SAPIENZA
UNIVERSITÀ DI ROMA

Consiglio di Amministrazione

Seduta del

18 SET. 2012

Nell'anno **duemiladodici**, addì **18 settembre** alle ore **16.00**, presso l'Aula degli Organi Collegiali, si è riunito il Consiglio di Amministrazione, convocato con nota rettorale prot. n. 0054260 del 13.09.2012, 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**, prof. Francesco Avallone; i consiglieri: dott.ssa Francesca Pasinelli, prof. Giorgio Graziani, prof. Alberto Sobrero, prof. Maurizio Saponara (entra alle ore 16.25), prof. Antonio Mussino, prof. Maurizio Barbieri, prof.ssa Roberta Calvano, prof. Marco Merafina, prof. Marco Biffoni, dott. Roberto Ligia, sig. Sandro Mauceri, sig. Marco Cavallo, sig.ra Paola De Nigris Urbani, dott. Pietro Lucchetti, dott. Paolo Maniglio, dott. Massimiliano Rizzo, sig. Giuseppe Romano, sig. Alberto Senatore; il **direttore generale**, Carlo Musto D'Amore, che assume le funzioni di segretario.

E' assente giustificato: prof. Aldo Laganà

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

…….. O M I S S I S ……..

DELIBERA
194/12

BREVETTI
11/1

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DOMANDA DI BREVETTO N. USA 61/325952: CONTRATTO DI LICENZA CON ISTITUTO EUROPEO DI ONCOLOGIA (IEO).

Il Presidente sottopone all'attenzione del Consiglio di Amministrazione la seguente relazione predisposta dal Settore Trasferimento Tecnologico e Spin Off dell'Ufficio Valorizzazione Ricerca Scientifica e Innovazione.

L'Università è titolare al 33%, con Università di Pavia (33%), Università di Milano (16,5%) e Fondazione dell' Istituto Europeo di Oncologia (16,5%), della domanda di brevetto n. USA 61/325952 del 20.04.2010 dal titolo "TRANYLCYPROMINE DERIVATIVES AS INHIBITORS OF HISTONE DEMETHYLASE LSD1 AND/OR LSD2", la cui tutela è stata estesa a livello internazionale con domanda n. PCT/EP2001/055990 del 15.04.2011 – inventori Antonello Mai (Sapienza), Andrea Mattevi (UNIPV), Saverio Minucci (I.E.O.).

La quota di titolarità di Sapienza è stata acquisita, in conformità alla normativa prevista dal Codice di Proprietà Industriale (D.lgs. n. 30/2005) e al Regolamento Brevetti di Ateneo emanato con D.R. n. 490 del 16.10.09, con contratto di cessione sottoscritto con il Prof. Antonello Mai in data 19.04.10.

Le successive attività di trasferimento tecnologico, implementate dall'Ufficio in coordinamento con i corrispondenti Uffici degli Enti co-titolari, hanno condotto alla negoziazione della proposta di licensing di cui in narrazione con l'Istituto Europeo di Oncologia (I.E.O.), Ente promotore della omonima Fondazione co-titolare del brevetto.

Quest'ultimo, tramite "*TT Factor*" struttura operativa di trasferimento tecnologico ad esso afferente, si farà carico dello sviluppo sperimentale ed applicativo della tecnologia, coordinando le attività dei ricercatori coinvolti e cercando al contempo di attivare opportuni canali di investimento pubblici/privati.

Il Contratto di Licenza, che si sottopone all'approvazione di questo Consesso, messo a punto a valle delle trattative tra i co-titolari della domanda di brevetto e l'I.E.O., prevede, in sintesi, le principali seguenti condizioni:

1. concessione all'I.E.O., in regime di licenza esclusiva con possibilità di sub-licenza, dei diritti di proprietà industriale inerenti la tecnologia brevettata;
2. concessione al medesimo I.E.O. di tutti i miglioramenti e perfezionamenti connessi alla tecnologia brevettata;
3. definizione di un Accordo di Collaborazione di Ricerca fra le Università partecipanti e l'I.E.O. volto a disciplinare le attività dei ricercatori riguardanti la proprietà intellettuale congiunta;
4. previsione di un Piano di sviluppo congiunto della suddetta IP la cui responsabilità di gestione spetta al Licenziatario (I.E.O.), e il cui controllo e supervisione è affidato ad un Comitato Direttivo (JOINT STEERING COMMITEE) con ruolo consultivo;
5. previsione di un sistema di royalties derivanti dalla vendita o sub licenza a terzi del prodotto licenziato le cui percentuali spettanti alle parti licenzianti sono legate al conseguimento delle seguenti

UFFICIO VAL. R.S. e INNOVAZIONE
SettoreTrasferimento Tecnologico e Spin Off
Il Responsabile
(dott. Daniele RICCIONI)

PERVENUTO IL
13 SET. 2012
RIP. V - SETT. III

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Milestone, meglio specificate nell'allegato D del Contratto di Licenza:

Licenzianti	**Milestone 1**	**Milestone 2**	**Milestone 3**
	ADME/PK	PC	IND
UNIMI	10%	5%	3.75%
FOND. I.E.O.	10%	5%	3.75%
UNIROMA	20%	10%	6.25%
UNIPV	20%	10%	6.25%

6. obbligo del Licenziatario di provvedere alle spese e agli oneri di mantenimento e prosecuzione del brevetto;
7. diritto di prelazione riconosciuto al Licenziatario (I.E.O.) su eventuali brevetti aggiuntivi dei licenzianti relativi alla proprietà intellettuale congiunta;
8. impegno del Licenziatario (I.E.O.) allo sviluppo commerciale del prodotto licenziato.

