE) -- Vaxxinity, Inc. (Nasdaq: VAXX), a U.S. company pioneering the development of a new class of medicines, today announced new data from a Phase 1 clinical trial demonstrating that antibodies derived from its investigational immunotherapeutic for Parkinson's disease (PD), UB-312, slows seeding of alpha-synuclein (aSyn) in cerebrospinal fluid (CSF) of patients with PD as demonstrated using multiple target engagement assays. These data signify that UB-312 has established clear target engagement in PD patient CSF, and provides further validation of Vaxxinity's platform technology in neurodegenerative disease.

"This is a major milestone for Vaxxinity in our quest to help Parkinson's patients. Our candidate has shown target engagement of the toxic species of alpha-synuclein in patients, demonstrating not only proof of our technology platform, but also proof of the mechanism of our vaccine-derived antibodies specifically engaging with the toxic target *in vivo*," said Mei Mei Hu, CEO of Vaxxinity. "Showing target engagement has always been a key challenge to overcome in neurodegeneration, and is of critical importance when demonstrated – a milestone worth celebrating. It is beyond our expectation to see this in our Phase 1 trial. We are endlessly grateful to the patients who participated, and to The Michael J. Fox Foundation and our collaborators for their work on these cutting-edge assays that supported this breakthrough."

UB-312 is designed to target aggregated forms of aSyn, the toxic species that underlies Parkinson's disease and other synucleinopathies. Last month, Vaxxinity announced clinical data from Part B of its Phase 1 clinical trial of UB-312 demonstrating that UB-312 was well-tolerated and induced anti-aSyn antibody responses in participants with early PD, and that antibodies were detectable in the CSF. As part of this trial, The Michael J. Fox Foundation (MJFF) funded a 2-year collaborative project between Vaxxinity, the Mayo Clinic, and UTHealth Houston to analyze CSF collected from patients, and to conduct exploratory research to characterize the anti-aSyn antibodies produced after UB-312 administration and assess target engagement.

Analyses from this and related research yielded insights about the pharmacodynamic effects of anti-aSyn antibodies generated by UB-312 in the Phase 1 trial.

- UB-312-derived antibodies show preferential binding to aggregated aSyn isolated from patients with PD and Multiple System Atrophy (MSA), as measured by dot blot. Preclinical data published in *Alzheimer's Research & Therapy* in 2020 showed similar characteristics of UB-312-derived antibodies.
- UB-312-derived antibodies successfully demonstrate inhibition of aggregation of aSyn in both a seed amplification assay (SAA) and a protein misfolding cyclic amplification assay (PMCA). These techniques can potentially be used to identify people with PD, and also to measure the treatment response and pharmacodynamic properties of UB-312-derived antibodies from subjects in clinical trials.
- Importantly, aSyn aggregation was slowed down in CSF samples from PD patients who received UB-312, as compared to those who received placebo, in the Phase 1 trial.

Vaxxinity plans to continue analyses of the clinical data as part of the collaborative project with MJFF, in addition to completing other target engagement assays and additional antibody characterization studies for binding kinetics and specificity. Mark Frasier, Ph.D., Chief Scientific Officer of MJFF, commented, "Integration of critical biomarker insight into therapeutic development programs is essential for building confidence in the treatment approach, and for designing informative trials. We're pleased to support efforts of this kind that can have major impact for people with Parkinson's disease."

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 antibodies that target aggregated aSyn, and that these antibodies slow the aggregation of alpha-synuclein in the cerebrospinal fluid of patients with PD. 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.

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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