UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): September 26, 2019

ZIOPHARM Oncology, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	**001-33038**	**84-1475642**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

One First Avenue, Parris Building 34, Navy Yard Plaza
Boston, Massachusetts **02129**
(Address of Principal Executive Offices) **(Zip Code)**

(617) 259-1970
(Registrant's telephone number, including area code)

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	**ZIOP**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act (17 CFR 230.405) or Rule 12b-2 of the Exchange Act (17 CFR 240.12b-2).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 1.01 Entry into a Material Definitive Agreement.

On January 10, 2017, Ziopharm Oncology, Inc. (the "Company") announced the signing of a Cooperative Research and Development Agreement (the "CRADA") with the National Cancer Institute ("NCI") for the development of adoptive cell transfer ("ACT") -based immunotherapies genetically modified using the *Sleeping Beauty* system to express T-cell receptors ("TCRs") for the treatment of solid tumors.

Under the CRADA, the Company is granted an option to exclusively license inventions made pursuant to the research plan included in the CRADA, as described in more detail below. On May 28, 2019, the Company entered into a patent license agreement (the "License") with the NCI, pursuant to which the Company holds an exclusive, worldwide license to certain intellectual property for manufacturing technologies, invented under the CRADA's research plan, to develop and commercialize autologous, peripheral blood T-cell therapy products engineered by non-viral gene transfer to express TCRs. In addition, pursuant to the License, the Company holds an exclusive, worldwide license to certain intellectual property to develop and commercialize patient-derived (autologous), peripheral blood T-cell therapy products engineered by transposon-mediated gene transfer to express TCRs reactive to mutated KRAS, p53 and EGFR. The terms of the License were described in the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission (the "SEC") on May 28, 2019.

On June 11, 2019, the Company announced that the investigational new drug application submitted by the NCI had received clearance from the U.S. Food and Drug Administration for a clinical trial to evaluate TCR T-cell therapy in solid tumors utilizing the Company's *Sleeping Beauty* system pursuant to the CRADA. As a result of recent updates from the NCI, the Company has now determined that the CRADA is material to the Company.

The CRADA, dated January 9, 2017, was entered into by the NCI, the Company and Intrexon Corporation ("Intrexon"). Intrexon assigned its rights and obligations under the CRADA to Precigen, Inc. ("Precigen") pursuant to Amendment #1 to the Cooperative Research and Development Agreement, dated March 23, 2018 (the "First Amendment"), and Precigen assigned its rights and obligations to the Company pursuant to Amendment #2 to the Cooperative Research and Development Agreement, dated February 1, 2019 (the "Second Amendment").

Under the CRADA, the parties intend to develop and evaluate ACT for patients with advanced cancers using autologous peripheral blood lymphocytes genetically modified using the non-viral *Sleeping Beauty* system to express TCRs that recognize neoantigens expressed within a patient's cancer. Research conducted under the CRADA will be at the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI, in collaboration with the Company.

Under the CRADA, as amended by the First Amendment and the Second Amendment, the Company is required to pay the NCI $2.5 million per year, payable quarterly, during the term of the CRADA. To date, the Company has paid the NCI $6.9 million. The CRADA terminates on January 9, 2022 unless it is extended in writing by the parties. Either party may terminate the CRADA by providing at least 60 days' prior written notice to the other party.

Each party has granted the other party rights to use their respective background inventions solely to the extent necessary to conduct the research and development activities under the CRADA. Subject to the U.S. government's nonexclusive, nontransferable, irrevocable right to practice any CRADA invention for research or other government purposes, the producing party will own any inventions, data and materials produced by its employees, and the parties will jointly own all any inventions jointly invented by the parties. The Company is granted an exclusive option to elect an exclusive or nonexclusive commercialization license with a field of use that does not exceed the scope of the CRADA research plan. Any such license will be in substantially the form of the applicable U.S. Public Health Service's model agreement, with terms that reflect the nature of the licensed technology, among other things. The CRADA also contains customary representations, warranties, indemnification and confidentiality obligations.

The foregoing descriptions of the CRADA, the First Amendment and Second Amendment are not complete and are qualified in their entireties by reference to the full texts of the CRADA, the First Amendment and Second Amendment, copies of which are filed herewith as Exhibits 10.1, 10.2, and 10.3 respectively, and are incorporated by reference herein.

Item 7.01 Regulation FD Disclosure.

The Company has updated its corporate presentation to include a slide describing the Company's agreements with the NCI. The corporate presentation will be used by the Company's management in future meetings regarding the Company.

A copy of the slide describing the NCI agreements is furnished as Exhibit 99.1 to this Current Report on Form 8-K. The information in this Item 7.01 and Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, except as expressly set forth by specific reference in such filing. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
10.1†	Cooperative Research and Development Agreement, dated January 9, 2017, by and among the National Cancer Institute, Ziopharm Oncology, Inc. and Intrexon Corporation.
10.2	Amendment #1 to the Cooperative Research and Development Agreement, dated March 23, 2018, by and among the National Cancer Institute, Ziopharm Oncology, Inc., Intrexon Corporation and Precigen, Inc.
10.3†	Amendment #2 to the Cooperative Research and Development Agreement, dated February 1, 2019, by and among the National Cancer Institute, Ziopharm Oncology, Inc. and Precigen, Inc.
99.1	Slide describing Ziopharm Oncology, Inc.'s agreements with the National Cancer Institute.

† Certain portions of this exhibit (indicated by "[***]") have been omitted pursuant to confidential treatment.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ZIOPHARM ONCOLOGY, INC.

By: /s/ Robert Hadfield
Name: Robert Hadfield
Title: General Counsel and Secretary

Date: September 26, 2019

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM IF PUBLICLY DISCLOSED.

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT FOR INTRAMURAL-PHS CLINICAL RESEARCH

This Agreement is based on the model Cooperative Research and Development Agreement ("CRADA") adopted by the U.S. Public Health Service ("PHS") Technology Transfer Policy Board for use by components of the National Institutes of Health ("NIH"), the Centers for Disease Control and Prevention ("CDC"), and the Food and Drug Administration ("FDA"), which are agencies of the PHS within the Department of Health and Human Services ("HHS").

This Cover Page identifies the Parties to this CRADA:

The U.S. Department of Health and Human Services, as represented by
National Cancer Institute
an Institute or Center (hereinafter referred to as the "**IC**") of the
National Institutes of Health

and

Intrexon Corporation,
hereinafter referred to as "Intrexon",
having offices at 20374 Seneca Meadows Parkway, Germantown MD 20876,
created and operating under the laws of Virginia.

and

ZIOPHARM Oncology, Inc.,
hereinafter referred to as "ZIOPHARM",
having offices at One First Avenue, Paris Building 34, Boston, MA 02129,
created and operating under the laws of Delaware.

Article 1. INTRODUCTION

This CRADA between IC and Collaborator will be effective when signed by the Parties, which are identified on both the Cover Page and the Signature Page. The official contacts for the Parties are identified on the Contacts Information Page. Publicly available information regarding this CRADA appears on the Summary Page. The research and development activities that will be undertaken by IC and Collaborator in the course of this CRADA are detailed in the Research Plan, attached as Appendix A. The staffing, funding, and materials contributions of the Parties are set forth in Appendix B. Any changes to the model CRADA are set forth in Appendix C.

Article 2. DEFINITIONS

The terms listed in this Article will carry the meanings indicated throughout the CRADA. To the extent a definition of a term as provided in this Article is inconsistent with a corresponding definition in the applicable sections of either the United States Code (U.S.C.) or the Code of Federal Regulations (C.F.R.), the definition in the U.S.C. or C.F.R. will control.

"**Adverse Event**" or **"AE**" means any untoward medical occurrence associated with the use of a Test Article in humans, whether or not considered related to the Test Article (21 C.F.R §§ 312.32, 308.3; see also FDA Good Clinical Practice Guideline, International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance, 62 Federal Register 25,691 (1997)).

"Affiliate" means any corporation or other business entity controlled by, controlling, or under common control with Collaborator at any time during the term of the CRADA. For this purpose, "control" means direct or indirect beneficial ownership of at least fifty percent (50%) of the voting stock or at least fifty percent (50%) interest in the income of the corporation or other business entity.

"Annual Report" means the report of progress of an IND-associated investigation that IC, as the IND Sponsor, must submit to the FDA within sixty (60) days of the anniversary of the effective date of the IND (pursuant to 21 C.F.R.§ 312.33).

"Background Invention" means an Invention conceived and first actually reduced to practice before the Effective Date.

"Clinical Investigator" means, in accordance with 21 C.F.R. § 312.3, an individual who actually conducts a clinical investigation, that is, who directs the administration or dispensation of Test Article to a subject, and who assumes responsibility for studying Human Subjects, for recording and ensuring the integrity of research data, and for protecting the welfare and safety of Human Subjects.

"Collaborator Material" means all tangible materials not first produced in the performance of this CRADA that are owned or controlled by Collaborator and used in the performance of the Research Plan. The term "Collaborator Materials" does not include "Test Article" (defined below).

"**Confidential Information**" means confidential scientific, business, financial information, or Identifiable Private Information provided that the information does not include:

(a) information that is publicly known or that is available from public sources;

(b) information that has been made available by its owner to others without a confidentiality obligation;

(c) information that is already known by the receiving Party, or information that is independently created or compiled by the receiving Party without reference to or use of the provided information; or

(d) information that relates to potential hazards or cautionary warnings associated with the production, handling, or use of the subject matter of the Research Plan.

"Cooperative Research and Development Agreement" or "**CRADA**" means this Agreement, entered into pursuant to the Federal Technology Transfer Act of 1986, as amended (15 U.S.C. §§ 3710a *et seq.*), and Executive Order 12591 of April 10, 1987.

"CRADA Data" means all recorded information first produced in the performance of the Research Plan.

"CRADA Materials" means all tangible materials first produced in the performance of the Research Plan other than CRADA Data.

"CRADA Principal Investigator(s)" or "**CRADA PI(s)**" means the person(s) designated by the Parties who will be responsible for the scientific and technical conduct of the Research Plan. The CRADA PI may also be a Clinical Investigator.

"CRADA Subject Invention" means any Invention of either or both Parties, conceived or first actually reduced to practice in the performance of the Research Plan.

"Drug Master File" or "**DMF**" is described in 21 C.F.R. Part 314.420. A DMF is a submission to the FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs.

"Effective Date" means the date of the last signature of the Parties executing this Agreement.

"Government" means the Government of the United States of America.

"Human Subject" means, in accordance with the definition in 45 C.F.R. § 46.102(f), a living individual about whom an investigator conducting research obtains:

(a) data through intervention or interaction with the individual; or

(b) Identifiable Private Information.

"IC Materials" means all tangible materials not first produced in the performance of this CRADA that are owned or controlled by IC and used in the performance of the Research Plan.

"IND" means an "**Investigational New Drug Application**", filed in accordance with 21 C.F.R. Part 312 under which clinical investigation of an experimental drug or biologic (Test Article) is performed in Human Subjects in the United States or intended to support a United States licensing action.

"Identifiable Private Information" **or "IPI**" about a Human Subject means private information from which the identity of the subject is or may readily be ascertained. Regulations defining and governing this information include 45 C.F.R. Part 46 and 21 C.F.R. Part 50.

"Institutional Review Board" or "**IRB**" means, in accordance with 45 C.F.R. Part 46, 21 C.F.R. Part 56, and other applicable regulations, an independent body comprising medical, scientific, and nonscientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of the Human Subjects involved in a study.

"Invention" means any invention or discovery that is or may be patentable or otherwise protected under Title 35 of the United States Code, or any novel variety of plant which is or may be protectable under the Plant Variety Protection Act, 7 U.S.C. §§ 2321 *et seq*.

"Investigator's Brochure" means, in accordance with the definition in 21 C.F.R. § 312.23(a)(5), a document containing information about the Test Article, including animal screening, preclinical toxicology, and detailed pharmaceutical data, including a description of possible risks and side effects to be anticipated on the basis of prior experience with the drug or related drugs, and precautions, such as additional monitoring, to be taken as part of the investigational use of the drug.

"Patent Application" means an application for patent protection for a CRADA Subject Invention with the United States Patent and Trademark Office ("U.S.P.T.O.") or the corresponding patent-issuing authority of another nation.

"Patent" means any issued United States patent, any international counterpart(s), and any corresponding grant(s) by a non-U.S. government in place of a patent.

"Placebo" means an inactive substance identical in appearance to the material being tested that is used to distinguish between drug action and suggestive effect of the material under study.

"Protocol" means the formal, detailed description of a study to be performed as provided for in the Research Plan. It describes the objective(s), design, methodology, statistical considerations, and organization of a trial. For the purposes of this CRADA, the term, Protocol, for clinical research involving Human Subjects, includes any and all associated documents, including informed consent forms, to be provided to Human Subjects and potential participants in the study.

"**Raw Data**" means the primary quantitative and empirical data first collected from experiments and clinical trials conducted within the scope of this CRADA.

"**Research Plan**" means the statement in Appendix A of the respective research and development commitments of the Parties. The Research Plan should describe the provisions for sponsoring the IND, clinical and safety monitoring, and data management.

"**Sponsor**" means, in accordance with the definition in 21 C.F.R. § 312.3, an organization or individual who assumes legal responsibility for supervising or overseeing clinical trials with Test Articles, and is sometimes referred to as the IND holder.

"**Steering Committee**" means the research and development team whose composition and responsibilities with regard to the research performed under this CRADA are described in Appendix A.

"**Summary Data**" means any extract or summary of the Raw Data, generated either by, or on behalf of, IC or by, or on behalf of, Collaborator. Summary Data may include extracts or summaries that incorporate IPI.

"**Test Article**" means, in accordance with 21 C.F.R. § 50.3 (j), any drug (including a biological product), medical device, food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act that is intended for administration to humans or animals, including a drug or biologic as identified in the Research Plan and Appendix B, that is used within the scope of the Research Plan. The Test Article may also be referred to as Investigational Agent, Study Material, or Study Product.

Article 3. COOPERATIVE RESEARCH AND DEVELOPMENT

3.1 **Performance of Research and Development**. The research and development activities to be carried out under this CRADA will be performed solely by the Parties identified on the Cover Page, unless specifically stated elsewhere in the Agreement. The CRADA PIs will be responsible for coordinating the scientific and technical conduct of this project on behalf of their employers. Any Collaborator employees who will work at IC facilities will be required to sign an agreement appropriately modified in view of the terms of this CRADA.

3.2 **Research Plan.** The Parties recognize that the Research Plan describes the collaborative research and development activities they will undertake and that interim research goals set forth in the Research Plan are good faith guidelines. Should events occur that require modification of these goals, then by mutual agreement the Parties can modify them through an amendment, according to Paragraph 13.6.

3.3 **Use and Disposition of Collaborator Materials and IC Materials**. The Parties agree to use Collaborator Materials and IC Materials only in accordance with the Research Plan and Protocol(s), not to transfer these materials to third parties except in accordance with the Research Plan and Protocol(s) or as approved by the owning or providing Party, and, upon expiration or termination of the CRADA, to dispose of these materials as directed by the owning or providing Party.

3.4 **Third-Party Rights in Collaborator's CRADA Subject Inventions**. If Collaborator has received (or will receive) support of any kind from a third party in exchange for rights in any of Collaborator's CRADA Subject Inventions, Collaborator agrees to ensure that its obligations to the third party are both consistent with Articles 6 through 8 and subordinate to Article 7 of this CRADA.

3.5 **Disclosures to IC**. Prior to execution of this CRADA, Collaborator agrees to disclose to IC all instances in which outstanding royalties are due under a PHS license agreement and in which Collaborator had a PHS license terminated in accordance with 37 C.F.R. § 404.10. These disclosures will be treated as Confidential Information upon request by Collaborator in accordance with the definition in Article 2 and Paragraphs 8.3 and 8.4.

3.6 **Clinical Investigator Responsibilities**. The Clinical Investigator will be required to submit, or to arrange for submission of, each Protocol associated with this CRADA to the IRB. In addition to the Protocol all associated documents, including informational documents and advertisements, must be reviewed and approved by the IRB before starting the research. The research will be done in strict accordance with the Protocol(s) and no substantive changes in a finalized Protocol will be made unless mutually agreed upon, in writing, by the Parties. Research will not commence (or will continue unchanged, if already in progress) until each substantive change to a Protocol, including those required by either the FDA or the IRB, has been integrated in a way acceptable to the Parties, submitted to the FDA (if applicable) and approved by the IRB.

3.7 **Investigational Applications**.

3.7.1 If an IND is required, IC will be the IND Sponsor and will submit an IND. All Clinical Investigators must have completed registration documents on file (1572 forms).

3.7.2 When IC files the IND, Collaborator agrees to provide IC background data and information necessary to support the IND. Collaborator further agrees to provide a letter of cross-reference to all pertinent regulatory filings sponsored by Collaborator. Collaborator's employees will be reasonably available to respond to inquiries from the FDA regarding information and data contained in the Collaborator's IND, DMF, other filings, or other information and data provided to IC by the Collaborator pursuant to this Article 3.

3.7.3 If Collaborator supplies Confidential Information to IC in support of an IND filed by IC, this information will be protected in accordance with the corresponding confidentiality provisions of Article 8.

3.7.4 Collaborator may sponsor its own clinical trials and hold its own IND for studies performed outside the scope of this CRADA. These studies, however, should not adversely affect the ability to accomplish the goal of the Research Plan, for example, by competing for the same study population. All data from those clinical trials are proprietary to Collaborator for purposes of this CRADA.

3.8 **Test Article Information and Supply**. Collaborator agrees to provide IC without charge and on a schedule that will ensure adequate and timely performance of the research, a sufficient quantity of formulated and acceptably labeled, clinical-grade Test Article (and, as required by the Protocol(s), Placebo) to complete the clinical trial(s) agreed to and approved under this CRADA. Collaborator will provide a Certificate of Analysis to IC for each lot of the Test Article provided.

