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UCB Zilucoplan trial arm stopped early in HEALEY ALS Platform

The independent Data and Safety Monitoring Board (DSMB) recommended stopping the zilucoplan regimen in the HEALEY ALS Platform Trial after a pre-scheduled interim analysis demonstrated futility.

The Healey ALS Platform Trial is a master platform trial led by the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) in collaboration with the Northeast ALS Consortium (NEALS).

The trial is designed using an efficient trial design that permits rolling initiation of new regimens and the possibility of early stopping if a candidate drug is found to be ineffective. The regimen testing zilucoplan (NCT04436497) was one of the first three regimens initiated in July 2020. Zilucoplan is an experimental C5 complement inhibitor manufactured by UCB.

The decision to stop the zilucoplan regimen early was based on the recommendation of the DSMB following pre-specified criteria for early stopping that are evaluated as part of regular interim analyses. At the most recent interim analysis, zilucoplan was found to have a low probability of meaningfully slowing disease progression.

“The platform trial includes early stopping rules and other adaptive features to accelerate the testing of investigational products for ALS," says Merit Cudkowicz, MD, MSc, principal investigator and sponsor of the HEALEY ALS Platform Trial, director of the Sean M. Healey & AMG Center for ALS, chief of the Department of Neurology at MGH, and the Julieanne Dorn Professor of Neurology at Harvard Medical School. “While we are disappointed by the results of the zilucoplan regimen, we know it is important to have early read-outs when results are clear so that efforts can be quickly refocused on other investigational products. We have to move forward to find new treatments as quickly as possible. We are extremely grateful to the many participants in the trial and the members of our patient advisory group for their contributions to ALS science and therapy development.”

“We would like to sincerely thank the participants in the zilucoplan regimen who committed their time, energy, and hope in the trial as well as the investigators and study staff who dedicated their effort and expertise," says Sabrina Paganoni, MD, PhD, a physician-scientist at the Healey & AMG Center and lead investigator of the zilucoplan regimen. “Even though the trial results were negative, participants' involvement in the trial contributed greatly to ALS research by providing substantial clinical and biomarker data that will help us better understand ALS disease mechanisms and the role of the complement system in people living with ALS.”

Participants who enrolled in the zilucoplan regimen are discontinuing study medication and will complete any necessary follow-up activities over the next few days. Full data from the trial are expected to be available later in 2022.

Additional products under investigation in the platform trial include: 1) verdiperstat, a brain-penetrant myeloperoxidase enzyme inhibitor, 2) CNM-Au8, a cellular energetic nanocatalyst, 3) pridopidine, a selective sigma-1 receptor agonist, and 4) SLS-005 (trehalose), a molecule that stabilizes proteins and activates autophagy. Enrollment is complete for the verdiperstat, CNM-Au8, and pridopidine regimens, while enrollment for the SLS-005 regimen has recently started. The trial is active and enrolling at nationwide.

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