सत्यमेव जयते

GOVERNMENT OF INDIA
CENTRAL DRUGS STANDARD CONTROL ORGANISATION(Headquarter)(Directorate General ofHealthServices) Ministry of Health & Family Welfare
FDA Bhavan
ITO, Kotla Road
New Delhi - 110002 (Delhi)
Phone No.:91-11-23216367
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File No. CT/22/000107

To

M/s. GSK Pharma India Private Limited,
C/o GlaxoSmithKline Pharmaceuticals Limited,
Dr. Annie Besant Road, Worli, Mumbai,
Maharashtra (India) – 400030.

Sir,

With reference to your application no. GCT/CT04/FF/2022/33966 (GCT/107/22) dated 17-09-2022, please find enclosed herewith the permission in Form CT-06 for conduct of clinical trial titled," **Phase 3 Multicenter, Randomized, Double-Blind, Study to Assess the Efficacy and Safety of Treatment with Bepirovirsen in HBeAg-negative Nucleos(t)ide Analogue-treated Participants with Chronic Hepatitis B Virus (B-Well 2)" Protocol no. 219288, Version no. 00 dated 31/Aug/2022 with a total of up-to 80 subjects from the country** 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, namely:-

(i) **The study should be conducted initially in 20 subjects from India. The applicant should submit safety data of these 20 Indian subjects along with recommendations of independent data safety monitoring committee/board to CDSCO for further review by the Subject Expert Committee (SEC). Once data reviewed by SEC, trial might be continued;**

(ii) **Being a placebo controlled trial, SoC/background therapy should be provided to the trial subjects free of cost throughout the conduct of the trial;**

(iii) 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;

(iv) 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;

(v) 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;

(vi) 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;

(vii) 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;

(viii) 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;

(ix) 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;

(x) 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;

(xi) 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;

(xii) 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;

(xiii) 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;

(xiv) 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;

(xv) 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;

(xvi) 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;

(xvii) 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;

(xviii) 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;

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

(xx) 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;

(xxi) 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,

VENUGOPAL G SOMANI

Digitally signed by VENUGOPAL G SOMANI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL ORGANIZATION, ou=DRUGS CONTROLLER GENERAL (INDIA), pseudonym=112046a34e21727bacb255748732c456d249073e55e953d9cb5b5b5874bee3113c, postalCode=110002, st=DELHI, serialNumber=e97241aa0c0bba4152525ff2c07054[illegible], cn=VENUGOPAL G SOMANI
Date: 2023.02.13 10:35:55 +05'30'

(Dr. V. G. Somani)
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. GSK Pharma India Private Limited, C/o GlaxoSmithKline Pharmaceuticals Limited, Dr. Annie Besant Road, Worli, Mumbai, Maharashtra (India) – 400030 Telephone No.: 912224959595 FAX: 912224959494** to conduct clinical trial of the new drug or investigational new drug as per **Protocol no. 219288, Version no. 00 dated 31/Aug/2022** 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 _____

VENUGOPAL G SOMANI
(Dr. A.G. Somani)
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	GSK3228836 Solution for Injection 150 mg/mL (Bepirovirsen)
Therapeutic class:	2 MOE modified phosphorothioate ASO
Dosage form:	Solution for injection
Composition:	Water for injection = 0.0000 qs to 1 ml U.S.P., J.P., Ph. Eur Inactive Sodium Hydroxide = 0.0000 qs to pH 8 U.S.P., J.P., Ph. Eur Inactive Hydrochloric Acid = 0.0000 qs to pH 8 U.S.P , JP, Ph. Eur Inactive Bepirovirsen sodium = 150.0000 mg/ml In House Specification Active
Indications:	For the treatment of adult participants (18 years of age) with chronic hepatitis B infection.

