January 18, 2025

BSE Limited **Code: 532321**
P J Towers,
Dalal Street,
Mumbai-400001

National Stock Exchange of India Limited **Code: Zyduslife**
Exchange Plaza,
C/1, Block G,
Bandra-Kurla Complex, Bandra (East),
Mumbai-400051

Re.: Press Release

Dear Sir / Madam,

Please find enclosed a copy of press release dated January 18, 2025, titled "**Zydus Lifesciences receives approval from USFDA to conduct Phase II(b) clinical trial for Usnoflast, a novel oral NLRP3 inflammasome inhibitor in patients with Amyotrophic Lateral Sclerosis (ALS)**".

The contents of the press release give full details.

Please bring the aforesaid news to the notice of the members of the exchange and the investors at large.

The submission of press release got delayed as coordination between teams spread globally across different time zones.

Thanking you,

Yours faithfully,
For, **ZYDUS LIFESCIENCES LIMITED**
DHAVAL NARENDRA SONI
Digitally signed by DHAVAL NARENDRA SONI
Date: 2025.01.18 13:16:52 +05'30'
DHAVAL N. SONI
COMPANY SECRETARY

Encl.: As above

Zydus Lifesciences receives approval from USFDA to conduct Phase II(b) clinical trial for Usnoflast, a novel oral NLRP3 inflammasome inhibitor in patients with Amyotrophic Lateral Sclerosis (ALS)

Ahmedabad, India, January 18, 2025

Zydus, a leading, discovery-based, global pharmaceutical company today announced that it has received approval from USFDA to conduct Phase II(b) clinical trial for Usnoflast, a novel oral NLRP3 inflammasome inhibitor in patients with Amyotrophic Lateral Sclerosis (ALS).

Under the leadership of Principal Investigator Prof Merit Cudkowicz, MD, Director of the Sean M. Healey & AMG Centre for ALS; Chair of Neurology, Massachusetts General Hospital; Julieanne Dorn Professor of Neurology, Harvard Medical School, the Phase 2(b), randomized, double-blind, placebo-controlled, parallel-group, multicentre study will evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of Usnoflast administered to adult subjects with ALS. This study consists of 36- week treatment phase, followed by a 16-week open label extension. This study will enrol 210 ALS patients and study doses of 50 mg and 75 mg Usnoflast versus placebo. The change in ALSFRS-R total score from baseline through week 36 will be measured as the primary endpoint of this trial. The key secondary endpoints will include change in SVC (Slow Vital Capacity), CSF levels of NfL (neurofilament). In addition, the biomarkers including high sensitivity C-reactive protein, (hs-CRP), interleukin (IL)-18, IL-6, IL-1β, NLRP3 and serum amyloid A (SAA), will also be evaluated.

Speaking on the development, Chairman of Zydus Lifesciences Limited, Pankaj Patel, said, “We are excited to report the approval from USFDA to initiate this randomised, double blind, placebo- controlled Phase 2(b) clinical trial in ALS patients. Zydus is committed to unlocking new frontiers in neuroscience and develop transformative breakthrough medicines.”

People living with ALS have an average survival of approximately two to five years from diagnosis, with most ALS patients dying from respiratory failure. 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 Centre for Disease Control and Prevention (CDC). More than 30,000 people are estimated to be

PRESS RELEASE

For further information please contact :
The Corporate Communications Department

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CIN : L24230GJ1995PLC025878

living with ALS in Europe (European Union and United Kingdom), while India has an estimated 75,000 people living with ALS.

Usnoflast (ZYIL1) is a novel, oral small molecule NLRP3 inhibitor. Usnoflast has been studied in several pre-clinical models of neuroinflammation, Parkinson's disease, Inflammatory Bowel Disease (IBD) and Multiple Sclerosis (MS). 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 previously completed a Phase 2(a) randomized, double-blind, placebo controlled clinical trial in 24 ALS patients across 7 clinical trial sites in India. [ClinicalTrials.gov Identifier: NCT05981040]. It is planned to present this Phase 2(a) trial data in upcoming medical conference and publish in medical journal.

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

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
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)

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CIN : L24230GJ1995PLC025878

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.

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