

**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  
**National Cancer Institute**  
an Institute or Center (hereinafter referred to as the “IC”) of the  
**National Institutes of Health**

and

**Kite Pharma, Inc.**  
hereinafter referred to as the “Collaborator”,  
having offices at 2225 Colorado Avenue, Santa Monica, CA 90404,  
created and operating under the laws of Delaware.

## COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT FOR INTRAMURAL-PHS CLINICAL RESEARCH

### **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 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 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 inventorship, 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. § 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 [http://www.ott.nih.gov/policy/research\\_tool.aspx](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:



\_\_\_\_\_  
James H. Doroshow, M.D.  
Deputy Director for Clinical and Translational Research, NCI

12/23/15  
\_\_\_\_\_  
Date

FOR COLLABORATOR:



\_\_\_\_\_  
Cynthia M. Butitta  
Chief Financial Officer and Chief Operating Officer

1/4/16  
\_\_\_\_\_  
Date

## CONTACTS INFORMATION PAGE

### CRADA Notices

#### For NCI:

Technology Transfer Specialist  
for Experimental Transplantation and  
Immunology Branch  
National Cancer Institute  
9609 Medical Center Drive  
Bethesda, MD 20892-9702 MSC 9702  
Rockville, MD 20850-9702 (express mail)  
Tel: 240-276-5530  
Fax: 240-276-5504

#### For Collaborator:

David Chang, M.D., Ph.D.  
EVP R&D & Chief Medical Officer  
Kite Pharma, Inc.  
2225 Colorado Avenue  
Santa Monica, CA 90404  
Tel: (310) 824-9999  
Email: dchang@kitepharma.com

### Patenting and Licensing

#### For IC:

National Cancer Institute  
Technology Transfer Center  
9609 Medical Center Drive  
Room 1E530, MSC 9702  
Rockville, MD 20850  
Bethesda, MD 20892 (business mail)  
Rockville, MD 20850 (courier/visitors)  
Tel: 240-276-5523  
Fax: 240-276-5524

#### For Collaborator (if separate from above)

Adrian Bot, M.D., Ph.D.  
VP of Translational Medicine  
Kite Pharma, Inc.  
2225 Colorado Avenue  
Santa Monica, CA 90404  
Tel: 310 622 9105  
Email: abot@kitepharma.com

### Delivery of Materials Identified in Appendix B (if any)

#### For IC:

James N. Kochenderfer, M.D.  
National Cancer Institute  
Building 10 - CRC - Room 3-3888  
Bethesda, MD 20892  
Tel: 301-594-5340  
Email: kochendj@mail.nih.gov

#### For Collaborator:

Adrian Bot, M.D., Ph.D.  
VP of Translational Medicine  
Kite Pharma, Inc.  
2225 Colorado Avenue  
Santa Monica, CA 90404  
Tel: 310 622 9105  
Email abot@kitepharma.com

### Clinical Contact (as needed for Article 4.4.2)

Same as above

## SUMMARY PAGE

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

TITLE OF CRADA: Clinical Evaluation of NCI-hCD19-CAR, a CD19-Targeting Chimeric Antigen Receptor (CAR) for the Treatment of B Cell Lymphoma and B cell Leukemia, and the Development of Novel CARs Targeting B Cell Malignancies

PHS [IC] Component: National Cancer Institute  
IC Principal Investigator: James N. Kochenderfer, M.D.

Collaborator: Kite Pharma, Inc.  
Collaborator Principal Investigator: David Chang, M.D., Ph.D.

TERM OF CRADA: Five (5) years from the Effective Date.

### ABSTRACT OF THE RESEARCH PLAN:

The National Cancer Institute and Kite Pharma, Inc. have entered into a Cooperative Research and Development Agreement (CRADA) to: 1) evaluate an NCI-developed monomeric chimeric antigen receptor (CAR) targeting CD19 for the treatment of B cell lymphoma and B cell leukemia, and 2) pursue the development of novel CARs for the treatment of B cell lymphoma and B cell leukemia.

