

**CLINICAL TRIAL AGREEMENT FOR THE CONDUCT OF AN INDEPENDENT CLINICAL TRIAL ON MEDICINAL PRODUCTS “\_\_\_\_\_”**

**BETWEEN**

\_\_\_\_\_ (*indicate name of Healthcare Facility*) (from now on the "**Institution**"), headquartered in \_\_\_\_\_, Tax Code and VAT no. \_\_\_\_\_, acting through its legal representative \_\_\_\_\_, in her/his capacity as \_\_\_\_\_ (*indicate whether Director General, CEO, Extraordinary Commissioner, etc.*) with appropriate signing powers

**AND**

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

\_\_\_\_\_ (*indicate name of Institution, Scientific Society, Foundation, Association*), headquartered in \_\_\_\_\_, Tax Code and VAT no. \_\_\_\_\_, in the person of legal representative \_\_\_\_\_ (hereinafter the "**Sponsor**")

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

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

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

\_\_\_\_\_ (*indicate the entity 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 \_\_\_\_\_<sup>1</sup>, acts as the representative of the Sponsor of the Trial, \_\_\_\_\_, headquartered in \_\_\_\_\_, Tax Code and VAT no. \_\_\_\_\_, in the person of its legal representative \_\_\_\_\_,<sup>2</sup>(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:

- A.** 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 code no. \_\_\_\_\_ at the Institution, under the responsibility of Dr./Prof. \_\_\_\_\_, in his capacity as Scientific Responsible for the experimentation which is the subject of this Agreement (from now on "**Principal Investigator**"), at \_\_\_\_\_ (*indicate the Operating Unit, Department, etc.*) (from now on "**Trial Centre**");
- B.** the Trial presents the requirements of D.M. 30 November 2021, art. 1, paragraph 2, letter .... ;
- C.** 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 par falling within its competence by notifying the Institution in writing;
- D.** the Trial Centre has 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;

<sup>1</sup> A copy of the mandate (and related modifications) necessary for verifying the representative's powers will be inserted in the Trial Master File referred to in art. 2.7.

<sup>2</sup> 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.

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- E.** 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;
- F.** except as otherwise subsequently agreed in writing by the Parties, the Institution shall only conduct the Trial in its facilities.
- G.** (i) (in the event the loan of the equipment is **not** required):  
The Institution is equipped with suitable equipment for the Trial as indicated in the Protocol.
- or
- (ii) (in the event there is a loan for the use of equipment):  
The Institution receives the equipment and/or goods listed in Art. 5 of this Agreement necessary for the performance of the Trial.
- H.** The Trial has been duly authorised under Chapter II of the Regulation<sup>3</sup>, 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 Territorial Committee \_\_\_\_\_ or, in the absence of such a decision, by lapse of time in accordance with Art. 8 of the Regulation;
- I.** (if the case occurs) during the negotiation of this Agreement, the Parties relied on the scheme approved by the National Coordination Center of Territorial Ethics Committees under Article 2, Paragraph 6, of the Law no.3 of 11 January 2018 and, respecting the homogeneity of the administrative, economic, insurance aspects referred to therein, have decided to integrate and/or modify the relative provisions, to regulate the specificities and peculiarities of the Trial, based on the following reasons specified below for each addition or modification<sup>4</sup>:  
(specify) art. \_\_\_\_\_ reason:.....

In consideration of the preceding, it is at this moment agreed as follows

## **Art. 1 – Entirety of Agreement**

1.1. 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 Institution 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 formalised through the necessary deeds of amendment, duly signed.

or

(where the CRO is not empowered to sign the contract): The Sponsor declares that it has appointed the Contract Research Organization \_\_\_\_\_ (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 Medicinals (OsSC), for the performance of activities related to the Trial, conferring on it, through the relevant

<sup>3</sup> for "exhaustion" 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

<sup>4</sup> do not constitute additions or amendments to be indicated in the foreword the indications inserted in specially prepared spaces (filling in the blanks), nor the exercise of the option between two formulations of the same article, with possible elimination of the case that does not recur (e.g. Art. 2.6a or b), or the adoption of shorter or longer time limits, provided that they are within the limits provided for by the applicable legislation (e.g. Art. 2.7 and 10.1).