Su tale Contratto di Licenza la Commissione Tecnica Brevetti, nella seduta del 15.6.12, ha espresso il proprio parere favorevole per ciò che concerne gli aspetti di competenza.

Il Prof. Antonello Mai del Dipartimento di Chimica e Tecnologie del Farmaco e co-inventore del brevetto, con nota del 06.09.12, ha espresso il proprio consenso alla sottoscrizione del Contratto di Licenza ed all'assunzione in prima persona degli gli obblighi di collaborazione nella ricerca previsti nel Contratto stesso.

ALLEGATI PARTE INTEGRANTE:

- contratto di licenza con l'I.E.O.

ALLEGATI IN VISIONE:

- estratto del verbale della Commissione Tecnica Brevetti del 15.6.12;
- dichiarazione di impegno del Prof. Antonello Mai.

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

DELIBERAZIONE N. 194/12

IL CONSIGLIO DI AMMINISTRAZIONE

- **Letta la relazione istruttoria;**
- **Visto lo Statuto dell'Università degli Studi di Roma "La Sapienza";**
- **Visto il D.lgs. n. 30/2005 (Codice di Proprietà Industriale);**
- **Visto il Regolamento Brevetti di Sapienza emanato con D.R. n. 490 del 16.10.2009;**
- **Vista la domanda di brevetto n. USA 61/325952 del 20.04.2010 e relativa estensione PCT n. PCT/EP2001/055990 del 15.04.2011 dal titolo "TRANYLCYPROMINE DERIVATIVES AS INHIBITORS OF HISTONE DEMETHYLASE LSD1 AND/OR LSD2", – inventori Antonello Mai, Andrea Mattevi, Saverio Minucci - di titolarità in via derivativa (giusto contratto di cessione del 19.04.10) della Sapienza per il 33%, dell'Università di Pavia per il 33%, dell'Università di Milano per il 16,5% e della Fondazione I.E.O. per il 16,5%;**
- **Vista la proposta avanzata dall'Istituto Europeo di Oncologia volta all'acquisizione dei diritti di utilizzo della proprietà intellettuale inerenti la domanda di brevetto in parola;**
- **Esaminata la bozza di contratto di licenza concordata con l'I.E.O. sopra citato e gli altri co-titolari del Brevetto;**
- **Visto il parere favorevole espresso dalla Commissione Tecnica Brevetti in data 15.6.12;**
- **Preso atto della dichiarazione di impegno sottoscritta dall'Inventore della Sapienza, Prof. Antonello Mai, con nota del 6.9.12;**
- **Presenti e votanti n. 15: con voto unanime espresso nelle forme di legge dal rettore, dal prorettore, dal direttore generale e dai consiglieri: Barbieri, Biffoni, Calvano, Cavallo, Graziani, Ligia, Mauceri, Merafina, Sobrero, Lucchetti, Maniglio e Senatore**

DELIBERA

- **di approvare il testo del Contratto di Licenza concordato con l'Istituto Europeo di Oncologia (I.E.O.) avente ad oggetto la domanda di brevetto n. USA 61/325952 del 20.04.10 e relativa estensione PCT n. PCT/EP2001/055990 del 15.04.2011 da titolo "TRANYLCYPROMINE DERIVATIVES AS INHBITORS OF HISTONE DEMETHYLASE LSD1 AND/OR LSD2";**

[redacted]

Consiglio di Amministrazione

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- **di autorizzare il Rettore alla sottoscrizione del suddetto Contratto di Licenza.**

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 .....

LICENSE AND DEVELOPMENT AGREEMENT

between

UNIVERSITA' DI ROMA, UNIVERSITA' DEGLI STUDI DI MILANO, UNIVERSITA' DI PAVIA AND FONDAZIONE IEO - LICENSORS

and

IEO, Istituto Europeo di Oncologia - LICENSEE

LICENSE AGREEMENT

This License Agreement (the "**Agreement**") is made and entered into effective as of **September 10, 2012** (the "**Effective Date**") by and between

Università degli Studi di Milano, with registered offices in via Festa del Perdono 7, in person of Enrico Decleva; Università di Pavia, with registered offices in c.so Strada Nuova 65, represented by Angiolino Stella; Università di Roma, with registered offices in Piazzale Aldo Moro 5, represented by Luigi Frati; Fondazione IEO, with registered offices in via Filodrammatici 10, represented by Marco Agnelli ("**Licensors**")

and

IEO - Istituto Europeo di Oncologia S.r.l., with registered offices in via Filodrammatici 10, Milano represented by Mauro Melis, Milano ("**Licensee**").

Licensors and Licensee are sometimes referred to herein individually as a "**Party**" and collectively as the "**Parties**."

RECITALS

WHEREAS, Licensors jointly own or otherwise control certain patents, patent applications, identified in Exhibit A, and technology, know-how and scientific and technical information relating to potential anticancer compounds known as tranylcypromine inhibitors derivatives; and

WHEREAS, the Licensee has extensive experience and expertise in the research and development of pharmaceutical products in oncology; and

WHEREAS, Licensors wish to grant to Licensee an exclusive worldwide license to use the Joint Intellectual Property Rights and the relevant Dependent Improvements under the terms and conditions hereinafter set forth;

NOW, THEREFORE, in consideration of the premises and the mutual promises and conditions hereinafter set forth, the Parties intend to be legally bound, do hereby agree as follows:

ARTICLE I: Definitions

Unless otherwise specifically provided herein, the following terms shall have the following meanings:

1.01 **"Affiliate"** shall mean, any corporation, company, partnership, joint venture, firm, entity and/or person which controls, is controlled by or is under common control with a Party. The term "control" means possession, direct or indirect, of the power to direct or cause the direction of the management and policies of any of the above mentioned entities, whether through the ownership of voting securities, by contract or otherwise.

1.02 **"Agreement"** shall mean this License Agreement.

