**CLINICAL TRIAL AGREEMENT FOR THE DRUG(S) “\_\_\_\_\_\_\_\_\_\_”**

**PROT. \_\_\_\_\_\_**

**ID FPG \_\_\_\_\_\_**

**BETWEEN**

**Fondazione Policlinico Universitario Agostino Gemelli IRCCS**(hereinafter for brevity “**Policlinico**”), headquartered in Rome, Italy, Largo Francesco Vito 1 – 00168, Value Added Tax and Fiscal Code No. 13109681000, represented by General Manager Mr. Daniele Piacentini, resident for his position at Policlinico

**AND**

**Clinical Trial Center S.p.A.** (hereinafter for brevity **“CTC”**), headquartered in Rome, Largo A. Gemelli 8 – 00168, Value Added Tax and Fiscal Code No. 14361101000, in the person of the Sole Director Massimo Dalfelli, resident for his position at CTC

(a) (*in case of direct signature of the Agreement with the Sponsor*):

\_\_\_\_\_\_\_\_\_\_\_\_\_(*indicate name of Sponsor*), headquartered in \_\_\_\_\_\_\_, Tax Code and VAT no. \_\_\_\_\_\_\_, in the person of legal representative \_\_\_\_\_\_\_ (hereinafter the “**Sponsor**”), as \_\_\_\_\_\_\_\_\_

(b) (*in case of signature of the Agreement with:*

i. *the representative of the Sponsor headquartered outside the European Union, under art. 74 of the Regulation*.

ii. *a company belonging to the same group as the Sponsor, duly empowered to sign the Agreement;*

iii. *a Contract Research Organization, or CRO, duly empowered also to sign the Contract*):

\_\_\_\_\_\_\_\_\_ (indicate the company or CRO), headquartered in \_\_\_\_\_\_\_, Tax Code and VAT no. \_\_\_\_\_\_\_, in the person of its legal representative, \_\_\_\_\_\_\_\_\_\_\_ in her/his capacity as \_\_\_\_\_\_\_, which, by mandate conferred on\_\_\_\_\_\_\_\_[[1]](#footnote-2), acts as the representative of the Sponsor of the Trial,\_\_\_\_\_\_\_, headquartered in \_\_\_\_\_\_\_, Tax Code and VAT no. \_\_\_\_\_\_\_, in the person of its legal representative \_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_,[[2]](#footnote-3)(from now on referred to as “**Sponsor**”), to which, therefore, the situations, rights and obligations related to the role will continue to be referable, even if formally assumed by or otherwise referred for operational purposes to the aforesaid company, which therefore acts in the capacity mentioned above

From now on, both will be referred to individually/collectively as "**Party/Parties**."

Whereas:

1. It is in the interest of the Sponsor to carry out, under Regulation (EU) no. 536/2014 (from now on the "**Regulation**"), the clinical trial entitled: "\_\_\_\_\_\_\_" (from now on the "**Trial**"), having as its object the Protocol version no. \_\_\_\_ of \_\_\_\_\_ and its subsequent duly approved amendments (from now on the "**Protocol**"), EudraCT (or EU-CT in case of studies submitted through CTIS) code no. \_\_\_\_\_\_ at the Policlinico, under the responsibility of Dr./Prof. \_\_\_\_\_\_, in his/her capacity as Scientific Responsible for the experimentation which is the subject of this Agreement (from now on "**Principal Investigator**"), at \_\_\_\_\_\_ (indicate the Operating Unit) (from now on "**Trial Centre**”);
2. The Sponsor has identified Dr. \_\_\_\_\_ as the scientific contact for the part of its competence. The Sponsor may change the scientific and technical contact for the part falling within its competence by notifying the Policlinico in writing;
3. the Trial Centre and CTC have the technical and scientific know-how to carry out the Trial and is a suitable facility for the Trial to be conducted by the applicable regulations;
4. the Principal Investigator and their direct healthcare staff qualified according to the Protocol to intervene with discretionary powers in the execution of the Protocol (from now on "**Co-investigators**”), as well as all other subjects playing any part in the Trial under the supervision of the Principal Investigator are qualified to conduct the Trial by the applicable regulations, are familiar with the Protocol and the standards of good clinical practice and possess the necessary regulatory and legal requirements including compliance with the current rules regarding the conflict of interest;
5. except as otherwise subsequently agreed in writing by the Parties, the Policlinico shall only conduct the Trial in its facilities.
6. *(i) (in the event the loan of the equipment is* ***not*** *required):*

The Policlinico are equipped with suitable equipment necessary to carry out the Trial as indicated in the Protocol.

*or*

(ii) (*in the event there is a loan for the use of equipment*):

The Policlinico receives the equipment and/or goods listed in Art. 5 of this Agreement necessary for the performance of the Trial;

1. The Trial has been duly authorised under Chapter II of the Regulation[[3]](#footnote-4), following the AIFA national authorisation decision uploaded on the EU portal referred to in Article 80 of the Regulation on \_\_\_\_\_\_\_, which includes the opinion issued by the Ethics Committee \_\_\_\_\_\_\_ or, in the absence of such a decision, by lapse of time in accordance with Art. 8 of the Regulation;
2. In accordance with Art. 76 of the Regulation and the applicable national provisions, Sponsor took out an insurance policy as detailed in Article 8 of this Agreement.
3. (*where the CRO is not empowered to sign the contract*): The Sponsor declares that it has appointed the Contract Research Organization \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, headquartered \_\_\_\_\_, Tax Code and VAT no. \_\_\_\_\_\_\_ (from now on referred to as "**CRO**"), regularly operating in accordance with D.M. 15 November 2011 and registered with the National Observatory on Clinical Trials of Drugs (OsSC), for the performance of activities related to the Trial, conferring on it, through the relevant agreement dated \_\_\_\_\_\_, the necessary powers and the related mandate with representation. The Policlinico is aware of this appointment.
4. CTC is a joint-stock Company controlled by Policlinico whose corporate purpose is the performance - in favour of Companies in the pharmaceutical sector, healthcare facilities, universities, research entities and other subjects - of services and management activities for clinical trials as a Site Management Organisation (SMO);
5. CTC and Policlinico commit themselves directly in respect of the Sponsor to carry out the Trial, in the terms and modalities established by the single clinical trial Agreement;
6. during the negotiation of this Agreement, the Parties relied on the scheme approved by the National Coordination Center of Territorial Ethics Committees pursuant to Article 2, Paragraph 6, of the Law no.3 of 11 January 2018 respecting the homogeneity of the administrative, economic, insurance aspects referred to therein;

In consideration of the foregoing, it is hereby agreed as follows

**Art. 1 – Entirety of Agreement**

* 1. The recitals, the Protocol – even if not physically attached – and all the Annexes, including the budget (Annex A) and the data protection glossary (Annex B), form an integral and substantial part of this Agreement.

**Art. 2 – Subject matter of the Agreement**

2.1. The Sponsor hereby entrusts the Policlinico with the execution of the Trial under the terms of this Agreement, in accordance with the Protocol (and any subsequent amendments thereof) and with the amendments to this Agreement/budget resulting from such amendments and formalized through the necessary deeds of amendment, duly signed.

The Parties agree that in the context of the Trial the activities relating to administrative and support management such as Site Management Organisation shall be carried out under the direct responsibility of CTC and shall be, by way of example only, the following:

- administrative activities in support of clinical trials;

- invoicing management.

2.2. The Trial must be conducted in strict compliance with the Protocol, in the version in force as accepted by the Principal Investigator and approved by the Ethics Committee and the Competent Authority in conformity with the laws applicable to clinical drug trials and the principles of ethics and medical practice followed by the healthcare staff involved in the Trial in any capacity.

2.3. The Trial shall also be conducted by the principles of the Convention on Human Rights and Biomedicine, the updated version of the Helsinki Declaration, the current rules of good clinical practice, and the applicable laws on transparency, anti-corruption and the current data protection regulations.

2.4. By signing this Agreement, the Parties declare that they know and accept the contents of the above rules and regulations. Each Party declares, to the best of its knowledge, that the activities provided in this Agreement do not involve a breach of its commitments to third parties.

