सत्यमेव जयते

GOVERNMENT OF INDIA
CENTRAL DRUGS STANDARD CONTROL
ORGANISATION (Headquarter)
(Directorate General of Health Services)
Ministry of Health & Family Welfare
FDA Bhavan
ITO, Kotla Road
New Delhi - 110002 (Delhi)
Phone No.: 91-11-23216367
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E-Mail : dci@nic.in

File No. CT/25/000138

To

M/s. PPD Pharmaceutical Development (India) Pvt. Ltd.,
102, A Wing, Fulcrum, Hiranandani Business Park,
Sahar Road, Andheri East, Mumbai – 400099, India.

Sir,

With reference to your application no. GCT/CT04/FF/2025/52084 dated 19-Sep-2025, please find enclosed herewith the permission in Form CT-06 for conduct of clinical trial titled, "**ZENITH:A Phase 3 Global, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Zilebesiran in Addition to Standard of Care in Reducing Major Adverse Cardiovascular Events in Adult Patients with Hypertension Not Adequately Controlled and With Either Established Cardiovascular Disease or High Risk for Cardiovascular Disease" Protocol no.: ALN-AGT01-008 version no. original protocol dated 15- JUL-2025 with a total of up-to 688 subjects from India** under the provisions of New Drugs and Clinical Trial Rules, 2019.

The permission granted by the Central Licensing Authority to conduct clinical trial shall be subject to following conditions, specifically::-

(i) **Human biological samples i.e. Whole blood and urine samples related to clinical trial shall be permitted to be exported for analysis subject to the clearance by port offices of CDSCO. Further, ICMR/DHR permission shall be obtained for export of optional biological samples as per DGFT notification number 72/2023 dated 11.03.2024.**

(ii) Clinical trial at each site shall be initiated after approval of the clinical trial protocol and other related documents by the Ethics Committee of that site, registered with the Central Licencing Authority under rule 8;

(iii) Where a clinical trial site does not have its own Ethics Committee, clinical trial at that site may be initiated after obtaining approval of the protocol from the Ethics Committee of another trial site; or an independent Ethics Committee for clinical trial constituted in accordance with the provisions of rule 7:
Provided that the approving Ethics Committee for clinical trial shall in such case be responsible for the study at the trial site or the centre, as the case may be:
Provided further that the approving Ethics Committee and the clinical trial site or the bioavailability and bioequivalence centre, as the case may be, shall be located within the same city or within a radius of 50 kms of the clinical trial site;

(iv) In case an ethics committee of a clinical trial site rejects the approval of the protocol, the details of the same shall be submitted to the Central Licensing Authority prior to seeking approval of another Ethics Committee for the protocol for conduct of the clinical trial at the same site;

(v) The Central Licencing Authority shall be informed about the approval granted by the Ethics Committee within a period of fifteen working days of the grant of such approval;

(vi) Clinical trial shall be registered with the Clinical Trial Registry of India maintained by the Indian Council of Medical Research before enrolling the first subject for the trial;

(vii) Clinical trial shall be conducted in accordance with the approved clinical trial protocol and other related documents and as per requirements of Good Clinical Practices Guidelines and the provisions of these rules;

(viii) Status of enrolment of the trial subjects shall be submitted to the Central Licencing Authority on quarterly basis or as appropriate as per the duration of treatment in accordance with the approved clinical trial protocol, whichever is earlier;

(ix) Six monthly status report of each clinical trial, as to whether it is ongoing, completed or terminated, shall be submitted to the Central Licencing Authority electronically in the SUGAM portal;

(x) In case of termination of any clinical trial the detailed reasons for such termination shall be communicated to the Central Licencing Authority within thirty working days of such termination;

(xi) Any report of serious adverse event occurring during clinical trial to a subject of clinical trial, shall, after due analysis, be forwarded to the Central Licencing Authority, the chairperson of the Ethics Committee and the institute where the trial has been conducted within fourteen days of its occurrence as per Table 5 of the Third Schedule and in compliance with the procedures as specified in Chapter VI;

(xii) In case of injury during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of the receipt of order issued by Central Licencing Authority in accordance with the provisions of the said Chapter;

(xiii) In case of clinical trial related death or permanent disability of any subject of such trial during the trial, compensation shall be provided in accordance with Chapter VI and details of compensation provided in such cases shall be intimated to the Central Licencing Authority within thirty working days of receipt of the order issued by the Central Licencing Authority in accordance with the provisions of the said Chapter;

