SAPIENZA
UNIVERSITÀ DI ROMA

Consiglio di Amministrazione

Seduta del

- 5 DIC. 2013

Nell'anno **duemilatredici**, addì **5 dicembre** alle ore **15.50**, presso il **Salone di rappresentanza**, si è riunito il Consiglio di Amministrazione, convocato con nota rettorale prot. n. 0070666 del 29.11.2013, per l'esame e la discussione degli argomenti iscritti al seguente ordine del giorno:

..... **O M I S S I S** .....

Sono presenti: il **rettore**, prof. Luigi Frati; il **prorettore vicario**, prof. Antonello Biagini; i consiglieri: prof.ssa Antonella Polimeni, prof. Maurizio Barbieri, prof. Bartolomeo Azzaro, prof. Michel Gras, Sig. Domenico Di Simone, dott.ssa Angelina Chiaranza, sig. Luca Lucchetti, sig.ra Federica Di Pietro; il **direttore generale**, Carlo Musto D'Amore, che assume le funzioni di segretario.

È assente giustificato: dott.ssa Francesca Pasinelli.

Il **presidente**, constatata l'esistenza del numero legale, dichiara l'adunanza validamente costituita e apre la seduta.

..... **O M I S S I S** .....

D. 288/13
Tecnol. inf.
10.1

[redacted]

SAPIENZA
UNIVERSITÀ DI ROMA

Consiglio di Amministrazione

Seduta del

- 5 DIC. 2013

RATIFICA DELL'ACCORDO PER LA CREAZIONE DELL'INTERNATIONAL ASSOCIATED LABORATORY (LIA)

Il Presidente sottopone al Consiglio di Amministrazione la relazione predisposta dall' Area per l'Internazionalizzazione relativa all'approvazione, a ratifica, dell'accordo tra Sapienza Università di Roma, il Centre National de la Recherche Scientifique – CNRS, l'Université des sciences et technologies de Lille – Lille 1 e l'Istituto Neuromed, già approvata dal Senato accademico nella seduta del 26 novembre 2013.

SAPIENZA UNIVERSITÀ DI ROMA
Area per l'Internazionalizzazione
Il Direttore
Dott.ssa Antonella Cammisa

L'Accordo, già firmato da tutte le parti, è stato proposto dal prof. Nencini, Direttore del Dipartimento di Farmacologia e Fisiologia e si inserisce nel quadro della pluriennale collaborazione scientifica tra Italia e Francia nell' ambito delle Neuroscienze, nonché, più in particolare, della collaborazione tra il laboratorio di Farmacologia della Sapienza e vari team di ricerca francesi.

L'Accordo è finalizzato alla creazione dell'International Associated Laboratory (LIA) "Prenatal stress and Neurodegenerative Diseases". Lo scopo del LIA è quello di realizzare un progetto di ricerca (descritto nell'Annex 1 dell'Accordo allegato come parte integrante alla presente relazione) in materia di impatto dello stress nei primi anni di vita sulle malattie neurologiche da adulti.

Il LIA non ha status o capacità legale. L'Accordo non comporta e non può in alcun modo essere interpretato come finalizzato alla formazione, la creazione, l'implementazione di una società comune, o di un rapporto di agenzia, società, gruppo di interesse o di qualsiasi altro tipo di raggruppamento commerciale o ente o società di fatto tra le Parti.

Il LIA sarà coordinato congiuntamente da due co-Direttori: la prof.ssa Stefania Maccari, per la Francia, e il prof. Ferdinando Nicoletti, per l'Italia.

L'Accordo ha durata quadriennale, rinnovabile solo una volta.

Ciò premesso, il Presidente sottopone all'approvazione del Consiglio di amministrazione l'approvazione, a ratifica, dell'accordo.

Allegato parte integrante:

[redacted]

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- Accordo tra Sapienza Università di Roma, il Centre National de la Recherche Scientifique – CNRS, l'Université des sciences et

- technologies de Lille – Lille 1 e l'Istituto Neuromed finalizzato alla creazione dell'International Associated Laboratory (LIA) "Prenatal stress and Neurodegenerative Diseases"

SAPIENZA UNIVERSITÀ DI ROMA
Area per l'Internazionalizzazione
Il Direttore
Dott.ssa Antonella Cammisa

SAPIENZA
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..... O M I S S I S .....

Consiglio di Amministrazione

Seduta del

- 5 DIC. 2013

DELIBERAZIONE N. 288/13

IL CONSIGLIO DI AMMINISTRAZIONE

- **Letta la relazione istruttoria;**
- **Visto l'Accordo culturale tra l'Italia e la Francia del 4/11/1949;**
- **Visto l'Accordo di Cooperazione scientifica e tecnologica tra il Governo della Repubblica francese e il Governo della Repubblica italiana del 29/01/2001;**
- **Visto l'Accordo di collaborazione culturale e scientifica bilaterale tra Sapienza Università di Roma e l'Université des sciences et technologies de Lille del 15/02/2007;**
- **Considerato l'interesse e l'opportunità di creare l'International Associated Laboratory (LIA) "Prenatal stress and Neurodegenerative Diseases", avente come scopo quello di realizzare un progetto di ricerca in materia di impatto dello stress nei primi anni di vita sulle malattie neurologiche da adulti;**
- **Vista la necessità di ratificare l'Accordo già sottoscritto tra Sapienza Università di Roma, il Centre National de la Recherche Scientifique – CNRS, l'Université des sciences et technologies de Lille – Lille 1 e l'Istituto Neuromed, finalizzato alla creazione dell'International Associated Laboratory (LIA) "Prenatal stress and Neurodegenerative Diseases";**
- **Vista la delibera del Senato accademico n. 438/13 del 26 novembre 2013;**
- **<u>Presenti 11, votanti 9</u>: con voto unanime espresso nelle forme di legge dal rettore e dai consiglieri: Polimeni, Barbieri, Azzaro, Gras, Di Simone, Chiaranza, Lucchetti e Di Pietro**

DELIBERA

di ratificare l'Accordo già sottoscritto tra Sapienza Università di Roma, il Centre National de la Recherche Scientifique – CNRS, l'Université des sciences et technologies de Lille – Lille 1 e l'Istitutt Neuromed, finalizzato alla creazione dell'International Associated Laboratory (LIA) "Prenatal stress and Neurodegenerative Diseases".

