

## **Template Clinical Trial Agreement**

(Template agreement for industry initiated and sponsored Clinical Trials, with human subjects, conducted in the Netherlands by academic (NFU) and non-academic (STZ) hospitals and NKI/AvL)

### **Scope of use:**

This template clinical trial agreement is created in joint cooperation between the Nationale Federatie van Universitair Medische Centra (NFU), de vereniging Samenwerkende Topklinische opleidingsZiekenhuizen (STZ), Vereniging Innovatieve Geneesmiddelen (previously Nefarma), Stichting Het Nederlands Kanker Instituut - Antoni van Leeuwenhoek Ziekenhuis (NKI/AvL) and the Associatie van Contract Research Organisaties in Nederland (ACRON), to facilitate conducting clinical trials in the Netherlands. The clauses on termination and publication meet the Revised Directive on the Assessment of the Clinical Trial Agreement of the CCMO (Centrale Commissie Mensgebonden Onderzoek) of 2011.

In case a Contract Research Organization (CRO) is signing this agreement on behalf of the Sponsor or in its own name, please note that depending on the Power of Attorney / Delegation of Authority given by sponsor to the CRO, a separate indemnity letter signed by Sponsor may be needed.

If no CRO is involved, “Sponsor and/or CRO” must be read as solely “Sponsor” throughout the Agreement. If a CRO is involved, references to “Sponsor and/or CRO” must be checked on accuracy and applicability.

This template can be modified as agreed upon between the Parties for accommodating the correct party structure, study-specific requirements, financial arrangements or any other terms and conditions which are relevant for the purpose of the collaboration. During the negotiations any modifications should be marked and explained.

## TABLE OF CONTENT

# Clinical Trial Agreement

Clinical Trial: *[insert title]*

Protocol: *[insert EUDRACT number or Dutch Registration NL-number, date and version number]*

Study Drug: *[insert name]*

Effective date of agreement: date of last signature on this Agreement

## The undersigned,

- A. *[insert name of the sponsor]*, whose registered office is at *[insert address]*, lawfully represented by *[insert name(s) and function(s)]* (hereinafter referred to as “**Sponsor**”) OR CRO *[insert name of CRO]* acting in its own name and for and on behalf of *[insert name of Sponsor]*, whose registered office is at *[insert address of CRO]* (hereinafter referred to as “**CRO**”)

and

- B. *[insert name of institution]*, whose address is at *[insert address]*, lawfully represented by *[insert name(s) and function(s)]* (hereinafter referred to as “**Institution**”)

[N.B. In case the “medisch specialistisch bedrijf” will cosign the agreement, the following text can be used for the Institution:]

“*[Name of the hospital]*, located at *[adres]*, the Netherlands, lawfully represented by *[name and function]* (hereinafter referred to as “*[name of hospital]*”); and *[name of medisch specialistisch bedrijf]*, located at *[adres]*, the Netherlands, lawfully represented by *[name and function]* (hereinafter referred to as “*[name of MSB]*”); (hereinafter *[name of hospital]* and *[name of MSB]* jointly referred to as “Institution”)

## **If the Principal Investigator is not an employee of Institution and acts as a party:]**

and

**[INVESTIGATOR]**, *[insert: name of physician ...», ...[function], [tax/office address and chamber of commerce registration number, if applicable]* (hereinafter referred to as “**Principal Investigator**” )

**[ OR if the Principal Investigator is an employee of the Institution and not a Party: ]**

in the presence of

Institution's employee, [INVESTIGATOR] [*insert investigator's title, name and department of Institution where the investigator is employed*], the supervisor under whose responsibility the conduct of the Clinical Trial will be carried out (hereinafter referred to as “**the Principal Investigator**”)

WHEREAS, the Sponsor is a pharmaceutical company involved in research, development, registration, manufacture and/or sale of medicines for use in humans;

WHEREAS, the Sponsor has designed the Clinical Trial identified hereof, to evaluate Sponsor's drug [*insert study drug(s)*] (“**Study Drug**”) in accordance with the Protocol defined below; and

**[ONLY INSERT IF APPLICABLE]** WHEREAS, the Sponsor contracted the CRO to perform one or more of a Sponsor's clinical trial-related duties and functions as summarized in the Power of Attorney / Delegation of Authority attached herein as Annex 8 [and to enter into this Agreement on Sponsor's behalf] ;

WHEREAS, the Principal Investigator and Institution are concerned with the diagnosis, treatment and prevention of disease and/or clinical research for the improvement of healthcare;

WHEREAS, the Institution has facilities and personnel with the requisite skills, experience, and knowledge required to support the performance of the Clinical Trial by the Principal Investigator; and

WHEREAS, Principal Investigator, having reviewed the Protocol for the Clinical Trial, the investigator brochure and having been supplied with sufficient information by Sponsor regarding the Investigational Product in order to evaluate and determine its interest in participating in the Clinical Trial, wishes to participate in the Clinical Trial and the Principal Investigator assures that he/she has sufficient authority, competence and experience in conducting clinical trials.

In consideration of the undertakings and commitments set forth herein, the Parties agree to enter into this Clinical Trial Agreement.

## **1. DEFINITIONS**

The following words and phrases have the following meanings:

- a. “**Affiliate**” means any business entity which controls, is controlled by, or is under the common control. For the purposes of this definition, a business entity shall be deemed to control another business entity if it owns, directly or indirectly, in excess of 50% of the voting interest in such business entity or the power to direct the

- management of such business entity or to elect or appoint 50% or more of the members of the management of such business entity;
- b. “**Agent**” shall include, but shall not be limited to, any person providing services to a Party under a contract for services or otherwise, to include without limitation any pharmacist, clinical chemist, nurse or other health professional.
  - c. “**Agreement**” means this agreement comprising its recitals, clauses, schedules and any appendices attached to it, including the Protocol and including any amendments to the Agreement agreed between the Parties;
  - d. “**Auditor**” means a person who is authorised to carry out a systematic review and independent examination of clinical trial related activities and documents to determine whether the evaluated clinical trial related activities were conducted, and the data were recorded, analysed and accurately reported according to the Protocol, the Standard Operating Procedures of Sponsor and/or CRO, ICH GCP and the applicable regulatory requirements;
  - e. “**Clinical Trial**” means the investigation to be conducted at the Trial Site in accordance with the Protocol as defined below;
  - f. “**Clinical Trial Authorisation**” means a Clinical Trial authorised in accordance with the article 2 and 13i of the Dutch *Medical Research Involving Human Subjects Act*;
  - g. “**Clinical Trial Subject**” means a person enrolled to participate in the Clinical Trial;
  - h. “**Competent Authority**” means the authority appointed to evaluate the Clinical Trial in accordance with 13i and 13k of the Dutch *Medical Research Involving Human Subjects Act*, based on article 9 of the European Clinical Trial Directive 2001/20/EC;
  - i. “**Confidential Information**” means information provided by a Party (the Disclosing Party) to the other Party (the Receiving Party) or to any other of such Receiving Party’s employees or agents, and means all information (including, without limitation, study protocols, case report forms, clinical data, other data, reports, specifications, computer programs or models and related documentation, know-how, trade secrets, or business or research plans) of the Disclosing Party or the Disclosing Party’s Affiliates that are provided in connection with this Agreement or the Clinical Trial. Sponsor’s Confidential Information shall include Clinical Trial data, results, or reports created by Institution, Principal Investigator, or Research Staff in direct connection with the Clinical Trial (except for a Clinical Trial Subject’s medical records); and cumulative Clinical Trial data, results, and reports from all sites conducting the Clinical Trial;
  - j. “**CRF**” means the case report form in a format prepared by Sponsor and documenting the administration of the Investigational Product to Clinical Trial Subjects as well as all tests and observations related to the Clinical Trial;
  - k. “**eCRF**” means a CRF in electronic form;
  - l. “**CRO**” means Contract Research Organization which is the organization to which a sponsor may transfer some of its tasks and obligations. Any such transfer should be defined in writing. (*And according to 21CFR312.52: Transfer of Obligations to a CRO: CRO shall comply with the same regulations/ CRO is subject to the same regulatory actions*)