1.02 **"Business Day"** shall mean a day other than a Saturday or Sunday on which banking institutions in Italy are open for business.

1.03 **"Confidential Information"** shall have the meaning set forth in Section 3.02.

1.04 **"Development Plan"** shall have the meaning assigned to it in Exhibit B.

1.05 **"Dependent Improvements"** shall mean any improvement or enhancement (whether patentable or not) dependent from Joint Intellectual Property Right covered by this Agreement that is discovered and/or developed by the Inventors after the Effective Date

1.06 **"Effective Date"** shall mean the date written above and shall be the Effective date of this Agreement.

1.07 **"Field"** shall means any and all indications for diagnosis, prevention, treatment and management of solid tumors and hematological malignancies.

1.08 **"First Right to Negotiate"** set forth in Section 2.05

1.09 **"Information"** shall mean all technical, scientific and other know-how and information, trade secrets, knowledge, technology, means, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, technical assistance, designs, drawings, assembly procedures, computer programs, apparatuses, specifications, data, results and other material, including: biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and

quality control data and information, including study designs and protocols; assays and biological methodology; (whether or not confidential, proprietary, patented or patentable) in written, electronic or any other form now known or hereafter developed.

1.10 "Inventors" shall mean Saverio Minucci, Antonello Mai, Andrea Mattevi.

1.11 "Joint Intellectual Property Rights" shall mean i) the Joint Patents as listed in Exhibit A; and ii) the Joint Know-how as set forth in Section 1.13 and 1.14 hereto.

1.12 "Joint Patents" Patents and Patent's applications listed in Exhibit A and all applications, patents, reissues, re-examinations, extensions, continuations, continuations in part, continuing prosecution applications, and divisions of such applications; and foreign counterparts to any of the foregoing, including without limitation utility models.

1.13 "Joint Know-how" shall mean any Information related to the Licensed Products, whether or not patented or patentable, that are conceived, discovered, developed or otherwise made, data, specifications, test results, ideas, methods, characterization and techniques which are known to the Licensors on the Effective Date and which are necessary or useful for the discovery, development, manufacture, use or sale of the Licensed Products.

1.14 "Joint Steering Committee" or "JSC" shall have the meaning set forth in Section 5.0 hereto.

1.15 "Licensed Products" any chemical entity covered by at least one valid claim, as set forth in Section 1.28 hereto, under the Joint Intellectual Property Rights and the relevant Dependent Improvements

1.16 "Licensee" shall have the meaning set forth in the preamble hereto.

1.17 "Licensors" shall have the meaning set forth in the preamble hereto

1.18 "Licensee Net Considerations" shall mean the net payments received by Licensee from Third Party for granting the sublicense of the Licensed Products either in the form of up-front or milestones payments or royalties on Net Sales of the Licensed Products, less (a) direct administration and legal costs related to the Licensed Products and duly documented by the Licensee (b) Past and future Patent and Intellectual Property costs and (c) any license fees or other considerations due for any further intellectual property needed to commercialize the Licensed Products.

1.19 "Net Sales" shall mean the gross billing price Third Party, its Affiliates and sub-licensees charge to their customers for the Licensed Products, less (a) credits, allowances, discounts and rebates to, and charge-backs

from the account of, such independent customers for spoiled, damaged, out-dated, rejected or returned Licensed Products; (b) actual freight and insurance costs incurred in transporting such Licensed Products to such customers; (c) cash, quantity and trade discounts and other price reduction programs; and (d) sales, use, occupation, value-added, excise and other direct taxes incurred. Such amounts shall be determined from the books and records of Licensee and/or its Affiliates maintained in accordance to the applicable generally accepted accounting principles, consistently applied.

1.20 "New Patent and Independent Improvements" shall mean any New Patent and/or patentable Improvements developed by the Inventors, which are independent from the Joint Intellectual Property Rights and which can ameliorate the performance of the Licensed Products or have the same Mechanism of Action of Inhibition of Histone Demethylases LSD1 and LSD2 inhibition in the Field. For the sake of clarity they do not include "Research Collaboration IP".

1.21 "Party" and "Parties" shall have the meaning set forth in the preamble hereto.

1.22 "Payments" shall have the meaning set forth in Section 6.

1.23 "Research Collaborations" shall mean any agreements between Licensee and Universita' di Pavia and/or Universita' di Roma whereby the Licensee commissions research activities in the area of LSD1 and LSD2 inhibitors to Inventors and/or their direct collaborators.

1.24 "Research Collaboration IP": shall mean any patentable or non-patentable results originated in the performance of the Research Collaborations.

1.25 "Term" shall have the meaning set forth in Section 10.

1.26 "Third Party" shall mean any Person other than Licensors, Licensee and their respective Affiliates.

1.27 "Territory" shall mean the entire world.

1.28 "Valid Claim" shall mean a claim of an issued and unexpired patent included within the Joint Intellectual Property Rights (Exhibit A), which has not been held permanently revoked, unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, un-appealable or un-appealed within the time allowed for appeal, and which has not been admitted to be invalid or unenforceable through reissue or disclaimer or otherwise.

ARTICLE II. License Grant

Section 2.01 **License Grant.** The Licensors hereby grant to Licensee and its Affiliates an exclusive, royalty-bearing, sub-licensable license under the Joint Intellectual Property Rights and the relevant Dependent Improvements generated by the Licensors to develop, make, have made, use, and/or sell the Licensed Products in the Field in the Territory, subject to the milestones indicated in Exhibit B and further extensions.

Section 2.02 **Sublicense.** Licensee shall have the right to grant sub-licenses to Third Parties under the Joint Intellectual Property Rights and the relevant Dependent Improvements to develop, make, have made, use and sell the Licensed Products, provided that such sub-licenses shall be in writing and expressly subject and subordinate to, and consistent with, the terms and conditions of this Agreement. Licensee agrees to be reasonably responsible for the performance hereunder by its sub-licensees.

