

**INDEPENDENT CLINICAL TRIAL AGREEMENT FOR THE DRUG(S)**

“ \_\_\_\_\_ ”

**BETWEEN**

“ \_\_\_\_\_ ” (*insert the name of Healthcare facility*) (hereinafter the “Entity”), headquartered in \_\_\_\_\_, city \_\_\_\_\_, Tax Code and VAT Code \_\_\_\_\_, in the person of its legal representative Dr./Prof. \_\_\_\_\_, in quality of (*indicate whether General manager, CEO, Extraordinary commissioner, etc.*) who has been duly empowered to sign this deed on \_\_\_\_\_, (*title of signatory*) (hereinafter referred to as “ \_\_\_\_\_ ”)

**AND**

(a) (*in case of an agreement with the Sponsor*):

The Institute/Company/Foundation/Association \_\_\_\_\_ headquartered in \_\_\_\_\_, Tax Code and VAT \_\_\_\_\_ (hereinafter “Sponsor”) in the person of the General Manager Legal representative (or delegated person), on the one hand, as Sponsor

(a1) (*in case of a trial with a Sponsor established outside the European Union and concluded by its representative in the territory of the European Union*):

\_\_\_\_\_ (*indicate the Company*), headquartered in \_\_\_\_\_ Tax Code and VAT \_\_\_\_\_, in the person of the Legal Representative \_\_\_\_\_ in quality of \_\_\_\_\_ (hereinafter the “Company”), which by proxy/mandate in \_\_\_\_\_ acts in its own name and on behalf of the Sponsor of the trial \_\_\_\_\_, headquartered in \_\_\_\_\_, Tax Code and VAT \_\_\_\_\_ (hereinafter “Sponsor”)

(b) (*in case of assignment to a CRO also for the execution of the Agreement*):

\_\_\_\_\_ (*indicate the name of the Contract Research Organization – CRO*), headquartered in \_\_\_\_\_, Tax Code and VAT \_\_\_\_\_, in the person of the Legal Representative \_\_\_\_\_, in quality of \_\_\_\_\_ (hereinafter “CRO”), acting in the name and on behalf of \_\_\_\_\_ (hereinafter “Sponsor”), by virtue of appropriate power of attorney/mandate/proxy granted on \_\_\_\_\_

Hereinafter individually/collectively the “Party/Parties”.

Whereas:

A) The Sponsor is interested in conducting, in accordance with EU Regulation 536/2014 (hereinafter the “Regulation”) the clinical trial entitled “ \_\_\_\_\_ ” (hereinafter the “Trial”) relating to the Protocol version no. “ \_\_\_\_\_ ”, duly approved (hereinafter the “Protocol”), EudraCT code no “ \_\_\_\_\_ ” at the Entity, under the responsibility of Dr./Prof. “ \_\_\_\_\_ ”, as the Scientific Director of the trial covered by this Agreement (the “Principal Investigator”), at “ \_\_\_\_\_ ” (*insert name of Unit, Department, etc.*) (“Trial Centre”);

B) The Trial fulfils the requirements of the Ministerial Decree of 30 November 2021, Article 1, para. 2, lett. “ \_\_\_\_\_ ”;

C) The Sponsor has appointed prof./dr. \_\_\_\_\_ as the scientific contact for the part under its responsibility. The Sponsor may change the scientific contact by given written notice to the Entity;

D) The Trial Centre has the technical and scientific know-how to carry out the Trial and is suitable facility for the Trial to be conducted in accordance with the applicable regulations;

E) The Principal Investigator and his/her direct staff, qualified according to the Protocol to intervene with discretionary powers in the execution of it (hereinafter “Co-investigators”), as well as all other subjects

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playing any part in the Trial under the supervision of the Principal Investigator are qualified to conduct the Trial in accordance with 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 regulations regarding the conflict of interest;

F) Except as otherwise agreed upon in writing by the Parties, the Entity shall only conduct the Trial in its own facilities;

G) (1) (in the event that there is no need to loan the equipment for use): the Entity is equipped with suitable equipment necessary for the execution of the Trial as indicated in the Protocol;

**Or**

(2) (in the event that the loan for use of equipment is required): the Entity, while being provided with equipment suitable for the execution of the Trial, shall receive on gratuitous loan for use from the Sponsor, pursuant to and for the purposes of the Civil Code, the equipment and/or goods essential for the successful completion of the Trial, listed in Article 5 of this Agreement;