- m. “**Effective Date**” the date this Agreement comes into effect, being the date mentioned in the cadre on the first page;
- n. “**Ethics Committee**” means the accredited medical research ethics committee competent to review the Clinical Trial in accordance with article 2 of the Dutch *Medical Research Involving Human Subjects Act*, and to which the Protocol has been submitted for approval;
- o. “**ICF**” means the Informed Consent Form as approved by the Ethics Committee, in which the Clinical Trial Subject consents to his participation in the Clinical Trial;
- p. “**ICH-GCP**” means the ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95 together with such other good clinical practice requirements as are specified in Directives 2001/20/EC and 2005/28/EC of the European Parliament and the Council relating to medicinal products for human use and in guidance published by the European Commission pursuant to such Directives;
- q. “**Independent Committee**” means a committee such as a Data and Safety Monitoring Board (DSMB), which is a group of individuals with pertinent expertise that have oversight of and reviews on a regular basis accumulating data from one or more ongoing clinical trials and that advise the Sponsor regarding the continuing safety of Clinical Trial Subjects and those to be recruited to the Clinical Trial, as well as the continuing validity and scientific merit of the Clinical Trial.
- r. “**Intellectual Property Rights**” means patents, trademarks, trade names, service marks, domain names, copyrights, rights in and to databases (including rights to prevent the extraction or reutilisation of information from a database), design rights, topography rights and all rights or forms of protection of a similar nature or having equivalent or the similar effect to any of them which may subsist anywhere in the world, whether or not any of them are registered and including applications for registration of any of them;
- s. “**Investigational Product**” means the Study Drug identified above and the control material, as further detailed in the Protocol;
- t. “**Know How**” means all technical and other information which is not in the public domain (other than as a result of a breach of confidence), including but not limited to information comprising or relating to concepts, discoveries, data, designs, formulae, ideas, inventions, methods, models, procedures, designs for experiments and tests and results of experimentation and testing, processes, specifications and techniques, laboratory records, manufacturing data and information contained in submissions to regulatory authorities, whether or not protected by Intellectual Property Rights or any applications for such rights;
- u. “**Law**” means any applicable international, European Union and Dutch law and regulations, as well as generally accepted international conventions applicable to the performance of the Clinical Trial. Such Law including, but not limited to:
- Directives 2001/20/EC and 2005/28/EC of the European Parliament and the Council relating to medicinal products for human use and in guidance published by the European Commission pursuant to such Directives and any implementation in Institution’s national Law,

- ICH Harmonised Tripartite Guideline for Good Clinical Practice (CPMP/ICH/135/95),
- Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (*General Data Protection Regulation* or *GDPR*), and any applicable national implementing legislation.
- the Dutch Medical Research Involving Human Subjects Act (*Wet Medisch-wetenschappelijk Onderzoek met Mensen* or *WMO*),
- the Dutch Medical Treatment Agreements Act (*Wet op de geneeskundige behandelingsovereenkomst* or *Wgbo*),
- the Directives on “the assessment of Clinical Trial Agreements (2011)” and on “External Review (2012)” issued by the CCMO,
- the principles of the Dutch Code of Conduct regarding the adequate procurement, management and use of bodily human tissue published by the Federation of Dutch Medical Scientific Societies, and
- the Declaration of Helsinki, the most recent version;

References to EU Council Directives and Dutch Law include any amendments or replacements of such Law.

- v. “**Party**” means the Sponsor and/or CRO, the Institution or, only if the Principal Investigator is a separate party to this Agreement, the Principal Investigator, and “**Parties**” shall mean all of them;
- w. “**Personal Data**” means personal data as defined in the GDPR (General Data Protection Regulation), i.e. any information relating to an identified or identifiable Clinical Trial Subject.
- x. “**Principal Investigator**” means the person who will take primary responsibility for the conduct of the Clinical Trial at the Trial Site or any other person as may be agreed between the Parties as a replacement;
- y. “**Protocol**” means the document signed by the Principal Investigator, as defined in the cadre on page 1 of this Agreement, detailing all aspects of the Clinical Trial, a copy of which is at **Annex 1** to this Agreement. The Protocol includes all amendments thereto for which Clinical Trial Authorisation has been obtained;
- z. “**Research Staff**” means the persons who will undertake the conduct of the Clinical Trial at the Trial Site on behalf of the Principal Investigator and under the supervision of the Principal Investigator;
- aa. “**Samples**” means any human biological materials, including but not limited to blood, body tissue, plasma and any other material containing human cells;
- bb. “**Site Parties**” shall refer to the Principal Investigator and the Institution jointly;
- cc. “**Sponsor**” means the Party commissioning for the Clinical Trial to be conducted, acting as “**verrichter**” as defined in Article 1.1(f) of the WMO ;
- dd. “**Target**” means the estimated number of Clinical Trial Subjects to be included in the Clinical Trial as referred to in clause 5.2;

- ee. “**Timelines**” means the dates set out in **Annex 2** hereto as may be amended by agreement between the Sponsor and the Principal Investigator and “**Timeline**” shall mean any one of such dates;
- ff. “**Trial Monitor**” means one or more persons appointed by the Sponsor and/or CRO to monitor compliance of the Clinical Trial with GCP and the Protocol and to conduct source data verification;
- gg. “**Trial Site(s)**” means the premises at the Institution where the Clinical Trial will be conducted;

## **2. OBLIGATIONS**

- 2.1. The Parties agree to perform the Clinical Trial in accordance with the terms and conditions of this Agreement.
- 2.2. The Parties represent and warrant that they each have the authority to enter into this Agreement. In case the Principal Investigator is not a party to this Agreement, Institution shall ensure the performance of the responsibilities assigned to the Principal Investigator under this Agreement and by no means shall the Principal Investigator liable hereunder in person. The Institution will ensure the availability of and/or access to any resources necessary to perform the Clinical Trial at the Trial Site, including departments, facilities and Research Staff and support personnel, and the Institution certifies that Principal Investigator holds the necessary registration and has the necessary qualifications, expertise and time to perform the Clinical Trial.
- 2.3. The Institution shall notify the Sponsor and/or CRO if the Principal Investigator ceases to be associated with the Institution where the Clinical Trial will be conducted or if he/she is otherwise unavailable to continue as Principal Investigator, and Institution (or Principal Investigator, if he/she is a Party to this Agreement) shall use all reasonable endeavours to find a qualified successor acceptable to the Sponsor and/or CRO, subject to the Principal Investigator’s overriding obligations in relation to Clinical Trial Subjects and individual patient care.
- 2.4. The Institution shall procure the performance of the obligations of the Research Staff as set out in this Agreement.
- 2.5. Institution, and if the Principal Investigator is a party, the Principal Investigator, will guarantee the availability of sufficient and adequately trained and experienced Research Staff. This will include the participation of the Principal Investigator and Research Staff in any training provided by Sponsor reasonably required for the sound conduct of the Clinical Trial.
- 2.6. Institution ensures that subject to the Principal Investigator’s overriding obligations in relation to Clinical Trial Subjects and individual patient care, the Principal Investigator shall not, and the Institution shall ensure that the Research Staff shall not, during the term of this Agreement conduct any other trial which might jeopardize the Principal Investigator’s ability to recruit, enrol and study the required cohort of Clinical Trial Subjects.



- 2.7. Terms and conditions on any equipment provided by Sponsor, shall be described in **Annex 5**.
- 2.8. The Site Parties acknowledge that Sponsor and/or CRO and their respective Affiliates and/or subsidiaries need to adhere to the provisions of (i) the Bribery Act 2010 of the United Kingdom (“**Bribery Act**”); (ii) the Foreign Corrupt Practices Act 1977 of the United States of America (“**FCPA**”) and (iii) any other applicable anti-corruption legislation (together the *Applicable Anti-Corruption Legislation*). A summary of the key principles underlying the Bribery Act and the FCPA is set out in **Annex 6**. The Institution and the Principal Investigator shall not and shall not permit or induce employees, agents, consultants or other representatives, whether directly or indirectly, to engage in any activity that is prohibited by the Applicable Anti-Corruption Legislation including bribery, kickbacks, payoffs or other corrupt business practices, as outlined in the summary in **Annex 6**. Sponsor shall be responsible for keeping the summary up to date in case of any changes to the Bribery Act and the FCPA.