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agreement dated \_\_\_\_\_, the necessary powers and the related mandate with representation. The Institution is aware of this appointment.

2.2. The Trial is to 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. To the greatest extent necessary and the best of its knowledge, each Party declares 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 (and the latter will inform 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 Institution expects to include, provisionally, \_\_\_\_ patients by \_\_\_\_ (*insert estimated date*). The Parties acknowledge that any increase in the number of patients included at the Institution's investigation centre must be agreed in writing in advance between the Parties and sent to the Ethics Committee and Competent Authority as an appropriate amendment. Any increase in the caseload 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 Agency 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.

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 Institution. 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 Institution 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 (or for a more extended period, if required by other applicable rules or by an agreement between Institution and Sponsor). After the expiry of this period, the Parties may agree on the conditions for a further storage period.

2.8. The Institution and the Sponsor, within their respective sphere of responsibility, shall also use document digitalisation (or dematerialisation) forms, where applicable under the legislation. 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 Institution and the Sponsor shall take all the physical and technical measures referred to in Article 32 of said 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 Institution may rely on external service providers to manage the archiving obligation.

2.9. The Sponsor, the Institution 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 from the Institution. 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 on the Protocol, 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 radiation or suspension hypotheses that intervened for some of them during the Trial.

3.2. The Parties acknowledge that the Principal Investigator, as the general contact person of the Institution in relation to the Sponsor, is responsible for compliance with all the obligations imposed on the Institution by current legislation on clinical trials of medicinal products.

3.3. The present contractual relationship is between the Sponsor and the Institution. Each Party is not related to the other's relations with its representatives and/or employees (in particular, the Sponsor to those between the Institution, the Principal Investigator, the Co-investigators and all other personnel participating in the Trial, and the Institution 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 Institution ends for any reason, the Institution 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 Institution 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 Institution 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 Institution, or if the Institution does not suggest a substitute, the Sponsor may terminate this Agreement by the provisions of Article 7.

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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 entity 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 pseudonymised, 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 Institution 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 Institution 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 favourable 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 Institution 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 Institution;

3.9.3. the Sponsor warrants that the Institution's use of the Products indicated above, in the context of the Trial, shall not create any obligation for the Institution 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 Institution 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 Institution, 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 Institution of its contractual obligations towards its direct suppliers;

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

3.10. the Institution shall promptly inform the Sponsor if a regulatory authority informs the Institution of an inspection/audit about the Trial and, unless expressly refused by the Competent Authority, the Institution 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 institutional activity of the Institution.;

3.11. The Institution 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 acts of address 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. For the purposes of this Agreement, "Investigational Medicinal Products" shall be defined as the investigational medicinal products (\_\_\_\_), as well as (i) the other medicinal products covered by the Protocol under D.M. 21 December 2007, Annex 1, item 3, Table I, including medicinal products to be used in association or combination with each other, whenever the subject-matter of the study is the association or combination, and (ii) auxiliary medicinal products and background therapy *i.e.* the standard of care for the pathology under trial, if included, according to the Protocol, in the comparison between the different treatment strategies being tested. The Investigational Medicinal Products shall be supplied to the Institution for the duration of the Trial and in the quantities necessary and sufficient for the execution of the Trial. The reception and tracking of drugs should be done with the registration of batches. The Institution remains responsible for the background therapies not included in the comparison therapeutic strategies. The quantities of Investigational Medicinal Products should be appropriate to the number of cases covered. In respect of the Investigational Medicinal Products:

- a) *(if the Investigational Medicinal Products have a Marketing Authorization ("AIC") and are used according to the same indication, at the expense of the National Health Service ("SSN"))*: Under Art. 2 paragraph 2 of the Ministerial Decree 30 November 2021, the Investigational Medicinal Products, having an AIC and being used according to the indications of the same and dispensed by the SSN, will be provided by the Sponsor (or: will be procured by the Institution).
- b) *(if the Investigational Medicinal Products have an AIC but are used according to other indications and are supplied free of charge by the Pharmaceutical Company)*: The Sponsor shall ensure, under its supervision, direct or indirect free supply, or reimbursement, of the Investigational Medicinal Products, not used according to the indications of the AIC, subject to a specific contractual support agreement with the Pharmaceutical Company \_\_\_\_\_, which will provide them free of charge.
- c) *(in the event that the Investigational Medicinal Products are equipped with ACIs but are used according to different indications and are not provided free of charge by the Sponsor or by other funds, but covered by the Institution's corporate fund)*: Pursuant to art. 2 paragraph 3 of the ministerial decree of 30 November 2021, the cost of Experimental Medicinal Products, if not covered by ad hoc funds, will be covered by the fund referred to in paragraph 4 of the same article, within the limits of the financial resources of the competent health facility, and respecting the economic planning of the same structure.

