



NEWS RELEASE

eidos therapeutics initiates phase 2 clinical trial for ag10 targeting transthyretin amyloidosis cardiomyopathy

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SAN FRANCISCO, May 3, 2018 /PRNewswire/ — Eidos Therapeutics, Inc., a clinical stage biopharmaceutical company developing a novel oral therapy to treat transthyretin (TTR) amyloidosis (ATTR), today announced dosing of the first patient in the Phase 2 clinical trial of AG10 in patients with ATTR cardiomyopathy (**NCT03458130**).

The Phase 2 trial will enroll approximately 45 symptomatic ATTR cardiomyopathy patients in a randomized, double-blind, placebo-controlled design. The trial will include a minimum of 30% of patients with mutant ATTR cardiomyopathy, with the remainder having wild type ATTR cardiomyopathy.

Patients will be randomized in a 1:1:1 fashion to placebo or one of two different doses of AG10 on a background of stable heart failure therapy. If all doses are well-tolerated, patients will be treated for 28 days.

“ATTR cardiomyopathy represents a significant unmet need with a poor prognosis and limited existing treatment options, and further, the prevalence of the disease is increasing dramatically with improved awareness and novel, non-invasive diagnostic techniques,” said Rodney Falk, M.D., director of the cardiac amyloidosis program at Brigham and Women’s Hospital and associate professor of medicine at Harvard Medical School. “The preclinical and Phase 1 data describing AG10 indicate that it could be a valuable treatment option for these patients, and I am eager to participate in the trial and learn more about AG10’s potential.”

The primary objective of this trial is to evaluate the safety and tolerability of AG10. The trial will also characterize the pharmacokinetics of AG10 administered twice daily. Finally, the trial will measure and confirm TTR stabilization by

validated ex vivo assays, namely fluorescent probe exclusion and immunoblotting. As previous clinical studies have demonstrated that increasing levels of TTR stabilization lead to improved clinical benefit, the trial aims to provide clinical proof of concept to support potential subsequent pivotal trials.

This Phase 2 trial follows the successful completion of a Phase 1 trial of AG10 in healthy volunteers, reported at the 16th International Symposium on Amyloidosis in Kumamoto, Japan on March 29, 2018. The Phase 1 trial included single ascending dose, multiple ascending dose (MAD) and food effect components. AG10 was found to be well-tolerated at all doses. No serious adverse events were observed in the trial, vital signs and cardiac safety measures revealed no findings of clinical concern, and liver, kidney and hematological parameters were all within normal limits.

“The positive results of our Phase 1 trial of AG10 in healthy volunteers encouraged our rapid advancement into a Phase 2 trial in patients with ATTR cardiomyopathy,” said Jonathan Fox, M.D., Ph.D., the company’s president and chief medical officer. “Our preclinical and Phase 1 data provide evidence that AG10 could be beneficial for both wild type and mutant ATTR cardiomyopathy patients, and this Phase 2 trial aims to provide additional information in these specific populations.”

Pharmacokinetic measurements demonstrated that AG10 is rapidly and consistently absorbed with a terminal half-life of approximately 25 hours. Ex vivo pharmacodynamic assays demonstrated 100% TTR stabilization at peak plasma concentrations and >95% stabilization on average in the final MAD cohort. TTR stabilization measurements were highly correlated between assays and a clear dose-dependency of stabilization was observed.

“Based on genetic evidence and previous clinical trials, we believe that increasing levels of TTR stabilization lead to increased clinical benefit,” said Uma Sinha, Ph.D., the company’s chief scientific officer. “The ex vivo measurements used in our Phase 1 trial demonstrate that AG10 potently binds TTR tetramers and prevents their dissociation into monomers, which is thought to be the rate limiting step in ATTR pathogenesis. These data support our belief that AG10 could become a best-in-class TTR stabilizer treatment for ATTR patients.”

The company expects to report topline results from this Phase 2 trial by the end of 2018. Eidos expects to launch a second Phase 2 trial in patients with ATTR polyneuropathy later this year.

about ag10

AG10 is an orally-administered, small molecule designed to potently stabilize tetrameric TTR, thereby halting at its outset the series of molecular events that give rise to ATTR. Eidos’ approach, based on over 25 years of research, mimics a naturally-occurring genetic rescue mutation that protects high-risk individuals from developing ATTR by stabilizing the TTR tetramer. In fact, the binding of AG10 to tetrameric TTR creates strong molecular bonds at the same locations as the rescue mutation known as T119M, which “super-stabilizes” TTR and has been shown to

enhance survival. This specific binding mode underlies AG10's ability at peak blood concentrations to completely stabilize tetrameric TTR and prevent its dissociation into disease-causing TTR monomers in the bloodstream. Based on data from previous clinical trials in ATTR demonstrating that preventing the generation of TTR monomers from circulating in the bloodstream leads to improved clinical outcomes, Eidos believes that AG10 could be a best-in-class therapy.

about transthyretin amyloidosis (attr)

ATTR represents a significant unmet need, with a comparatively large patient population in the context of rare genetic diseases and an inadequate current standard of care. There are three distinct diseases that comprise the ATTR family: wild-type ATTR cardiomyopathy (ATTRwt-CM), mutant ATTR cardiomyopathy (ATTRm-CM), and ATTR polyneuropathy (ATTR-PN). The worldwide prevalence of each disease is approximately 200,000 patients, 40,000 patients and 10,000 patients, respectively, although Eidos believes the cardiomyopathic forms of the disease are significantly underdiagnosed due to non-specific symptoms and a historical reliance on an invasive heart biopsy for diagnosis. Eidos believes that improving

disease awareness and the introduction of a non-invasive, imaging-based diagnostic scan, coupled with appropriate blood tests, are significantly increasing rates of diagnosis for ATTRwt-CM and ATTRm-CM.

All three forms of ATTR are progressive and fatal, and no disease-modifying therapies have been approved by the FDA. For patients with ATTRwt-CM and ATTRm-CM, symptoms usually manifest later in life (age 50+), with median survival of three to five years from diagnosis. ATTR-PN either presents in a patient's early 30s or later (age 50+), and results in a median life expectancy of five to ten years from diagnosis. Progression of all forms of ATTR causes significant morbidity, impacts productivity and quality of life, and creates a significant economic burden due to the costs associated with progressively greater patient needs for supportive care.

about eidos therapeutics

Eidos is a clinical stage biopharmaceutical company focused on addressing the large and growing unmet need in diseases caused by transthyretin (TTR) amyloidosis (ATTR). Eidos seeks to treat this well-defined family of diseases at their collective source by stabilizing TTR, a therapeutic approach that is supported by genetic evidence as well as previous clinical trials. The company's product candidate, AG10, is an orally-administered small molecule designed to potently stabilize TTR, suggesting a best-in-class treatment with the potential to halt the progression of ATTR. The development of AG10 is led by a proven management team who are responsible for developing over 30 molecules through IND applications and more than 10 approved drugs. Together with patients and physicians, Eidos aims to bring a safe, effective and disease-modifying treatment for ATTR to market as quickly as possible.