April 25, 2022

BSE Limited **Code: 532321**
1st Floor,
P J Towers,
Dalal Street,
Mumbai-400001

National Stock Exchange of India Limited **Code: Zyduslife**
Exchange Plaza, 5th Floor,
Plot No. C/1, G Block,
Bandra-Kurla Complex, Bandra (East),
Mumbai-400051

Re.: Press Release

Dear Sir / Madam,

Please find enclosed a copy of press release dated April 25, 2022 titled **Zydus announces publication of "DREAM-ND" and "DREAM-D" Phase 3 trials of Desidustat in "American Journal of Nephrology"**.

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.

Thanking you,

Yours faithfully,
For, **ZYDUS LIFESCIENCES LIMITED**
(Formerly known as Cadila Healthcare Limited)

DHAVAL NARENDRA SONI
Digitally signed by DHAVAL NARENDRA SONI
Date: 2022.04.25 09:31:45 +05'30'

DHAVAL N. SONI
COMPANY SECRETARY

Encl.: As above

Zydus announces publication of "DREAM-ND" and "DREAM-D" Phase 3 trials of Desidustat in "American Journal of Nephrology"

Ahmedabad, India, 25 April 2022,

Zydus Lifesciences Ltd. (formerly known as Cadila Healthcare Ltd.), a discovery-driven, global lifesciences company today announced the publication of two manuscripts detailing the DREAM-ND and DREAM-D Phase 3 study results of Desidustat, a novel HIF-PH inhibitor in the prestigious American Journal of Nephrology.

Desidustat's development is based on the Nobel Prize in Medicine winning science on discoveries of the oxygen sensing mechanism of cells through hypoxia-inducible factor (HIF). Desidustat works by stabilizing the HIF complex and stimulating endogenous erythropoietin production in Chronic kidney disease (CKD) patients thereby improving haemoglobin levels and treating anemia. CKD patients irrespective of their dialysis status have been reported to develop anemia leading to significant morbidity, mortality, progression of kidney disease and higher blood transfusion rates. Chronic Kidney Disease patients are often on 8-13 different medications and are at safety risks of drug-drug interactions.

"We are pleased as the results of our DREAM-ND and DREAM-D trials are published in the American Journal of Nephrology", said Mr. Pankaj R. Patel, Chairman, Zydus Lifesciences Ltd. "In our quest to develop a potential best-in-class HIF-PH inhibitor, our research team had envisaged to develop a candidate which achieves primary and secondary end-points, requires less frequent dosing and has a reduced potential for drug-drug interactions. The results published in American Journal of Nephrology demonstrates that Desidustat met all the primary and secondary end-points with thrice a week oral dosing regimen, was well-tolerated and also ensured a durable treatment effect in both non-dialysis and dialysis dependent Chronic Kidney Disease patients with anemia."

In the DREAM-ND trial, Desidustat oral dose was administered thrice a week compared to Darbepoetin subcutaneous injection in 588 Chronic Kidney Disease patients not-on-dialysis (randomized 1:1). In the Desidustat group the mean baseline Hemoglobin level was 8.97 g/dL which improved to 10.90 g/dL in Weeks 16–24, and in the Darpepoetin group the mean baseline haemoglobin levels was 8.92 g/dL which improved to 10.77 g/dL, which met prespecified non-inferiority of Desidustat to Darbepoetin as per protocol. The hemoglobin responders were significantly higher in the Desidustat group compared to the Darbepoetin group. There was a statistically significant reduction in hepcidin and LDL-c in the Desidustat

PRESS RELEASE

For further information please contact :
The Corporate Communications Department

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CIN : L24230GJ1995PLC025878

arm as compared to the injectable Darbepoetin arm. The safety profile of the Desidustat oral tablet was comparable with the Darbepoetin alfa injection in CKD patients not on dialysis.