### **3. CLINICAL TRIAL GOVERNANCE AND COMPLIANCE**

- 3.1. The Sponsor shall be responsible for obtaining and maintaining Clinical Trial Authorisation for the Clinical Trial and substantial amendments to the Protocol. The Sponsor may require, by written notice the Principal Investigator to apply for the Clinical Trial Authorisation for Sponsor, in which case the Principal Investigator shall keep the Sponsor fully apprised of the progress of Ethics Committee submissions and shall upon request provide the Sponsor with all correspondence relating to such submissions.
- 3.2. The Principal Investigator shall not consent to any change in the Protocol requested by the Ethics Committee or Competent Authority without the prior written consent of the Sponsor.
- 3.3. In the event of any substantial amendments being made to the Protocol, the amendments shall be signed by the Principal Investigator and shall be implemented by the Research Staff as required by the Sponsor or CRO after approval of the amendments by the Competent Authority and a favourable opinion of the Ethics Committee.
- 3.4. The Clinical Trial shall be performed at the Trial Site. The Principal Investigator shall be responsible for obtaining authorization from the representatives of the Trial Site to perform the Clinical Trial at the Trial Site, which shall include but not be limited to the engagement of sub-investigators, to the extent applicable the pharmacist of the Institution (unless a separate Pharmacy Agreement is made as set out in article 7.1 below), clinical chemists, and the Research Staff required to perform the Clinical Trial as set out in this Agreement.
- 3.5. The Sponsor shall submit the Clinical Trial for listing on a free, publicly accessible clinical trial registry like [www.clinicaltrials.gov](http://www.clinicaltrials.gov) or on websites managed by a

registry conforming to WHO standards ([http://www.who.int/ictcp/network/criteria\\_summary/en/index.html](http://www.who.int/ictcp/network/criteria_summary/en/index.html)) after Clinical Trial Authorization. Upon request of the Institution or the Principal Investigator the Sponsor will disclose the registry and the date of submission.

- 3.6. The Parties shall conduct the Clinical Trial in accordance with:
  - a. the Agreement;
  - b. the Protocol;
  - c. the terms and conditions of the Clinical Trial Authorisation granted by the Competent Authority and the opinion of the Ethics Committee; and
  - d. the applicable Law.
- 3.7. The Site Parties shall make and retain records regarding the Clinical Trial as required by the Protocol, applicable Law, and in accordance with the Institution's standard archiving procedures. Institution will retain such records for a minimum of time as put out in the applicable Law. At least ninety (90) days prior to the expiry of such retention period, Sponsor will contact Institution. If indicated by Sponsor that such is reasonably required for regulatory purposes, Institution shall retain the records for a longer period of time at Sponsor's expense.
- 3.8. The Site Parties shall notify Sponsor immediately (not later than 24 hours) of any serious adverse events in accordance with the Protocol and applicable Law, and will cooperate with Sponsor in connection with any reports or filings related to such serious adverse event.

#### **4. LIABILITIES, INDEMNIFICATION AND INSURANCE**

- 4.1. Subject to the limitations set out hereinafter, Sponsor shall indemnify (in Dutch "*schadeloosstellen*") and hold harmless (in Dutch "*vrijwaren*") Institution, its employees, Agents, the Principal Investigator and the Research Staff (the "Indemnitees") against all claims, demands, actions or proceedings (to include any settlements or ex gratia payments made with the consent of the Parties hereto and reasonable legal and expert costs and expenses) made or brought (whether successfully or otherwise): (i) by or on behalf of any Clinical Trial Subject in connection with personal injury or death – including also costs for medical treatment in relation to such injury or death – arising out of the administration or use of the Investigational Product during or as a result of the Clinical Trial, or of any clinical intervention or procedure provided for or required by the Protocol, to which the Clinical Trial Subject would not have been exposed but for its participation in the Clinical Trial. In addition, Sponsor shall compensate Institution and/or the Principal Investigator for reasonable and necessary costs and expenses incurred for medical treatment of Clinical Trial Subjects who have suffered such personal injury. (ii) by or on behalf of any Clinical Trial Subject or by a data protection authority for a Personal Data breach, as defined in applicable Law, which is attributable to Sponsor or its Affiliates.

- 4.2. Sponsor's indemnification and defence of the Indemnitees shall not apply to any claim or proceeding pursuant to clause 4.1, and Sponsor shall not be liable
- a. to the extent that said personal injury (including death) is caused by any of the Indemnitees' failure to comply with this Agreement; or
  - b. to the extent that said personal injury (including death) is caused by gross negligence, willful recklessness or willful conduct or willful misconduct (in Dutch: *bewuste roekeloosheid of opzettelijk handelen of nalaten*) of any of the Indemnitees, unless the clinical trial insurance of Sponsor is providing coverage for the claim;
  - c. if any of the Indemnitees shall have made any admission in respect of such claim or proceeding or taken any action relating to such claim or proceeding prejudicial to the defence of it, without the written consent of Sponsor, provided that this condition shall not be treated as breached by any statement properly made by any of the Indemnitees in connection with the operation of Institution's internal complaint procedures, accident reporting procedures or disciplinary procedures or where such a statement is required by law.
- 4.3. Sponsor shall keep Site Parties reasonably informed of the progress of any such claim or proceeding.
- 4.4. The Parties will each use their reasonable endeavours to inform each other promptly of any circumstances reasonably thought likely to give rise to any claim or proceeding resulting from the Clinical Trial of which it is directly aware. Parties shall keep each other reasonably informed of developments in relation to any such claim or proceeding. The Parties will use reasonable efforts to consult with each other on the nature of any defence to be advanced.
- 4.5. Institution, Principal Investigator and Sponsor will each give to the other such help as may reasonably be required for the efficient conduct and prompt handling of any claim or proceeding made or brought by or on behalf of Clinical Trial Subjects (or their dependants).
- 4.6. Nothing in this clause 4 shall operate so as to restrict or exclude the liability of any Party vis-à-vis the Clinical Trial Subjects in relation to their death or personal injury caused by the negligence of that Party or their servants or employees or to restrict or exclude any other liability of a Party which cannot be so restricted or excluded by law.
- 4.7. In no circumstances shall any Party be liable to the other in contract or otherwise howsoever arising or whatever the cause thereof, for any indirect or consequential damages of any nature, such as but not limited to any loss of profit, business, goodwill, reputation, contracts, revenues or anticipated savings which arise directly or indirectly from any default on the part of Sponsor, Institution or the Principal Investigator, except and to the extent such damages
- a. shall be covered under and paid out of any insurance policy of the liable party, or
  - b. are caused by gross negligence, willful recklessness or willful conduct or willful misconduct (in Dutch: *bewuste roekeloosheid of opzettelijk handelen of nalaten*) of any of the Indemnitees and cannot be so restricted or excluded by law.

- 4.8. The liability of the Site Parties for a claim or proceeding of Sponsor under this Agreement shall be limited to an amount of three (3) times the total contract sum which is paid out under this Agreement, or the amount covered and paid out under the insurance policy taken out in accordance with clause 4.10 below, whichever is the highest; except and to the extent such claim or proceeding is made for damages caused by gross negligence, willful recklessness or willful conduct or willful misconduct (in Dutch: *bewuste roekeloosheid of opzettelijk handelen of nalaten*) of any of the Site Parties and cannot be so restricted or excluded by law.
- 4.9. Sponsor will take out or maintain
- a. insurance cover in respect of its potential liability for damages to Clinical Trial Subjects resulting from the Clinical Trial in accordance with the requirements set out in the (Dutch) Medical Research Involving Human Subjects Act and the Decree on Obligatory Insurance for Medical Studies involving Human Subjects unless this requirement has been waived by the Ethics Committee, and
  - b. further appropriate insurance cover in respect of its other potential liability under this Agreement. Sponsor shall produce to Institution, on request, copies of such insurance certificates. Except for the limitations stated in clause 4.7 above, the terms of any insurance or the amount of cover shall not relieve Sponsor of any liabilities under this Agreement.
- 4.10. Institution will take out or maintain an insurance cover in respect of the potential liability of Institution, the Research Staff, the Principal Investigator and any other employees and Agents involved with the conduct of the Clinical Trial pursuant to this Agreement. Institution shall produce to Sponsor, on request, copies of insurance certificates, together with evidence that the policies to which they refer remain in full force and effect during the term of this Agreement and any period thereafter as may be required by mandatory law. Except for the limitations stated in clause 4.7 and 4.8 above, the terms of any insurance or the amount of cover shall not relieve Institution or the Principal Investigator of any liabilities under this Agreement. Where the Institution cannot cover Agents under its insurance, it shall verify that such Agents have sufficient insurance and inform the Sponsor of such insurance upon request.
- 4.11. CRO expressly disclaims any liability in connection with the content of the Protocol and the Investigational Product, including any liability for any claim arising out of a condition caused by or allegedly caused by the administration of such Investigational Product and/or any Clinical Trial procedures associated with such Investigational Product except to the extent that such liability is caused by the gross negligence, willful recklessness or willful conduct or willful misconduct or otherwise cannot be excluded by operation of law by CRO.

