SAPIENZA
UNIVERSITÀ DI ROMA

Consiglio di Amministrazione

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Nell'anno **duemilaundici**, addì **5 luglio** alle ore **15.45**, presso l'Aula degli Organi Collegiali, si è riunito il Consiglio di Amministrazione, convocato con nota rettorale prot. n. 0044357 del 30.06.2011, 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: prof. Aldo Laganà, prof. Giorgio Graziani, prof. Massimo Moscarini (entra alle ore 16.00), prof. Maurizio Saponara, 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 (entra alle ore 16.00), dott. Matteo Fanelli, dott. Pietro Lucchetti, dott. Paolo Maniglio (entra alle ore 16.35), sig. Gianfranco Morrone; il **direttore generale**, Carlo Musto D'Amore, che assume le funzioni di segretario.

È assente giustificato: dott.ssa Francesca Pasinelli.

È assente: sig. Giuseppe Romano.

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
173/11

BREVETTI
13/1

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DOMANDA DI BREVETTO N. USA 61/256846: TERM SHEET DI LICENZA E COLLABORAZIONE NELLA RICERCA CON LA SOCIETA' VESTA THERAPEUTICS INC.

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 50% con l'University North Carolina (U.N.C.), della domanda di brevetto n. USA 61/256846 del 30.10.2009 dal titolo "Multipotent stem cells from the estrahepatic biliary tree and methods of isolating same", la cui tutela è stata estesa a livello internazionale con domanda PCT n. 12/926,161 del 28.10.10 – inventori Alvaro Domenico, Gaudio Eugenio, Carpino Guido, Vincenzo Cardinale, Lola M. Reid, Yunfang Wang.

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. nr. 490 del 16.10.09, giusti contratti di cessione sottoscritti con gli inventori della Sapienza in data 25.10.10, e altresì, con il dott. Carpino, afferente all'Università degli Studi di Roma "Foro Italico", in data 21.12.10.

Le successive attività di trasferimento tecnologico, implementate dall'Ufficio e finalizzate alla valorizzazione del brevetto in oggetto, hanno condotto al recepimento di una proposta di licensing da parte di Vesta Therapeutics Inc., per l'acquisizione in licenza della quota di diritti di sfruttamento della proprietà intellettuale di cui è titolare l'Ateneo e, inoltre, per stabilire i termini di collaborazione nello sviluppo industriale della tecnologia.

Tale Società è stata fondata nel 2002 da un fondo di investimento focalizzato sulla medicina rigenerativa denominato Toucan Capital Corp., il quale non presenta alcun collegamento con gli inventori della tecnologia oggetto del presente Term Sheet.

Vesta Therapeutics Inc. ha sede nel Maryland (USA) ed impegnata nel campo dello sviluppo di terapie cellulari da impiegare principalmente contro le patologie del fegato, è intenzionata a portare avanti principalmente lo sviluppo clinico (terapeutico) e collateralmente l'uso pre-clinico.

Il Term Sheet, che si sottopone all'approvazione di questo Consesso e messo a punto dopo diversi mesi di trattative condotte dal Settore Trasferimento Tecnologico e Spin Off con Vesta Therapeutics, è prodromico alla successiva conclusione del contratto di licenza che verrà sottoscritto da Sapienza e al relativo "*sponsored reserarch agreement*" per il finanziamento dello sviluppo che verrà sottoscritto, per competenza, dal Dipartimento di Scienze Anatomiche, Istologiche, Medico Legali e dell' Apparato Locomotore.

Tale Term Sheet prevede le principali condizioni che regoleranno il successivo rapporto, qui di seguito schematicamente riportate:

a) la concessione in licenza esclusiva dei diritti di sfruttamento della domanda di brevetto per ciò che concerne l'uso clinico (terapeutico) per tutta la durata di vita del brevetto (pari a venti anni dal primo deposito USA);