Section 2.03 **Use for Research Purposes.** It is understood that the granting of any license hereunder is subject to the non-transferable right of Licensors and its respective employees, to use the Joint Intellectual Property Rights and the Relevant Dependent Improvements solely for internal research and educational purposes.

Section 2.04 **New Patents and Independent Improvements.** Following the execution of this Agreement any New Patent and or patentable Independent Improvement generated by Licensee will be owned by Licensee and any New Patent or patentable Independent Improvements generated by Licensors regarding new molecular entities with the same mechanism of action (Histone Demethylases LSD1 and LSD2 inhibition) in the Field will be owned by Licensors and subject to Section 2.05.

Notwithstanding the above, the Parties acknowledge that the **Research Collaboration IP** is disciplined in the corresponding Research Collaborations agreement between IEO with each of Universita' di Pavia and/or Universita' di Roma as the case may be. For the sake of clarity such Research Collaboration IP will be owned by IEO.

Section 2.05 **First Right to Negotiate.** Licensors shall offer to Licensee the right to negotiate in good faith exclusively with Licensors for a period of ninety (90) days the terms of an agreement pursuant to which Licensee, alone or in collaboration with Licensors and or with a Third Party, would develop and/or sublicense and/or commercialize the New Patents and or Independent Improvements, in the Territory. The Licensors shall send, as soon as possible, a negotiation notice to Licensee together with a report summarizing available

data with respect to the New Patent and/or Independent Improvements, Licensee shall notify Licensors in writing within thirty (30) days after receipt of the notice whether or not it wishes to exercise the First Right to Negotiate. If Licensee wishes to exercise the First Right to Negotiate, Licensors and Licensee shall negotiate in good faith for a period of ninety (90) days after receipt of the response of Licensee the terms of a license agreement based on the actual fair market value; provided that neither Party shall have any obligation to execute a licensee agreement. Should the Parties enter into in a license agreement related to the New Patents and Independent Improvement, the New Patents and Independent Improvement shall become part of the Joint Intellectual Property rights.

Section 2.06 Patent ownership. Subject to the terms of this Agreement Joint Patent and Joint Know-how will remain property of the Licensors.

ARTICLE III. Disclosure of Inventions, Confidentiality and Representations

Section 3.01 Disclosure of Inventions. The Licensors agree promptly after the Effective Date of this Agreement to deliver and to disclose to duly authorized representatives of Licensee, all proprietary technical data, methods, processes on the Joint Intellectual Property Rights and the relevant technology.

Section 3.02 Mutual Confidentiality. Licensors and the Licensee realize that some information received by one Party from the other pursuant to this Agreement shall be confidential. It is therefore agreed that any Information received by one Party from the other, shall not be disclosed by either Party to any third Party and shall not be used by either Party for purposes other than those contemplated by this Agreement for a period of five (5) years from the termination of this Agreement, unless or until:

(a) said information shall become known to third Parties not under any obligation of confidentiality to the disclosing Party, or shall become publicly known through no fault of the receiving Party, or

(b) said information was already in the receiving Party's possession prior to the disclosure of said information to the receiving Party, except in cases when the information has been covered by a preexisting Confidentiality Agreement, or

(c) said information shall be subsequently disclosed to the receiving Party by a third Party not under any obligation of confidentiality to the disclosing Party, or

(d) said information is approved for disclosure by prior written consent of the disclosing Party,

(e) is developed by a Party independent of any Confidential Information of the other Party, such independent development being performed solely by persons not having access whatsoever to the other Party's Confidential Information, as evidenced by contemporaneous written evidence of same; or

(f) said information is required to be disclosed by Court order or governmental law or regulation, provided that the receiving Party gives the disclosing Party prompt notice of any such requirement and cooperates with the disclosing Party in attempting to limit such disclosure.

Section 3.03 Corporate Action. Licensors and Licensee represent and warrant to the other Party that they have full power and authority to enter into this Agreement and carry out the transactions contemplated hereby, and that all necessary corporate actions had been duly taken in this regard.

Section 3.04 Press Releases. All press releases or other similar public communications by either Party relating to this Agreement shall be approved in advance by the other Party, which approval shall not be unreasonably withheld or delayed, except for those communications required by applicable law, disclosures of information for which consent has previously been obtained or information that has been previously disclosed publicly or as otherwise set forth in this Agreement; provided that the other Party is given a reasonable opportunity to review and comment on any such press release or public communication in advance thereof. In any case, after fifteen (15) days from the receipt of the press release of other similar communication no response is given by the Party receiving the press release or other similar communication, it will be conclusively presumed that the publication may proceed without delay.

Section 3.05 Publications. The Licensee shall have the right to review any paper proposed for publication by the Licensors, including any oral presentation or abstract, that contains studies with respect to the Joint Intellectual Property Right or includes other data generated under this Agreement or that includes Confidential Information of the Licensors. Before any such paper is submitted for publication or an oral presentation is made, the Licensors shall deliver a complete copy of the paper or materials for oral presentation to the Licensee at least thirty (30) days prior to submitting the

paper to a publisher or making the presentation. The Licensee shall review any such paper and give its comments to the Licensors within fifteen (15) days from the receipt of such paper from the Licensors. In case of objections to publication, Licensors may refer the matter to the JSC for resolution together with the reasons for withholding approval. Notwithstanding the foregoing, Licensors shall comply with the Licensee request to delete references to Licensee Confidential Information in any such paper and will withhold publication of any such paper or any presentation of the same for an additional sixty (60) days in order to permit Licensee to obtain Patent protection.