## APPENDIX A

### RESEARCH PLAN

#### SCOPE AND GOALS OF THIS CRADA RESEARCH PLAN

PROPRIETARY INFORMATION

#### INTRODUCTION

B cell malignancies represent a diverse collection of diseases that include most non-Hodgkin lymphomas and some leukemias. It is estimated that in 2015, over eighty thousand people will be diagnosed with these diseases and, as some B cell malignancies cannot be fully cured by conventional treatments such as chemotherapy and monoclonal antibodies, they will cause more than twenty-two thousand deaths.

Immunotherapies such as the anti-CD20 monoclonal antibody rituximab and the bispecific antibody blinatumomab have been shown to be useful when combined with chemotherapy. However, as a single agent, rituximab is not curative. Allogeneic hematopoietic stem cell transplantation (alloHSCT) is an approach that has been shown to be effective, but is associated with significant transplant-related mortality and chronic graft-versus-host disease. These results demonstrate that immunotherapy can be effective in patients with B cell malignancies; however, there remains a significant need for novel immunotherapy approaches with improved efficacy and decreased toxicity.

Cell-based immunotherapy is a promising treatment modality for B cell malignancies. In this approach, a patient's own T cells are removed, genetically modified to express a specialized receptor called a chimeric antigen receptor (CAR), and infused back into the patient, allowing the immune cells to target and eliminate malignant cells expressing specific antigens. Recent clinical data have shown in several patients that treatment with autologous T cells genetically modified to express CARs targeting the B cell antigen CD19 resulted in durable and lengthy complete remissions of lymphoma or chronic lymphocytic leukemia. To date, numerous clinical trials of genetically modified T cells targeting a variety of malignancies have been carried out.

CARs generally incorporate the scFv (single-chain variable fragment) from a monoclonal antibody as the antigen-targeting domain. This is fused to a protein spacer element followed by a transmembrane spanning domain and intracellular signaling elements. Thus, the CAR protein contains both tumor antigen recognition domains and T cell signal domains in the same hybrid molecule. The design of CARs has evolved over the decades since their first description, with the goal of enhancing T cell signaling functions. Dr. James Kochenderfer in NCI's Experimental Transplantation and Immunology Branch (ETIB) has recently identified CD19-targeted CARs and evaluated their efficacy both in vitro and in vivo (NIH Ref #E-042-2014 and corresponding US Provisional Application 62/006,313).

PROPRIETARY INFORMATION

#### **EXPERTISE OF THE PARTIES**

James Kochenderfer, M.D. is a tenure-track Investigator in the Experimental Transplantation and Immunology Branch (ETIB) of the National Cancer Institute (NCI). For the past 7 years, Dr. Kochenderfer has focused on a full range of chimeric antigen receptor (CAR) research from designing and constructing new CARs to conducting clinical trials. Dr. Kochenderfer had



previously designed another anti-CD19 CAR, conducted preclinical studies on the CAR, and then participated in its clinical trial as the Lead Associate Investigator. He has designed and constructed multiple novel CARs and has extensive expertise in cellular and molecular immunology needed to assess CAR safety and efficacy.

Kite Pharma is a biopharmaceutical company founded in 2009 with a goal of developing T cell therapies for cancer. Kite is now a publicly-traded company with extensive academic collaborations including a CRADA with the Surgery Branch of the National Cancer Institute, as well as industry collaborations. Kite has substantial scientific and product development capability with extensive laboratory space and scientific expertise, including a team of physicians with experience in managing clinical trials and commercially developing immunotherapies.

#### **EXPERIMENTAL PLAN**

The experimental details that follow are preliminary and may be changed upon mutual agreement of Parties. Any substantive change to the Research Plan will be by mutual agreement and written Amendment to this CRADA.

PROPRIETARY INFORMATION, WITHHELD THROUGH PAGE 31

## 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 three (3) 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 one (1) person-year of effort per year will be required to complete the CRADA research.

