Zydus Lifesciences announces completion of Phase II(a) clinical trial of Usnoflast, a novel oral NLRP3 inflammasome inhibitor in patients with Amyotrophic Lateral Sclerosis (ALS)

- *Usnoflast, is a "First-in-class" NLRP3 inhibitor to demonstrate proof-of-concept in Phase 2(a) clinical study in ALS patients*
- *Usnoflast was well-tolerated in the 12-week Phase 2(a) trial with target levels achieved in both plasma and Cerebrospinal Spinal Fluid (CSF) of ALS patients [ClinicalTrials.gov ID: NCT05981040]*
- *Usnoflast showed favorable trend towards reduction in Neurofilament Light chain (NfL), an established biomarker of neurodegeneration, in the CSF of ALS patient*
- *Improvement in ALS Functional Rating Scale (ALSFRS-R) and Slow Vital Capacity (SVC) were also observed*

Ahmedabad, India, 10 September, 2024

Zydus, a leading discovery-based, global pharmaceutical company, announced the completion of its Phase II(a) clinical study of NLRP3 inhibitor 'Usnoflast (ZYIL1)' in patients with Amyotrophic Lateral Sclerosis (ALS).

ALS patients experience neuroinflammation and rapid neurodegeneration. Axonal neurodegeneration leads to formation of neurofilaments which first accumulate in CSF of ALS patients, and then slowly these neurofilaments enter blood circulation. Owing to rapid neurodegeneration, steady loss of the ability to move, speak, eat, eventually breathe, paralysis and death have been reported in ALS patients.

ALS affects approximately 32,000 people in the U.S.A and on an average 5,000 new patients are diagnosed every year with this disease in USA as per statistics from Centers for Disease Control and Prevention (CDC). More than 30,000 people are estimated to be living with ALS in Europe (European Union and United Kingdom), while India has an estimated 75,000 people living with ALS. People living with ALS have an average survival of approximately two to five years from diagnosis, with most ALS patients dying from respiratory failure.

PRESS RELEASE

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CIN : L24230GJ1995PLC025878

Speaking on the development, Mr. Pankaj Patel, Chairman, Zydus Lifesciences Limited said "This is a first-in-class innovation and represents a significant scientific breakthrough in our quest for finding new medicines for treating ALS patients. We are excited to report that Usnoflast has been able to reach therapeutic concentrations in CSF of ALS patients and reduce the neurofilaments in CSF in this initial Phase 2(a) study. Clinicians have reported improvements in ALSFRS-R score. The improvement observed in SVC (Slow Vital Capacity) in ALS patients has been encouraging in this 12-week trial. We now look forward to conducting a larger Phase 2b clinical trial in consultation with the regulatory authorities."

The Phase 2(a) randomized, double-blind, placebo controlled clinical trial recruited 24 ALS patients across 7 clinical trial sites in India and evaluated the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Usnoflast in Subjects with ALS [ClinicalTrials.gov Identifier: NCT05981040]. Zydus will publish the detailed clinical trial results in leading medical journals and upcoming scientific conferences.

Usnoflast (ZYIL1) is a novel, oral small molecule NLRP3 inhibitor. Studies have demonstrated that Usnoflast is highly potent in human whole blood assay and can suppress inflammation caused by the NLRP3 inflammasome. Usnoflast was found distributed in the brain and CSF of various nonclinical species including mice, rats and non-human primates. The efficacy of Usnoflast has been established in several pre-clinical models of neuroinflammation, Parkinson's disease[8], Inflammatory Bowel Disease (IBD) and Multiple Sclerosis (MS). Usnoflast, has an acceptable Absorption, Distribution, Metabolism, Excretion (ADME) profile, with a good safety margin. In Phase I studies, Usnoflast was found to be safe and well-tolerated [NCT04731324, NCT04972188]. Zydus has established the Phase 2 proof-of-concept in CAPS patients [NCT05186051] and had earlier published the data in journal 'Clinical Pharmacology in Drug Development'. The USFDA has granted Zydus an 'Orphan Drug Designation' for Usnoflast to treat patients with Cryopyrin Associated Periodic Syndrome (CAPS), a rare auto-inflammatory disease. Zydus has initiated a Phase 2 clinical study of Usnoflast in Ulcerative Colitis [ClinicalTrials.gov ID NCT06398808].

References:

1. ClinicalTrials.gov Identifier: NCT04972188 A Phase I, Prospective, Open Label, Multiple Dose Study of ZYIL1 Administered Via Oral Route to Investigate The Safety, Tolerability, Pharmacokinetics And Pharmacodynamics In Healthy Adult Subjects

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2. ClinicalTrials.gov Identifier: NCT04731324 A Phase 1, Prospective Open Label, Single Dose, Single Arm Study of ZYIL1 Administered Via Oral Route to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Healthy Adult Human Subjects
3. ClinicalTrials.gov Identifier: NCT05186051 A Phase 2a, Prospective, Open-Label Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ZYIL1 in Subjects With Cryopyrin Associated Periodic Syndromes (CAPS)
4. ClinicalTrials.gov ID NCT06398808 A Study to Evaluate the Efficacy and Safety of ZYIL1 Oral Capsules for the Treatment of Patients With Mild to Moderately Active Ulcerative Colitis Resistant or Intolerant to Oral Aminosalicylates
5. ClinicalTrials.gov ID NCT05981040 A Phase 2, Proof-of-concept, Placebo Controlled, Randomized, Multi-centre, Double Blind Study of ZYIL1 to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Patients With Amyotrophic Lateral Sclerosis (ALS)
6. Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of the Oral NLRP3 Inflammasome Inhibitor ZYIL1: First-in-human Phase 1 studies (Single Ascending Dose and Multiple Ascending Dose), Clinical Pharmacology in Drug Development, 2022. DOI: 10.1002/cpdd.1162
7. Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of ZYIL1 in Three Patients with Cryopyrin-Associated Periodic Syndromes, Clinical Pharmacology in Drug Development, 2023, 0(0) 1–8. DOI: 10.1002/cpdd.1318.
8. A novel selective NLRP3 inhibitor shows disease-modifying potential in animal models of Parkinson's disease. Brain Res. 2024 Jul 27;1842:149129. doi: 10.1016/j.brainres.2024.149129.

About Zydus

Zydus Lifesciences Ltd. with an overarching purpose of empowering people with freedom to live healthier and more fulfilled lives, is an innovative, global lifesciences company that discovers, develops, manufactures, and markets a broad range of healthcare therapies. The group employs over 27,000 people worldwide, including 1,400 scientists engaged in R & D, and is driven by its mission to unlock new possibilities in lifesciences through quality healthcare solutions that impact lives. The group aspires to transform lives through pathbreaking discoveries. Over the last decade, Zydus has introduced several innovative, first-in class products in the market for treating unmet healthcare needs with vaccines, therapeutics, biologicals and New Chemical Entities. For more details visit www.zyduslife.com

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