AMANDEMEN KETIGA
No: 0003/Agr-Amd/KGBIO/XI/2021
TERHADAP PERJANJIAN UJI KLINIS
No: 008/KGBio-Legal/MEDICAL/III/2020

Amandemen Ketiga Perjanjian Uji Klinis (selanjutnya disebut "**Amandemen**") ini dibuat dan efektif pada tanggal **23 November 2021** (selanjutnya disebut "**Tanggal Efektif**") oleh dan antara :

1. **PT KALBE GENEXINE BIOLOGICS**, sebuah perusahaan yang didirikan di Republik Indonesia, yang memiliki tempat usaha di Gedung Kalbe 1 Lantai 3, Jln. Letjend Soeprapto Kav. 4 No. 1, Cempaka Putih Timur, Cempaka Putih, Jakarta Pusat 10510, Indonesia (selanjutnya disebut "**Sponsor**"); dan

2. **RSUPN DR. CIPTO MANGUNKUSUMO,** dalam hal ini diwakili oleh **dr. Lies Dina Liastuti, SpJP(K), MARS, FIHA** selaku **Direktur Utama RSUPN Dr. Cipto Mangunkusumo**, berdasarkan Surat Keputusan Menteri Kesehatan Republik Indonesia Nomor: KP.03.03/ Menkes/ 254/ 2018 tanggal 14 Mei 2018 tentang Pemberhentian dan Pengangkatan Dari dan Dalam Jabatan Pimpinan Tinggi Pratama di Lingkungan Kementerian Kesehatan Republik Indonesia, dan oleh karenanya sah dan berwenang dalam bertindak untuk dan atas nama **RSUPN Dr. Cipto Mangunkusumo**, berkedudukan hukum di Jalan Diponegoro No. 71 Jakarta Pusat, Indonesia, (selanjutnya disebut "**Institusi**").

Sponsor dan Institusi secara bersama-sama selanjutnya disebut sebagai "**Para Pihak**".

MENERANGKAN

A. Bahwa, Para Pihak telah menandatangani:
   1. Perjanjian Uji Klinis No. 008/KGBio-Legal/MEDICAL/III/2020 tertanggal 19 Maret 2020;
   2. Perjanjian Uji Klinis No. 008/KGBio-Legal/MEDICAL/VI/2020-AMD1 tertanggal 9 Juli 2020; dan
   3. Perjanjian Uji Klinis No. 008/KGBio-Legal/MEDICAL/III/2020-AMD2 tertanggal 31 Mei 2021,

   (selanjutnya disebut sebagai "**Perjanjian**").

B. Bahwa Para Pihak sepakat untuk mengubah ketentuan dalam Perjanjian.

OLEH KARENA ITU, dengan mempertimbangkan premis-premis sebelumnya dan persetujuan bersama yang tercantum di sini, Para Pihak dalam Perjanjian ini

THIRD AMENDMENT
No: 0003/Agr-Amd/KGBIO/XI/2021
TO THE CLINICAL TRIAL AGREEMENT
No: 008/KGBio-Legal/MEDICAL/III/2020

This Third Amendment to the Clinical Trial Agreement (hereinafter referred to as "**Amendment**") is entered into and is effective as of **November 23rd, 2021** (hereinafter referred to as "**Effective Date**") by and between:

1. **PT KALBE GENEXINE BIOLOGICS**, a company incorporated in Republic of Indonesia, having its place of business at Kalbe Building 1, 3rd Floor, Jln. Letjend Soeprapto Kav. 4 No. 1, Cempaka Putih Timur, Cempaka Putih, Central Jakarta 10510, Indonesia (hereinafter referred to as "**Sponsor**"); and

2. **RSUPN DR. CIPTO MANGUNKUSUMO**, represented by **dr. Lies Dina Liastuti, SpJP(K), MARS, FIHA,** as **President Director of RSUPN Dr. Cipto Mangunkusumo**, based on the Decree of the Minister of Health of the Republic of Indonesia Number: KP.03.03/Menkes/254/2018 dated May 14, 2018 on Dismissal and Appointment of and in *Jabatan Pimpinan Tinggi Pratama* within the Ministry of Health of the Republic of Indonesia, in this matter acting for and on behalf of **RSUPN Dr.Cipto Mangunkusumo**, with legal domicile at Jl. Diponegoro No. 71 Jakarta Pusat, Indonesia (hereinafter referred to as "**Institution**").