#### *Funding Contributions*

Collaborator agrees to provide \$2,500,000 in total 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:

Collaborator will provide funds in equal  installments, as described below. The first installment will be due within thirty (30) days of the Effective Date. Each of the subsequent installments will be due within  of each anniversary of the Effective Date. Collaborator agrees that IC can allocate the funding between the various categories in support of the CRADA research. In addition, to cover the production cost of a clinical vector, upon execution of the CRADA, Collaborator will also provide a one-time funding contribution of \$220,000 due within thirty (30) days of the Effective Date.

#### **FUNDING CONTRIBUTIONS:**

##### **Annual contribution**

##### Research support:

Ph.D. scientist for *ex vivo* assay & pre-clinical CAR studies  
Supplies for *ex vivo* assays (antibodies, flow-cyto, ELISA kits, PCR..etc)  
Preclinical supplies for *in vitro* and *in vivo* murine assays

##### Clinical support:

Ph.D. scientist for clinical cell production

\$
----

Research nurse  
Partial coverage of cell production costs  
Workstation, software, travel and office supplies for new personnel

Annual contribution

\$
----

**Total Funding Contribution:**

One-time contribution for clinical vector	\$220,000
Annual contribution x <input type="text" value="0"/>	\$2,280,000
<b>Total</b>	<b><u>\$2,500,000</u></b>

**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](http://www.pay.gov).

**CRADA TRAVEL PAYMENTS:**

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

*Materials/Equipment Contributions*

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

NCI-hCD19-CAR 47G4-CD828Z vector and accompanying sequence information

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

Collaborator Materials: None

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 INTRAMURAL-PHS CLINICAL CRADA

Amend the definition of “**Background Invention**” in Article 2 to read as follows:

“**Background Invention**” means an Invention conceived and first actually reduced to practice before the Effective Date or an Invention conceived and first actually reduced to practice by either Party outside the scope of the Research Plan.

Amend the definition of “**CRADA Data**” in Article 2 to read as follows:

“**CRADA Data**” means all recorded information first produced in the performance of the Research Plan. IC and PHS acknowledge and agree that notwithstanding the foregoing, the expression “CRADA Data” expressly excludes any and all data, results and information generated by or for or otherwise in the possession of either Party before the Effective Date, or generated or otherwise acquired by or on behalf of either Party after the Effective Date outside of the scope of this CRADA, which data, results and information shall be deemed to be the exclusive property of the Party possessing such data, results and information.

Amend the definition of “**CRADA Materials**” in Article 2 to read as follows:

“**CRADA Materials**” means all tangible materials first produced in the performance of the Research Plan other than CRADA Data. IC and PHS acknowledge and agree that notwithstanding the foregoing, the expression “CRADA Materials” expressly excludes any and all materials generated by or for or otherwise in the possession of either Party before the Effective Date, or generated or otherwise acquired by or on behalf of either Party after the Effective Date outside of the scope of this CRADA, which materials shall be deemed to be the exclusive property of the Party possessing such materials.

Amend the definition of “**Protocol**” in Article 2 to read as follows:

“**Protocol**” means the formal, detailed and written 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. Protocols written and conducted under the Research Plan during the term of the CRADA will be mutually agreed to by the Parties. Associated documents for such Protocols will also be mutually agreed to by the Parties.

Amend the definition of “**Test Article**” in Article 2 to read as follows:

“**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. For the purposes of this CRADA, "Test Article" shall be provided solely by the Party which is the IND holder for a clinical study.

**Amend Section 3.2** to read as follows:

**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. The Parties shall use reasonable efforts to achieve the goals and objectives of the Research Plan in an efficient and expeditious manner.

**Amend Section 3.3** to read as follows:

**3.3 Use and Disposition of Collaborator Materials and IC Materials.** The Parties agree to use Collaborator Materials and IC Materials (together with all related written information) only in accordance with the Research Plan and Protocol(s), not to transfer these materials or written information 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 and written information as directed by the owning or providing Party.