Letto, approvato seduta stante per la sola parte dispositiva.

IL SEGRETARIO
Carlo Musto D'Amore

IL PRESIDENTE
Luigi Frati

..... O M I S S I S .....

[redacted]

AGREEMENT TO CREATE THE INTERNATIONAL ASSOCIATED LABORATORY "Prenatal stress and neurodegenerative diseases" (LIA PSND)

The **Centre National de la Recherche Scientifique** (French National Center for Scientific Research), hereinafter referred to as "**CNRS**", a public scientific and technological organization, headquartered at 3, rue Michel-Ange, 75794 Paris cedex 16 (France), represented by its President, Professor **Alain FUCHS**,

And

The **Université des sciences et technologies de Lille**, hereinafter referred to as "**Lille 1**", a public institution of higher education and research, headquartered Cité Scientifique 59655 Villeneuve d'Ascq Cedex (France), represented by its President, Professor **Philippe ROLLET**,

acting in their own names and jointly on behalf of the following joint research unit:

Unité de glycobiologie structurale et fonctionnelle, UMR 8576 (CNRS - Lille 1), directed by Dr Christophe D'HULST.

And

The **Sapienza Università di Roma,** hereinafter referred to as "**Sapienza**", a public institution of academic education and research, headquartered 5, Piazzale Aldo Moro 00185 Roma (Italy), represented by its President, Professor **Luigi FRATI**,

Acting in its own name and on behalf of:

Department of Physiology and Pharmacology "V. Erspamer", directed by Pr. Paolo NENCINI.

And

The **Neuromed Institute**, hereinafter referred to as "**Neuromed**", a private institution of research, clinical studies and education, recognized by the Italian Ministry of Health as Hospital and Clinical Institution with Scientific Purpose (IRCCSS), headquartered at Via Atinense 18, 86077 Pozzilli (IS) (Italy), represented by its President, Professor **Erberto MELARAGNO**,

Acting in its own name and on behalf of:

Laboratory of Molecular NeuroPharmacology (MNP), directed by Pr. Ferdinando NICOLETTI.

Hereinafter referred to collectively as the "Parties" or individually as the "Party".

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IN ACKNOWLEDGMENT OF

- The Cultural agreement between French and Italian governments signed on the 4th of November 1949;

- The Scientific agreement of cooperation between the government of the French Republic and the government of the Italian Republic signed on the 29th of January 2001;

- The cultural and scientific frame agreement on the bilateral collaboration between the University of Lille 1 and the Sapienza signed on the 15th February 2007;

- The agreement between CNRS and Lille 1;

- The French decree n°2009-645 of June 9, 2009 on the management between the French public institutions of the industrial property of the results from research conducted by French state-employees, and which determines a French public mandatory responsible for the protection and exploitation of said results;

- The constitutive agreement of the International Scientific Coordination Network entitled "Early Programming of Modern Diseases" (abbreviated as GDRE EPMD) (2009-2012), signed on the 17th of March 2010.

PREAMBLE

The scientific collaboration on neurosciences between France and Italy started more than 20 years ago. In particular, the collaboration between the laboratory of Pharmacology at Sapienza University of Rome and French research teams from Bordeaux started in October 1988. Several grants for mobility were obtained in the framework of several national and international programs such as the Partenariat Hubert Curien (PHC) Galileo and the ERASMUS program, short fellowship from the European Union and private grants from industries. Several PhD students took their PhD and Italian students became Researchers or Professors in France, such as S. Maccari herself, who became first Assistant Professor at the University of Bordeaux 2 and after Professor at the University of Lille 1. A new collaboration was created between Lille and the Institute of Neurosciences in Rome (CNR). A frame agreement was also signed between University of Lille 1 and the Sapienza University of Rome in 2007. This agreement permitted the nomination of French researchers as Visiting Professors at the Sapienza University of Rome and in return the nomination of Italian researchers as Visiting Professors at the University of Lille 1. Furthermore, mobility of PhD students and Postdocs was improved thanks to this agreement, which supported the annual summer schools of neurosciences organised by S. Maccari. A financial support for the summer schools was obtained from the Federation of European Neurosciences Societies (FENS). In 2008, a two-day meeting on "Programming and Epigenetic" was organized in Lille, funded by the French Neurosciences Society.

Thanks to the support of CNRS, an International Scientific Coordination Network, the GDRE 691 "Early programming of modern diseases" (EPMD) was created in 2009 by the Parties, Consiglio Nazionale delle Ricerche (CNR) and Università Cattolica del Sacro Cuore, with S. Maccari (for France) and Dr. A Moles (for Italy) as coordinators. Aim of EPMD was to consolidate the international network around behavioural epigenetics, an innovative theme of neurosciences. This consortium grouped high level researchers, internationally recognized in different neuroscience fields: prenatal stress animal model of depression (PRS) (S. Maccari); animal models of neurodegenerative diseases (F. Nicoletti and B. Bioulac) and antidepressant action on plasticity (A. Daszuta); eating disturbancies (A. Moles, V. Prévot) and circadian disorders (P. Pevet, J. Mairesse); proteomics and epigenetics (S. Morley-Fletcher; A. Benecke).

In particular, the GDRE has supported a bilateral collaboration between S. Maccari and F. Nicoletti, internationally acknowledged as experts of the neurobiology of prenatal stress and of neurodegenerative disorders, respectively.