2.5. The Sponsor and the Principal Investigator, having an obligation to protect patients' safety, where required in the circumstances, may take urgent, appropriate measures to protect patients' safety, such as temporarily suspending the study (interrupting of treatment for patients already enrolled or interruption of the enrolment of new patients), in the manner provided for by Article 38 of Regulation (EU) 536/2014, subject to the Sponsor's obligation to immediately inform the Ethics Committee, the Competent Authority and the Testing Centers, as well as the participants in the study, of the new events, the measures taken and the programme of measures to be taken, by promptly completing the procedures provided for by current legislation. The Sponsor, having received communication from the investigator of a severe adverse event, shall promptly communicate to the electronic database all suspected severe and unexpected adverse reactions within the terms of paragraph 2 of the art. 42 of Regulation (EU) No. 536/2014, also by reporting under paragraph 3.

2.6. *(a) (In the event of non-competitive inclusion of patients)*:

The Policlinico expects to include, provisionally, \_\_\_\_ patients by \_\_\_\_ (*insert estimated date*). The Parties acknowledge that any increase in the number of patients included at the Policlinico's Trial Centre must be agreed in writing in advance between the Parties and sent to the Ethics Committee and Competent Authority as a substantial amendment. Any increase in the number of patients made by the above conditions does not require the stipulation of an addendum to this Agreement if the financial conditions per patient, as agreed herein, apply to all the additional patients.

*or*

2.6. (*b) (In the event of a multi-centre Trial with competitive inclusion*):

Since the Trial provides for the competitive inclusion (competitive recruitment) of patients, the Policlinico is expected to include approximately …..with the limit of the maximum …..number of patients eligible for trial at the global level and the time limits provided by the Sponsor.

Any possible modification of the number of patients to be recruited at the Trial Site must be noticed between Sponsor/CRO and Principal Investigator and notified to CTC and to the Research Office of Università Cattolica del Sacro Cuore to the email addresses detailed at art. 12 “*Amendments*” of the Contract and no amendments to the Contract will be necessary.

The planned period of inclusion is liable to change in light of developments at the international level. Upon reaching the total number of patients expected for the entire Trial, the inclusion of additional patients will be automatically closed, regardless of the number of patients included with the Policlinico. The parties acknowledge the informed consent given to patients before inclusion provides such a hypothesis. The Sponsor will send the appropriate and timely notice of the closure of the competitive inclusion. In the case of patients who have already given their consent to participate in the Trial, the inclusion in the Trial cannot take place without the prior permission of the Sponsor.

2.7. The Policlinico and the Sponsor will keep the documentation concerning the Trial (permanent "Trial Master File") for the period and according to the specifications indicated by current legislation that is twenty-five (25) years. The Sponsor is obligated to inform the Centre of the expiry date of the mandatory conservation period at the request of the Sponsor. After the expiry of this period, the Parties may agree on the conditions for a further storage period.

2.8. The Policlinico and the Sponsor, within their respective sphere of responsibility, shall also use document digitalisation (or dematerialisation) forms, where applicable. Regardless of whether or not the archived Trial documentation contains personal data (of a unique nature or otherwise), according to the definitions in Regulation (EU) no. 679/2016 (from now on "**GDPR**"), the Policlinico, the CTC and the Sponsor shall take all the physical and technical measures referred to in Article 32 of GDPR. It shall carry out any security checks as required by the applicable regulation to protect the data, information and documents (both printed and digital). The archiving system shall guarantee the integrity of the data, information and printed/digital documents and their future legibility throughout the mandatory conservation period. To fulfil such obligation, the Sponsor and the Policlinico may rely on external service providers to manage the archiving obligation.

2.9. The Sponsor, the Policlinico, the CTC and the Principal Investigator shall comply with the directions, indications, instructions and recommendations from the Ethics Committee and the Competent Authority.

**Art. 3 – Principal Investigator and Co-investigators**

3.1. The Principal Investigator will be assisted in the execution of the Trial by direct collaborators, qualified according to the Protocol to intervene with discretionary powers in the execution of it (from now on "**Co-investigators**"), as well as by staff, sanitary and not sanitary, charged by the Policlinico. Co-investigators and other staff will operate under the responsibility of the Principal Investigator for aspects related to the Trial. The above subjects must be qualified for the conduct of the Trial and have received adequate training, under current legislation, from the Sponsor in advance; each of them must have expressed her/his willingness to participate in the Trial. In particular, the Principal Investigator shall be responsible for ensuring that the activities of the Co-investigators and other personnel participating in the Trial are carried out regularly, with particular reference to debarment or suspension cases that might occur for any of them during the Trial.

3.2. The Parties acknowledge that the Principal Investigator, is bound by all the responsibilities and obligations imposed on their role by the applicable regulations on clinical trials regarding medicines.

3.3. The present contractual relationship is between the Sponsor, the Policlinico and CTC. The Sponsor is extraneous to the relations between the Policlinico, the Principal Investigator, the Co-Investigators and all other personnel participating in the Trial, and the Policlinico to those between the Sponsor, the Company/CRO or any other representative and/or employee of the Sponsor), thus being relieved of any claim they might make about the Trial.

3.4. In respect of the Trial covered by this Agreement, the Parties acknowledge that they have complied with the provisions of Article 7 of the Regulation as well as Article 6, Paragraph 4 of Legislative Decree no. 52 of 14 May 2019, as amended by Article 11-bis of Law no. 77 of 17 July 2020, converting Legislative Decree no. 34 of 19 May 2020 (“**Decreto Rilancio**”).

3.5. If the relationship between the Principal Investigator and the Policlinico ends for any reason, the Policlinico will inform the Sponsor in writing, indicating the name of a replacement and reporting it in the European electronic database. The name of a replacement must be approved by the Sponsor and the competent Ethics Committee. The Policlinico guarantees that the new Principal Investigator is qualified to continue the Trial, accept the terms and conditions of this Agreement, and agree to respect the Protocol when executing the Trial. Pending approval of the substantial amendment for the change of Principal Investigator, the Investigator indicated by the Policlinico shall carry out the necessary continuity in the Trial activities. If the Sponsor does not intend to accept the name of the replacement proposed by the Policlinico, or if the Policlinico does not suggest a substitute, the Sponsor may terminate this Agreement by the provisions of Article 7.

The Sponsor is required to notify the addresses smo@clinicaltrialcenter.it, amministrazione@clinicaltrialcenter.it, of the submission and approval of the substantial amendment relating to the change of the Principal Investigator, enclosing adequate documentation.

3.6. Before starting the Trial, the Principal Investigator shall obtain the informed consent of the patient or his/her legal representative, by the current laws on clinical trials, as well as the consent for the processing of personal data by the current Italian and EU rules on data protection, as specified in Article 11 below.

3.7. The Principal Investigator is obliged to register and document, in detail, all adverse events and serious adverse events and report them to the Sponsor within the terms established by current legislation. Furthermore, the Principal Investigator has to provide any other clinical information indicated in the Protocol (*e.g.,* pregnancy) that is directly or indirectly related to the execution of the Trial, by the provisions of the Protocol, the rules of Good Clinical Practice and the laws applicable to pharmacovigilance and clinical drugs trials.

3.8. The Policlinico guarantees the correct performance of the Trial by the Principal Investigator and the personnel under his responsibility by the highest standards of diligence. In particular:

3.8.1. the Principal Investigator shall submit all properly completed Case Report Forms (CRFs), duly compiled and pseudonymized, by the terms and conditions of the Protocol for the Trial and with the applicable regulations, in printed or digital form and any case on time as per GCP, by the date indicated in the Trial Protocol;

3.8.2. the Principal Investigator shall also resolve any queries raised by the Sponsor by the date indicated in the Trial Protocol;

3.8.3. to verify the correspondence between the data recorded on the CRF and the data contained in the original clinical records, the Policlinico and the Principal Investigator shall allow direct access to the source data during the monitoring visits and any audits by the Sponsor and inspections by the Competent Authorities including remote methods, provided that the laws on confidentiality and patient privacy are respected;

3.8.4. The Policlinico and the Principal Investigator, having been informed sufficiently in advance, shall allow the correct execution of the monitoring, auditing, and inspections at the Trial Centre by the Sponsor and by the Competent Authority, such activities to guarantee the proper execution of the Trial.