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

PERVENUTO IL
30 GIU. 2011
RIP. V - SETT. III

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b) la concessione non esclusiva dei diritti di sfruttamento del brevetto per uso non terapeutico;
c) l'accollo dei costi di mantenimento del brevetto da parte di Vesta Therapeutics Inc. ;
d) le seguenti obbligazioni economiche che prevedono a carico di Vesta Therapeutics Inc il pagamento a favore di Sapienza di:
- un upfront iniziale di € 50.000,00, (di cui € 10.000,00 corrisposti alla firma del presente Term Sheet);
- annual license payments di € 30.000,00 il II anno, di € 35.000,00 il III e IV anno, e di € 40.000,00 dal quinto anno fino alla scadenza del brevetto;
- royalties minime garantite pari a € 50.000,00 il I e II anno e € 100.000,00 dal III anno in poi fino alla scadenza del brevetto;
- royalties variabili pari al 2% del fatturato netto realizzato da Vesta;
- tre milestones di € 40.000,00, € 60,000,00 e € 100.000,00 legate al conseguimento di individuati steps di sperimentazione;
- compensi derivanti da eventuali sub-licenze pari al 20% di tutte le roaylties incassate da Vesta con un minimo garantito di € 20.000,00 e pari al 10% di tutti i compensi diversi dalle royalties percepiti da Vesta con un minimo garantito di € 10.000,00;
- finanziamento alla ricerca tramite la sottoscrizione (da parte del Dipartimento di afferenza degli Inventori) di uno *sponsored research agreement* per un importo annuo di € 250.000,00, per almeno tre anni;
- *additional fee* minima garantita su eventuali risultati migliorativi del brevetto sviluppati in regime di cotitolarità di € 10.000,00;
e) riconoscimento di un diritto di prelazione a favore di Vesta sui diritti di proprietà intellettuale occasionalmente scaturiti dalla collaborazione nella ricerca con Sapienza che non costituiscono meri miglioramenti del brevetto originario e di un diritto di prelazione sui diritti di proprietà intellettuale sviluppati in proprio da Sapienza al di fuori della collaborazione nella ricerca con Vesta;
f) la possibilità di revocare il regime di esclusività sui diritti per lo sviluppo clinico in caso di grave inadempimento delle milestones predeterminate;
g) la risoluzione del contratto in caso di inadempimenti di carattere monetario o non monetario.

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Settore Trasferimento Tecnologico e Spin Off
Il Responsabile
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Conseguentemente, il valore complessivo dell'operazione di licensing considerando i soli proventi fissi, ivi compresi i finanziamenti alla ricerca, è pari a € 3.360.000,00 (tremilionitrecentosessantamila) ai quali si potranno aggiungere in futuro i corrispettivi eventuali e/o variabili (come da prospetto riassuntivo allegato alla presente).

Su tale Term Sheet la Commissione Tecnica Brevetti, nella seduta dell'8.6.11, ha espresso il proprio parere favorevole per ciò che concerne gli aspetti di competenza riguardanti la cessione in licenza della domanda di brevetto.

Gli inventori, con lettera di intenti del 9.6.11, hanno preso visione del Term Sheet, dichiarando di essere disposti ad assumere formalmente gli

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obblighi di collaborazione nella ricerca individuati nel Term Sheet e derivanti dal futuro *sponsored research agreement.*

Il Direttore del Dipartimento di Scienze Anatomiche,Istologiche, Medico Legali e dell'Apparato Locomotore ed il Responsabile dell'afferente Sezione di Anatomia Umana, con nota del 14.6.11 hanno, altresì, dichiarato di aver preso visione del Term Sheet e di essere disposti, in qualità di rappresentanti delle strutture competenti, ad assumere formalmente gli impegni che deriveranno dallo *sponsored research agreement.*

A seguito della sottoscrizione di tale Term Sheet, si addiverrà alla fase di negoziazione, finalizzata alla conclusione dei definitivi contratti di licenza e di ricerca.

Si specifica, infine, che la University North Carolina, titolare del restante 50%, ha concesso autonomamente, ed in conformità alle normative brevettuali internazionali, i diritti di utilizzo della propria quota del 50% a Vesta Therapeutics Inc.

ALLEGATI PARTE INTEGRANTE:

- Term Sheet tra Sapienza e Vesta Therapeutics Inc.;
- Verbale della Commissione Tecnica Brevetti dell'8.6.11;
- Prospetto riassuntivo delle condizioni economiche del Term Sheet

ALLEGATI IN VISIONE:

- Lettera di intenti degli inventori del 9.6.11;
- Lettera del Direttore del Dipartimento di Scienze Anatomiche, Istologiche, Medico Legali e dell'Apparato Locomotore del 14.6.11

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SettoreTrasferimento Tecnologico e Spin Off
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DELIBERAZIONE N.173/11

