AGREEMENT FOR CONDUCTING THE CLINICAL TRIAL: _____

(Protocol code___, Foundation code number___/__)

Madrid, on ____ _____ 2014

BEING ASSEMBLED

(fill in with your own data)
Of the one part, **Mr/Ms/Mrs.** _____ with Tax Identity Number ..... acting respectively on behalf and in representation of … (hereinafter the **SPONSOR**), with Tax Identity Code … and registered address … , duly authorized to execute this document by virtue of a deed of power of attorney duly registered with the Companies Register of _____, authorized by the Notary Public Mr/Ms/Mrs_____, of the Notary Association of _____ on _____ (date), number ____ of his/her records, with VAT number _____,

Mr/Ms/Mrs._____ *(name of the legal representative of the CRO)*, with Tax Identity Code _____ acting as legal representative of _____ *(name of the CRO) and* with registsred address_____*(full address of the CRO),*_____*(town/city and post code), with Tax Identity Code/VAT number* _____, (hereinafter '**CRO'**), acting on behalf and in representation of the **SPONSOR** _____ *(full name of the sponsoring entity –pharmaceutical laboratory, scientific association/entity, corporate person),* (hereinafter '**SPONSOR'**), authorized to execute this document by virtue of a deed of power of attorney duly registered with the Companies Register of _____, authorized by the Notary Public Mr/Ms/Mrs_____, of the Notary Association of _____ on _____ _____ _____. This is without prejudice of the Sponsor's responsibility under RD 223/2004;

Of another part, **Javier Maldonado González**, with Tax Identity Numver 378 887-P, Managing Director of the **RAMON Y CAJAL UNIVERSITY HOSPITAL** (hereinafter, **HOSPITAL**), domiciled at, Carretera de Colmenar Viejo, Km 9,100 P.O. 28034 Madrid, Spain, with C.I.F. No Q-2877004-H, acting under the authority delegated by Resolution of February 25,2011 the Deputy Ministry of Healthcare of the Ministry of Heath of the Community of Madrid.

Of another part, **José Ignacio Flores Nicolás**, with Tax Identity Number 5.629.501-K, acting on behalf and in representation of the **RAMÓN Y CAJAL UNIVERSITY HOSPITAL FOUNDATION FOR BIOMEDICAL RESEARCH**, (hereinafter '**FOUNDATION'**), with registered address Carretera de Colmenar Viejo, Km 9,100, Madrid, 280434, with VAT number G-8372984, duly authorized to execute the present document by virtue of the power of attorney authorized in Madrid on 15 January 2010 by the Notary Public of Madrid Mrs Carmen Boulet Alonso, with number 48 of her record,

And of another part, Mr/Ms/Mrs ---, with Tax Identity Number ----, acting on his/her own behalf and representation (hereinafter '**PRINCIPAL INVESTIGATOR'**), with domicile for notification purposes the ------ Service of the **HOSPITAL** with address at …..*)*

The Parties mutually acknowledge their capacity to enter into, and the binding force of, this Agreement (hereinafter **the Parties**),

THEY STATE

That ***SPONSOR*** expresses its interest in conducting the **CLINICAL TRIAL** described in the First Clause of the Agreement.

*That the **CRO**, as the **SPONSOR'S** legal representative, is authorized to carry out payments on behalf of the **SPONSOR**, and that the CRO's signature is not required for the amendment/change of all other aspects of the Agreement in which the CRO is not directly involved.*

That according to the provisions of the Agreement signed on 17 June 2009 between the **FOUNDATION** and the SERMAS, the ***FOUNDATION's*** functions are, among others, the management of any **CLINICAL TRIAL**s to be conducted at the **RAMÓN Y CAJAL UNIVERSITY HOSPITAL**

Also, that by virtue of the agreement between the **HOSPITAL** and the **FOUNDATION** for the development of clinical trials, it is the FIBIO-HRC responsibility to enter into the required agreements and to effectively execute any clinical trials to be conducted at the **RAMON Y CAJAL UNIVERSITY HOSPITAL.**

Now, therefore, the Parties express their interest to execute this Agreement according to the following

CLAUSES

ONE.- OBJECT

1.1. The purpose of this Agreement is to conduct a **CLINICAL TRIAL** under the title _____(hereinafter the '**CLINICAL TRIAL'**) with protocol code _____ (hereinafter the '**PROTOCOL'**), to be conducted mainly within the **HOSPITAL's** premises identified above, under the leadership and responsibility of Dr……. acting as **PRINCIPAL INVESTIGATOR** in said trial. The **CLINICAL TRIAL** shall be conducted according to the specifications detailed in the **PROTOCOL**, **version no.** …..**of** …. (date), i.e., the same as has been reported to the **HOSPITAL**...'s CREC (Clinical Research Ethics Committee) and with the Favourable Opinion of the CREC of reference (details of the CREC of reference) dated _____.