3.9 **Test Article Delivery and Usage**. Collaborator will ship the Test Article and, if required, Placebo to IC in containers marked in accordance with 21 C.F.R. § 312.6. IC agrees that the Clinical Investigators will keep appropriate records and take reasonable steps to ensure that the Test Article is used in accordance with the Protocol(s) and applicable FDA regulations. In addition, IC agrees that the Test Article (and all Confidential Information supplied by Collaborator relating to the Test Article) will be used solely for the conduct of the CRADA research and development activities. Furthermore, IC agrees that no analysis or modification of the Test Article will be performed without Collaborator's prior written consent. At the completion of the Research Plan, any unused quantity of Test Article will be returned to Collaborator or disposed as directed by Collaborator. Pharmacy contacts at IC will be determined by IC and communicated to Collaborator.

3.10 **Monitoring**. Subject to the restrictions in Article 8 concerning IPI, and with reasonable advance notice and at reasonable times, IC will permit Collaborator or its designee(s) to monitor the conduct of the research, as well as to audit source documents containing Raw Data, to the extent necessary to verify compliance with FDA Good Clinical Practice (International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance; 62 Federal Register 25, 691 (1997)) and the Protocol(s).

3.11 **FDA Meetings/Communications**. All meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and IC in advance. Each Party reserves the right to take part in setting the agenda for, to attend, and to participate in these meetings. IC will provide Collaborator with copies of FDA meeting minutes, all transmittal letters for IND submissions, IND safety reports, formal questions and responses that have been submitted to the FDA, Annual Reports, and official FDA correspondence, pertaining either to the INDs under this CRADA or to the Clinical Investigators on Protocols performed in accordance with the Research Plan, except to the extent that those documents contain the proprietary information of a third party or dissemination is prohibited by law.

Article 4. REPORTS

4.1 **Interim Research and Development Reports**. The CRADA PIs should exchange information regularly, in writing. This exchange may be accomplished through meeting minutes, detailed correspondence, circulation of draft manuscripts, Steering Committee reports, copies of Annual Reports and any other reports updating the progress of the CRADA research. However, the Parties must exchange updated Investigator's Brochure, formulation and preclinical data, and toxicology findings, as they become available.

4.2 **Final Research and Development Reports**. The Parties will exchange final reports of their results within six (6) months after the expiration or termination of this CRADA. These reports will set forth the technical progress made; any publications arising from the research; and the existence of invention disclosures of potential CRADA Subject Inventions and/or any corresponding Patent Applications.

4.3 **Fiscal Reports**. If Collaborator has agreed to provide funding to IC under this CRADA and upon the request of Collaborator, then concurrent with the exchange of final research and development reports according to Paragraph 4.2, IC will submit to Collaborator a statement of all costs incurred by IC for the CRADA. If the CRADA has been terminated, IC will specify any costs incurred before the date of termination for which IC has not received funds from Collaborator, as well as for all reasonable termination costs including the cost of returning Collaborator property or removal of abandoned Collaborator property, for which Collaborator will be responsible.

4.4 **Safety Reports**.

4.4.1 In accordance with FDA requirements IC, as the IND Sponsor, will establish and maintain records and submit safety reports to the FDA, as required by 21 C.F.R. § 312.32 and 21 C.F.R. § 812.150(b)(1), or other applicable regulations. In the conduct of research under this CRADA, the Parties will comply with specific IC guidelines and policies for reporting AEs, as well as procedures specified in the Protocol(s). IC must provide Collaborator with copies of all Safety Reports concurrently with their submission to the FDA, and with any other information affecting the safety of Human Subjects in research conducted under this CRADA.

4.4.2 During and for a period of two years after the completion of a Protocol, the Collaborator shall promptly provide to the IC any information that Collaborator has reasonably determined could directly affect the health or safety of past or current Human Subjects or influence the conduct of the Protocol. Such information may arise from any source, for example, Safety Reports provided to the FDA, study results, information in site monitoring reports or data safety monitoring committee reports. IC shall be free to communicate the relevant safety information to each Human Subject and the IRB.

4.5 **Annual Reports**. IC will provide Collaborator a copy of the Annual Report concurrently with the submission of the Annual Report to the FDA. Annual Reports will be kept confidential in accordance with Article 8.

Article 5. STAFFING, FINANCIAL, AND MATERIALS OBLIGATIONS

5.1 **IC and Collaborator Contributions**. The contributions of any staff, funds, materials, and equipment by the Parties are set forth in Appendix B. The Federal Technology Transfer Act of 1986, 15 U.S.C. § 3710a(d)(1) prohibits IC from providing funds to Collaborator for any research and development activities under this CRADA.

5.2 **IC Staffing**. No IC employees will devote 100% of their effort or time to the research and development activities under this CRADA. IC will not use funds provided by Collaborator under this CRADA for IC personnel to pay the salary of any permanent IC employee. Although personnel hired by IC using CRADA funds will focus principally on CRADA research and development activities, Collaborator acknowledges that these personnel may nonetheless make contributions to other research and development activities, and the activities will be outside the scope of this CRADA.

5.3 **Collaborator Funding**. Collaborator acknowledges that Government funds received by Collaborator from an agency of the Department of Health and Human Services may not be used to fund IC under this CRADA. If Collaborator has agreed to provide funds to IC then the payment schedule appears in Appendix B and Collaborator will make payments according to that schedule. If Collaborator fails to make any scheduled payment, IC will not be obligated to perform any of the research and development activities specified herein or to take any other action required by this CRADA until the funds are received. IC will use these funds exclusively for the purposes of this CRADA. Each Party will maintain separate and distinct current accounts, records, and other evidence supporting its financial obligations under this CRADA and, upon written request, will provide the other Party a Fiscal Report according to Paragraph 4.3, which delineates all payments made and all obligated expenses, along with the Final Research Report described in Paragraph 4.2.

5.4 **Capital Equipment**. Collaborator's commitment, if any, to provide IC with capital equipment to enable the research and development activities under the Research Plan appears in Appendix B. If Collaborator transfers to IC the capital equipment or provides funds for IC to purchase it, then IC will own the equipment. If Collaborator loans capital equipment to IC for use during the CRADA, Collaborator will be responsible for paying all costs and fees associated with the transport, installation, maintenance, repair, removal, or disposal of the equipment, and IC will not be liable for any damage to the equipment.

Article 6. INTELLECTUAL PROPERTY

6.1 **Ownership of CRADA Subject Inventions, CRADA Data, and CRADA Materials**. Subject to the Government license described in Paragraph 7.5, the sharing requirements of Paragraph 8.1 and the regulatory filing requirements of Paragraph 8.2, the producing Party will retain sole ownership of and title to all CRADA Subject Inventions, all copies of CRADA Data, and all CRADA Materials produced solely by its employee(s). The Parties will own jointly all CRADA Subject Inventions invented jointly and all CRADA Materials developed jointly.

6.2 **Reporting**. The Parties will promptly report to each other in writing each CRADA Subject Invention reported by their respective personnel, and any Patent Applications filed thereon, resulting from the research and development activities conducted under this CRADA. Each Party will report all CRADA Subject Inventions to the other Party in sufficient detail to determine inventor ship, which will be determined in accordance with U.S. patent law. These reports will be treated as Confidential Information in accordance with Article 8. Formal reports will be made by and to the Patenting and Licensing Offices identified on the Contacts Information Page herein.

6.3 **Filing of Patent Applications**. Each Party will make timely decisions regarding the filing of Patent Applications on the CRADA Subject Inventions made solely by its employee(s), and will notify the other Party in advance of filing. Collaborator will have the first opportunity to file a Patent Application on joint CRADA Subject Inventions and will notify PHS of its decision within sixty (60) days of an Invention being reported or at least thirty (30) days before any patent filing deadline, whichever occurs sooner. If Collaborator fails to notify PHS of its decision within that time period or notifies PHS of its decision not to file a Patent Application, then PHS has the right to file a Patent Application on the joint CRADA Subject Invention. Neither Party will be obligated to file a Patent Application. Collaborator will place the following statement in any Patent Application it files on a CRADA Subject Invention: "This invention was created in the performance of a Cooperative Research and Development Agreement with the **National Institutes of Health**, an Agency of the Department of Health and Human Services. The Government of the United States has certain rights in this invention." If either Party files a Patent Application on a joint CRADA Subject Invention, then the filing Party will include a statement within the Patent Application that clearly identifies the Parties and states that the joint CRADA Subject Invention was made under this CRADA.

6.4 **Patent Expenses**. Unless agreed otherwise, the Party filing a Patent Application will pay all preparation and filing expenses, prosecution fees, issuance fees, post issuance fees, patent maintenance fees, annuities, interference expenses, and attorneys' fees for that Patent Application and any resulting Patent(s). If a license to any CRADA Subject Invention is granted to Collaborator, then Collaborator will be responsible for all expenses and fees, past and future, in connection with the preparation, filing, prosecution, and maintenance of any Patent Applications and Patents claiming exclusively licensed CRADA Subject Inventions and will be responsible for a pro-rated share, divided equally among all licensees, of those expenses and fees for non-exclusively licensed CRADA Subject Inventions. Collaborator may waive its exclusive option rights at any time, and incur no subsequent financial obligation for those Patent Application(s) or Patent(s).

6.5 **Prosecution of Patent Applications**. The Party filing a Patent Application will provide the non-filing Party with a copy of any official communication relating to prosecution of the Patent Application within thirty (30) days of transmission of the communication. Each Party will also provide the other Party with the power to inspect and make copies of all documents retained in the applicable Patent Application or Patent file. The Parties agree to consult with each other regarding the prosecution of Patent Applications directed to joint CRADA Subject Inventions. If Collaborator elects to file and prosecute Patent Applications on joint CRADA Subject Inventions, then Collaborator agrees to use the U.S.P.T.O. Customer Number Practice and/or grant PHS a power(s) of attorney (or equivalent) necessary to assure PHS access to its intellectual property rights in these Patent Applications. PHS and Collaborator will cooperate with each other to obtain necessary signatures on Patent Applications, assignments, or other documents.

Article 7. LICENSING

7.1 **Background Inventions.** Other than as specifically stated in this Article 7, nothing in this CRADA will be construed to grant any rights in one Party's Background Invention(s) to the other Party, except to the extent necessary for the Parties to conduct the research and development activities described in the Research Plan.

7.2 **Collaborator's License Option to CRADA Subject Inventions**. With respect to Government rights to any CRADA Subject Invention made solely by an IC employee(s) or made jointly by an IC employee(s) and a Collaborator employee(s) for which a Patent Application was filed, PHS hereby grants to Collaborator an exclusive option to elect an exclusive or nonexclusive commercialization license. The license will be substantially in the form of the appropriate model PHS license agreement and will fairly reflect the nature of the CRADA Subject Invention, the relative contributions of the Parties to the CRADA Subject Invention and the CRADA, a plan for the development and marketing of the CRADA Subject Invention, the risks incurred by Collaborator, and the costs of subsequent research and development needed to bring the CRADA Subject Invention to the marketplace. The field of use of the license will not exceed the scope of the Research Plan.

7.3 **Exercise of Collaborator's License Option.** To exercise the option of Paragraph 7.2 Collaborator must submit a written notice to the PHS Patenting and Licensing Contact identified on the Contacts Information Page (and provide a copy to the IC Contact for CRADA Notices) within three (3) months after either (i) Collaborator receives written notice from PHS that the Patent Application has been filed or (ii) the date on which Collaborator files the Patent Application. The written notice exercising this option will include a completed "Application for License to Public Health Service Inventions" and will initiate a negotiation period that expires nine (9) months after the exercise of the option. If PHS has not responded in writing to the last proposal by Collaborator within this nine (9) month period, the negotiation period will be extended to expire one (1) month after PHS so responds, during which month Collaborator may accept in writing the final license proposal of PHS. In the absence of Collaborator's exercise of the option, or upon election of a nonexclusive license, PHS will be free to license the CRADA Subject Invention to others. These time periods may be extended at the sole discretion of PHS upon good cause shown in writing by Collaborator.

7.4 **Government License in IC Sole CRADA Subject Inventions and Joint CRADA Subject Inventions.** Pursuant to 15 U.S.C. § r3710a(b)(1)(A), for CRADA Subject Inventions owned solely by IC or jointly by IC and Collaborator, and licensed pursuant to the option of Paragraph 7.2, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government. In the exercise of this license, the Government will not publicly disclose trade secrets or commercial or financial information that is privileged or confidential within the meaning of 5 U.S.C. § 552(b)(4) or which would be considered privileged or confidential if it had been obtained from a non-federal party.

7.5 **Government License in Collaborator Sole CRADA Subject Inventions**. Pursuant to 15 U.S.C. § 3710a(b)(2), for CRADA Subject Inventions made solely by an employee of Collaborator, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government for research or other Government purposes.

7.6 **Third Party License**. Pursuant to 15 U.S.C. § 3710a(b)(1)(B), if PHS grants Collaborator an exclusive license to a CRADA Subject Invention made solely by an IC employee or jointly with a Collaborator employee, the Government will retain the right to require Collaborator to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the CRADA Subject Invention in Collaborator's licensed field of use on terms that are reasonable under the circumstances; or, if Collaborator fails to grant a license, to grant a license itself. The exercise of these rights by the Government will only be in exceptional circumstances and only if the Government determines (i) the action is necessary to meet health or safety needs that are not reasonably satisfied by Collaborator, (ii) the action is necessary to meet requirements for public use specified by federal regulations, and such requirements are not reasonably satisfied by Collaborator; or (iii) Collaborator has failed to comply with an agreement containing provisions described in 15 U.S.C. § 3710a(c)(4)(B). The determination made by the Government under this Paragraph is subject to administrative appeal and judicial review under 35 U.S.C. § 203(b).

7.7 **Third-Party Rights In IC Sole CRADA Subject Inventions**. For a CRADA Subject Invention conceived prior to the Effective Date solely by an IC employee that is first actually reduced to practice after the Effective Date in the performance of the Research Plan, the option offered to Collaborator in Paragraph 7.2 may be restricted if, prior to the Effective Date, PHS had filed a Patent Application and has either offered or granted a license in the CRADA Subject Invention to a third party. Collaborator nonetheless retains the right to apply for a license to any such CRADA Subject Invention in accordance with the terms and procedures of 35 U.S.C. § 209 and 37 C.F.R. Part 404.

Article 8. RIGHTS OF ACCESS AND PUBLICATION

8.1 **Right of Access to CRADA Data and CRADA Materials**. IC and Collaborator agree to exchange all CRADA Data and to share all CRADA Materials. If the CRADA is terminated, both Parties agree to provide CRADA Materials in quantities needed to complete the Research Plan. Such provision will occur before the termination date of the CRADA or sooner, if required by the Research Plan. If Collaborator possesses any human biological specimens from clinical trials under the CRADA, the specimens must be handled as described in the Protocol or as otherwise directed by IC before the termination date of the CRADA.

8.2 **Use of CRADA Data and CRADA Materials**. The Parties will be free to utilize CRADA Data and CRADA Materials internally for their own purposes, consistent with their obligations under this CRADA. The Parties may share CRADA Data or CRADA Materials with their Affiliates, agents or contractors provided the obligations of this Article 8.2 are simultaneously conveyed.

8.2.1 **CRADA Data**.
Collaborator and IC will use reasonable efforts to keep CRADA Data confidential until published or until corresponding Patent Applications are filed. To the extent permitted by law, each Party will have the right to use any and all CRADA Data in and for any regulatory filing by or on behalf of the Party.

8.2.2 **CRADA Materials**.
Collaborator and IC will use reasonable efforts to keep descriptions of CRADA Materials confidential until published or until corresponding Patent Applications are filed. Collaborator acknowledges that the basic research mission of PHS includes sharing with third parties for further research those research resources made in whole or in part with NIH funding. Consistent with this mission and the tenets articulated in "Sharing of Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts", December 1999, available at http://www.ott.nih.gov/policy/research tool.aspx, following publication either Party may make available to third parties for further research those CRADA Materials made jointly by both PHS and Collaborator. Notwithstanding the above, if those joint CRADA Materials are the subject of a pending Patent Application or a Patent, or were created using a patent-pending or patented material or technology, the Parties may agree to restrict distribution or freely distribute them. Either Party may distribute those CRADA Materials made solely by the other Party only upon written consent from that other Party or that other Party's designee.

8.3 **Confidential Information**. Each Party agrees to limit its disclosure of Confidential Information to the amount necessary to carry out the Research Plan, and will place a confidentiality notice on all this information. A Party orally disclosing Confidential Information to the other Party will summarize the disclosure in writing and provide it to the other Party within fifteen (15) days of the disclosure. Each Party receiving Confidential Information agrees to use it only for the purposes described in the Research Plan. Either Party may object to the designation of information as Confidential Information by the other Party.

8.4 **Protection of Confidential Information**. Confidential Information will not be disclosed, copied, reproduced or otherwise made available to any other person or entity without the consent of the owning or providing Party except as required by a court or administrative body of competent jurisdiction, or federal law or regulation. Each Party agrees to use reasonable efforts to maintain the confidentiality of Confidential Information, which will in no instance be less effort than the Party uses to protect its own Confidential Information. Each Party agrees that a Party receiving Confidential Information will not be liable for the disclosure of that portion of the Confidential Information which, after notice to and consultation with the disclosing Party, the receiving Party determines may not be lawfully withheld, provided the disclosing Party has been given a reasonable opportunity to seek a court order to enjoin disclosure.

8.5 **Human Subject Protection**. The research to be conducted under this CRADA involves Human Subjects or human tissues within the meaning of 45 C.F.R. Part 46, and all research to be performed under this CRADA will conform to applicable federal laws and regulations. Additional information is available from the HHS Office for Human Research Protections (http://www.hhs.gov/ohrp/).

8.6 **Duration of Confidentiality Obligation**. The obligation to maintain the confidentiality of Confidential Information will expire at the earlier of the date when the information is no longer Confidential Information as defined in Article 2 or three (3) years after the expiration or termination date of this CRADA, except for IPI, for which the obligation to maintain confidentiality will extend indefinitely. Collaborator may request an extension to this term when necessary to protect Confidential Information relating to products not yet commercialized.