## **5. CLINICAL TRIAL SUBJECT RECRUITMENT AND ENROLLMENT**

- 5.1. The Institution shall make sure that the Clinical Trial Subjects (and/or their legal representatives) will, in accordance with applicable Law, be duly informed and that each give his informed consent prior to his participation in the Clinical Trial.

Institution shall submit for approval to Sponsor/CRO the content of any Clinical Trial recruitment materials (including the ICF) directed to potential Clinical Trial Subjects before such materials are used, regardless of medium.

- 5.2. The Institution, through its Principal Investigator, shall use reasonable endeavours to recruit the Target within the Timelines as specified in **Annex 2**. As soon as the Principal Investigator expects to reach the Target, he shall notify the Sponsor and/or CRO.
- 5.3. If circumstances or events have occurred or will occur that will substantially delay or are likely to substantially delay the progress of recruitment or enrolment of the Clinical Trial Subjects, the Principal Investigator shall without undue delay inform the Sponsor and/or CRO in writing. In each such event the Parties shall discuss the consequences of the delay and each Party shall undertake reasonable endeavours to agree on measures to address the delay.
- 5.4. In the event that the Clinical Trial is part of a multi-centre clinical trial, the Sponsor may amend the number of Clinical Trial Subjects to be recruited pursuant to the Target as per clause 5.2 above subject to this clause 5.4.
  - a. The Sponsor may require further recruitment of Clinical Trial Subjects at the Trial Site to cease if:
    - i. in the reasonable opinion of the Sponsor recruitment of Clinical Trial Subjects at the Trial Site will not meet or will not likely meet the Target within the Timelines or is proceeding at a rate below that required to enable the relevant Timeline to be met, and upon Sponsor's request to increase the inclusion rate, the Principal Investigator is unable to comply, or
    - ii. if the global recruitment target for all clinical centres of Sponsor and its affiliates has been reached.
  - b. Upon receipt of a notice subject to clause 5.4.a, the Principal Investigator shall immediately stop the recruitment and inclusion of Clinical Trial Subjects. The terms and conditions of this Agreement regarding the Clinical Trial Subjects shall also apply to individuals who, at the time of receipt of such notice, have signed the ICF. Payments shall only be made according to the number of Clinical Trial Subjects recruited and included up to the date of receipt of the notice. The Sponsor will not take any responsibility or have a duty to make any payment for the Clinical Trial Subjects recruited after the date of receipt of its notice.
  - c. If recruitment of Clinical Trial Subjects is proceeding at a rate above that required to meet the relevant Timelines the Sponsor may with the agreement of the Principal Investigator increase the number and amend the rate of Clinical Trial Subjects to be recruited and enrolled at the Trial Site.

## **6. QUALITY ASSURANCE AND CONTROL**

- 6.1. The Site Parties shall ensure that all procedures defined in the Protocol are complied with, so that all data generated at the Trial Site are reliable and have been processed

correctly (especially the randomization lists, and the blind character of the Clinical Trial as the case may be) and will ensure that the content of the CRFs or e-CRFs will accurately reflect source documents.

- 6.2. The Site Parties will permit the Sponsor to examine the conduct of the Clinical Trial and the Trial Site upon reasonable advance notice and in the company of a Site Party's representative, during regular business hours at mutually agreed times, and at Sponsor's sole expense to determine that the Clinical Trial is being conducted in accordance with the Protocol, this Agreement and applicable Law, provided Trial Monitor will comply with all internal policies and regulations of the Trial Site to the extent these are sufficiently communicated to the Trial Monitor.
- 6.3. The Site Parties shall permit the Trial Monitor and any Auditor access to all relevant clinical data of Clinical Trial Subjects and relevant source documents for monitoring of the progress of the Clinical Trial, the proper collection and recording of Clinical Trial data, the welfare of the Clinical Trial Subjects, and altogether the good quality of the Clinical Trial and compliance with applicable Law and Sponsor's and/or CRO's Standard Operating Procedures. For the avoidance of any doubt, the Sponsor shall be responsible for the confidential handling of all Personal Data of Clinical Trial Subjects and other patients which the Trial Monitor and any Auditor comes across with during its monitoring or auditing activities. Before the start of the monitoring visits, the Sponsor shall provide the Institution with the name and date of birth of the appointed monitor, and declare that such Trial Monitor has signed a confidentiality statement regarding the above.
- 6.4. The Site Parties shall promptly inform the Sponsor and/or CRO of any intended or actual inspection, written enquiry and/or visit to the Trial Site by any regulatory authority in connection with the Clinical Trial and forward to the Sponsor copies of any correspondence from any such regulatory authority relating to the Clinical Trial. The Site Parties shall allow Sponsor and/or CRO representatives to be present during any such visit as permitted by Law.
- 6.5. The Site Parties shall permit authorized representatives of the Ethics Committee and Competent Authorities to have access to, copy and verify information relating to the Clinical Trial, as required by and in accordance with applicable Law. Furthermore Sponsor and/or CRO acknowledges and agrees that the Institution executive management (or a local review board appointed by such management) will have the right to audit the performance of the Clinical Trial at the Trial Site. Parties acknowledge that the Clinical Trial is subject to inspection by regulatory authorities worldwide and that such inspections may occur after the completion of the Clinical Trial.
- 6.6. In the event that the Sponsor and /or CRO reasonably believes there has been any research misconduct in relation to the Clinical Trial, Site Parties shall provide all reasonable assistance to any investigation into any alleged research misconduct undertaken by or on behalf of the Sponsor and/or CRO, the results of which the Party on whose behalf the investigation was undertaken shall, subject to any obligations of confidentiality, communicate to the Principal Investigator. In the event

that the Principal Investigator reasonably believes there has been any research misconduct in relation to the Clinical Trial, the Sponsor shall provide all reasonable assistance to any investigation undertaken by or on behalf of the Principal Investigator, the results of which shall, subject to any obligations of confidentiality, be communicated to the Sponsor. The Site Parties shall take appropriate measures and cause the Research Staff to take appropriate measures and corrective actions without delay as the Sponsor and/or CRO may reasonably require in order to solve all problems found and reported by the Trial Monitors and any of the aforesaid Auditors, or representatives of the Ethics Committee, Competent Authority or other regulatory authority.

- 6.7. It is expressly agreed between the Parties that
  - a. the Sponsor will not compensate the Principal Investigator nor any member of the Research Staff for the assistance or guidance of representatives of the Ethics Committee, Competent Authority or other regulatory authority and
  - b. the assistance or guidance of Trial Monitors or Sponsor's Auditors by the Principal Investigator and the Research Staff shall be deemed included in the remuneration paid pursuant to clause 13 hereinafter unless expressly agreed otherwise in writing.
- 6.8. The Principal Investigator and any member of the Research Staff will be trained by Sponsor with respect to the use of eCRFs.