3.9. *(Where appropriate, taking into account the current regulations on data protection)* having received the favorable opinion of the competent facility, the IT product (from now on the "**Product**") intended for \_\_\_\_\_\_\_\_\_ will be supplied for free. Concerning the same, it is understood that:

3.9.1. for the use of the network infrastructure and information systems, the Sponsor shall agree on the procedure for the installation and delivery of the Product after the competent local centre has issued a positive report on feasibility and technical compatibility with the standards in place at the Policlinico and on medium-term sustainability with the existing services;

3.9.2. in the same way, the Sponsor undertakes to de-install the Product on completion of the Trial, at no cost to the Policlinico;

3.9.3. the Sponsor warrants that the Policlinico’s use of the Products indicated above, in the context of the Trial, shall not create any obligation for the Policlinico to purchase or subscribe to the Sponsor’s supplies or services, that it does not infringe any third party licenses or rights and that it does not bind the Policlinico to use the Product beyond the date provided for in the Trial;

3.9.4. the Sponsor further warrants that the use of the Product in the context of the Trial shall not entail, for the Policlinico, any costs relating to the servicing, modification or upgrading of any of the hardware/software components in its IT network and, therefore it shall not lead to any breach by the Policlinico of its contractual obligations towards its direct suppliers;

3.9.5. in any event, the Sponsor shall indemnify the Policlinico concerning any direct or indirect losses deriving from the use of the Product by the instructions of the manufacturer/supplier;

3.10. the Policlinico shall promptly inform the Sponsor if a regulatory authority informs the Policlinico of an inspection/audit about the Trial and, unless expressly refused by the Competent Authority, the Policlinico will authorise the Sponsor to take part while sending the Sponsor all the written communications received for the inspection/audit. These activities must not in any way affect the performance of the ordinary Policlinico activity of the Policlinico;

3.11. The Policlinico and the Sponsor guarantee that the biological samples (blood, urine, saliva, etc.) of the patients involved in the Trial referred to in this Agreement will be used exclusively for the Trial covered by this Agreement or for any substudies included in the protocol and subject to informed consent by the patient, according to the provisions of current legislation. Any storage and subsequent use are subject to the acquisition of specific informed consent by the patient (or the parent/legal guardian), the favourable opinion of the Ethics Committee, and must be carried out within the limits and with the guarantees provided by the current rules and by the guidelines referred to in art. 1, paragraph 1, letter b, of D. Lgs. 14 May 2019 n. 52.

**Art. 4 – Trial Drugs – Materials and Services**

4.1. The Sponsor shall provide the Policlinico, free of charge and directly, for the duration of the Trial, with the necessary and sufficient quantities of the pharmaceutical products relating to the Trial \_\_\_\_\_\_\_ and shall provide free of charge the other drugs provided for in the Protocol, by Ministerial Decree of 21 December 2007, Annex 1, Paragraph 3, Table I, including the drugs to be used in association or combination, whenever the object of the study relates to such an association or combination (the “**Trial Drugs**"). The Sponsor shall also provide at its own expense the supply of auxiliary medicines and the background therapy, that is, the therapeutic standard for the pathology subject of the Trial, if included, according to the Trial Protocol, in the comparison among the different therapeutic strategies being tested. The quantities of Trial Drugs, auxiliary medicines, and background therapy charged to the Sponsor must be adequate for the number of cases treated. The receipt and tracking of drugs must occur upon the batches' registration. Background therapies not included in the comparison therapeutic strategies remain the responsibility of the Policlinico. Sponsor also undertakes to provide, at its own expense, any other materials necessary for the execution of the Trial (the "**Materials**") as well as laboratory, diagnostic or monitoring tests relating to the use of the Trial Drugs or primary and secondary objectives of the Trial (from now on "**Services**”).

4.2. In accordance with point 34 of the Helsinki Declaration and good practices on continuity of treatment, the Sponsor undertakes, where applicable, to make the medicinal product which is the subject of the Trial available after the end of the Trial, beyond the follow-up period, for patients who have obtained clinical benefit from it, assessed on the basis of the judgement and under the responsibility of the Principal Investigator (regardless of the applicability or not of D.M. 7 September 2017 "Regulation of the therapeutic use of medicinal product undergoing clinical trials"). In patients with clinical benefit, the drug supply will continue until it is made available through ordinary channels of dispensation to ensure therapeutic continuity. Any reasons that determine an unavailability of the Sponsor to ensure therapeutic continuity must be specified in writing by the Sponsor to the Policlinico and be evaluated by the Ethics Committee. Information on whether or not the Sponsor is willing to ensure post-trial access to the drug referred to above, with the related reasons, should be made clear to participants in the trial in the informed consent documents that, in the event of reasons arising, they should be updated.

4.3. The Sponsor shall send the Trial Drugs to the Pharmacy of Policlinico, which will record them, store them appropriately, and deliver them to the Principal Investigator by the provisions of the Protocol and the current regulations.

4.4. An adequate transport note shall accompany the Trial Drugs addressed to the Pharmacy, describing the type of drug, the quantity, batch, storage requirements, expiry date and references to the Trial (Protocol code, Principal Investigator and Trial Centre).

4.5. The Policlinico and the Principal Investigator shall use the Trial Drugs and Materials supplied by the Sponsor exclusively in the context and conduct of the Trial. The Policlinico shall not transfer or assign to a third party the Trial Drug and/or Materials/Services supplied by the Sponsor under the terms of this Agreement.

4.6. All the expired or otherwise unusable Trial Drugs or those that have not been used at the conclusion of the Trial will be collected by the Sponsor (or its representative) and disposed of at the Sponsor's expense.

**Art. 5 – Loan (where applicable)**

5.1. The Sponsor grants on gratuitous loan to the Policlinico, which accepts under and for articles 1803 et seq. of the Italian Civil Code, the Instruments described below, together with the relevant material for use (from now cumulativelythe *“***Instrument***”) \_\_\_\_\_\_\_\_ (description of the asset and corresponding value in Euro*). The ownership of the Instrument, as by law, is not transferred to the Policlinico. The effects of this loan shall commence from the date of delivery of the Instruments and shall cease at the end of the Trial when the Instruments shall be returned to the Sponsor at no cost to the Policlinico. The Parties also agree that any additional Instruments deemed necessary for the conduct of the study during the Trial, should the characteristics and conditions thereof be met, shall be granted on gratuitous loan for use by the provisions of this Agreement. The Policlinico and the Sponsor shall proceed with a specific loan agreement or with an addendum/amendment to the Agreement if the Instruments are provided after the conclusion of the present Agreement.

5.2. It is required that the Instruments supplied have such characteristics and in particular, are configured to comply with the following requirements:

* physical encryption of hard disks or, where this is not possible, provision of the device for
* remote locking and logical encryption of files;
* installation of antivirus with an active licence;
* access to the Tools via password authentication;
* operating system with active support for updates/patches.

The Instruments in question must be provided with a declaration of conformity with European standards and directives. The Instrument(s) in question will be subjected to acceptance testing, if the instrument has a direct action on the patient or other machinery present in the Policlinico by the technicians appointed by the Policlinico, in the presence of a delegate of the Sponsor, subject to prior agreements, for verification of correct installation and functionality and compliance with current regulations. At the time of delivery of the materials supplied on loan by the Sponsor to the Policlinico, adequate documentation shall be drawn up to certify the delivery.

5.3. The Sponsor shall be responsible for the transport and installation of the Instruments and undertakes to provide, at its own expense, the technical assistance necessary for their operation and any consumables for their use, at no cost to the Policlinico.

5.4. In accordance with the provisions of the technical manual of the Instrument, the Sponsor will carry out, at its own expense, in cooperation with the Principal Investigator, all the technical interventions necessary for the proper functioning of the Equipment, such as quality controls, calibrations and periodic safety checks. In the event of malfunction or failure of the Equipment, promptly communicated by the Principal Investigator, the Sponsor will proceed, directly or through specialised personnel, with corrective maintenance or repair or replacement with a similar Equipment.

5.5. The Sponsor will bear all costs and responsibilities for any damage that may result to persons or property about the use of the equipment in question according to the indications of the Protocol and the instructions of the manufacturer, if due to a defect thereof unless such damage is caused by willful misconduct and/or gross negligence of the Policlinico. For this purpose, it will be affixed on the Instrument/s the appropriate plate or other suitable indication of the property.

