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Avenue Therapeutics Announces First Patient Dosed in Phase 1b/2a Clinical Trial of AJ201 for the Treatment of Spinal and Bulbar Muscular Atrophy (Kennedy's Disease)

Topline data expected in 2024

MIAMI, July 27, 2023 (GLOBE NEWSWIRE) -- Avenue Therapeutics, Inc. (Nasdaq: ATXI) ("Avenue" or the "Company"), a specialty pharmaceutical company focused on the development and commercialization of therapies for the treatment of neurologic diseases, today announced that the first patient has been dosed in the Phase 1b/2a clinical trial of AJ201 for the treatment of spinal and bulbar muscular atrophy ("SBMA"), also known as Kennedy's Disease. A recent study used genetic analysis to estimate disease prevalence of 1:6,887 males.[1] AJ201 is currently the lead drug candidate in the clinic for SBMA and enrollment in the trial is expected to be complete by the end of 2023 or early 2024 with potential topline data in 2024.

"We are excited to announce that the first patient has been dosed in our Phase 1b/2a clinical trial evaluating AJ201 for the treatment of SBMA, a progressive and devastating neurodegenerative disease that currently has no approved treatments available," said Alexandra MacLean, M.D., Chief Executive Officer of Avenue. "We are encouraged by the Phase 1 clinical data of AJ201 that demonstrate the drug's excellent safety profile in healthy volunteers. Additionally, compelling preclinical data in a mouse model showed efficacy signals, including improvement in motor function, robust degradation of mutant androgen receptors ("AR"), a disease-signaling protein, and activation of the Nrf1 and Nrf2 pathways. In this Phase 1b/2a clinical trial, we aim to demonstrate how AJ201's novel, multi-fold mechanism of action reduces accumulation of mutant AR aggregates to potentially decrease neuroinflammation, protect cells from oxidative stress, and ultimately, improve clinical outcomes for SBMA patients. We look forward to advancing this much needed drug, as we continue to deliver on our mission of bringing impactful therapies to people suffering from neurologic diseases."

The 12-week, multicenter, randomized, double-blind Phase 1b/2a clinical trial of AJ201 is expected to enroll approximately 24 patients, randomly assigned to AJ201 (600 mg/day) or

placebo. The primary endpoint of the study is to assess safety and tolerability of AJ201 in subjects with clinically and genetically defined SBMA. Secondary endpoints include pharmacodynamic data measuring change from baseline in mutant AR protein levels in skeletal muscle and changes in the fat and muscle composition as seen on MRI scans, which are believed to be biomarkers indicating likelihood for longer term clinical improvement. Further details about this study can be found at ClinicalTrials.gov (Identifier: NCT05517603).

About Spinal and Bulbar Muscular Atrophy

Spinal and bulbar muscular atrophy ("SBMA") is a rare, X-linked genetic neuromuscular disease primarily affecting men. The condition is caused by the trinucleotide CAG repeat expansion in the androgen receptor ("AR") which leads to production of a mutant polyglutamine ("polyQ") AR protein that forms aggregates responsible for muscular atrophy focused in the limbs and bulbar region of the body. The weakening of the bulbar muscles affects chewing, speech and swallowing, with patients prone to choking or inhaling foods or liquids, resulting in airway infection. SBMA also affects muscles in the limbs, leading to difficulty walking and injury caused by falling. Although there is a range of cited prevalence rates in scientific literature, a recent study used genetic analysis to estimate disease prevalence of 1:6,887 males.[1] Currently, there are no treatments approved by the U.S. Food and Drug Administration or European Medicines Agency available for patients. For more information about SBMA, also known as Kennedy's Disease, please visit https://kennedysdisease.org/.

About AJ201

AJ201 is a novel, first-in-class asset in development for the treatment of spinal and bulbar muscular atrophy. It was designed to modify SBMA through multiple mechanisms including degradation of the abnormal androgen receptor protein and by stimulating the Nrf1 and Nrf2 pathways, which are involved in protecting cells from oxidative stress which can lead to cell death. A first-in-human Phase 1 study of AJ201 in 72 healthy volunteers revealed an excellent safety and pharmacokinetic profile. It is currently being studied in a Phase 1/2a multicenter, randomized, double-blind clinical trial in six clinical sites across the U.S., which aims to evaluate the safety, PK/PD data and clinical response of AJ201 in patients suffering from SBMA. AJ201 has been granted Orphan Drug Designation by the FDA for multiple polyQ diseases, including SBMA, Huntington's disease and spinocerebellar ataxia. Avenue exclusively licensed AJ201 from AnnJi Pharmaceuticals in the United States, Canada, European Union, Great Britain, and Israel.