8.7 **Publication**. The Parties are encouraged to make publicly available the results of their research and development activities. Before either Party submits a paper or abstract for publication or otherwise intends to publicly disclose information about a CRADA Subject Invention, CRADA Data, or CRADA Materials, the other Party will have thirty (30) days to review proposed manuscripts and three (3) days to review proposed abstracts to assure that Confidential Information is protected. Either Party may request in writing that the proposed publication or other disclosure be delayed for up to thirty (30) additional days as necessary to file a Patent Application.

Article 9. REPRESENTATIONS AND WARRANTIES

9.1 **Representations of IC**. IC hereby represents to Collaborator that:

9.1.1 IC has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that IC's official signing this CRADA has authority to do so.

9.1.2 To the best of its knowledge and belief, neither IC nor any of its personnel involved in this CRADA is presently subject to debarment or suspension by any agency of the Government which would directly affect its performance of the CRADA. Should IC or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, IC will notify Collaborator within thirty (30) days of receipt of final notice.

9.2 **Representations and Warranties of Collaborator**. Collaborator hereby represents and warrants to IC that:

9.2.1 Collaborator has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that Collaborator's official signing this CRADA has authority to do so.

9.2.2 Neither Collaborator nor any of its personnel involved in this CRADA, including Affiliates, agents, and contractors are presently subject to debarment or suspension by any agency of the Government. Should Collaborator or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, Collaborator will notify IC within thirty (30) days of receipt of final notice.

9.2.3 Subject to Paragraph 12.3, and if and to the extent Collaborator has agreed to provide funding under Appendix B, Collaborator is financially able to satisfy these obligations in a timely manner.

9.2.4 The Test Article provided has been produced in accordance with the FDA's current Good Manufacturing Practice set out in 21 C.F.R. §§ 210-211 and ICH QA7, and meets the specifications cited in the Certificate of Analysis and Investigator's Brochure provided.

Article 10. EXPIRATION AND TERMINATION

10.1 **Expiration**. This CRADA will expire on the last date of the term set forth on the Summary Page. In no case will the term of this CRADA extend beyond the term indicated on the Summary Page unless it is extended in writing in accordance with Paragraph 13.6.

10.2 **Termination by Mutual Consent**. IC and Collaborator may terminate this CRADA at any time by mutual written consent.

10.3 **Unilateral Termination**. Either IC or Collaborator may unilaterally terminate this CRADA at any time by providing written notice at least sixty (60) days before the desired termination date. IC may, at its option, retain funds transferred to IC before unilateral termination by Collaborator for use in completing the Research Plan. If Collaborator terminates this Agreement before the completion of all approved or active Protocol(s), then Collaborator will supply enough Test Article (and Placebo, if applicable) to complete these Protocol(s) unless termination is for safety concerns.

10.4 **Funding for IC Personnel**. If Collaborator has agreed to provide funding for IC personnel and this CRADA is mutually or unilaterally terminated by Collaborator before its expiration, then Collaborator agrees that funds for that purpose will be available to IC for a period of six (6) months after the termination date or until the expiration date of the CRADA, whichever occurs sooner. If there are insufficient funds to cover this expense, Collaborator agrees to pay the difference.

10.5 **New Commitments**. Neither Party will incur new expenses related to this CRADA after expiration, mutual termination, or a notice of a unilateral termination and will, to the extent feasible, cancel all outstanding commitments and contracts by the termination date. Collaborator acknowledges that IC will have the authority to retain and expend any funds for up to one (1) year subsequent to the expiration or termination date to cover any unpaid costs obligated during the term of the CRADA in undertaking the research and development activities set forth in the Research Plan.

10.6 **Collaborator Failure to Continue Development**. If Collaborator suspends development of the Test Article without the transfer of its active development efforts, assets, and obligations to a third party within ninety (90) days of discontinuation, Collaborator agrees that IC may continue developing the Test Article. In that event, the following will apply:

10.6.1 Collaborator agrees to transfer to IC all information necessary to enable IC to contract for the manufacture of the Test Article and, unless abandoned for reasons relating to safety as determined by the data safety monitoring board, to provide the Test Article (and Placebo, if any) in Collaborator's inventory to IC.

10.6.2 Further, Collaborator hereby grants to IC a nonexclusive, irrevocable, world-wide, paid-up license to practice, or have practiced for or on behalf of the Government, any Background Invention that Collaborator may currently have or will obtain on the Test Article, its manufacture, or on any method of using the Test Article for the indication(s) described in the Research Plan, including the right to sublicense to third parties.

Article 11. DISPUTES

11.1 **Settlement**. Any dispute arising under this CRADA which is not disposed of by agreement of the CRADA Principal Investigators will be submitted jointly to the signatories of this CRADA. If the signatories, or their designees, are unable to jointly resolve the dispute within thirty (30) days after notification thereof, the Assistant Secretary for Health (or his/her designee or successor) will propose a resolution. Nothing in this Paragraph will prevent any Party from pursuing any additional administrative remedies that may be available and, after exhaustion of such administrative remedies, pursuing all available judicial remedies.

11.2 **Continuation of Work**. Pending the resolution of any dispute or claim pursuant to this Article 11, the Parties agree that performance of all obligations will be pursued diligently.

Article 12. LIABILITY

12.1 **NO WARRANTIES**. EXCEPT AS SPECIFICALLY STATED IN ARTICLE 9, THE PARTIES MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO ANY MATTER WHATSOEVER, INCLUDING THE CONDITIONS OF THE RESEARCH OR ANY INVENTION OR MATERIAL, WHETHER TANGIBLE OR INTANGIBLE, MADE OR DEVELOPED UNDER OR OUTSIDE THE SCOPE OF THIS CRADA, OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE RESEARCH OR ANY INVENTION OR MATERIAL, OR THAT A TECHNOLOGY UTILIZED BY A PARTY IN THE PERFORMANCE OF THE RESEARCH PLAN DOES NOT INFRINGE ANY THIRD-PARTY PATENT RIGHTS.

12.2 **Indemnification and Liability**. Collaborator agrees to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses and losses arising out of the use by Collaborator for any purpose of the CRADA Data, CRADA Materials or CRADA Subject Inventions produced in whole or part by IC

employees under this CRADA, unless due to the negligence or willful misconduct of IC, its employees, or agents. The Government has no statutory authority to indemnify Collaborator. Each Party otherwise will be liable for any claims or damages it incurs in connection with this CRADA, except that IC, as an agency of the Government, assumes liability only to the extent provided under the Federal Tort Claims Act, 28 U.S.C. Chapter 171.

12.3 ***Force Majeure***. Neither Party will be liable for any unforeseeable event beyond its reasonable control and not caused by its own fault or negligence, which causes the Party to be unable to perform its obligations under this CRADA, and which it has been unable to overcome by the exercise of due diligence. If a *force majeure* event occurs, the Party unable to perform will promptly notify the other Party. It will use its best efforts to resume performance as quickly as possible and will suspend performance only for such period of time as is necessary as a result of the *force majeure* event.

Article 13. MISCELLANEOUS

13.1 **Governing Law**. The construction, validity, performance and effect of this CRADA will be governed by U.S. federal law, as applied by the federal courts in the District of Columbia. If any provision in this CRADA conflicts with or is inconsistent with any U.S. federal law or regulation, then the U.S. federal law or regulation will preempt that provision.

13.2 **Compliance with Law**. IC and Collaborator agree that they will comply with, and advise any contractors, grantees, or agents they have engaged to conduct the CRADA research and development activities to comply with, all applicable Executive Orders, statutes, and HHS regulations relating to research on human subjects (45 C.F.R. Part 46, 21 C.F.R. Parts 50 and 56) and relating to the appropriate care and use of laboratory animals (7 U.S.C. § 2131 *et seq.*; 9 C.F.R. Part 1, Subchapter A). IC and Collaborator will advise any contractors, grantees, or agents they have engaged to conduct clinical trials for this CRADA that they must comply with all applicable federal regulations for the protection of Human Subjects, which may include the Standards for Privacy of Individually Identifiable Health Information set forth in 45 C.F.R. Part 164. Collaborator agrees to ensure that its employees, contractors, and agents who might have access to a "select agent or toxin" (as that term is defined in 42 C.F.R. §§ 73.4-73.5) transferred from IC is properly licensed to receive the "select agent or toxin".

13.3 **Waivers**. None of the provisions of this CRADA will be considered waived by any Party unless a waiver is given in writing to the other Party. The failure of a Party to insist upon strict performance of any of the terms and conditions hereof, or failure or delay to exercise any rights provided herein or by law, will not be deemed a waiver of any rights of any Party.

13.4 **Headings**. Titles and headings of the articles and paragraphs of this CRADA are for convenient reference only, do not form a part of this CRADA, and will in no way affect its interpretation.

13.5 **Severability**. The illegality or invalidity of any provisions of this CRADA will not impair, affect, or invalidate the other provisions of this CRADA.

13.6 **Amendments**. Minor modifications to the Research Plan may be made by the mutual written consent of the CRADA Principal Investigators. Substantial changes to the CRADA, extensions of the term, or any changes to Appendix C will become effective only upon a written amendment signed by the signatories to this CRADA or by their representatives duly authorized to execute an amendment. A change will be considered substantial if it directly expands the range of the potential CRADA Subject Inventions, alters the scope or field of any license option governed by Article 7, or requires a significant increase in the contribution of resources by either Party.

13.7 **Assignment**. Neither this CRADA nor any rights or obligations of any Party hereunder shall be assigned or otherwise transferred by either Party without the prior written consent of the other Party. The Collaborator acknowledges the applicability of 41 U.S.C. § 15, the Anti Assignment Act, to this Agreement. The Parties agree that the identity of the Collaborator is material to the performance of this CRADA and that the duties under this CRADA are nondelegable.

13.8 **Notices**. All notices pertaining to or required by this CRADA will be in writing, signed by an authorized representative of the notifying Party, and delivered by first class, registered, or certified mail, or by an express/overnight commercial delivery service, prepaid and properly addressed to the other Party at the address designated on the Contacts Information Page, or to any other address designated in writing by the other Party. Notices will be considered timely if received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Notices regarding the exercise of license options will be made pursuant to Paragraph 7.3. Either Party may change its address by notice given to the other Party in the manner set forth above.

13.9 **Independent Contractors**. The relationship of the Parties to this CRADA is that of independent contractors and not agents of each other or joint venturers or partners. Each Party will maintain sole and exclusive control over its personnel and operations.

13.10 **Use of Name; Press Releases**. By entering into this CRADA, the Government does not directly or indirectly endorse any product or service that is or will be provided, whether directly or indirectly related to either this CRADA or to any patent or other intellectual-property license or agreement that implements this CRADA by Collaborator, its successors, assignees, or licensees. Collaborator will not in any way state or imply that the Government or any of its organizational units or employees endorses any product or services. Each Party agrees to provide proposed press releases that reference or rely upon the work under this CRADA to the other Party for review and comment at least five (5) business days before publication. Either Party may disclose the Title and Abstract of the CRADA to the public without the approval of the other Party.

13.11 **Reasonable Consent**. Whenever a Party's consent or permission is required under this CRADA, its consent or permission will not be unreasonably withheld.

13.12 **Export Controls**. Collaborator agrees to comply with U.S. export law and regulations. If Collaborator has a need to transfer any CRADA Materials made in whole or in part by IC, or IC Materials, or IC's Confidential Information to a person located in a country other than the United States, to an Affiliate organized under the laws of a country other than the United States, or to an employee of Collaborator in the United States who is not a citizen or permanent resident of the United States, Collaborator will acquire any and all necessary export licenses and other appropriate authorizations.

13.13 **Entire Agreement**. This CRADA constitutes the entire agreement between the Parties concerning the subject matter of this CRADA and supersedes any prior understanding or written or oral agreement.

13.14 **Survivability**. The provisions of Paragraphs 3.3, 3.4, 3.8, 4.2, 4.3, 4.4.2, 5.3, 5.4, 6.1-9.2, 10.3-10.6, 11.1, 11.2, 12.1-12.3, 13.1-13.3, 13.7, 13.10 and 13.14 will survive the expiration or early termination of this CRADA.

SIGNATURES BEGIN ON THE NEXT PAGE

SIGNATURE PAGE

ACCEPTED AND AGREED

BY EXECUTING THIS AGREEMENT, EACH PARTY REPRESENTS THAT ALL STATEMENTS MADE HEREIN ARE TRUE, COMPLETE, AND ACCURATE TO THE BEST OF ITS KNOWLEDGE. COLLABORATOR ACKNOWLEDGES THAT IT MAY BE SUBJECT TO CRIMINAL, CIVIL, OR ADMINISTRATIVE PENALTIES FOR KNOWINGLY MAKING A FALSE, FICTITIOUS, OR FRAUDULENT STATEMENT OR CLAIM.

FOR IC:

/s/ James H. Doroshow	1/9/17
James H. Doroshow, M.D. Deputy Director for Clinical and Translational Research, NCI	Date

FOR INTREXON CORPORATION:

/s/ Donald P. Lehr	January 9, 2017
Donald P. Lehr Chief Legal Officer	Date

FOR ZIOPHARM ONCOLOGY INC.:

/s/ Laurence Cooper	January 9, 2017
Laurence Cooper, M.D., Ph.D. Chief Executive Officer	Date

CONTACTS INFORMATION PAGE

CRADA Notices

For NCI:

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For Collaborators:

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Patent and Licensing

For NCI:

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For Collaborators:

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Delivery of Materials Identified in Appendix B (if any)

For NCI:

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For Collaborators:

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Clinical Contact (as needed for Article 4.4.2)

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SUMMARY PAGE

EITHER PARTY MAY, WITHOUT FURTHER CONSULTATION OR PERMISSION, RELEASE THIS SUMMARY PAGE TO THE PUBLIC.

TITLE OF CRADA: Development and Evaluation of Intrexon Corporation's Proprietary Non-viral *Sleeping Beauty* Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods

PHS NCI Component:	National Cancer Institute (NCI)
IC Principal Investigator:	Steven A. Rosenberg, M.D., Ph.D.
Collaborator:	Intrexon Corporation
Collaborator Principal Investigator:	Tim Chan, Ph.D.
Collaborator:	ZIOPHARM Oncology, Inc.
Collaborator Principal Investigator:	Laurence Cooper, M.D., Ph.D.
TERM OF CRADA:	Three (3) years from the Effective Date.

ABSTRACT OF THE RESEARCH PLAN:

The principal goal of this CRADA is to develop and evaluate adoptive cell transfer-based immunotherapies (ACT) using NCI proprietary methods for the isolation of tumor-reactive T Cell Receptors (TCRs) targeting unique, patient specific mutated neoantigen(s) and introduction of said TCRs into T cell subsets isolated from peripheral blood using proprietary Intrexon Corporation ("Intrexon") Non-Viral Sleeping Beauty Transposon and Transposascs for the treatment of patients with solid tumor malignancies.

APPENDIX A
RESEARCH PLAN

Title of CRADA

Development and Evaluation of Intrexon Corporation's Proprietary Non-viral *Sleeping Beauty* Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods

NCI Principal Investigator
Steven A. Rosenberg, M.D., Ph.D.
Chief, Surgery Branch
Center for Cancer Research (CCR)
National Cancer Institute (NCI)

Collaborator Investigator
Tim Chan, Ph.D.
Intrexon Corporation, Inc. (Intrexon)

Collaborator Investigator
Laurence Cooper, M.D., Ph.D.
ZIOPHARM Oncology, Inc. (Ziopharm)

Term of CRADA
Three (3) years from the date of the final CRADA signature.

GOALS AND SCOPE OF THIS CRADA
[*Eight (8) Pages Redacted in their Entirety***]**

[***] = CERTAIN CONFIDENTIAL INFORMATION OMITTED.

APPENDIX B

STAFFING, FUNDING AND MATERIALS/EQUIPMENT CONTRIBUTIONS OF THE PARTIES

Staffing Contributions

IC will provide scientific staff and other support necessary to conduct the research and other activities described in the Research Plan. IC's scientific staff will include IC's Principal Investigator and technical staff.

IC estimates that 6-8 person-years of effort per year will be required to complete the CRADA research.

Collaborator will provide scientific staff and other support necessary to conduct the research and other activities described in the Research Plan. Collaborator's scientific staff will include Collaborator's Principal Investigator and technical staff.

Collaborator estimates that 3-4 person-years of effort per year will be required to complete the CRADA research.

Funding Contributions

Ziopharm agrees to provide funds in the amount of $2,500,000.00 per year of the CRADA for IC to use to acquire technical, statistical, and administrative support for the research activities, as well as to pay for supplies and travel expenses. Ziopharm will provide funds in the amount of $625,000.00 on a quarterly basis. The first quarterly installment of $625,000.00 will be due within thirty (30) days of the Effective Date. Each subsequent installment will be due within thirty (30) days of each quarterly anniversary of the Effective Date. Collaborator agrees that IC can allocate the funding between the various categories in support of the CRADA research as IC's CRADA Principal Investigator sees fit.

CRADA PAYMENTS:

Collaborator has three options for making CRADA payments. See CRADA Payment Options at http://ttc.nci.nih.gov/forms/crada.php for specific information on making payments using each option.

Option 1: Collaborator sends checks to the NCI.
Option 2: Collaborator makes payments via wire transfer.
Option 3: Collaborator makes payments using www.pay.gov.

Collaborator may make CRADA payments via www.pay.gov. If Collaborator makes CRADA payments by check, Collaborator will make the checks payable to the National Cancer Institute and will reference the CRADA number 03111 and title "Development and Evaluation of Intrexon Corporation's Proprietary Non-Viral *Sleeping Beauty* Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods" on each check, and will send them via trackable mail or courier to:

CRADA Funds Coordinator
Technology Transfer Center, NCI
9609 Medical Center Drive, Rm 1-E530
Rockville, MD 20850-9702

CRADA Travel Payments:

Travel arrangements for all Government staff will be made in accordance with the Federal Travel Rules and Regulations, whether arranged by ICD and funded using either appropriated funds or CRADA funds, or arranged and funded directly by Collaborator.