H) (1) (*for Trials proposed under the Regulation*): The Trial has been duly authorized in accordance with Chapter II of the Regulation, following the AIFA national authorization 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**

(2) (*for Trials proposed on a transitional basis pursuant to Directive 2001/20 and the Italian legislation still in force*): The Sponsor filed, by the legal deadline, and application for authorization of the Trial with AIFA (the "Competent Authority") by virtue of Italian Legislative Decree no. 158 of 13 September 2012 ("Balduzzi Decree"), converted by Law no. 189 of 8 November 2012, within the time limits set out in the regulations, the application for authorization to carry out the Trial;

(2.a) (*in the event that the Entity is the Coordinating Centre in Italy*): On \_\_\_\_\_, the Ethics Committee competent for the Entity has expressed its single opinion in favour of carrying out the trial at the Entity, as Coordinating Centre for the trial in Italy;

(2.b) (*if the Entity is not the Coordinating Centre in Italy*): Pursuant to Article 7 of Legislative Decree no. 211 of 24 June 2003, on \_\_\_\_\_, the Sponsor obtained the sole opinion in favour of the conduct of the Trial from the Ethics Committee \_\_\_\_\_, to which the Coordinating Centre of the Trial for Italy belongs; and, on \_\_\_\_\_, the Ethics Committee responsible for the Entity expressed a favourable opinion on the conduct of the Trial, accepting the aforementioned favourable sole opinion;

I) (*if the case applies*) in negotiating this Agreement, the Parties have based themselves on the outline approved by the National Coordination Centre of Territorial Ethics Committees pursuant to Article 2, Paragraph 6, of Law no. 3 of 11 January 2018 and, in compliance with the homogeneity of the administrative, economic, insurance aspects referred to therein, have deemed it necessary to supplement and/or amend the relevant provisions for the purpose of regulating the specificities and peculiarities of the Trial, on the basis of the following reasons (specify): \_\_\_\_\_;

J) Pursuant to Article 76 of the Regulation, the Sponsor has taken out a suitable insurance policy as detailed in Article 8 of this Agreement;

in consideration of the foregoing, it is hereby 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 Entity with the execution of the Trial under the terms of this Agreement, in accordance with the Protocol and any subsequent amendments, and with the amendments to this Agreement/budget resulting from such amendments formalized by the necessary deeds of amendment, duly signed.

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 in accordance with 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 in accordance with 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.

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 (interruption 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 Trial centers as well as the participants in the study, of any new events, the measures taken and the program of measures to be taken in the future, and will duly complete the procedures required by the applicable laws. The Sponsor, having been informed by the Principal Investigator of a serious adverse event, promptly communicates to the electronic database all the serious and suspected adverse events within the terms referred to in Paragraph 2 of Article of Regulation (EU) 536/2014, also pursuant to Paragraph 3 by reporting.

2.6. (a) *(In the event of non-competitive inclusion of patients)*: The Entity expects to include, provisionally, \_\_\_\_ patients by \_\_\_\_ (insert estimated date). The Parties acknowledge that any increase in the number of patients to be enrolled at the Entity's investigation 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 caseload made in accordance with 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)*: as the Trial involves the competitive inclusion of patients, the Entity expects to include approximately \_\_\_\_ patients, with a global maximum of

\_\_\_\_\_ patients eligible for the Trial and limited to the terms provided for by the Sponsor. The enrolment period may be changed depending on the national or international trend in enrolment. When the total number of patients permitted for the entire Trial has been reached, the inclusion of further patients will be closed automatically, regardless of the number of patients enrolled at the Centre, apart from patients who have already provided their consent to take part in the Trial, unless the patients themselves withdraw their consent. The Sponsor will timely notify the Entity accordingly.

2.7. The Entity and the Sponsor will keep the Trial documentation (the permanent “Trial Master File”) for the period of time and as specified in the applicable laws (or for a longer period if required by other applicable laws or by a financial agreement between Entity and the Sponsor). The Sponsor must inform the Centre of the expiry of the mandatory conservation period at the request of the Sponsor, after expiry of the mandatory conservation period, the Parties may agree the terms of a further conservation period, anonymizing the data in advance.

2.8. The Entity and the Sponsor, each within their own sphere of responsibility, shall also use forms of document digitalization (or dematerialization), if applicable. Regardless of whether or not the archived Trial documentation contains personal data (of a special nature or otherwise), according to the definitions in Regulation (EU) no. 679/2016 (hereinafter “GDPR”), the Entity and the Sponsor shall take all the physical and technical measures referred to in Article 32 of said GDPR and 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 not only the integrity of the data, information and printed/digital documents but also their future legibility throughout the mandatory conservation period. To fulfil such obligation both the Sponsor and the Entity may rely on external service providers to manage the archiving obligation.