Sponsor and Institution together referred to as the "**Parties**".

RECITALS

A. Whereas, the Parties have signed:
   1. Clinical Trial Agreement No. 008/KGBio-Legal/MEDICAL/III/2020 dated 19th March 2020;
   2. Clinical Trial Agreement No. 008/KGBio-Legal/MEDICAL/VI/2020-AMD1 dated 9 July 2020; and
   3. Clinical Trial Agreement No. 008/KGBio-Legal/MEDICAL/III/2020-AMD2 tertanggal 31 May 2021

   (hereinafter referred to as the "**Agreement**").

B. Whereas the Parties agree to change provision in the Agreement.

THEREFORE, in consideration of the foregoing premises and the mutual covenants contained herein, the Parties hereto agree as follows:

menyetujui ketentuan sebagai berikut:

PASAL I

Para Pihak sepakat untuk mengubah Pasal 4 ayat 2 huruf d tentang jumlah rekrutmen Subjek Uji Klinis dari 13 (tiga belas) subjek menjadi 26 (dua puluh enam) subjek, sehingga untuk selanjutnya mengatur sebagai berikut:

PASAL 4
KEWAJIBAN PARA PIHAK DAN PENELITI

2. Institusi wajib memastikan bahwa:
   d. Peneliti harus melakukan upaya terbaiknya untuk merekrut **26 (dua puluh enam)** Subjek Uji Klinis untuk berpartisipasi dalam Uji Klinis dan akan melakukan Uji Klinis sesuai dengan jadwal ("**Timeline**") sebagaimana ditentukan dalam Lampiran Perjanjian ini.

PASAL II

Para Pihak sepakat untuk mengubah Lampiran 2 tentang Timeline dan Lampiran 3 tentang Biaya Penelitian.

PASAL III

1. Apabila tidak ditentukan lain dalam Amandemen ini, maka semua ketentuan yang diatur dalam Perjanjian akan tetap berlaku dan mengikat untuk dilaksanakan oleh Para Pihak;

2. Amandemen ini berikut Lampirannya, baik yang dilekatkan pada saat ini maupun kemudian, merupakan satu-kesatuan dan bagian yang tidak terpisahkan dengan Perjanjian;

3. Amandemen ini diintepretasikan sesuai dengan dan administrasi dan pelaksanaannya tunduk pada hukum Republik Indonesia; dan

4. Amandemen ini dibuat dalam bahasa Inggris dan Indonesia. Dalam hal terdapat suatu pertentangan, ketidaksesuaian atau perbedaan pengertian antara ke-2 (Ketiga) versi, maka Bahasa Indonesia akan berlaku dan mengatur.

ARTICLE I

The Parties agree to amend Article 4 paragraph 2 alphabet d, concerning the number of Clinical Trial Subjects from 13 (thirteen) subjects to 26 (twenty six) subjects, so as to further regulate the following:

ARTICLE 4
OBLIGATIONS OF THE PARTIES AND THE INVESTIGATOR

2. Institution shall ensure that:
   d. Investigator shall use its best endeavors to recruit **26 (twenty six)** Clinical Trial Subjects to participate in the Clinical Trial and shall conduct the Clinical Trial in accordance with the timeline ("**Timeline**") as prescribed in Appendix of this Agreement.

ARTICLE II

The Parties agree to change Appendix 2 concerning Timeline and Appendix 3 concerning Study Budget.

ARTICLE III

1. Save as otherwise specified in this Amendment, all provisions stipulated in the Agreement shall remain in force and binding to be conducted by the Parties;

2. This Amendment including its Appendix, whether or not attached herein or in the future, constitute an integral and inseparable part of the Agreement ;

3. This Amendment shall be interpreted in accordance with, and its administration and performance governed by the laws of the Republic of Indonesia; and

4. This Amendment is made in English and Indonesian language. In the event there is a conflict, inconsistency or difference in meaning between the two (2) versions, the Indonesian language shall prevail and control.

