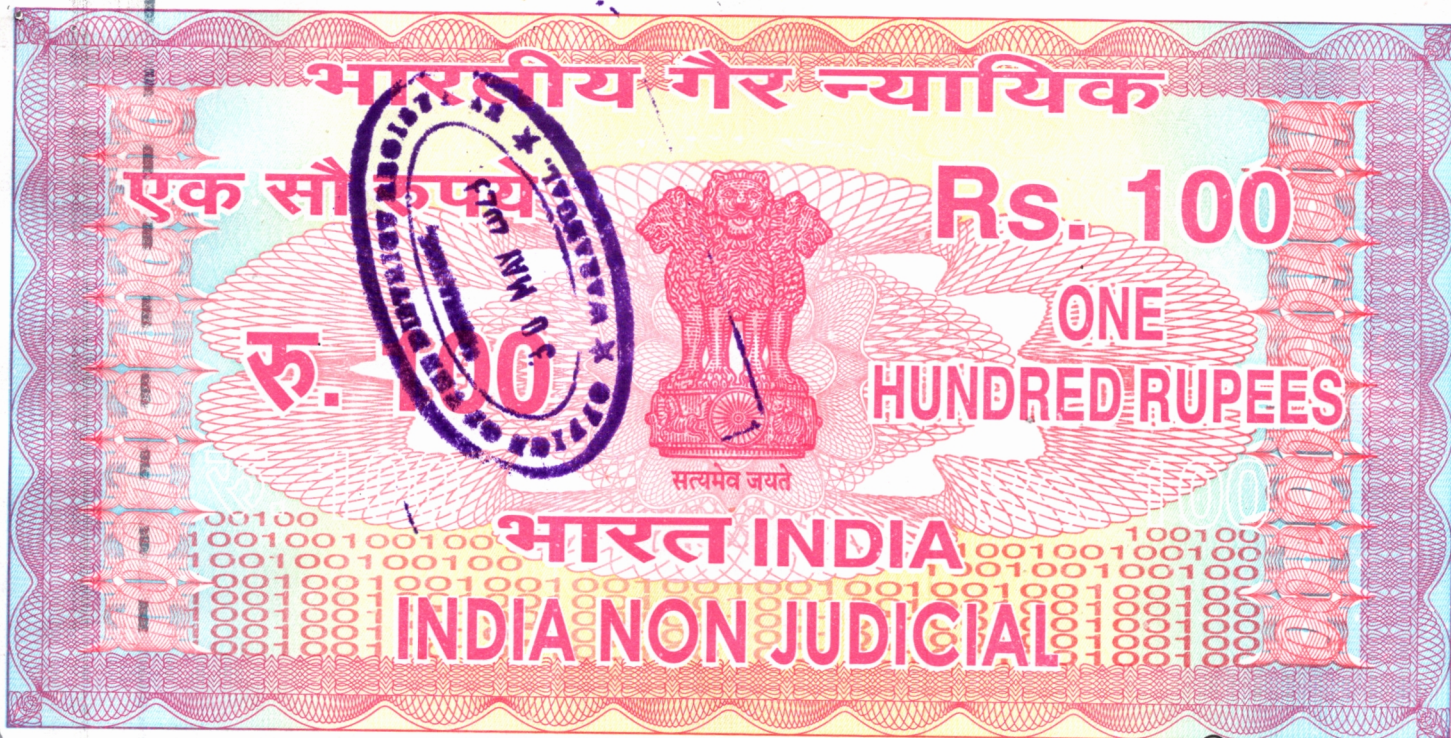




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Hyderabad
For Whom M/s Nmc Clinical Services
CLINICAL TRIAL AGREEMENT

A Manjula
AW 605246
A. MANJULA
Licenced Stamp Vendor
L.No. 21-11-71/2014 R.L. No. 21-11-6/2023
8-10-51, Near: Radhika Talkies, WARANGAL.
Pin: 506 002 (T.S) Cell : 9704638101

