**CLINICAL TRIAL AGREEMENT WITH THE RESEARCH CENTRE**

In Valencia on, 18 October 2023

# BY AND BETWEEN

**The party of the first part** **(Centre)** Ms. Goitzane Marcaida Benito in her capacity as General Manager of the Healthcare Centre Consorcio Hospital General Universitario de Valencia [General University Hospital Consortium of Valencia] and on behalf of that organization, with address at Avda. Tres Cruces, s/n de Valencia (46014) and Tax Identification Code No. Q 4601065H.

**The party of the second part (Foundation)** Ms. Carmen Escobedo Lucea, in her capacity as Manager of the Fundación de la Comunidad Valenciana Hospital General para la Investigación Biomédica, Docencia y Desarrollo de las Ciencias de la Salud [Valencian Community Foundation General Hospital for Biomedical Research, Teaching and Development of Health Sciences] and on behalf of said organization, with registered address at Av. Tres Cruces s/n, with Tax Identification Code G-96792221

**Party of the third part**

**And the party of the fifth part (Principal Investigator)** xxxxxxxxx with D.N.I. xxxxx assigned to the Department xxxxxxx of the Healthcare Centre as Principal Investigator and acting in their own name and behalf, by way of acceptance and in compliance with the obligations they have undertaken.

**PURSUANT TO**

The provisions of Spanish legislation in force on clinical trials with medications and medical devices, and in accordance with ethical standards and Good Clinical Practice and laboratory practice applicable to the conduct of Clinical Trials.

**THE PARTIES HEREBY STATE**

The parties acknowledge each other’s necessary and sufficient capacity to be bound by this contract (“Agreement”).

The PURPOSE of this contract is to conduct at the Healthcare Centre of the General University Hospital Consortium of Valencia the CLINICAL TRIAL (“Clinical Trial”) entitled “**xxxxxxxxxx**code **xxxxxxxxxx** (hereinafter protocol) promoted by which will be directed by **Dr. xxxxxxx** (called Principal Investigator) of Department of **xxxxxx**of the healthcare Centre Healthcare Centre General University Hospital Consortium of Valencia (called Centre or Research Centre), in accordance with Clinical Trial Protocol with EUDRACT number: **xxxxxxxxx.**

**I.** That, to do so, the Sponsor has selected the most appropriate investigator according to their qualification and available means to carry out, direct and supervise the Clinical Trial at the Centre facilities, in accordance with the Protocol **xxxxxxx**, in accordance with the approval of the Spanish Agency of Medicines and Medical Devices.

**II.** That said Clinical Trial is intended to demonstrate xxxxxxxxxxxx with Protocol number **xxxxxx** EUDRACT **xxxxxxxxx** and which describes in detail the procedures and scope of the clinical trial to be conducted.

**III.** The Clinical Trial will be conducted after obtaining the mandatory authorization from the Spanish Agency of Medicines and Medical Devices and the favorable opinion from the Drug Clinical Research Ethics Committee (CEIC) of reference xxxxxxxxxxx dated xxxxxxxxxxxx)

That based on the above principles and objectives, the parties agree to enter into this contract under the following:

**CLAUSES**

**ONE.- Object**

Under this Agreement, the Centre hereby authorizes the conduct of the Clinical Trial at its facilities, referred to in APPENDIX I, II, III, which will be carried out, directed and supervised personally by the Principal Investigator to whom the research work is expressly conferred. Moreover, the Clinical Trial is conducted with an estimated number of xxxxx participating subjects and within an estimated maximum period of xxxxx months, as detailed in the Protocol, and said number and period may be modified when deemed necessary, after approval of the corresponding budget. Any deviation from this amount shall be reported by the Sponsor to the corresponding Drug Clinical Research Ethics Committee (CEIC).

**TWO.- Performance conditions.**

**2.1.- Protocol and Good Clinical Practice (GCP).**

The conditions for conducting the Clinical Trial shall be those established in the regulations in force, in the GCP standards and in this Agreement. The parties shall comply with the provisions of the Protocol, including any amendments or modifications that may be introduced therein from time to time, provided they have been signed and accepted by the Principal Investigator and the Sponsor, which shall keep in their files copies of the amendments and modifications that are made to the Protocol, upon approval of the modifications and amendments by the CEIC and the Competent Authority regarding clinical trials and medical devices in accordance with the provisions of Article 26 of Royal Decree 1090/2015, of December 4, regulating clinical trials with medicinal products, the Drug Research Ethics Committees and the Spanish Registry of Clinical Studies.

**2.2.-** **Term and duration.**

This Agreement will be effective from last signature’s date till end of Clinical Trial.

The Clinical Trial will start on the date on which authorization is obtained from the Competent Authority for clinical trials and medical devices or on the date this agreement is signed, whichever occurs later, and will have an estimated duration of **xxxxxx** months or more.