2.9. The Sponsor, the Entity and the Principal Investigator shall comply with the directions, indications, instructions and recommendations given by the Ethics Committee and by the Competent Authority

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

3.1. The Principal Investigator shall be assisted in the execution of the Trial by direct collaborators, qualified under the Protocol to intervene with discretionary powers in the execution of the Trial (hereinafter “Co-investigators”), as well as by the healthcare and non-healthcare personnel engaged by the Entity. Co-investigators and other personnel will operate under the responsibility of the Principal Investigator for all aspects pertaining to the Trial; they will have to be qualified to conduct the Trial and have previously received adequate training by the Sponsor, in accordance with applicable regulations and each of them must have declared her/his willingness to take part in 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. This Agreement is made between the Sponsor and the Entity. The Sponsor is extraneous to the relations between the Entity, the Principal Investigator, the Co-investigators and all other personnel participating in the Trial and is thus indemnified in respect of any claim that they may take in relation to the Trial.

3.4. In relation to 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.

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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 Entity ends for any reason, the Entity 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 by the competent Ethics Committee. The Entity guarantees that the new Principal Investigator is qualified to continue the Trial, that he will accept the terms and conditions of this Agreement and that he will 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 Entity shall ensure the necessary continuity in the Trial activities. If the Sponsor does not intend to accept the name of the replacement proposed by the Entity, or if the Entity does not propose a substitute, the Sponsor may terminate this Agreement in accordance with the provisions of Article 7.

3.6. Before starting the Trial, the Principal Investigator shall obtain the informed consent of the patient or his/her legal representative, in accordance with the current laws on clinical trials, as well as the consent for the processing of personal data in accordance with the current Italian and EU laws 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 to 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, in accordance with 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 its responsibility in accordance with the highest standards of diligence. In particular:

3.8.1. The Principal Investigator shall submit all properly completed Case Report Forms (CRFs), duly compiled, in accordance with the terms and conditions of the Protocol for the Trial and with the applicable regulations, in printed or digital form and in any case in a timely manner 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 Entity 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 Entity and the Principal Investigator, having been informed sufficiently in advance, shall allow the correct execution of the monitoring and auditing and inspections at the Trial Centre \_\_\_\_\_ by the Sponsor and by the Competent Authority, such activities to be carried out 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 (hereinafter the “Product”), intended for \_\_\_\_\_, will be supplied for free. With reference to the same it is understood that:

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3.9.1. For the use of the network infrastructure and information systems, the Sponsor shall agree 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 Entity 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 Entity;

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

3.9.5. In any event the Sponsor shall indemnify the Entity respect of any direct or indirect losses deriving from use of the Product in accordance with the instructions of the manufacturer/supplier.

3.10. The Entity shall promptly inform the Sponsor if a regulatory authority informs the Entity of an inspection/audit in relation to the Trial and, unless expressly refused by the Competent Authority, the Entity will authorize the Sponsor to take part, while sending the Sponsor all the written communications received for the purposes of the inspection/audit.

3.11. These activities must in no way prejudice the ordinary institutional activities of the Entity.

3.12. The Entity and the Sponsor guarantee that the biological samples (blood, urine, saliva, etc.) that may be collected from patients undergoing the Trial covered by this Agreement shall only be used for the purposes of the Trial in accordance with the provisions of the Protocol and of the current regulations. Any conservation and subsequent use are subject to the acquisition of specific informed consent from the patient (or the parent/legal guardian) to the favourable opinion of the Ethics Committee in accordance with the limits and guarantees provided for in the current regulations and guidelines referred to in Article 1 of Legislative Decree 52 of 14 May 2019.

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

4.1. For the purposes of this Agreement, "Trial Drugs" are defined as the pharmaceutical products subject to the Trial (\_\_\_\_\_), as well as (i) the other medicinal products envisaged by the protocol in compliance with Ministerial Decree 21 December 2007, Annex 1, Point 3, Table I, including medicinal products to be used in combination or association with each other, whenever the association or combination is the object of the study, and (ii) ancillary medicinal products and background therapy, i.e. the therapeutic standard for the pathology under Trial, if included, according to the trial protocol, in comparing the different therapeutic strategies under Trial. Trial Drugs must be supplied to the Institution for the duration of the Trial and in the quantities necessary and sufficient for the conducts of the trial. Receipt and tracking of the drugs must take place with batch registration. Background therapies not included in the comparative therapeutic strategies remain the responsibility of the Institution. The quantities of Trial Drugs must be appropriate to the number of cases treated. In relation to the Trial Drugs:

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a) *(in the event that the Trial Drugs have a Marketing Authorisation and are used according to the same indication, at the charge of the NHS):* Pursuant to Article 2, Paragraph 2 of the Ministerial Decree of 30 November 2021, Trial Drugs, having a Marketing Authorisation (MA), used according to its indications and dispensed at the charge of the National Health Service, will be provided by the Sponsor (or: will be procured by the Institution).

b) *(in the event that the Trial Drugs have a MA but are used according to a different indication and are supplied free of charge by the pharmaceutical company):* the Sponsor guarantees, under its own supervision, the free direct or indirect supply, or reimbursement, of Trial Drugs, not used according to the indications of the AIC subject to a specific supporting contractual agreement entered into with the pharmaceutical company \_\_\_\_\_ which will supply the drug(s) free of charge.

c) *(in the event that the Trial Drugs have a marketing authorization but are used according to a different indication and are not provided free of charge by the Sponsors, but are covered by the Entity's corporate fund):* Pursuant to Article 2, Paragraph 3 of the Ministerial Decree of 30 November 2021, the cost of the Trial Drugs, 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 structure, and in compliance with the economic planning of the same structure.

4.2. Upon fulfilment of the conditions laid down in the current regulations on the therapeutic use of a drugs undergoing clinical trials, with particular regard to the Declaration of Helsinki and good practice in the field of therapeutic continuity, the Sponsor agrees, where applicable and in the absence of reasons (to be specified in writing) to the contrary, to make the drug undergoing clinical trials available at the end of the Trial, beyond the follow-up period, for patients who have obtained a clinical benefit from the investigational drug, assessed according to the judgment of the Principal Investigator (regardless of whether or not the Ministerial Decree of 7 September 2017 "Discipline of therapeutic use of investigational medicinal product" applies). In patients with clinical benefit, the supply of the drug will be continued until the same is made available through the ordinary dispensing channels, so as to ensure therapeutic continuity. In accordance with the Declaration of Helsinki, information about the availability or non-availability of post-trial access by the Sponsor should be made known to the Trial participants in the informed consent documents.

4.3. The Trial Drugs shall be sent by the Sponsor to the Pharmacy of the Entity, which will record them, store them appropriately and deliver them to the Principal Investigator in accordance with the provisions of the Protocol and the current regulations.

4.4. The Trial Drugs shall be accompanied by an adequate transport document, 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 agrees to provide free of charge or reimburse the Entity, for the entire duration of the Trial and in the quantities necessary and sufficient for the execution of the Trial, any materials necessary for the execution of the Trial (hereinafter "Materials"), as well as laboratory, diagnostic or monitoring tests, related to the use of the Trial Drugs or the primary and secondary endpoints of the Trial (hereinafter, "Services"). The Entity and the Principal Investigator must use the Investigational Medicinal Products and Materials/Services provided by the Sponsor exclusively within the scope of and for the performance of the Trial. The Entity shall not transfer or assign to any third party any Trial Drugs 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):*

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

**Or**

(b) *(In the event of disposal of the Trial Drugs by the Entity):*

All the expired or otherwise unusable Trial Drug or those that have not been used upon conclusion of the Trial will be disposed of by the Entity, at the Sponsor's expense. The Entity shall provide the Sponsor with certification of disposal, in accordance with current regulations. With regard to the disposal of unused Trial Drugs and the related operations, the Sponsor shall pay the Entity the amount indicated in Annex A (Paragraph "Costs and Payments" – Part 1) attached to this Agreement. The Entity 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 Entity, which accepts pursuant to and for the purposes of articles 1803 et seq. of the Italian Civil Code, the Instruments described below, together with the relevant material for use (hereinafter 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 Entity. 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 Entity. The Parties also agree that any additional Instruments deemed necessary for the conduct of the study during the course of the Trial, should the characteristics and conditions thereof be met, shall be granted on gratuitous loan for use in accordance with the provisions of this Agreement. The Entity 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 Instruments 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 direct action on the patient or on other machinery present in the Entity by the technicians appointed by the Entity, 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 materials supplied on loan for use by the Sponsor to the Entity, suitable 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 its operation as well as any consumables for its use, at no cost to the Entity.