This Clinical Trial Agreement (hereinafter "Agreement") is made on 14th July 2023

by and between

NMC Clinical Services acts as a Clinical Research Consultancy having its registered office at #12-52, Road No. 2, P&T Colony, Medipally, Hyderabad -500 039 represented through its authorized signatory (hereinafter known as the "NMC", which expression shall unless be repugnant to the context include its successors and assigns) of the **FIRST PART**

And

DR. YOGESH PREET SINGH, working at Himalayan Institute of Medical Sciences, an academic unit of Swami Rama Himalayan University having its place of business at Swami Ram Nagar, Jolly Grant, Dehradun, Uttarakhand-248016, India (hereinafter referred to as "**Principal Investigator**" (which expression unless repugnant to the context, shall mean and include his permitted assigns) of the **SECOND PART**

And

SWAMI RAMA HIMALAYAN UNIVERSITY, a University established under section 2(f) of UGC Act, 1956 and enacted vide Uttarakhand Act no. 12 of year 2013, having its registered office at Swami Ram Nagar, Jolly Grant 248 016, Dehradun, Uttarakhand, India through its Registrar Dr. Susheela Sharma (hereinafter referred to as "**Institution**" which expression shall unless repugnant to meaning or context mean and include its successors and permitted assigns) of the **THIRD PART**



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NMC, Principal Investigator and Institution are hereinafter individually referred to as the “Party” and jointly as the “Parties”.

WHEREAS:

- A. Virchow Healthcare Pvt. Ltd. (“Virchow” or “Sponsor”) wishes to sponsor a clinical trial study entitled “*Comparative pharmacokinetic, pharmacodynamic, safety, efficacy and immunogenicity study of VBRTXM01 (Virchow Rituximab) versus Ristova (Roche Rituximab) in patients with Rheumatoid Arthritis*” (hereinafter referred to as “Study”) to be conducted by Principal Investigator at the Institution under the appended protocol carrying study code VBRTXM01/2020-CT1 (“Protocol”) and all its subsequent amendments.
- B. Virchow has delegated responsibility for the management of this Study, including contracting and Study monitoring, to NMC, and has authorized NMC to bind Virchow to all commitments within this Agreement identified as belonging to Virchow.
- C. Principal Investigator is professionally equipped to undertake the Study and has agreed to perform the Study on the terms and conditions hereinafter set forth.

NOW, THEREFORE, in consideration of the premises and the mutual promises and covenants expressed herein, the parties agree as follows:

1. STUDY

The Principal Investigator will perform the project set forth in the appended protocol carrying the study code **VBRTXM01/2020-CT1**.

Any additional work not identified in the protocol, but indicated during the course of the study, will be separately agreed upon by Sponsor and Principal Investigator.

2. PERIOD OF PERFORMANCE AND TERMINATION

The Study will be conducted during the period starting from 14 July 2023 to 13 June 2024 and may be extended by mutual agreement in writing, duly signed by all the Parties to this Agreement. This Agreement shall be terminated by the Parties in writing with at least thirty days prior notice to the other Party.

3. PROVISION OF MATERIAL AND INFORMATION

NMC agrees to provide:

1. All trial materials necessary for the conduct of the study;
2. All relevant clinical pharmacology and toxicology information and advice to the Principal Investigator and the Institution for the proper planning and conduct of the study throughout the study period. Such information will include any serious adverse drug experience, all relevant clinical, pharmacological and toxicology data; and



3. Supervision, training and monitoring support during the conduct of the Study.

4. CONDUCT OF THE STUDY

Principal Investigator and Institution shall conduct the Study in accordance with any and all applicable laws, regulations, guidelines and protocols, including but not limited to, the terms of the Study Protocol, the trial authorisation given by the Drug Control General of India, New Drugs and Clinical Trials Rules, 2019 Guidelines issued by the Central Drug Standard Control Organization, Ministry of Health, Government of India, Ethical Guidelines for Biomedical Research on Human subjects issued by the Indian Council for Medical Research and in accordance with the ethical principles that have their origin in the declaration of Helsinki and other ethical conditions imposed by the Institutional Ethics Committee.