5.6. The Instruments shall be used by the Policlinico's staff and/or patients and for the sole and exclusive purposes of this Agreement's Trial object, by the Protocol's provisions. The Policlinico undertakes to keep and store the Instruments appropriately and with the necessary care, not to use it/them for any other use than the one envisaged above, not to transfer even temporarily the use of the Instruments to third parties, be it free of charge or for a consideration, and to return the Instruments to the Sponsor in the state in which it/they were delivered to the Policlinico, except for normal deterioration due to the effect of use.

5.7. The Sponsor reserves the right to demand the immediate return of the Instruments if the Instruments are used improperly or otherwise in a manner inconsistent with the provisions of this Agreement.

5.8. in the event of theft or loss of the Instruments, the Policlinico shall promptly, at the knowledge of the event, file a formal complaint with the competent public authority and notify the Sponsor within the same time limit. In all other cases of damage or destruction, the Policlinico shall notify the Sponsor promptly after knowledge of the event. Any fraudulent or unauthorised use must be reported immediately by the Principal Investigator to the Sponsor. In the event of irreparable damage or theft of the Instruments, the Sponsor shall replace the Instruments, at no cost to the Policlinico, unless the event is the result of willful misconduct intent on the part of the Policlinico.

5.9. It is understood that for Instruments that will be directly handled or managed by the patients/parents/legal guardians (*e.g.,* electronic diaries), the Sponsor acknowledges that the Policlinico is relieved from any responsibility deriving from tampering, damage or theft of the same Instruments attributable to the patients/parents/legal guardians. In the event of failure and/or loss by the subjects participating in the study, the Sponsor will replace the equipment at its own expense; the Policlinico will be responsible for the delivery of the equipment to the recipient, including the registration and delivery of the Sponsor's instructions, as well as the collection at the time of the subject's exit, for whatever reason, from the study; the Policlinico will also be responsible for promptly informing the Sponsor of any failure to return the equipment by the subjects participating in the study.

5.10. The authorisation to grant loan-free use of the Instrument was given by the Policlinico following and according to its internal procedures.

**Art. 6 – Remuneration**

6.1. The remuneration agreed, previously evaluated by the Policlinico through CTC for each eligible assessable patient and who has completed the trial treatment according to the Protocol and for whom the related CRF/eCRF has been duly redacted, including all the costs incurred by the Policlinico and CTC in execution of the Trial and the costs to cover all the related activities, is detailed in the Study Budget approved by the CTC as per Annex A.

6.2. The Sponsor will pay to Policlinico through CTC the amount due under the terms of this article based on a valid statement of account/supporting document agreed between the Parties.

The above amount will be paid at the intervals indicated in the Budget (Annex A), based on the number of patients enrolled during the period, the treatments carried out according to the Protocol and in the presence of the duly completed CRF/ECRF duly compiled and validated by the Sponsor based on the activities carried out.

Payment will be made by the obligee only following receipt of a regular invoice by the CTC. This invoice needs to be required from the Sponsor/CRO according to the instructions about frequency and methods indicated in Annex A. No amount will have to be paid in the absence of a regular invoice.

6.3. The laboratory/ instrumental tests required by the Protocol approved by the Ethics Committee and indicated in Annex A will not burden the Policlinico in any way, even if carried out outside the Policlinico. All laboratory/instrumental tests not included in the agreed fee per eligible patient, as well as any additional services/activities requested by the Sponsor and provided for by the Protocol approved by the Ethics Committee, will be reimbursed to the Policlinico and invoiced to the Sponsor in addition to the agreed fee per eligible patient.

6.4. The Policlinico will receive no remuneration for patients who cannot be assessed due to failure to observe the Protocol, violation of the rules of Good Clinical Practice or failure to comply with the laws applicable to clinical drug trials. The Policlinico will have no right to receive any remuneration for any patient enrolled after notification of interruption and/or conclusion of the Trial by the Sponsor, or any number beyond the maximum number of patients stipulated under this Agreement, if not agreed with the Sponsor.

6.5. The Sponsor shall also reimburse the Policlinico through CTC for all the additional costs of medical/diagnostic activities, including hospital admissions, which are not provided for in the Protocol or amendments to the Protocol and which are not already covered by the above payments if such activities are essential for the proper clinical treatment of a patient undergoing the Trial. The reimbursement will only be paid on condition that such activities and costs have been adequately communicated, with justification, and have been documented in writing to the Sponsor and approved in writing by the Sponsor, provided that the patient's data is transmitted in anonymised form.

6.6. If, during the Trial, it is necessary to increase the financial support to Policlinico, the Sponsor may supplement this Agreement by an addendum/amendment authorising the appropriate increase to the attached Budget.

6.7. The amounts will be paid to the CTC within the terms set out in Annex A (Table 5).

The Sponsor will have the right to dispute the amounts within a maximum term of 60 days from the date of issue of such invoice and in any case within the fiscal year to which the invoice refers. The CTC and the Policlinico will not take into consideration any complaints received after the aforementioned deadlines.

6.8. The payments made for the Policlinico's services (i) represent the fair market value for those services, as they reflect the tariff scale applied by the Policlinico, (ii) were negotiated under normal market conditions, and (iii) were not agreed based on the volume or value of prescriptions or about those prescriptions or other financial activities between the Parties. Neither the Policlinico nor the Principal Investigator shall request any compensation or reimbursement from any other party in return for the activities performed or costs incurred by including the patients in the Trial, which the Sponsor is obligated to pay for.

6.9. Within the limits and by the procedures provided for in the Protocol and approved by the Ethics Committee, the Sponsor shall make available to the patients participating in the Trial the reimbursement of out of pockets expenses, provided they are actually incurred and documented, related to participation in the Trial at the Policlinico, through procedures previously approved by the Ethics Committee.

The reimbursement can be made through the administration of the Policlinico, which will follow its procedures in this matter. In this case, for coverage by the Sponsor, each patient will submit the list of expenses to the Policlinico; this list will be duly codified by the Policlinico, which, in consideration of the duration of the study, agrees on the deadlines for submitting to the Sponsor the list of total costs incurred by patients in the reference period. The Sponsor/CRO will be able to check the amounts requested by comparing them with the services provided to patients, validating them also during the monitoring visits if requested by the Trial Center, and will make the relevant payments to the Policlinico through CTC. Upon the collection of invoice, it will, therefore, be the responsibility of the Policlinico to provide reimbursement to each patient involved, according to the amounts of respective relevance.

Policlinico/CTC will not reimburse to patient any of the sums requested but after it has verified the collection of the invoice and Policlinico/CTC will not be liable towards patient for the default of payment from the Sponsor/CRO.

The provisions of the previous paragraphs will also apply, where provided for in the Protocol, to compensatory allowances for expenses and loss of earnings directly related to participation in the Trial, recognised under Art. 31, 32 and 33 of the Regulation.

The settlement of the amounts of out of pockets expenses must be made by bank transfer, upon presentation of the invoice to CTC, with an invoicing period independent of that provided in Annex A, which is no later than thirty (30) days date of the invoice. A 20% increase shall be applied to the amounts to be invoiced as reimbursement of management costs.

6.10 All costs related to items not specified in Annex A or provided in the Protocol will not be reimbursed, except those provided in article 6.5 and for the reimbursements of out of pockets expenses described in article 6.9.

To all amounts invoiced, including those invoiced for the purpose of reimbursement of out-of-pocket expenses, will be added VAT and/or the applicable tax charges, in accordance with current legislation and the VAT will be all charged to the Promoter/CRO.

The Parties agree that any bank charges due for foreign transfers must be fully charged to the payer and, in no case, may be deducted from the amount credited to the payee.

**Art. 7 - Duration, termination and cancellation**

7.1 This Agreement shall take effect from the date of the last signature (“**Effective Date**"). It shall remain in force until the conclusion of the Trial at the Policlinico, as provided for in the study Protocol for …..… (*insert date*), subject to any amendments agreed by the Parties. Without affecting the preceding provision, this Agreement shall remain in full force and effect following the issue of formal authorisation by the Competent Authority.