The study completion date is estimated to be xxxxxxxx.

The enrollment period is expected to end according to the protocol.

In the event that either the commencement or the duration of the Clinical Trial should be modified, it must be reported by the Sponsor to the Hospital and the CEIC.

**2.3.**- **Modification.**

The Protocol may not be amended unilaterally by the Principal Investigator, but rather will require the prior consent and approval of the Sponsor. The amendment of the authorized Protocol must be reported to the relevant Ethics Committee, Spanish Agency of Medicines and Medical Devices, and must have the approval of the Principal Investigator of the Clinical Trial.

Protocol modifications or amendments must be reported to the Centre, through the local CEIC. The Centre may, if it considers them to be an essential amendment or modification, by mutual agreement with the Sponsor, proceed to make the appropriate amendments to the Agreement and/or APPENDIX es thereto.

**2.4.-** **Ethical and Legal Standards.**

All parties undertake to comply with the Spanish legislation in force on Clinical Trials with Medicines: Royal Legislative Decree 1/2015, of July 24, which approves the revised text of the Law on guarantees and rational use of medicines and medical devices, Royal Decree 1090/2015 of December 4, Agreement of April 4, 1997 for the Protection of Human Rights and Dignity of Human Beings with respect to the obligations of Biology and medicine, ratified by instrument of July 23, 1999- date of entry into force in Spain on January 1, 2000 and other concordant regulations.

In the case of clinical trials with medical devices, these will be conducted in accordance with Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 regarding medical devices, which lays down the general requirements regarding clinical investigations with medical devices, and Royal Decree 192/2023 of 21 March, which regulates medical devices.

It is hereby agreed to be conducted in accordance with the Provisions of the latest version of the Declaration of Helsinki and in accordance with the ICH (International Conference of Harmonization Guideline) Good Clinical Practice (GCP) guideline.

The Hospital shall request that in the conduct of the Clinical Trial the fundamental rights of the person are fully respected, in accordance with the essential standards of Bioethics, Health and Good Practice standards applicable to the trial, without replacing the functions entrusted to the Sponsor, Principal Investigator and CEIC,and the applicable provisions of Law 14/2007, of 3 July concerning Biomedical Research.

**2.5.-** **Patient’s Informed Consent.**

The Principal Investigator, or his/her Co-Investigators to whom he/she has delegated this task, must inform the patient, in understandable verbal and written language, of the nature of the trial, and shall obtain the informed consent of said patient and/or his or her representative, in accordance with current legislation. The patient will receive a copy of this document and may withdraw their consent at any time.

Furthermore, the patient will be informed, through the informed consent, about the processing of their personal data pursuant to Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 regarding the protection of natural persons with respect to the processing of personal data and the free movement of such data, and Organic Law 3/2018 of 5 December regarding the Protection of Personal Data and guarantee of digital rights.

Both declarations of consent must be obtained prior to the subject’s enrollment in the Clinical Trial, and will be dated and signed. The Clinical Trial participant should be able to give consent after having been duly informed about the nature, significance, implications and risks entailed in their participation in the Clinical Trial, as well as alternative treatments. When the subject is not able to give consent or is not in a position to do so, the decision must be made taking into account the requirements of Royal Decree 1090/2015 of 4 December.

The versions of the patient information sheet (PIS) and informed consent form (ICF) for data processing will be those approved by the Ethics Committee.

The CEIC must approve the patient information sheet (PIS) and the Informed Consent Form (ICF) and the data processing consent form.

A copy of the informed consent forms shall be filed in the patient’s medical record with due retention standards.

For the duration of time that the electronic informed consent form does not exist or is not available, the copy of the informed consent form will be kept in the Principal Investigator’s file.

**2.6.-** **Access.**

The CEIC will have access at any time to the documentation relating to the Clinical Trial, necessary to follow-up on clinical trials set forth in regulations, especially to the informed consent forms of the patients participating in the Clinical Trial.

The clinical trial monitor will also have access at each visit to the relevant clinical documentation of patients included in the Clinical Trial. In any case, he/she must respect the confidentiality of the data in accordance with the laws in force. Similarly, the competent Health Authorities and monitors will have access to the patient’s clinical documentation to perform inspections and GCP audits.

**2.7.-** **Publication of results.**

The Sponsor undertakes to publish the results of this Clinical Trial. This publication will be submitted to the CRECs involved in the conduct of the Clinical Trial and the Principal Investigator for their knowledge. The Principal Investigator may present the results at an appropriate scientific meeting and/or publish them in a recognized scientific journal, undertaking to provide the Sponsor with a copy of the manuscript or original, sufficiently in advance, so that they have the opportunity to know such information or informative material to make their comments on the content of such communications or publications. Within the period specified in the Protocol and, failing that, within 30 days of receipt thereof.

