



Kynexis Announces Positive Topline Results from Phase 1 Study of KYN-5356, a Potential Treatment for Cognitive Impairment Associated with Schizophrenia

KYN-5356, an innovative, first-in-class small molecule inhibitor of KAT-II, a key enzyme in the kynurenine pathway implicated in schizophrenia, was shown to be safe and well-tolerated in the Phase 1 study in healthy volunteers

Initial data shows clear evidence of target engagement and suggestive evidence of cognitive improvement, adding to body of evidence that supports further study of KYN-5356 in patients with cognitive impairment associated with schizophrenia (CIAS), which is among the most debilitating symptoms of the disease

Clinical trial in patients anticipated to begin in 2025

Naarden, The Netherlands – December 17, 2024 – Kynexis, a biotechnology company focused on precision therapeutics for brain diseases, today announced positive topline results from its first-in-human phase 1 clinical trial. The phase 1 study in healthy volunteers evaluated the safety, tolerability, and pharmacokinetics of single and multiple ascending oral doses of KYN-5356, a first-in-class small molecule inhibitor of KAT-II, being developed for the treatment of cognitive impairment associated with schizophrenia (CIAS). The study also evaluated central pharmacodynamic biomarkers and cognitive performance to determine target engagement in the multiple ascending part.

Results show that KYN-5356 was safe and well-tolerated and exhibited excellent pharmacokinetic (PK) properties in both plasma and cerebrospinal fluid (CSF), suggesting appropriate penetration and exposure of KYN-5356 in the central nervous system (CNS). The study also tested exploratory pharmacodynamic (PD) endpoints, where KYN-5356 demonstrated statistically significant improvements in electroencephalography (EEG) activity relevant to cognitive pathways, as well as early, suggestive evidence of cognitive improvement. Findings further showed a dose-dependent reduction of kynurenic acid levels in the CSF, which have been shown to be elevated in people with schizophrenia and are believed to be a key driver of CIAS.

“Cognitive impairment is a primary driver of disability for people with schizophrenia and affects most people with the disease. While still early, these data represent a milestone for Kynexis as we advance this potentially first-in-class treatment for cognitive impairment associated with schizophrenia, or CIAS,” said Kees Been, Chief Executive Officer of Kynexis. “As the first KAT-II inhibitor studied in humans, KYN-5356 has demonstrated an excellent safety profile and promising pharmacokinetic data, including evidence of significant brain penetration. The observed dose-dependent reductions in CSF kynurenic acid levels, the effects on EEG activity, and the early evidence of cognitive benefit further validate our precision-medicine approach to targeting the kynurenine pathway for CIAS.”

Dr. Jens Wendland, Chief Medical Officer at Kynexis, continued, “All subjects successfully completed the study, and the data provide critical insights into the brain effects of KYN-5356. These findings, including data showing clear target engagement across several biomarker modalities, build on the body of evidence

supporting its potential to treat cognitive impairment associated with schizophrenia. We look forward to sharing the full phase 1 results at a scientific conference next year and are now moving swiftly toward initiating our first-in-patient clinical study in 2025.”

About Kynexis

Kynexis is advancing precision therapeutics for brain diseases by taking a biomarker-based approach to advance a potential treatment for cognitive impairment associated with schizophrenia (CIAS). By harnessing large data to identify and stratify patients based on the underlying causal human biology of the disease, Kynexis is targeting KAT-II, a key enzyme in the kynurenine pathway. The company’s lead candidate, KYN-5356, is a first-in-class small molecule that is potent and highly selective for KAT-II. The Company has a subsidiary in the United States, which is based in Cambridge, Mass. (Kynexis Therapeutics Inc.). Learn more at kynexistx.com and follow us on [LinkedIn](#) and [X](#).

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