**Amend Section 3.6** to read as follows:

**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. The CRADA Principal Investigators shall conduct the Study and use his/her reasonable efforts to complete the research in a professional manner in accordance with the highest professional standards. The NCI CRADA Principal Investigator shall be an employee of IC. Neither Party shall be a party to any agreement nor have any obligation that conflicts with the provisions of this CRADA, and shall not enter into such any conflicting agreement during the research conducted under this CRADA. If either researcher designated as the CRADA Principal Investigator is removed, unable or unwilling to continue in his or her role as CRADA Principal Investigator or terminates his or her employment relationship with the respective Party, then that Party shall promptly provide written notice to the other Party, and shall use its reasonable efforts to find a suitable replacement to assume the role of CRADA

Principal Investigator. The other Party, in its sole discretion, may elect not to accept such replacement, in which event either Party shall have the right to terminate the research and this CRADA subject to the terms in Article 10 of this CRADA. In the event that the other Party accepts such replacement, a Party shall ensure that in such replacement, its CRADA Principal Investigator agrees to adhere to the terms and conditions applicable to the CRADA Principal Investigator under this CRADA.

**Amend Section 3.7** to read as follows:

**3.7 Investigational Applications.**

- 3.7.1 If an IND is required, ~~IC~~the Parties will decide which Party will be the IND Sponsor and the IND Sponsor will submit an IND. All Clinical Investigators must have completed registration documents on file (FDA form 1572 forms).
- 3.7.2 When ~~IC~~a Party files the IND, ~~Collaborator~~the other Party agrees to provide ~~IC~~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~~Party's IND, DMF, other filings, or other information and data provided to ~~IC~~one Party by the ~~Collaborator~~other Party pursuant to this Article 3.
- 3.7.3 If ~~Collaborator~~a Party supplies Confidential Information to ~~IC~~the other Party in support of an IND that is 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.

**Amend Section 3.8** to read as follows:

**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. IC agrees to supply a sufficient quantity of formulated and acceptably labeled, clinical-grade Test Article to complete the clinical trial(s) under this CRADA. IC will maintain a Certificate of Analysis for each lot of the Test Article provided.~~

Section 3.9 is deleted in its entirety:

~~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.~~

Amend Section 4.1 to read as follows:

4.1 **Interim Research and Development Reports.** The CRADA PIs ~~should~~shall exchange information regarding the status of the work hereunder and the results thereof regularly (and not less than quarterly), 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. Additionally, each Party shall update the other Party orally and respond orally to inquiries not less than monthly regarding the status of the work hereunder and the results thereof. Such updates shall be either by telephone or in person, as mutually agreed by the Parties; provided, that not less than once every [ ] the Parties anticipate that such updates shall be in person at a mutually agreed location.

Amend Section 5.2 to read as follows:

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 ~~thesuch other~~ activities will be outside the scope of this CRADA.

Section 5.4 is deleted in its entirety and is of no force or effect in this CRADA.

~~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.~~

**Amend Section 6.5** to read as follows:

**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 or filing relating to prosecution of the Patent Application within 0 of transmission of the communication or filing. The non-filing Party shall have reasonable opportunity to comment thereon, and the filing Party shall reasonably consider such comments. 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.

**Amend Section 7.1** to read as follows:

**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.

Collaborator understands that any license agreement executed by Collaborator for a CRADA Subject Invention or Background Invention grants Collaborator rights to the NIH-owned intellectual property specified in the license agreement within the agreed field of use. This license agreement(s) should not be construed by Collaborator as a license to any third party proprietary agents utilized in the CRADA Research Plan or as freedom to operate in view of any third party proprietary agents.

**Amend Section 7.2** to read as follows:

**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 IC~~ hereby grants to Collaborator an exclusive option to elect an exclusive or, (in the sole discretion of Collaborator) nonexclusive, commercialization license. The license will be substantially in the form of the appropriate model ~~PHS NIH~~ 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 and third party intellectual property and technology 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.