In the DREAM-D trial, Desidustat oral tablets were administered thrice a week compared to Epoetin alfa subcutaneous injection in 392 Chronic Kidney Disease patients on dialysis (randomized 1:1). In the Desidustat group the mean baseline hemoglobin level was 9.57 g/dL which improved to 10.47 g/dL in weeks 16–24 and in the Epoetin group the mean baseline haemoglobin level was 9.46 g/dL which improved to 10.32 g/dL, which met prespecified non-inferiority of Desidustat to Epoetin as per protocol. The number of haemoglobin responders were significantly higher in the Desidustat group as compared to the Epoetin alfa group. There was a statistically significant reduction in hepcidin and LDL-c in the Desidustat arm as compared to the injectable Epoetin alfa arm. The safety profile of the Desidustat oral tablet was comparable with the epoetin alfa injection in CKD patients on dialysis.

Desidustat is currently approved only in India as Oxemia™ for patients with CKD induced anemia. It is currently undergoing Phase III clinical development in China for anemia in Chronic Kidney Disease Patients. Desidustat is under Phase I(b) clinical evaluation under a IND with the United States Food and Drug Administration (USFDA) for Chemotherapy Induced Anemia (CIA) in cancer patients.

Previously, results of multiple other studies on Desidustat have been published in international peer-reviewed scientific journals of repute such as European Journal of Pharmacology, Journal of Medicinal Chemistry, Drug Development Research, Drug Research (Stuttg), Xenobiotica, American Journal of Nephrology and Clinical Pharmacokinetics.

Publications on Desidustat / ZYAN1:

1. Desidustat in Anemia due to Non- Dialysis-Dependent Chronic Kidney Disease: A Phase 3 Study (DREAM-ND). Am J Nephrol. 2022. DOI: 10.1159/000523961
2. Desidustat in Anemia due to Dialysis-Dependent Chronic Kidney Disease: A Phase 3 Study (DREAM-D). Am J Nephrol. 2022. DOI: 10.1159/000523949
3. Outcomes of Desidustat Treatment in People with Anemia and Chronic Kidney Disease: A Phase 2 Study. Am J Nephrol. 2019; 49:470–478.
4. Phase I Clinical Study of ZYAN1, A Novel Prolyl-Hydroxylase (PHD) Inhibitor to Evaluate the Safety, Tolerability, and Pharmacokinetics Following Oral Administration in Healthy Volunteers. Clin Pharmacokinet. 2018 Jan; 57(1):87-102.
5. Pharmacological Characterization of ZYAN1, a Novel Prolyl Hydroxylase Inhibitor for the Treatment of Anemia. Drug Res (Stuttg). 2016 Feb; 66(2):107-12.

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6. Influence of acute and chronic kidney failure in rats on the disposition and pharmacokinetics of ZYAN1, a novel prolyl hydroxylase inhibitor, for the treatment of chronic kidney disease induced anemia. Xenobiotica. 2018 Jan; 48(1):37-44.
7. A sensitive assay for ZYAN1 in human whole blood and urine utilizing positive LC-MS/MS electrospray ionization. Bioanalysis. 2017 May; 9(9):719-732.
8. Pharmacological inhibition of prolyl hydroxylase protects against inflammation-induced anemia via efficient erythropoiesis and hepcidin downregulation. Eur J Pharmacol. 2019 Jan 15; 843:113-120.
9. Prolyl Hydroxylase Inhibitors: A Breakthrough in the Therapy of Anemia Associated with Chronic Diseases. J Med Chem. 2018 Aug 23; 61(16):6964-6982.
10. Prolyl hydroxylase inhibitor desidustat protects against acute and chronic kidney injury by reducing inflammatory cytokines and oxidative stress. Drug Dev Res. 2021; 1–9.

About Zydus

The Zydus Group 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 23000 people worldwide and is driven by its mission to unlock new possibilities in life-sciences through quality healthcare solutions that impact lives. The group aspires to transform lives through path-breaking discoveries. For more details visit www.zyduslife.com.

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