4.1. IP to Be Used Only for Study

Principal Investigator shall not make any use of IP provided by Sponsor other than for the performance of the Study.

4.2. Valid Subjects' Recruitment

Principal Investigator shall use his best effort to recruit only valid subjects and shall not knowingly enrol any subjects, which in Principal Investigator's best professional judgment do not adequately meet the criteria for a valid subject.

4.2.1. Number of subjects

The study anticipates an average enrolment of 25 completed and evaluable patients from the Principal Investigator. Recruitment for this study will be through competitive enrolment and Principal Investigator may enrol more or less depending on the enrolment at other sites.

4.2.2. Timeline

Principal Investigator shall recruit the eligible patients in the stipulated time schedule of 3 months after site initiation of the study.

4.3. Case Report Forms

Principal Investigator shall complete the Case Report Form provided by Sponsor promptly and accurately. Principal Investigator shall give these forms and make available any source documents related to the Study to Sponsor and NMC at periodic monitoring visits or otherwise promptly upon request. Principal Investigator shall assist Sponsor and NMC to resolve any discrepancies, errors or missing information in the Case Report Forms. Principal Investigator shall assist Sponsor to conduct audits of original case records, laboratory reports, and/or raw data sources underlying data recorded in the Case Report Forms. Such audits shall be conducted with due regard to patient confidentiality.

4.4. No Ancillary Study



Principal Investigator agrees that no valid subject in this Study may participate concurrently in any ancillary study (technique, procedure, questionnaire, or observation other than those set forth in the Protocol) without prior approval in writing from Sponsor.

4.5 Ethics Committee's Approval

Principal Investigator shall be responsible for obtaining approval of the Protocol, Informed Consent and any alteration to or waiver of any valid subject authorization permitting the disclosure of confidential valid subject information in connection with the Study, from the appropriate Ethics Committee prior to commencement of the Study and notifying the same with sponsor and NMC.

4.6. Changes to Protocol or Informed Consent

In the event the Ethics Committee requires changes in the contents of the Protocol or the Informed Consent, such changes shall not be implemented until Sponsor is notified and gives its approval. The contents of the Protocol or the Informed Consent shall not be revised without the prior written agreement of Sponsor and the Ethics Committee.

4.7. Informed Consent to Be Signed

Principal Investigator shall be responsible for obtaining an Informed Consent document signed and dated by or on behalf of each valid subject, prior to the valid subject's participation in the Study. Principal Investigator shall also be responsible for audio visual recording of informed consent process while adhering to the principles of confidentiality.

5. Monitoring of the Study

5.1 Inspections/Audits

During the term of this agreement, and subject to prevailing patient confidentiality, Principal Investigator agrees to permit representatives of the Sponsor or other appropriate governmental authorities direct access to examine (a) the facilities where the Study is being conducted, (b) include Informed Consent Form (c) raw Study data including original valid subjects' records and (d) any other relevant information (and to make copies) necessary for Sponsor to confirm that the Study is being conducted in conformance with the Protocol and in compliance with federal laws and state laws. Principal Investigator agrees to take any reasonable actions requested by the Sponsor to cover deficiencies noted pursuant to the Study during an audit or inspection.

5.2. Adverse Event

Principal Investigator shall promptly notify Sponsor and NMC in writing of any serious or unexpected adverse events or claim of illness or injury actually or allegedly due to the adverse reaction to the IP and allow Sponsor to handle such claim (including settlement negotiations) and shall co-operate fully with Sponsor in its handling of the claim.