Materials/Equipment Contributions:

IC will provide the following ICD Materials for use under this CRADA:

Test Article: None.

IC Materials: PBL collected under NCI protocol 03-C-0277 entitled “Cell Harvest and Preparation for Surgery Branch Adoptive Cell Therapy Protocols.”

Capital Equipment: None

Collaborator will provide the following Collaborator Materials and/or capital equipment for use under this CRADA:

Test Article: Research grade and cGMP grade Intrexon proprietary SB system. Collaborator agrees to provide SB system cassettes, cGMP materials, protocols, specifications and certificates of analysis sufficient to treat the number of patients agreed upon during the three-year term of the CRADA for IC to use for the approved protocol(s).

Collaborator Materials: For cellular assays, preclinical studies, and clinical studies, sequences each containing the Sleeping Beauty Transposon/Transposase system.

Capital Equipment: None

If either Party decides to provide additional Materials for use under this CRADA, those materials will be transferred under a cover letter that identifies them and states that they are being provided under the terms of the CRADA.

APPENDIX C

MODIFICATIONS TO THE MODEL CRADA

Underlining indicates additions and strikeout indicates deletions.

Amend Article 1 "Introduction" to read as follows:

This CRADA between IC and Collaborator will be effective when signed by the Parties, which are identified on both the Cover Page and the Signature Page. The official contacts for the Parties are identified on the Contacts Information Page. Publicly available information regarding this CRADA appears on the Summary Page. The research and development activities that will be undertaken by IC and Collaborator in the course of this CRADA are detailed in the Research Plan, attached as Appendix A. The staffing, funding, and materials contributions of the Parties are set forth in Appendix B. Any changes to the model CRADA are set forth in Appendix C. Should the Collaborator hire an employee to work on the premises of the IC for the purposes of performing activities under the Research Plan of this Agreement, the "NIH Research Collaborator (RC) Agreement" will be used for this purpose and is attached as Appendix D. A Letter of Intent ("LOI") to enter into this CRADA was executed by the Parties, as of October 6th, 2016, which LOI is attached hereto as Appendix E. Articles 2, 6, 7, 8, and 9 of the Model PHS CRADA shall be deemed to have become effective between the Parties on the date of execution of the LOI and shall survive through the Effective Date of this CRADA; provided, that as of the Effective Date, such LOI and the Model PHS CRADA terms shall be of no further force or effect and shall be superseded by the terms of this CRADA. The Research Plan of this CRADA hereby replaces and supersedes the Research Plan of the LOI.

Add the Definition of "Multi-Party Data" in Article 2 to read as follows:

"Multi-Party Data" means data from studies sponsored by IC pursuant to Clinical Trial Agreements (CTA) or CRADAs, where such data are collected under Protocols involving combinations of investigational agents supplied from more than one CTA or CRADA collaborator. "Multi-Party Data" also means data from studies where such data are collected pursuant to research involving combinations of proprietary materials from more than one collaborator as documented in more than one agreement.

Amend **the Definition of "Annual Report" in Article** 2 to read as follows:

"Annual Report" means the report of progress of an IND-associated investigation that IC or Collaborator, as the IND Sponsor, must submit to the FDA within sixty (60) days of the anniversary of the effective date of the IND (pursuant to 21 C.F.R.§ 312.33).

Add the Definition of "Collaborator" in Article 2 to read as follows:

"Collaborator" means, as context dictates, collectively Intrexon and ZIOPHARM, or individually Intrexon or ZIOPHARM.

Add the Definition of " Third Party" in Article 2 to read as follows:

"**Third Party**" means an entity not a Party to this CRADA.

Amend Section 3.7 to read as follows:

3.7 **Investigational Applications.**

3.7.1 If an IND is required, ~~IC will be the IND Sponsor and will submit an IND~~the Parties will file and/or amend sponsorship of INDs as agreed upon in Appendix A of this CRADA. All Clinical Investigators must have completed registration documents on file (1572 forms).

3.7.2 When ~~ICD~~ a Party files the IND, ~~Collaborator~~ the other Party agrees to provide ~~ICD~~ the filing party background data and information necessary to support the IND. ~~Collaborator~~ The Parties further agrees to provide a letter of cross-reference to all data and pertinent regulatory filings sponsored by ~~Collaborator. Collaborator's~~ a Party under this CRADA. Both Parties' employees will be reasonably available to respond to inquiries from the FDA regarding information and data contained in the ~~Collaborator's~~ Party's IND, DMF, other filings, or other information and data provided to ~~ICD~~ one Party by the Collaborator other Party pursuant to this Article 3.

3.7.3 If ~~Collaborator~~ a Party supplies Confidential Information to ~~ICD~~the other Party in support of an IND that is filed, ~~by ICD~~ this information will be protected in accordance with the corresponding confidentiality provisions of Article 8.

~~3.7.4 Collaborator may sponsor its own clinical trials and hold its own IND for studies performed outside the scope of this CRADA. These studies, however, should not adversely effect the ability to accomplish the goal of the Research Plan, for example, by competing for the same study population. All data from those clinical trials are proprietary to Collaborator for purposes of this CRADA.~~

Amend Section 3.11 to read as follows:

3.11 **FDA Meetings/Communications.** All meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and IC in advance. Each Party reserves the right to take part in setting the agenda for, to attend, and to participate in these meetings, as appropriate. ~~IC~~ Sponsor will provide ~~Collaborator~~ the other Party with copies of FDA meeting minutes, all transmittal letters for IND submissions, IND safety reports, formal questions and responses that have been submitted to the FDA, Annual Reports, and official FDA correspondence, pertaining either to the INDs under this CRADA or to the Clinical Investigators on Protocols performed in accordance with the Research Plan, except to the extent that those documents contain the proprietary information of a third party or dissemination is prohibited by law.

Amend Section 7.2 to read as follows:

7.2 **Collaborator's License Option to CRADA Subject Inventions.** Intrexon Corporation shall take the lead in exercising Collaborator's License Option under Article 7. Thus "Collaborator" shall mean Intrexon Corporation in Articles 7.2, 7.3, 7.4, 7.6 and 7.7. With respect to Government rights to any CRADA Subject Invention made solely by an IC employee(s) or made jointly by an IC employee(s) and a Collaborator employee(s) for which a Patent Application was filed, PHS hereby grants to Collaborator an exclusive option to elect an exclusive or nonexclusive ~~commercialization license~~ or co-exclusive, if applicable, commercialization license. The option to elect a co-exclusive license shall apply when a CRADA Subject Invention is also an Invention made under another agreement resulting from mutually agreed upon studies, as described in Section 8.8 (regarding Multi-Party Data Rights), and the field of use of this co-exclusive license shall be limited to the use of the combination of the Test Article with another agent(s) commensurate with the scope of the Research Plan. The license will be substantially in the form of the appropriate model PHS license agreement and will fairly reflect the nature of the CRADA Subject Invention, the relative contributions of the Parties to the CRADA Subject Invention and the CRADA, a plan for the development and marketing of the CRADA Subject Invention, the risks incurred by Collaborator, and the costs of subsequent research and development needed to bring the CRADA Subject Invention to the marketplace. The field of use of the exclusive or non-exclusive license will not exceed the scope of the Research Plan.

Amend Section 7.6 to read as follows:

7.6 **Third Party License.** Pursuant to 15 U.S.C. § 3710a(b)(1)(B), if PHS grants Collaborator an exclusive license or co-exclusive license to a CRADA Subject Invention made solely by an IC employee or jointly with a Collaborator employee, the Government will retain the right to require Collaborator to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the CRADA Subject Invention in Collaborator's licensed field of use on terms that are reasonable under the circumstances; or, if Collaborator fails to grant a license, to grant a license itself. The exercise of these rights by the Government will only be in exceptional circumstances and only if the Government determines (i) the action is necessary to meet health or safety needs that are not reasonably satisfied by Collaborator, (ii) the action is necessary to meet requirements for public use specified by federal regulations, and such requirements are not reasonably satisfied by Collaborator; or (iii) Collaborator has failed to comply with an agreement containing provisions described in 15 U.S.C. § 3710a(c)(4)(B). The determination made by the Government under this Paragraph is subject to administrative appeal and judicial review under 35 U.S.C. § 203(b).

Amend Section 8.3 to read as follows:

8.3 Confidential Information. Each Party agrees to limit its disclosure of Confidential Information to the amount necessary to carry out the Research Plan, and will place a confidentiality notice on all this information. A Party orally disclosing Confidential Information to the other Party will reduce the disclosure to writing within fifteen (15) days of the disclosure.

Each Party receiving Confidential Information agrees to use it only for the purposes described in the Research Plan. Either Party may object to the designation of information as Confidential Information by the other Party. Notwithstanding any other provision in this Agreement, although certain information concerning Collaborator Materials or Test Article provided under this Agreement is confidential and will be so stamped, Collaborator recognizes that the NCI PI may need to disclose certain information concerning CONFIDENTIAL materials to patients (or to physicians or scientists where such disclosure is made in order to directly facilitate the ongoing treatment of a patient, or the development of a treatment for a patient). Collaborator hereby authorizes such limited disclosures, and the NCI PI agrees to promptly acknowledge to Collaborator the making of any such disclosure.

Amend Section 8.4 to read as follows:

8.4 Protection of Confidential Information. Subject to Paragraph 8.3, Confidential Information will not be disclosed, copied, reproduced or otherwise made available to any other person or entity without the consent of the owning or providing Party except as required by a court or administrative body of competent jurisdiction, or federal law or regulation. Each Party agrees to use reasonable efforts to maintain the confidentiality of Confidential Information, which will in no instance be less effort than the Party uses to protect its own Confidential Information. Each Party agrees that a Party receiving Confidential Information will not be liable for the disclosure of that portion of the Confidential Information which, after notice to and consultation with the disclosing Party, the receiving Party determines may not be lawfully withheld, provided the disclosing Party has been given a reasonable opportunity to seek a court order to enjoin disclosure.

Amend Section 8.6 to read as follows:

8.6 Duration of Confidentiality Obligation. The obligation to maintain the confidentiality of Confidential Information as described in Paragraph 8.3, will expire at the earlier of the date when the information is no longer Confidential Information as defined in Article 2 or three (3) years after the expiration or termination date of this CRADA, except for IPI, for which the obligation to maintain confidentiality will extend indefinitely. Collaborator may request an extension to this term when necessary to protect Confidential Information relating to products not yet commercialized.

Add Section 8.8 as follows:

8.8 **Multi-Party Data Rights.** For clinical Protocol(s) mutually agreed upon by IC and Collaborator where Test Article is used in combination with another investigational agent supplied to IC pursuant to a CTA or CRADA between IC and an entity not a Party to this CRADA (hereinafter referred to as "Third Party"), or for non-clinical study(ies) where research involving combinations of proprietary materials from more than one collaborator as documented in more than one agreement, the access and use of Multi-Party Data by the Collaborator and Third Party shall be co-exclusive as follows:

8.8.1 IC will provide both Collaborator and Third Party with notice regarding the existence and nature of the agreements governing the use of the Test Article and Third Party's investigational agent, the design of the proposed combination Protocol(s) or non-clinical study(ies), and the existence of any obligations that might restrict IC's participation in the proposed combination Protocols or non-clinical study(ies).

8.8.2 Collaborator shall agree to permit use of the Multi-Party Data from these trials by Third Party to the extent necessary to allow Third Party to develop, obtain regulatory approval for, or commercialize its own investigational agent(s). However, this provision will not apply unless Third Party also agrees to Collaborator's reciprocal use of Multi-Party Data.

8.8.3 Collaborator and Third Party must agree in writing prior to the commencement of the combination Protocol(s) or non-clinical study(ies) that each will use the Multi-Party Data solely for the development, regulatory approval, and commercialization of its own investigational agent(s).

8.84 The sharing of Multi-Party Data does not alter the ownership of the Multi-Party Data or obligations of IC, Collaborator and Third Party to keep Confidential Information owned by any other Party or Parties confidential.

Amend the Definition of "Independent Contractors" in Section 13.9 to read as follows:

13.9 **Independent Contractors.** The relationship of the Parties to this CRADA is that of independent contractors and not agents of each other or joint venturers or partners. Each Party shall maintain sole and exclusive control over its personnel and operations. If Collaborator elects to perform any portion of the Research Plan through an agent, contractor or consultant, Collaborator agrees to incorporate into such contracts all provisions necessary to ensure that the work of such agents, contractors or consultants is governed by the terms of the CRADA, including, but not limited to a provision for the assignment of Inventions of the agent, contractor or consultant to the Collaborator.

Amend the Definition of "Entire Agreement" in 13.13 to read as follows:

13.13 **Entire Agreement**. This CRADA constitutes the entire agreement between the Parties concerning the subject matter of this CRADA and supersedes any prior understanding or written or oral agreement between the Parties relating to the subject matter of this CRADA, including, without limitation the LOI executed on October 6th, 2016, and the corresponding terms of the Model PHS CRADA referred to in Article 1. The Material Transfer Agreement (MTA) between the parties (NCI no. 32360-11), effective date 6/29/11, is hereby superseded and succeeded by the terms of this CRADA. Specifically, the transfer of materials and data shall be governed by the terms of this CRADA as if they had been exchanged after the execution of the CRADA, and not by terms of the MTA.

APPENDIX D

(from NIH Manual 2300-308-4, Appendix 2)

NIH Research Collaborator (RC) Agreement for Use with IC CRADA # 03111

The Parties acknowledge that an employee of (print CRADA Collaborator name) ("Collaborator") will work at the NIH to advance the research goals enumerated in the Research Plan of the Cooperative Research and Development Agreement reference number (*# 03111*) ("CRADA"), between the Collaborator and NCI ("IC") as a Research Collaborator (Non-Clinical) OR Research Collaborator (Clinical) ("RC"). The RC will be assigned to work within the Surgery Branch, Center for Cancer Research of the NCI. The RC agrees to the following terms:

I, (print RC full name) (select one and delete the other:) CRADA Research Collaborator (Non-Clinical) OR CRADA Research Collaborator (Clinical), in consideration of acceptance by NIH as a RC understand and agree to the following terms.

1. The intent of the work performed under this RC Agreement will be according to the Research Plan (Appendix A) of the CRADA referenced above. In addition, the RC is bound by the Confidentiality terms of the CRADA and shall treat all confidential or proprietary material accordingly. CRADA Subject Inventions resulting from the RC's activities done under the Research Plan of the CRADA during the term of assignment at IC as a RC funded by the CRADA Collaborator, shall be treated as CRADA Subject Inventions of the Collaborator (either joint or sole) and will be governed by the terms of the CRADA.
2. RC will make written disclosure promptly to the Technology Development Coordinator of the NIH Institute/Center (IC), of all inventions which are conceived or first actually reduced to practice during the term of work at IC.
3. Publication of results from the RC's activities done under the Research Plan of the CRADA during the term of assignment at IC shall be addressed by the terms of CRADA.
4. In the event that an invention results from work done outside the scope of the Research Plan of the CRADA and thus is not a CRADA Subject Invention, the following will govern reporting and disposition of the confidential and proprietary information/material:

(a.) RC agrees to be bound by all provisions of USPHS Technology Transfer Manual Chapter 203 approved March 22, 2007, in accordance to which patent rights for all inventions conceived or first actually reduced to practice by the RC while at the NIH are NIH property. RC agrees to disclose promptly to the appropriate NIH officials, all inventions which RC may conceive or first actually reduce to practice during RC's visit to the NIH. RC hereby assigns all right, title and interest worldwide in such inventions to the U.S. Government and agrees to sign any papers necessary to comply with attendant formalities.

(b.) The work the RC will perform may require access to knowledge and information of a confidential nature to the IC. RC agrees to maintain such knowledge and information in confidence, and the RC shall not publish or disclose, or authorize anyone else to publish, disclose or make use of any such information or knowledge without prior written authorization from the IC. This responsibility to protect said confidential information extends for a period of 5 years beyond the RC status with the IC.

(c.) All documents, written information and other items, including but not limited to notes, sketches, laboratory reports, experiments, notebooks, papers, publications, project reports, records, and information relating to inventions or improvements, kept or obtained by the RC while engaged as a RC by the IC, shall be the exclusive property of the U.S. Government and shall be delivered to the IC upon termination of RC status or at any time as requested by the IC.

(d.) RC will submit publications resulting from work at NIH to be cleared for conformance with NIH's publication policies and practices, including Public Access requirements.

5. RC will waive any and all claims for compensation from the Government of the United States for any services performed incidental to the personal research RC performs, and absolve NIH of any responsibility in case of personal injury or death arising out of those research activities, and/or failure or damage to RC's experiments or equipment.

6. While on NIH premises, RC will conform to all applicable administrative instructions and requirements of the Department of Health and Human Services and NIH, including all regulations and procedures concerning conduct, safety, patient care, and animal care.

7. RC agrees to obtain, prior to the beginning of this assignment, health insurance coverage substantially comparable to that provided by the Federal Employee's Health Benefits Plan and show proof of coverage prior to beginning RC appointment. Furthermore, non-immigrant foreign nationals sponsored as J-1 Exchange Visitors must maintain adequate health insurance coverage for themselves and any J-2 dependents as required by the U.S. Department of State.

8. If not a U.S. citizen or permanent resident, RC agrees to provide evidence of valid non-immigrant status and RC eligibility to the Division of International Services, ORS, for the duration of the RC appointment.

Research Collaborator Signature Date

It is understood that the RC is an employee of (print CRADA Collaborator name) and that (print CRADA Collaborator Name) accepts these terms for the work the RC will be conducting during the term of the RC appointment.