SEBAGAI BUKTI, Para Pihak telah menandatangani Perjanjian ini melalui wakilnya masing - masing yang sah pada Tanggal Efektif.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives as of the Effective Date.

Ditandatangani atas nama:

Signed on behalf of the:

SPONSOR
PT KALBE GENEXINE BIOLOGICS

Sie Djohan
Presiden Direktur

INSTITUSI
RSUPN Dr. CIPTO MANGUNKUSUMO

dr. Lies Dina Liastuti, SpJP(K), MARS, FIHA
Direktur Utama

PENELITI
Saya dengan ini mengakui bahwa saya telah membaca ketentuan-ketentuan Perjanjian ini, termasuk Protokol, dan saya akan bertindak dan melakukan tugas-tugas saya sebagai Penyelidik Utama dari Percobaan ini sesuai dengan ICH-GCP.

INVESTIGATOR
I hereby acknowledge that I have read the terms of this Agreement, including the Protocol, and I will act and perform my duties as the Principal Investigator of this Trial in accordance with ICH-GCP.

dr. Pringgodigdo Nugroho, Sp.PD-KGH
Penyakit Dalam Sub Spesialis Ginjal dan Hipertensi

Appendix II
Timeline

	Nov-21				Dec-21				Jan-22				Feb-22				Mar-22				Apr-22				May-22				Jun-22				Mar-23			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Amandment (2 weeks)																																				
Subject recruitment (4 months)																																				
Subject following up (13 months/subject)																																				

Appendix 3: Study Budget

FINANCIAL PAYMENT

Subject 1-13

No	Remarks	Cost (IRD)	Subjects	Total cost (IRD)	Notes
1	Investigator fee	Rp7.000.000	13	Rp91.000.000	
2	Nurse	Rp2.000.000	13	Rp26.000.000	Blood specimen collection and inject the drug
3	Study room	Rp20.000.000		Rp20.000.000	
4	Drug storage	Rp10.000.000		Rp10.000.000	Some drug will have to be stored in pharmacy
5	Institutional fee	20%		Rp27.400.000	
6	Clinical trial administration fee			Rp5.000.000	
	Total cost			Rp179.400.000	

Additional Fee For Other Doctors

	Remarks	Cost (IDR)	Subjects/site	Total cost (IDR)	Notes
1	References other doctor fee*	Rp2.500.000 per subject		Rp2.500.000 per subject	Subject fulfil the inclusion and exclusion criteria

Payment Schedule (Subject 1-13)

Payment No	Milestone	Payment amount
1	Initial Payment + Institutional fee + Clinical trial administration fee	Rp57.000.000,00
2	After 4 subjects completed*	Rp40.800.000 + *
3	After 9 subjects completed*	Rp40.800.000 + *
4	Final payment after all case report forms are completed and close out visit is complete*	Rp40.800.000 + *
	Total Payment*	Rp 179.400.000,00 + *

Subject 14-26 (based on 3rd Amendment)

No	Remarks	Cost (IRD)	Subjects	Total cost (IRD)	Notes
1	Investigator fee	Rp7.000.000	13	Rp91.000.000	
2	Nurse	Rp2.000.000	13	Rp26.000.000	Blood specimen collection and inject the drug
	Total Cost			Rp117.000.000	

Additional Payment Schedule For Subject 14-26

Payment No	Milestone	Payment amount	Notes
1	After 4 additional subject recruited	Rp19.500.000	Payment will be made immediately even though the recruitment has not been achieved if the research has been completed (the amount paid is in accordance with what was achieved).
2	After 4 additional subject completed	Rp19.500.000	
3	After 8 additional subject recruited	Rp19.500.000	
4	After 8 additional subject completed	Rp19.500.000	
5	After 13 additional subject recruited	Rp19.500.000	
6	After 13 additional subject completed	Rp19.500.000	
	Total Payment	Rp117.000.000	