IL CONSIGLIO

- **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. nr. 490 del 16.10.2009;**
- **Vista la domanda di brevetto n. USA 61/256846 del 30.10.09 e relativa estensione PCT n. 12/926,161 del 28.10.10, dal titolo "Multipotent stem cells from the estrahepatic biliary tree and methods of isolating same", – inventori Alvaro Domenico, Gaudio Eugenio, Carpino Guido, Vincenzo Cardinale, Lola M. Reid, Yunfang Wang- di titolarità in via derivativa (giusto contratto di cessione del 25.10.10) di Sapienza per il 50% e di UNC (Università del North Carolina) per il restante 50%;**
- **Vista la proposta avanzata dalla Società americana Vesta Therapeutics Inc. volta all'acquisizione dei diritti di utilizzo della proprietà intellettuale inerenti la domanda di brevetto in parola;**
- **Esaminati la bozza di Term Sheet, concordata con Vesta Therapeutics Inc. per la concessione, relativamente alla quota di titolarità del 50% appartenente a Sapienza, dei diritti di sfruttamento per usi clinici (in esclusiva) e per gli usi non clinici (non esclusiva) dell'invenzione, le relative condizioni contrattuali ed il profilo economico ivi previsti;**
- **Considerato che Vesta Therapeutics Inc corrisponderà immediatamente dopo la firma del Term Sheet di cui in narrazione, la somma iniziale di € 10.000,00;**
- **Preso Atto del parere favorevole espresso al riguardo dalla Commissione Tecnica Brevetti, nella seduta dell'8.6.11;**
- **Preso Atto delle dichiarazioni di intenti espresse dagli inventori, con nota del 9.6.11;**
- **Preso Atto altresì, della nota del 14.6.11, sottoscritta dal Direttore del Dipartimento di Scienze Anatomiche, Istologiche, Medico Legali e dell'Apparato Locomotore e dal Responsabile dell'afferente Sezione di Anatomia Umana, circa la disponibilità ad assumere formalmente gli impegni derivanti dalla collaborazione nella ricerca con la società Vesta Therapeutics Inc;**
- **<u>Presenti e votanti n. 20</u>: con voto unanime espresso nelle forme di legge dal rettore, dal prorettore, dal direttore generale e dai consiglieri: Barbieri, Biffoni, Calvano, Cavallo, Graziani, Laganà, Ligia, Mauceri, Merafina, Moscarini, Mussino, Saponara, De Nigris Urbani, Fanelli, Lucchetti, Maniglio e Morrone**

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- **di approvare il testo del Term Sheet concordato con la Società Vesta Therapeutics Inc. avente ad oggetto la domanda di brevetto n. USA 61/256846 del 30.10.09 e relativa estensione PCT n. 12/926,161 del 28.10.10, dal titolo "Multipotent stem cells from the estrahepatic biliary tree and methods of isolating same";**
- **di autorizzare il Rettore alla sottoscrizione del Term Sheet in premessa;**
- **di autorizzare la Ragioneria ad introitare sul conto in entrata n. E 1.3.1.4.5 "Royalties Brevetti di Ateneo" B.U. es. fin. 2011, la somma di € 10.000,00 quale corrispettivo iniziale spettante a Sapienza a seguito della sottoscrizione del Term Sheet tra L'Università degli Studi di Roma "La Sapienza" e Vesta Therapeutics Inc.**

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 .....

SUMMARY OF TERMS & CONDITIONS:
LICENSE TO VESTA THERAPEUTICS, INC.

Confidentiality	Receipt of this Proposal by the University (and any other persons assisting the University) will be deemed to constitute agreement to keep both the existence and contents of this Proposal confidential. The University (and any other persons assisting the University) will not directly or indirectly deliver a copy of all or any part of this Proposal to any other person, and will not communicate with any other person about any of the terms, conditions, scope or contents of this Proposal or the identity of the party making this Proposal.
Licensor	Universita di Roma, Sapienza ("Sapienza" or "Licensor" or "University")
Licensee	Vesta Therapeutics, Inc. ("Vesta" or "Company")
Licensed Patents	Biliary Tree patent application, and subsequent improvements dependent upon this patent
Territory	Worldwide (with all patent costs borne by Vesta)
License Grant	Exclusive license for human clinical applications. ("Clinical applications" will be defined in more detail in the definitive license document but is meant to cover use of cells in or for a human patient, relating to potential diseases or medical conditions in that human patient. Products for such uses would include the stem cells and their progeny or derivatives.) (The scope of "clinical applications" is not intended to "reach through" to the broad spectrum of all types of drug compounds which may be discovered through the drug discovery and toxicity testing under the "non-clinical applications" scope (below).) Non-exclusive license for uses other than human clinical applications.. (Such non-clinical applications will be defined in more detail in the definitive license document but are meant to include, without limitation, uses for drug discovery and toxicity testing.) The University retains rights for educational and non-commercial research use. This includes the ability to carry out non-sponsored clinical trials and experimental research, supported by institutional funds, involving biliary tree stem cells and their progeny and derivatives. The University could also collaborate with other non-commercial entities in research involving biliary tree stem cells and their progeny and derivatives. The foregoing provisions of this paragraph are subject to the condition that such clinical trials and/or research shall not lead to or result in any commercialization without Vesta that would otherwise be within the scope of this License.
Sub-Licensing	The Company will actively pursue sub-licensing and partnering arrangements