Printed Name of CRADA Collaborator Responsible Official and Position Title

Authorized Signature of CRADA Collaborator Responsible Official Date

Signature of NIH IC Approving Official and Printed Name and Position Title Date

APPENDIX E

LOI Executed October 6th, 2016 between the Parties.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute
Technology Transfer Center
9609 Medical Center Drive
Room 1-E530 MSC 9702
Bethesda, MD 20892
240-276-5530 / 240-276-5504 (fax)

September 30th, 2016

Dr. Laurence Cooper, CEO
ZIOPHARM Oncology, Inc.
One First Avenue, Parris Building 34, Navy Yard Plaza
Boston, MA 02129

Donald Lehr, Chief Legal Officer
Intrexon Corporation
20374 Seneca Meadows Parkway
Germantown, MD 20876

Letter of Intent for a Cooperative Research and Development Agreement ("CRADA")

NCI CRADA #: 03111
NCI Principal Investigator: Steven A. Rosenberg
Collaborator Investigators: Laurence Cooper (for Ziopharm), and Tim Chan (for Intrexon)
Title: Development and Evaluation of Intrexon Corporation's Proprietary Non-viral Sleeping Beauty Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods

Dear Dr. Cooper and Mr. Lehr:

It is my understanding that a cooperative research and development project between the parties referenced below is being considered. Accordingly, until the formal Cooperative Research and Development Agreement (CRADA) is reviewed by the NIH CRADA Subcommittee and approved by the Director, National Cancer Institute (NCI), this Letter is offered to permit the joint research to commence. If human clinical trials are a part of the joint research, the parties agree that all such trials which may begin prior to the execution of the formal CRADA shall be preceded by the appropriate regulatory approvals (U.S. Food and Drug Administration IND approval or international equivalents thereof).

It is acknowledged by the parties below that cooperative research pursuant to the Research Plan, attached as Appendix A, will be conducted informally by the NCI, Intrexon, and Ziopharm pending formal approval of the CRADA. It is further acknowledged that patentable inventions may be made by NCI employees and employees of the Intrexon and/or Ziopharm. Pursuant to its authority under the Federal Technology Transfer Act of 1986, as amended, NCI agrees that should this CRADA be approved, it will have retroactive effect to the date that the last party has executed this Letter for any inventions that may be made under this Research Plan. NCI further agrees that should this CRADA be approved it will have retroactive effect to the date that the last party has executed this Letter for confidentiality obligations specified in the NIH Model CRADA. The NIH Model CRADA provisions for the protection of proprietary information are incorporated in this Letter by reference and are considered controlling during the period of informal joint research. These provisions include, but are not limited to Article 2 and Article 8. The NIH Model CRADA is attached as Appendix B. In addition, a separate Confidential Disclosure Agreement (CDA) and Material Transfer Agreement (MTA) will accompany this Letter. If the CRADA is subsequently executed, it will supersede the CDA and MTA.

You understand, however, that this Letter is not a commitment on the part of either party to enter into a CRADA. Further, this Letter is effective for a term not to exceed six (6) months. The six-month term may be extended, provided the CRADA is under active negotiation and the collaborative research is continuing. Assuming that the necessary approvals are forthcoming, we look forward to a successful collaboration.

Sincerely,

/s/ Kathleen Carroll

Kathleen Carroll, Ph.D., MBA
Associate Director, Technology Transfer Center
National Cancer Institute

AGREED AND ACCEPTED:

National Cancer Institute

/s/ James Doroshow
James Doroshow, M.D.
Deputy Director for Clinical and Translational Research, NCI

10/5/16
Date

ZIOPHARM Oncology, Inc. ("Ziopharm")

/s/ Laurence Cooper
Laurence Cooper, M.D., Ph.D.
CEO

October 6, 2016
Date

Intrexon Corporation ("Intrexon")

/s/ Donald Lehr
Donald Lehr
CLO

October 6, 2016
Date

Attachments: **Appendix A - Letter of Intent Research Plan**
Appendix B - Model NIH CRADA (version MODEL ADOPTED June 18, 2009, Revised May 15, 2014)

APPENDIX A
[*Four (4) Pages Redacted in their Entirety***]**

[***] = CERTAIN CONFIDENTIAL INFORMATION OMITTED.

APPENDIX B

PUBLIC HEALTH SERVICE

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT
FOR INTRAMURAL-PHS CLINICAL RESEARCH

This Agreement is based on the model Cooperative Research and Development Agreement ("CRADA") adopted by the U.S. Public Health Service ("PHS") Technology Transfer Policy Board for use by components of the National Institutes of Health ("NIH"), the Centers for Disease Control and Prevention ("CDC"), and the Food and Drug Administration ("FDA"), which are agencies of the PHS within the Department of Health and Human Services ("HHS").

This Cover Page identifies the Parties to this CRADA:

The U.S. Department of Health and Human Services, as represented by
[INSERT the full name of the IC]
an Institute or Center (hereinafter referred to as the "IC") of the
[INSERT as appropriate: NM, CDC, or FDA]

and

[INSERT Collaborator's official name],
hereinafter referred to as the "Collaborator",
having offices **at [INSERT Collaborator's address]**,
created and operating under the laws of **[INSERT State of Incorporation]**.

Article 1. Introduction

This CRADA between IC and Collaborator will be effective when signed by the Parties, which are identified on both the Cover Page and the Signature Page. The official contacts for the Parties are identified on the Contacts Information Page. Publicly available information regarding this CRADA appears on the Summary Page. The research and development activities that will be undertaken by IC and Collaborator in the course of this CRADA are detailed in the Research Plan, attached as Appendix A. The staffing, funding, and materials contributions of the Parties are set forth in Appendix B. Any changes to the model CRADA are set forth in Appendix C.

Article 2. Definitions

The terms listed in this Article will carry the meanings indicated throughout the CRADA. To the extent a definition of a term as provided in this Article is inconsistent with a corresponding definition in the applicable sections of either the United States Code (U.S.C.) or the Code of Federal Regulations (C.F.R.), the definition in the U.S.C. or C.F.R. will control.

"**Adverse Event**" or "**AE**" means any untoward medical occurrence associated with the use of a Test Article in humans, whether or not considered related to the Test Article (21 C.F.R §§ 312.32, 308.3; see also FDA Good Clinical Practice Guideline, International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance, 62 Federal Register 25,691 (1997)).

"**Affiliate**" means any corporation or other business entity controlled by, controlling, or under common control with Collaborator at any time during the term of the CRADA. For this purpose, "control" means direct or indirect beneficial ownership of at least fifty percent (50%) of the voting stock or at least fifty percent (50%) interest in the income of the corporation or other business entity.

"**Annual Report**" means the report of progress of an IND-associated investigation that IC, as the IND Sponsor, must submit to the FDA within sixty (60) days of the anniversary or the effective date of the IND (pursuant to 21 C.F.R.§ 312.33).

"**Background Invention**" means an Invention conceived and first actually reduced to practice before the Effective Date.

"**Clinical Investigator**" means, in accordance with 21 C.F.R. § 312.3, an individual who actually conducts a clinical investigation, that is, who directs the administration or dispensation of Test Article to a subject, and who assumes responsibility for studying Human Subjects, for recording and ensuring the integrity of research data, and for protecting the welfare and safety of Human Subjects.

"**Collaborator Materials**" means all tangible materials not first produced in the performance of this CRADA that are owned or controlled by Collaborator and used in the performance of the Research Plan. The term "Collaborator Materials" does not include "Test Article" (defined below).

"**Confidential Information**" means confidential scientific, business, financial information, or Identifiable Private Information provided that the information does not include:

(a) information that is publicly known or that is available from public sources;

(b) information that has been made available by its owner to others without a confidentiality obligation;

(c) information that is already known by the receiving Party, or information that is independently created or compiled by the receiving Party without reference to or use of the provided information; or

(d) information that relates to potential hazards or cautionary warnings associated with the production, handling, or use of the subject matter of the Research Plan.

"**Cooperative Research and Development Agreement**" or "**CRADA**" means this Agreement, entered into pursuant to the Federal Technology Transfer Act of 1986, as amended (15 U.S.C. §§ 3710a *et seq*.), and Executive Order 12591 of April 10, 1987.

"**CRADA Data**" means all recorded information first produced in the performance of the Research Plan.

"**CRADA Materials**" means all tangible materials first produced in the performance of the Research Plan other than CRADA Data.

"**CRADA Principal Investigator(s)**" or "**CRADA PI(s)**" means the person(s) designated by the Parties who will be responsible for the scientific and technical conduct of the Research Plan. The CRADA PI may also be a Clinical Investigator.

"**CRADA Subject Invention**" means any Invention of either or both Parties, conceived or first actually reduced to practice in the performance of the Research Plan.

"**Drug Master File**" or "**DMF**" is described in 21 C.F.R. Part 314.420. A DMF is a submission to the FDA that may be used to provide confidential detailed information about facilities, processes, or articles used in the manufacturing, processing, packaging, and storing of one or more human drugs.

"**Effective Date**" means the date of the last signature of the Parties executing this Agreement.

"**Government**" means the Government of the United States of America.

"**Human Subject**" means, in accordance with the definition in 45 C.F.R. § 46.102(f), a

living individual about whom an investigator conducting research obtains:

(a) data through intervention or interaction with the individual; or

(b) Identifiable Private Information.

"**IC Materials**" means all tangible materials not first produced in the performance of this CRADA that are owned or controlled by IC and used in the performance of the Research Plan.

"**IND**" means an "**Investigational New Drug Application**", filed in accordance with 21 C.F.R. Part 312 under which clinical investigation of an experimental drug or biologic (Test Article) is performed in Human Subjects in the United States or intended to support a United States licensing action.

"**Identifiable Private Information**" or "**IPI**" about a Human Subject means private information from which the identity of the subject is or may readily be ascertained. Regulations defining and governing this information include 45 C.F.R. Part 46 and 21 C.F.R. Part 50.

"**Institutional Review Board**" or "**IRB**" means, in accordance with 45 C.F.R. Part 46, 21 C.F.R. Part 56, and other applicable regulations, an independent body comprising medical, scientific, and nonscientific members, whose responsibility is to ensure the protection of the rights, safety, and well-being of the Human Subjects involved in a study.

"**Invention**" means any invention or discovery that is or may be patentable or otherwise protected under Title 35 of the United States Code, or any novel variety of plant which is or may be protectable under the Plant Variety Protection Act, 7 U.S.C. §§ 2321 *et seq.*

"**Investigator's Brochure**" means, in accordance with the definition in 21 C.F.R. § 312.23(a)(5), a document containing information about the Test Article, including animal screening, preclinical toxicology, and detailed pharmaceutical data, including a description of possible risks and side effects to be anticipated on the basis of prior experience with the drug or related drugs, and precautions, such as additional monitoring, to be taken as part of the investigational use of the drug.

"**Patent Application**" means an application for patent protection for a CRADA Subject Invention with the United States Patent and Trademark Office ("U.S.P.T.O.") or the corresponding patent-issuing authority of another nation.

"**Patent**" means any issued United States patent, any international counterpart(s), and any corresponding grant(s) by a non-U.S. government in place of a patent.

"**Placebo**" means an inactive substance identical in appearance to the material being tested that is used to distinguish between drug action and suggestive effect of the material under study.

"**Protocol**" means the formal, detailed description of a study to be performed as provided for in the Research Plan. It describes the objective(s), design, methodology, statistical considerations, and organization of a trial. For the purposes of this CRADA, the term, Protocol, for clinical research involving Human Subjects, includes any and all associated documents, including informed consent forms, to he provided to Human Subjects and potential participants in the study.

"**Raw Data**" means the primary quantitative and empirical data first collected from experiments and clinical trials conducted within the scope of this CRADA.

"**Research Plan**" means the statement in Appendix A of the respective research and development commitments of the Parties. The Research Plan should describe the provisions for sponsoring the IND, clinical and safety monitoring, and data management.

"**Sponsor**" means, in accordance with the definition in 21 C.F.R. § 312.3, an organization or individual who assumes legal responsibility for supervising or overseeing clinical trials with Test Articles, and is sometimes referred to as the IND holder.

"**Steering Committee**" means the research and development team whose composition and responsibilities with regard to the research performed under this CRADA are described in Appendix A.

"**Summary Data**" means any extract or summary of the Raw Data, generated either by, or on behalf of, IC or by, or on behalf of, Collaborator. Summary Data may include extracts or summaries that incorporate IPI.

"**Test Article**" means, in accordance with 21 C.F.R. § 50.3 (j), any drug (including a biological product), medical device, food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act that is intended for administration to humans or animals, including a drug or biologic as identified in the Research Plan and Appendix B, that is used within the scope of the Research Plan. The Test Article may also be referred to as Investigational Agent, Study Material, or Study Product.

Article 3. Cooperative Research and Development

3.1 **Performance of Research and Development.** The research and development activities to be carried out under this CRADA will be performed solely by the Parties identified on the Cover Page, unless specifically stated elsewhere in the Agreement. The CRADA PIs will be responsible for coordinating the scientific and technical conduct of this project on behalf of their employers. Any Collaborator employees who will work at IC facilities will be required to sign an agreement appropriately modified in view of the terms of this CRADA.

3.2 **Research Plan.** The Parties recognize that the Research Plan describes the collaborative research and development activities they will undertake and that interim research goals set forth in the Research Plan are good faith guidelines. Should events occur that require modification of these goals, then by mutual agreement the Parties can modify them through an amendment, according to Paragraph 13.6.

3.3 **Use and Disposition of Collaborator Materials and IC Materials.** The Parties agree to use Collaborator Materials and IC Materials only in accordance with the Research Plan and Protocol(s), not to transfer these materials to third parties except in accordance with the Research Plan and Protocol(s) or as approved by the owning or providing Party, and, upon expiration or termination of the CRADA, to dispose of these materials as directed by the owning or providing Party.

3.4 **Third-Party Rights in Collaborator's CRADA Subject Inventions.** If Collaborator has received (or will receive) support of any kind from a third party in exchange for rights in any of Collaborator's CRADA Subject Inventions, Collaborator agrees to ensure that its obligations to the third party are both consistent with Articles 6 through 8 and subordinate to Article 7 of this CRADA.

3.5 **Disclosures to IC**. Prior to execution of this CRADA, Collaborator agrees to disclose to IC all instances in which outstanding royalties are due under a PHS license agreement and in which Collaborator had a PHS license terminated in accordance with 37 C.F.R. § 404.10. These disclosures will be treated as Confidential Information upon request by Collaborator in accordance with the definition in Article 2 and Paragraphs 8.3 and 8.4.

3.6 **Clinical Investigator Responsibilities.** The Clinical Investigator will be required to submit, or to arrange for submission of, each Protocol associated with this CRADA to the IRB. In addition to the Protocol all associated documents, including informational documents and advertisements, must be reviewed and approved by the IRB before starting the research. The research will be done in strict accordance with the Protocol(s) and no substantive changes in a finalized Protocol will be made unless mutually agreed upon, in writing, by the Parties. Research will not commence (or will continue unchanged, if already in progress) until each substantive change to a Protocol, including those required by either the FDA or the IRB, has been integrated in a way acceptable to the Parties, submitted to the FDA (if applicable) and approved by the IRB.

3.7 **Investigational Applications.**

3.7.1 If an IND is required, IC will be the IND Sponsor and will submit an IND. All Clinical Investigators must have completed registration documents on file (1572 forms).

3.7.2 When IC files the IND, Collaborator agrees to provide IC background data and information necessary to support the IND. Collaborator further agrees to provide a letter of cross-reference to all pertinent regulatory filings sponsored by Collaborator. Collaborator's employees will be reasonably available to respond to inquiries from the FDA regarding information and data contained in the Collaborator's IND, DMF, other filings, or other information and data provided to IC by the Collaborator pursuant to this Article 3.

3.7.3 If Collaborator supplies Confidential Information to IC in support of an IND filed by IC, this information will be protected in accordance with the corresponding confidentiality provisions of Article 8.

3.7.4 Collaborator may sponsor its own clinical trials and hold its own IND for studies performed outside the scope of this CRADA. These studies, however, should not adversely affect the ability to accomplish the goal of the Research Plan, for example, by competing for the same study population. All data from those clinical trials are proprietary to Collaborator for purposes of this CRADA.

3.8 **Test Article Information and Supply.** Collaborator agrees to provide IC without charge and on a schedule that will ensure adequate and timely performance of the research, a sufficient quantity of formulated and acceptably labeled, clinical-grade Test Article (and, as required by the Protocol(s), Placebo) to complete the clinical trial(s) agreed to and approved under this CRADA, Collaborator will provide a Certificate of Analysis to IC for each lot of the Test Article provided.

3.9 **Test Article Delivery and Usage.** Collaborator will ship the Test Article and, if required, Placebo to IC in containers marked in accordance with 21 C.F.R. § 312.6. IC agrees that the Clinical Investigators will keep appropriate records and take reasonable steps to ensure that the Test Article is used in accordance with the Protocol(s) and applicable FDA regulations. In addition, IC agrees that the Test Article (and all Confidential Information supplied by Collaborator relating to the Test Article) will be used solely for the conduct of the CRADA research and development activities. Furthermore, IC agrees that no analysis or modification of the Test Article will be performed without Collaborator's prior written consent. At the completion of the Research Plan, any unused quantity of Test Article will be returned to Collaborator or disposed as directed by Collaborator. Pharmacy contacts at IC will be determined by IC and communicated to Collaborator.

3.10 **Monitoring.** Subject to the restrictions in Article 8 concerning IN, and with reasonable advance notice and at reasonable times, IC will permit Collaborator or its designee(s) to monitor the conduct of the research, as well as to audit source documents containing Raw Data, to the extent necessary to verify compliance with FDA Good Clinical Practice (International Conference on Harmonisation (ICH) E6: "Good Clinical Practice: Consolidated Guidance; 62 Federal Register 25, 691 (1997)) and the Protocol(s).