Very recent results obtained in this bilateral cooperation indicate that PRS can induce a latent state of Parkinsonism, raising the interesting possibility that this pathology can be programmed by stressful events occurring in early life. Parkinson's disease is a disorder of the brain characterized by slowness of movement

and locomotion (bradykinesia, rigidity and tremor). It is one of the most common nervous system disorders of the elderly. Parkinson's disease has an incidence of about 50,000 new cases per year in the U.S. The average age of clinical onset is about 60. Dopamine is involved in the control of motor programming. Parkinson's disease occurs when the dopaminergic neurons are slowly degenerated. Depletion in dopamine alters nigro-striatal motor pathway. This leads to a deep alteration of motor planning. The damage gets worse over time. Nowadays, the reasons of this important cell death are poorly known. Our studies suggest that early life events can induce changes in the dopaminergic motor system during the adult life, affecting behavior and neurochemical transmission. These researches also highlight the importance to detect the early signs of a latent parkinsonism.

Based on these encouraging scientific results, the Parties recognize the quality of the research collaboration emerged thanks to the GDRE EPMD and decided to support this successful bilateral cooperation through a structuring partnership allowing a long term development of further joint research activity on prenatal stress and neurodegenerative diseases.

Consequently, the Parties agree, on the basis of this Agreement, to form an "International Associated Laboratory - LIA" devoid of legal status and governed by the following provisions.

TITLE I – CREATION, TERM, NAME, PURPOSE AND COMPOSITION OF THE LIA

Article 1 - Creation and term

The International Associated Laboratory (LIA) "**Prenatal stress and Neurodegenerative Diseases**", abbreviated as "PSND", hereinafter referred to as "LIA" or "LIA PSND", shall be effective on **1 January 2013** for a term of four (4) years, renewable once.

Article 2 - Purpose

The purpose of the LIA is to carry out the research project described in Annex 1 attached hereto in the field of impact of early life stress on neurological adult diseases.

Article 3 - Composition

The LIA "PSND" consists of the following laboratories:

- Neuroplasticity Team, headed by Pr. Stefania MACCARI - Unité de glycobiologie structurale et fonctionnelle, UMR 8576 (CNRS, Université Lille 1), directed by Dr Christophe D'HULST;
- Psychopharmacology Group, headed by Pr. Ferdinando NICOLETTI - Department of Physiology and Pharmacology "V. Erspamer", Sapienza, directed by Pr. Paolo NENCINI;
- Laboratory of Molecular NeuroPharmacology, IRCCSS NEUROMED, directed by Pr. Ferdinando NICOLETTI.

The personnel and teams list (hereinafter referred to as "LIA Members"), as of January 1st 2013 is set out in Annex 2.

According to the research program realised in the framework of the LIA, researchers from other laboratories can participate in the LIA research. If deemed necessary, their participation will be subject to a specific Agreement or to an Amendment to the Agreement according to art 16.

Article 4 – Type of cooperation

The LIA has no legal status or capacity.

This Agreement neither sets out to nor results in, nor should anything in it be construed as either forming, creating, implementing or recognizing the creation of a joint company, agency relationship, corporation, interest group or any other type of commercial grouping or entity or de facto company by the Parties.

TITLE II - ORGANIZATION

Article 5 – Co-directors

The LIA is run by two co-directors. The management of the LIA is jointly provided by:

- Pr. Stefania MACCARI, for France,
- Pr. Ferdinando NICOLETTI, for Italy,

hereinafter referred to as "Co-directors".

In accordance with the practice of their home institutions, the Co-directors jointly assume responsibility for the scientific program and each one individually manages his part of the LIA. As necessary, they shall establish the bylaws of the LIA.

The Co-directors shall prepare the research program, provisional budget and annual financial and scientific reports to be submitted to the Steering Committee and to the Parties.

The directors of the French Joint Research Units (UMR) participating in the LIA are solely responsible administratively with regard to staff management and use of funding resources allocated to the LIA vis-à-vis the Parties overseeing their unit.

The Co-directors may take advice from a Scientific Advisory Board composed of scientific experts, not involved in the LIA whose names are listed in Annex 2.B.

Article 6 – Steering Committee

6.1. – Composition

A Steering Committee for the LIA PSND is constituted. This Committee shall be composed of 2 representatives per country, chosen from outside the staff of those laboratories making up the LIA:

- 2 representatives of French Parties:
  - the Director of the Institute of Biological Sciences of CNRS, or his/her representative,
  - the Vice President for Research of Lille 1, or his/her representative,

- 2 representatives of Italian Parties:
  - the President of Sapienza, or his/her representative,
  - the President of Neuromed, or his/her representative.

All members possess equal voting rights.

Subject to the execution of a nondisclosure agreement, all Parties may invite members of their administrative organization and/or outside parties, to attend the steering committee meetings. Such invited guests shall sit in a consultative capacity.
The list of representatives as of January 1st, 2013 is set out in Annex 2.C.

The LIA Co-directors shall attend the Steering Committee meetings in a consultative capacity.

6.2. - Chairperson

The Parties appoint one of the Steering Committee members as Chairperson in rotation for two years in order to preside the Steering Committee.

The Chairperson as of January 1st 2013, is the Director of the Institute of Biological Sciences of CNRS, or his/her representative.

6.3. – Meetings and decisions

The Steering Committee shall meet at least once every two (2) years and, at the initiative of its Chairperson and at the request of its members or the Co-directors, as often as required by the interests of the LIA.

Decisions require the unanimity of members either present or represented, the quorum being reached at ¾ of its members.
In the event of practical impossibility of a physical meeting, the Steering Committee may meet via teleconferencing or any other means.

6.4. – Role

The Steering Committee:
- formulates recommendations on the project presented by the Co-directors and the state and direction of the research carried out by the LIA;
- approves the funding necessary to run the LIA;
- may make recommendations or propose reorientations;
- defines the collaboration policy of the LIA taking into account the Parties' interests;
- defines the Party in charge of negotiation;
- provides an opinion on any modification of the LIA structure and on the admission of new laboratories or Parties to the LIA;
- provides an advice as to the renewal of the LIA based on the evaluation report;
- may also study any matter relating to the LIA.

Meeting minutes for all Steering Committee meetings shall be provided by the Chairperson to all Parties within 30 days.