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 Investigator, all the technical interventions necessary for the



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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 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 shall bear all burden and liability in relation to any damage that may be caused to persons or things in connection with the use of the equipment in question according to the indications of the Protocol and the manufacturer's instructions, if due to a defect of the same, except in the case where such damage is caused by willful misconduct and/or gross negligence on the part of the Entity. To this end, a plate or other suitable indication of ownership shall be affixed to the Instruments.

5.6. The Instruments shall be used by the Institution's staff and/or patients and for the sole and exclusive purposes of the Trial object of this Agreement, in accordance with the provisions of the Protocol. 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 Entity, 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 Entity shall promptly, upon 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 Entity shall notify the Sponsor promptly after knowledge of the event. Any fraudulent or otherwise unauthorized 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 Entity, unless the event is the result of willful misconduct on the part of the Entity.

5.9. It is understood that with regard to the Instruments that will be directly handled or managed by the patients/parents/legal guardians (e.g., electronic diaries), the Sponsor acknowledges that the Entity 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 Entity 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 Entity 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. Authorisation for the free loan of the Instruments was granted by the Entity following its internal procedures.

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

6.1. The remuneration agreed, previously evaluated by the Entity 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 compiled, including all the costs incurred by the Entity in execution of the Trial and the costs to

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cover all the related activities, is € \_\_\_\_ + VAT (if applicable) per patient (a total of € \_\_\_\_ + VAT (if applicable) for an estimated no. \_\_\_\_ of patients) as specified in greater detail in the Budget annexed (sub A).

6.2. The Sponsor will pay the amount due under the terms of this article on the basis of 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, Paragraph "Liquidation and Invoices"), on the basis of 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.

*(if the Trial does not provide for any consideration, Articles 6.1. and 6.2. are replaced by the following, re-numbering accordingly):*

6.1. Given the nature of the Parties and the absence of any profit-making purpose, no consideration is envisaged in favour of the Entity for carrying out the Trial.

6.3. (a) *(If the tests are done by a centre external to the Entity):* All the laboratory/Instrument test indicated in Annex A, required by the Protocol and approved by the Ethics Committee, will not burden the Entity as they will be carried out centrally.

**Or**

6.3. (b) *(If the tests are carried out on the Entity's premises):* All the laboratory/instrument tests and any other services or additional activities not covered by the price agreed per eligible patient and requested by the Sponsor as approved by the Ethics Committee and Competent Authority and as detailed in Annex A (Paragraph "Costs and payments" – Part 2), shall be reimbursed and invoiced by the Sponsor in addition to the price paid for each eligible patient.

6.4. The Entity 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 trials regarding drugs. The Entity 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 the terms of this Agreement, if not agreed with the Sponsor.

6.5. The Sponsor shall also reimburse the Entity with 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 properly communicated, with justification, and have been documented in writing to the Sponsor and approved in writing by the Sponsor, and provided that the patient's personal data is communicated in anonymized form.

6.6 *(to be omitted in case of no consideration):* If during the course of the Experimentation it becomes necessary to increase the financial support to the Entity, the Sponsor may supplement, by an addendum/amendment, this Contract, providing for the appropriate increase in the Budget attached hereto.

6.7. *(to be omitted in case of no consideration):* In compliance with the legislation on the obligation of electronic invoicing for the supply of goods and for the provision of services also between private

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individuals, the Entity shall issue invoices in XML (Extensible Markup Language) format and transmitted through the Interchange System (SDI).

The Sponsor shall communicate the necessary data for the issuance of the electronic invoice:

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

ADDRESSEE CODE/PEC: \_\_\_\_\_

FISCAL CODE \_\_\_\_\_

VAT NUMBER \_\_\_\_\_

BANKING INSTITUTION DETAILS \_\_\_\_\_

6.8 *(to be omitted in case of no consideration)*: Payments made for services performed by the Entity (i) represent the fair market value of such services as adjusted against the applicable fee schedule at the Entity, (ii) have been negotiated on normal commercial terms, and (iii) have not been defined on the basis of the volume or value of prescriptions or otherwise by reference to such prescriptions or other economic activity generated between the Parties. Neither the Entity nor the Principal Investigator shall seek any other reimbursement or consideration from any other party in respect of any activities performed or expenses incurred including Investigational Patients to which the Sponsor/CRO is obligated to pay.

6.9 *(if the conditions provided by law are applicable)*

6.9.1 The Sponsor offers to patients participating in the Trial the reimbursement of the expenses directly incurred for participation (such as, for example, accommodation and food expenses), in relation to each medical service provided at the Institution, according to the eligibility criteria, procedures and maximum amounts approved in advance by the Ethics Committee.