**Amend Section 7.3** to read as follows:

**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 IC** Patenting and Licensing Contact identified on the Contacts Information Page ~~(and provide a copy to the IC Contact for CRADA Notices)~~ within  after either (i) Collaborator receives written notice from **PHS IC** 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~~ **National Institutes of Health** Inventions" and will initiate a negotiation period that expires  after the exercise of the option. If **PHS IC** has not responded in writing to the last proposal by Collaborator within this  period, the negotiation period will be extended to expire  after **PHS IC** so responds, during which month Collaborator may accept in writing the final license proposal of **PHS IC**. In the absence of Collaborator's exercise of the option, or upon election of a nonexclusive license, **PHS IC** will be free to license the CRADA Subject Invention to others. These time periods may be extended at the ~~sole~~reasonable discretion of **PHS IC** upon good cause shown in writing by Collaborator.

**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 IC** 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).

**Amend Section 7.7** to read as follows:

**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 IC** 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.

**Amend Section 8.2.2** to read as follows:

**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](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.

PROPRIETARY INFORMATION

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.

**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 summarize the disclosure in writing and provide it to the other Party within  of the disclosure. Each Party receiving Confidential Information agrees to use it only for the purposes described in the Research Plan. Subject to the requirements as set out in Section 8.6 regarding IPI, Collaborator shall have the right to share CRADA Data, information on CRADA Materials, reports and other Confidential Information relating to this CRADA with third party contractors, actual or potential collaborators or licensees, and actual or potential investors, in each case subject to written confidentiality obligations no less restrictive than those as set out in this CRADA. Either Party may object to the designation of information as Confidential Information by the other Party. Notwithstanding any other provision in this CRADA, although certain information concerning Collaborator Materials or Test Article provided under this Agreement is confidential and will be so stamped, Collaborator recognizes that the NIH 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 NIH 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.** Except as otherwise set forth in this CRADA and 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~~five (35) 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.

**Amend Section 8.7** to read as follows:

**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  to review proposed manuscripts and  to review proposed abstracts and/or other disclosures 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   as necessary to file a Patent Application, or for such other period as may be required by applicable law or regulation.

**Amend Section 9.1** to read as follows:

**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  of receipt of final notice.

9.1.3 The execution and delivery of this CRADA and the performance of IC's obligations hereunder (a) do not conflict with or violate any requirement of applicable laws or regulations, and (b) do not conflict with, or constitute a default under, any contractual obligation of IC.

**Amend Section 9.2** to read as follows:

**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  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.~~ The execution and delivery of this CRADA and the performance of Collaborator's obligations hereunder (a) do not conflict with or violate any requirement of applicable laws or regulations, and (b) do not conflict with, or constitute a default under, any contractual obligation of Collaborator.

**Amend Section 10.3** to read as follows:

**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. Upon any termination of this CRADA, each Party shall return or destroy (as directed by the disclosing Party) any Confidential Information provided by the other Party under this CRADA except that each Party shall be entitled to retain one archival copy thereof for the purposes of determining its obligations under this CRADA. Further, upon termination or suspension for any reason, the Parties shall cooperate and assist the other to promptly wind down all research and development activities under this CRADA, continuing only those activities deemed necessary by reasonable medical judgment to protect the health of the Human Subjects.

**Amend Section 10.4** to read as follows:

**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 already received by IC for that purpose will be available to IC for a period of  after the termination date or until the expiration date of the CRADA, whichever occurs sooner. If, as a result of Collaborator not meeting payment obligations stated in Appendix B, there are insufficient funds to cover this expense, Collaborator agrees to pay the difference.

**Amend Section 10.5** to read as follows:

**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 already received by IC for up to  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.

**Section 10.6** is deleted in its entirety and is of no force or effect in this CRADA.

~~**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.~~

**Amend Section 13.7** to read as follows:

**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 except that Collaborator without such consent may assign this Agreement and its rights and obligations hereunder to any one or more of its Affiliates. Collaborator will notify NIH upon such assignment to its Affiliates of such rights or obligations hereunder. Collaborator shall always have the right to perform any or all of its obligations and exercise any or all of its rights under this Agreement through any one or more of its Affiliates. 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.