## **7. INVESTIGATIONAL PRODUCTS**

- 7.1. Parties acknowledge and agree that the Institution's pharmacy, or such other pharmacy as appointed by Sponsor, the Principal Investigator and the Institution, will be responsible for certain tasks in relation to the handling of the Investigational Product. Any agreements between the pharmacy and any of the Parties will be in writing and must be in accordance with the Institution's internal policies. Any such agreements will be annexed to this Agreement as Annex 4, if applicable.
- 7.2. Subject to the foregoing, the Sponsor and/or CRO will provide the Principal Investigator and the pharmacy with all necessary information on the Investigational Product(s), quality and handling instructions thereof and sufficient quantities needed to conduct the Clinical Trial free of charge.
- 7.3. The Site Parties shall not use or permit the Research Staff or any third party to use the Investigational Product for any purpose other than the conduct of the Clinical Trial and upon termination or expiration of this Agreement all unused Investigational Product shall, at the Sponsor's option, either be returned to the Sponsor or disposed of in accordance with the Protocol or the Sponsor's written instructions.

## **8. CONFIDENTIALITY AND DATA PROTECTION**

- 8.1 *Medical Confidentiality Data protection and data controlling*
  - a. In line with the current position of the CCMO, the Institution and Sponsor are

considered joint controllers for the processing of the Personal Data and will both handle all Personal Data in accordance with the GDPR and any other to the performance of the Clinical Trial applicable laws or regulations covering the protection of Personal Data (collectively “Data Protection Law”).

b. With respect to the coded Personal Data from this Clinical Trial provided to Sponsor, CRO (if applicable) will be regarded as a processor on behalf of Sponsor. All will act in accordance with the Data Protection Law. Sponsor and CRO (if applicable) will enter into an appropriate processor agreement in accordance with Data Protection Law. Furthermore, the Institution and Sponsor will fully cooperate with each other as joint controllers and shall take the necessary measures in order to comply with the Data Protection Law, such cooperation shall duly reflect the respective roles and relationships of the joint controllers vis-à-vis the Clinical Trial Subjects as data subjects, in particular as regards the exercising of the rights of these data subjects and the joint controllers’ respective duties to provide the information referred to in Articles 13 and 14 of the GDPR. Each joint controller shall maintain a record of processing activities under its responsibility.

*In the event law and interpretation by the CCMO and/or a relevant data protection authority or a court decision should prescribe or indicate another qualification of the roles of the parties in clinical trial agreements, the Parties hereto shall consult with each other and shall adapt the qualification of their roles and change arrangements as may be deemed appropriate.*

c. Both Sponsor and Institution shall implement appropriate technical and organizational measures to meet the requirements of the GDPR.

d. If Sponsor or Institution becomes aware of a Personal Data breach, that Party discovering such breach shall promptly notify the other Party/ies. In such a case Sponsor and Institution will fully cooperate with each other to fulfil the (statutory) notification obligations timely. Institution will not be responsible for compliance by CRO (if applicable), as processor on behalf of Sponsor, of applicable Data Protection Law. A Personal Data breach refers to: a Personal Data breach as meant in article 4 paragraph 12 GDPR and further determined by articles 33 and 34 of the GDPR.

- 8.2. When based outside the EU, Sponsor will appoint a representative in the EU in order to fulfil its duties under GDPR. For processing of their Personal Data consent will be obtained from Clinical Trial Subjects. All processing of Personal Data will be in accordance with the GDPR
- 8.3. The Parties agree to adhere to the principles of medical confidentiality in relation to Clinical Trial Subjects.
- 8.4. Sponsor acknowledges that Clinical Trial Subjects – and/or their legal representatives on their behalf – may withdraw or change their initial informed consent. Principal Investigator shall promptly notify Sponsor of any withdrawal of or changes in the informed consent of a Clinical Trial Subject, which may affect the use of such Clinical Trial Subject’s clinical data under this Agreement. The Principal



Investigator will communicate with Sponsor on behalf of the Clinical Trial Subject. However, the procedure followed upon a withdrawal of a Clinical Trial Subject's consent will be according to the instructions in the Protocol and the ICF and in accordance with the (Data Protection) Law.

- 8.5. Sponsor shall refrain from tracing and/or identifying any Clinical Trial Subject, except where Sponsor is under a legal obligation to do so. In the event any Clinical Trial Subject, for any other than aforementioned reason, becomes identifiable to Sponsor, Sponsor agrees to preserve, at all times, the confidentiality of information pertaining to such Clinical Trial Subjects.

#### Confidential Information

- 8.6. The Receiving Party shall ensure that only those of its officers and employees (and those of its Affiliates and members of the Research Staff) and Agents directly concerned with the carrying out of this Agreement have access to the Confidential Information of the Disclosing Party. The Receiving Party shall take all practicable steps to ensure that such persons abide by the same obligations of confidentiality as apply to the Receiving Party under this Agreement. The Receiving Party undertakes to treat as strictly confidential and not to disclose to any third party any Confidential Information of the Disclosing Party, except where disclosure is required by a regulatory authority or by law, in which case the Receiving Party shall inform the Disclosing Party of such requirement and the information to be disclosed and Disclosing Party take reasonable steps to limit the scope of such disclosure. Notification will be within a reasonable time prior to being required to make the disclosure or if such time is not available, immediately upon becoming known of the requirement to disclose Confidential Information. The Receiving Party undertakes not to make use of any Confidential Information of the Disclosing Party, other than in accordance with this Agreement, without the prior written consent of the Disclosing Party.
- 8.7. The obligations of confidentiality and non-use set out in clause 8.6 shall not apply to information which as evidenced by written records:
- a. is or becomes part of the public domain by any other means than a wrongful act or breach of this Agreement by the Receiving Party;
  - b. was or becomes in the Receiving Parties' lawful possession prior to the disclosure without restriction on disclosure;
  - c. has been independently developed by the Receiving Party without the use of Confidential Information of the Disclosing Party;
  - d. has been obtained by the Receiving Party from a third party who is not subject to a duty of confidentiality; or
  - e. is published in accordance with clause 11 hereof.

#### Principal Investigator and Research Staff's Personal Data

- 8.8. Prior to and during the course of the Clinical Trial, Sponsor and/or CRO may request to collect Personal Data which may be subject to the GDPR relating to the Clinical

Trial from the Institution, including from its investigators, sub-investigators, other Institution staff or personnel involved in the conduct of the Study. Institution agrees to help Sponsor and/or CRO obtain any express consents, as may be necessary in accordance with GDPR, for the processing of any Personal Data collected by the Sponsor and/or CRO from its Principal Investigator, sub-investigators, other Institution staff and personnel involved in the conduct of the Clinical Trial. Such consent may authorize the transfer of Personal Data to countries other than the Institution's own country, including without limitation the United States, even though data protection may not exist or be as developed in those countries as in the Institution's own country, for the following purposes:

- a. the conduct and interpretation of the Clinical Trial;
- b. review by governmental or regulatory agencies, Sponsor, and its agents, affiliates and collaborators;
- c. satisfying legal or regulatory requirements;
- d. publication on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and other websites and databases that serve a comparable purpose;
- e. upon request of individual patients and doctors provision to individual patients and doctors who may be interested in participating in a clinical trial at Institution;
- f. storage in Sponsor's and/or CRO's databases for use in selecting sites in future clinical trials. Sponsor warrants the correct handling of this data, according to the GDPR.

## **9. INTELLECTUAL PROPERTY**

- 9.1. All Intellectual Property Rights and Know How owned by or licensed to any of the Parties prior to and after the date of this Agreement other than any Intellectual Property Rights and Know How arising from the Clinical Trial are and shall not be affected by this Agreement.
- 9.2. The Sponsor shall own the Intellectual Property Rights and Know How arising from and directly related to the Clinical Trial, the Protocol (Sponsor Intellectual Property and Know How) and the Study Drug (including but not limited to its formulation and use alone or in combination with other drugs), but excluding (1) any clinical procedure and improvements thereto that are clinical procedures of the Institution and/or Principal Investigator and (2) copyrights on work published by the Principal Investigator in accordance with clause 11 hereinafter, which copyrights shall either vest in the Institution or, if made by the Principal Investigator and other authors, in the Institution and the other co-author(s) in accordance with applicable copyright laws or as mutually agreed between the Parties, or shall vest in the publisher of such work upon the transfer of copyrights by the author(s). The Intellectual Property Rights and Know How as described in the previous sentence as Sponsor's property, is hereinafter referred to as ("Sponsor Intellectual Property and Know How").