6.9.2 The above expenses, duly documented, will be reimbursed exclusively through the Entity's administration. To this end, each patient shall submit the list of expenses to the Entity, or to the organization delegated by the Entity, which shall codify the list and, in consideration of the duration of the study, shall agree on the deadlines for the submission to the Sponsor of the total list of expenses to be reimbursed during the reference period.

6.9.3 The Sponsor will be able to check the amounts claimed against the examinations performed by the patients and will make the relevant payments to the Institution. It shall then be the responsibility of the Entity to make the reimbursements to the patients, in accordance with the amounts set out in the Budget attached hereto sub A (paragraph "Charges and Fees" - part 3).

6.9.4 Any bank charges and fees shall be charged in full to the payor and in no case may they be deducted from the amount credited to the payee.

6.9.5 Refunds other than those mentioned above are not permitted.

6.9.6 *(if specifically envisaged by the Protocol)*: A compensatory allowance is envisaged for the loss of earnings directly connected with participation in the trial, which may be extended to the companion of patients unable to travel alone (such as, for example, minor patients, incapacitated subjects, frail patients). This allowance may be granted according to the eligibility criteria, procedures and ceilings previously approved by the Ethics Committee. To this end, each patient shall submit a request to the Entity, or to the entity delegated by the Entity, which shall codify the requests and, in consideration of the duration of the study, shall agree on the deadlines for submitting to the Sponsor the overall list of the allowances to be disbursed in the reference period. Articles 6.9.3, 6.9.4 and 6.9.5 shall apply to the disbursement.

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

7.1 This Agreement shall take effect from the date of the last signature ("Effective Date") and shall remain in force until conclusion of the Trial at the Entity, as provided for in the study Protocol, subject to any

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amendments agreed by the Parties. Without affecting the foregoing provision, this Agreement shall remain in full force and effect following the issue of formal authorisation by the Competent Authority.

7.2 The Entity may terminate this Agreement in writing with 30-day 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 Entity – 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 from the time when the Sponsor receives the above communication.

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

Termination by the Sponsor will not affect the obligations assumed and costs paid by the Entity on the date of notification of termination. In particular, the Sponsor will pay the Entity all the documented, non-revocable expenses, contained in Annex A, that it has incurred in order to ensure the correct, efficient execution of the Trial (where applicable, including the costs incurred by the Entity 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 Entity during the Trial and also thereafter, if deriving from or related to the Trial.

7.4. In case of termination of the Trial, in accordance with applicable regulation, Sponsor will pay the Entity the expenses and considerations that have accrued and are documented up until that time.

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

7.6. This Agreement shall automatically cease to have effect pursuant to Article 1454 of the Civil Code in the event that 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.

The provisions of Articles 1218 et seq. of the Italian Civil Code shall apply in any event.

7.7. If this Agreement is terminated for reasons not due to non compliance by the Entity, the Entity shall have the right to reimbursement of the expenses incurred in relation to the Trial prior to receipt of the notice of termination, and to payment for the services rendered in accordance with the Protocol and this Agreement, proportionately to the activities performed up until the time of termination. The Entity shall repay the Sponsor any amounts already paid in relation to activities that were not completed.

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

### **Art. 8 – Insurance coverage**

8.1. The Sponsor is required to guarantee, according to current legislation, 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 coverage provided by the Sponsor guarantees with respect to the hypotheses of civil liability of the Sponsor, the health entity where the Trial is conducted, the Principal Investigator, and the other Investigators involved at the Entity.

8.3 a) The Sponsor declares that it has taken out an adequate insurance policy (no. \_\_\_\_\_, with the Company \_\_\_\_\_) for third party civil liability, to cover the risk of any damages deriving to patients from participation in the trial referred to in this Agreement, in accordance with the provisions of the Ministerial Decree of 14 July 2009. The insurance policy was deemed by the Ethics Committee to be compliant with the terms of the law and adequately protecting the subjects involved in the Clinical Trial.

**Or**

8.3 b) The Entity declares that the risks of third party liability for any damage caused to patients as a result of their participation in the trial referred to in this Agreement are covered by the general policy it has taken out. The insurance policy has been deemed by the Ethics Committee to be in compliance with the terms of the law and adequately protecting the subjects involved in the Clinical Trial.

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

8.5. In particular, in the event that 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, in accordance with Article 2 par. 3 of M.D. of 17/07/09.