3.11 **FDA Meetings/Communications.** All meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and IC in advance. Each Party reserves the right to take part in setting the agenda for, to attend, and to participate in these meetings. IC will provide Collaborator with copies of FDA meeting minutes, all transmittal letters for IND submissions, IND safety reports, formal questions and responses that have been submitted to the FDA, Annual Reports, and official FDA correspondence, pertaining either to the INDs under this CRADA or to the Clinical Investigators on Protocols performed in accordance with the Research Plan, except to the extent that those documents contain the proprietary information of a third party or dissemination is prohibited by law.

Article 4. Reports

4.1 **Interim Research and Development Reports.** The CRADA PIs should exchange information regularly, in writing. This exchange may be accomplished through meeting minutes, detailed correspondence, circulation of draft manuscripts, Steering Committee reports, copies of Annual Reports and any other reports updating the progress of the CRADA research. However, the Parties must exchange updated Investigator's Brochure, formulation and preclinical data, and toxicology findings, as they become available.

4.2 **Final Research and Development Reports.** The Parties will exchange final reports of their results within six (6) months after the expiration or termination of this CRADA. These reports will set forth the technical progress made; any publications arising from the research; and the existence of invention disclosures of potential CRADA Subject Inventions and/or any corresponding Patent Applications.

4.3 **Fiscal Reports.** If Collaborator has agreed to provide funding to IC under this CRADA and upon the request of Collaborator, then concurrent with the exchange of final research and development reports according to Paragraph 4.2, IC will submit to Collaborator a statement of all costs incurred by IC for the CRADA. If the CRADA has been terminated, IC will specify any costs incurred before the date of termination for which IC has not received funds from Collaborator, as well as for all reasonable termination costs including the cost of returning Collaborator property or removal of abandoned Collaborator property, for which Collaborator will be responsible.

4.4 **Safety Reports.**

4.4.1 In accordance with FDA requirements IC, as the IND Sponsor, will establish and maintain records and submit safety reports to the FDA, as required by 21 C.F.R. § 312.32 and 21 C.F.R. § 812.150(b)(1), or other applicable regulations. In the conduct of research under this CRADA, the Parties will comply with specific IC guidelines and policies for reporting AEs, as well as procedures specified in the Protocol(s). IC must provide Collaborator with copies of all Safety Reports concurrently with their submission to the FDA, and with any other information affecting the safety of Human Subjects in research conducted under this CRADA.

4.4.2 During and for a period of two years after the completion of a Protocol, the Collaborator shall promptly provide to the IC any information that Collaborator has reasonably determined could directly affect the health or safety of past or current Human Subjects or influence the conduct of the Protocol. Such information may arise from any source, for example, Safety Reports provided to the FDA, study results, information in site monitoring reports or data safety monitoring committee reports. IC shall be free to communicate the relevant safety information to each Human Subject and the IRB.

4.5 **Annual Reports.** IC will provide Collaborator a copy of the Annual Report concurrently with the submission of the Annual Report to the FDA. Annual Reports will be kept confidential in accordance with Article 8.

Article 5. Staffing, Financial, and Materials Obligations

5.1 **IC and Collaborator Contributions.** The contributions of any staff, funds, materials, and equipment by the Parties are set forth in Appendix B. The Federal Technology Transfer Act of 1986, 15 U.S.C. § 3710a(d)(1) prohibits IC from providing funds to Collaborator for any research and development activities under this CRADA.

5.2 **IC Staffing.** No IC employees will devote 100% of their effort or time to the research and development activities under this CRADA. IC will not use funds provided by Collaborator under this CRADA for IC personnel to pay the salary of any permanent IC employee. Although personnel hired by IC using CRADA funds will focus principally on CRADA research and development activities, Collaborator acknowledges that these personnel may nonetheless make contributions to other research and development activities, and the activities will be outside the scope of this CRADA.

5.3 **Collaborator Funding.** Collaborator acknowledges that Government funds received by Collaborator from an agency of the Department of Health and Human Services may not be used to fund IC under this CRADA. If Collaborator has agreed to provide funds to IC then the payment schedule appears in Appendix B and Collaborator will make payments according to that schedule. If Collaborator fails to make any scheduled payment, IC will not be obligated to perform any of the research and development activities specified herein or to take any other action required by this CRADA until the funds are received. IC will use these funds exclusively for the purposes of this CRADA. Each Party will maintain separate and distinct current accounts, records, and other evidence supporting its financial obligations under this CRADA and, upon written request, will provide the other Party a Fiscal Report according to Paragraph 4.3, which delineates all payments made and all obligated expenses, along with the Final Research Report described in Paragraph 4.2.

5.4 **Capital Equipment.** Collaborator's commitment, if any, to provide IC with capital equipment to enable the research and development activities under the Research Plan appears in Appendix B. If Collaborator transfers to IC the capital equipment or provides funds for IC to purchase it, then IC will own the equipment. If Collaborator loans capital equipment to IC for use during the CRADA, Collaborator will be responsible for paying all costs and fees associated with the transport, installation, maintenance, repair, removal, or disposal of the equipment, and IC will not be liable for any damage to the equipment.

Article 6. Intellectual Property

6.1 **Ownership of CRADA Subject Inventions, CRADA Data, and CRADA Materials.** Subject to the Government license described in Paragraph 7.5, the sharing requirements of Paragraph 8.1 and the regulatory filing requirements of Paragraph 8.2, the producing Party will retain sole ownership of and title to all CRADA Subject Inventions, all copies of CRADA Data, and all CRADA Materials produced solely by its employee(s). The Parties will own jointly all CRADA Subject Inventions invented jointly and all CRADA Materials developed jointly.

6.2 **Reporting.** The Parties will promptly report to each other in writing each CRADA Subject Invention reported by their respective personnel, and any Patent Applications filed thereon, resulting from the research and development activities conducted under this CRADA. Each Party will report all CRADA Subject Inventions to the other Party in sufficient detail to determine inventor ship, which will be determined in accordance with U.S. patent law. These reports will be treated as Confidential Information in accordance with Article 8. Formal reports will be made by and to the Patenting and Licensing Offices identified on the Contacts Information Page herein.

6.3 **Filing of Patent Applications.** Each Party will make timely decisions regarding the filing of Patent Applications on the CRADA Subject Inventions made solely by its employee(s), and will notify the other Party in advance of filing. Collaborator will have the first opportunity to file a Patent Application on joint CRADA Subject Inventions and will notify PHS of its decision within sixty (60) days of an Invention being reported or at least thirty (30) days before any patent filing deadline, whichever occurs sooner. If Collaborator fails to notify PHS of its decision within that time period or notifies PHS of its decision not to file a Patent Application, then PHS has the right to file a Patent Application on the joint CRADA Subject Invention. Neither Party will be obligated to file a Patent Application. Collaborator will place the following statement in any Patent Application it files on a CRADA Subject Invention: "This invention was created in the performance of a Cooperative Research and Development Agreement with the **[INSERT into Agency's model as appropriate: National Institutes of Health, Food and Drug Administration, Centers for Disease Control and Prevention]**, an Agency of the Department of Health and Human Services. The Government of the United States has certain rights in this invention." If either Party files a Patent Application on a joint CRADA Subject Invention, then the filing Party will include a statement within the Patent Application that clearly identifies the Parties and states that the joint CRADA Subject Invention was made under this CRADA.

6.4 **Patent Expenses.** Unless agreed otherwise, the Party filing a Patent Application will pay all preparation and filing expenses, prosecution fees, issuance fees, post issuance fees, patent maintenance fees, annuities, interference expenses, and attorneys' fees for that Patent Application and any resulting Patent(s). If a license to any CRADA Subject Invention is granted to Collaborator, then Collaborator will be responsible for all expenses and fees, past and future, in connection with the preparation, filing, prosecution, and maintenance of any Patent Applications and Patents claiming exclusively licensed CRADA Subject Inventions and will be responsible for a pro-rated share, divided equally among all licensees, of those expenses and fees for non-exclusively licensed CRADA Subject Inventions. Collaborator may waive its exclusive option rights at any time, and incur no subsequent financial obligation for those Patent Application(s) or Patent(s).

6.5 **Prosecution of Patent Applications.** The Party filing a Patent Application will provide the non-filing Party with a copy of any official communication relating to prosecution of the Patent Application within thirty (30) days of transmission of the communication. Each Party will also provide the other Party with the power to inspect and make copies of all documents retained in the applicable Patent Application or Patent file. The Parties agree to consult with each other regarding the prosecution of Patent Applications directed to joint CRADA Subject Inventions. If Collaborator elects to file and prosecute Patent Applications on joint CRADA Subject Inventions, then Collaborator agrees to use the U.S.P.T.O. Customer Number Practice and/or grant PHS a power(s) of attorney (or equivalent) necessary to assure PHS access to its intellectual property rights in these Patent Applications. PHS and Collaborator will cooperate with each other to obtain necessary signatures on Patent Applications, assignments, or other documents.

Article 7. Licensing

7.1 **Background Inventions.** Other than as specifically stated in this Article 7, nothing in this CRADA will be construed to grant any rights in one Party's Background Invention(s) to the other Party, except to the extent necessary for the Parties to conduct the research and development activities described in the Research Plan.

7.2 **Collaborator's License Option to CRADA Subject Inventions.** With respect to Government rights to any CRADA Subject Invention made solely by an IC employee(s) or made jointly by an IC employee(s) and a Collaborator employee(s) for which a Patent Application was filed, PHS hereby grants to Collaborator an exclusive option to elect an exclusive or nonexclusive commercialization license. The license will be substantially in the form of the appropriate model PHS license agreement and will fairly reflect the nature of the CRADA Subject Invention, the relative contributions of the Parties to the CRADA Subject Invention and the CRADA, a plan for the development and marketing of the CRADA Subject Invention, the risks incurred by Collaborator, and the costs of subsequent research and development needed to bring the CRADA Subject Invention to the marketplace. The field of use of the license will not exceed the scope of the Research Plan.

7.3 **Exercise of Collaborator's License Option.** To exercise the option of Paragraph 7.2 Collaborator must submit a written notice to the PHS Patenting and Licensing Contact identified on the Contacts Information Page (and provide a copy to the IC Contact for CRADA Notices) within three (3) months after either (i) Collaborator receives written notice from PHS that the Patent Application has been filed or (ii) the date on which Collaborator files the Patent Application. The written notice exercising this option will include a completed "Application for License to Public Health Service Inventions" and will initiate a negotiation period that expires nine (9) months after the exercise of the option. If PHS has not responded in writing to the last proposal by Collaborator within this nine (9) month period, the negotiation period will be extended to expire one (1) month after PHS so responds, during which month Collaborator may accept in writing the final license proposal of PHS. In the absence of Collaborator's exercise of the option, or upon election of a nonexclusive license, PHS will be free to license the CRADA Subject Invention to others. These time periods may be extended at the sole discretion of PHS upon good cause shown in writing by Collaborator.

7.4 **Government License in IC Sole CRADA Subject Inventions and Joint CRADA Subject Inventions.** Pursuant to 15 U.S.C. § 3710a(b)(1)(A), for CRADA Subject Inventions owned solely by IC or jointly by IC and Collaborator, and licensed pursuant to the option of Paragraph 7.2, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government. In the exercise of this license, the Government will not publicly disclose trade secrets or commercial or financial information that is privileged or confidential within the meaning of 5 U.S.C. § 552(b)(4) or which would be considered privileged or confidential if it had been obtained from a non-federal party.

7.5 **Government License in Collaborator Sole CRADA Subject Inventions.** Pursuant to 15 U.S.C. § 3710a(b)(2), for CRADA Subject Inventions made solely by an employee of Collaborator, Collaborator grants to the Government a nonexclusive, nontransferable, irrevocable, paid-up license to practice the CRADA Subject Invention or have the CRADA Subject Invention practiced throughout the world by or on behalf of the Government for research or other Government purposes.

7.6 **Third Party License.** Pursuant to 15 U.S.C. § 3710a(b)(1)(B), if PHS grants Collaborator an exclusive license to a CRADA Subject Invention made solely by an IC employee or jointly with a Collaborator employee, the Government will retain the right to require Collaborator to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the CRADA Subject Invention in Collaborator's licensed field of use on terms that are reasonable under the circumstances; or, if Collaborator fails to grant a license, to grant a license itself. The exercise of these rights by the Government will only be in exceptional circumstances and only if the Government determines (i) the action is necessary to meet health or safety needs that are not reasonably satisfied by Collaborator, (ii) the action is necessary to meet requirements for public use specified by federal regulations, and such requirements are not reasonably satisfied by Collaborator; or (iii) Collaborator has failed to comply with an agreement containing provisions described in 15 U.S.C. § 3710a(c)(4)(B). The determination made by the Government under this Paragraph is subject to administrative appeal and judicial review under 35 U.S.C. § 203(b).

7.7 **Third-Party Rights In IC Sole CRADA Subject Inventions.** For a CRADA Subject Invention conceived prior to the Effective Date solely by an IC employee that is first actually reduced to practice after the Effective Date in the performance of the Research Plan, the option offered to Collaborator in Paragraph 7.2 may be restricted if, prior to the Effective Date, PHS had filed a Patent Application and has either offered or granted a license in the CRADA Subject Invention to a third party. Collaborator nonetheless retains the right to apply for a license to any such CRADA Subject Invention in accordance with the terms and procedures of 35 U.S.C. § 209 and 37 C.F.R. Part 404.

Article 8. Rights of Access and Publication

8.1 **Right of Access to CRADA Data and CRADA Materials.** IC and Collaborator agree to exchange all CRADA Data and to share all CRADA Materials. If the CRADA is terminated, both Parties agree to provide CRADA Materials in quantities needed to complete the Research Plan. Such provision will occur before the termination date of the CRADA or sooner, if required by the Research Plan. If Collaborator possesses any human biological specimens from clinical trials under the CRADA, the specimens must be handled as described in the Protocol or as otherwise directed by IC before the termination date of the CRADA.

8.2 **Use of CRADA Data and CRADA Materials.** The Parties will be free to utilize CRADA Data and CRADA Materials internally for their own purposes, consistent with their obligations under this CRADA. The Parties may share CRADA Data or CRADA Materials with their Affiliates, agents or contractors provided the obligations of this Article 8.2 are simultaneously conveyed.

8.2.1 **CRADA Data**.
Collaborator and IC will use reasonable efforts to keep CRADA Data confidential until published or until corresponding Patent Applications are filed. To the extent permitted by law, each Party will have the right to use any and all CRADA Data in and for any regulatory filing by or on behalf of the Party.

8.2.2 **CRADA Materials.**
Collaborator and IC will use reasonable efforts to keep descriptions of CRADA Materials confidential until published or until corresponding Patent Applications are filed. Collaborator acknowledges that the basic research mission of PHS includes sharing with third parties for further research those research resources made in whole or in part with NIH funding. Consistent with this mission and the tenets articulated in "Sharing of Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts", December 1999, available at https://www.gpo.gov/fdsys/pkg/FR-1999-12-23/pdf/99-33292.pdf; following publication either Party may make available to third parties for further research those CRADA Materials made jointly by both PHS and Collaborator. Notwithstanding the above, if those joint CRADA Materials are the subject of a pending Patent Application or a Patent, or were created using a patent-pending or patented material or technology, the Parties may agree to restrict distribution or freely distribute them. Either Party may distribute those CRADA Materials made solely by the other Party only upon written consent from that other Party or that other Party's designee.

8.3 **Confidential Information.** Each Party agrees to limit its disclosure of Confidential Information to the amount necessary to carry out the Research Plan, and will place a confidentiality notice on all this information. A Party orally disclosing Confidential Information to the other Party will summarize the disclosure in writing and provide it to the other Party within fifteen (15) days of the disclosure. Each Party receiving Confidential Information agrees to use it only for the purposes described in the Research Plan. Either Party may object to the designation of information as Confidential Information by the other Party.

8.4 **Protection of Confidential Information.** Confidential Information will not be disclosed, copied, reproduced or otherwise made available to any other person or entity without the consent of the owning or providing Party except as required by a court or administrative body of competent jurisdiction, or federal law or regulation. Each Party agrees to use reasonable efforts to maintain the confidentiality of Confidential Information, which will in no instance be less effort than the Party uses to protect its own Confidential Information. Each Party agrees that a Party receiving Confidential Information will not be liable for the disclosure of that portion of the Confidential Information which, after notice to and consultation with the disclosing Party, the receiving Party determines may not be lawfully withheld, provided the disclosing Party has been given a reasonable opportunity to seek a court order to enjoin disclosure.

8.5 **Human Subject Protection.** The research to be conducted under this CRADA involves Human Subjects or human tissues within the meaning of 4S C.F.R. Part 46, and all research to be performed under this CRADA will conform to applicable federal laws and regulations. Additional information is available from the NHS Office for Human Research Protections (http://www.hhs.gov/ohrp/).

8.6 **Duration of Confidentiality Obligation.** The obligation to maintain the confidentiality of Confidential Information will expire at the earlier of the date when the information is no longer Confidential Information as defined in Article 2 or three (3) years after the expiration or termination date of this CRADA, except for IPI, for which the obligation to maintain confidentiality will extend indefinitely. Collaborator may request an extension to this term when necessary to protect Confidential Information relating to products not yet commercialized,

8.7 **Publication.** The Parties are encouraged to make publicly available the results of their research and development activities. Before either Party submits a paper or abstract for publication or otherwise intends to publicly disclose information about a CRADA Subject Invention, CRADA Data, or CRADA Materials, the other Party will have thirty (30) days to review proposed manuscripts and three (3) days to review proposed abstracts to assure that Confidential Information is protected. Either Party may request in writing that the proposed publication or other disclosure be delayed for up to thirty (30) additional days as necessary to file a Patent Application.

Article 9. Representations and Warranties

9.1 **Representations of IC.** IC hereby represents to Collaborator that:

9.1.1 IC has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that IC's official signing this CRADA has authority to do so.

9.1.2 To the best of its knowledge and belief, neither IC nor any of its personnel involved in this CRADA is presently subject to debarment or suspension by any agency of the Government which would directly affect its performance of the CRADA. Should IC or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, IC will notify Collaborator within thirty (30) days of receipt of final notice.