and Partnering	to maximize development of the technology (see Development Plan section, below). The Company will ensure that any sub-license, assignment or partnering agreement requires the sub-licensee, assignee or partner to comply with applicable regulations, and with the requirements of this license (including recordkeeping and consent requirements). The Company will consult with the University in advance about all such potential sub-license or partnering arrangements. (UNC License has no consultation provision, but the Company consults anyway.) The University will receive a portion of any payments the Company receives in connection with sub-licensing and partnering arrangements (see Royalties and Sub-license Revenues sections below).
Upfront License Fee	€50,000 – €10,000 upon execution of the Term Sheet, and €40,000 upon execution of the License. (UNC License upfront fee was USD$45,000 for multiple patents, then $10,000 for subsequent additional patents added to the License)
Upfront Expense Reimbursement	In addition, after execution of the License, the legal fees for its negotiation and completion incurred by outside legal counsel on behalf of the University will be reimbursed by the Licensee.
Annual License Payment	Annual License Payments will be made at the beginning of each year under the License until Minimum Royalty payments begin to apply (starting with Year 2, since Year 1 is deemed satisfied by the Upfront License Fee). The amounts of such Annual License payments will be as follows: • Year 2 (payable on first anniversary of License execution): €30,000 • Years 3 and 4: €35,000 • Years 5 and beyond: €40,000 (UNC License does not have any annual license payment)
Annual Sponsored Research	Estimate: €200-250,000 per year (amount is flexible, according to the work program as described below) (UNC SRAs have ranged from USD$125,00 to $450,000 per year over the last 10 years, for work program covering many aspects of liver and endodermal research, as well as "productization" research such as cryopreservation) Vesta considers further development of this technology very important, in order to move it toward commercialization. Vesta considers it desirable for further development to be done by (or in collaboration with) the investigators who have done the research so far. Accordingly, Vesta is interested and willing (if the investigators are interested and willing) to enter into an annual sponsored research arrangement, separate from the License but connected with it. This sponsored research will be part of the development plan and activities described below, and will help ensure rapid progress.

Such sponsored research arrangements would be entered into at the same time as (or, if the University or investigators prefer, promptly after) execution of the License, and would include subjects such as the following:

- Further exploration of the biliary tree and duodenum tissues and stem cell niches
- Further characterization of the biliary tree-derived stem cells
- Exploration of the differentiation of the biliary tree-derived cells into various endodermal tissues, starting with liver and pancreas
- Exploration of culture conditions and expansion potential
- Other, as suggested by the investigators

Additional Upfront License Fees

The Sponsored Research Agreement would provide that additional IP developed through the sponsored research and defined as an Improvement (see definition below) would be added to the scope of the License, upon payment of an additional Upfront Fee of €10,000 per additional patent. Additional products would be subject to separate Milestone Payments and Royalties, which will be agreed upon on a case-by-case basis using the below amounts as reference.
(UNC License is USD$10,000 per additional patent).

Milestone License Payments

Milestone license payments will be payable in connection with clinical development of each product:

- €40,000 per product for the initial IND approval or its equivalent (i.e., initiation of the first Phase I trial)
  (UNC license milestone is USD$40,000)
- €60,000 per product at the initiation of the first Phase III clinical trial or its equivalent
  (UNC license milestone is USD$60,000)
- €100,000 per product for the initial product approval (BLA or equivalent) in the first country where such approval is received
  (UNC license milestone is USD$100,000)

Royalties – Earned Royalties

Earned Royalties will be payable on all Net Sales by the Company. On Net Sales by sub-licensees and/or partners, the Company will pay Pass-Through Royalties as provided below. ("Net Sales" means the usual definition in biotech licenses: gross sales minus selling commissions and discounts, transportation discounts, etc. Cost of goods sold, etc. are not subtracted in determining "Net Sales.")

The Earned Royalties will be 2% of Net Sales, subject to a 50% stacking provision.

(The Earned Royalties under the UNC License are:

- 1.0% of Net Sales up to $50 million
- 1.5% of Net Sales between $50-100 million
- 2% of the net sales in excess of $100 million)

Minimum Royalties

Minimum Royalties would be payable as follows:

- Year 1 and 2: €50,000 (UNC License provides USD$50,000)
- Year 3 and beyond: €100,000 (UNC License provides USD$100,000)

Such Minimum Royalties would credit against the Earned Royalties due.

