EIP Pharma announces that final results of the AscenD-LB phase 2 clinical study demonstrates neflamapimod has disease-modifying potential in dementia with Lewy Bodies

Results presented at 14th Clinical Trials in Alzheimer's Disease (CTAD) meeting in Boston

Neflamapimod treatment led to significant improvement relative to placebo in cognition, motor function, and cognition & function (dementia progression)

Boston, Mass., November 10th, 2021 – EIP Pharma Inc., a clinical-stage pharma company focused on the development of disease-modifying treatments for dementia and neurodegenerative diseases announces that the final results of the AscenD-LB phase 2 clinical study of their oral investigational drug, neflamapimod, in mild-to-moderate dementia with Lewy bodies were presented at the 14th Clinical Trials in Alzheimer's Disease (CTAD) meeting that will be held in Boston November 9th through 12th, 2021. The results demonstrated that neflamapimod treatment led to significant improvement relative to placebo in cognition (assessed by cognitive test battery), motor function (specifically functional mobility assessed by Timed Up and Go test) and cognition & function (dementia progression, assessed by Clinical Dementia Rating scale Sum of Boxes). In addition, patients with "pure DLB" (identified by excluding patients with concomitant Alzheimer's-related tau pathology using a plasma biomarker) had particularly robust and high efficacy, a finding consistent with neflamapimod acting on the underlying, and specific disease process in DLB.

"Neflamapimod significantly improves relative to placebo cognition, motor function, and cognition & function (dementia progression) in mild-to-moderate dementia with Lewy bodies, consistent with a disease-modifying effect on basal forebrain cholinergic degeneration", concluded Dr. John Alam, CEO at EIP Pharma, at the end of his oral presentation at the meeting.

"The final results of the AscenD-LB study are extremely exciting for patients with DLB, caregivers and clinicians as we may be looking at the first DLB treatment that modifies the underlying disease", said Dr. James Galvin, Professor of Neurology and Director of the Lewy Body Dementia Research Center of Excellence at the University of Miami Miller School of Medicine. "Combined with the scientific studies that preceded the clinical study, the results suggest that neflamapimod has the potential to change the course of the disease and significantly improve function and quality of life in patients with DLB. In addition, AscenD-LB has also advanced the field by increasing our understanding of the disease and the tools we can use to measure drug treatment effects in clinical trials in dementia with Lewy bodies."

AscenD-LB Clinical Study Results

AscenD-LB was a Phase 2 double-blind, placebo-controlled, 16-week treatment proof-of-concept study ("AscenD-LB") of neflamapimod in mild-to-moderate dementia with Lewy bodies

(DLB) conducted at 22 centers in the United States and two centers in the Netherlands. 91 patients were enrolled between October 2019 and March 2020 and randomized to receive 40 mg neflamapimod capsules or matching placebo capsules (randomized 1:1) for 16 weeks. The dosing regimen was based on weight, with study participants weighing less than 80 kg receiving capsules twice-daily (BID) and those weighing greater than or equal to 80 kg received capsules three-times-a-day (TID). The primary objective was to evaluate the effect of neflamapimod on cognition as assessed in a DLB-specific Neuropsychological Test Battery (NTB) that was designed to evaluate attention and executive function. Secondary endpoints included the Timed Up and Go (TUG) test and the Clinical Dementia Rating scale Sum of Boxes (CDR-SB). The AscenD-LB study is registered at clinicaltrials.gov as study NCT04001517.

Initial results presented at the 13th CTAD meeting in November 2020 demonstrated that 40mg TID led to a significant improvement relative to placebo in cognitive function, particularly with respect to attention, as well in the time required to complete the TUG test.