- 9.3. The Site Parties will promptly inform the Sponsor of any invention or discovery arising from and directly related to the Clinical Trial, the Investigational Product (including but not limited to its formulation and use alone or in combination with other drugs) or the Protocol to be owned by Sponsor in accordance with clause 9.2, and Institution and/or Principal Investigator hereby assigns and transfers, and shall procure that the Research Staff shall assign and transfer, without additional consideration, all assignable rights and title in relation to such Sponsor Intellectual Property Rights and Know How (for the avoidance of any doubt: excluding (1) any clinical procedure and improvements thereto that are clinical procedures of the Institution and/or Principal Investigator and (2) copyrights on work published by the Principal Investigator in accordance with clause 11 hereinafter), and will provide reasonable assistance to the Sponsor in filing or prosecuting Sponsor Intellectual Property Rights, at the expense of the Sponsor.
- 9.4. Nothing in this clause 9 shall be construed so as to prevent or hinder the Institution or the Principal Investigator from using the Sponsor Know How generated in the Clinical Trial for its internal hospital and/or non-commercial research and/or educational activities, such research or educational activities whether or not in collaboration with other non-commercial institutions, to the extent such use does not result in the disclosure or misuse of Confidential Information or the infringement of any Sponsor Intellectual Property Rights.
- 9.5. In case a third party brings a claim or initiates proceedings against the Site Parties for the use of Intellectual Property of Sponsor in conducting the Clinical Trial in accordance with this Agreement, Sponsor shall indemnify the Site Parties against such claims or proceedings, provided the Site Parties shall have notified Sponsor promptly in writing of it and shall, upon Sponsor's request and at Sponsor's costs, have permitted Sponsor to have full care and control over the claim or proceeding using legal representation of its own choosing in accordance with clause 4.3-4.5.

## **10. PUBLICITY**

- 10.1. The Sponsor and/or CRO will not use the logo or name of the Site Parties, nor of any member of the Research Staff, in any publicity, advertising or news release without the prior written approval of the Site Parties, such approval not to be unreasonably withheld.
- 10.2. The Site Parties will not, and will ensure that the Research Staff will not, use the name or logo of the Sponsor and/or CRO or of any of its employees, nor the name of the Clinical Trial, nor the name of the Investigational Product, in any publicity, advertising or news release without the prior written approval of the Sponsor and/or CRO, such approval not to be unreasonably withheld.
- 10.3. The Site Parties will not issue and will ensure the Research Staff will not issue any information or statement to the press or public, including but not limited to advertisements for the enrolment of Clinical Trial Subjects, without, where

appropriate, the review and the delivery of a favourable opinion from the Ethics Committee and the prior written permission of the Sponsor and/or CRO.

- 10.4. Unless required by Law, Parties shall not disclose terms of this Agreement without the prior written approval of the other Party.

## **11. PUBLICATION AND AUTHORSHIP**

### *Principles*

- 11.1. The Sponsor, Institution and the Principal Investigator each acknowledge the importance of public disclosure/publication of information collected or generated as a result of or related to the Clinical Trial, under the condition that public disclosure/publication takes place under the provisions of this clause 11.
- 11.2. Upon completion of the Clinical Trial (whether prematurely or otherwise) the Principal Investigator and Sponsor may co-operate in producing a report of the Clinical Trial detailing the methodology, results and containing an analysis of the results and drawing appropriate conclusions.

### *Publication by Sponsor*

- 11.3. The Site Parties each acknowledge that the Sponsor may present at symposia, national or regional professional meetings, and publish in journals, theses or dissertations, or otherwise of their own choosing, methods and results of the Clinical Trial and in particular, but without limiting the foregoing, post a summary of Clinical Trial results in on-line clinical trials register(s) before or after publication by any other method. Sponsor shall coordinate a multi-centre publication, in which case the Principal Investigator shall be provided the opportunity to review and provide his input on each draft of such multi-center publication. The participation of the Principal Investigator or other representatives of the Institution as a named author shall be determined in accordance with generally accepted academic standards for authorship as outlined in 11.8 below. If the Principal Investigator or other representative of the Institution is a named author of the multi-centre publication, such person shall have access to the Clinical Trial data from all Clinical Trial sites as necessary to participate fully in the development of the multi-centre publication.

### *Publication by Principal Investigator*

- 11.4. The Sponsor agrees that the Principal Investigator or any of the Research Staff who fulfills the ICMJE authorship criteria and is highly involved in the Clinical Trial, shall be permitted to present at symposia, national or regional professional meetings, and to publish in journals, theses or dissertations, or otherwise of its own choosing, methods and results of the Clinical Trial, subject to this clause 11 and any publication policy described in the Protocol, provided any such policy does not obstruct publication unreasonably. Principal Investigator shall appropriately disclose Sponsor's role in the Clinical Trial in any such publication or presentation.
- 11.5. If the Clinical Trial is a multi-centre Clinical Trial, any publication based on the results obtained at the Trial Site (or a group of sites) shall not be made before the first multi-centre publication or presentation unless otherwise agreed in writing. If a

publication concerns the analyses of sub-sets of data from a multi-centre Clinical Trial the publication shall make reference to the relevant multi-centre publication(s). Notwithstanding the foregoing, if a multi-centre publication is not published within twelve (12) months after completion of the Clinical Trial and lock of the Clinical Trial database at all research sites that are part of the multi-centre Clinical Trial or any earlier termination or abandonment of the Clinical Trial, or if Sponsor informs the Principal Investigator that such multi-centre publication will not take place, or if publication has been agreed otherwise, the Principal Investigator shall have the right to publish or present the methods and results of the Clinical Trial in accordance with the provisions of this clause 11. The foregoing provided however, that any such publication will take in account the rights and interests of all investigators involved in the multi-centre Clinical Trial and authorship will be determined in accordance with clause 11.8.

- 11.6. Material for public dissemination will be submitted to the Sponsor for review at least thirty (30) days prior to submission for publication, public dissemination, or review by a publication committee. If Sponsor does not respond within this period Institution and/or the Principal Investigator is/are free to proceed with the intended publication or presentation without further delay.
- 11.7. During the thirty (30) period for review of a proposed publication referred to in clause 11.6 above, the Sponsor shall be entitled to
  - a. comment on the scientific content of the proposed publication. The Principal Investigator agrees that all reasonable comments made by the Sponsor in relation to a proposed publication or presentation will be incorporated into the publication or presentation. Reasonable comments for the purposes of this clause 11.7 shall mean such comments and suggestions that, with a view to the scientific interest or the treatment of patients, will clarify or improve the proposed publication or presentation of the results of the Clinical Trial or the conclusions drawn from such results, and such other comments that aim to avoid that such publication or presentation will misrepresent the results;
  - b. make a reasoned request to the Principal Investigator that publication be delayed for an additional period of sixty (60) days (following the 30 day period referred to in clause 11.6) in order to enable the Sponsor to take steps to protect its proprietary information and/or Intellectual Property Rights and Know How, and the Principal Investigator shall not unreasonably withhold its consent to such a request; and
  - c. may cause the Principal Investigator to remove from the projected publication any Sponsor Confidential Information received by Principal Investigator that are not constituted results of the Clinical Trial. The Institution shall not unreasonably withhold or delay its consent to the reasoned request from the Sponsor.

Authorship and Copyrights

- 11.8. Publications will be in accordance with international recognized scientific and ethical standards concerning publications and authorship, including the Uniform

Requirements for Manuscripts Submitted to Biomedical Journals, established by the International Committee of Medical Journal Editors. Copyrights concerning Publications of the Clinical Trial remain with the authors of the Publication, regardless of any other provisions regarding intellectual property rights.