Principal Investigator responsibilities in case of serious adverse events (SAE)



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- Principal Investigator shall report all SAE to the Licensing Authority, Sponsor and Ethics committee, which accorded approval to the study protocol within 24 hrs of occurrence.
- In case of death, Principal Investigator shall forward his/her reports on SAE after due analysis to Chairman of the Expert committee and Chairman of Ethics Committee with a copy of the report to Licensing Authority and head of the Institution where the trial has been conducted, within 10 days of occurrence of death.
- In case of SAEs other than deaths, PI shall forward his/her report on SAE after due analysis to Chairman of Ethics Committee, Licensing Authority and head of the Institution where the trial has been conducted, within 10 days of occurrence of SAE.
- Ensure adequate follow-up.
- Report any Principal Investigator Notifications to respective EC.
- Sponsor agrees to reimburse the Institution or Principal Investigator for reasonable and necessary medical expenses incurred by the Institution or Principal Investigator as a direct result of diagnosing and treating of an SAE resulting from the use of the Trial drugs when administered in strict accordance with the Protocol and Sponsor's instructions, provided that the SAE did not occur as a direct result of the Institution's or Principal Investigator's negligence or misconduct. The Institution and Principal Investigator agree to treat any such illness or injury. Payments will be made following an invoice per treatment and confirmation by Sponsor that the treatment was performed as a result of an SAE. Institution or Principal Investigator will provide all information reasonably requested by Sponsor to confirm such treatment.
- If during the course of the Trial any injury occurs to a patient ("**Patient Injury**"), Sponsor agrees to pay financial compensation as well as reimbursement of reasonable and necessary medical expenses to the patient or his legal heirs. However, where the Patient Injury is due to (i) the failure of the Institution or Principal Investigator, or their officers, agents, or employees to follow the Protocol or administer the Trial drugs in strict accordance with the Protocol or Sponsor's instructions or (ii) their negligence, the Institution and Principal Investigator agree to pay any such compensation to the patient.

5.3. Change in Principal Investigator

In the event of a change of Principal Investigator, the Principal Investigator shall alert NMC within three (3) days. If NMC considers that Principal Investigator's non-affiliation with the Institution would adversely affect the Study, NMC may in its absolute discretion shall sign the agreement with the new Principal Investigator who shall be required to agree to the terms and conditions of this agreement.

6. Payments

In consideration for performance under terms of this AGREEMENT, NMC agrees to pay **PI per patient** per visit, in accordance with the appended BUDGET in Annexure through Cheque(s)/Online payable to the Principal Investigator.

If to PI

Payee Name: SRHU SCIENTIFIC AND INDUSTRIAL RESEARCH

Bank Name: STATE BANK OF INDIA

Bank Account No.: - 33082676422




Bank IFSC code: SBIN0010580

Bank Branch Address: HIHT, Jolly Grant , P.O. Doiwala , Dehradun

PAN Number: AAAJH0463L

GST Number: 05AAAJH0463LIZC

7. Term and Termination

7.1. Term

The term of this Agreement shall begin on the Effective Date and shall end on the date, unless sooner terminated in accordance with the terms hereof. The parties agree that the term may be extended by mutual written agreement if events beyond the parties' control delay completion of the Study beyond the expiration date.

7.2. Termination

This agreement may be terminated by NMC at any time in the exercise of its sole discretion upon thirty (30) days prior written notice to Principal Investigator and Institution. Upon receipt of such notice, Principal Investigator agrees to promptly terminate conduct of the Study, to the extent medically permissible, for all valid subjects.

Principal Investigator or Institution may terminate the Study immediately upon 30 (thirty) days prior written notice to NMC if such termination is required to protect the health of Study Subjects or in case of material breach of any term of this agreement by the NMC or Sponsor.

7.3. Continuing Obligations

Except as otherwise specifically provided, termination of this Agreement shall not relieve any party from any obligation under this Agreement that accrued or arose from facts and circumstances in existence prior thereto.

7.4. Return of Materials

Principal Investigator shall return to Sponsor any unused IP, any infrastructure provided by the sponsor and all Sponsor Confidential Information, as defined in the Confidentiality provision of this agreement, at the conclusion of the Study or termination of this Agreement, whichever is earlier.

8. Ownership of Data and Confidentiality

8.1. Proprietary information

At the completion of Study services by Institution, all original data, regardless of the method of storage or retrieval, shall at the direction and written request of Sponsor either be (1) delivered to Sponsor; (2) retained by Institution in connection with Study services rendered hereunder for a period of two (2) years following the date a marketing application is approved for the study Drug for the indication which is being investigated, or until 2 years after Sponsor has provided written notice to Institution that the investigation has been discontinued; or (3) disposed of by Institution at Sponsor's written request.