Article 7 – Scientific evaluation

The LIA activities shall be assessed regularly and in any case before its expiration date by the relevant authorities of both parties, in accordance with the applicable procedures of these bodies. The Parties may also propose to form an *Ad Hoc* Committee, particularly prior to LIA renewal, in order to evaluate its scientific activities and issue recommendations on the LIA scientific orientation and functioning.
Evaluation reports shall be addressed to the Steering Committee and the Parties.

TITLE III – FINANCIAL AND HUMAN RESOURCES

Article 8 – Funding provisions

Every calendar year, the budget required to carry out the LIA research is prepared and submitted by the LIA Co-directors to the Steering Committee for approval.

Annex 3 attached hereto, sets out the projected budget allocated by the Parties as of the date the LIA enters into effect. This budget is updated annually by the LIA Co-directors, following a vote by the Steering Committee.

Each LIA Party shall manage its respective resources, such as the internal budget allocation for the LIA purposes or external resources.

Resources obtained jointly within the framework of agreements concluded on behalf of the LIA shall be shared and managed by the Parties in accordance with their participation in such projects.

A report is provided annually by each Party to the others on the resources it allocated over the past year (including equipment, premises and tenured or temporary personnel).

Moreover, the funds allocated to the LIA and managed by both LIA Co-directors are subject to the customary monitoring mechanisms in their respective countries to verify their legitimate use in relation to the purpose of this Agreement.

Article 9 – Personnel

Personnel assigned to contribute to the LIA shall remain administratively dependent on their original institution and unit and shall carry out its work under the administrative supervision of their unit director.

Annex 2 summarizes the schedule and extent of the participation of personnel in the joint scientific project.

The exchange of personnel (secondment, etc.) is subject to execution of an agreement setting out terms and conditions of compensation, ownership of results and subordination.

While on assignment, visitors are subject to the bylaws and procedures of the hosting laboratory.

Article 10 – Facilities and equipment

LIA members shall have access to the facilities and/or equipment listed in Annex 4 throughout the term of this Agreement for purposes of carrying out the research project described in Annex 1.

The Party, in whose possession the facilities and/or equipment are located, remains liable therefore.

For information purposes, the amount of depreciation allowance for facilities and equipment made available to the LIA must be provided (according to the terms in effect for each Party).

The use of facilities and/or equipment is subject to the safety and security rules in force.

The Parties' premises are made available to LIA use subject to compliance with the bylaws and procedures of the owner Party and the execution of a hosting agreement.
In the event of a loan or rental of facilities and equipment, a loan agreement shall be executed by the Parties concerned, including reference to the purpose and term, any applicable fees, the Parties' liabilities and the terms of maintenance and return of the property.

Article 11 – Research contracts

All research contracts that the LIA shall execute with third-party bodies, public or private, require approval of and signature by all Parties, and are subject to the paragraph 6.4 on the role of the Steering Committee.

They shall be negotiated by the Party having express authority to so act, following the Co-directors' proposition and recommendations of the Steering Committee and with the agreement of the other Parties. The authorized Party shall keep the other Parties informed of the results of all negotiations. The latter shall dispose of fifteen (15) days to respond, after which the negotiation is deemed approved.

The use of LIA PSND title by the Parties must include that LIA is devoid of legal personality and the LIA Parties are financially and legally independent and separate liable partners.

The nondisclosure clauses included in such research contracts must not preclude the concerned researchers from including their research in activity reports or the students to defend their PhD dissertation.

The contracts shall make explicit provisions for reimbursing overheads associated with activities developed under said contracts, which have been paid by the Party involved in the research. The corresponding amounts, determined by agreement between the Parties, shall be allocated to the budgetary contribution of said Party.

[redacted]

TITLE IV – PUBLICATIONS, CONFIDENTIALITY, INTELLECTUAL PROPERTY AND VALORISATION

Article 12 – Mutual informing and Publications

Each Party undertakes to share with the other Parties all information needed to carry out the joint research work. The publication of scientific results shall be made according the usual custom and practice of the scientific community; Parties' recommendations on scientists' affiliation and with prior consent of all scientific contributors to the results and entitled Parties.

Publications related to the joint research efforts of the LIA research project shall include reference to the LIA Parties or other French overseeing authorities and bearing the mandatory statement ***"Research conducted in the scope of the PSND International Associated Laboratory (LIA)"***.

Throughout the term of the LIA and for a subsequent period of two (2) years, each Party shall request the consent of the other Party for its own publication related to the LIA. Such consent may not be unreasonably withheld.

In any case, a publication cannot be delayed beyond nineteen (19) months from the date of receipt of a notice by the Parties. Where a publication or paper contains important information of an industrial, commercial or strategic nature related to the activities of certain Parties the decision regarding the nature and term of nondisclosure shall be taken by the Steering Committee (allowed: activity reports by personnel, closed session dissertation defenses). The Steering Committee shall make its decision known within a maximum period of one (1) month as from the receipt date of the enquiry. This decision can consist in:

a) Accepting the publication unreservedly; or
b) Requesting that the publication or communications project be postponed, owing to real and serious reasons in particular if specific information must be subject to protection under intellectual property provisions. In such case, the Parties agree to either remove the objecting Party's Confidential Information or to delay the planned publication for a period of up to a maximum of eighteen (18) months after objection to allow for protection or other appropriate steps.

Article 13 – Non-disclosure

Within the framework of information exchange necessary to carry out the joint research work, the Parties shall refrain from disclosure, protection (patent) or exploitation of commercial or industrial nature of any confidential information belonging to the other Party,

Information (of any kind, contained in any medium) is confidential when explicitly identified as "confidential".

The period of confidentiality runs for the term of the LIA and a subsequent 5-year period.

Parties are responsible for ensuring compliance with duty of non-disclosure by their employees during LIA and following expiration of its term or following termination of their employment, as well as by hosted personnel.

However, this clause shall not impede CNRS researchers from fulfilling their obligation of producing an activity report, which shall not constitute disclosure within the meaning of the laws governing industrial property, nor students from defending their doctoral thesis or internship report relating to the work conducted under this cooperative activity. If necessary, the examination may take place behind closed doors.