(xiv) The premises of the sponsor including his representatives and clinical trial sites, shall be open for inspection by officers of the Central Licencing Authority who may be accompanied by officers of the State Licencing Authority or outside experts as authorised by the Central Licencing Authority, to verify compliance of the requirements of these rules and Good Clinical Practices Guidelines, to inspect, search and seize any record, result, document, investigational product, related to clinical trial and furnish reply to query raised by the said officer in relation to clinical trial;

(xv) Where the new drug or investigational new drug is found to be useful in clinical development, the sponsor shall submit an application to the Central Licencing Authority for permission to import or manufacture for sale or for distribution of new drug in India, in accordance with Chapter X of these rules, unless otherwise justified;

(xvi) The laboratory owned by any person or a company or any other legal entity and utilised by that person to whom permission for clinical trial has been granted used for research and development, shall be deemed to be registered with the Central Licensing Authority and may be used for test or analysis of any drug for and on behalf of Central Licensing Authority;

(xvii) The Central Licencing Authority may, if considered necessary, impose any other condition in writing with justification, in respect of specific clinical trials, regarding the objective, design, subject population, subject eligibility, assessment, conduct and treatment of such specific clinical trial;

(xviii) The sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial.

(xix) Merely granting permission to conduct the **clinical trial** with the Investigational Drug Product does not convey or imply that, based on the **clinical trial study data** generated with the investigational drug, permission to market this drug in the country will automatically be granted to you;

(xx) The permission to initiate clinical trial granted under rule 22 in form CT-06 or automatic approval under rule 23 in Form CT 4A shall remain valid for a period of **two years** from the date of its issue, unless extended by the Central Licencing Authority.

Yours faithfully,

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
Date: 2026.03.19 16:51:57 +05'30'

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India) &
Central Licencing Authority
Stamp

FORM CT-06

(See rules 22,25,26,29 and 30)

PERMISSION TO CONDUCT CLINICAL TRIAL OF NEW DRUG OR INVESTIGATIONAL NEW DRUG

1. The Central Licensing Authority hereby permits **M/s. PPD Pharmaceutical Development (India) Pvt. Ltd., 102, A Wing, Fulcrum, Hiranandani Business Park, Sahar Road, Andheri East, Mumbai (India) – 400099** to conduct clinical trial of the new drug or investigational new drug as per **Protocol no.: ALN-AGT01-008 version no. original protocol dated 15- JUL-2025** in the below mentioned clinical trial sites [As per Annexure].-

2. Details of new drug or investigational new drug and clinical trial site [As per Annexure].

3. This permission is subject to the conditions prescribed in part A of Chapter V of the New Drugs and Clinical Trials Rules, 2019 under the Drugs and Cosmetics Act, 1940.

Place: New Delhi
Date _____

RAJEEV SINGH RAGHUVANSHI
Digitally signed by RAJEEV SINGH RAGHUVANSHI
Date: 2026.03.19 16:52:06 +05'30'

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India) &
Central Licencing Authority
Stamp

Note: The permission to initiate clinical trial granted under rule 22 in form CT-06 shall remain valid for a period of **two years** from the date of its issue, unless extended by the Central Licencing Authority.

Annexure:

Details of new drug or investigational new drug:

Names of the new drug or investigational new drug	Zilebesiran
Therapeutic class:	siRNA targeting liver angiotensinogen mRNA
Dosage form:	Solution for injection
Composition:	Zilebesiran =200.0000 mg/ml In House Specification Active
Indications:	To reduce the risk of CV death, nonfatal myocardial infarction (MI), nonfatal stroke, and heart failure (HF) events (hospitalization for HF or urgent HF visit) in adult patients with hypertension and with either established CVD or high risk for CVD

Annexure:

Details of clinical trial site:

S. No.	Name and address of clinical trial site	Ethics Committee Details	Name of Investigator
1.	King George Hospital, Department of Cardiology, King George Hospital, Andhra Medical College, Maharanipeta, Visakhapatnam Andhra Pradesh - 530002	IEC King George hospital ECR/197/Inst/KGH/2013/RR-20	Dr Jenny Madhuri Gudivada
2.	KIMS-Kingsway Hospitals, SPANV Medisearch Lifesciences Private Limited, 44 Kingsway Road, Near Kasturchand Park Nagpur	KIMS KINGSWAY HOSPITALS ETHICS ECR/1269/Inst/MH/2025	Dr Rishi Lohiya
3.	SMC Heart Institute and IVF Research Centre, VIP Estate, Vidhan Sabha Rd, In Front Of Bsnl Office, Near Ashoka Ratan, Shankar Agar Raipur Chhattishgarh - 492014	SMC Heart Institute Institutional Ethics Committee ECR/1522/Inst/CG/2021	Dr Satish Suryavanshi
4.	SCB Medical College and Hospital, Srirama Chandra Bhanja Medical College and Hospital-SCBMCH Manglabag Cuttack Orissa - 753007	Institutional Ethics Committee SCB Medical College and Hospital, Cuttack ECR/2094/Inst/OD/2025	Dr Dipak Ranjan Das
5.	Marengo CIMS Hospital, Ahmedabad a Unit of Marengo Asia Healthcare Private Limited, Plot No 67 by 1, Panchamrut bunglows, Near Shukan Mall, Off Science City Road, Sola Ahmedabad Gujarat - 380060	Ethics Committee of CIMS ECR/206/Inst/GJ/2013/RR-24	Dr Milan Chag
6.	JSS Hospital, M G Road, Ramachandra Agrahara Mysore Karnataka - 570004	Institutional Ethics Committee, JSS Medical College ECR/387/Inst/KA/2013/RR-22	Dr Manjappa Mahadevappa
7.	All India Institute of Medical Sciences, Sijua, Patrapada Bhubaneswar Orissa - 751019	INSTITUTIONAL ETHICS COMMITTEE, Faculty Research, AIIMS Bhubaneswar ECR/534/Inst/OD/2014/RR-25	Dr Rama Chandra Barik
8.	Apex Heart Institute, Block G-K, Mondeal Business Park, Near Gurudwara, S G Road Ahmedabad Gujarat - 380059	Ethics Committee Apex Heart Institute ECR/514/Inst/GJ/2014/RR-25	Dr Tejas Madhusudan Patel
9.	Nanjappa Life Care, 5619, Gadikoppa, Sagar Road Shivamogga Karnataka - 577205	Nanjappas Institutional Ethics Committee ECR/537/Inst/KA/2014/RR-20	Dr Narendra J
10.	Amrita Institute of Medical Sciences and Research	Institutional Ethics Committee	Dr Navin Mathew

	Centre, Dept. of Cardiology, A Block, 5th Floor Tower 1, Amrita Institute of Medical Sciences and Research Centre, AIMS-Ponekkara. P.O Kochi Kerala -682041	ECR/129/Inst/KL/2013/RR-24	
11.	Rhythm Heart Institue- A Unit of Synergy Lifecare Pvt. Ltd., Near Siddharth Bunglows, Sama-Savli Road Vadodara Gujarat - 390022	Rhythm Heart Institute Ethics Committee ECR/224/Inst/GJ/2013/RR-24	Dr Nirav Chandulal Bhalani
12.	Sengupta Hospital and research Institute, Sengupta Hospital and research Institute, Ravinagar Square Nagpur Maharashtra - 440033	Sengupta Hospital and Research Institute ECR/675/Inst/MH/2014/ RR-20	Dr Shantanu Sengupta
13	Fortis Escorts Heart Institute, Okhla Road New Delhi Delhi -110025	INSTITUTIONAL ETHICS COMMITTEE ECR/261/Inst/DL/2013/RR-24	DR VISHAL RASTOGI
14	Vijan Hospital and Research Centre Vijan Cardiac and Critical Care Centre, Dr Vijan Hospital Marg, College Road Nashik Maharashtra - 422005	VIJAN HOSPITAL ETHICS COMMITTEE ECR/406/Inst/MH/2013/RR-12	Dr Vinodkumar M Vijan
15	S.M.S Hospital, Department of Cardiology, Bangar Building, Gate no. 5, JLN Marg Jaipur Rajasthan - 302004	Ethics committee, S.M.S medical college and Attached Hospital ECR/26/Inst/RJ/2013/RR-24	Dr Chandra Bhan Meena
16	Manipal Hospital Mysuru, 85-86, Mysuru Bengaluru Ring Road Junction, Bannimantap A layout, Siddiqui Nagar Bengaluru Karnataka - 570015	I E C Columbia Asia Hospital Mysore ECR/1106/Inst/KA/2018/RR-21	Dr Keshavamurthy C B
17	Vardhaman Mahavir Medical College and Safdarjung Hospital, VMMC and Safdarjung Hospital New Delhi Delhi - 110029	Institutional Ethics Committee VMMC and Safdarjung Hospital ECR/593/Inst/DL/2014/RR-20	Dr Sandeep Bansal
18	Medanta- The Medicity, Sector-38 Gurugram Haryana -122001	Medanta Institutional Review Board (MIRB)+ Medanta Institutional Ethics (MIEC) ECR/282/Inst/HR/2013/RR-25	Dr Sanjay Mittal
19	LPS Institute of Cardiology, GSVM Medical College, Swaroop Nagar Kanpur Uttar Pradesh - 208002	ETHICS COMMITTEE GSVM MEDICAL COLLEGE ECR/680/Inst/UP/2014/RR-20	Dr Awadhesh Kumar Sharma
20	Asian Institute of Gastroenterology – AIG Hospitals, Plot No 2-3-4-5, Survey No 136, 1, Mindspace Road, Gachibowli Hyderabad Telangana - 500032	Institutional Ethics Committee, Asian Institute of Gastroenterology (IEC-AIG) ECR/346/Inst/AP/2013/RR-22	Dr Narasimhan Calambur
21	Sir Ganga Ram Hospital, SGRH Marg, Rajinder Nagar New Delhi Delhi - 110060	Sir Ganga Ram Hospital Ethics Committee ECR/20/Inst/DL/2013/RR-24	Dr Ashwani Mehta