The Principal Investigator undertakes to respect the agreements established in the Clinical Trial protocol that make special reference to the publication of the data, undertaking not to publish/disclose the data obtained at the Centre, until the Clinical Trial data has been published as a whole.

If requested by the Sponsor, in order to adequately ensure the protection of inventions or developments arising from the Clinical Trial, the Principal Investigator agrees to delay the presentation of the proposed publication, for a period not exceeding 6 months.

The Sponsor undertakes not to prevent and/or hinder the dissemination of joint results that, being scientifically sound and unquestionable, demonstrate the lack of efficacy or adverse effects of the treatment.

The Sponsor shall comply fully with article 42 on publications of Royal Decree 1090/2015 of 4 December, which regulates clinical drug trials.

**2.8.-** **Confidentiality and Data protection.**

All Clinical Trial-related information either before or after the Clinical Trial, provided or collected, are confidential. In any case, if the information is disclosed to a third party connected to the Clinical Trial, this third party will agree in writing to respect the secrecy and confidentiality of the information under these same terms.

This confidentiality agreement shall remain in force indefinitely after termination of this contract. The Principal Investigator agrees to have all members of the research team and any third party to whom they disclose confidential information relating to this study sign a confidentiality commitment in terms similar to those provided for in this agreement, or their compliance with the contents of this agreement, before commencing their collaboration in this study.

Finally, all parties and collaborating personnel must take the appropriate measures to keep the confidentiality of the personal data of which they become aware as a consequence of carrying out the Clinical Trial, preventing unauthorized third parties from accessing them. The Centre will respect it, and together with the Principal Investigator will restrict access to the information to those cases necessary for proper execution of the protocol.

In this regard, the Organic Law 3/2018 of 5 December on Personal Data Protection and guarantee of digital rights and Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016, on Data Protection (GDPR), Law 41/2002 of 14 November, basic regulation of patient autonomy and rights and obligations in terms of information and clinical documentation and Law 10/2014 of 29 December on health in the Valencian Community, must be strictly observed.

As long as the postulates of Article 2.7 are respected, the Hospital shall not be entitled to reveal or disseminate by any means the results, data and information that directly or indirectly result from the conduct of the Clinical Trial, even for scientific purposes, without written authorization from the Sponsor.

The personal data of the Principal Investigator provided to the Sponsor may be processed by the Sponsor. This data will allow the Sponsor to maintain the relationship with the Principal Investigator, send them information about the products and projects of the Sponsor and may be communicated to other companies of the group for the same purposes respecting in all cases the requirements derived from Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 regarding the protection of natural persons with respect to the processing of personal data and the free movement of such data. The Principal Investigator reserves the power to exercise their rights of access, rectification, erasure, limitation of processing, opposition, right to the portability and revocation of consent, by sending a written notice to the Sponsor.

All Parties agree to comply with the provisions of the Data Protection APPENDIX A of this contract.

**2.9.-** **Filing of documentation:**

Patient records will have a permanent, expeditious and fast system to identify that a patient participates or has participated in a clinical trial.

The obligations included in the Organic Law 3/2018 of 5 December on Personal Data Protection and Guarantee of the Digital Rights and Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on Data Protection (GDPR) must be guaranteed.

The media used to preserve essential documents shall ensure that the documents remain complete and legible, and that they are available to the competent authorities if requested during the provided retention period.

Where the media used to retain essential documents are in electronic form, they shall ensure that any modification of the records is traceable, allowing the initial and corrected data to be known, as well as the date and signature of the author, including at least the following:

- Accreditation resolutions and subsequent modifications.

- Curriculum vitae of current or former members of the Committee.

- Summons to and minutes of Committee meetings.

- Standard operating procedures of the Committee, current version and historical archive.

- Record book.

**THREE.- Participants and Conduction Centre**

**3.1.-** **Participants**

**3.1.1.- Sponsor**

**3.1.2.- Principal Investigator**:

The Principal Investigator shall take care and guarantee that all participants in the Clinical Trial and, especially, its collaborators faithfully comply with this agreement and its APPENDIX es, having been sufficiently informed of its details.

**3.1.3. – Collaborators:**

**3.1.3.1-. Collaborative team:**

The Principal Investigator’s team of co-investigators, consisting of the staff who, together with the Principal Investigator and under their coordination, participates in the Clinical Trial, must be approved by the CEIC and be trained to successfully comply with the foreseen Clinical Trial, complying with the requirements of the certificate of suitability.

The Principal Investigator is committed to notify the CEIC and the Centre’s management of all modifications and updates of the functions of the team involved in the Agreement.

**3.1.4. - Other staff**:

If, for the development of this Clinical Trial, contracting personnel from outside of the Centre is required, the hiring will be reported at the Centre for the purposes of inspection and the authorization of access, and for participation in the protocol via the relevant accreditation.