TWO.- START AND DURATION

2.1. This Agreement is effective as of the date of execution and shall remain valid and in force until the **CLINICAL TRIAL** has been fully completed, without prejudice to the provisions of Clause NINE. To such effects, the **CLINICAL TRIAL** shall only been considered as fully completed upon due execution by each Party of their respective obligations of this Agreement.

2.2. The **CLINICAL TRIAL** shall not be initiated unless and until the mandatory permission of the Spanish Agency for Drugs and Health Products ('Agencia Española de Medicamentos y Productos Sanitarios') (hereinafter '**AEMPS'**) has been obtained in the terms provided by Royal Decree 223/2004, and also until the authorizations of both the competent CREC, the **HOSPITAL** Management and any other, if any, required by the laws have been obtained**.** The effectiveness of this Agreement, with protocol version.... of date .... is subject to the authorizations above being obtained in due course. The Parties acknowledge that each of them is responsible for the execution of the **CLINICAL TRIAL** exactly as per the specifications contained in the **PROTOCOL.**

2.3. The estimated duration of the **CLINICAL TRIAL** is ... month(s), as specified in the **PROTOCOL.**

THREE.- APPLICABLE LAWS

3.1. The Parties agree to abide by and to respect at all times the applicable laws both upon the execution of this Agreement and at all times during its term. The applicable laws shall be in force with respect of the Agreement even if any of them is amended, which amendment shall be

automatically applicable to the Agreement. The Parties also agree expressly to abide by the ethical principles and policies, and in particular:

3.1.1. Act 10/2013, of 24 July, implementing in Spain Directive 2010/84/EU of the European Parliament and the Council, of 15 December 2010, on Pharmacovigilance, and Directive 2011/62/EU of the European Parliament and the Council, of 8 June 2011, on prevention of the entry into the legal supply chain of falsified medicinal products, and amending Act 29/2006, of 26 July, on Guarantee and the Rational Use of Medicinal Products, and Act 28/2009, of 30 December, amending the former.

3.1.2. ROYAL DECREE 223/2004, of 6 February, governing the conduct of **CLINICAL TRIAL**s with medicinal products (hereinafter, 'RD 223/2004')

3.1.3. DECREE 39/1994, of 28 April, governing competencies in the field of **CLINICAL TRIAL**s with medicinal products of the Madrid Community.

3.1.4. Order SCO 256/2007, of 5 February, establishing detailed principles and guidelines of good clinical practice, and requirements to authorize drug manufacturing or imports for research on human subjects, and Order SCO/362/2008, of 4 February, amending the former.

3.2. Act 15/1999, of 13 December, of Personal Data Protection, and Act 41/2002, of 14 November, governing the Basic Aspects of Patients' Autonomy.

3.3. Act 1/1998 of the Madrid Community, of 2 March, of Foundations. Under its article 23, patrons may contract with the foundation either on their own behalf or in that of a third party, subject to obtaining prior authorization from the Foundations Authority.

3.4. The Parties agree also to comply with the rules on incompatibilities of the staff at the service of Public Administrations under Act 53/1984, of 26 December, and Royal Decree 598/1985, of 30 April.

3.5. The Parties agree that the **CLINICAL TRIAL** shall be conducted under the Principles of the Helsinki Declaration and according to the International Conference of Harmonization (ICH) Guideline for Good Clinical Practice; they shall comply also with the applicable deontological principles and the international and local anti-bribery and anti-corruption laws, in particular those adopted under the OECD Convention of 21 November 1997, the Foreign Corrupt Practices Act and any other that may be applicable to the Parties of the Agreement.

FOUR.- DUTIES OF THE PARTIES

4.1. The contracting parties are bound to fully implement all clauses of this Agreement in its own terms, as well as those of the **PROTOCOL**. Each party shall comply with their respective obligations as per the legislation indicated in Clause THREE. Each party's obligations, duties and functions under RD/2004 are deemed binding content of the present Agreement, and consequently any violation thereof shall be considered as non-compliance of the Agreement.