22	Shri Guru Ram Rai Institute of Medical and Health Sciences and Shri Mahant Indiresh Hospital, Patel Nagar Dehradun Uttarakhand - 248001	Institutional Ethics Committee SGRR Institute Of Medical Health Sciences ECR/710/Inst/UK/2015/RR-21	Dr Tanuj Bhatia
23	KLES Dr Prabhakar Kore Hospital and Medical Research Centre, Nehrunagar Belagavi Karnataka - 590010	IEC, KLE University's KLE Dr PK Hospital & MRC ECR/211/Inst/KA/2013/RR-24	Dr Sanjay Porwal
24	Chopda Medicare and Research Centre Pvt. Ltd Magnum Heart Institute, 3-5, Patil Lane No. 1, Laxmi Nagar, Near K.B.H. Vidyalaya, Canada Corner Nashik Maharashtra -422005	Magna-care Ethics Committee ECR/79/Inst/MH/2013/RR-24	Dr Manojkumar Bhavarilal Chopada
25	All India Institute of Medical Sciences, Room No- 2, Department of Cardiology, Sri Aurobindo Marg, Ansari Nagar New Delhi Delhi - 110029	Institute Ethics Committee, All India Institute of Medical Sciences ECR/538/Inst/DL/2014/RR-25	Dr Sandeep Seth
26	Kamalnayan Bajaj Hospital, Gut no. 43, Satara Paisar, Beed bypass road Chh Sambhajinagar Maharashtra - 431010	Ethics Committee Kamalnayan Bajaj Hospital ECR/444/Inst/MH/2013/RR-24	Dr Ajit Bhagwat
27	Shrikrishna Hrudayalaya and Critical Care Centre, Tikekar Road, Congress Nagar Square Dhantoli Nagpur Maharashtra- 440012	Virtuous Institutional Medical Research EC ECR/548/Inst/MH/2014/RR-25	Dr Mahesh Fulwani
28	Galaxy Life Care Services Pvt. Ltd., Plot No. 4-7, Dayal Enclave, Mahmoorganj Varanasi Uttar Pradesh - 221010	Galaxy Hospital Ethics Committee ECR/877/Inst/UP/2016/RR-24	Dr Ajay Kumar Pandey
29	EPIC Hospital A Unit of Vatsalya Healthcare LLP, Rajpath Rangoli Road, Opp. Pandit Dindayal Auditorium Hall, Behind Rajpath Club, Bodakdev Ahmedabad Gujarat - 380054	EPIC Hospital Ethics Committee ECR/1372/Inst/GJ/2020	Dr Anil Ranjeetmal
30	Ashirwad Hospital and Research Centre, Maratha section Near Jijamata Udyan Ulhasnagar Maharashtra - 421004	Ashirwad Ethics Committee ECR/247/Inst/MH/2013/RR-24	Dr Shrikant Deshpande
31	Charak Hospital and Research Centre, Hardoi Road, Dubagga Lucknow Uttar Pradesh - 226003	IEC Charak Hospital and Research Centre ECR/1255/Inst/UP/2019/RR-24	Dr Manish Kumar Jha
32	Supe Heart and Diabetes Hospital And Research Centre, Opp. Adhar Ashram, Near Rungta School, Gharpure Ghat, Ashok Stambh Nashik	Supe Hospital Ethics Committee, Supe Heart and Diabetes Hospital and Research Centre ECR/272/Inst/MH/2013/RR-24	Dr Pravin Supe

	Maharashtra - 422002		
33	Arneja Heart and Multispeciality Hospital, 123, Ramdaspeth Nagpur Maharashtra - 440010	Arneja's Institutional Ethics Committee ECR/726/Inst/MH/2015/RR-21	Dr Jaspal Singh

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