7.2 The Policlinico and CTC may terminate this Agreement with a 30-day prior written notice sent to the Sponsor by registered post or certified email in the following cases:

* insolvency of the Sponsor, proposal of composition arrangements, also extrajudicially, with the creditors of the Sponsor or the commencement of enforcement action against the Sponsor. If the situation indicated above relates to the CRO, the Sponsor is obligated to take over from the CRO and to continue the activities unless the intervention of another CRO – approved by the Policlinico – is obtained to replace the insolvent CRO;
* the sale of all or part of the assets of the Sponsor to the creditors or the Agreement of a moratorium with creditors.

The notice will take effect when the Sponsor receives the above communication.

7.3. The Sponsor, in accordance with Art. 1373(2) of the Italian Civil Code, may terminate this Agreement at any time by sending a 30-day prior written notice by registered post or certified email. The notice will take effect when the Policlinico receives such communication.

Termination by the Sponsor will not affect the obligations assumed and costs paid by the Policlinico and CTC on the date of notification of termination. In particular, the Sponsor will pay the Policlinico through CTC all the documented, non-revocable expenses, contained in Annex A, that it has incurred to ensure the correct, efficient execution of the Trial (*where applicable*, including the costs incurred by the Policlinico and CTC towards the patients/participants) and all the payments accruing up until that time.

In case of early termination, the Sponsor may, as the original owner, receive all the complete and partial data and results obtained by the Policlinico during the Trial and thereafter, if deriving from or related to the Trial.

7.4. If the Trial is terminated, the Sponsor will pay the Policlinico through CTC the expenses and considerations contained in Annex A that have accrued and are documented until that time, as required by the applicable regulation.

7.5. It is also agreed that the early termination of this Agreement shall not give either Party any right to claim from the other Party any compensation or requests for payment other than those already agreed.

7.6. This Agreement shall cease to have effect automatically under Article 1454 of the Civil Code if either Party has not fulfilled one of its obligations as provided for herein within 30 days from a written notice to perform sent by the other Party.

Articles 1218 et seq. of the Italian Civil Code shall apply.

7.7. If this Agreement is terminated for reasons not due to non-compliance by the Policlinico, the Policlinico shall have the right to reimbursement of the expenses incurred about the Trial before receipt of the notice of termination, and to payment for the services rendered by the Protocol and this Agreement, proportionately to the activities completed up to the date of termination. The Policlinico through CTC shall repay the Sponsor any amounts already paid for activities that still need to be completed.

7.8. In all cases of interruption or termination of this Agreement, full precautions will be taken to protect the patients already involved, by the Protocol approved by the Ethics Committee, guaranteeing, within the limits and the modality set in Article 4.2, continuity of treatment

**Art. 8 – Insurance coverage**

8.1. According to current legislation, The Sponsor is required to guarantee compensation for damages suffered by patients and attributable to participation in the clinical Trial, in accordance with the Protocol, commensurate with the nature and extent of the consequent risks.

8.2. Without prejudice to the provisions of Article 76 of the Regulation and of Law 8 March 2017, n. 24 and the respective implementing measures, the insurance cover provided by the Sponsor guarantees concerning the civil liability of the Sponsor, where the Trial is conducted, CTC the Principal Investigator, and the other Investigators involved at the Centre of the Policlinico.

8.3. The Sponsor confirms, by signing this Agreement, that it has taken out a third-party liability insurance policy (no. \_\_\_\_\_, with the insurer \_\_\_\_\_) to cover the risk of injury to patients from taking part in the Trial, by M.D. of 14 July 2009. The Ethics Committee considered that the insurance policy complies with the provisions of the law and adequately protects the patients taking part in the Trial.

8.4. By signing this Agreement, the Sponsor confirms that it is liable for any consequences resulting from any present or future deficiencies in the insurance cover mentioned above, integrating them where necessary by the provisions of Article 8.1.

8.5. In particular, if the Sponsor intends to withdraw from the Agreement, the Sponsor warrants that the insurer shall, in all cases, guarantee the coverage of patients already included in the clinical trial also during the continuation of the Trial, by Article 2 par. 3 of M.D. of 14/07/09.

**Art. 9 – Final report, ownership and use of results**

9.1. The Sponsor will publish the study results even if the results are negative.

9.2 The Sponsor is liable for preparing the final clinical report and for sending a summary of the results of the Trial to the Principal Investigator and Ethics Committee by the applicable legal deadline. Regardless of the outcome of a clinical trial, within one year (and six months in the case of pediatric studies) from its conclusion, the Sponsor sends a summary of the results of the Trial to the EU database by the procedures set out in Article 37.4 of the Regulation (UE) n. 536/2014.

9.3. All the data, results, information, materials, discoveries and inventions deriving from the execution of the Trial in pursuit of its objectives is the exclusive property of the Sponsor, without prejudice to the right of the Investigators, if the conditions are met, to be recognised as authors.

In the event of a procedure activated by the Sponsor for the filing of a patent application concerning inventions obtained during the Trial, the Policlinico, and for it the Principal Investigator, undertake to provide the Sponsor, at the expense of the same, the support, also documentary, helpful for this purpose.

9.4. The Policlinico may use the data and the results of the Trial, for which processing it is an autonomous data controller according to the applicable regulation for its own institutional, scientific and research purposes only. Such use must not affect the secrecy and the patent protection of the related intellectual property rights due to the Sponsor.

The Parties mutually acknowledge they will at all times remain the owners of industrial and intellectual property rights relating to their background knowledge and to their own knowledge developed or obtained in the course of the Trial, but regardless and irrespectively from the way it is conducted (sideground knowledge).

9.5. The provisions of this article will remain valid and binding even after termination or cancellation of this Agreement.

**Art. 10 – Secrecy of technical and commercial information and dissemination of data**

10.1. By signing this Agreement, each Party undertakes to treat as private for the entire duration of this Agreement, all the technical and commercial information provided by the other Party and/or developed during the Trial and in pursuit of its objectives, which may be classified as "Commercial Secrets" within the meaning of articles 98 and 99 of the Industrial Property Code (legislative decree 30/2005 as amended by legislative decree 63/2018 enacting Directive EU 2016/943), and shall take all the contractual, technological or physical measures necessary to protect such information, also about their employees, contractors, subcontractors, successors or assigns.

Each Party also represents and warrants as follows:

(i) Its Commercial Secrets have been acquired, used and disclosed legally. There are not – as far as is known to it – any legal actions, disputes, claims for compensation or indemnity, whether judicial or extrajudicial, brought by any third party claiming ownership of such secrets.

(ii) It shall, therefore, indemnify the other Party regarding any legal actions, complaints, claims for compensation or indemnity, whether judicial or extrajudicial, brought by any third party claiming ownership of such secrets.

10.2. The Parties are obligated to adequately and accurately disclose and publish the results of the Trial and to communicate them adequately to the patients taking part and to their representatives. Under the terms of the applicable regulations, the Sponsor is required to promptly publish the results of the Trial, even if harmful, obtained at the end of the Trial as soon as they become available from all the participating Centres and any case no later than the deadlines for this purpose established by the applicable provisions of the European Union.

10.3. The Principal Investigator has the right to disseminate and publish, without limitation, the results of the Trial obtained from the Policlinico, by the current laws on the confidentiality of sensitive data, data protection and intellectual property, and by the terms and conditions of this Agreement.

To ensure that the data processing is correct and accurate, and the results of the Trial obtained at the Policlinico, given their presentation or publication, at least 60 days before them, the Principal Investigator will send the Sponsor the text of the document Intended to be presented or published. Should issues arise about the scientific integrity of the document and/or problems regarding regulatory aspects, patents or the protection of intellectual property, the Parties and the Principal Investigator will proceed over the next 60 days to review the document. The Principal Investigator shall agree to take into account the Sponsor's suggestions in the publication or presentation, only if necessary to protect the confidentiality of information, personal data and to protect intellectual property, provided that the amendments do not conflict with the reliability of the data, or the rights, safety and well-being of the patients.

10.4. The Sponsor acknowledges that it has no right to request the deletion of information contained in the document except where such requests and amendments are necessary for data confidentiality, data protection and intellectual property protection.