None of the provisions of this contract constitutes or may constitute an employment relationship between the Centre and persons outside the Centre who participate in the Clinical Trial.

**3.1.5.- Monitor:**

The Sponsor, in compliance with the provisions of Article 39 and 40 of Decree 1090/2015 of 4 December, designates as Clinical Trial monitor of the company **xxxxxxxx.**

In case of replacement, the Sponsor will inform of the identity of the new designated monitor.

**3.2.-** **Centre:**

The Clinical Trial regulated under this Agreement will be conducted in the Service, Unit, Department/s, centre/s of Oncology of the healthcare Centre General University Hospital Consortium of Valencia.

**FOUR.- Product Supply and extra equipment:**

**4.1. - Product:**

The Sponsor shall supply, through the Hospital Pharmacy Department the products for the conduct of the Clinical Trial at no cost to the Centre, as established in Art. 39.f. of Royal Decree 1019/2015; in exceptional situations and with prior written agreement, other means of supply or funding may be used. Said product may not be used, sold or supplied to any third party without prior written approval from the Sponsor

In the event that, after completion of the Clinical Trial, the product is in surplus, the Principal Investigator and the Centre shall be obliged to return it to the Sponsor as soon as possible. The Centre shall take the necessary measures to ensure that the refund is paid. Upon completion of the Clinical Trial, the Sponsor shall agree with the Hospital the procedure for withdrawing, disposing, or transferring such surplus (if marketed products).

**4.2. - Equipment:**

In the event that special equipment is required to conduct the Protocol, it will be acquired and installed by the SPONSOR, with the authorization and supervision of the SITE. Furthermore, the SPONSOR will be responsible for its maintenance costs during the trial. Upon completion of the protocol, the sponsor may collect the extraordinary equipment at its own expense. In the event of a transfer of machinery by the Sponsor, this must be done under a due contractual agreement.

In the present trial, the equipment is the following: **xxxxxxxxxx**

**4.3. - Additional tests:**

The tests to be performed on patients at the Centre to conduct the Clinical Trial, which are not usually administered for their process during their stay at the Centre, will be defrayed by the Sponsor, who will be billed per APPENDIX II.

**FIVE - Financial relations:**

The financial report for the Clinical Trial should specify the following sections:

**5.1. -Budget and Financial report.**

According to the financial report attached as APPENDIX II to this Agreement: The initial Clinical Trial budget should include all trial remuneration, i.e., payments to the Centre and Foundation (clinical trial management, direct and indirect costs), to the research team and to patients travel reimbursements, and should be broken down into the following sections:

**I. Extraordinary costs for the Centre and patients:**

I.a. Administrative management of Clinical Trials

I.b. Compensation to Foundation.

I.c. Compensation to patients (if applicable): (only reimbursement of patient travel costs..

**II. Regular Clinical Trial costs (patient recruited):**

II.a. Indirect costs (in phase I and II studies it will be 30% of the budget established for each patient recruited, in phase III and IV studies it will be 40% of the budget established for each patient recruited).

II.b. Compensation for Principal Investigator and collaborators (in phase I and II studies it will be 70% of the budget calculated for each evaluable patient recruited, in phase III and IV studies it will be 60% of the budget calculated for each evaluable patient recruited)

- Principal Investigator

- Collaborators

- Consideration to other departments

- Other personnel costs

II.c. Compensation for the Pharmacy Department, in case of clinical trials, and other (up to 10%).

**III. Patients who do not complete the Clinical Trial.**

**5.1.1. – Extraordinary costs for the Centre and patients:**

1. For **administrative management** of the Clinical Trial, the one-time amount of **€1500 + VAT** will be paid regardless of the number of agreements generated. The payment will be made against the presentation of the corresponding invoice correctly issued to the sponsor within a period not exceeding 60 days from receipt thereof.

Payment to the Foundation shallbe made upon submission of the corresponding invoice within a period of no more than 60 days from the signing of the document by the Centre’s management, and before starting the study, to the following address and bank account:

**Entity:** CAIXABANK, S.A.

**Address:** PINTOR SOROLLA 2-4 46002 VALENCIA

**Account No.:** 2100-8706-3713-0033-8021

**IBAN**: ES54-2100-8706-3713-0033-8021

**SWIFT**: CAIXESBBXXX

**In the name of:** FUNDACIÓN Hospital universitario DE VALENCIA para la INVESTIGACIÓN biomédica, DOCENCIA Y DESARROLLO DE LAS CIENCIAS DE LA SALUD.

b) The **Centre’s extraordinary direct costs** shall include all those tests or specific materials necessary for carrying out the Clinical Trial. The extraordinary direct costs will be specified in detail by the Principal Investigator in APPENDIX II and accepted by the Sponsor and by the Centre. The extraordinary costs of the Centre will be billed to the Sponsor taking as reference the rates of the Law of Generalitat Valenciana’s [Government of Valencia] fee for Health Services Billing, the Valencian Health Agency, or, in its absence, for the cost thereof.

c) **Remuneration to patients**. Where appropriate, due to participation in the Clinical Trial, and as agreed with the sponsor, patients shall be reimbursed the amount budgeted in APPENDIX II.