Use of Vesta's Complementary IP

Through more than a decade of collaboration with UNC on endodermal stem cell technology (originally on liver and including other endodermal tissues, such as pancreas, in the last couple of years), Vesta has built up an enormous patent estate of >150 patents and patent applications, including some important blocking positions.

Portions of this other IP are likely to be needed in order to commercialize certain kinds of products under the Biliary Tree patent. In connection with this License, Vesta will make available such other IP that may be necessary or desirable for use in its commercialization of products under the Biliary Tree patent.

Third Party IP

The Company will use commercially reasonable efforts to identify protected intellectual property that is owned or controlled by third parties, and that is necessary for freedom to operate in the use of the intellectual property licensed hereunder. The Company will also be responsible for any commercially reasonable efforts to license or acquire any such third party IP, provided, however, that the Company cannot and does not provide any guarantee or warranty of any kind that it will be able to license or acquire any such third party IP on commercially reasonable terms and the Company shall determine what is commercially reasonable in its sole discretion.

[Note: Of course, as a practical matter, the Company has a shared interest with the University in the desirability of obtaining freedom to operate.]

Sub-Licenses/ Partnering –

The Company will share with the University any payments the Company receives from sub-licensees and/or partnering arrangements, as follows:

Pass-through Royalties on Net Sales

- The Company will pay a pass-through percentage of at least twenty percent (20%) of any royalties it receives on Net Sales by sub-licensees and/or partners. Upon the closing of a sub-license agreement involving pass-through royalties, the Company will pay to the University a minimum amount of such royalties equal to €20,000, which shall be credited towards the earned royalties.

Other Payments

- The Company will pay to the University ten percent (10%) of any payments other than royalties on Net Sales that it receives from sub-licensees and/or partners (e.g., license issue fees; annual license maintenance fees; milestone payments; minimum royalty payments); provided however that purchases of equity in the Company, loans, research funding and payments for manufacturing costs shall be excluded. Upon the closing of a sub-license agreement not involving pass-through royalties or other payments, the Company will pay to the University a minimum payment equal to €10,000, which shall be credited towards the earned amounts of the other payments.

Patent Costs and Filings

The Company will be responsible for filing, prosecuting and maintaining the Licensed Patents, and paying all costs involved including those of Societa Italiana Brevetti. In regard to all patent filings and prosecution, the Company will consult in advance with the University and cooperate with any patent counsel designated by the University, including providing the University or it's designated patent counsel with copies of all papers involved in filing, prosecuting and maintaining the Licensed Patents. Any limitation or abandonment of patent rights in the US or Europe will require an explicit approval of the University, which shall not be unreasonably withheld or delayed and which shall be granted for a limitation or partial abandonment which is required in order to overcome office action rejections or to pursue an appeal.

Royalty Stacking

In the event that the Company must pay royalties to a third party for a Licensed Product that is also covered by this License, the royalties paid to the third party will be credited against royalties payable to the University for the sale of the same Licensed Product; provided that, in no event shall the royalties due the University be reduced by more than 50%.

Development Plan; Diligence

In order for the Biliary Tree stem cell technology to move toward commercialization, 3 main stages of development work will be needed, as described below. The amount of time and funding required for each stage will need to be determined or confirmed in consultation with the investigators. Below are rough estimates. A default provision, linked to the diligence plan, is provided

- Stage 1: Further development of the technology.
  Estimated time: 2 years.
  This will include the kind of work listed in the Sponsored Research section above.

- Stage 2: Pre-clinical development of particular products.
  Estimated time: at least 2 years (which can probably overlap with the second year of Stage 1).
  Focus will be selection and development of at least 1 product for liver applications and 1 product for pancreatic applications. By developing 2 products, involving different endodermal tissues, in parallel, this will maximize the opportunities for early partnering arrangements, if desired.

- Stage 3: Clinical trials, Phase I and Phase II.
  Estimated time: 5-7 years (timeframes can be relatively short and aggressive if any of the following strategies are followed: (a) conduct trials in India or Asia where liver is the #1 cause of death and regulators are supportive; (b) choose orphan disease applications and obtain fast-track regulatory treatment; (c) choose personalized treatments and make use of the Hospital Exemption under the EU's Advanced Therapy Medicinal Products [ATMP] Regulation, or the Conditional Approval regulatory category).
  Following completion of Phase II clinical trial, if the data are positive,

then a partnering or acquisition with a big pharma company would typically occur.