Section 3.06 Return of Confidential Information. Upon the effective date of the termination of this Agreement for any reason, either Party may request in writing, and the other Party shall either, with respect to Confidential Information to which such other Party does not retain rights hereunder: (a) promptly destroy all copies of such Confidential Information in the possession of the other Party and confirm such destruction in writing to the requesting Party; or (b) promptly deliver to the requesting Party, at the other Party's expense, all copies of such Confidential Information in the possession of the other Party*; provided, however*, the other Party shall be permitted to retain one (1) copy of such Confidential Information for the sole purpose of performing any continuing obligations hereunder or for archival purposes. Notwithstanding the foregoing, such other Party shall be permitted to retain such additional copies of or any computer records or files containing such Confidential Information that have been created solely by such Party's automatic archiving and back-up procedures, to the extent created and retained in a manner consistent with such other Party's standard archiving and back-up procedures, but not for any other use or purpose. All Confidential Information shall continue to be subject to the terms of this Agreement for the period set forth in Section 3.02.

ARTICLE IV. Development Plan

Section 4.01 Development. Licensee itself or through its Affiliates and/or its sub-licensees shall use reasonable efforts and due diligence to develop the Joint Intellectual Property Rights which are licensed hereunder into commercially viable products as promptly as is reasonably and commercially feasible. Licensee will use its best efforts to implement the Development Plan described in Exhibit B.

Section 4.02 Extension of Time. Notwithstanding the above, if Licensee and/or its Affiliates believe that they cannot, within the exercise of prudent and reasonable business judgment, reach the development milestones within the established time period set forth under Exhibit B, Licensee shall, at Joint

Steering Committee discretion, have the right to extend the duration of the program referring to specific milestones of one (1) year with respect to the originally proposed timelines, such an extension to be done no more than two times during the development period. These extensions shall be considered independently from any amendment to the Development Plan proposed by the JSC as set forth under Article 5.02.

Section 4.03 Development Responsibilities. It is understood that the Licensee at its sole discretion will be responsible for the Development Plan implementation and for the decision to terminate the development or sublicense the Licensed Products.

ARTICLE V. Joint Steering Committee

Section 5.01 Formation of Joint Steering Committee. The Parties shall establish a joint steering committee (the "Joint Steering Committee" or "JSC"), which shall have an advisory role in overviewing the implementation of the Development Plan until the Licensed Products are sublicensed to any Third Party.

Section 5.02 Specific Responsibilities of the JSC. JSC will have the following advisory tasks: (a) overseeing development activities of the Licensed Products; (b) reviewing technical and scientific data coming from the implementation of Development Plan; (c) propose amendments to the Licensee approval; (d) every six months prepare in writing a progress report with technical and scientific data. Such responsibilities of the JSC shall be in force until the earliest of the following: (1) termination of the development activities by the Licensee; (2) completion of the Development Plan; (3) sublicense of the Licensed Products to a Third Party.

Section 5.03 JSC Membership. The members of the JSC are set forth in Exhibit C.

Section 5.04 Meetings. The JSC shall meet at least quarterly, or as otherwise agreed to by the Parties. The members shall agree on the minutes of each meeting promptly, but in no event later than the next meeting of the JSC.

ARTICLE VI. Payments, Records and Reports

Section 6.01 Payments. In consideration for the grant of license of the of Joint Intellectual Property Rights and Dependent Improvements Licensee shall pay to the Licensors a percentage of the Licensee Net Consideration, which meaning is set forth in Section no.1.18. Such compensation from Licensee to Licensors is subject to Section 6.01 (a) and (b) below and the amount due to the Licensors is described in Exhibit D.

Licensee shall pay to Licensors in EURO. The payment from Licensee to Licensors will be made within sixty (60) days following Licensee reception on its bank account of the corresponding payment from Third Party.

(a) **Valid Claim.** In case the patent of the Licensed Products sub-licensed to a Third Party by Licensee still retains at least one Valid Claim, which meaning is set forth in Section 1.28, of the Joint Intellectual Property Rights, the Licensee will pay the Licensors a percentage of the Licensee Net Considerations received by Third Party as result from the transaction between Licensee to Third Party. Payments by Licensee to Licensors will be done according to what set forth in Exhibit D.

c) **No Valid Claim.** In case the patent of the product sub-licensed by Licensee to Third Party does not contain any Valid Claim of the Joint Intellectual Property Right described in Exhibit A, in such a case, the product licensed to Third Party is considered to be completely independent from the Joint Intellectual Property Rights and therefore nothing is due by Licensee to Licensors.

ARTICLE VII. Intellectual Property

Section 7.01 Licensors' Rights. The Licensee shall control all future preparation, filing, prosecution and maintenance of the Joint Patents. Notwithstanding the foregoing, the Licensors shall have the obligation to provide the required support to Licensee to maintain the Joint Patents in a manner that best furthers the rights and interests granted to Licensee under this Agreement.

Section 7.02 Licensee's Rights. The Licensors agrees to promptly provide Licensee with copies of: (i) all patent applications included in the Joint Patents; (ii) all prior art searches in its possession related to said patent applications and the subject matter of this Agreement; and (iii) all correspondence to and from the United States Patent and European Patent Office and foreign Patent Office related to the Joint Patents. Licensee shall

have the right, but not the obligation, to consult with the Licensors with respect to the filing, prosecution and maintenance of the Joint Patents; however all final decisions respecting conduct of the prosecution of said patent applications shall rest solely in the discretion of the Licensee.