Exceptions in which the Confidentiality obligations shall not apply:

- if the confidential information becomes publicly available by means other than a breach of the recipient's confidentiality obligations;

- if the disclosing party subsequently informs the recipient that the confidential information is no longer confidential;
- if the confidential information is communicated to the recipient without any obligation of confidence by a third party who is in lawful possession thereof and under no obligation of confidence to the disclosing party;
- if the confidential information, at any time, was developed by the recipient completely independently of any such disclosure by the disclosing party; or
- if the confidential information was already known to the recipient prior to disclosure.
- if a Party is required, to disclose confidential information in order to comply with applicable laws or regulations or with a court or administrative order, provided however that it shall, to the extent it is lawfully able to do so, prior to any such disclosure
  - notify the owning party, and
  - comply with the owning party's reasonable instructions to protect the confidentiality of the information.

Article 14 – Intellectual Property

Definitions

- "Proprietary Results":

Results, including software and databases, which may or may not be protected by intellectual property rights and belonging to one of the Parties, obtained prior to joining the present Agreement or simultaneous to and independent of the scope of LIA activities.

- "Joint Results":

Results, including software and databases, which may or may not be protected by intellectual property rights to which two or more Parties jointly contributed in a substantial or inventive manner and which are a direct or indirect result of the LIA activities.

- "Qualified Know-How":

All practical results unprotected by intellectual property rights which are: (a) confidential, (b) substantial, i.e. significant and useful for the manufacture of particular products and (c) identified, i.e. described in such a way as to be understandable and adequate to confirm the elements of (a) and (b).

14.1. – Ownership of Results

Proprietary Results remain the property of the owning Party.
Proprietary Results or Qualified Know-how that are not free of access for the purposes of LIA are set out in Annex 5, which shall be regularly updated by the Parties. All Proprietary Results, which are not listed in Annex 5, are free of access for the purposes of LIA.

Joint Results are the joint property of the entitled Parties (hereinafter referred to as "Joint Owners"), which shall hold such rights in the following proportions:
- 50% to CNRS and Lille 1 (in their names and in the name and on behalf of other LIA Members employers, unless theses employers explicitly waive their rights),
- 50% to Sapienza and Neuromed.

The above allocation shall be the default in cases of Joint Results, but the Parties may negotiate, however, from case to case, a more appropriate allocation of share according to the inventive contributions, if such contributions are substantially not comparable.
In case of disagreement between the parties regarding to such contributions, the share should be discussed in an amicable way in the framework of the Steering Committee. In case of persisting disagreement such share shall be determined by an external independent patent attorney.

Any transfer of ownership, grant of license or similar right over the Joint Results shall require the prior written consent of the other Joint Owners.

The Joint Owners agree to negotiate in good faith an Inter-Institutional-Agreement ("IIA") settling their rights and duties with regard to any Joint Result.

To the extent possible, such IIA shall be based on the terms and conditions with regard to the regulation, the administration and the commercial exploitation of the Joint Result agreed by the Joint Owners and specified in this section.

A result obtained in the framework of the LIA activities (hereinafter the "LIA Result"), which is not a Joint Result, shall be solely owned by the Party who obtained it, and shall not be subject to the provisions regarding the Joint Results.

14.2. – Patent protection of Joint Results

Inventors of a Joint Result shall inform both Co-directors and the Steering Committee and declare their invention to each of the entitled Parties, which shall evaluate any interest in protecting said invention.

The Joint Owners shall jointly decide whether or not to patent a Joint Result. In the event a patent is filed, they shall jointly decide on the countries or regions to be covered by the registration. Patent applications shall be filed in the names and for the joint benefit of the Joint Owners; the name(s) of the inventor(s) shall be mentioned pursuant to his/her/their rights.

One or more Joint Owner(s) have the right to file a patent in its (their) name and at its (their) expense, if one or more Joint Owners expressly waive and assign their rights to do so. The Joint Owner who waived and assigned his right should take all steps and/or execute all documents necessary in order to give full force and effect to any such assignment. Such Joint Owner shall be entitled however, to assign its rights in the Joint Result to its inventor/s without obtaining the other Party's approval, provided that the inventor/s has/have undertaken in writing to the other Party to be bound by the provisions of this Agreement.

The remaining Joint Owners has the right to recover the patent rights in their name(s) if, during the term of protection, one of the Joint Owners decides to withdraw its involvement from the patent. Such Joint Owner shall be entitled however, to assign its rights in the Joint Result to its inventor/s without obtaining the other Party's approval, provided that the Inventor/s has/have undertaken in writing to the other Party to be bound by the provisions of this Agreement.

A Joint Owner who does not join in protecting a Joint Result or who withdraws its involvement in the patent protection, shall lose its rights (including the right to remuneration or compensation in respect of such patent rights or such assignment), save for the right to use the Joint Results for internal research purposes.

The Joint Owners involved in such protection shall be the sole beneficiaries of the income generated from commercial exploitation of the patent in the corresponding countries.

Each Joint Owner involved in the protection of a Joint Result is solely liable for ensuring compliance with duties relative to its employees' rights over the invention.

14.3. – Appointment of an Administrator

The Joint Owner most able to valorize or exploit one or more Joint Results of the LIA, identified by mutual agreement between the Parties upon recommendation by the Steering Committee and subject to the French decree n°2009-645, shall administer the protection and exploitation of the(se) Joint Results (hereinafter the "Administrator").

[redacted]

14.4. – Patent infringement actions

In the event that one of the Joint Owners learns of an alleged infringement of a patent owned jointly by the Parties, or of an application pending or a patent belonging to a third party and interfering with the patent held jointly the Parties, the information shall be immediately communicated between the Joint Owners.

The Joint Owners involved in the protection of a Joint Result shall mutually agree on measures to be taken in the event of infringement. The Administrator, who shall be vested with all specific powers in relation thereto, is responsible for such measures; he shall take all necessary steps in order to take cognizance of and put a stop to the infringing action.

