18-04769-E

Sectilis

FOIA / PA Officer John Livornese
U.S. Securities & Exchange Commission
FOIA Office
100 F Street NE, Mail Stop 5100
Washington, DC 20549

June 12, 2018

Dear Mr. Livornese:

I request pursuant to the Freedom of Information Act (FOIA) 5 U.S.C. § 552. As Amended by Public Law No. 104-231,110 Stat. 3048, copies of the following agreements:

Exhibit 10.6 to Form 10KSB filed on 03/28/2003 by Microislet Inc

Exhibit Title: Research Funding And Option Agreement

CIK: 1092050

Sectilis will pay up to $61 for research, copies and review fees for all of the abovementioned agreements. Please forward all releasable material for copying. My daytime telephone number is 202-798-8809. Please call me or e-mail at research@sectilis.com to discuss the total cost or estimated cost of this research/copies should the amount exceed the price indicated in this request.

Sincerely,

Stella Vasconcellos
Research Assistant
Sectilis LLC
6931 Arlington Rd. # 580
Bethesda, MD 20814

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
STATION PLACE
100 F STREET, NE
WASHINGTON, DC 20549-2465

Office of FOIA Services

July 5, 2018

Ms. Stella Vasconcellos
Sectilis LLC
6931 Arlington Rd. # 580
Bethesda, MD 20814

RE: Freedom of Information Act (FOIA), 5 U.S.C. § 552
Request No. 18-04769-E

Dear Ms. Vasconcellos:

This letter is in response to your request, dated and received in this office on June 12, 2018, for a copy of Exhibit 10.6 to the Form 10KSB filed on March 28, 2003 by Microislet, Inc.

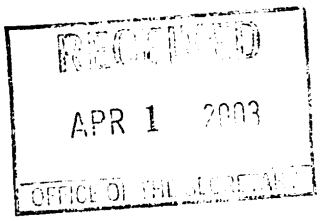
The search for responsive records has resulted in the retrieval of the enclosed eight pages which are being released in their entirety. Because this exhibit was released in response to a previous FOIA request, no chargeable processing fees have been incurred.

If you have any questions, please contact Amy Gbenou of my staff at Gbenoua@sec.gov or (202) 551-5327. You may also contact me at foiapa@sec.gov or (202) 551-7900 as a FOIA Public Liaison or contact the Office of Government Information Services (OGIS) for dispute resolution services. OGIS can be reached at 1-877-684-6448 or Archives.gov or via e-mail at ogis@nara.gov.

Sincerely,

Jeffery Ovall
FOIA Branch Chief

Enclosure



Confidential Treatment

Exhibit A
To
Research Funding and Option Agreement

Specific Funding Proposal

Title: Xenotransplantation of porcine islets protected by alginate encapsulation.

Principal Investigator: Daniel R. Salomon, M.D.
Department of Molecular and Experimental Medicine
The Scripps Research Institute

Funding Company: MicroIslet, Inc.
Contacts: William G. Kachioff, CPA
Chief Financial Officer
Tel. (858) 657-0287
FAX. (619) 374-7049
wkachioff@microislet.com

Haro Hartounian, Ph.D.
President/Chief Operating Officer
mailto:haro@microislet.com

Definition of Field: Encapsulation of pancreatic islets for transplantation

Introduction: This Specific Funding Proposal is designed to test the thesis that successful porcine islet xenotransplantation can be accomplished using a novel encapsulation strategy being developed by MicroIslets, (La Jolla, CA). This strategy is based on the use of an ultrapure alginate preparation and several proprietary encapsulation technologies developed by the Company's scientists. The ultrapure alginate is a superior, low endotoxin material (~~< 50 eu/g~~[***]) that allows construction of highly reproducible spherical capsules with minimal capsule fragmentation. As such, this alginate preparation is a major advance over previous attempts to encapsulate islets for transplantation. Ultrapure alginate preparations previously manufactured by MicroIslet scientists have already been approved by the FDA for use in several unrelated clinical situations such as the experimental treatment of cerebral vascular aneurysms. The production process now being developed and refined by MicroIslets is also being designed for scale-up to clinical grade processing (U.S. patent numbers: 6,303,355 and 6,365,385). The key objective of using ultrapure alginate in combination with a ~~refined capsule production~~[***] technology is the production of encapsulated porcine islet preparations producing little host inflammatory or immune responses after transplantation. In turn, over a decade of experience with encapsulation technologies indicates that minimizing or eliminating these posttransplantation reactions will significantly enhance successful islet survival and function.

Project Strategy: The initial phase of studies will be done in ~~mouse~~[***] models of xenotransplantation. The strategy is to start with ~~encapsulated rat islets into mice~~[***], then ~~pig islets into mice~~[***] and finally, ~~pig islets~~[***] into nonhuman primates as a pre-clinical model.