10.5. The Sponsor may, to present a patent application and, if necessary, ask the Principal Investigator to delay the publication or presentation of the document by a further 90 days. The Trial being multicentre, the Principal Investigator may not publish the data or the results of his or her own Centre until all data and results of the Trial have been published in whole or for at least 12 months from the conclusion of the Trial, it’s interruption or early termination. Suppose a publication containing the results of a multicentre trial, published by the Sponsor or the third party designated by the Sponsor, is completed after 12 months from the end of the multicentre Trial. In that case, the Investigator may publish the results obtained at the Policlinico based on the article's contents.

**Art. 11 – Data protection**

11.1. In executing the contractual activities the Parties shall treat all the personal data they receive for any reason about the clinical Trial by the objectives of the preceding articles and in conformity with the provisions of Regulation (EU) 2016/679 of the European Parliament and Council of 27 April 2016 (GDPR), and with the related requirements of law and orders of national administrations, including any subsequent amendments (collectively the "**Data Protection Laws**”) as well as any regulations of the Entities.

11.2. The terms used in this article, in this Agreement, in the informed consent documents and any other documents used for the Trial shall be construed and utilised by the meanings given in Annex B.

11.3. The Policlinico and Sponsor are independent data controllers for Article 4, paragraph 7 of the GDPR. Each Parties will arrange at its own expense, as part of its organisational structure, for the appointment of Data Processors and assignment of functions and tasks to designated subjects, who operate under their authority by the GDPR and current legislation.

11.4. For the Trial, personal data relating to the following categories of data subjects will be processed: persons taking part in the trial and persons operating on the Parties' behalf. Such data subjects will be appropriately informed of the processing of their data. For the Trial, the following types of personal data will be processed: the data referred to in Article 4 paragraph 1 of the GDPR; data classified as "sensitive" – and in particular, data relating to health, sexual life and genetic data – referred to in Article 9 GDPR. Such data shall be processed by the principles of legality, fairness, transparency, adequacy, relevance and necessity as contained in Article 5 paragraph 1 of the GDPR.

11.5. The Sponsor may send the data to other affiliates of the Sponsor's group and third parties operating on its behalf, including those abroad, in countries outside of the EU, only in compliance with the conditions set out in Articles 44 and ss. of the GDPR. In this case, the Sponsor will guarantee adequate personal data protection also through the use of the *Standard Contractual Clauses* approved by the European Commission. Where the Sponsor is established in a State that does not fall within the scope of European Union law and that the European Commission has decided that this country does not guarantee an adequate level of protection under Articles 44 and 45 of the EU GDPR 2016/679, the Sponsor and the Policlinico must complete and sign the document *Standard Contractual Clauses* *(the latter is not attached to this Agreement)*.

11.6. The Parties warrant that the persons authorised by them to process personal data for the Trial will comply with the principles in force to safeguard data protection and the right to confidentiality and that any persons having access to the personal data will be obligated to process the data by the instructions given, by this article, by the data controller.

11.7. The Policlinico has identified the Principal Investigator as a person authorised for the data processing for Article 29 GDPR and as a designated party for Article 2 quaternities of the Italian Law Decree 196/2003.

11.8 The Principal Investigator shall provide clear, complete information to all patients before the Trial starts (also before the preliminary phases or screening) to all patients, regarding the nature, purpose, results, consequences, risks and methods of the processing of personal data; in particular, all patients must be informed that the national and international authorities and the Ethics Committee may, in connection with the monitoring, checking and control of the Trial, have access to the related documentation and also to the original healthcare records of the patient, and that the Monitors and Auditors may also access the data in connection with their respective duties.

11.9. After the patient has been duly informed, the Principal Investigator shall obtain the consent form for participation in the Trial and consent to processing personal data. The Policlinico is responsible for keeping the consent forms.

11.10 Without prejudice to the obligations deriving from articles 33 and 34 of EU Regulation 2016/679, if a Personal Data Breach occurs in relation to any Subjects’ Personal Data processed, the Parties undertake to inform each other about the Personal Data Breach, in order to guarantee the correct continuation of the Trial.

**Art. 12 – Amendments**

12.1 This Agreement and its annexes/addenda, together with the Protocol, form an integral part of this Agreement and constitute the entire Agreement between the Parties.

12.2 This Agreement may only be amended/supplemented with the written consent of both Parties. Any amendments will be contained in a supplement to this Agreement and will take effect from the date of signature unless agreed otherwise by the Parties.

**If to Policlinico/CTC:**

For all administrative and management communications:

Clinical Trial Center S.p.A., c/o Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Largo Agostino Gemelli, n. 8 - 00168 Rome, Italy

Telephone: +39 06 3015.7200 (Secretariat); +39 06 3015.7261 (Administration Section)

E-mail: [amministrazione@clinicaltrialcenter.it](mailto:amministrazione@clinicaltrialcenter.it)

**If to Policlinico/CTC:**

For all communications regarding this Agreement:

Clinical Trial Center S.p.A., c/o Ufficio Ricerca

Università Cattolica del Sacro Cuore

Largo Francesco Vito n. 1 - 00168 Rome, Italy

Telephone: +39 06 3015.6309

E-mail: [contratti@clinicaltrialcenter.it](mailto:contratti@clinicaltrialcenter.it)

**If to Sponsor/CRO:**

Address:

Email:

**Art. 13 – Anti-corruption provisions and for the prevention of crimes**

13.1. The Policlinico and the Sponsor will comply with the anticorruption laws applicable in Italy.

13.2 The Sponsor confirms that it has taken supervisory and control measures to ensure compliance with and implementation of, the provisions of Italian Legislative Decree no. 231 of 8 June 2001 and, where applicable and not conflicting with laws in Italy, the principles of the US Foreign Corrupt Practices Act and its amendments. The Policlinico and its clinical and administrative facilities undertake to collaborate in good faith according to the provisions of Italian law mentioned above. They will cooperate with the Sponsor's personnel and management to facilitate full, accurate implementation of the resulting obligations and the implementation of the operational procedures developed by the Sponsor for that purpose.

13.3

The Sponsor declares that it has adopted its code of ethics, which can be viewed at the webpage (…) *(insert a link to the website*).

13.4. The Policlinico and the Sponsor shall immediately inform each other of any violation of this article by the other Party, which they become aware of, and will provide complete information and documents for all the appropriate investigations.

13.5 the Sponsor may disclose the terms of this Agreement or any amendments to this Agreement for any legitimate purpose within the limits of the data protection laws.

13.6 If the relationship of trust between the parties is affected by violating any provisions of this article, it will constitute a severe breach of this Agreement under Article 1456 of the Italian Civil Code.

**Art. 14 – Transfer of rights, assignment of contract and subcontracting**

14.1 This Agreement is fiduciary and, therefore, the Parties may not assign or transfer the same to third parties, in whole or in part, without the prior written consent of the other Party.

In any event, the assignee must explicitly accept all terms and conditions of this Agreement. Any rights transfer in the absence of these conditions will be considered null and void and will never occur.

14.2 In the event of a change in the name of the Policlinico, the amendment to this Agreement will not be necessary. However, the Policlinico will be required to notify the Sponsor of such a change of name without delay.

**Art. 15 – Subscriptions and taxes**

***OPTION A: DIGITAL SIGNATURE in PADES mode (NO DOCUSIGN; digital signature is preferable for speed)***

15.1. This Agreement is signed digitally in accordance to art. 24 of Legislative Decree 82/2005, pursuant to the provisions of art. 15, paragraph 2bis of Law no. 241/1990, as added by art. 6, Legislative Decree 10/18/2012, no. 179, converted into Law 12/17/2012 no. 22.. All taxes and duties relating to or resulting from the stipulation of this Agreement, including the revenue stamp on the digital original as referred to in Article 2 of the table in Annex A – tariff part I of Presidential Decree 642/1972, and the registration tax, must be paid by the applicable regulations.

***OPTION B: AUTOGRAPH SIGNATURE (by sending original paper material: option with longer lead times)***

15.2 This Agreement is drawn up in legal paper pursuant to Art. 2 of Tariff (Part I) of the stamp duty referred to in Italian Presidential Decree No. 642 of 26 October 1972 and subsequent modifications and integrations (s.m.i.), and shall be subject to registration only in the event of use pursuant to Art. 5 second paragraph of the Consolidated Text (“Testo Unico”) of the provisions concerning the registration tax, approved with Italian Presidential Decree No. 131 of 26 April 1986.