The legal fees, costs, damages and interest shall be shared between/among the Joint Owners acting jointly according to their share in the ownership. Joint Owners who do not participate in the action shall not collect any sums resulting from legal recourse.

14.5. – Rights of access

Each Party holds, subject to third-party rights, a non-exclusive, non-transferable right to use the LIA Results – including those that are not Joint Results - and the Proprietary Results, except for those listed in Annex 5, free of charge for purposes of the LIA research.

Each Joint Owner holds a non-exclusive, non-transferable right to use the Joint Results – including the structure and content of Joint software and databases - free of charge for their own internal research needs, with the exception of any activity which is of an industrial or commercial nature and necessitates execution of an agreement defining the scope, terms and conditions of licensing.

Third-party access to Joint Results including software and databases is subject to the prior consent of the Joint Owners and subject to a written agreement.

14.6. – Commercial exploitation of Joint Results

The consent of all Joint Owners is required to grant third-party rights, as licenses to use and exploit any Joint Result.

The Joint Owners shall agree, with regard to each commercial negotiation with a third party, on the principal financial terms, which shall form part of the commercial agreement with such third party in advance (hereinafter "the Term Sheet").

Express powers are granted to the Administrator by other Joint Owners to act and undertake all activities to commercially exploit the Joint Results.

The Administrator shall regularly inform the Joint Owners of the progress and conclusion of negotiations.

The Joint Owners agree that, after the Term Sheet shall be agreed upon by them, the Administrator shall be entitled to negotiate license and other commercialization agreements on the Joint Owners' behalf in respect of the Joint Results, based on the terms of the Term Sheet and the provisions set out below ("Additional Terms"). The Joint Owners shall jointly execute any such agreements, and shall not be entitled to withhold their signature thereon provided the Administrator has complied with the terms hereof.

In addition to the specific terms of the Term Sheet that shall be agreed by the Joint Owners as aforesaid, an Agreement for any license granted in respect of the Joint Results shall include, *inter alia:*

- a definition of the products for which the Joint Results may be used for their development, manufacture and sale;
- terms securing full indemnification, without exception, and holding harmless of the Parties, and those employed by them, against and from any claim, damage or expense of any kind resulting

from any use the Licensee or those authorized by the Licensee may make of the Joint Results or other licensed information;
- a disclaimer as to any representations and/or warranties in respect of the Joint Results, their potential, use, exploitability and/or that it does not infringe third party's rights;
- the license agreement may not be sublicensed, transferred or assigned without the prior written consent of the Joint Owners;
- financial terms: in return for the license agreement the Joint Owners shall get financial return, as royalties (in the form of percentage from sales), part of any consideration other than from sales received in connection with a grant of sub-license, an annual license fee and an equity (in start-up companies). The exact mixture of the above and the terms securing it will be negotiated;
- specific undertakings of commercialization of the licensee (such as, but not limited to achieving milestones for developing and sale of the products (to avoid "shelving" of the technology), receiving prior approval before the grant of any sub-license etc.) ;
- limitation on the use of the names of the Inventors, CNRS, Lille 1, Sapienza, NEUROMED and their employees;
- payment/reimbursement of past and future patent expenses by the licensee;
- patent prosecution and maintenance shall be done by the Administrator.

Notwithstanding anything to the contrary herein, in the event that a potential licensee rejects any of the above terms, the Joint owners shall in good faith seek solutions that will be subject to all Joint Owners' written approval, to be advised timeously, and not to be unreasonably withheld.

Licensing agreements shall require signature of all Joint Owners.

The Administrator shall transfer to the Joint Owners their share of the royalties from the license granted over the Result(s) according to their share in the Result(s), after having deducted the Administrator's commercial development fees, capped at 10% of said royalties. For the avoidance of doubt, research funding received from a licensee by either Party shall not be regarded as payment from commercialization of the Invention and/or the Patents.

TITLE V – MISCELLANEOUS PROVISIONS

Article 15 – Renewal

This Agreement may be renewed once for a second term of four (4) years, by amendment executed by the Parties, following a decision by the Parties on advice from the Steering Committee, the relevant evaluating bodies of the Parties and the LIA Co-directors.

Article 16 – Modification – Membership

All modifications to the present Agreement require the mutual consent of all Parties by Amendment.

All additions of members to the LIA, including that of a new laboratory of one of the Parties, require the unanimous consent of the Steering Committee.

Any admission of a new laboratory under the authority of a Party requires the update of Annexes, in particular Annexes 2 and 3, to be provided by the Co-directors to all Parties.

The addition of new parties to the LIA shall require an amendment to this Agreement.
All admission amendments to this Agreement shall be signed by the new parties and CNRS, authorized by this Agreement to so act on behalf of the other Parties.
The sole purpose of an admission amendment is to join new Parties to the LIA. It in no way modifies the scope of the present Agreement.

[redacted]

Article 17 – Cancellation

In the event of an unresolved dispute, the Parties, following consultation with the Steering Committee and the LIA Co-directors, may mutually consent to canceling the present Agreement before the expiration of its term, upon six (6) months' notice. In such a case, the Parties shall conclude joint actions undertaken prior to notice given.

The decision to cancel shall be taken by the Parties following consultation with the Steering Committee and the LIA Co-directors.

The withdrawal of a Party prior to term, notified to the other Parties with six months' notice shall terminate the present Agreement.

Non-disclosure, publication, intellectual property and exploitation provisions shall continue to apply for their respective terms.

Article 18 – Internal communication between Parties

Internal communication between Parties shall be done in writing (registered letter with acknowledgement of receipt, sent via postal or electronic means, facsimile, etc.).

The names and addresses are the following:

at CNRS:

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at Neuromed

[redacted]

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Article 19 – Liability

Each Party remains liable, without right of action against the other Parties, except in case of gross or intentional negligence, for repairing damage to its own property during and owing to the implementation of this Agreement.
Should damage be caused to physical assets acquired by the Parties under this Agreement, the latter shall pay repair or replacement charges for said assets on a pro rata basis of their respective financial contributions to the acquisition thereof.
According to the rules of ordinary law, each Party is liable for damage / loss of any nature caused to third parties during the implementation of this Agreement.