4.2. In accordance with point 34 of the Helsinki Declaration and good practice 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 Institution and be evaluated by the Ethics Committee. Information on whether or not the Sponsor is willing to

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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 Institution's pharmacy, 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 Sponsor undertakes to provide free of charge or refund to the Institution, for the duration of the Trial and in the quantities necessary and sufficient for the execution of the Trial, any material necessary for the execution of the Trial (hereinafter, "Materials"), as well as laboratory, diagnostic or monitoring tests, related to the use of the Investigational Medicinal Products or the primary and secondary objectives of the Trial (hereinafter, "Services"). The Institution and the Principal Investigator shall use the Experimental Medicinal Products and the Materials /Services provided by the Sponsor exclusively within and for the execution of the Trial. The Institution shall not transfer or transfer to third parties the Investigational Medicinal Products and/or Materials provided by the Sponsor under this Agreement.

4.6. (a) *(in the event of collection of the Trial Drugs by the Sponsor):*

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.

*or*

4.6. (b) *(in the event of destruction of the Trial Drugs by the Institution):*

All the expired or otherwise unusable Trial Drugs or those that have not been used upon conclusion of the Trial will be disposed of by the Institution at the Sponsor's expense. The Institution shall provide the Sponsor with certification of disposal by current regulations. Concerning the disposal of unused Trial Drugs and the related operations, the Sponsor shall pay the Institution the amount indicated in Annex A (Paragraph "Costs and Payments" – Part 1) attached to this Agreement. The Institution will invoice the indicated amount plus VAT at the ordinary rate, with the description "Ancillary cost for the disposal of expired or unused Trial Drugs".

### **Art. 5 – Loan for use (where applicable)**

5.1. The Sponsor grants on gratuitous loan to the Institution, 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 on, individually or cumulatively, the "Instrument") \_\_\_\_\_ *(description of the asset and corresponding value in Euro)*. The ownership of the Instrument, as by law, is not transferred to the Institution. 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 Institution. 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 Institution 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;

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- 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 Institution by the technicians appointed by the Institution, in the presence of a delegate of the Sponsor, subject to prior Agreement, for verification of correct installation and functionality and compliance with current regulations. At the time of delivery of the Instrument, appropriate documentation is drawn up certifying 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 Institution.

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 Instrument 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 wilful misconduct and/or fault of the Institution. For this purpose, it will be affixed on the/ the Instrument/ the appropriate plate or other suitable indication of the property.

5.6. The Instruments shall be used by the Institution's staff and/or patients and for the sole and exclusive purposes of this Agreement's Trial object, by the Protocol's provisions. The Institution 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 Institution, 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 Institution 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 Institution 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 Institution, unless the event is the result of willful misconduct intent on the part of the Institution.

5.9. It is understood that about the Instruments that will be directly handled or managed by the patients/parents/legal guardians (*e.g.*, electronic diaries), the Sponsor acknowledges that the Institution 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 Institution 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 Institution will also be



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responsible for promptly informing the Sponsor of any failure to return the equipment by the subjects participating in the study.

5.10. It is acknowledged that the authorisation to grant loan-free use of the Instrument was given by the Authority following and according to its internal procedures.

#### **Art. 6 – Remuneration (if applicable)**

6.1. The remuneration agreed, previously evaluated by the Institution for each eligible assessable patient who has completed the trial treatment according to the Protocol and for whom the related CRF/eCRF has been duly compiled, including all the costs incurred by the Institution in execution of the Trial and the costs to cover all the associated activities, is € \_\_\_\_ + VAT (*if applicable*) per patient as specified in greater detail in the Budget annexed (*sub A*).