15.3 Stamp duty costs are borne by the Sponsor/CRO, while registration fees are borne by the requesting Party.

15.4 This Agreement is drawn up in No. 3 original copies (of which, No. 2 stamped original copies).

**Art. 16 – Governing law and forum**

16.1. This Agreement is governed by the laws of Italy.

16.2. For any disputes that may arise about the interpretation, application and execution of this Agreement, without prejudice to the Parties' commitment to make a prior attempt at out-of-court settlement, the Court of the Rome registered office shall have exclusive jurisdiction. 16.3 The Parties mutually acknowledge that every single clause of this Agreement has been duly drafted, understood and accepted by each Party following fair and reciprocal negotiations and that, therefore, the provisions of Articles 1341 and 1342 of the Italian Civil Code shall not apply.

**Art. 17 – Language**

17.1. If there is any discrepancy between the English language version and the Italian version of this Agreement, the Italian version shall prevail.

**\*\*\* \*\*\* \*\*\***

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, \_\_/\_\_/\_\_\_\_\_\_ (place and date)

**For the Sponsor**

Legal Representative or her/his delegate (or CRO)

Mr./Mrs. \_\_\_\_\_\_\_\_\_\_\_\_

Signature \_\_\_\_\_\_\_\_\_\_\_\_\_

Rome, \_\_/\_\_/\_\_\_\_\_\_

**For Fondazione Policlinico Universitario Agostino Gemelli IRCSS**

General Manager

Mr. Daniele Piacentini

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature

Rome, \_\_/\_\_/\_\_\_\_\_\_

**For Clinical Trial Center S.p.A.**

The Sole Director

Mr. Massimo Dalfelli

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature

**ANNEX A – BUDGET**

**Prot. N. …………**

**ID FPG N. ………………….**

The maximum total fee for the entire Trial, applied and calculated on the complete enrollment of N. .... patients, beyond the fixed costs, is intended to include the institutional Overhead equal to 25%, when foreseen, and is detailed below:

**Table 1.  TRIAL COMPENSATION**

|  |  |
| --- | --- |
| **Estimated total compensation for all Patients to be enrolled (total arm 1,2 pcs etc.)** |  |
| *Total number of Trial arms (if there are more arms, please specify what required in the order indicated - see examples of arms 1 and 2 below)* | *N. XX* |
| Estimated compensation for each Patient to be enrolled in arm 1 | € XXXX,00 |
| Estimated total number of Patients to be enrolled in arm 1 | *N. XX* |
| *Total estimated compensation for all Patients to be enrolled in arm 1* | € XXXX,00 |
| Estimated compensation for each Patient to be enrolled in arm 2 | € XXXX,00 |
| Estimated total number of Patients to be enrolled in arm 2 | € XXXX,00 |
| *Total estimated compensation for all Patients to be enrolled in arm 2* | € XXXX,00 |
| *(In case of additional arms to arms 1 and 2, please add other lines)* |  |
|  |  |
| **Total compensation for fixed costs Trial costs (NON REFUNDABLE) to be paid also in case of non activation of the Site** | **€ XXXX,00** |
| Administrative Start Up *(Administrative fee for managing and starting the Trial contract)* | € XXXX,00 |
| Centre/PI Clinical Site Set Up *(Fee for activities performed by the Centre/PI for Trial activation at the experimental Site)* | € XXXX,00 |
| Pharmacy fee *(Fee for activities carried out by the Pharmacy and preparatory to the study activation at the Site, as well as for the reception, the storage and restitution of the drug* | € XXXX,00 |
| Other possible fees | € XXXX,00 |
|  |  |
| **MAXIMUM TOTAL COMPENSATION** | **€ XXXX,00** |

Maximum total compensation for the Clinical Trial shall cover:

* clinical activities under the Trial Protocol;
* tasks performed by the Principal Investigator;
* activities carried out by CTC that were necessary for initiation and support of the Trial and invoicing the amounts accrued for the execution of the Trial;
* the fixed costs as indicated above;
* coverage of all general costs, including the expected institutional Overheads, equal to 25%;

Total compensation for the Trial shall not cover:

* billable clinical activities and/or health procedures as extra costs patient visit that shall be subject of specific reporting and billing indicated at Table 3;
* any other possible study costs foreseen in Table 4

**Table 2. PATIENT VISITS COSTS**

*PLEASE ATTACH EXCEL FILE FOR DETAILS OF THE AGREED UPON BUDGET (clean version)*

**Table 3. COSTS OF CLINICAL ACTIVITIES AND/OR HEALTH PROCEDURES** **BILLABLE AS PATIENT VISIT EXTRA COSTS**

*Enter all budget items accountable per patient and not included in visits calculation*

**Table 4. OTHER TRIAL COSTS**

|  |  |
| --- | --- |
| Administration fee for management and starting of each contractual amendment | € XXXX,00 |
| Trial Master File archiving in accordance with the current Law (for 25 years) | € XXXX,00 |
| Daily administrative fee for possible audits and inspections at the Centre | € XXXX,00 |

**TERMS AND MANNERS OF INVOCING AND PAYMENT**

All compensations accrued for the Trial shall be billed entirely by CTC as follows:

* upon signature of the Agreement, the non-refundable fees (Pharmacy Fee; Administrative Startup Fee; Site Set up Clinical Centre/PI, any other agreed fees); these fees shall be paid compulsorily aside from the subsequent activation of the Center and in no case will be refunded;
* On a (*please specify if quarterly solar/half-yearly solar/annual*) basis, what accrued in the reference period, both for the patient visit costs as well as for the billable clinical activities and/ or healthcare procedures extra costs patient ‘s visit;
* At the conclusion of the Study: archiving of the Trial Master File according to current Laws (25 years) and any other agreed fees (see Table 4);
* upon the occurrence: the administrative fee for management of each contract amendment, the daily administrative fee for any audits and inspections at the Center, any other agreed one-time costs;
* the balance shall be calculated on the basis of evaluable subjects at the end of the Trial.
* at the end of the study all the unbilled and/or possible adjustments costs will be calculated.

In case of interruption and/or suspension and/or early closing and/or withdrawal from the Study, beyond the fixed costs (Table 1), all the fees accrued as specified in Tables 2, 3 and 4 will be due, that shall be paid on a pro-rata basis according to the progress of visits.

For the purpose of issuing the invoice, the Sponsor/CRO or its delegate will have to send to the CTC, according to the foreseen timeline (see Table 5), the details of the activities eligible for the payment, both if they are patient’s visits, extra clinical activities, extra costs visits or any other potential fees agreed upon, in Excel format. The payment of the accrued fees will take place only after issuing the invoice by the CTC, taking care to indicate in the reason of the bank transfer mandatorily the invoice number to which the payment refers (see Table 6).

Billing requests must be sent only by e-mail to the address amministrazione@clinicaltrialcenter.it, with reference in the subject line of the e-mail request to the following data:

1. ID FPG;
2. Protocol Number, indicated in this Agreement;
3. PI;
4. Reference period and/or type of costs to be billed;

In case of Sponsor and/or CRO needs to insert in the invoice its identifying data (N. of purchase order, payer agent, name of the Sponsor, name of the CRO, VAT references , site number, etc.), they must have to provide written communication to the CTC no later than 10 working days starting from the notification of the final signature of the current agreement, to the address amministrazione@clinicaltrialcenter.it.

Once 10 working days elapsed and without such communication, the CTC will issue the relevant invoice without the abovementioned reference.

In case of invoicing requests for an amount lower than 500,00€, it is required to merge this amount to the next invoicing request, consistently with the foreseen invoicing timeline (Table 5), or, in case the amount is overall still lower than 500,00€, to send again the invoice request at the end of the relevant year.

Any claim and/or adjustment of the amounts invoiced or already paid for by the Sponsor and/or the CRO, must be made within the maximum period of 60 days starting from the date of the issuance of the disputed invoice, and, in any case, within the fiscal year of reference. The CTC and Policlinico will not take into consideration any claim received beyond the above specified terms.