8.6. At the time of the accident, the Entity is required to disclose the existence of policies for liability RCT Medical Malpractice (to cover the Entity and the medical staff administering the drug) in accordance with Article 1910 of the Italian Civil Code.

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

9.1. The Sponsor will publish the results of the Study 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 in accordance with the procedures set out in Article 37.4 of the Regulation.

9.3. All 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 recognized as authors. If the Sponsor takes action to file an application for a patent relating to inventions obtained during the course of the Trial, the Entity and the

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Principal Investigator shall provide to Sponsor, at the expense of the latter, all the assistance and documentary support necessary for that purpose.

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

The Parties mutually acknowledge they will still be 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 (time limit extendable in the course of negotiation until their fall into public domain, if necessary on the basis of any agreements with the licensors), all the technical and/or commercial information provided by the other Party and/or developed during the course of 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 with regard to their own employees, contractors, subcontractors, successors or assigns.

Each Party also represents and warrants as follows:

- a) its own Commercial Secrets have been acquired, used and disclosed legally and 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.
- b) It shall therefore indemnify the other Party in respect of any legal actions, complaints, claims for compensation or indemnity, whether judicial or extrajudicial, brought by any third party claiming ownership to such secrets.

10.2. The Parties are obligated to adequately and accurately disclose and publish the results of the Trial as well as to communicate them adequately to the patients taking part and to the patients’ representatives. Under the terms of the applicable regulations, the Sponsor is required to promptly publish the results of the Trial even if negative, 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. Pursuant to Article 5(2) (c) of M.D. of 8 February 2013, the Principal Investigator has the right to disseminate and publish, without limitation, the results of the Trial obtained from the Entity, in accordance with the current laws on the confidentiality of sensitive data, data protection and intellectual property, and in accordance with 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 Entity, in view of their presentation or publication, at least 60 days before them, the Principal Investigator

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will send the Sponsor the text of the document intended to be presented or published. Should issues arise in relation to the scientific integrity of the document and/or issues 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 the protection of intellectual property.

10.5. The Sponsor may, for the purposes of presenting a patent application and if necessary, ask the Principal Investigator to delay the publication or presentation of the document by a further 90 days. Should the Trial be 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 full or for at least 12 months from conclusion of the Trial, its interruption or early termination.

If the publication containing the results of a multi-centre trial, published by the Sponsor or by the third party designated by the Sponsor is not completed within 12 months (at least twelve months under the current regulations) from the end of the multi-centre Trial, the Investigator may publish the results obtained at the Entity, in accordance with the contents of this article.

### **Art. 11 – Data protection**

11.1. In executing the contractual activities the Parties shall treat all the personal data they receive for any reason in relation to the clinical Trial in accordance with the objectives of the foregoing 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 provisions 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 in any other documents used for the purposes of the Trial shall be construed and utilized in accordance with the meanings given in Annex B.

11.3. The Entity and Sponsor are independent data controllers for the purposes of article 4 paragraph 7 of the GDPR. Each of the Parties will arrange at its own expense, as part of its organizational structure, for any appointment of Data Processors and assignment of functions and tasks to designated subjects, who operate under their authority, in accordance with the GDPR and current legislation.

11.4. For the purposes of the Trial, personal data relating to the following categories of data subjects will be processed: persons taking part in the trial; persons operating on the Parties' behalf. Such data subjects will be appropriately informed of the processing of their data. For the purposes of 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 in accordance with the principles of legality, fairness, transparency, adequacy, relevance and necessity as contained in Article 5 paragraph 1 of the GDPR.

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11.5. The Sponsor may send the data to other affiliates of the Sponsor's group and to 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 an adequate level of protection of personal data 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 does not guarantee an adequate level of protection pursuant to Articles 44 and 45 of the EU GDPR 2016/679, the Sponsor and the Entity must complete and sign the Standard Contractual Clauses document (this last document is not attached to this Agreement).

11.6. The Parties warrant that the persons authorized by them to process personal data for the purposes of 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 in accordance with the instructions given, in accordance with this article, by the data controller.

11.7. The Principal Investigator has been identified by the Entity as a person authorized for the data processing for the purposes of Article 29 GDPR and as a designated party for the purposes of Article 2 quaterdecies 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 data may also be accessed by the Monitors and Auditors 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 also the consent to the processing of personal data. The Entity is responsible for keeping the consent forms.

11.10 If either Party discovers a data breach, the other Party shall be informed within 48 hours from the breach having been verified, without prejudice to such Party's independent assessment of the existence 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/addenda together with the Protocol, form an integral part hereof, 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 an addendum 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 Entity and the Sponsor will comply with the anticorruption laws applicable in Italy.