## **12. TERM AND TERMINATION**

- 12.1. This Agreement commences on the Effective Date and shall continue in force until the earlier of:
- a. completion of final Clinical Trial report and the final payment under this Agreement; or
  - b. early termination in accordance with clauses 12.2, 12.3 or 12.5 of this Agreement;
- 12.2. Each Party may terminate this Agreement upon written notice to the other Parties with immediate effect in the following events:
- a. the approval by the Ethics Committee in charge of the Clinical Trial is not granted or irrevocably revoked;
  - b. it can be reasonably concluded that the Clinical Trial must be terminated in the interests of the health of the Clinical Trial Subjects;
  - c. it becomes apparent, following confirmation of the Ethics Committee or the Independent Committee, that continuation of the Clinical Trial cannot serve a scientific purpose, and this is notified to the Ethics Committee;
  - d. the Sponsor and/or the Institution become or are declared insolvent or a petition in bankruptcy has been filed against it or if one of them is dissolved;
  - e. circumstances beyond a Party's control occur that render continuation of the Clinical Trial unreasonable as outlined in Clause 16;
  - f. one of the Parties fails to comply with the obligations arising from the Agreement and, if capable of remedy, is not remedied within 30 days after receipt of written notice from the other Party specifying the non-compliance and requiring its remedy, unless failure to comply is not in reasonable proportion to the premature termination of the Clinical Trial.
- 12.3. Sponsor and/or CRO may terminate this Agreement if the Principal Investigator is no longer able (for whatever reason) to act as Principal Investigator and no mutually acceptable replacement has been found within a reasonable period, in accordance with Clause 2.3, provided that the Sponsor will not unreasonably withhold its approval of the proposed replacement of Principal Investigator.
- 12.4. In all circumstances causing the termination of this Agreement, the Sponsor shall confer with the Principal Investigator and use their best endeavours to minimise any inconvenience or harm to Clinical Trial Subjects. Parties agree that in case of termination of this Agreement, they will in good faith make arrangements concerning the continuation of the treatment of the enrolled Clinical Trial Subjects if such is in their medical best interest.

- 12.5. Up until a Clinical Trial Subject has signed the ICF, Sponsor and/or CRO may terminate this Agreement upon written notification to the Principal Investigator and the Institution, with immediate effect, in the following events:
  - a. for lack of recruitment at the Trial Site in case the Clinical Trial is conducted at one Site only; or
  - b. in case of a multicentre trial, if termination at the Trial Site does not affect performance of the Protocol.
- 12.6. Upon notice of termination of this Agreement, Site Parties will not recruit and/or enroll additional Clinical Trial subjects, and will cooperate with the Sponsor in the orderly discontinuation of the Clinical Trial, including, without limitation, discontinuing Investigational Product as soon as medically appropriate, allowing Sponsor and/or CRO access to records and facilities as required for Clinical Trial close-out procedures at mutually agreed times, and requiring Principal Investigator to complete any actions required by the role Principal Investigator.
- 12.7. In case of early termination of this Agreement, the financial provisions of 13.3 and 13.4 shall apply.
- 12.8. At close-out of the Trial Site following termination or expiration of this Agreement the Parties shall upon request immediately deliver, or destroy with confirmation thereof, if requested, to the other Party all Confidential Information, except for copies to be retained in order to comply with Institution's archiving obligations or for evidential purposes. Furthermore the Site Parties shall immediately deliver to the Sponsor any equipment provided to them pursuant to the terms and conditions of **Annex 5**.
- 12.9. Termination of this Agreement will be without prejudice to the accrued rights and liabilities of the Parties under this Agreement.

### **13. FINANCIAL PROVISIONS**

- 13.1. The Sponsor (through CRO, if applicable) will provide funding in support of the Clinical Trial, as set out in **Annex 3**. All payments shall occur on the conditions as set out in this **Annex 3**. The Parties agree that no payments are being provided for the purpose of inducing anyone to purchase or prescribe any drugs, devices or products. In addition, Site shall not (i) bill any patient, insurer, or governmental agency for any items, visits, services or expenses provided or paid for by, or on behalf of, Sponsor, or (ii) provide any money or item of value to any government official or representative to improperly influence government actions.
- 13.2. In the event that amendments to the Protocol require changes to the Clinical Trial financing arrangements, an amended financial schedule will be agreed upon and signed by the Parties which will replace the existing **Annex 3**.
- 13.3. If the Agreement is terminated for one of the reasons in clauses 12.2, 12.3 or 12.5, except for material breach by the Institution and/or the Principal Investigator under clause 12.2.f, and subject to an obligation on the Institution and the Principal Investigator to mitigate any loss, the Sponsor (through CRO, if applicable) shall pay

all fees and expenditures falling due for payment to the Principal Investigator and/or the Institution up to the date of termination in accordance with Annex 3, and also all expenditure falling due for payment after the date of termination which arises from uncancellable commitments reasonably and necessarily incurred by the Principal Investigator and/or Institution for the performance of the Clinical Trial prior to the date of termination, in accordance with Annex 3. In the case of termination for material breach by the Institution and/or the Principal Investigator under clause 12.2.f, and subject to an obligation on the Institution and the Principal Investigator to mitigate any loss, Sponsor (through CRO, if applicable) shall pay all fees and expenditures falling due for payment of properly performed services up to the date of the material breach by the Institution and/or the Principal Investigator in accordance with Annex 3. In case of termination for fraud, bribery or corruption, Sponsor will not pay for fees and expenditures directly related to such fraud, bribery or corruption.

- 13.4. In the event of early termination, if payment has been made by the Sponsor (through CRO if applicable) to the Institution or the Principal Investigator in advance for work not completed in accordance with Article 13.3, the Institution and/or the Principal Investigator shall issue a credit note and repay the remainder of the monies within 45 days of receipt of written notice from the Sponsor and/or CRO

#### **14. MISCONDUCT AND DEBARMENT**

- 14.1. The Institution and/or Principal Investigator represent and warrant that neither the Principal Investigator nor, to their best knowledge, any collaborator of the Principal Investigator involved in conducting the Clinical Trial nor any member of the Research Staff, has been debarred, excluded, disqualified or restricted in their ability to practice medicine, participate in a clinical trial, or perform services in connection with the evaluation of a pharmaceutical product under any laws, regulations or professional code of conduct including without limitation United States Code of Federal Regulations (“U.S.C.” or “CFR”) title 21 section §335a and section §312.70.
- 14.2. The Institution and/or Principal Investigator shall immediately notify Sponsor should the Principal Investigator or any collaborators or any member of the Research Staff involved in conducting the Clinical Trial, be so debarred, excluded, disqualified or restricted, or should a procedure or action be initiated against any of them that could result in their being so debarred, excluded, disqualified or restricted, at any time during the term of this Agreement and during the twelve months following the expiration or termination of the Agreement.

#### **15. DISCLOSURE OF FINANCIAL INTEREST**

- 15.1. Principal Investigator shall ensure that he/she and collaborators and any member of the Research Staff involved in this Clinical Trial at Principal Investigator’s Clinical Trial Site provide Sponsor with the appropriate financial disclosures required for



Sponsor's compliance with CFR title 21 Part 54, on Sponsor's request and on such forms as Sponsor may supply or approve.

- 15.2. During the term of this Agreement and for one (1) year following termination or completion of the Clinical Trial, Principal Investigator shall promptly notify Sponsor of any material change in the information disclosed on a previous form.
- 15.3. Parties may disclose the financial terms of this Agreement only if required by Law or transparency regulations.

## **16. FORCE MAJEURE**

No Party shall be liable to the other Parties or shall be in default of its obligations hereunder if such default is the result of war, hostilities, terrorist activity, revolution, civil commotion, strike, fire, flood, and epidemic or because of any other cause beyond the reasonable control of the Party affected. The Party affected by such circumstances shall promptly notify the other Parties in writing when such circumstances cause a delay or failure in performance and where they cease to do so. However, such non-performance or delay is excused under this provision only for the duration of the qualifying event.

## **17. GOVERNING LAW AND DISPUTE RESOLUTION**

This Agreement shall be exclusively governed by, and construed in all respects in accordance with the laws of The Netherlands without regard to its conflicts of laws rules. Any claims, controversies or disputes arising out of or in connection with this Agreement which cannot be settled amicably between the Parties, shall be subject to the exclusive jurisdiction of the competent court in the Netherlands.

