File No. CT/149/23-DCG(I)

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
Fax No.: 91-11-23236973
E-Mail : dci@nic.in

File No. CT/23/000149

To,

M/s InVentiv International Pharma Services Pvt. Ltd ,
4th Floor Block -2, DLF Downtown, Commercial Site,
Block-V, DLF City, Phase III Sector 25A, Gurugram
DLF Qe Gurugram (India) – 122002.

Sir,

With reference to your application No. GCT/CT04/FF/2023/40571 (GCT/149/23) dated 24-11-2023, please find enclosed herewith the permission in Form CT-06 for conduct of phase III b clinical trial titled, "**A Randomised, Double-blind, Parallel Group, Equivalence, Multicentre Phase III Trial to Compare the Efficacy, Safety, and Immunogenicity of AP063 to Herceptin® in Subjects with HER2+ Breast Cancer" Protocol No.: AP063-003 Version No. 2.0 Protocol Date 31-JUL-2023 with a total of up-to 200 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, namely:-

(i) 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;

(ii) 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;

(iii) 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;

(iv) 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;

(v) 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;

(vi) 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;

(vii) 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;

(viii) 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;

(ix) 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;

(x) 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;

(xi) 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;

(xii) 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;

(xiii) 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;

(xiv) 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;

(xv) 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;

(xvi) 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;

(xvii) the sponsor and the investigator shall maintain the data integrity of the data generated during clinical trial;

(xviii) 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;

(xix) 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.

RAJEEV SINGH RAGHUVANSHI

Digitally signed by RAJEEV SINGH RAGHUVANSHI
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL ORGANIZATION, cn=RAJEEV SINGH RAGHUVANSHI, 2.5.4.20=80c62f6a23e4eafbe8a239774cdeb03c2769041015a06564fe67f54b765db1cb, postalCode=600034, st=TAMIL NADU, serialNumber=657F5E47D940985D8F03BDC902D0E1FE73CFA12A1A126EA94FA5701124A19013, cn=RAJEEV SINGH RAGHUVANSHI
Date: 2024.05.07 11:47:30 +05'30'

Yours faithfully,

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

File No. CT/149/23-DCG(I)

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 Inventiv International Pharma Services Pvt Ltd , 4th Floor Block -2,DLF Downtown, Commercial Site, Block-V, DLF City, Phase III Sector 25A, Gurugram DLF Qe Gurugram (India) -122002 Telephone No.: 9811362577 FAX: 020-30569158 E-Mail :SM_INVENTIV_REGULATORY@SYNEOSHEALTH.COM** to conduct clinical trial of the new drug or investigational new drug as per **Protocol No.: AP063-003 Version No. 2.0 Protocol Date 31-JUL-2023** 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
DN: c=IN, o=CENTRAL DRUGS STANDARD CONTROL ORGANIZATION, ou=RAJEEV SINGH RAGHUVANSHI, 2.5.4.20=80c62f6a23e4eafbe8a239774cdeb03c2769041015a06564fe67f54b765db1cb, postalCode=600034, st=TAMIL NADU, serialNumber=657F5E47D940985D8F03BDC902D0E1FE73CFA12A1A126EA94FA5701124A19013, cn=RAJEEV SINGH RAGHUVANSHI
Date: 2024.05.07 11:47:46 +05'30'

(Dr. Rajeev Singh Raghuvanshi)
Drugs Controller General (India) &
Central Licensing 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	AP063
Therapeutic class:	Anticancer
Dosage form:	Powder for concentrate for solution for infusion
Composition:	Trastuzumab =156.0000 milligram(mg) In House Specification Active L-histidine hydrochloride monohydrate = 3.4900 milligram(mg) Ph. Eur Inactive L-histidine =2.2000 milligram (mg) U.S.P., Ph. Eur Inactive alpha, aplha-trehalose dihydrate=141.6000 milligram (mg) U.S.P., Ph. Eur Inactive

	Polysorbate 20 =0.6200 milligram(mg) U.S.P., Ph. Eur Inactive
Indications:	Breast Cancer

Annexure:

Details of clinical trial site:

Names and address of clinical trial site	**Ethics committee details**	**Name of investigator**
SIR GANGA RAM HOSPITAL, SIR GANGA RAM HOSPITAL Old Rajinder Nagar, New Delhi,110060 Delhi Delhi - 110060	Sir Ganga Ram Hospital Ethics Committee, Dept. of Ethics, RoomNo-1643,6th Floor, old building sir ganga ram hospital, Rajinder Nagar, New Delhi- 110060, India ECR/20/INST/DL/2013/RR-19	Dr Shyam Aggarwal
Bhagwan Mahaveer Cancer Hospital, Bhagwan Mahaveer Cancer Hospital, J L N marg, Jaipur, 302017- India Jaipur Rajasthan - 302017	Institutional Ethics Committee, Bhagwan Mahaveer Cancer Hospital& Research Center, Jawahar Lal Nehru Marg, Jaipur-302017(Raj) India. ECR/19/Inst/RJ/2013/RR-20	Dr Pawan Agarwal
Apex Wellness Hospital, Apex Wellness Hospital, GOVINDNAGAR, Nashik, Maharashtra, 422009, India Nashik Maharashtra - 422009	Apex Wellness Ethics Committee, Apex Wellness Hospital, Survey no. 799, Plot No. 187, Behind Prakash Petrol Pump, Govind Nagar, Nashik-422009, Maharashtra, India ECR/1500/Inst./MH/2021	Dr Shailesh Bondarde
KLE University - Jawaharlal Nehru Medical College, KLE University - Jawaharlal Nehru Medical College JNMC Belgaum Belgaum, Karnataka, 590010 , India Belgaum Karnataka - 590010	Institutional Ethics Committee, KLE University' KLE Dr PK Hospital & MRC JNMC Campus Nehrunagar Belagavi-590010, Karnataka, India. ECR/211/Inst/KA/2013/RR-19	Dr Rohan Bhise
Grant Medical Foundation Ruby Hall Clinic, Grant Medical Foundation Ruby Hall Clinic, 40, Sassoon	POONA MEDICAL RESEARCH FOUNDATION, INSTITUTIONAL ETHICS COMMITTEE, E4-C to E4-F, 4th floor, Fifth Avenue,	Dr Sadanand Karandikar