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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 applicable in Italy, the principles of the US Foreign Corrupt Practices Act and its amendments. The Entity and its clinical and administrative facilities undertake to collaborate in good faith in accordance with the provisions of Italian laws mentioned above and will collaborate 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 For the purposes of Law 190 of 6 November 2012 ("Anticorruption Act") as amended, the Entity 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 own code of ethics which can be viewed at the webpage (...) *(insert link to website)*.

13.4. The Entity and the Sponsor shall immediately inform each other of any violation of this article by the other Party, of which they become aware, and will provide full 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 The violation of any provisions of this article will constitute serious breach of this Agreement pursuant to Article 1456 of the Italian Civil Code, if the relationship of trust between the Parties is affected.

**Art. 14 – Transfer of rights, assignment of contract and subcontracting, transfer of Trial data and/or results for registration purposes**

14.1. This Agreement is fiduciary in nature and therefore the Parties may not assign or transfer this Agreement to any third party without the prior consent of the other Party.

Each Party will allow the other Party to assign and/or transfer all or part of the rights and obligations received directly or indirectly from the signing of this Agreement to a successor or to a company or entity affiliated to it, on condition of acceptance by the transferee of all the terms and conditions hereof. Any transfer of rights taking place in the absence of such conditions shall be considered null and void and shall be disregarded.

14.2 In the event of a change of name of the Entity, no amendment to this Agreement shall be necessary. However, the Entity is required to duly inform the Sponsor of its change of name.

14.3 Any sale, licensing or transfer for any reason whatsoever (hereinafter referred to as "Transfer") of data and/or results of the Trial Drugs for the purpose of registration or development of the Trial Drugs may be made only in the manner set forth in Article 3 of the Ministerial Decree of 30 November 2021.

Pursuant to paragraph 2, letter a of said article and pending the issuance of the ministerial decree referred to in Article 1, paragraph 2, letter g no. 6 of Law no. 3 of 11 January 2018, the estimate of the value of the assets to be divested must take adequate account of the contribution of the public research centres to the conception and development of the data and/or results to be divested, providing for mechanisms of compensation or participation in any profits and benefits deriving from their commercialisation. All the proceeds of the divestment must be used for the unconditional financing of independent research projects.

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In relation to the provisions of Article 3, paragraph 5 of the Ministerial Decree of 30 November 2021, the Parties undertake to give notice of the transfer on their institutional websites, as information to patients involved in the trial.

#### **Art. 15 – Fiscal obligations**

15.1. This Agreement is signed digitally in accordance with the applicable regulations. All the 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 in accordance with the applicable regulations.

#### **Art. 16 – Governing law and Forum (*please refer to Circular letter no. 5 of the National Coordination Centre for the identification of governing law and competent forum (<https://www.aifa.gov.it/centro-coordinamento-comitati-etici>), Section “Circulars”*)**

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 the 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 \_\_\_\_\_, without prejudice, however, to the rules of necessary application of Italian law, in particular with regard to the protection of patients’ rights.

16.2. For any disputes that may arise in relation to 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 Courts of the \_\_\_\_\_’s headquarters shall have exclusive jurisdiction.

#### **Art. 17 – Language**

17.1. In the event of any discrepancy between the English language version and the Italian version of this Agreement, the Italian version shall prevail.

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

For the Sponsor

Legal Representative or his/her delegate (the CRO)

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

Signature \_\_\_\_\_

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

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For the Entity

The legal Representative or his/her delegate

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/or of 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 and unscheduled visit, as well as for 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 Entity for the trial <sup>1</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 there are no additional costs 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/or lab tests to be carried out according to the Tariff of the Entity (or over cost on the basis of 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/caregivers involved in the clinical trial: (if applicable)

<sup>1</sup> General administrative costs, costs incurred by the Pharmacy service in managing the Trial drug(s).

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

**LIQUIDATION AND INVOICES**

- The payment must be made within \_\_\_\_ days (state number) from receipt of the invoice.
- 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 on sets of personal data, whether or not by automated means, such as collection, recording, organization, 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. 4 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. 4 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 authorized 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 organizational structure, pursuant to art. 2 quaterdecies " 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 a clear 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, unauthorized disclosure, or access to, personal data transmitted, stored or otherwise processed;
- Medical Data - personal data pertaining to the physical or mental health of an individual including the provision of medical services, which may reveal information about his or her 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;

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- 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.