Vesta has experience in the development process for a spectrum of products from liver stem cells and differentiated hepatocytes. (The liver stem cells are believed to be in the lineage chain 1 or 2 steps below the biliary tree stem cells covered by the patent application to be covered by this License). One product (liver stem cells themselves, developed to treat late stage liver failure) was developed in collaboration with a center of excellence in Hyderabad, India, has completed a Phase I/II clinical trial of 100 patients, and is now starting a Phase III randomized controlled trial with another 100 patients. Another product (liver grafts) is being developed through collaboration with UNC and has been in mid-pre-clinical stage animal studies, funded by Vesta, for a year now.

Vesta also has experience with pancreatic tissues, through its UNC collaboration, through clinical collaboration in Israel and through its cancer affiliate (addressing pancreatic cancers, which appear to arise from pancreatic or endodermal stem cells, similar to those covered by the biliary tree patent which are malfunctioning).

Vesta's affiliates have pioneering experience with the EU's ATMP Regulation for cell therapies (partnering with Kings College in London and the Fraunhofer Institute in Germany), Named Patient programs (partnering with 2 clinics in Spain) and clinical trials.

Diligence Provisions: The Company shall use best efforts to proceed diligently with the development, clinical testing, manufacture and sale of Licensed Products.

- The Company agrees to enter into Annual Sponsored Research with the University investigators if they are interested and willing, as described above.
- The Company will also continue with its annual Sponsored Research program with UNC, as it has since 2002 (and its predecessor company did since the late 1990s).
- The Company will use best efforts to file an IND or equivalent application to begin clinical trials of a Licensed Product on or before the 4th anniversary of the execution of this License.
- The Company will use best efforts to complete Phase II clinical trials or achieve a major corporate partnering or acquisition agreement with a big pharma company in accordance with the diligence schedule outlined above.

Diligence Default

If the Company fails to meet the diligence schedule outlined above, then subject to the exceptions below, the following default provisions shall apply:

- If the delay does not exceed 12 months beyond the applicable milestone in the diligence schedule above, the Company shall pay to the University a Default Penalty of €10,000 for each month of delay after the first 3 months (i.e., €10,000 per month for months 4 - 12 of delay). The license shall remain in force as is, with the diligence

schedule deemed to be correspondingly amended.

- If the delay is more than 12 months beyond the applicable milestone, the Company shall submit to the University a written description of the reasons for the delay and a plan for completion of the applicable milestone. The University shall evaluate the description and plan, and reasonably determine, in good faith, whether the Company has demonstrated reasonable diligence. If the University reasonably determines, in good faith, that the Company has not demonstrated reasonable diligence, the University may amend the license to remove the exclusivity and make the license non-exclusive with respect to all applications, including clinical ones. If the University reasonably determines, in good faith, that the Company has demonstrated reasonable diligence, then the University and the Company shall negotiate a mutually agreeable amendment of the diligence provisions.

The diligence default provisions shall not apply, and the Company shall not be considered in default of the diligence provisions, if the failure to fulfil the diligence schedule is materially attributable to a change in regulatory requirements, change in the biliary tree technology being developed pursuant to this license, or unforeseen difficulties with the biliary technology that have not been solved by the sponsored research work.

Improvements	All improvements, modifications or alterations or enhancements (collectively "Improvements") based on the Licensed Patent and developed in whole or in part through sponsored research will be owned by the Licensor, but included within the definition of the Licensed Patents under this License. "Improvements" means intellectual property which is dependent upon the IP licensed hereunder – i.e., IP which, if practiced without a license to the IP covered in this License, would infringe in whole or in part this Licensed IP. Regarding any Improvements developed without any sponsored research, the Licensee will receive a Right of First Refusal on the same terms as provided (below) for New IP. If separate patent applications are filed on Improvements, the Company will pay an Upfront Fee of €10,000 per additional patent. Additional products would be subject to separate Milestone Payments and Royalties, which will be agreed upon on a case-by-case basis. If new IP is developed through sponsored research, which does not constitute "Improvements" (the "New IP"), such New IP will not be included in this License automatically. If the New IP has been developed in whole or substantial part through sponsored research paid for by the Licensee, the Licensee will receive a Right of First Refusal (ROFR) to license the New IP, on terms no less favorable than the University would provide to any other party. The University and the Licensee will negotiate in good faith to reach agreement on a license to the New IP (which may either be a separate license or an addition to this License, as determined jointly by the parties). The negotiation period will be at least one hundred twenty (120) days, and may be extended for two further periods of thirty (30) days each, if the Licensee so requests and the Licensee is proceeding with the negotiations promptly and in good faith.