Annexure:

Details of clinical trial site:

S. No.	Name and address of clinical trial site	Ethics Committee Details	Name of Investigator
1.	Institute of Liver and Biliary Sciences, D-1, Vasant Kunj, New Delbi-11 0070.	Institutional Ethics Committee, Institute of Liver and Biliary Sciences, D-1, Vasant Kunj, New Delhi-I I 0070. ECR/67/Inst/DL/2013/RR-19	Dr Shiv Kumar Sarin
2.	Global Hospital - Super Speciality & Transplant Centre, (A unit of Centre for Digestive & Kidney Disease (India) PVT LTD) 35, Dr. E. Borges Road, Hospital Avenue, Opp. Shirodkar High School, Pare!, Mumbai - 400012, Maharashtra, India	Institutional Ethics Committee Global Hospital, Mumbai Room No. 222, 2nd Floor Dr. E. Borges Road, Hospital A venue, Opp. Shirodkar High School, Pare!, Mumbai: 400012, Maharashtra, India ECR/493/Inst/MH/2014/RR- 19	Dr. Alisha Nitin Chaubal
3.	Centre for Clinical Research-JCMLRI, Indian Institute of Liver & Digestive Sciences, Sitala East, Sonarpur, Kolkata 700150.	Human Research Ethics Committee, Indian Institute of Liver & Digestive Sciences, Sitala East, Sonarpur, Kolkata 700150 ECR/1568/Inst/WB/2021	Dr. Abhijit Chowdhury
4.	Yashoda Hospitals, Secunderabad, Hyderabad, Telangana-500003	Institutional Ethics Committee, Yashoda Academy Of Medical Education and Research, Yashoda Hospitals, Behind Hari Hara Kalabhavan, Alexander Road, Secunderabad, Hyderabad, Telangana-500003 ECR/49/Inst/AP/2013/RR-22	Dr. Dharmesh Kapoor
5.	Grant Medical Foundation Ruby Hall Clinic, 40, Sassoon Road, Pune - 411 001, Maharashtra, India	Institutional Ethics Committee Poona Medical Research Foundation, E 4 - C to E 4- F, 4th Floor, Fifth Avenue Condominium, Dhole Patil Road, Pune-411001 Maharashtra , India ECR/24/MH/2013/RR-22	Dr. Pai Nitin Vikas
6.	All India Institute of Medical Sciences, Ansari Nagar, New Delhi110029,India	The Institute Ethics Committee, Room No. 102, first floor, Old OT Block, All India Institute of Medical Sciences, Ansari Nagar, New Delhi-110029, India	Dr. Shalimar

		ECR/538/Inst/DL/2014/RR-20	
7.	Apollo Speciality Hospital No. 320, Padma Complex, Anna Salai, Chennai-600 035, Tamil Nadu, India.	Institutional Ethics Committee-Clinical Studies, Apollo Hospitals Enterprise Limited, No. 21, Greams Lane, Off Greams Road, Thousand lights, Chennai-600 006, Tamil Nadu, India ECR/37/Inst/TN/2013/RR-19	Dr. Ganesh Subramanian
8.	Midas Multispeciality Hospital Pvt. Ltd., Midas Heights 07 Central Bazar _Road, Ramdaspeth, Nagpur-440010 (MS) INDIA	Ethics Committee of Midas Multispeciality Hospital, Midas Multispeciality Hospital Pvt. Ltd., Midas Heights 07 Central Bazar _Road, Ramdaspeth, Nagpur-440010 (MS) INDIA ECR/494/Inst/MH/2014/RR-20	Dr. Mukewar Shrikant Vasantrao
9.	Dept of Gastroenterology Amrita Institute of Medical Sciences & Research Centre, Department of Gastroenterology, Ponekkara P.O., Kochi 682041	Institutional Ethics Committee Amrita Institute of Medical Sciences & Research Centre, Department of Gastroenterology, Ponekkara P.O., Kochi 682041 ECR/129/Inst/KL/2013/RR-19	Dr. Shine Sadashivan
10.	Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai-400022	Institutional Ethics Committee Human Research, 2ndFloor, Room no .17 Lokmanya Tilak Municipal Medical college & General Hospital Sion Mumbai-400022 ECR/266/Lokmanya/Inst/MH/2013/RR-19	Dr. Meghraj Ingle
11.	Medanta - The Medicity, Sector 38, Gurgaon, Haryana-122001, India	Medanta Institutional Ethics Committee (MIEC), 10th floor, A-wing (POCU), Medanta -The Medicity, Sector 38, Gurgaon, Haryana 122001, India ECR/282/Inst/HR/2013/RR -20	Dr. Neeraj Saraf

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