Compensations shall be subject to VAT and/or all the foreseen fiscal costs under current legislation.

The Parties agree that any applicable tax and bank charges in accordance with current Laws shall be charged entirely to the purchaser and under no circumstances can be deducted from the amount that is credited to the beneficiary.

**Table 5. DATA FOR ADMINISTRATIVE MANAGEMENT AND BILLING**

The amounts shall be paid by the Promoter/CRO following receipt of an invoice issued by CTC.

The invoicing will be based on the information given in the following Table.

The invoices will be registered only to the subject indicated in the line “billing Party”. All the invoice holder information (company name, address, VAT number/TAX ID, etc.) will be filed in the specific registers established in the Nation of registered office.

|  |  |
| --- | --- |
| Trial Protocol No. |  |
| FPG ID No. | *XXX* |
| PI | *Name and surname* |
| Date of Agreement expiry/  end of Trial | *Month and year* |
| Invoice Holder | *Enter only the data relating to the company name pf the invoice holder (NO c/o)* |
| Billing Party Address | *Enter the invoice holder's registered office address* |
| Postal/Zip Code |  |
| City (Province) |  |
| Country |  |
| VAT No. | *VAT No. to be entered must coincide with Invoice Holder’s VAT No.* |
| Tax ID/Fiscal Code | *Fiscal Code to be entered must coincide with Invoice Holder’s Fiscal Code* |
| Office Unique Code\* | *Code necessary for electronic invoicing purposes in Italy* |
| Additional information to be included on the invoice | *Specify any information you wish to appear on the invoice (PO number, paying agent, Sponsor name, VAT references)* |
| Billing Frequency | *Please specify if quarterly solar/ half-yearly solar/annual solar* |
| Invoice Payment Days | *30 – end of the month – invoice date* |
| PEC Address for invoice sending |  |
| Email Address for invoice sending | *Address of the institutional e-mail reserved to the invoices receipt* |
| Contact Person for billing | *Name and Surname* |
| Contact Person Email |  |
| Contact Person Tel.No. |  |
| Authorised Third Paying Agent | *Please specify the name of Third Paying Agent if not coinciding with Invoice holder’s name The CTC*  *The CTC wil be entitled to enter in the free text field of the invoice, any reference to the Third Paying Agent. Notwithstanding this, the invoice holder will always and solely remain the subject indicated in the field “Invoice holder”.* |

*\*In compliance with the 2018 Budget Law (paragraph 909) requiring mandatory e-nvoicing for sales of goods and services among private individuals, Policlinico, through CTC, shall issue invoices in XML (Extensible Markup Language) format. Invoices must be sent through the Interchange System (SDI).*

In case of using payment systems by means of web-based electronical systems, the Trial center declares itself as "non-adopter", therefore any required operation must be carried out by the SPONSOR/CRO (invoice upload, data entry, etc.). CTC will send the issued invoices only by email and, where required, through the Exchange System (SDI).

**Table 6. DETAILS OF BENEFICIARY**

The amounts shall be paid by the SPONSOR/CRO by Bank Transfer upon receipt of a invoice from the CTC, according to the instructions foreseen by the article 6.7, as specified below, taking care to indicate the invoice reference number in the reason for the payment:

|  |  |
| --- | --- |
| Business Name | Clinical Trial Center Spa |
| Registered Office Address | Largo Gemelli, 8 |
| Operational Headquarters Address | Largo Gemelli, 8 |
| Postal/Zip Code | 00168 |
| City | ROMA |
| Country | ITALIA |
| VAT No. | 14361101000 |
| Tax/Fiscal Code No. | 14361101000 |
| Bank Name | BANCO BPM |
| Bank Address | Piazza Mercanti, 5 |
| CIN Code | D |
| ABI Code | 05034 |
| CAB Code | 01633 |
| Current Account (C/A) No. | 000000006278 |
| Office Unique Code | MZO2A0U |
| IBAN Code | IT92D0503401633000000006278 |
| SWIFT Code | BAPPIT21M85 |
| Reason for Bank ransfer | *Strictly specify the invoice number to which collection refers* |
| Reference Email | [amministrazione@clinicaltrialcenter.it](mailto:amministrazione@clinicaltrialcenter.it) |

All administrative and management communications related to the Trial under this Agreement must be addressed to: [amministrazione@clinicaltrialcenter.it](mailto:amministrazione@clinicaltrialcenter.it)

**ANNEX B - GLOSSARY RELATING TO THE PROTECTION OF PERSONAL DATA (terminology referring to the GDPR - UE Reg. n. 2016/679 - ad to the Italian implementing rules)**

* **Personal Data** - any information relating to an identified or identifiable, natural person (the "Data Subject"). An identifiable natural person is a person who can be identified directly or indirectly using an identifier such as a name, an identification number, location data, an online identifier or one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of the individual;
* **Processing** - any operation or set of operations which is performed on personal data or sets of personal data, whether or not by automated means, such as collection, recording, organisation, structuring, storage, adaptation or alteration, retrieval, consultation, use, disclosure by transmission, dissemination or otherwise making available, alignment or combination, restriction, erasure or destruction;
* **Pseudonymisation** - the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organisational measures to ensure that the personal data are not attributed to an identified or identifiable individual;
* **Data Subject -** the natural person to whom the personal data refer (art. four n.1 GDPR);
* **Data Controller** - the natural or legal person, public authority, agency or any other entity which, alone or jointly with others, determines the purposes and means of the processing of personal data; where the purposes and means of such processing are determined by Union or Member State law, the controller or the specific criteria for its nomination may be provided for by Union or Member State law (art. four n. 7 GDPR) ;
* **Data Processor** - a natural or legal person, public authority, agency or other body which processes personal data on behalf of the data controller;
* **Other Subjects processing personal data -** persons authorised to process personal data under the direct authority of the Data Controller or the Data Processor (art. 28, n. 3, letter b, 29 and 32, n. 4 GDPR), including therefore the natural persons to whom the Data Controller or the Data Processor has assigned specific tasks and functions related to the processing, who operate under the Data Controller's authority and within the organisational structure, under art. two quaternities " of Legislative Decree 196/2003 as amended by Legislative Decree 101/2018;
* **Consent of the Data Subject** - any freely given, specific, informed and unambiguous indication of the data subject's wishes by which he or she, by a statement or by an explicit affirmative action, signifies Agreement to the processing of personal data relating to him or her;
* **Personal Data Breach** - any breach of security leading to the accidental or unlawful destruction, loss, alteration, unauthorised disclosure, or access to, personal data transmitted, stored or otherwise processed;
* **Medical Data** - personal data about the physical or mental health of an individual, including the provision of medical services, which may reveal information about their state of health;
* **Genetic data** - personal data relating to the hereditary genetic or acquired characteristics of an individual which provides unequivocal information about the physiology or health of that individual and which results, in particular, from the testing of a biological sample from the individual in question;
* **Biological sample** - any sample of biological material from which the characteristic genetic data of an individual can be extracted;
* **Sponsor** - the person, company, institution or body that is responsible for starting, managing and/or funding a clinical trial;
* **CRO** – the contractual research organisation to which the sponsor may entrust all or part of its competencies relating to clinical trials;
* **Monitor** – the party responsible for monitoring the Trial, appointed by the Sponsor;
* **Auditor** – the party responsible for auditing the conduct of the Trial as an integral part of quality assurance, appointed by the Sponsor

1. A copy of the mandate (and the relative modifications) necessary for verifying the representative's powers will be inserted in the Trial Master File referred to in art. 2.7. [↑](#footnote-ref-2)
2. For subjects belonging to countries outside the European Union, the tax references (Fiscal Code, VAT number) should be replaced with appropriate homologous references of the country of origin. [↑](#footnote-ref-3)
3. for *trials* proposed on a transitional basis under Directive 2001/20 and the Italian legislation still in force): the Trial has been authorised by the AIFA according to D. L. n. 158 of 13 September 2012, converted with L. n. 189 of 8 November 2012, within the time limits provided for by that legislation; the application for authorisation to carry out the Trial and on \_\_\_\_\_, the competent Ethics Committee has delivered a favourable opinion on the Trial [↑](#footnote-ref-4)