Infringement	(1) Licensors and Licensee will each inform the other of any suspected infringement by third parties and will cooperate in pursuing infringers and defending the Licensed Patents. Licensee shall have a 120-day option to pursue infringers. If Licensee is unsuccessful in persuading the alleged infringer to desist and/or is not diligently prosecuting an infringement action, or if Licensee notifies Licensors that it does not intend to bring suit against the alleged infringer, Licensor may prosecute such matter at its own expense and retain the proceeds of any settlement. (2) If Licensee is prosecuting or defending Licensed Patents by litigation(s) or settlement action(s), after the Licensee has incurred an aggregate of at least €35,000 of legal fees and expenses, then Licensee may start withholding up to fifty percent (50%) of the royalties otherwise thereafter due Licensors under the license agreement and apply them toward reimbursement of Licensee's litigation fees and expenses. Any recovery of damages by Licensee will be applied to (i) satisfy unreimbursed litigation fees and expenses; (ii) reimburse Licensors for royalties withheld; and (iii) reimburse Licensee for lost sales and Licensors for lost royalties on account of lost sales. Amounts that exceed compensatory damages will be shared equally between Licensee and Licensors.
Indemnification	The Company will indemnify the University for claims, losses, damages, litigation, etc. arising from or relating to Licensed Products and the Company's activities with respect to Licensed Products or pursuant to this license, provided however, that in no event will the Company be liable for indirect or consequential damages. The Company will maintain customary insurance (e.g., general liability, products liability) in customary amounts in the industry.
Legal Fees	The Company will be responsible for payment of all legal fees and expenses associated with this license, including with respect prosecution and maintenance of patents, infringement of patents, regulatory compliance, contractual matters with third parties, and claims and proceedings covered by the Indemnification, provided that the Company has the authority to select the attorneys, decide any strategy matters and direct the execution of the legal work involved. The Company will keep the University informed in a timely manner and consult with the University about all legal matters, and any strategy and execution matters relating thereto.
Term and Termination	The term of the License will continue until expiration of the last valid (issued) claim of the Licensed Patents. In the event of material breach of this License, the non-breaching party will deliver notice of such breach to the breaching party and provide an opportunity for the breaching party to cure such preach. In the event of breaches consisting of failure to make a payment, the cure period shall be thirty (30) days. In the event of non-monetary breaches, the cure period shall be up to one hundred eighty (180) days, or such other period as is reasonably necessary. Sub-licenses will survive termination, and shall be deemed to become a license agreement directly with the University.

Dispute Resolution	Any disputes between the parties shall be decided by binding arbitration, in accordance with the rules of the International Arbitration Association. Any such arbitration shall take place in _____, and each party hereby consents to jurisdiction in _____ and waives any objection thereto. Official written transcripts shall be made of all proceedings and sessions involved in any such arbitration, and shall be available to the parties.
Assignment	Neither party may assign the Agreement to any third party without the prior written consent of the other party, which consent shall not be unreasonably withheld. Either party may assign the Agreement to any third party that purchases substantially all of the assigning party's stock or assets relating to the Agreement.
Definitive Documents	The definitive license documents will include the terms stated above plus other customary provisions, including standard representations and warranties, publication provisions, dispute resolution, etc.

[signatures on following page]

CONFIDENTIAL

The parties hereby agree that execution of this Term Sheet constitutes a binding commitment to enter into a license on the terms and conditions set forth above, as more fully expressed in the definitive documents. Following execution of this Term Sheet, the parties will use best efforts, in good faith, as promptly as reasonably practicable, to agree upon and execute the definitive license documents.

Agreed and Accepted:

LA SAPIENZA UNIVERSITY

By:_____

Name:

Title:

Date:_____

By:_____

Name:

Title:

Date:_____

VESTA THERAPEUTICS, INC.

By: Linda F Powers

Name: Linda F Powers

Title: Chairman

Date: 14 June 2011

SAPIENZA
UNIVERSITÀ DI ROMA

VERBALE DELLA
COMMISSIONE TECNICA BREVETTI
8 giugno 2011

Il giorno 8 giugno 2011 alle ore 14.00 nella Sala Commissioni al piano terra del palazzo del Rettorato, è convocata la riunione della Commissione Tecnica Brevetti per discutere il seguente ordine del giorno:

1. Comunicazioni
2. Esame e valutazione delle seguenti domande di brevetto:
   - 2.1 Nuova proposta di invenzione brevettabile – prof. Sciubba
   - 2.2 Nuova proposta di invenzione brevettabile – prof. Santini
   - 2.3 Nuova proposta di invenzione brevettabile – prof.ssa Fini
   - 2.4 Nuova proposta di invenzione brevettabile – prof. Naviglio – ratifica
   - 2.5 Nuova proposta di invenzione brevettabile – prof. Pierelli
   - 2.6 Nuova proposta di invenzione brevettabile – prof. Bruzzese_1
   - 2.7 Nuova proposta di invenzione brevettabile – prof. Bruzzese_2
   - 2.8 Domanda internazionale PCT/FR2009/051642 – prof. Scrosati
3. Esame eventuali proposte di cessione di invenzione brevettabile pervenute dopo la presente convocazione
4. Proposta di licenza della domanda di brevetto PCT 12/926,161 – prof. Gaudio
5. Varie ed eventuali