6.2. The Sponsor undertakes to pay its due under this Article based on an appropriate statement/statement of reasons agreed between the Parties.

The above fee will be paid with the frequency indicated in the Budget (Annex A) based on the number of patients involved in the relevant period, the processing carried out by them according to the Protocol, and the presence of the relevant CRF/eCRF duly completed and deemed valid by the Sponsor based on the activities carried out.

*(If the trial does not provide for any fee, Articles 6.1 and 6.2 are replaced by the following. Renumber accordingly):* 6.1 In consideration of the nature of the Parties and the absence of profit purposes, there will be no consideration in favor of the Institution for the performance of the Trial.

6.3. The laboratory/instrumental tests, indicated in Annex A, required by the Protocol, as approved by the Ethics Committee, and indicated in Annex A hereto will not be at the charge of the Institution in any way even if carried out outside the Institution. All laboratory/instrumental tests and any other additional performance/activity not included in the agreed fee for eligible patient, requested by the Sponsor and provided for by the Protocol approved by the Ethics Committee, will be invoiced to the Sponsor in addition to the agreed fee per eligible patient.

6.4. The Institution 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 Institution 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 Institution 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. *(to be omitted in case of no consideration)* If, during the Trial, it is necessary to increase the Institution's financial support, the Sponsor may supplement this Agreement by an addendum/amendment authorising the appropriate increase to the attached Budget.

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6.7. *(to be omitted in case of no consideration)* By the regulation on mandatory e-invoicing for sales of goods and services among private individuals, the Institution shall issue invoices in XML (Extensible Markup Language) format. Invoices are to be sent through the interchange system (SDI).

To this end:

- the Sponsor communicates its data:

COMPANY NAME \_\_\_\_\_

CONSIGNEE CODE/PEC: \_\_\_\_\_

C.F. \_\_\_\_\_

P.IVA \_\_\_\_\_

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- the Institution shall disclose its data:

COMPANY NAME \_\_\_\_\_

CONSIGNEE CODE/PEC: \_\_\_\_\_

C.F. \_\_\_\_\_

P.IVA \_\_\_\_\_

BANK DETAILS \_\_\_\_\_

6.8. *(to be omitted in case of no consideration)* The payments made for the Institution's services (i) represent the fair market value for those services, as they reflect the tariff scale applied by the Institution, (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 Institution 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 living expenses, provided they are actually incurred and documented, related to participation in the Trial at the Institution, through procedures previously approved by the Ethics Committee.

The reimbursement can be made through the administration of the Institution, 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 Institution; this list will be duly codified by the Institution, 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 will be able to check the amounts requested by comparing them with the services provided to patients and will make the relevant payments to the Institution. It will, therefore, be the responsibility of the Institution to provide reimbursement to each patient involved, according to the amounts of respective relevance. Alternatively, the reimbursement may be materially provided to patients by an external specialised organisation (from now on referred to as "**Service Provider**"), to which a specific task must have been assigned in writing by the Institution, with appointment to the person in charge of the treatment of the personal data of the patients, of which the Institution is independent owner. The Service Provider may also be suggested and reimbursed by the Sponsor (insofar as *e.g.* performing a similar service in other Centres and/or Countries), but must remain independent and may not in any way transfer to the Sponsor personal data of patients, of which the same is not the controller. Each patient must explicitly consent, subject to appropriate notice, to receive reimbursement of the costs due through the Service Provider.

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.

Any and all costs relating to items not specified in Annex A or provided for in the Protocol will not be reimbursed.

TRANSLATION (for convenience only)

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.

The criteria and the modalities indicated in paragraph 3 will apply, insofar as compatible, to other cases of outsourcing of services related to the Trial, which have been regulated by the Protocol and evaluated favourably by the Ethics Committee, such as the provision of home nursing services or the home delivery of medicines for self-administration by the patient.

#### **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 Institution, as provided for in the study Protocol, 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 Institution 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 Institution – 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 Institution receives such communication.

Termination by the Sponsor will not affect the obligations assumed and costs paid by the Institution on the date of notification of termination. In particular, the Sponsor will pay the Institution 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 Institution 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 Institution 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 Institution 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 Art. 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 Institution, the Institution 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 Institution 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 for low-level intervention trials, the insurance cover provided by the Sponsor guarantees concerning the civil liability of the Sponsor, the health institution of the Trial, the Principal Investigator, and the other Experimenters involved at the Centre of the Institution.