Section 7.03 Patent Costs. Licensee shall pay for all future expenses incurred after the Effective Date in connection with the preparation, filing, prosecution and maintenance of the Joint Patents. If Licensee chooses to discontinue prosecution or maintenance of any patent or patent application, which is a subject of the Joint Patents, it will so inform the Licensors within a reasonable time before implementation of such decision but in no event will be less than ninety (90) days prior to the date on which any action is required to avoid said application(s) or patent(s) becoming effectively abandoned. The Licensors then shall have the right to prosecute or maintain such patent or patent application on its own and at its own expenses, in which case the license to Licensee under such patent or patent application will terminate.

Section 7.04 New Patents Applications and Independent Improvement. The Licensors shall promptly notify Licensee in writing of any possible New Patent and or Independent Improvement, as defined in Section 1.20, of the Joint Intellectual Property Rights on the Licensed Products. In accordance with Section 2.05, Licensee shall have the option, exercisable upon written notification to the Licensors, to assume full responsibility and to prosecute the New Patent and or Independent Improvement in which event all such New Patents and or Independent Improvements shall be promptly licensed by the Licensors to Licensee under terms and conditions to be agreed upon, from which time such Independent Improvements shall become part of the Joint Intellectual Property Right.

Section 7.05 Action Against Joint Patent. Each Party shall promptly notify the other Party of any action for declaratory judgment, nullity or revocation action, opposition or interference proceedings, or similar proceedings against a Joint Patent. Licensee may decide, at its sole discretion, to defend such action on any such Joint Patent. If Licensee exercises such right, (a) Licensee shall select legal counsel and pay all legal fees and costs of defending such action, and (b) Licensee also shall have the right to settle such action; provided, however, no settlement may be entered without the Licensors' written consent (which shall not be unreasonably withheld or delayed) if such settlement would (i) materially and adversely affect the Licensors' interest or (ii) admit non-infringement or invalidity or unenforceability or narrow the claim construction of a Joint Patent. The Licensors shall reasonably cooperate, at Licensee expense, to facilitate the defence of all such suits. To the extent that Licensee is unsuccessful in defending such action, including a holding of any Joint Patent invalid or narrow

claim construction (provided that such outcome does not result from the gross negligence, wilful misconduct or breach of this Agreement by Licensee), Licensee shall incur no liability to the Licensors as a consequence of such outcome.

Section 7.06 Infringement. Each Party shall promptly notify the other Party of any potential infringement of a Joint Patent. In the event that a third party infringes on a Joint patent, Licensee may decide, at its sole discretion, to bring legal action to enforce any such patent. If Licensee exercises such right, Licensee shall (a) select legal counsel and pay all legal fees and cost of prosecution of such action, and (b) have the right to file suit for patent infringement and the right to settle such suits; provided, however, no settlement may be entered without the Licensors' written consent (which shall not be unreasonably withheld or delayed) if such settlement would (i) materially and adversely affect the Licensors' interest or (ii) admit non-infringement or invalidity or unenforceability or narrow the claim construction of a Joint Patent. Licensee shall keep Licensors reasonably apprised of all developments in the action and shall seek Licensors input on any substantive submissions or positions taken in the litigation regarding the scope, validity or enforceability of such Joint Patent. To the extent that Licensee is unsuccessful in enforcing such Joint Patent, including a holding that such Joint Patent was not infringed (provided that such outcome does not result from the gross negligence, wilful misconduct or breach of this Agreement by Licensee), Licensee shall incur no liability to the Licensors as a consequence of such outcome.

In the event that Licensee shall choose not to take such action, the Licensors shall have the right, at its option and its own expense, to prosecute any action to enjoin such infringement or to prosecute any claim for damages. To the extent that the Licensors are unsuccessful in enforcing such Joint Patent, including a holding that such Joint Patent was not infringed (provided that such outcome does not result from the gross negligence, wilful misconduct or breach of this Agreement by the Licensors), the Licensors shall incur no liability to Licensee as a consequence of such outcome.

Licensee shall have the right to enter into any commercial and/or settlement agreements with any third Party which has been identified by Licensee and/or the Licensors as an actual or potential infringer of the Joint Intellectual Property Rights provided that such agreement includes a sublicense of the Joint Patents under the terms and conditions of this Agreement.

Section 7.07 Proceeds. The Party prosecuting any such infringement action shall be entitled to retain the remaining funds received as a result of

settlement or judgment of such action. The Parties may also agree to jointly pursue infringes. After deduction and payment to the Parties of their respective out of pocket costs and fees (including without limitation reasonable attorney's fees) incurred in prosecuting any such actions, the remaining funds obtained as a result of settlement or of judgment of any such jointly prosecuted action shall be divided in the following manner: 100% of all the net funds shall be equally divided between the Parties. If funds are insufficient to pay all costs and fees then all of the funds shall be paid to the Parties in the proportion to the amount of legal fees and costs incurred by the Parties in the prosecution of such action.

Section 7.08 Cooperation. In any suit, proceeding or dispute involving the infringement of any Joint Patent, the Parties shall provide each other with reasonable cooperation, and, upon the request and at the reasonable expense of the Party bringing suit, the other Party shall make available to the Party bringing suit, at reasonable times and under appropriate conditions, all relevant personnel, records, papers, information, samples, specimens, and the like in its possession.

ARTICLE VIII. Commercial Development

Section 8.01 Commercial Development. During the term of this Agreement, Licensee agrees to use reasonable efforts commensurate in scope with efforts used by Licensee for similar products to effectively develop and/or sublicense the Licensed Products.
It is understood that in case the Licensee will not be able to negotiate an agreement with Third Parties having per object the commercial exploitation of the Joint Patents within the terms of the Agreement, nothing will be due to Licensors.

Section 8.02 Name. Licensee shall not use and shall not permit to be used by any other person or entity the name of the Licensors nor any adaptation thereof, or the name of Licensors' employees, in any advertising, promotional or sales literature, or for any other purpose without prior written permission of the Licensors, except that Licensee may state that it is licensed by the Licensors under the Joint Patents and the licensed technology.