The final results of AscenD-LB includes additional analyses of the TUG and CDR-SB, and efficacy analyses after discriminating patients within the study by whether they had "pure DLB" based on a plasma biomarker for co-existing Alzheimer's related tau pathology. These new results were presented in an oral communication and a poster presentation at this year's meeting:

- ***OC5 - Effects of the oral p38α kinase inhibitor neflamapimod on motor function (gait) in patients with mild-to-moderate dementia with Lewy bodies (DLB)***
  New results presented were around the TUG and CDR-SB (note: all p-values reported are from mixed model for repeated measures, MMRM, analyses):

  - Timed up and Go (TUG) Test: in the full efficacy analysis population, the comparison of all neflamapimod (N=39, including both 40mg BID and 40mg TID participants) *vs.* all placebo (N=38), there was a significant difference (p=0.044) in the change from baseline in time required to complete TUG, favoring neflamapimod. The positive effect was dose-dependent with a significant effect also demonstrated in the comparison of 40mg TID vs. all placebo (p=0.024). For both comparisons, the mean difference between active drug and placebo was 1.4 seconds.
  - Clinical Dementia Rating scale Sum of Boxes (CDR-SB): in the full efficacy analysis population, the comparison of all neflamapimod (N=42, including both 40mg BID and 40mg TID participants) *vs.* all placebo (N=41), there was a significant difference (p=0.024) in the change from CDR-SB scores, favoring neflamapimod, over the course of the study. At week 16, compared to placebo there was a 65% reduction with neflamapimod treatment in worsening of dementia, as assessed by change in CDR-SB. Significant effect improvement (p=0.007) was also demonstrated in the comparison of 40mg TID (N=20) vs. all placebo (N=41).

- ***LP14 Impact of Alzheimer's disease (AD) related co-pathology on treatment effects of the oral p38α kinase inhibitor neflamapimod in mild-to-moderate dementia with Lewy bodies (DLB)***

  The primary pathology in dementia with Lewy bodies is in the region of the brain called the basal forebrain. In addition, one-third to half of patients with DLB have "AD co-pathology", particularly tau pathology, indicative of neurodegeneration, outside the basal forebrain. To understand the relative impact of neflamapimod treatment in these sub-groups, baseline samples from AscenD-LB were assayed at VUMc in Amsterdam for plasma p-tau181, a biomarker that is predictive of cortical tau pathology in patients with DLB (Hall et al, *Movement Disorders,* 2021). At baseline, 22 of 41 (53%) of placebo and 22 of 42 (54%) of neflamapimod participants had plasma ptau181 < 2.2 pg/mL (cut-off for co-pathology at VUMc). When efficacy was analyzed using plasma ptau181 status to identify patients with or without co-pathology, patients without co-pathology ("pure DLB", predicted to have pathology confined to basal forebrain) demonstrated better efficacy than patients with co-pathology (predicted to have neurodegeneration outside basal forebrain), with effect size ranging from 0.56 to 0.78 for the major efficacy endpoints for the comparison of 40mg TID vs. placebo in patients.

  As disease expression in the patients with "pure DLB" is expected to be most specifically driven by basal forebrain cholinergic dysfunction (the therapeutic target of neflamapimod), the specificity for, and magnitude of the clinical efficacy in the patients without co-pathology further supports that neflamapimod has potent and specific activity against basal forebrain cholinergic dysfunction.

About Neflamapimod: Neflamapimod is an investigational drug that is brain-penetrant, oral small molecule that inhibits the intra-cellular enzyme p38 MAP kinase alpha (p38a). P38a, which is expressed in neurons under conditions of stress and disease, plays a major role in inflammation-induced synaptic toxicity, leading to impairment of synaptic function (i.e., synaptic dysfunction). In pre-clinical studies, neflamapimod reverses synaptic dysfunction, including and particularly within the part of the brain most impacted in dementia with Lewy bodies (DLB) - the basal forebrain cholinergic system. Results from the AscenD-LB Phase 2 clinical study demonstrated proof of concept for neflamapimod as a treatment for DLB. In that study, neflamapimod significantly improved cognition, as assessed by a DLB specific Neuropsychological Test Battery (NTB) designed to evaluate attention and executive function. In addition, neflamapimod significantly improved cognition and function as measured by the gold standard dementia rating test, the Clinical Dementia Rating Sum-of-Boxes (CDR-SB), and also showed significant impact on motor function as measured by the Timed Up and Go test (TUG). Neflamapimod is the first treatment with potential impact on cognition, function and motor function in patients with DLB. The combined pre-clinical and clinical data is consistent with neflamapimod treating the underlying disease process and having the potential to be the first disease-modifying treatment for DLB.

About EIP Pharma: EIP Pharma, Inc. is a private, Boston, MA company advancing CNS-focused therapeutics to benefit patients with neurodegenerative diseases.

For more information, please visit www.eippharma.com

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