4.2. The Parties are committed also to:

4.2.1. Collaborating in the **CLINICAL TRIAL** follow-up visits conducted by: (i) the CREC, (ii) the monitors and auditors acting on behalf of the **SPONSOR**, and (iii) the competent authorities when conducting inspection interventions. There shall be at least a one week notice prior to these visits (unless the Parties agree otherwise). Technical and organizational steps will be

taken during these follow-up, monitoring and audit visits to ensure full compliance with any applicable personal data protection statute.

4.2.2. The **PRINCIPAL INVESTIGATOR**, the **SPONSOR**, the monitors and the auditors shall comply with both the **HOSPITAL** and the **FOUNDATION** internal rules as shall be notified by them, and with the instructions from the monitoring CREC about the execution of the **CLINICAL TRIAL**.

4.2.3. Not entering into any agreements or commitments related to the implementation of the **CLINICAL TRIAL** that might result in exceptions or contradictions with its content. Therefore, each Party states that, at this date, none of them is a party in any agreement or pact that might contradict its content. In particular, by virtue of this Clause, the Parties agree that they shall in no event compromise or pay any compensation whatsoever other than those provided for in the Agreement, without prejudice to the expenses incurred for the attendance to/celebration of the meetings required to organize and supervise the execution of the STUDY and the meetings designed to analyze or make the STUDY's results public (presentations or scientific publications).

4.3. In addition to the obligations stated in the applicable norms, the **SPONSOR** shall provide constant support to the PRINCIPAL INVESTIGATOR and shall provide him/her and the CREC with any new information related to the drug under research that may be relevant.

4.4. It is the **FOUNDATION**'s responsibility to manage the financial aspect of this **CLINICAL TRIAL**. To such affect, the **FOUNDATION** shall receive any payments made by the **SPONSOR/CRO** and shall distribute them according to the provisions of Schedule 1.

4.5. The **PRINCIPAL INVESTIGATOR** agrees to safeguard the patient identification codes. The **SPONSOR** and the **PRINCIPAL INVESTIGATOR** agree to maintain the essential documents of the **CLINICAL TRIAL** during the period and according to the conditions set forth by the laws curently in force.

4.6. It is the **PRINCIPAL INVESTIGATOR'S** responsibility also to select the members of the research team and the support staff for the **CLINICAL TRIAL**. These can be either natural or legal persons, or organizations of a different nature, in any case with adequate material and human resources for its implementation. Attached as Schedule 2 is a comprehensive list of the current members of the research team at the date of execution of this Agreement. Any change in the list of members of the research team shall be notified to the CREC as per the laws in force.

FIVE.- FINANCIAL ASPECTS

5.1. The cost of this **CLINICAL TRIAL** has been initially estimated at _____EURO (VAT not included) (€____) (hereinafter the '**CLINICAL TRIAL Budget'**). This cost has been determined by applying a cost of _____ EUROS (____ €) per subject to be evaluated, as per the Financial Schedule attached as Schedule 1 to this Agreement, where full detail of the financial aspects of the **CLINICAL TRIAL** is given. This amount does not cover or provide for any obligation or commitment for the **HOSPITAL**, the **FOUNDATION** and/or the **PRINCIPAL INVESTIGATOR** to recommend, endorse, prescribe, purchase, use or agree the use of any of the **SPONSOR**'s products.

5.2. The sum to be paid by the **SPONSOR/CRO** during the implementation of the **CLINICAL TRIAL** shall be set according to the specifications of Schedule 1, and shall be paid to the **FOUNDATION** as detailed below:

5.2.1. The remainder of the **CLINICAL TRIAL** budget shall be paid, at least each semester, as detailed in the table of cost per visit and recruited patient included as Schedule 1 until the

total cost of the budget is fully paid off. The **SPONSOR** and the **PRINCIPAL INVESTIGATOR** shall report to the **FOUNDATION** on a biyearly basis.

5.2.2. These instalments shall be considered as partial payments, subject to the settlement of the final total expenses of the **CLINICAL TRIAL**.

5.3. The final contribution of the **SPONSOR** for the implementation of the **CLINICAL TRIAL** shall be determined by the activities actually carried out while conducting the **CLINICAL TRIAL** ('Final cost'). Final cost shall be estimated as follows:

5.3.1. Within a maximum of three (3) months from completion of the **TRIAL** at the **HOSPITAL**, the **SPONSOR/CRO** and the **PRINCIPAL INVESTIGATOR** shall report in writing to the **FOUNDATION** the total number of (1) recruited and evaluated subjects, (2) actual number of visits, (3) resulting incidents, as well as (4) any tests, analyses, examinations, consultations or hospital stays of special nature that might have occurred, whether or not included in the Financial Schedule (Schedule 1).