**5.1.2. – Regular Clinical Trial costs (patient recruited):**

a) The Sponsor agrees to pay the amount of €.**xxxxxxx** per concluded and evaluable patient as described in the Protocol, amount to which **€0** of extraordinary tests and processes carried out with Centre means shall be discounted. The maximum number of patients to enroll will be 10 patients.

b)For general partnership **(indirect costs)** for the conduct of the Clinical Trial, the amount of **xxxxxxx** per patient will be paid. This amount will be understood to cover indirect costs, with the Foundation issuing the corresponding invoice, to which the corresponding VAT will be added.

c) Payment of compensation to the Principal Investigator, as well as the additional legal obligations is the responsibility of the Sponsor. Remuneration for Principal Investigator will be € **xxxxxxxx** per patient (compensation will not exceed 70% of the amount budgeted per patient). Wherever possible, if there is capacity to do so, payments to Principal Investigator should be made by the Foundation or Ste, not directly by the Sponsor.

**There will be a single Additional Payment of €600 t+ VAT for archival custody: Through this payment, the Principal Investigator, and the Sponsor commission the Valencian Community General Hospital Foundation to safeguard the master file of the Principal Investigator, under the conditions required by Article 43 of R.D. 1090/2015, in an archive external to the “Valencia General Hospital” University Hospital, managed by the company GRUPO ENTORNO DOCUMENTAL, S.A. (GEDSA). In the aforementioned file, the Sponsor’s documents that allow the identification of the Clinical Trial subjects will also be safeguarded.**

**5.1.3. – Financial statement:**

The overall financial cost of the Clinical Trial is calculated at “**xxxxxxxx** euros” per patient (not including VAT). The breakdown of the Clinical Trial is included in APPENDIX II of this contract FINANCIAL REPORT OF THE CLINICAL TRIAL IN PHASES III AND IV), which specifies both the direct and indirect costs of the Clinical Trial (financial compensation for investigators, administration and management costs, Clinical Trial Centre and process costs, financial compensation for Clinical Trial subjects, and other costs).

In the event that a patient, for whatever reason, abandons the Clinical Trial before the end of the Clinical Trial, the Sponsor will be obliged in any case to pay the proportional part of his/her participation in the Clinical Trial. To such amounts the corresponding VAT shall be applied, which shall be paid by the Sponsor, in accordance with the provisions of clause 5.1.2.

In the event of the early termination of the Clinical Trial, for whatever reason, the amount to be paid will be modified proportionately according to the number of patients included and the length of time they remained in the Clinical Trial.

**5.1.4. Payment methods:**

The following payment periodicity is established:

The amount shall be paid on a quarterly basis according to the number of visits completed by the patients enrolled in the Clinical Trial protocol in that period.

In the event that the sample size is expanded and modified in the protocol, or new patients are enrolled in the Clinical Trial, the Sponsor will communicate to the Hospital the modification of the protocol and will proceed to revise the financial report, through an APPENDIX thereto in the billable items.

The sponsor undertakes to provide to the financial directorate of the Foundation **Fundación de la Comunidad Valenciana Hospital General para la Investigación Biomédica, Docencia y Desarrollo de las Ciencias de la Salud** upon completion of the Clinical Trial with code **xxxxxxxxxx** a copy of the settlement of expenses corresponding to the aforementioned trial.

The Sponsoring Entity states that it has not, nor will it establish agreements apart from this contract with the Principal Investigator, their collaborators, or with any institution directly or indirectly involved in the performance of this Clinical Trial, from which arise additional financial payments or considerations in kind. In the event that for any reason it is necessary to sign a supplementary agreement, it will be appended as an amendment to this Agreement.

**SIX.- Clinical Trial Sponsor’s obligations:**

Established in accordance with current clinical trial laws.

Regarding clinical trials with medical products, the Sponsor, agrees to provide said products free of charge, taking into account the current legislation regarding administrative contracting.

The Sponsor must inform the CEIC and the Hospital Management of the start and end of the Clinical Trial.

The Sponsor must make an initial visit to the Pharmacy Department to agree on the details of the development of the Clinical Trial on medicinal products.

**SEVEN.- Monitor’s obligations:**

Established in accordance with current clinical trial laws.

**EIGHT.- Obligations of the Principal Investigator:**

The Principal Investigator is responsible for the Clinical Trial meeting the requirements and conditions established in the corresponding administrative authorization, in accordance with the obligations contained in the current legislation on clinical trials.