9.2 **Representations and Warranties of Collaborator.** Collaborator hereby represents and warrants to IC that:

9.2.1 Collaborator has the requisite power and authority to enter into this CRADA and to perform according to its terms, and that Collaborator's official signing this CRADA has authority to do so.

9.2.2 Neither Collaborator nor any of its personnel involved in this CRADA, including Affiliates, agents, and contractors are presently subject to debarment or suspension by any agency of the Government. Should Collaborator or any of its personnel involved in this CRADA be debarred or suspended during the term of this CRADA, Collaborator will notify IC within thirty (30) days of receipt of final notice.

9.2.3 Subject to Paragraph 12.3, and if and to the extent Collaborator has agreed to provide funding under Appendix B, Collaborator is financially able to satisfy these obligations in a timely manner.

9.2.4 The Test Article provided has been produced in accordance with the FDA's current Good Manufacturing Practice set out in 21 C.F.R. §§ 210-211 and ICH QA7, and meets the specifications cited in the Certificate of Analysis and Investigator's Brochure provided.

Article 10. Expiration and Termination

10.1 **Expiration.** This CRADA will expire on the last date of the term set forth on the Summary Page. In no case will the term of this CRADA extend beyond the term indicated an the Summary Page unless it is extended in writing in accordance with Paragraph 13.6.

10.2 **Termination by Mutual Consent.** IC and Collaborator may terminate this CRADA at any time by mutual written consent.

10.3 **Unilateral Termination.** Either IC or Collaborator may unilaterally terminate this CRADA at any time by providing written notice at least sixty (60) days before the desired termination date. IC may, at its option, retain funds transferred to IC before unilateral termination by Collaborator for use in completing the Research Plan. If Collaborator terminates this Agreement before the completion of all approved or active Protocol(s), then Collaborator will supply enough Test Article (and Placebo, if applicable) to complete these Protocol(s) unless termination is for safety concerns.

10.4 **Funding for IC Personnel.** If Collaborator has agreed to provide funding for IC personnel and this CRADA is mutually or unilaterally terminated by Collaborator before its expiration, then Collaborator agrees that funds for that purpose will be available to IC for a period of six (6) months after the termination date or until the expiration date of the CRADA, whichever occurs sooner. If there are insufficient funds to cover this expense, Collaborator agrees to pay the difference.

10.5 **New Commitments.** Neither Party will incur new expenses related to this CRADA after expiration, mutual termination, or a notice of a unilateral termination and will, to the extent feasible, cancel all outstanding commitments and contracts by the termination date. Collaborator acknowledges that IC will have the authority to retain and expend any funds for up to one (1) year subsequent to the expiration or termination date to cover any unpaid costs obligated during the term of the CRADA in undertaking the research and development activities set forth in the Research Plan.

10.6 **Collaborator Failure to Continue Development.** If Collaborator suspends development of the Test Article without the transfer of its active development efforts, assets, and obligations to a third party within ninety (90) days of discontinuation, Collaborator agrees that IC may continue developing the Test Article. In that event, the following will apply:

10.6.1 Collaborator agrees to transfer to IC all information necessary to enable IC to contract for the manufacture of the Test Article and, unless abandoned for reasons relating to safety as determined by the data safety monitoring board, to provide the Test Article (and Placebo, if any) in Collaborator's inventory to IC.

10.6.2 Further, Collaborator hereby grants to IC a nonexclusive, irrevocable, world-wide, paid-up license to practice, or have practiced for or on behalf of the Government, any Background Invention that Collaborator may currently have or will obtain on the Test Article, its manufacture, or on any method of using the Test Article for the indication(s) described in the Research Plan, including the right to sublicense to third parties.

Article 11. Disputes

11.1 **Settlement.** Any dispute arising under this CRADA which is not disposed of by agreement of the CRADA Principal Investigators will be submitted jointly to the signatories of this CRADA. If the signatories, or their designees, are unable to jointly resolve the dispute within thirty (30) days after notification thereof, the Assistant Secretary for Health (or his/her designee or successor) will propose a resolution. Nothing in this Paragraph will prevent any Party from pursuing any additional administrative remedies that may be available and, after exhaustion of such administrative remedies, pursuing all available judicial remedies.

11.2 **Continuation of Work.** Pending the resolution of any dispute or claim pursuant to this Article 11, the Parties agree that performance of all obligations will be pursued diligently.

Article 12. Liability

12.1 **NO WARRANTIES.** EXCEPT AS SPECIFICALLY STATED IN ARTICLE 9, THE PARTIES MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO ANY MATTER WHATSOEVER, INCLUDING THE CONDITIONS OF THE RESEARCH OR ANY INVENTION OR MATERIAL WHETHER TANGIBLE OR INTANGIBLE, MADE OR DEVELOPED UNDER OR OUTSIDE THE SCOPE OF THIS CRADA, OR THE OWNERSHIP, MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE RESEARCH OR ANY INVENTION OR MATERIAL, OR THAT A TECHNOLOGY UTILIZED BY A PARTY IN THE PERFORMANCE OF THE RESEARCH PLAN DOES NOT INFRINGE ANY THIRD-PARTY PATENT RIGHTS.

12.2 **Indemnification and Liability.** Collaborator agrees to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses and losses arising out of the use by Collaborator for any purpose of the CRADA Data, CRADA Materials or CRADA Subject Inventions produced in whole or part by IC employees under this CRADA, unless due to the negligence or willful misconduct of IC, its employees, or agents. The Government has no statutory authority to indemnify Collaborator. Each Party otherwise will be liable for any claims or damages it incurs in connection with this CRADA, except that IC, as an agency of the Government, assumes liability only to the extent provided under the Federal Tort Claims Act , 28 U.S.C. Chapter 171.

12.3 ***Force Majeure*.** Neither Party will be liable for any unforeseeable event beyond its reasonable control and not caused by its own fault or negligence, which causes the Party to be unable to perform its obligations under this CRADA, and which it has been unable to overcome by the exercise of due diligence. If a *force majeure* event occurs, the Party unable to perform will promptly notify the other Party. It will use its best efforts to resume performance as quickly as possible and will suspend performance only for such period of time as is necessary as a result of the *force majeure* event.

Article 13. Miscellaneous

13.1 **Governing Law.** The construction, validity, performance and effect of this CRADA will be governed by U.S. federal law, as applied by the federal courts in the District of Columbia. If any provision in this CRADA conflicts with or is inconsistent with any U.S. federal law or regulation, then the U.S. federal law or regulation will preempt that provision.

13.2 **Compliance with Law.** IC and Collaborator agree that they will comply with, and advise any contractors, grantees, or agents they have engaged to conduct the CRADA research and development activities to comply with, all applicable Executive Orders, statutes, and NHS regulations relating to research on human subjects (45 C.F.R. Part 46,

21 C.F.R. Parts 50 and 56) and relating to the appropriate care and use of laboratory animals (7 U.S.C. § 2131 *et seq.*; 9 C.F.R. Part 1, Subchapter A). IC and Collaborator will advise any contractors, grantees, or agents they have engaged to conduct clinical trials for this CRADA that they must comply with all applicable federal regulations for the protection of Human Subjects, which may include the Standards for Privacy of Individually Identifiable Health Information set forth in 45 C.F.R. Part 164. Collaborator agrees to ensure that its employees, contractors, and agents who might have access to a "select agent or toxin" (as that term is defined in 42 C.F.R. §§ 73.4-73.5) transferred from IC is properly licensed to receive the "select agent or toxin".

13.3 **Waivers.** None of the provisions of this CRADA will be considered waived by any Party unless a waiver is given in writing to the other Party. The failure of a Party to insist upon strict performance of any of the terms and conditions hereof, or failure or delay to exercise any rights provided herein or by law, will not be deemed a waiver of any rights of any Party.

13.4 **Headings.** Titles and headings of the articles and paragraphs of this CRADA are for convenient reference only, do not form a part of this CRADA, and will in no way affect its interpretation.

13.5 **Severability.** The illegality or invalidity of any provisions of this CRADA will not impair, affect, or invalidate the other provisions of this CRADA.

13.6 **Amendments.** Minor modifications to the Research Plan may be made by the mutual written consent of the CRADA Principal Investigators. Substantial changes to the CRADA, extensions of the term, or any changes to Appendix C will become effective only upon a written amendment signed by the signatories to this CRADA or by their representatives duly authorized to execute an amendment. A change will be considered substantial if it directly expands the range of the potential CRADA Subject Inventions, alters the scope or field of any license option governed by Article 7, or requires a significant increase in the contribution of resources by either Party.

13.7 **Assignment.** Neither this CRADA nor any rights or obligations of any Party hereunder shall be assigned or otherwise transferred by either Party without the prior written consent of the other Party. The Collaborator acknowledges the applicability of 41 U.S.C. § 15, the Anti Assignment Act, to this Agreement. The Parties agree that the identity of the Collaborator is material to the performance of this CRADA and that the duties under this CRADA are nondelegable.

13.8 **Notices.** All notices pertaining to or required by this CRADA will be in writing, signed by an authorized representative of the notifying Party, and delivered by first class, registered, or certified mail, or by an express/overnight commercial delivery service, prepaid and properly addressed to the other Party at the address designated on the Contacts Information Page, or to any other address designated in writing by the other Party. Notices will be considered timely if received on or before the established deadline date or sent on or before the deadline date as verifiable by U.S. Postal Service postmark or dated receipt from a commercial carrier. Notices regarding the exercise of license options will be made pursuant to Paragraph 7.3. Either Party may change its address by notice given to the other Party in the manner set forth above.

13.9 **Independent Contractors.** The relationship of the Parties to this CRADA is that of independent contractors and not agents of each other or joint venturers or partners. Each Party will maintain sole and exclusive control over its personnel and operations.

13.10 **Use of Name; Press Releases.** By entering into this CRADA, the Government does not directly or indirectly endorse any product or service that is or will be provided, whether directly or indirectly related to either this CRADA or to any patent or other intellectual-property license or agreement that implements this CRADA by Collaborator, its successors, assignees, or licensees. Collaborator will not in any way state or imply that the Government or any of its organizational units or employees endorses any product or services. Each Party agrees to provide proposed press releases that reference or rely upon the work under this CRADA to the other Party for review and comment at least five (5) business days before publication. Either Party may disclose the Title and Abstract of the CRADA to the public without the approval of the other Party.

13.11 **Reasonable Consent.** Whenever a Party's consent or permission is required under this CRADA, its consent or permission will not be unreasonably withheld.

13.12 **Export Controls.** Collaborator agrees to comply with U.S export law and regulations. If Collaborator has a need to transfer any CRADA Materials made in whole or in part by IC, or IC Materials, or IC's Confidential Information to a person located in a country other than the United States, to an Affiliate organized under the laws of a country other than the United States, or to an employee of Collaborator in the United States who is not a citizen or permanent resident of the United States, Collaborator will acquire any and all necessary export licenses and other appropriate authorizations.

13.13 **Entire Agreement.** This CRADA constitutes the entire agreement between the Parties concerning the subject matter of this CRADA and supersedes any prior understanding or written or oral agreement.

13.14 **Survivability.** The provisions of Paragraphs 3.3, 3.4, 3.8, 4.2, 4.3, 4.4.2, 5.3, 5.4, 6.1-9.2, 10.3-10.6, 11.1, 11.2, 12.1-12.3, 13.1-13.3, 13.7, 13.10 and 13.14 will survive the expiration or early termination of this CRADA.

SIGNATURES BEGIN ON THE NEXT PAGE

SIGNATURE PAGE

ACCEPTED AND AGREED

BY EXECUTING THIS AGREEMENT, EACH PARTY REPRESENTS THAT ALL STATEMENTS MADE HEREIN ARE TRUE, COMPLETE, AND ACCURATE TO THE BEST OF ITS KNOWLEDGE. COLLABORATOR ACKNOWLEDGES THAT IT MAY BE SUBJECT TO CRIMINAL, CIVIL, OR ADMINISTRATIVE PENALTIES FOR KNOWINGLY MAKING A FALSE, FICTITIOUS, OR FRAUDULENT STATEMENT OR CLAIM.

FOR IC:

_____ _____

Signature Date

Typed Name:
Title:

FOR COLLABORATOR:

_____ _____

Signature Date

Typed Name:
Title:

CONTACTS INFORMATION PAGE

CRADA Notices

For NCI:

Technology Transfer Specialist
National Cancer Institute
9609 Medical Center Drive
Bethesda, MD 20892-9702 MSC 9702
Rockville, MD 20850-9702 (express mail)
Tel: [***]
Fax: [***]

For Collaborator:

_____
_____

Tel:
Fax:

Patenting and Licensing

For IC:

_____

Technology Transfer Specialist
National Cancer Institute
9609 Medical Center Drive
Room 1-E530, MSC 9702
Rockville, MD 20850-9702
Tel: [***]
Fax: [***]

For Collaborator (if separate from above)

_____
_____

Tel:
Fax:

Delivery of Materials Identified in Appendix B (if any)

For IC:

_____

Tel:

Fax:

For Collaborator:

_____

Clinical Contact (as needed for Article 4.4.2)

For IC:
Tel:
Fax:

[***] = CERTAIN CONFIDENTIAL INFORMATION OMITTED.

SUMMARY PAGE

EITHER PARTY MAY, WITHOUT FURTHER CONSULTATION OR PERMISSION, RELEASE THIS SUMMARY PAGE TO THE PUBLIC.

TITLE OF CRADA: _____

_____

PHS [IC] Component: _____

IC Principal Investigator: _____

Collaborator: _____

Collaborator Principal Investigator: _____

TERM OF CRADA: _____ (___) years from the Effective Date.

ABSTRACT OF THE RESEARCH PLAN:

_____

_____

_____

_____

_____

_____

APPENDIX A

RESEARCH PLAN

[The Research Plan should be a short, concise explanation of the research project that will be conducted by NIH with the materials provided under the CRADA. Each Research Plan should include the following sentence, "The scope of the Research Plan is....."]

APPENDIX B

STAFFING, FUNDING AND MATERIALS/EQUIPMENT CONTRIBUTIONS OF THE PARTIES

APPENDIX C

MODIFICATIONS TO THE MODEL INTRAMURAL-PHS CLINICAL CRADA

CONFIDENTIAL DISCLOSURE AGREEMENT
FOR CRADA LETTER OF INTENT

This Agreement is made by and between the National Cancer Institute, NCI, an agency of the United States Government, (hereinafter referred to as "IC"), ZIOPHARM Oncology, Inc. (hereinafter referred to as "Ziopharm") and Intrexon Corporation (hereinafter referred to as "Intrexon"). Ziopharm and Intrexon each may be hereinafter referred to individually as "Collaborator" and collectively as "Collaborators." Collectively or individually, the IC and Collaborator shall also be referred to as "Parties" or "Party."

WHEREAS, Collaborators have certain confidential information relating to non-viral *Sleeping Beauty* vectors for genetic modification of peripheral blood lymphocytes and the therapeutic use thereof (hereinafter referred to as the "Confidential Information" belonging to Collaborator); and

WHEREAS, IC has certain confidential information relating to methods for identifying mutation reactive T-cell receptors and use of T cells for cancer therapy (hereinafter referred to as the "Confidential Information" belonging to IC); and

WHEREAS, each Party is interested in examining the Confidential Information of the other Party in order to conduct research described in the attached Research Plan under a Letter of Intent for proposed Cooperative Research And Development Agreement #03111 entitled Development and Evaluation of Intrexon Corporation's Proprietary Non-viral Sleeping Beauty Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been identified Using NCI Proprietary Methods;

NOW, THEREFORE, in consideration of the premises and mutual covenants contained herein, the Parties hereto agree as follows:

1. Each Party shall disclose and transmit Confidential Information to the other Party in sufficient detail to enable such other Party to conduct the research described in the Research Plan of the CRADA Letter of Intent.

2. Each Party agrees to accept the Confidential information and employ all reasonable efforts to maintain the Confidential information of the other Party secret and confidential, such efforts to be no less than the degree of care employed by each Party to preserve and safeguard its own confidential information. The Confidential Information of the disclosing Party shall not be disclosed, revealed, or given to anyone by the receiving Party except employees, contract employees, and volunteers who are under an obligation of confidentiality to the receiving Party and who have a need for the Confidential Information in connection with the receiving Party's research activities. Such individuals shall be advised by the receiving Party of the confidential nature of the Confidential Information and that the Confidential Information shall be treated accordingly,

3. Each Party agrees that it will not use the Confidential Information of the other Party for any purpose except as set forth herein.

4. "**Confidential Information**" means confidential scientific, business, or financial information provided that such information does not include information which:

   a) is publicly known or is available from public sources;

   b) has been made available by its owner to others without a confidentiality obligation;

   e) is already known by the receiving Party, or information that is independently created or compiled by the receiving Party without reference to or use of the provided information;

   d) relates to potential hazards or cautionary warnings associated with the production, handling, or use of the subject matter of the Research Plan of the proposed CRADA;

   e) is required to be disclosed by law or court order.

5. The term of this Confidential Disclosure Agreement shall be the same as that of the CRADA Letter of Intent, including any extensions. If the CRADA is executed, this Agreement shall be superseded by the terms of the CRADA. If the CRADA is not executed, or the Letter of Intent is terminated or expires, each Party's obligations under Paragraphs 2 and 3 shall extend for a period of three (3) years from the date of final signature of this Agreement.

6. All information to be deemed confidential under this Agreement shall be clearly marked "**CONFIDENTIAL**," by the disclosing Party. Any Confidential Information which is orally disclosed must be reduced to writing and marked "**CONFIDENTIAL**" by the disclosing Party and such notice must be provided to the other Party within thirty (30) days of such disclosure.