5.3.2. As soon as possible after the information of the previous point has been notified, the **FOUNDATION** shall calculate and notify the **SPONSOR/CRO** the final payment of the **CLINICAL TRIAL**, as well as the outstanding sums, if any, which shall be paid within one (1) month without further requirement. This settlement of the final payment shall be regarded to all effects as due compliance by the **SPONSOR** of his financial obligations**.**

5.4. All payments shall be made upon the presentation of an invoice; the corresponding VAT shall be included as per current legislation at the time of payment, at the name of the **SPONSOR** or the **ENTITY/PERSON IN CHARGE OF FINANCIAL ASPECTS** (invoicing details)

Name:

VAT number / Tax ID Number:

Domicile / Registered Address:

5.5. All payments to the **FOUNDATION** shall be by bank transfer (with bank fees being paid by the payer) to:

Beneficiary: Foundation para la Investigación Biomédica del the RAMÓN Y CAJAL UNIVERSITY HOSPITAL

Banking entity: La Caixa

Account nbr.: 2100 4065 12 2200091823

IBAN: ES19 2100 4065 12 2200091823

SWIFT CODE: CAIXESBBXXX

5.6. Payments by the **SPONSOR/CRO** to the **FOUNDATION** shall be in full satisfaction by the former of its obligations, being the **FOUNDATION**'s responsibility to pay the sums, if any, due to the researchers and/or the subjects of the trial.

SIX.- INSURANCE AND LIABILITY

The **SPONSOR** has a civil liability policy that meets all requirements under RD 223/2004. This policy**,** number _____, has been issued by the insurance company _____, and

covers any damages arising from the participation of subjects in the **CLINICAL TRIAL** under this Agreement, and is fully effective, since the **SPONSOR** is up to date with the payment of all premiums. The coverage of this policy expressly includes the **PRINCIPAL INVESTIGATOR** and his/her collaborators, the **HOSPITAL**, and the **FOUNDATION** (copy of the policy or certificate is attached).

SEVEN.- CONFIDENTIALITY ASSURANCE AND PROTECTION OF PERSONAL DATA.

7.1. To comply with all requirements under current legislation, the Parties agree to take all necessary steps within their means to ensure the confidentiality of the information collected for the implementation of the **CLINICAL TRIAL,** as well as the personal data of participants in the trial. Exceptions are: (i) public domain information, (ii) information previously known by the **PRINCIPAL INVESTIGATOR** or the **FOUNDATION** at the moment of disclosure, or (iii) mandatory disclosure of information enforced by law.

7.2. All parties, insofar as they access and deal with personal data from the **CLINICAL TRIAL** participants, have to take all necessary steps to protect these data and to prevent access by unauthorized third parties. The Parties are bound to the utmost strict observance of the provisions of Act 15/1999 of 13 December 1999, on Personal Data Protection, the regulation implementing said Act (RD 1720/2007), Act 8/2001, of 13 July 2001, on Personal Data Protection at the Madrid Community, and Act 41/2002, of 14 November 2002, which regulates patient autonomy. The statutes above are applicable also to all personal data contained in this Agreement.

7.3. Both the **PRINCIPAL INVESTIGATOR** and the **FOUNDATION** shall treat the personal data of any person participating in the **CLINICAL TRIAL** in a manner that they cannot be traced to and/or be used to identify any particular individual by the **SPONSOR/CRO**. Access to the personal data of any person participating in the **CLINICAL TRIAL** shall be granted, subject to the terms governing Informed Consent, solely to the monitors and/or representatives designated by the **SPONSOR/CRO**, auditors and competent authorities, and strictly within the exercise of their respective professional duties.

EIGHT.- DRUGS UNDER RESEARCH

8.1. **SPONSOR** shall provide, free of cost, the drugs under research, including comparison drugs and those used as placebo, as per RD 223/2204 guidelines.

8.2. The drug under research shall be supplied through the **HOSPITAL** Pharmacy Service and shall be administered in a controlled manner, as specified by the **PROTOCOL** guidelines.

8.3. The drugs under research shall not be available to researchers unless a favourable **CREC** report and the mandatory authorization of the **AEMPS** have been obtained.

NINE.- AMENDMENTS, TERMINATION AND SUSPENSION OF THE AGREEMENT

AMENDMENTS

9.1. Amendments to the terms of the Agreement shall be in writing duly signed by the Parties and as an *addendum* thereto. In any case, amendments shall conform with the provisions of section 25, RD 223/2004.