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8.2 Confidentiality

All information, including, but not limited to the Protocol, the IP or Sponsor's operations, such as Sponsor's patent application, formulas, manufacturing processes, basic scientific data, prior clinical data and formulation information supplied by Sponsor to Principal Investigator and not previously published (the "Sponsor Confidential Information") are considered confidential and shall remain the sole property of Sponsor. Both during and after the term of this Agreement, Principal Investigator shall use diligent efforts to maintain in confidence and use only for the purposes contemplated in this Agreement

9. Intellectual Properties

All intellectual Properties rights to any discovery or invention conceived or conceived and reduced to practice as a result of the work conducted under this Agreement in accordance with the Protocol shall belong exclusively to Sponsor.

10. Publications

The Institution and the Principal Investigator shall not, without the prior written consent of the NMC/Sponsor, publish the results or make or give any public announcements, press releases or statements to the public or the press regarding the study. The results of the study may be published in a scientific journal in the event of which the Sponsor undertakes not to identify the patient by name. The Principal Investigator will provide a thirty (30) day review period prior to publication to afford the Sponsor the opportunity to identify and prevent disclosure of any proprietary information that may have been inadvertently included in a proposed release. Being a multicentre study, Principal Investigator agree that the results shall be made in conjunction with the presentation of joint, multicentre publication of the Study results with the Principal Investigators from all study sites contributing data, analysis and comments.

11. Indemnification

Virchow shall indemnify, defend and hold harmless the Institution, Investigator, and/or other affiliated and cooperating hospitals and institutions, as well as the directors, officers, agents, employees, students, the members of their Ethics Committee/Institutional Review Boards, and others holding appointments within those institutions and their respective heirs, successors, and assigns, from any liability, loss, or damage they may suffer as a result of claims or final judgments that arise from the participation in and/or performance of the subject Study.

NMC will ensure that the Sponsor agrees to execute and deliver to the Principal Investigator, other Staff Involved in Study and Institution, Members of Ethics Committee as necessary, an indemnity in form of Insurance policy provided by ICICI Lombard for any and all liabilities, claims to cover for the study patient during the entire study period, to the extent that such Liabilities are caused by the Study procedures or the Study Drug and then only if the Study is conducted in accordance with (i) this Agreement and the Protocol, (ii) all written instructions delivered by NMC/Sponsor concerning administration of the Study, (iii) all applicable government laws, rules and regulations and (iv) the manner required of a reasonable and prudent clinical Principal Investigator. The details of the Clinical Trials Liability Insurance Policy, provided by ICICI Lombard will be made available to the Principal Investigator on receipt of the requisite details of the patient.

12. Representations and Warranties



Virchow/NMC warrants that it has insurance for the Trial Subjects included in the Trial in place at Trial start as per the Applicable Laws.

The Institution warrants that it has appropriate and adequate professional indemnity insurance to cover claims or damages for which it shall be liable under this Agreement.

The Principal Investigator warrants that he has appropriate medical liability insurance.

Each party warrants that each party would maintain appropriate/applicable licenses, approvals, permits, certifications and the like necessary to lawfully perform its respective obligations under this Agreement.

Each Party represents to the other that it has the necessary right and authority to enter into this Agreement and to the best of its knowledge, it is not party to any agreement which would prevent it from fulfilling its obligations under this Agreement.

13. Dispute Resolution

In case of any dispute between the Parties, the Parties shall initiate steps to resolve the same amicably. If such discussions fails, the dispute shall be settled through arbitration in accordance with the provisions of Indian Arbitration and Conciliation Act, 1996 as amended from time to time. The venue of the Arbitration shall be in Dehradun and arbitration proceedings shall be conducted in English language. The award of the arbitrator shall be final and binding on the Parties.

14. Governing Law: This agreement shall be construed and interpreted in accordance with the laws of India and Jurisdiction at Dehradun.