Animal studies will be conducted to address the following questions:

Is the technology effective in relevant diabetes models?
Dose and duration?
Islet integrity, function and differential gene expression?

Is the technology safe?
Biocompatible?
Donor- and/or xeno-specific immune responses?
Potential for transmission of infectious disease (PERV)?

What is the fate of the capsules and alginate in vivo?
Capsule distribution?
Capsule degradation and clearance?

Preliminary Studies:

A number of preliminary studies will be done to develop the systems required for the formal experiments described in the next sections. First, a number of ~~rat and mouse islet isolations~~[***] will be done to validate the technique and establish the yield and viability in our hands. Second, islet preparations will be encapsulated and tested for ~~glucose-stimulated insulin release~~[***] and ~~insulin content after culture for up to one week~~[***]. Third, several pilot studies of transplanting ~~rat (xeno)~~[***] or ~~mouse (allo)~~[***] islets will be done into ~~STZ-induced diabetic mice~~[***], some into ~~NOD/SCIDs~~[***] and others into ~~immune competent Balb/c~~[***]. The purpose of these preliminary studies is to make sure the individual technical elements of the system from islet isolation to encapsulation and transplantation are established prior to the formal experiments and hypothesis testing outlined next. An important question is whether the results will be significantly ~~different for rat (xeno) and mouse (allo) islet~~[***] transplants. Our hypothesis is that the challenges represented by islet isolation and encapsulation are ~~the same for rat and mouse islets~~[***]. We also predict that a successful encapsulation technology will protect a ~~rat islet~~[***] from rejection in a ~~mouse (a concordant xenograft)~~[***] as well as a ~~mouse islet~~[***] in a ~~mouse (an allotransplant)~~[***]. If this is not correct, then appropriate adjustments in our experimental plan will be made to further investigate the basis for such ~~a difference~~[***] between ~~encapsulated xeno~~[***] and ~~allotransplants~~[***].

Upon completion of the Preliminary Studies we will initiate the following Series of formal experiments.

Series #1: ~~Rat islets~~[***] encapsulated and transplanted into ~~immunodeficient NOD/SCID mice~~[***]. Islets will be retrieved at ~~3, 7, 14, 21 and 28 days posttransplant (n=4 animals/group, 20 animals total/experiment, 2 experiments total)~~[***].

Experimental questions/Outcome parameters: Can ~~rat islets~~[***] be purified, encapsulated, transplanted, retrieved and tested for integrity in an animal model with no adaptive ~~immune response and a reduced innate immunity~~[***]? Islet integrity will be

assessed post retrieval by ~~histology, staining for insulin, determinations of insulin content and testing of glucose-stimulated insulin release~~[***]. Capsule integrity will be tested by MicroIslet using their engineering criteria.

Series #2: ~~Rat islets~~[***] encapsulated and transplanted into ~~STZ-induced diabetic, immunodeficient NOD/SCID mice~~[***]. Islets will be retrieved at ~~1, 3, 6 and 12 months posttransplant or until the last day of measurable function (n=4 animals/group, 16 animals total/experiment, 2 experiments total)~~[***].

Experimental questions/Outcome parameters: Can encapsulated ~~rat islets~~[***] cure diabetic ~~mice~~[***] and function for up to one year? Will islet integrity be affected by concommitant diabetes? This model is designed to remove issues related to adaptive immunity from the interpretation of the results. In combination with Series #3 it will allow a first prediction on a requirement for immunosuppression (see below). Function of encapsulated islets will be followed by serial blood glucose and body weight determinations, monthly intravenous glucose tolerance, Hgb A1C testing and C-peptide monitoring.

Series #3: ~~Rat islets~~[***] encapsulated and transplanted into ~~STZ-induced diabetic Balb/c mice~~[***]. Islets will be retrieved at ~~1, 3, 6 and 12 months posttransplant or until the last day of measurable function (n=4 animals/group, 16 animals total/experiment, 2 experiments total)~~[***].

Experimental questions/Outcome parameters: Can encapsulated ~~rat islets~~[***] cure diabetic ~~mice~~[***] and function for up to one year? Will islet integrity be affected by immune responses either to the ~~rat islets~~[***] or to the capsules? In combination with Series #2 the intent is to determine what additional impact an intact adaptive immune system might have on the survival and function of encapsulated xenogeneic islets. If there is a significant difference between the outcome parameters comparing Series #2 to #3, then additional experiments will be done to determine if immunosuppression will be necessary for an optimal therapy strategy.