## **18. HUMAN SAMPLES**

- 18.1. As part of the Protocol, Samples may be transferred to Sponsor or another organization indicated by Sponsor only if this is arranged for in the ICF.
- 18.2. Sponsor, and the other organization mentioned above in this clause 18.1, shall have the right to store, transfer and use the Samples only in accordance with the applicable Law, the Protocol and ICF (as approved by the Ethics Committee). Principal Investigator shall promptly notify Sponsor of any withdrawal of or changes in the informed consent of a Clinical Trial Subject, which may affect the use of such Clinical Trial Subject's Samples under this Agreement. In such event, Sponsor shall destroy or return the affected Samples if necessary.
- 18.3. Upon termination or expiration of the Clinical Trial, and at least at any time the Samples are no longer needed to be retained by Sponsor for any pending registration purpose related to the Study Drug in relation to the Protocol or as defined in the ICF, or as required per any Applicable Law or regulation the remainder of the Samples in Sponsor's or any of its designee's possession will be returned to the Site Parties,

retained by the Sponsor in accordance with clause 18.2 or destroyed by the Sponsor, as described in the Protocol and/or the ICF.

- 18.4. For the avoidance of any doubt, the control (in Dutch: zeggenschap) of the Samples remains at all times at the Clinical Trial Subjects they are derived from, with the Institution and/or Sponsor acting as custodian of the Samples, as described in the Protocol.

## **19. MISCELLANEOUS**

- 19.1. Sponsor and CRO shall have the right to assign this Agreement to an Affiliate or another CRO upon prior written notification to Institution. Institution shall have the right to assign this Agreement to an Affiliate upon prior written approval from Sponsor or CRO, which approval shall not be withheld unreasonably. Any approval by a Party of an assignment, transfer or encumbrance by the other Party shall not release the assigning Party of any of its obligations under this Agreement due up until such assignment. Subject to the foregoing, this Agreement shall bind and inure to the benefit of the respective Parties and their successors and assignees.
- 19.2. Institution or the Principal Investigator may not sub-contract the performance of all or any of their obligations under this Agreement without the prior written consent of the Sponsor and/or CRO, such consent not to be unreasonably withheld or delayed. Any Party who so sub-contracts shall be responsible for the acts and omissions of its sub-contractors as though they were its own.
- 19.3. Nothing shall be construed as creating a joint venture, partnership or contract of employment between the Parties.
- 19.4. Any agreement to amend, vary or modify the terms of the Agreement in any manner shall be valid only if effected in writing and signed by duly authorized representatives of each of the Parties hereto.
- 19.5. Should there be any inconsistency between the Protocol and the terms of this Agreement, or any other document incorporated therein, the Protocol shall prevail in case such inconsistency concerns clinical matters and the Agreement shall prevail the inconsistency concerns non-clinical matters. For the avoidance of doubt, Termination and Publication provisions of this Agreement shall always prevail above the Protocol.
- 19.6. Unless otherwise agreed, formal notices to the respective Parties required by this Agreement shall be given, made or served if in writing and delivered personally or sent by registered mail or by facsimile with receipts confirmed to the contact details as set out in **Annex 7**. Other communication between the Parties may also be effected by other means such as e-mail with acknowledgement of receipt, which fulfils the conditions of written form. Change of the contact details has to be notified to the other Party or Parties, but shall not require amendment of this Agreement.
- 19.7. The clauses 1 (Definitions); 3.8; 4 (Liabilities, Indemnification and Insurance); 6 (Quality Assurance and Control); 7.3 (Use of Investigational Product); 8 (Confidentiality and Data Protection); 9 (Intellectual Property); 10 (Publicity); 11

(Publication); 12.4 and 12.6-12.9 (Termination); 13.3 and 13.4 (Financial Provisions); 14.2 (Misconduct and Debarment); 15.2 (Disclosure of Financial Interest); 16 (Force Majeure); 17 (Governing Law and Dispute Resolution); 18 (Human Samples) and this clause 19.7 (Surviving Clauses) or other clauses (including but not limited to those in Annexes) contemplating performance after termination, shall survive termination or expiry of this Agreement. Notwithstanding the above, the provisions of clause 8.6 and 8.7 (Confidential Information) shall remain in force for a period of [five (5)] / [ ten (10)] years as from the date of termination or expiration of this Agreement.

- 19.8. Each person signing this Agreement represents and warrants that he or she is duly authorized and has legal capacity to execute and deliver this Agreement. Each party represents and warrants to the other that the execution and delivery of the Agreement and the performance of such party's obligations hereunder have been duly authorized and that the Agreement is a valid and legal agreement binding on such party and enforceable in accordance with its terms.

#### Annexes

Annex 1: Protocol

Annex 2: Timelines

Annex 3: Financial arrangements

Annex 4: Pharmacy agreement

Annex 5: Equipment

Annex 6: Bribery and Corruption Statement

Annex 7: Contact details

Annex 8: Power of Attorney / Delegation of Authority to CRO

[The remainder of this page is intentionally left blank; for signatures, see next page]

Signed on behalf of the **Sponsor / CRO**

Signature: .....

Name: .....

Title: .....

Date: .....

Signed on behalf of the **Institution**

Signature: .....

Name: .....

Title: .....

Date: .....

*[If Principal Investigator is NOT a contracting party, insert: The undersigned Principal Investigator hereby declares that he/she has read the above Agreement between the Parties and that he/she acknowledges the provisions of the Agreement relative to his/her role, responsibilities and duties concerning the Clinical Trial:]*

Signed by the **Principal Investigator**

Signature: .....

Name: .....

Title: .....

Date: .....

ANNEX 1

**PROTOCOL**

(by reference only)

ANNEX 2

**TIMELINES**

ANNEX 3

**FINANCIAL ARRANGEMENTS**

ANNEX 4

**PHARMACY AGREEMENT**



ANNEX 5

**EQUIPMENT**

## ANNEX 6

### **BRIBERY AND CORRUPTION**

- A. The Site Parties must at all times act with integrity and honesty and comply with the highest ethical standards.
- B. The Site Parties must not make, give, or offer any payment, gift or other benefit or advantage to any person for the purposes of:
- i. securing any improper advantage; or
  - ii. inducing the recipient or another person to do or omit to do any act in violation of their duties or responsibilities (or for the purposes of rewarding such conduct).
- C. This restriction applies at all times and in all contexts. For the avoidance of any doubt, it applies both to dealings with "public officials" and to dealings with employees and agents of commercial enterprises.
- D. Nevertheless, particular care must be exercised with dealings with public officials. The Site Parties must not make, give or offer any payment, gift or other benefit or advantage for the purposes of influencing any act or decision of a public official (or inducing such official to use their influence with another person, entity or government instrumentality or to affect or influence any act or decision of such other person, entity or government instrumentality).
- E. The term "**Public Official**" includes any person acting on behalf of any government department, agency or instrumentality or any state-owned or controlled enterprise. By way of example, this includes health care professionals employed by a state- or local municipality-run hospital or clinic, and representatives of public international organizations.
- F. The Site Parties must not make, give or offer any payment, gift or other benefit or advantage to any person whilst knowing or suspecting that all or a portion of such money, gift, benefit or advantage will be used, whether directly or indirectly, in breach of (B) or (C) above.
- G. The Site Parties shall make and keep books, records, and accounts, which, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the Site Parties, in accordance with Dutch law.
- H. The Site Parties shall devise and maintain a system of internal accounting controls in accordance with Dutch law, sufficient to provide reasonable assurances that –
- i. transactions are executed in accordance with management's general or specific authorization;
  - ii. transactions are recorded as necessary
    - (I) to permit preparation of financial statements in conformity with generally accepted accounting principles or any other criteria applicable to such statements, and

- (II) to maintain accountability for assets;
- iii. access to assets is permitted only in accordance with management's general or specific authorization; and
- iv. the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences.

ANNEX 7

**CONTACT DETAILS**

Recipients of Notice in accordance with clause 19.6 of this Agreement:

**If to Sponsor / CRO**

*For scientific matters:*

Name:

Address:

Tel.:

Mail:

*For legal matters:*

Name:

Address:

Tel.:

Mail:

*For financial matters:*

Name:

Address:

Tel.:

Mail:

**If to Institution / Principal Investigator**

*For scientific matters:*

Name:

Address:

Tel.:

Mail:

*For legal matters:*

Name:

Address:

Tel.:

Mail:

*For financial matters:*

Name:

Address:

Tel.:

Mail:

ANNEX 8

**POWER OF ATTORNEY / DELEGATION OF AUTHORITY TO CRO**