15. Notices

Any notices given hereunder shall be deposited in the mail, sent by fax or personally delivered, with postage prepaid, as follows:

If to NMC

Name: R. Praveen Kumar

Title: Director

Address: #12 -52, Road No. 2, P&T Colony, Medipally,
Hyderabad -500 039, India

If to Principal Investigator:

Dr. Yogesh Preet Singh

Principal Investigator

Investigational Site (Hospital) Name: Himalayan Institute of Medical Sciences,

Address: Swami Rama Himalayan University and Swami Ram Nagar, Jolly Grant, Dehradun,
Uttarakhand-248 016

If to Institution:

Name: Dr Susheela Sharma

Title: Registrar

Investigational Site (Hospital) Name: Himalayan Institute of Medical Sciences

Address: Swami Rama Himalayan University and Swami Ram Nagar, Jolly Grant, Dehradun,
Uttarakhand-248 016



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14. Force Majeure

Neither party shall be liable nor deemed to be in default for any delays due to causes beyond the reasonable control of the Party (such as war, civil disorders, energy or other conservation matters, acts of God, or governmental action) provided that the affected Party promptly notifies the other of the cause and its effects on the Study and/or the Protocol. The Parties' obligations and the delivery dates shall be extended for the periods of such circumstances only so far as they affect the execution of the study and or other obligations in this agreement. The Party affected shall notify the other of the commencement and end of the said circumstances.

IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed by their duly authorized representatives as of the date first above written.

NMC Clinical Services

Signed By: _____



R. Praveen Kumar

Title: Director

Principal Investigator

Signed by _____

Yogesh Preet Singh 01/08/23

Dr. Yogesh Preet Singh
MD, DM (Clinical Immunology)
Consultant Rheumatologist

Dr. Yogesh Preet Singh

Title: Principal Investigator

Institution

Signed by _____

Susheela Sharma 13/08/23



Dr. Susheela Sharma

Title: Registrar, Swami Rama Himalayan University



BUDGET

(Payment Schedule)

ANNEXURE I

Patients are expected to be recruited on a competitive basis across all clinical trial centers.

ESTIMATE FOR ONE COMPLETED PATIENT: Fees Inclusive of all emoluments to Principal Investigator, Hospital charges, Co-Principal Investigator, Study coordinator and Study assistant and no extra charges will be paid for any kind of site supplies used for dosing.

Visit	PI fee (Rs.)	Institutional Over-head 20% (Rs.)	CRC Allowance	Patient travel (Rs.)	Total per Patient (INR)
V1- Screening	2000	400	500	500	3400
V2- Day 1	3000	600	500	500	4600
V3- Day 2	0	0	0	0	0
V4- Day 3	0	0	0	0	0
V5- Day 7	0	0	0	0	0
V6 – Day 15	3000	600	500	500	4600
V7 – Week 4	2000	400	500	500	3400
V8 – Week 8	1000	200	500	500	2200
V9 – Week 12	2000	400	500	500	3400
V10 – Week 16	1000	200	500	500	2200
V11 – Week 20	1000	200	500	500	2200
V12 – Week 24	2000	400	500	500	3400
Total	17000	3400	4500	4500	29400

Note: NMC will bear the Lab Investigational charges for all patients with the approval from Sponsor including those of screen failures (only five patients).



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Lab Investigational charges

Parameter	Cost
CBP,	350
Hb,	300
PLC	250
LFT	900
ALT	155
AST	200
RFT	1000
Sr. Creatinine	180
BUN	180
ESR	150
CRP	625
HbA1c,	600
HBsAg	500
Serum pregnancy	300
Anti-HCV	950
HIV	500
RA seropositive confirmatory test and Anti-CCP	2500
Total serum immunoglobulin (IgA, IgM, IgG)	1300

* Principal Investigator fee will be paid only for eligible patients. 10% TDS deduction is admissible for every payment made towards each visit or for every installment.

- The number of patients expected to be enrolled at each centre is 25.
- Any change from the above amount will be ratified with the mutual agreement with all the above involved parties.
- Sponsor would like to archive all the trial related documents at sponsor site itself.