ARTICLE IX. Indemnity, Disclaimers

Section 9.01 Disclaimer. Nothing contained in this Agreement shall be construed as:

(a) a warranty or representation by the Licensors as to the validity or scope of any Licensors' Patent Rights; or

(b) a warranty or representation that any Licensed Products manufactured, used or sold will be free from infringement of patents, copyrights, or third Parties, except that the Licensors represent that they have no knowledge of any existing issued patents or copyrights which might be infringed.

THE LICENSORS MAKE NO WARRANTIES, EXPRESS OR IMPLIED, AS TO THE MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OF LICENSED PRODUCTS. IN NO EVENT SHALL EITHER PARTY BE LIABLE FOR ANY LOST PROFITS OR SPECIAL OR INCIDENTIAL OR CONSEQUENTIAL DAMAGES REGARDLESS OF WHETHER ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

ARTICLE X. Duration and Termination

10.01 Term. This Agreement shall become effective upon the Effective Date, and unless sooner terminated in accordance with any of the provisions herein, shall remain in full force during the life of the last-to-expire patents under the Joint Patents and Dependent Improvements in the last-to-expire country in the Territory.

10.02 Termination.
Without prejudice of the provisions set forth under Section no. 2.01 of this Agreement, this Agreement can be terminated by the Licensors upon written request, in the case the Licensee does not meet on time the milestones within the timelines and their extensions indicated in Exhibit B and Article 2.01 of this Agreement.
It is understood that in case of failure by the Licensee to meet on time the development milestones due to partnering and negotiation activities aimed at sublicensing the Licensed Products, this Article 10.02 shall not apply.

10.03 Right of withdrawal. Licensee may withdraw from this Agreement at any time and for any reason upon thirty (30) days written notice to the Licensors.

10.04 Effect of Termination. Upon termination of this Agreement under Section 10.02 or 10.03 above, Licensee shall be entitled, for an additional period of three (3) months from such termination and on a non-exclusive basis, to continue to sell Licensed Products in inventory. Such sales shall be made subject to all of the provisions of this Agreement and to an accounting for and payment of a royalty thereon. Such accounting and payment shall be due and paid within sixty (60) days after the close of the said three (3) month period.

Upon termination of this Agreement under Section 10.02 or 10.03 above, the Joint Patents and all rights included therein shall revert to the Licensors and the Licensors shall be free to enter into agreements with any other third party for the granting of a license or to deal in any other manner with such right as it shall see fit at their sole discretion. Licensee shall return or transfer to the Licensors, within 30 days of termination of this Agreement, all material, in soft or hard copy, relating to the Joint Patents and Dependent Improvements generated by Licensors connected with the Licensors and it may not make any further use thereof.

Upon termination of this Agreement under Section 10.02 or 10.03 above, Licensee shall promptly notify the Licensors in writing of any possible Dependent Improvements and/or New Patents and or Independent Improvements generated by Licensee. Licensee shall offer to the Licensors the right to negotiate in good faith exclusively with Licensee for a period of ninety (90) days the terms of an agreement pursuant to which the Licensors would develop and or sublicense and or commercialize the New Patents and or Independent Improvements in the Territory. In accordance with above, the Licensors shall have the option, exercisable upon written notification to Licensee, to assume full responsibility and to prosecute the New Patent and or Independent Improvement in which event all such New Patents and or Independent Improvements shall be promptly licensed by Licensee to the Licensors under terms and conditions to be agreed upon, from which time such New Patent and or Independent Improvements shall become part of the Joint Intellectual Property Right. Licensee shall fully cooperate with the Licensors to effect such license and shall execute any document and perform any acts required to do so.

10.05 Prior Obligations and Survivability. Termination of this Agreement for any reason shall not release either Party from any obligation theretofore accrued. Sections 3.02, 6.01, 10.01 shall survive the termination of this Agreement.

ARTICLE X. Miscellaneous

11.01 Governing Law and Dispute resolution. This Agreement shall be construed by and governed in accordance with the Italian Law.
Any dispute, controversy or claim arising under, out of or relating to this Agreement and any subsequent amendments of this Agreement, including, without limitation, its formation, validity, binding effect, interpretation, performance, breach or termination shall be referred to Court Of Milan.

11.02 Notices. Any notice or communication required or permitted to be given by either Party hereunder, shall be deemed sufficiently given, if mailed by certified mail, return receipt requested, and addressed to the Party to whom notice is given as follows:

If to Licensee to:

Istituto Europeo di Oncologia (IEO)
Attention: Daniela Bellomo (TTFactor)
Via: Ripamonti 435
20141 Milano Italy
Fax: 02 94375991
Email: daniela.bellomo@ttfactor.com

If to Licensors collectively to:

Università degli Studi di Milano
Attention: Roberto Tiezzi (UNIMITT)
Via Festa del Perdono 7
20122 Milano Italy
Fax: 02 50312861
Email: roberto.tiezzi@unimi.it

Università degli Studi di Roma
Attention: Sabrina Luccarini (UNIROMA)
Piazzale Aldo Moro, 5
00185 Roma Italy
Fax: 06 49910692
Email: sabrina.luccarini@uniroma1.it

Università degli Studi di Pavia
Attention: Francesca Negri (UNIPAVIA)
C.so Strada Nuova 65
27100 Pavia Italy
Fax: 0382 984942
Email: francesca.negri@unipv.it

Fondazione Istituto Europeo di Oncologia (FIEO)
Attention: Marco Agnelli

Via Ramusio 1
20141 Milano Italy
Fax: 02 94379269
Email: marco.agnelli@ieo.it

11.03. Assignment. No Party may assign this Agreement without the prior written consent of the other Party, except that Licensee may assign it to its Affiliates provided that such Assignee shall abide to the conditions herein.