Sono presenti per la Commissione: proff. Misiti (Presidente), Carlucci Aiello, Valente, dott.ssa Siani.
Assume le funzioni di segretaria la dott.ssa Roberta Vincenzoni, responsabile del Settore Brevetti.
Assenti giustificati: Proff. Capaldo e Santoni

...omissis...

4. Proposta di licenza della domanda di brevetto PCT 12/926,161

In data 30 ottobre 2010 è stata presentata la domanda USA in co-titolarità Sapienza 50% e Università del North Caroline 50% inventori prof. Alvaro, Gaudio et al. rispondente alla Provisional n. 61/25684 (30.10.2009). In seguito a tale deposito l'UNC ha sottoscritto un contratto di licenza con la Società Vesta Therapeutics per il proprio 50% mentre la Sapienza ha la disponibilità della propria quota di titolarità. Da uno studio condotto attraverso alcuni corrispondenti locali, secondo la legislazione statunitense tale fattispecie è consentita. Al momento la domanda PCT è stata estesa nei seguenti Paesi: Argentina, Taiwan, Panama e Paesi GCC (Gulf Cooperation Council) ed i costi sono stati a carico della Vesta Therapeutics. L'ufficio per il trasferimento tecnologico in questi mesi ha avuto una lunga trattativa con la

Vesta T. e con la Gigacyte, altra società del settore interessata anch'essa ad una licenza sul brevetto. A tal proposito si consegna un prospetto che riassume sia le condizioni legali che economiche delle proposte pervenute dalle Società in argomento. La Commissione, valutate le carte in proprio possesso, le proposte contrattuali presentate ed udita la relazione dell'Ufficio per il trasferimento tecnologico, ritiene opportuno sottoscrivere una licenza di cui alla bozza contrattuale presentata dalla Società americana Vesta Therapeutics Inc. e alla relativa offerta economica, ritenuta oggettivamente più conveniente sia in termini finanziari che in termini di collaborazione per lo sviluppo. La Commissione comunque precisa che per quanto riguarda gli impegni relativi alla prosecuzione della ricerca questi siano assunti dai ricercatori insieme al Dipartimento.
La Commissione approva all'unanimità.
Letto ed approvato seduta stante.

...omissis...

Il Presidente
(prof. Domenico Misiti)

UNIVERSITA' DEGLI STUDI "LA SAPIENZA" ROMA

Il Segretario
(dott.ssa Roberta Vincenzoni)

Term Sheet Sapienza-Vesta

licenza esclusiva per uso clinico (terapeutico) Lic. non esclusiva (coesclusiva) X uso non clinico
Schema condizioni economiche
Data presunta sottoscrizione accordi finali settembre 2011 Totale anni contrattuali presunti 18 Brevetto depositato il 30.10.2009

COMPENSI FISSI CERTI

ANNUAL LICENSE PAYMENTS				
II anno	€	30.000,00		
III anno	€	35.000,00		
IV	€	35.000,00		
V anno in poi € 40.000 x 14	€	560.000,00		
MILESTONES				
per product for the inizial IND approval	€	40.000,00		
per product at the initiation of the first Phase II clincial trial	€	60.000,00		
per product for the iniziatil product approval (BLA..)	€	100.000,00		
ROYALTIES				
MINIMUM ROYALTIES				
anno I	€	50.000,00		
anno II	€	50.000,00		
anno dal III in poi 100,000,00 x 16	€	1.600.000,00		
TOTALE COMPENSI FISSI CERTI			€	**2.610.000,00**

COMPENSI VARIABILI EVENTUALI

earned royalties		2% sulle net sales		
minimun royalties		(-50% in caso di stacking provision= 1%)		
COMPENSI DA SUBLICENZE				
Minimum amount		+ 20% di tutte le royalties incassate da Vesta		
Minimum amount	€	20.000,00		
		+ 10% su tutti i compensi diversi da royalties incassati		
	€	10.000,00		
Additional fee sui brevetti migliorativi	€	10.000,00		
cotitolarità		più Milestone e roaylties da definire volta per volta		

FINANZIAMENTO ALLA RICERCA

ANNUAL SPONSORED RESEARCH				
- per anno (da definire il numero degli anni) almeno tre	€	250.000,00	€	**750.000,00**