Article 20 – Final provisions

The Parties undertake to settle their disputes out of court.
Failing that, disputes arising out of or in connection with this Agreement, which cannot be solved amicably, shall be finally settled under the Rules of Arbitration of the International Chamber of Commerce by one arbitrator appointed in accordance with the said Rules.
The place of arbitration shall be Paris or Rome at the defendant's total discretion.

Done in 4 (four) original copies.

Lille, on the 9th of October 2013

The National Center of Scientific Research

Alain Fuchs
President

By delegation
Franc Pattus
Deputy Director, Institute of Biological Sciences

The Sapienza University of Rome

Luigi Frati
President

University of Lille 1

Philippe Rollet
President

Neuromed

Erberto Melaragno
President

[redacted]

ANNEX 1

RESEARCH PROGRAM AND INDIVIDUAL PROJECTS

Prenatal stress and neurological disorders (PSND)

Prenatally restraint stressed (PRS) rats (i.e., the adult offspring of mothers exposed to chronic restraint stress during pregnancy, develop a pathological epigenetic programming that mainly targets synaptic transmission and plasticity in hippocampus and striatum. Alterations induced by PRS comprise an anxious depressive/profile related to a dysfunction of the hypothalamo-pituitary-adrenal axis, a disorganization of circadian rhythms and the sleep-wake cycle, an age-dependent impairment in spatial learning and reduction of hippocampal neurogenesis. With this purpose we opened the GDRE with the lecture of Pr F. Turek with whom S. Maccari's team has collaborated for long time on circadian rhythms and related mood disturbances.

We have proven evidence of the validity of PRS as a model of epigenetic programming that recapitulates some aspects of depression. Chronic treatment with different classes of antidepressants (imipramine, tianeptine or agomelatine, a novel antidepressant that behaves as a mixed MT1/MT2 melatonin receptor agonist/5-HT_{2c} serotonin receptor antagonist) reversed biochemical and behavioural changes including anxiety/depression and sleep alterations (Morley-Fletcher et al. 2011; Mairesse et al. 2012). Abnormalities of synaptic transmission and plasticity in the hippocampus represent an integral part of the altered programming triggered by early life stress. We have also shown that glutamate transmission in particular at the levels of metabotropic glutamate receptors mGlu 2/3 and mGlu5 is persistently impaired by PRS since infancy (Laloux et al. 2012) that epigenetic changes in mGlu2 and mGlu3 receptors lie at the core of the pathological programming induced by early-life stress (Matrisciano et al. 2011). A very recent study of our GDRE (Marrocco et al. Journal of Neuroscience 2012) shows that an impairment of glutamate release in the ventral hippocampus is a key component of the neuroplastic program induced by PRS, and that strategies aimed at enhancing glutamate release in the ventral hippocampus correct the "anxious phenotype" caused by early life stress.

Prenatal restraint stress (PRS) in rats programs the offspring to develop a pathological behavioral phenotype associated with abnormalities of the hypothalamic-pituitary-adrenal (HPA) axis (Darnaudery and Maccari, 2008). Chronic systemic treatment of PRS rats with the oxytocin receptor agonist, carbetocin, normalized the HPA response to a mild stress and the related changes in the expression of corticosteroid receptors in the hippocampus. All pathological behaviors of PRS rats (anxiety- and depressive-like behavior, and impaired social behavior and social memory) were corrected by carbetocin treatment. The negative correlation between anxiety-like behavior and social behavior in the entire cohort of rats suggested that reduction of anxiety lies at the core of the "therapeutic effect" of carbetocin in PRS rats. Carbetocin treatment also corrected the defect of depolarization-evoked glutamate release in ventral hippocampal synaptosomes of PRS rats, a neurochemical parameter that showed a tight correlation with both anxiety and social behavior. Remarkably, carbetocin had little, if any, effect in unstressed control rats, suggesting that its action was "disease dependent" (Mairesse et al., submitted). Thus, at least in this particular setting, activation of oxytocin receptors had no impact on normal brain functioning but corrected the pathological program induced by early life stress. Activation of oxytocin receptors in the SNC is a new potential strategy in the treatment of psychiatric disorders involving emotions and social behavior. These data strongly encourage the use of oxytocin receptor agonists in the treatment of stress-related disorders.

Very recently, joint research indicates that PRS can induce a latent state of parkinsonism, raising the interesting possibility that this pathology can be programmed by stressful events occurring in early life. Parkinson's disease is a disorder of the brain characterized by slowness of movement and locomotion (bradykinesia, rigidity and tremor). It is one of the most common nervous system disorders of the elderly. Parkinson's disease has an incidence of about 50,000 new cases per year in the U.S. The average age of clinical onset is about 60. Dopamine, is involved in the control of motor programming. Parkinson's disease occurs when the dopaminergic neurons are slowly degenerated. Depletion in dopamine alters nigro-striatal motor pathway. This leads to a deep alteration of motor planning. The damage gets worse over time. Nowadays, the reasons of this important cell death are poorly known. To investigate the possible causes of

vulnerability to Parkinson's disease we studied the effect of PRS in rats on dopamine neurons. This animal model has been proven for the study of brain adaptation occurring in response to early life stress. Male adult PRS rats (i.e., the adult offspring of mothers exposed to repeated episodes of restraint stress during pregnancy) showed impairment in behavioral tests (active avoidance, the grip strength test, and the pasta-matrix) that reflect the function of the nigro-striatal motor activity. Remarkably, PRS rats showed a marked reduction in dopamine release within these brain regions. Our studies suggest that early life events can induce changes in the dopaminergic motor system during the adult life, affecting behavior and neurochemical transmission. These researches also highlight the importance to detect the early signs of a latent pakinsonism. Indeed, subject "at risk" to develop Parkinson's disease could undergo clinical analysis of the dopaminergic system (i.e., by PET staining with ^{18}F-DOPA) to establish whether they can benefit of neuroprotective drugs despite the lack of motor symptoms. Finally, the identification of risk factors for Parkinson's disease may be of great help for the selection of patients that are eligible to an early neuroprotective treatment. Furthermore, we would like to extend our researches highlighting mechanisms of neuroprotection that can be altered in Alzheimer's brain. Among the risk factors that might increase the vulnerability to develop Alzheimer's disease, glucose metabolism impairments have a predominant role. We will focus on a post-translational glycosylation that is directly dependent on the neuronal ability to metabolize glucose: *O*-linked N-acetylglucosaminylation (*O*-GlcNAc). Triggering *O*-GlcNAc dynamics may pave the way for a generation of new therapeutic strategies against AD.