11.04 Entire Agreement. This Agreement represents the entire Agreement between the Parties as of the Effective Date hereof, and may only be subsequently altered or modified by an instrument in writing. This Agreement cancels and supersedes any and all prior oral or written agreements between the Parties which relate to the subject matter of this Agreement excluding the existing Research Collaborations.

11.05 Waiver. A failure by one of the Parties to this Agreement to assert its rights for or upon any breach or default of this Agreement shall not be deemed a waiver of such rights nor shall any such waiver be implied from acceptance of any payment. No such failure or waiver in writing by any one of the Parties hereto with respect to any rights shall extend to or affect any subsequent breach or impair any right consequent thereon.

11.06 Severability. The Parties agree that it is the intention of neither Party to violate any public policy, statutory or common laws, and governmental or supranational regulations; that if any sentence, paragraph, clause or combination of the same is in violation of any applicable law or regulation, or is unenforceable or void for any reason whatsoever, such sentence, paragraph, clause or combinations of the same shall be inoperative and the remainder of the Agreement shall remain binding upon the Parties.

11.07 Independent Contracts. Nothing herein shall be construed to create any relationship of employer and employee, agent and principal, partnership or joint venture between the Parties. Each Party is an independent contractor. No Party shall assume, either directly or indirectly, any liability of or for the other Party other than as expressly provided herein. No Party shall have the authority to bind or obligate another Party and no Party shall represent that it has such authority.

11.08 Force Majeure. Any delays in or failures of performance by either Party under this Agreement shall not be considered a breach of this Agreement if and to the extent caused by occurrences beyond the reasonable control of

the Party affected, including but not limited to: acts of God; acts, regulations or laws of any government; strikes or other concerted acts of workers; fires; floods; explosions; riots; wars; rebellions; and sabotage; and any time for performance hereunder shall be extended by the actual time of delay caused by such occurrence.

11.09 Headings. The headings of the paragraphs of this Agreement are inserted for convenience only and shall not constitute a part hereof.

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement, in duplicate originals, by their respective officers hereunto duly authorized, the day and year herein written.

IEO (Licensee)

By: _____

Date:_____

Name:

Title:

UNIVERSITA DEGLI STUDI DI MILANO (Licensor)

By: _____

Date: _____

Name:

Title:

UNIVERSITA DEGLI STUDI DI ROMA (Licensor)

By: _____

Date: _____

Name:

Title:

UNIVERSITA DEGLI STUDI DI PAVIA (Licensor)

By: _____

Date:_____

Name:

Title:

Fondazione IEO (Licensor)

By: _____

Date:_____

Name:

Title:

For the acceptance of Art. 2.01, 2.02, 2.03, 2.04, 2.05, 2.06, 3.06, 6.01, 7.02, 7.04

Antonello Mai

Andrea Mattevi

Saverio Minucci

EXHIBIT A

- Joint Intellectual property Rights –

Joint Patents:

US provisional n. 61/325,952 filed on 20th April 2010
PCT/EP2011/055990 filed on 15th April 2011 (publ. n. WO 2011/131576)

EXHIBIT B
Development Plan and Milestones

Within 31 December 2012: Lead ID

-Hit confirmation and expansion of patented chemical class
-Set up of primary biochemical assay for IC50 determination
-in cell: antiproliferative activity on selected cell lines
-in vitro ADMET of selected molecules

Within 31 December 2013: in vivo Model

-Hit2Lead and Lead optimization of patented chemical class
-in vitro: set up of secondary biochemical assays
-in cell: antiproliferative activity on selected cell lines
-determination of (cellular) mechanism of action (MOA)
-in vitro ADMET and preliminary PK of selected molecules
-preliminary in vivo experiment (Xenograft)

Within 30 June 2015: PC

-Preclinical Candidate (PC) identification
-Preclinical development plan

If the Licensee decides to continue the development until IND (or further), updated milestone schedule and timelines will be provided upon reaching PC.

EXHIBIT C
Joint Steering Committee Initial Members

-

Dott. Mario Varasi, Chairman (IEO – Istituto Europeo di Oncologia)
Prof. Andrea Mattevi (Universita' di Pavia)
Prof. Antonello Mai (Universita' di Roma)
Prof. Saverio Minucci (Universita' di Milano)
Dr. ssa Daniela Pezzi (Fondazione IEO)

EXHIBIT D

- Payments from Licensee to Licensor -

Percentage of Licensee Net Consideration due to Licensors by Licensee in case the Licensed Products sublicensed to a Third Party are covered by at least one valid claim of the Joint Patents and/or Dependent Improvements

	Milestone 1	**Milestone 2**	**Milestone 3**
Parties	ADME/ PK	PC	IND
	%	%	%
UNIMI	10	5	3.75%
F. IEO	10	5	3.75%
UNIROMA	20	10	6,25%
UNIPV	20	10	6,25%

Milestone 1: Licensee Net Considerations due to Licensors in case the Licensed Products are out-licensed by Licensee to a Third Party after completion of ADME/ PK studies and before Milestone 2

Milestone 2: Licensee Net Considerations due to Licensors in case the Licensed Products are out-licensed by Licensee to a Third Party after identification of the Preclinical Candidate (PC) and before Milestone 3

Milestone 3: Licensee Net Considerations due to Licensors in case the Licensed Products are out-licensed by Licensee to a Third Party after having prepared an Investigational New Drug (IND) application dossier

WHEREAS

- ADME/PK: Absorption, Distribution, Metabolism, Excretion
- PK: pharmacokinetic
- PC: identification of preclinical candidate

The Parties agree that if the Licensed Products are outlicensed later than Milestone 3 the parties will negotiate in good faith the revenue sharing conditions