Use of Electronic Data Capture. In this study Electronic Data Capture ("**EDC**") will be used to collect from Principal Investigator and deliver to Company study data, specifically as the electronic case report form ("eCRF"). Principal Investigator agrees that it will (i) enter such study data into EDC within 5 business days of the subject visit, and (ii) resolve all queries issued in the EDC system within 5 business days of the query being issued. In addition, Principal Investigator or sub-investigator shall review data entered into EDC for accuracy and completeness and apply electronic signature within 20 business days of Subject visit. In the event of delay(s) by Principal Investigator in complying with these timelines Company, at its option, may delay payment, suspend enrollment, conduct quality audit or pursue any other remedy.

**NINE.- Pharmacy Department Obligations:**

a) Maintain an updated file detailing the drugs used in the Clinical Trial until the end of the Clinical Trial, at which time the remaining medication may be transferred to the Sponsor together with the study master file, as well as control of the quantities issued and the respective dates of issue.

b) When agreed with the Sponsor, it will be responsible for ensuring that the randomization codes are safeguarded in a place that is accessible in the event of an emergency.

c) It will be responsible for the correct handling and preservation of the medication, understanding as such, oversight in receiving the medication, correct storage, oversight of dispensation and return to Sponsor of the surplus medication.

d) The Pharmacy Department will be involved in the decision to start each clinical trial that must have its cooperation. If the Principal Investigator does not inform the Pharmacy Department of the commencement of the Clinical Trial, the pharmacy may not provide the study medication, so the contract may be terminated.

**TEN.- Clinical Trial Documentation Archive:**

a) The Clinical Trial Sponsor and Principal Investigator are responsible for archiving Clinical Trial documentation as outlined in current applicable laws.

b) The Principal Investigator shall ensure that subject identification codes are retained for at least twenty-five years after the conclusion or discontinuation of the Clinical Trial.

c) The patient’s medical records and other original data shall be kept in accordance with the legislation in force

d) The Sponsor or data owner shall retain all other Clinical Trial-related documentation during the drug’s period of validity, in accordance with current clinical trial laws and the internal Centre rules.

e) Any change in the possession of the data shall be documented.

f) All data and documents shall be made available to the competent authorities on request.

g) The confidentiality of the data and documents contained in the archive shall be ensured in all cases.

h) In any case, the parties agree that they will conform to the model of rules ICH (International Conference of Harmonization Guideline) for Good Clinical Practices (GCPs).

**ELEVEN.- Reports and ownership of results:**

**11.1. - Reports:**

The parties agree to collaborate and reciprocally inform one another regarding the Clinical Trial, its follow-up, and the results thereof, complying to this effect with the requirements set out in Article 39 of Royal Decree 1090/2015. Within one year of the end of the Clinical Trial, the Sponsor shall submit to the Spanish Agency of Medicines and Medical Devices, and to the Clinical Research Ethics Committees involved, a summary of the final report on the outcomes of the Clinical Trial.

**11.2. - Ownership of results:**

The parties agree that all rights, data, results and discoveries or inventions, patentable or otherwise, made, obtained or generated in connection with the Clinical Trial, shall be the exclusive property of the Sponsor.

In the case of contracts with zero financial report, the parties agree that the intellectual and industrial ownership of the results deriving from this Clinical Trial be shared, in proportion to the contribution of each party to the research in question. In the instruments for the protection of the knowledge generated, this circumstance of co-ownership shall be expressly stated. The expenses necessary for the protection of such property, will be assumed by the parties in the same terms. Not Applicable.

**TWELVE.- Insurance and liabilities:**

12.1. The Sponsor of this Clinical Trial has contracted civil liability insurance, which covers the legal liabilities under the terms established by the regulations on clinical trials and the regulations on contracting insurance in our country. The policy’s certificate is attached to this Agreement.

The Sponsor undertakes to maintain insurance coverage for the duration of the Clinical Trial.

In the event of an increase in the number of patients, the Sponsor undertakes to extend the corresponding insurance coverage.

12.2. In all cases, the Centre shall notify the Sponsor each time it becomes aware of a complaint, grievance, claim, or legal action, whether real or potential if known.

**THIRTEEN.- Parties’ representation:**

The Centre does not represent the Sponsor before third parties in any way.

The Sponsor shall notify the hospital, through the Drug Clinical Research Ethics Committee (CEIC), of any amendment to the protocol that should be effected during the conduct of the same, such as an extension of the recruitment period, the renewal of the civil liability insurance policy, the renewal of the authorization of the investigational medicinal product, etc..., as well as the final report on the closure of the Clinical Trial, with the list of patients enrolled and the final sample balance (samples used and samples returned).