Road, Pune, Maharashtra, 411001, India Pune Maharashtra - 411001	condominium, Dhole Patil Road, pune-411001, Maharashtra, India. ECR/24/Inst/MH/2013/RR-22	
Karnataka Cancer Hospital and Research Centre, Karnataka Cancer Hospital and Research Centre Bangalore, No 99 J B KAVAL KRISHNA NANDA NAGAR NANDHINI LAYOUT, Bangalore, Karnataka, 560096, India bangalore Karnataka - 560096	Vagus Institutional Ethics Committee 6-8 , Malleswaram 18 Cross Bangalore , Karnataka - 560055 , India ECR/1181/Inst/KA/2019/RR-22	Dr Yathish Kumar
HCG Manavta Cancer Centre, HCG Manavta Cancer Centre, Behind Shivang Auto, Nashik, Maharashtra, 422002, India Nashik Maharashtra - 422002	Manavata clinical research institute Ethics committee, HCG Manavata Cancer center, Behind Shivang auto, Mumbai Naka, Nashik, Maharashtra -422002, India. ECR/500/Inst/MH/2013/RR-20	Dr Rajnish Nagarkar
All India Institute of Medical Sciences, All India Institute of Medical Sciences AIIMS New Delhi Dr. B.R.A Institute-Rotary Cancer Hospital, Ansari Nagar, New Delhi, 110029 Delhi Delhi -110029	Institution Ethics Committee, AIIMS, Old OT Block, Room No.102, AIIMS Hospital, Ansari Nagar, New Delhi-110029, India. ECR/538/Inst/DL/2014/RR-20	Dr Ajay Gogia
Sunshine Global Hospital, Sunshine Global Hospital, Piplod, Beside Big Bazar, Gaurav Path, Dumas Road, Surat-395007 , India surat Gujarat - 395007	Institutional Ethics Committee, Sunshine Global Hospital, beside big bazar, Gaurav Path, Dumas Road, Surat-395007, India. ECR/1341/Inst/GJ/2020	Dr Tanveer Maksud
Deenanath Mangeshkar Hospital Research Ctr, Deenanath Mangeshkar Hospital Research Ctr Near Mhatre Bridge Erandwane, Pune Maharashtra 411 004, India Pune Maharashtra - 411004	Institutional Ethics Committee, Deenanath Mangeshkar Hospital & Research Centre, 14th Floor, Superspeciality Building, Erandwane Pune Maharashtra-411004, India. ECR/15/Inst/Maha/2013/RR-22	Dr Chetan Deshmukh

File No. CT/149/23-DCG(I)

Mangalore Institute of Oncology MIO, Mangalore Institute of Oncology MIO, Pumpwell Circle, Kankanady, Mangalore, Karnataka, 575002, India Manglore Karnataka - 575002	Mangala Institutional Ethics Committee, Mangala Hospital, Kadri, Mangalore 575003, Karnataka, India. ECR/567/INST/KA/2014/RR20	Dr Krsihna Prasad
Nirmal Hospital Pvt Ltd, Nirmal Hospital Pvt Ltd, Ring Road Ring Road, Surat GUJARAT 395002, India Surat Gujarat - 395002	Nirmal Hospital Ethics Committee, Nirmal Hospital Pvt.Ltd., Ring Road, Surat, 395001, Gujarat, India. ECR/390/Inst/GJ/2013/RR-19	Dr Jayanti Patel
Meenakshi Mission Hosp and Research Centre, Meenakshi Mission Hosp and Research Centre , Lake Area, Melur Road Madurai, 625107, India Madurai Tamil Nadu - 625107	Institutional Ethics Committee, Room No. 6701, 6th floor, Meenakshi Mission Hospital & Research Center, Lake area, Melur Road, Madurai-625107, India. ECR/398/Inst/TN/2013/RR-19	Dr Anada Selvakumar P
Dr Ashish Kaushal, KD Hospital, Dr Ashish Kaushal, KD Hospital Ahmedabad, Near Vaishnav Devi Circle Ahmedabad Gujarat 382421, India ahmedabad Gujarat - 382421	KD Hospital Institutional Ethics Committee, KD Hospital, Nr. Vaishnodevi Circle, S.G. Highway, Ahmedabad, Gujarat -382421, India. ECR/1294/Inst/GJ/201	Dr Ashish Kaushal
Tata Memorial Hospital, Tata Memorial Hospital, Homi Babha Building, Dr Ernest Borges Rd, Parel East, Parel, Mumbai, Maharashtra, 400012 , India Mumbai Maharashtra - 40001	Institutional Ethics Committee I/II ,CRS Department , Main Building 3rd Floor , Dr E Borges Road . Parel (E) Mumbai 400012 India. ECR/170/Inst/MH/2013/RR-22	Dr Jyoti Bajpai

****