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Zydus announces 'first patient' randomised in EVIDENCES-X™ Phase II(b) clinical trial of Saroglitazar Mg in NASH

- Zydus has initiated enrolment of patients in EVIDENCES-X™ a global pivotal Phase 2(b) clinical trial
- Positive Results from the Phase 2(a) Clinical Trial Evaluating Saroglitazar Mg in patients with NASH were published in the October 2021 issue of Hepatology
- It is estimated that worldwide about 25% of adults suffer from Non-alcoholic Fatty Liver Disease (NAFLD) and 5 – 20 % adults suffer from Non-Alcoholic Steatohepatitis (NASH).

Ahmedabad, India, October 22, 2021

Zydus, a leading discovery based, global pharmaceutical company today announced that it has randomised the First patient into the Phase 2(b) Prospective, Multi-centre, Randomized, Double-blind, Placebo-controlled clinical trial to evaluate Efficacy and Safety of Saroglitazar Magnesium in subjects with Non-Alcoholic Steatohepatitis and Fibrosis. Zydus had earlier received permission from the USFDA [ClinicalTrials.gov Identifier: NCT05011305].

The EVIDENCES-X™ liver biopsy driven Phase 2(b) trial will be led by Prof. Naga Chalasani, M.D., Interim Chair, Department of Medicine, Indiana University School of Medicine and Prof. Arun J. Sanyal, M.D., Division of Gastroenterology, Virginia Commonwealth University as co-Principal Investigators. The EVIDENCES-X™ trial will randomise 240 subjects in a 1:1:1 ratio to Saroglitazar 2 mg, Saroglitazar 4 mg or Placebo and study the primary endpoint "Resolution of steatohepatitis with no worsening of fibrosis" over a period of 76 weeks. The secondary end-points will include improvement in liver fibrosis with no increase in NAS for ballooning, inflammation or steatosis, 2 points improvement in NAS, Improvement in steatosis, ballooning, inflammation and fibrosis from liver biopsy, Histological score changes in steatosis, ballooning, inflammation and fibrosis.

Incidences of Non-alcoholic Fatty Liver Disease (NAFLD) have been rising exponentially worldwide and are associated with co-morbidities including obesity, diabetes, hypertension and metabolic disorders. Experts estimate that about 25% of adults have NAFLD worldwide (K Nonalcoholic steatohepatitis: global impact and clinical consequences, Younossi et al., Endocr Connect. 2021 Oct 7;10(10):R240-R247. doi: 10.1530/EC-21-0048.). NASH is a progressive form of NAFLD and is characterised by histologic evidence of hepatic steatosis, lobular inflammation, hepatocyte ballooning with or without pericellular fibrosis, and/or Mallory-Denk bodies, which can progress to liver cirrhosis, liver cancer and need for liver transplant or death. Experts estimate about 5 – 20 % of adults worldwide have NASH placing significant clinical, economical, and health-related quality of life (HRQoL) burden for treating this liver disease (Source: Cost of non-alcoholic steatohepatitis in Europe and the USA: The GAIN study. Jamie O-Hare et. al., JHEP Reports 2020 vol. 2 j 100142). Analysts estimate the global market for Non-alcoholic steatohepatitis (NASH) treatment will reach $27 billion in 2029 (Source: Globaldata).

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Speaking on the new development, Chairman of Cadila Healthcare Ltd., Mr. Pankaj R. Patel said, "As there is currently no drug approved for the treatment of NASH in the USA, this life threatening liver disease is a high unmet medical need. We are committed to develop novel therapeutics for patients living with liver diseases and fibrosis. We stand encouraged that the findings from the earlier EVIDENCES-IV Phase 2 clinical study have been published as original article by Samer *et al* along with the editorial by Prof. Sven Francque, M.A. a leading hepatologist from Belgium in the October edition of Hepatology, the Journal of American Association for the Study of Liver Diseases (AASLD)".

NASH is a chronic liver disease characterised by fat accumulation and inflammation in the liver, which can progress to liver cirrhosis, need for liver transplant or death. Saroglitazar Mg is an investigational compound in the USA, and is yet to be approved by the U.S. Food & Drug Administration (USFDA) or European Medicines Agency (EMA). The USFDA has granted 'Orphan Drug Designation' and 'Fast Track Designation' to Saroglitazar Mg for PBC. The European Medicines Agency (EMA) has designated "Saroglitazar magnesium" with Orphan status for Treatment of Primary Biliary Cholangitis.

Publications

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- Siddiqui MS, Idowu MO, Parmar D, Borg BB, Denham D, Loo NM, Lazas D, Younes Z, Sanyal AJ. A Phase 2 Double Blinded, Randomized Controlled Trial of Saroglitazar in Patients With Nonalcoholic Steatohepatitis. *Clin Gastroenterol Hepatol*. 2020 Nov 2:S1542-3565(20)31509-3. doi: 10.1016/j.cgh.2020.10.051. Epub ahead of print. PMID: 33152542.
- Vuppalanchi R, Caldwell SH, Pyrsopoulos N, deLemos AS, Rossi S, Levy C, Goldberg DS, Mena EA, Sheikh A, Ravinuthala R, Shaikh F, Bainbridge JD, Parmar DV, Chalasani NP. Proof-of-concept study to evaluate the safety and efficacy of saroglitazar in patients with primary biliary cholangitis. *J Hepatol*. 2021 Sep 3:S0168-8278(21)02023-7. doi: 10.1016/j.jhep.2021.08.025. Epub ahead of print. PMID: 34487750.
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About Zydus

Zydus Cadila is an innovative, global pharmaceutical company that discovers, develops, manufactures and markets a broad range of healthcare therapies, including small molecule drugs, biologic therapeutics and vaccines. The group employs over 23,000 people worldwide, including 1400 scientists engaged in R & D, and is dedicated to creating healthier communities globally. www.zyduscadila.com

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