8.3. a) 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.

*or*

8.3 b) The Institution declares that the risks of civil liability to third parties for any damage arising to patients from participation in the Trial referred to in this contract are covered by the general policy stipulated by it under art. 3 of D.M. 14 July 2009. The Ethics Committee has deemed the insurance policy to respect the terms of the law and adequately protect the subjects involved in the clinical 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, or to be activated, by the Sponsor for the filing of a patent application concerning inventions obtained during the Trial, the Institution, 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 Institution 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.

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 (time limit extendable in the course of negotiation until they fall into the public domain), all the technical and commercial information provided by the other Party and/or developed during the Trial and in pursuit of its objectives( including but not limited to the Investigator Brochure, information, data and materials relating to the medicinal product being tested)), 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 Commercial 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 Institution, 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 Institution, 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 multi-centre, 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, its interruption or early termination. Suppose a publication containing the results of a multi-centre trial, published by the Sponsor or the third party designated by the Sponsor, is completed after 12 months (at least twelve months under the current regulations) from the end of the multi-centre Trial. In that case, the Investigator may publish the results obtained at the Institution 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, provided that it is communicated in advance and specifically to the Sponsor.

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 Institution 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 protection. 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, the Sponsor and the Institution, in the absence of other regulatory provisions, must complete and sign the document Standard Contractual Clauses approved by the European Commission (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 Institution 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 Institution is responsible for keeping the consent forms.

11.10 If either Party discovers a data protection breach, the other Party shall be informed within 48 hours of the breach being verified, without prejudice to such Party's independent assessment of the conditions and fulfilment of the obligations contained in Articles 33 and 34 GDPR.

## **Art. 12 – Amendments**

12.1 This Agreement and its annexes/appendices, 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.

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

13.1. The Institution 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 Institution 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 *If applicable*<sup>5</sup>In accordance with Law 190 of 6 November 2012 ("**Anticorruption Act**") as amended, the Institution confirms that it has adopted the Three-Year Anti-corruption Plan.

*(If applicable and if not conflicting with current regulations)* 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 Institution 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.

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<sup>5</sup> The provisions of art. 13.3 and 13.4 may be adapted for specific provisions of other legal systems.

TRANSLATION (for convenience only)

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, transfer of the Contract, transfer of data and/or results of the Trial for registration purposes**

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 Institution, which does not involve a change in its legal person, the amendment to this Agreement will not be necessary. However, the Authority will be required to notify the Sponsor of such a change of name without delay.

14.3 Any sale, licensing or transfer on any basis (hereinafter "transfer") of data and/or results of the Trial for registration or development of Investigational Medicinal Products may only be made in the manner provided by art. 3 of D.M. 30 November 2021.

Under paragraph 2, letter a of such article and pending issuance of the ministerial decree under art. 1, paragraph 2, letter g n. 6 of the Law of 11 January 2018, n. 3, the estimate of the value of the goods to be sold must take adequate account of the contribution of public research centres to the design and development of the data and/or results to be sold, providing mechanisms for compensation or participation in any profits and benefits arising from their marketing. All proceeds from the sale must be used for the unconditional funding of independent research projects.

As per the provision of art. 3 paragraph 5 of D.M. 30 November 2021, the Parties are committed to transparency. They undertake to give notice of the transfer on their institutional sites, ensuring that patients involved in the Trial are well-informed and feel part of the process.

**Art. 15 – Signatures and taxes**

15.1. This Agreement is signed digitally in accordance with applicable regulations. 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. (In case of exemption from the payment of stamp duty, please indicate the legal references that provide for it)

**Art. 16 – Governing law and forum**

(for the determination of the regulatory law and the competent court, please refer to the "*Guide to the assessment under art. 7 of EU Regulation No. 536/2014, by the Territorial Ethical Committees*," visible at the link (<https://www.aifa.gov.it/centro-coordinamento-comitati-etici>))

16.1. (a) (in general, and in any case if the Parties are both Italian): This Agreement is governed by the laws of Italy.  
or

16.1. (b) (in case of multi-centre international studies, if the parties have different nationalities and Italian law is not chosen, but rather the law uniformly applied by the Sponsor for all the participating centres, wherever located):

The governing law of this Agreement is the law \_\_\_\_\_ (insert nationality of the Sponsor), without prejudice, however, to mandatory rules of Italian law, particularly regarding the protection of patients' rights.