These results pave the way of research project of the PSND French-Italian associated laboratory, based upon the exchanges with and the expertise of the Italian Partner Pr. Ferdinando Nicoletti (Sapienza University/NEUROMED Institute) and French Partner Pr. Stefania Maccari (University of Lille 1, UMR 8576 CNRS). With this purpose, GDRE has been clotured and opened to LIA with the lecture of Pr McEwen in the last October 2012 in New Orleans, with whom S. Maccari's and F. Nicoletti's teams collaborate since a long time on stress induced alterations in brain.

[redacted]

ANNEX 2

COMPOSITION OF THE LIA AS OF JANUARY 1st 2013

LIA Members

COUNTRY	INSTITUTION	LABORATORY/TEAM	PERSONNEL/TITLE
FRANCE	CNRS and Lille1	UMR 8576 Neuroplasticity Team	*Permanent* Stefania MACCARI, Pr. Lille1 Sara MORLEY-FLETCHER, MdC Lille1 Gilles VAN CAMP, MdC Lille 1 Hammou BOUWALERH, IE Lille 1 *Temporary* Francesco MATRISCIANO, MD, PhD Jerome MAIRESSE, PostDoc Jordan MARROCCO, PostDoc Marie-Line REYNAERT, PhD student Eleonora GATTA, PhD student Lucie DERUYTER, Technician
ITALY	Sapienza and Neuromed	Psychopharmacology Group and Laboratory of Molecular NeuroPharmacology (MNP)	*Permanent* Ferdinando NICOLETTI, Pr. Valeria BRUNO, Pr. *Temporary* Giuseppe BATTAGLIA, CR Richard Teke NGOMBA, CR Carla BUSCETI, CR Francesca BIAGIONI, PostDoc Milena CANNELLA, CR Gemma MOLINARO, PostDoc

Composition of the LIA PSND Scientific Advisory Board

INSTITUTION/LABORATORIES	NAME	CITY, COUNTRY
CNRS - Collège de France	François TRONCHE	Paris, France
CNRS	Bernard BIOULAC	Bordeaux, France
Rockfeller University	Bruce MCEWEN	New York City, USA

[redacted]

Leiden University	Ron DE KLOET	Leiden, the Netherlands
Consiglio Nazionale delle Ricerche (CNR)	Anna MOLES	Rome, Italy
University of Milan	Maurizio POPOLI	Milan, Italy

Composition of the LIA PSND Steering Committee

INSTITUTION	TITLE, NAME, FUNCTION	CITY, COUNTRY
CNRS	- Dr Catherine JESSUS *, Director of INSB	Paris, France
Lille 1	- Pr. Philippe ROLLET, President	Lille, France
Sapienza	- Pr. Luigi FRATI, Rector	Rome, Italy
Neuromed	- Pr. Erberto MELARAGNO, President	Pozzilli (IS), Italy

* President for the first two-year mandate

[redacted]

ANNEX 3

CONSOLIDATED PROJECTED BUDGET FOR 2013

A. Specific allocations for the LIA PSND

The LIA PSND shall be supported by the allocation of earmarked financial contribution of each Party, mainly devoted to cover mobility expenses (short-term stays and meeting), in addition to other resources to which the relevant research teams have access.

COUNTRY	INSTITUTION	LABORATORY/ TEAM	TYPE OF RESOURCES ALLOCATED TO THE LIA PSND	AMOUNT (€ or FTE**)
France	CNRS	UMR8576 Team neuroplasticity	Specific funding	**Total amount : 15.000 €**
	Lille1	UMR8576 Team neuroplasticity	Specific funding	**Total amount : 10.000 €**
Italy	Sapienza	Psychopharmacology Group	Specific funding	**Total amount: 2.000 €**
	Neuromed	Laboratory of Molecular NeuroPharmacology (MNP)	Specific funding	**Total amount: 15.000 €**

** Additional specific funds such as co-supervised PhD funding, invited professor positions, Master students funding, subject to annual tenders.*

B. Preexisting staff effort devoted to the LIA PSND

COUNTRY	INSTITUTION	LABORATORY/ TEAM	TYPE OF RESOURCES ALLOCATED TO THE LIA	AMOUNT (FTE**)
France	Lille 1	UMR8576 Neuroplasticity Team	**Laboratory Staff** *Permanent* *Researchers* *Technicians* *Non-permanent* *PhD students* *PhD student MD* *Post-Docs* *Technician*	 1 0,2 0,9 0,3 0,6 1
Italy	Sapienza	Psychopharmacology Group	**Laboratory Staff** *Permanent*	 0,75
	Neuromed	Laboratory of Molecular NeuroPharmacology (MNP)	**Laboratory Staff** *Non-permanent* *Researchers* *Post-Docs*	 0,8 0,3

*** The staffing needs of the LIA are calculated based on the full time equivalent (FTE) by its members.*

[redacted]

ANNEX 4

FACILITIES AND EQUIPMENT

France

CNRS-Lille 1 - UMR 8576

Behavioural and proteomic platforms

Italy

Sapienza

Psychopharmacolgy platform

Neuromed

Molecular neuropharmacology platform

[redacted]

ANNEX 5

PROPRIETARY RESULTS EXCLUDED FROM THE PURPOSES OF LIA PSND

France

None

Italy

None

[redacted]