   Notwithstanding any other provision in this Agreement, although certain information provided under this Agreement is confidential and will be so marked, the Collaborators recognize that the NCI may need to disclose certain information concerning Confidential Information to patients (or to physicians or scientists where such disclosure is made in order to directly facilitate the ongoing treatment of a patient, or the development of a treatment for a patient). The Collaborators hereby authorize such limited disclosures, and the NCI agrees to promptly acknowledge to the Collaborators the making of any such disclosure.

7. It is understood that nothing herein shall be deemed to constitute, by implication or otherwise, the grant to either Party by the other of any license or other rights under any patent, patent application or other intellectual property right or interest. The grant of such right or license, if any, shall be formalized in a separate license agreement between the Parties.

8. It is understood and agreed by both Parties that each represents and warrants to the other Party that each Official signing this Agreement has authority to do so.

9. The illegality or invalidity of any provision of this Agreement shall not impair, affect or invalidate the other provisions of this Agreement.

10. The construction, validity, performance and effect of this Agreement shall be governed by Federal law, as applied by the Federal Courts in the District of Columbia.

SIGNATURES BEGIN ON THE FOLLOWING PAGE

ACCEPTED AND AGREED

The undersigned expressly certify or affirm that the contents of any statements made or reflected in this document are truthful and accurate. The undersigned further agree to examine and consider the subject matter of the Confidential Information on the foregoing basis.

FOR THE IC:

/s/ Kathleen Carroll

Date

Kathleen Carroll, Ph.D., MBA
Associate Director, Technology Transfer Center
National Cancer Institute
National Institutes of Health

FOR ZIOPHARM

/s/ Laurence Cooper — October 6, 2016

(Authorized Signatory for Ziopharm) — Date

Laurence Cooper, M.D., Ph.D.
Chief Executive Officer
ZIOPHARM Oncology, Inc.
One First Street, Parris Building 34, Navy Yard Plaza
Boston, MA 02129

FOR INTREXON

/s/ Donald Lehr — October 6, 2016

(Authorized Signatory for Intrexon) — Date

Donald Lehr
Chief Legal Officer
Intrexon Corporation
20374 Seneca Meadows Parkway
Germantown, MD 20876

MATERIAL TRANSFER AGREEMENT
for CRADA Letter of Intent

This Material Transfer Agreement ("MTA") has been adopted for use by the National Cancer Institute ("IC") for transfers of research material for research to be performed under a Cooperative Research and Development Agreement (CRADA) Letter of Intent. Collectively or individually, the IC and Collaborators shall also be referred to as "Parties" or "Party."

IC: National Cancer Institute

Collaborators: ZIOPHARM Oncology, Inc., and
Intrexon Corporation, Inc.

Proposed CRADA title: Development and Evaluation of Intrexon Corporation's Proprietary Non-viral *Sleeping Beauty* Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods

1. a. IC agrees to transfer to Collaborator the following IC Materials:

None.

b. Collaborators agree to transfer to IC the following Collaborator Materials:

i. clinical grade DNA plasmid for Sleeping Beauty transposon expressing CAR

ii. clinical grade DNA plasmid Sleeping Beauty transposase expressing SB11

iii. sequence information for both Sleeping Beauty transposase and transposon

In this MTA, IC Materials and Collaborator Materials will jointly be referred to as "Research Material."

2. THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS. The Research Material will only be used for research purposes by the receiving Party's Investigator in his/her laboratory, for the research project described in the Research Plan of the CRADA Letter of Intent (Appendix A), under suitable containment conditions. The Receiving Party agrees to comply with all Federal rules and regulations applicable to the Research Plan and the handling of the Research Material.

3. In all oral presentations or written publications concerning the Research Plan, the receiving Party will acknowledge the providing Party's contribution of this Research Material unless requested otherwise.

4. This Research Material represents a significant investment on the part of the providing Party and is considered proprietary to the providing Party. The receiving Party's Investigator therefore agrees to retain control over this Research Material and further agrees not to transfer the Research Material to other people not under her or his direct supervision without advance written approval of the providing Party. The providing Party reserves the right to distribute the Research Material to others and to use it for its own purposes. When the Research Plan is completed, the Research Material will be disposed of, if directed by the providing Party.

5. The Research Material IS BEING SUPPLIED TO THE RECEIVING PARTY WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. The providing Party makes no representations that the use of the Research Material will not infringe any patent or proprietary rights of third parties.

6. No indemnification for any loss, claim, damage, or liability is intended or provided by any Party under this agreement. Each Party shall be liable for any loss, claim, damage, or liability that said Party incurs as a result of its activities under this Agreement, except that IC, as an agency of the United States, assumes liability only to the extent as provided under the Federal Tort Claims Act, 28 U.S.C. 2671 et seq.

7. The term of this MTA shall be the same as that of the Letter of Intent including any extensions. If the CRADA is executed, this Agreement shall be superseded by the terms of the CRADA. If the CRADA is not executed, this Agreement shall expire at the same time as the expiration or termination of the Letter of Intent.

8. The undersigned providing Party and receiving Party expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

10. This MTA shall be construed in accordance with Federal law as applied by the Federal courts in the District of Columbia.

SIGNATURES BEGIN ON NEXT PAGE

10/5/16 /s/ Steven Rosenberg
Date Steven Rosenberg, M.D., Ph.D.
Chief, Surgery Branch, NCI

/s/ Kathleen Carroll
Date Kathleen Carroll, Ph.D., MBA
Associate Director, Technology Transfer Center
National Cancer Institute
National Institutes of Health

IC's Official and Mailing Address:

9609 Medical Center Drive, Rm 1E530
Rockville, MD 20850-9702 (for couriers)
Bethesda, MD 201192-9702 (for USPS mail)

October 7, 2016 /s/ Tim Chan
Date Tim Chan, Ph.D.
Senior Director, Intrexon

October 7, 2016 /s/ Donald Lehr
Date Authorized Signature for Intrexon Corporation and Title

Intrexon Corporation's Official and Mailing Address;

20374 Seneca Meadows Parkway
Germantown, MD 20876

October 6, 2016 /s/ Laurence Cooper
Date Laurence Cooper, M.D., Ph.D.
CEO ZIOPHARM Oncology, Inc.

Date Authorized Signature for ZIOPHARM Oncology, Inc. and Title

ZIOPHARM Oncology, Inc.'s Official and Mailing Address:

One First Avenue, Parris Building 34, Navy Yard Plaza
Boston, MA 02129

Any raise or misleading statements made, presented, or submitted to the Government, including any relevant omissions, under this Agreement and during the course of negotiation of this Agreement are subject to all applicable civil and criminal statutes including Federal statutes 31 U.S.C. § 3801-3812 (civil liability) and 18 U.S.C. § 1001 (criminal liability including line(s) and/or imprisonment).

Confidential

Amendment #1

Cooperative Research and Development Agreement # 03111

"Development and Evaluation of Precigen Inc.'s Proprietary Non-viral Sleeping Beauty Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods"

IC Principal Investigator: Steven A. Rosenberg, M.D., Ph.D.

Collaborators: Precigen Inc. and ZIOPHARM Oncology, Inc.

The purpose of this amendment is to change certain terms of the above-referenced Cooperative Research and Development Agreement (CRADA). These changes are reflected below, and except for these changes, all other provisions of the original CRADA remain in full force and effect. Underlining indicates additions, and strikeout indicates deletions.

The Parties agree:

1. Intrexon Corporation transfers all operating capabilities pertinent to this CRADA to Precigen Inc., an Intrexon wholly owned subsidiary. And thus, Intrexon assigns all its rights, titles, interests and benefits in and to CRADA #03111, along with its responsibilities under CRADA #03111, to Precigen Inc.

2. Intrexon Corporation is removed as the Collaborator, and Precigen Inc. is added as the Collaborator.

3. The CRADA title is modified to read as follows: "Development and Evaluation of ~~Intrexon Corporation's~~ Precigen Inc.'s Proprietary Non-viral Sleeping Beauty Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods".

4. The CRADA abstract is modified to read as follows: ~~The principal goal of this CRADA is to~~ Under a Cooperative Research and Development Agreement (CRADA), the National Cancer Institute (NCI), Precigen, Inc., and ZIOPHARM Oncology, Inc. will develop and evaluate adoptive cell transfer-based immunotherapies (ACT) using NCI proprietary methods for the isolation of tumor-reactive T Cell Receptors (TCRs) targeting unique, patient specific mutated neoantigen(s) and introduction of said TCRs into T cell subsets isolated from peripheral blood using proprietary ~~Intrexon Corporation ("Intrexon")~~ Precigen Inc. Non-Viral Sleeping Beauty Transposon and Transposases for the treatment of patients with solid tumor malignancies.

5. Article 3.7.2 is amended to read as follows:

   3.7.2 When a Party files the IND, the other Party agrees to provide the filing party background data and information necessary to support the IND

in electronic Common Technical Document (eCTD) format. The Parties further agree to provide a letter of cross-reference to all data and pertinent regulatory filings sponsored by a Party under this CRADA. Both Parties' employees will be reasonably available to respond to inquiries from the FDA regarding information and data contained in the Party's IND, DMF, other filings, or other information and data provided to one Party by the other Party pursuant to this Article 3.

6. Article 3.11 is amended to read as follows:

3.11 **FDA Meetings/Communications**. All formal meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and IC in advance. Each Party reserves the right to take part in setting the agenda for, to attend, and to participate in these meetings, as appropriate. Sponsor will provide the other Party with copies of FDA meeting minutes, ~~all transmittal letters for IND submissions~~, IND safety reports, formal questions and responses that have been submitted to the FDA, Annual Reports, and official FDA correspondence, pertaining either to the INDs under this CRADA or to the Clinical Investigators on Protocols performed in accordance with the Research Plan, except to the extent that those documents contain the proprietary information of a third party or dissemination is prohibited by law.

7. Article 4.1 is amended to read as follows:

4.1 Interim Research and Development Reports. The CRADA PIs should exchange information regularly, in writing. This exchange may be accomplished through meeting minutes, detailed correspondence, circulation of draft manuscripts, Steering Committee reports, copies of Annual Reports and any other reports updating the progress of the CRADA research. However, the Parties must exchange updated Investigator's Brochure, formulation and preclinical data, and toxicology findings, as they become available; these data and documents will be provided in eCTD format.

8. The IC's Clinical Contact (as needed for Article 4.4.2) is amended to read as follows:

Steven A. Rosenberg, M.D., Ph.D.
Surgery Branch, NCI
10 Center Drive, MSC 1201
Bldg. 10, CRC Room 3-3940
Bethesda, MD 20892-1201
Tel: [ ]
Fax: [ ]
and
[ ]

9. Add in a new Article 8.9 (Certificate of Confidentiality) as follows:

8.9 Certificate of Confidentiality. The CRADA Data collected under a Protocol conducted under this CRADA are covered under a Certificate of Confidentiality that has been issued by the NIH pursuant to Section 301(d) of the Public Health Service Act (42 U.S.C. 241(d)). Under this Certificate of Confidentiality, the Collaborator may not:

a) Disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or

b) Disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.

Provided that Collaborator will be permitted to disclose the information described in the points set forth above as follows:

a) If required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding;

b) If necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;

c) If made with the consent of the individual to whom the information, document, or biospecimen pertains; or

d) If made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of Human Subjects in research.

Prior to making any permitted disclosures, Collaborator will ensure that that any recipient of data protected by a Certificate of Confidentiality agrees to comply with the Certificate.

SIGNATURES ON THE NEXT PAGE

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/ James H. Doroshow	3/18/18
James H. Doroshow, M.D. Deputy Director for Clinical and Translational Research, NCI	Date

For Precigen Inc.:

/s/ Helen Sabzevari	March 13, 2018
Helen Sabzevari, Ph.D. President, Precigen	Date

For ZIOPHARM ONCOLOGY INC.:

/s/ Kevin Lafond	23 Mar 2018
Name: Kevin Lafond Title: SVP, Finance, CAO	Date

For Intrexon Corporation:

/s/ Jeffrey Perez	March 12, 2018
Jeffrey Perez SVP, Intellectual Property Affairs	Date

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM IF PUBLICLY DISCLOSED.

Confidential

Amendment #2

Cooperative Research and Development Agreement # 03111

"Development and Evaluation of Ziopharm Oncology, Inc.'s Proprietary Non-viral Sleeping Beauty Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods"

IC Principal Investigator: Steven A. Rosenberg, M.D., Ph.D.

Collaborators: Precigen, Inc. and Ziopharm Oncology, Inc.

The purpose of this amendment is to change certain terms of the above-referenced Cooperative Research and Development Agreement (CRADA). These changes are reflected below, and except for these changes, all other provisions of the original CRADA and Amendment #1 remain in full force and effect. Upon execution, NCI, Precigen Inc., and Ziopharm Oncology, Inc. will each retain a copy of this amendment. Underlining indicates additions, and strikeout indicates deletions.

The Parties agree:

1. Pursuant to that certain Exclusive License Agreement by and between Ziopharm Oncology, Inc., Precigen, Inc., and Intrexon Corporation, dated October 5, 2018, Precigen, Inc. has agreed to assign to Ziopharm Oncology Inc. all of Precigen Inc.'s rights, titles and interests in the CRADA. Thus, Precigen, Inc. hereby assigns all of its rights, titles, interests and benefits in and to CRADA #03111 to Ziopharm Oncology, Inc. In addition, Precigen, Inc. hereby assigns, and Ziopharm Oncology, Inc. hereby assumes, all of Precigen Inc.'s responsibilities under CRADA #03111 accruing on or after October 5, 2018. For clarity, Ziopharm Oncology, Inc. and NCI shall release Precigen, Inc. from all duties, claims, obligations and liabilities under CRADA #03111 upon execution of this amendment.

2. Precigen, Inc. is removed as a Collaborator, and Ziopharm Oncology, Inc is now the only Collaborator. All references in the CRADA to Collaborator and Precigen, Inc. shall be deemed to refer to Ziopharm Oncology, Inc. The definition of "Collaborator" is modified as follows: "Collaborator" means Ziopharm Oncology, Inc. ~~as the context dictates, collectively, Intrexon and ZIOPHARM, or individually Intrexon or ZIOPHARM.~~

3. Upon final signature, the term of the CRADA is extended for two (2) years from January 9, 2020 to January 9, 2022.

4. The CRADA title is modified to read as follows: "Development and Evaluation of ~~Precigen Inc.'s~~ Ziopharm Oncology, Inc.'s Proprietary Non-viral Sleeping Beauty Vectors for Genetic Modification of Peripheral Blood Lymphocytes with Genes Encoding Mutated Tumor Neoantigen-specific T Cell Receptors (also referred to as Mutation Reactive T Cell Receptors) that Have Been Identified Using NCI Proprietary Methods".

5. The CRADA abstract is modified to read as follows: Under a Cooperative Research and Development Agreement (CRADA), the National Cancer Institute (NCI), ~~Precigen, Inc.~~ and Ziopharm Oncology, Inc. will develop and evaluate adoptive cell transfer-based immunotherapies (ACT) using NCI proprietary methods for the isolation of tumor-reactive T Cell Receptors (TCRs) targeting unique, patient specific mutated neoantigen(s) and introduction of said TCRs into T cell subsets isolated from peripheral blood using ~~Precigen, Inc.~~ Ziopharm Oncology, Inc. Non-Viral Sleeping Beauty Transposon and Transposases for the treatment of patients with solid tumor malignancies.

6. The Contacts Information Page is deleted in its entirety and replaced with the Contacts Information Page in Exhibit 1.

ACCEPTED AND AGREED TO:

For the National Cancer Institute:

/s/ James H. Doroshow, M.D.	2/1/19
James H. Doroshow, M.D.	Date
Deputy Director for Clinical and Translational Research, NCI	

For Precigen Inc.:

/s/ Donald P. Lehr	January 10, 2019
Name: Donald P. Lehr	Date
Title: Director	

For Ziopharm Oncology, Inc.

/s/ Kevin Lafond	January 10, 2019
Name: Kevin Lafond	Date
Title: SVP, Finance, CAO	

Exhibit 1.

CONTACTS INFORMATION PAGES

CRADA Notices

[***] [***]

Patenting and Licensing

[***] [***]

Delivery of Materials Identified in Appendix B (if any)

[***] [***]

[***] = CERTAIN CONFIDENTIAL INFORMATION OMITTED.

Finances

[***] [***]

Clinical Contact (as needed for Article 4.4.2)

[***] [***]

[***] = CERTAIN CONFIDENTIAL INFORMATION OMITTED.

Summary of the NCI – Ziopharm Partnership

Ziopharm Controls Commercialization of its Sleeping Beauty TCR Program and Holds Full Commercial Economics Minus Fees, Milestone Payments and Single-Digit Royalties Payable to NCI

NCI as Development Partner; Licensed Key Intellectual Property to Ziopharm

January 2017 CRADA Summary

- NCI and Ziopharm developing adoptive cell transfer (ACT) - based immunotherapies genetically modified using *Sleeping Beauty* system to express TCRs for the treatment of solid tumors
- NCI performs early stage research and runs clinical trial(s)
  - Ziopharm retains all rights to develop oncology products for *Sleeping Beauty*; NCI has rights to use *Sleeping Beauty* solely for the purpose of conducting research under CRADA
- Ziopharm granted option to secure exclusive or non-exclusive license for IP generated by NCI under the CRADA
- Signed in January 2017 and extends through January 2022
- Ziopharm pays NCI $2.5M per year; paid $6.9M to date

May 2019 Patent License Agreement

- Ziopharm exclusively licensed intellectual property from the NCI:
  - *For Ziopharm to develop and commercialize* autologous, peripheral blood T-cell therapy products engineered by transposon-mediated gene transfer to express TCRs reactive to mutated **KRAS**, **p53** and **EGFR hotspots**
  - For manufacturing technologies to *develop and commercialize* autologous, peripheral blood T-cell therapy products engineered by non-viral gene transfer to express TCRs
    - Manufacturing technologies were originally developed under January 2017 CRADA
- License contemplates adding additional TCRs in the same hotspot families to this license
- Foundational IP will support further hotspot and personalized *Ziopharm sponsored* clinical trials