No information about Clinical Trial data may be disclosed by the Centre or Principal Investigator to the media or to personnel associated with financial market operators. The Principal Investigator, on their own behalf and that of the collaborators, agrees not make use of privileged information that their participation in the Clinical Trial may provide for their own benefit.

**FOURTEEN.- Audits and Inspections:**

The hospital and the Principal Investigator and his collaborators and Sponsor will enable health authorities to inspect their Clinical Trial Records and sources associated with the Clinical Trial, when requested.

The Hospital and the Principal Investigator and their co-investigators shall assist the monitor or auditor designed by the Sponsor to review (or examine) their Clinical Trial Records and sources associated with the Clinical Trial, when requested, if applicable.

**FIFTEEN.- Regulation and Jurisdiction:**

15.1- **Contractual.-** The parties agree that their relations are regulated by the content of this contract, without prejudice to the regulation set forth in the Protocol and other concordant documents that are signed in relation to this document. Any previous agreement, express or tacit, documented or not, from which economic considerations other than those set forth in this Contract derive, is null and void, and without effect. This contract shall only be deemed to have been modified or amended by written agreement of the parties and in accordance with subsection 2.1.- of this contract.

**15.2.- Legislative.-** This contract is subject to Spanish laws and regulations

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**15.3.- Jurisdiction.-** The parties submit to the jurisdiction of the Valencian Community, expressly renouncing any other jurisdiction that might be applicable.

**SIXTEEN.- Causes of suspension and termination**

Causes of termination:

**16.1*.-* Ordinary.-** The contract shall end at the end of the Clinical Trial.

**16.2- Extraordinary.-** This contract may be suspended or terminated, upon written notification, in the event of any of the causes set forth in Royal Legislative Decree 1/2015, of July 24, approving the consolidated text of the Law on guarantees and rational use of medicines and medical devices, or it may end, or be modified, in the following cases:

* Failure to include a minimum number of patients to allow the final assessment of the Clinical Trial within a reasonable amount of time.
* For a duly justified cause.
* Whether the total number of patients to be included in the Clinical Trial by the different investigators participating in the Clinical Trial is reached for a competitive, multicenter trial.
* Sponsor may terminate this Agreement early without cause upon 30 days prior written notice to the other parties.

In the event of suspension or early termination of the contract, the CRO will only pay the amount corresponding to the work done based on the number of visits made by the patients evaluable up to that time.

Upon suspension or termination of the Clinical Trial, the Principal Investigator and/or Centre shall return to Sponsor the supplied material and any unused medication in their possession.

**16.3.- Termination of the agreement** will lead to the settlement of the financial relationships between the parties, without prejudice to the liability insured in Clause Twelve.

Upon suspension of the Clinical Trial, the Principal Investigator shall return to the Sponsor any material supplied by said Sponsor and all unused medication that remains in its possession.

The Sponsor shall be liable for the payment of all services which have been provided up to the date of suspension, except:

- To the Centre, those services that, by being performed incorrectly, caused the suspension of the Clinical Trial.

- To the Principal Investigator if the suspension results from non-compliance with their duties and obligations.

The Clinical Trial shall be suspended before the scheduled date, regardless of its current phase, if any of the following circumstances occur:

a) If, from the available data, it is inferred that it is not safe or justified to continue administering the Clinical Trial drug and/or the comparative drug or placebo to the patients.

b) Due to breach by the Principal Investigator of any of the terms of this contract and/or the Protocol.

c) The suspension is agreed by common consent between the contracting parties. Such an agreement shall be in writing.

In the event of early termination, the Principal Investigator shall provide the Sponsor with a report of the results obtained up to the time of the discontinuation of the investigation.

In all these cases, the Sponsor will pay the Foundation and the Clinical Trial subjects the amounts corresponding to the work correctly carried out.

**SEVENTEENTH. -Anticorruption Clause**

Center and Foundation represent and warrant that they, or any person or company working on behalf of them, including but not limited to the Principal Investigator, shall not, directly or indirectly, offer, pay, promise to pay, or authorize such offer, promise or payment, of anything of value, to any person or entity for the purposes of obtaining or retaining business or any improper advantage in connection with this agreement, or that would otherwise violate any applicable laws, rules and regulations concerning or relating to public or commercial bribery or corruption (hereinafter, “AntiCorruption Laws”). Center and Foundation further represent and warrant that any invoices, or related records, that relate to this agreement or relate to any work conducted for or on behalf of Sponsor shall be complete and accurate. Center and Foundation further covenant and agree that Sponsor may, through CRO, terminate this agreement if Center and Foundation or any person or company working on their behalf (i) fails to comply with any anti-corruption laws or with the restrictions contained in this article, or (ii) if Sponsor has a good faith belief that Center or Foundation or any such person has violated, intends to violate, or has caused a violation of the anti-corruption laws. If Sponsor requires that Center or Foundation complete a compliances certification, Sponsor may also terminate this agreement if Center or Foundation (a) fails to complete a compliance certification, (b) fails to complete it truthfully and accurately, or (c) fails to comply with the terms of that certification. In particular, Center or Foundation shall comply with the provisions set out in the criminal code under the bribery and corruption among individuals section.