A limited immune testing strategy will include detecting ~~anti-rat~~[***] antibodies by testing serial animal plasma samples for staining against freshly isolated ~~rat~~[***] islets by flourescence immunohistology and flow cytometry. If positive, then ~~rat~~[***] islets and ~~rat~~[***] lymphocytes from two or more different strains will be tested to determine if the antibodies are directed to ~~MHC or islet-specific antigens~~[***]. ~~Cell-mediated immune~~ [***] responses will be tested for by modified ~~CTL assays~~[***] where ~~rat islet~~[***] cell populations will be targets for ~~splenocytes harvested~~[***] from transplanted ~~rats~~[***] at ~~one, three and six months~~[***] and cell killing assessed by measuring apoptosis with ~~flow cytometry~~[***] using labeled ~~annexin-V and anti-activated CASPASE-3 antibodies or by quantitative apoptosis ELISA assays~~[***].

Series #4: Pig islets encapsulated and transplanted into ~~STZ-induced diabetic NOD/SCID mice~~[***]. Islets will be retrieved at ~~7, 14 and 21 days posttransplant and at 1, 3, 6 and 12 months posttransplant or until the last day of measurable function (n=4 animals/group, 28 animals total/experiment, 2 experiments total)~~[***].

Experimental questions/Outcome parameters: Can encapsulated pig islets survive and function after encapsulation and transplantation in an immunodeficient animal? One additional outcome parameter applied in these studies will be production of porcine C-peptide that can be measured in ~~mice~~[***] with normal native islet function. A second outcome parameter will be measurements of ~~PERV expression~~[***] in the retrieved islets and various tissue compartments in the transplanted animals using quantitative ~~TaqMan PCR~~[***] methodology available in our laboratory. If evidence of ~~PERV~~[***] sequences in ~~mouse~~[***] tissues is detected by ~~DNA PCR~~[***] then additional studies for pig cell microchimerism will be done with pig cytochrome-specific ~~PCR primers~~[***] and for active ~~PERV~~[***] viral expression by ~~RT PCR~~[***] as we have previously published. The third outcome parameter will be detection of ~~PERV by PCR and RT PCR~~[***] in peritoneal washings of transplanted animals at serial time points posttransplant to determine if ~~PERV~~[***] is being shed by the encapsulated pig islets either directly through intact capsules or by loss of capsule integrity as a function of time. Parallel studies will be done with encapsulated pig islets in culture to demonstrate whether an intact capsule allows release of ~~PERV particles~~[***].

Series #5: Pig islets encapsulated and transplanted into ~~STZ-induced diabetic Balb/c mice~~[***]. Islets will be retrieved at ~~7, 14 and 21 days posttransplant and at 1, 3, 6 and 12 months posttransplant or until the last day of measurable function (n=4 animals/group, 28 animals total/experiment, 2 experiments total)~~[***].

Experimental questions/Outcome parameters: Can encapsulated pig islets survive and function after encapsulation and transplantation in a non-immunosuppressed animal with an intact adaptive immune response? The immune function testing will be identical to that described in Series #3 with the exception that ~~pig islet cells~~[***] and lymphocytes will serve as the targets.

~~PERV testing~~[***] will be identical to that described in Series #4 except that additional studies of ~~anti-PERV antibodies~~[***] will be done by ~~Western blotting of ultracentrifuged high titer PERV viral supernatants~~[***] with ~~serial plasma~~[***] samples from transplanted animals.

Series #6: Pig islets encapsulated and transplanted into ~~autoimmune-induced diabetic NOD mice~~[***]. Islets will be retrieved at ~~7 and 14 days and 1, 6 and 12 months posttransplant or until the last day of measurable function (n=4 animals/group, 20 animals total/experiment, 2 experiments total)~~[***].

Experimental questions/Outcome parameters: Can encapsulated pig islets survive and function after encapsulation and transplantation in a non-immunosuppressed animal with an active and islet-destructive immune response? Outcome parameters will be essentially the same as already described though ~~PERV~~[***] testing will be done only on a limited basis. An additional outcome parameter will be testing for ~~anti-pig islet cell antibodies~~[***] using ~~immunofluorescence or Western blotting~~[***]. If positive, then attempts to determine if ~~anti-pig islet~~[***] reactivity is due to ~~cross-reactive anti-islet antibodies (consistent with the preexisting autoimmune response)~~[***] or ~~pig MHC~~[***]

or ~~pig islet specific antigens~~[***]. A very interesting additional set of studies might be done to examine cell-~~mediated immunity~~[***] in these animals with transplanted pig islets to sort out autoimmune-mediated islet cell responses from ~~xenogeneic immunity~~[***]. However, these are challenging and complicated assays that are beyond the applied scope of this proposal, which is intended to set the stage for preclinical studies in a diabetic nonhuman primate model.