About Polyglutamine diseases

Polyglutamine diseases are a group of neurodegenerative disorders caused by expanded CAG repeats encoding a long polyQ tract in the affected proteins. To date, a total of nine polyQ disorders have been described. Mutant protein aggregation in affected tissues is the pathological hallmark of polyQ diseases. Neuroinflammation, oxidative stress and dysregulated protein quality control are thought to be key pathological factors that are either direct results of mutant protein aggregations and/or exacerbate the severity and progression of the diseases. Modulating multiple cellular pathways in enhancing degradation of mutant AR aggregates, inducing antioxidant and heat shock responses, and increasing proteasome expression simultaneously provide the rationale to develop AJ201 for the treatment of SBMA and potentially other polyQ diseases.

About Avenue Therapeutics

Avenue Therapeutics, Inc. (Nasdaq: ATXI) is a specialty pharmaceutical company focused on the development and commercialization of therapies for the treatment of neurologic diseases. It is currently developing three assets including AJ201, a first-in-class oral small molecule for spinal and bulbar muscular atrophy, BAER-101, an oral small molecule selective GABA-A α2/3 receptor positive allosteric modulator for CNS diseases, and IV Tramadol, which is in Phase 3 clinical development for the management of moderate-to-moderately-severe pain in adults in a medically supervised healthcare setting. Avenue is headquartered in Miami, FL and was founded by Fortress Biotech, Inc. (Nasdaq: FBIO). For more information, visit www.avenuetx.com.

Forward-Looking Statements

This press release contains predictive or "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements other than statements of current or historical fact contained in this press release, including statements that express our intentions, plans, objectives, beliefs, expectations, strategies, predictions or any other statements relating to our future activities or other future events or conditions are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "predict," "project," "will," "should," "would" and similar expressions are intended to identify forward-looking statements. These statements are based on current expectations, estimates and projections made by management about our business, our industry and other conditions affecting our financial condition, results of operations or business prospects. These statements are not guarantees of future performance and involve risks, uncertainties and assumptions that are difficult to predict. Therefore, actual outcomes and results may differ materially from what is expressed or forecasted in, or implied by, the forward-looking statements due to numerous risks and uncertainties. Factors that could cause such outcomes and results to differ include, but are not limited to, risks and uncertainties arising from: expectations for increases or decreases in expenses; expectations for the clinical and pre-clinical development, manufacturing, regulatory approval, and commercialization of our pharmaceutical product candidate or any other products we may acquire or in-license; our use of clinical research centers and other contractors; expectations for incurring capital expenditures to expand our research and development and manufacturing capabilities; expectations for generating revenue or becoming profitable on a sustained basis; expectations or ability to enter into marketing and other partnership agreements; expectations or ability to enter into product acquisition and in-licensing transactions; expectations or ability to build our own commercial infrastructure to manufacture, market and sell our product candidates; acceptance of our products by doctors, patients or payors; our ability to compete against other companies and research institutions; our ability to secure adequate protection for our intellectual property; our ability to attract and retain key personnel; availability of reimbursement for our products; estimates of the sufficiency of our existing cash and cash equivalents and investments to finance our operating requirements, including expectations regarding the value and liquidity of our investments; the volatility of our stock price; expected losses; expectations for future capital requirements; and those risks discussed in our filings which we make with the SEC. Any forward-looking statements speak only as of the date on which they are made, and we undertake no obligation to publicly update or revise any forward-looking statements to reflect events or circumstances that may arise after the date of this press release, except as required by applicable law. Investors should evaluate any statements made by us in light of these important factors.

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[1] M. Zanovello et al., Unexpected frequency of the pathogenic*AR*CAG repeat 2 expansion in the general population. Brain, 2023 Jul 3;146(7):2723-2729.

Source: Avenue Therapeutics