In witness whereof and after reading this contract, all parties sign three equal counterparts at the place and date indicated in the heading.

**xxxxxxxxxxxxx**

Signed: xxxxxxxxxx

**xxxxxxxxxxxxxxx**

Signed: **xxxxxxxxxxxxxxxx**

**BY THE CENTRE**

Signed: Ms. Goitzane Marcaida Benito

MANAGING DIRECTOR

**BY THE PRINCIPAL INVESTIGATOR BY THE FOUNDATION**

Signed: Signed: Ms. Carmen Escobedo Lucea FOUNDATION MANAGER

**APPENDIX I**

**TECHNICAL REPORT**

# DETAILS OF IDENTIFICATION OF THE CLINICAL TRIAL

**Clinical Trial Title:**

**Principal Investigator:**

**Protocol Code:**

**EUDRACT No.:**

**Protocol Version:**

**Patient Information Sheet and Informed Consent Form:**

**Reference EC:**

**Date of approval:**

**Appendix II**

**FINANCIAL REPORT OF THE CLINICAL TRIAL IN PHASES III AND IV**

**Trial name: “(no. of estimatied patients):**

**Protocol:**

**Sponsor:**

**Principal Investigator:**

**Service:**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **TOTAL TRIAL BUDGET:** | COST PER PATIENT | TOTAL (estimated PATIENTS) |
| **I.** | **Total Extraordinary costs for the Centre and Patients** | €\*\* | €\*\*\* |
|  | I.a. Administrative management of the Clinical Trial |  |  |
|  | I.b. Institution compensation |  |  |
|  | I.c. Patients compensation |  |  |
| **II.** | **Trial Ordinary costs (per recruited patient)** |  |  |
|  | II.a. Indirect costs (40%) |  |  |
|  | II.b. Compensation for Principal Investigator and Collaborators (60%) |  |  |
|  | Principal Investigator |  |  |
|  | Collaborators |  |  |
|  | Compensation to other services |  |  |
|  | Other staff costs |  |  |
|  | II.c. Compensation for Pharmacy Service and others |  |  |
|  | Pharmacy Service |  |  |
| **III** | Patients not completing the Trial |  |  |
|  | **TOTAL TRIAL BUDGET \*** |  |  |

\* The budget for complete, assessable patients is **12203.54 €** to which **€1500** have been added as set forth in article 2 of the Resolution of 16 July 2009, of the Ministry of Health [2009/8925)

THESE AMOUNTS DO NOT INCLUDE VAT

|  |  |  |
| --- | --- | --- |
| **VISITS** | **COST PER VISITA** | **I. Extraordinaty tests procedures** |
| Screening |  |  |
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| **TOTAL** |  |  |

\*\*Administrative Fee is not related to the no. of enrolled patients

**Fee Per Completed Subject:**

A detailed breakdown of the Study Budget can be found in the table above. CRO shall not be responsible for ensuring that Foundation makes any payments in this APPENDIX II to the Principal Investigator, Study Personnel and its internal departments.

**Other Payments:**

Payment for other fees or expenses that are not included in the Fees per Completed Subject (as defined above) will be made according to the Foundation’s fees as per published list of costs or up to the maximum amount established by the Sponsor according to the rates that constitutes fair market value.

Foundation shall submit invoices for Services performed and expenses incurred under this section, all payments will be made within forty-five (45) days of receipt from the date of receipt of valid invoice in accordance with this Payment Schedule.  All payments will be made by electronic wire to the bank account stated above.

|  |  |  |  |
| --- | --- | --- | --- |
| IV. OTHER Extraordinary TESTS and procedures | | | |
| **Type of test or procedure** | **No. of estimated tests** | **Cost per unit** | **Total cost** |
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|  |  | TOTAL |  |

**INVOICING DATA**

Issued to:

**CONTACT PERSON**

**APPENDIX III**

**RESEARCH TEAM LIST**

**CERTIFICATE OF SUITABILITY OF RESEARCH TEAM**

**Sponsor:**

**Title:**

**Protocol Code:**

**Dr Service, Principal Investigator of the Trial,**

**Hereby states:**

* That he has the material and human resources required for the correct and safe conduct of the Clinical Trial.
* That the Clinical Trial team required to conduct the Clinical Trial is that proposed and after its evaluation it has been deemed suitable.
* This team will consist of:

In Valencia, on 11 august of 2023

Signed:

Principal Investigator