Summary - Functional and Toxicity Outcome Parameters:

- Functional data for up to 12 mos. post-transplant
- Blood glucose levels (fasting and stimulated)
- Hgb A1c levels
- Endogenous ~~mouse~~[***] and porcine c-peptide levels (fasting and stimulated by glucose/arginine)
- Retrieval and testing of transplanted islets/capsules
- Selected immune response testing
- Testing possible impact of preexisting islet autoimmunity in ~~NOD mice~~[***]
- ~~PERV~~[***] expression and ~~viral production~~[***]/release testing
- General toxicity
    - Body weight change
    - Food consumption
    - Clinical observations
    - Clinical chemistries
    - Hematology
    - Urinalysis

[Biocompatibility and inflammatory/immune responses

A potential limitation of these studies is the possibility that some kind of bioincompatibility resulting in a limited inflammatory immune response will be documented very early in the testing protocol. In this case the reaction would presumably be to some component of the capsule formulation. If so, the nature and extent of this reaction will be measured using ~~immunohistochemistry~~[***] and other strategies such as ~~cytokine production~~[***] and ~~RNAse Protection~~[***] assays. It is also possible that inflammatory/immune reactions will only be seen at the point in these studies when we begin to transplant encapsulated ~~allogeneic islets~~[***]. Similarly it is also possible that the use of ~~xenogeneic islets~~[***] will be the trigger for such reactions or that these will be qualitatively or quantitatively different than those seen with ~~allogeneic islets~~[***]. In case of encountering any of these patterns they will be investigated. Moreover, we will test the potential of using a limited immunosuppression, ~~either low dose and/or short term, calcineurin inhibitor based or steroid based~~[***], to overcome these inflammatory/immune reactions.

We acknowledge that the requirement for any immunosuppression is a less than optimal result. However, the potential of circumventing the islet shortage by use of encapsulated pig islets would still be a major advance even if it required immunosuppression for success. To the extent that this immunosuppression would be less intense, more limited in numbers of drugs used and/or short term as compared to standard immunosuppressive regimes currently required, it would translate into a very viable

clinical strategy.]

Conclusions: The overarching rationale for the studies outlined here is to create a coherent data set that moves logically from ~~rat to mouse xenotransplantation to pig to mouse xenotransplantation~~[***]. In the process, we will create a large enough data set in several well characterized ~~rodent~~[***] models of islet xenotransplantation that presentation to scientists will convincingly demonstrate the utility of the MicroIslet encapsulation technology, set the stage for preclinical studies in diabetic nonhuman primates and can be presented to the FDA as part of the IND process for human clinical trials. Thus, even the redundancy that we acknowledge is created by the overlapping designs using ~~rat~~[***] and then ~~pig islets~~[***] for encapsulation will serve to better advance the agenda of developing the most robust data set to prove the utility of the technology.

Budget: continued on next page

Exhibit B
To
Research Funding and Option Agreement

Specific Funding Proposal: MicroIslet, Inc.
Principal Investigator: Daniel R. Salomon, M.D.
Project Title: Xenotransplantation of porcine islets protested by alginate encapsulation

Personnel	% Effort	Year 1 Salary/ Fringe	Year 2 Salary/ Fringe		
Daniel R. Salomon (P.I.)	~~5~~	~~$ 7,670~~[***]	[***]	~~$ 7,670~~	[***]
Alexander Szabo (Post-doc)	~~100~~	~~$45,738~~[***]	[***]	~~$45,738~~	[***]
TBD (Rsch Tech.)	~~100~~	~~$40,460~~[***]	[***]	~~$40,460~~	[***]
TOTAL Personnel		$93,868	$93,868		
Supplies					
Animals					
Purchase, board, care		~~$14,500~~	~~$14,500~~[***]		[***]
Chemicals		~~$ 5,132~~	~~$ 5,132~~[***]		[***]
Molecular reagents		~~$ 4,000~~	~~$ 4,000~~[***]		[***]
Plasticware/disposables		~~$ 4,000~~	~~$ 4,000~~[***]		[***]
Tissue culture materials		~~$ 2,500~~	~~$ 2,500~~[***]		[***]
Antibodies/assay materials		~~$ 1,000~~	~~$ 1,000~~[***]		[***]
TOTAL Supplies					
Total Direct		$125,000	$125,000		
IDC (85.2%)		$106,500	$106,500		
ISR (10%)		$ 23,150	$ 23,150		
TOTAL/YEAR		$254,650	$254,650		

Document comparison done by DeltaView on Wednesday, March 26, 2003 18:40:13

Input:	
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