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 \_\_\_\_\_'s registered office shall have exclusive jurisdiction.



TRANSLATION (for convenience only)

**Art. 17 – Language**

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

**Art. 18 - Knowledge and acceptance of the entire Contract**

The Parties mutually acknowledge, for mutual clarity, that this Agreement, drawn up based on the minimum content identified under Art. 2 paragraph 6 of Law 11 January 2018, n.3, is to be considered known and accepted in all its parts and that, therefore the provisions of art. 1341 and 1342 of the Civil Code.

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

**For the Sponsor**

Legal Representative or their delegate (or CRO)

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

Signature \_\_\_\_\_

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

**For the Institution**

The legal Representative or their delegate

Dr. \_\_\_\_\_

Signature \_\_\_\_\_

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

For confirmation of having seen the provisions concerning her/him: the Principal Experimenter

Prof/Dr. \_\_\_\_\_

Signature \_\_\_\_\_

**ANNEX A – BUDGET**

**COSTS AND PAYMENTS**

**Part 1 – Fixed costs and payments per patient involved in the study**

Include, by way of example, the following items:

- Supply of the Trial Drug(s) and any other materials required for the trial provided that there are no extra costs for the National Health Service (diagnostics kits, medical devices, etc.).
- Gross payment per patient involved in the study: € \_\_\_\_\_ + VAT (include multiple payments for studies that require different payments for each “arm” of the protocol).
- Compensation for screening failure, unscheduled visit, and the possible destruction of the Trial Drug as required by art. 4.6 of the Agreement.
- Payment per trial Centre for each completed patient (Payment for enrolled patient - company overheads - all the costs incurred by the Institution for the trial <sup>6</sup>): € \_\_\_\_\_ + VAT.
- Interim financial phases (if the patients do not complete the trial procedure): Examination: payment per patient (Examination no. \_\_\_\_ of € \_\_\_\_ + VAT; Contacts € \_\_\_\_ + VAT; Treatment cycles € \_\_\_\_ + VAT; Examination no. \_\_\_\_ € \_\_\_\_ + VAT).
- (*only include this paragraph if no extra costs are referred to in part 2*). All the reimbursable costs of the study, including those covered by the contribution per patient involved, shall not lead to any extra costs payable by the National Health Service (for example, there are no additional services, the instrumental and laboratory tests are routine for the patients in the trial, or the instrumental tests are routine for the patients in the trial and the lab tests will be carried out with diagnostic kits supplied by \_\_\_\_ or the lab tests will be done at a single centralised external laboratory, at Sponsor’s expenses).

**Part 2 – Additional costs for instrumental tests and lab tests to be carried out according to the Tariff of the Institution (or over cost based on the tariff nomenclator of the Region where the Trial Center is located) in force at the time of the provision of the respective services.**

Tariff Code	Description of test	No. Tests per patient	Amount € ____ + VAT
	-	-	-
-	-	-	-
-	-	-	-

**Part 3 – Payment Allowance for patients/careers involved in the clinical trial: (if applicable)**

- Reference is made to the model "Compensation for participants in the trial", included in the application dossier under Regulation (EU) no. 536/2014, to be understood as referred to in this Agreement as an integral and substantial part.

**LIQUIDATION AND INVOICES (if applicable)**

- The payment must be made within \_\_\_\_ days (*state number*) from receipt of the invoice.

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<sup>(6)</sup> General admin costs are costs incurred by the pharmacy service in managing the trial drug(s).

TRANSLATION (for convenience only)

- The invoice must be issued at the required intervals \_\_\_\_\_ (*quarterly/half yearly/annually or according to milestones*) based on the amounts accruing during the reference period and the request for invoice by the Sponsor.

**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/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;

TRANSLATION (for convenience only)

- **Auditor** – the party responsible for auditing the conduct of the Trial as an integral part of quality assurance, appointed by the Sponsor