GROUNDS FOR TERMINATION OR SUSPENSION

9.2. Either Party may terminate or suspend the **CLINICAL TRIAL** if any of the circumstances envisaged by section 26 RD 223/2004 occur, and also in any of the following cases:

9.2.1. Breach by either Party of their essential obligations under this Agreement.

9.2.2. Breach or defective compliance by either Party of any of their obligations not considered essential, where this is not remedied within fifteen (15) days after the other Party's requirement to comply, expressed in writing.

9.2.3. Mutual agreement of the Parties, expressed in writing.

EFFECTS OF TERMINATION

9.3. Upon termination or suspension of the **CLINICAL TRIAL,** the Party not being in breach of its contractual obligations shall be entitled to rescind the Agreement.

9.4. The Parties shall ensure the participants' safety upon termination of the **CLINICAL TRIAL** for whatever reason, guaranteeing also the continuity of the treatment administered and compliance with the current laws governing the subject matter.

TEN.- RESULTS AND PUBLICATIONS

10.1. All data and results obtained within the **CLINICAL TRIAL** as well as any derivative works and intelectual/industrial property rights arising therefrom are the property of the **SPONSOR**, and the Parties are bound to the provisions of the laws governing these issues. This does not preclude the right of the **PRINCIPAL INVESTIGATOR** and of the **FOUNDATION** to use the results in their respective professional activities subject to the **SPONSOR**'s intellectual/industrial property rights and to the terms of the **PROTOCOL**.

10.2. Under the provisions of RD 223/2004, upon completion of the **CLINICAL TRIAL,** the **SPONSOR** shall publish the results, whether positive of negative, in scientific media accessible to the public.

10.3. If the **SPONSOR** has not published the **CLINICAL TRIAL** final results, the **PRINCIPAL INVESTIGATOR** can disseminate any data, discoveries or inventions through journals or scientific publications, making reference at least to the **SPONSOR**. This shall be conducted according to following criteria: Trials on non-marketed products: during the first year, once authorized and marketed in any country; Trials conducted after product has been marketed, during the following year after the completion of the Trial, except when there is a commitment to publish the results in a medical journal submitted to peer review, or if there is an infringement to national law. The **SPONSOR** shall receive for his/her review, a copy of the text proposed for publication and/or dissemination at least forty-five (45) days before it is submitted to a scientific journal and at least twenty (20) days before it is summarized as an abstract. In any case, the **PRINCIPAL INVESTIGATOR** may only use these data subject to express prior written authorization from the **SPONSOR**.

ELEVEN.- CORRUPT PRACTICES

11.1. The anti-corruption policy provides that the members of the staff of _____(**SPONSOR**) and of any third party acting for the account or on behalf of the **SPONSOR** shall not have any personal interest or commitment that may conflict with or limit their capacity to comply in an ethically adequate manner with their respective obligations under this Agreement. Said policy provides also that any activities carried out in connection with this Agreement shall comply in all respects with the ethical standards and principles above and the applicable laws. _____(**SPONSOR**) considers that an ethical, transparent behaviour is of the essence and applies a zero-tolerance policy to any and all corrupt practices.

11.2. The members of the staff of _____(**SPONSOR**) and of any third party acting on behalf of the **SPONSOR** shall not initiate any contact or authorize directly or indirectly payments of any type to any of the parties participating in the **CLINICAL TRIAL** with the aim of securing an unfair advantage or to unduly influence any decision. The term 'Payment' shall include payments or commitments to pay any money or anyhing of value, or the offer of any other good or service.

11.3. The **FOUNDATION** shall keep a register of any economic transaction arising from this Agreement and shall make available to _____(**SPONSOR**), upon the latter's request in writing, any documents required to verify due compliance with the commitments aquired within this instrument.

TWELVE.- JURISDICTION

12.1. To resolve any dispute arising from the application or interpretation of the provisions of this Agreement, the parties submit to the jurisdiction of the courts in the city of the Madrid Community where the Hospital is located, expressly waiving their rights to any other jurisdiction that they might be subjected to.

12.2. Should a copy of this Agreement become available in any other language, the Spanish version shall prevail.

In witness whereof and as proof of consent, the Parties sign the present document in three (3) copies to a single effect.

For the **SPONSOR**,

For the **CRO**

For the **FOUNDATION**

For the **HOSPITAL**

José Ignacio Flores Nicolás

Javier Maldonado González

THE PRINCIPAL INVESTIGATOR

Schedule 2 List of investigators