

**NATIONAL INSTITUTES OF HEALTH**  
**COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT**  
**FOR**  
**NINDS NeuroNEXT PROGRAM**  
**EXTRAMURAL NIH CLINICAL RESEARCH**

This Agreement is based on the model Cooperative Research and Development Agreement (“CRADA”) adopted on December 8, 2010 by the National Institutes of Health (“NIH”).

This Cover Page identifies the Parties to this CRADA:

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

and

\_\_\_\_\_,  
hereinafter referred to as the “Collaborator,”  
having offices at \_\_\_\_\_,  
created and operating under the laws of \_\_\_\_\_.

# COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT FOR EXTRAMURAL-NIH 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, IC's grantees, 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 attached as Appendix B.

## 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 drug in humans, whether or not considered drug related, as defined under 21 C.F.R § 312.32. 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 the 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.

“**CCC**” means the Clinical Coordinating Center which oversees aspects of the organization and execution of the NeuroNEXT clinical studies and is funded by a Cooperative Agreement with IC.

**“Central IRB”** means the central IRB established by the CCC that will manage all required IRB communication and documentation including but not limited to tracking approvals, maintaining regulatory documents, communicating with Clinical Research Site IRBs, and handling adverse event reporting and notifications.

**“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 Investigational Agent 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.

**“Clinical Research Site(s)”** means the site(s) supported by a Cooperative Agreement at which the Protocol(s) described in the Research Plan will be performed.

**“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 “Investigational Agent” (defined below).

**“Confidential Information”** means confidential scientific, business, financial information, or Identifiable Private Information provided that Confidential 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 Investigational Agent.

**“Contract”** means a Funding Agreement that is a mechanism that provides that the contractor perform for the benefit of the Government, with an expectation of completion of the stated research goals and the delivery of a report, data, materials or other product. Generally, Contracts are administered under the Federal Acquisition Regulations (FAR) codified at Title 48 C.F.R., Chapter 1 or the Health Services Acquisition Regulations (HSAR) codified at Title 48 C.F.R., Chapter 3.

**“Cooperative Agreement”** means a Funding Agreement that is a species of a Grant, whereby the funding Federal agency intends to be substantially involved in carrying out the research program.

**“Cooperative Research and Development Agreement”** or **“CRADA”** means an 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 Collaborator Principal Investigator(s)”** or **“CRADA Collaborator PI(s)”** means the person(s) who will be responsible for the scientific and technical conduct of the Research Plan on behalf of the CRADA Collaborator.

**“CRADA Data”** means information developed by or on behalf of the Parties in the performance of the Research Plan, excluding Raw Data.

**“CRADA Materials”** means all tangible materials first produced in the performance of the Research Plan other than Raw Data, CRADA Data, Collaborator Materials or Investigational Agent. CRADA Materials do not include specimens collected from Human Subjects.

**“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.

**“DCC”** means the Data Coordinating Center which will oversee aspects of the data collection and management for NeuroNEXT clinical trials and is funded by a Cooperative Agreement from IC.

**“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.

**“DSMB”** means the Data Safety Monitoring Board, an independent board appointed by IC to monitor the conduct and safety of NeuroNEXT clinical studies.

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

**“Extramural Investigator”** means a Clinical Investigator who is conducting a NeuroNEXT clinical study at a Clinical Research Site as well as all personnel assisting the investigator in the performance of research under this CRADA.

**“Funding Agreement”** means a Contract, Grant, or Cooperative Agreement entered into between a Federal agency and another party for the performance of experimental, developmental or research work funded in whole or in part by the Federal Government.

**“Government”** means the Government of the United States of America.

“**Grant**” means a Funding Agreement that is an award of financial assistance that may be provided for support of basic research in a specific field of interest to the funding Federal agency.

“**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 (Investigational Agent) 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.

“**Intellectual Property Option**” mean those options included in the Funding Agreements with the Clinical Research Sites;  
[http://www.ninds.nih.gov/news\\_and\\_events/proceedings/IP\\_Options\\_to\\_CRADA\\_collaborators.pdf](http://www.ninds.nih.gov/news_and_events/proceedings/IP_Options_to_CRADA_collaborators.pdf)

“**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.*

“**Investigational Agent**” or Investigational New Drug means, in accordance with the definition in 21 C.F.R. § 312.3, a new drug or biological drug that is used in a clinical investigation. For this Agreement, Investigational Agent means \_\_\_\_\_ provided by or on behalf of Collaborator.

**“Investigator’s Brochure”** means, in accordance with the definition in 21 C.F.R. § 312.23(a)(5), a document containing information about the Investigational Agent, 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.

**“NeuroNEXT”** means the Network for Excellence in Neuroscience Clinical Trials, an IC-funded infrastructure to facilitate rapid development and implementation of protocols in neurological disorders affecting adult and/or pediatric populations.

**“NeuroNEXT Executive Committee”** means the team whose composition and responsibilities with regard to the research performed under this CRADA are described in Article 3.12.

**“NIH CRADA Extramural Investigator/Officer(s)”** means the extramural staff responsible for the conduct and/or management of the CRADA on behalf of the NIH IC.

**“Non-Clinical Investigator”** means any individual who conducts, directs, or assumes responsibility for Non-Clinical Studies as well as all personnel assisting the investigator in the performance of research under this CRADA.

**“Non-Clinical Studies”** means exploratory *in vitro*, *in vivo*, and *ex vivo* studies using defined biological models including cell lines, xenograft models, circulating tumor cells, normal tissue, blood and any of its components and may include ancillary correlative studies, proof-of-mechanism and proof-of-principle assays, development of imaging techniques, and evaluation of target linkage. Non-Clinical Studies may include studies using human materials derived from clinical trials. This defined term shall be limited to studies under this CRADA. Non-Clinical Studies can be performed by Clinical Investigators or Non-Clinical Investigators.

**“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.

**“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.

**“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 clinical investigation in which a drug is administered or dispensed to, or used involving, one or more Human Subjects. 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.

**“Protocol Steering Committee”** means the committee established to ensure efficient implementation of any NeuroNEXT clinical trial; Collaborator will have a voting seat on this committee.

**“Protocol Working Group”** means the group convened to finalize the Protocol for a NeuroNEXT clinical trial; Collaborator will have a voting seat on this group.

**“Raw Data”** means the primary quantitative and empirical data first collected from experiments and clinical trials conducted within the scope of this CRADA. Raw Data is blinded and includes case report forms but excludes IPI and original source documents.

**“Research Plan”** means the statement in Appendix A of the respective 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 Investigational Agents, and is sometimes referred to as the IND holder; for this CRADA, the Sponsor is the Collaborator.

**“Unauthorized Use”** means any unauthorized modifications to the Investigational Agent or the conduct of any unauthorized research using the Investigational Agent.

### **Article 3. Cooperative Research and Development.**

- 3.1 **Performance of CRADA Activities.** The activities to be carried out under this CRADA will be performed by the Parties identified on the Cover Page as well as by IC’s contractors or grantees as described in the Research Plan. However, IC’s contractors or grantees are not Parties to the CRADA, and this CRADA does not grant to Collaborator any rights to Inventions made by IC’s contractors or grantees. Section 8.8 addresses an Intellectual Property Option to Inventions made at Clinical Research Sites. The NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s) will be responsible for coordinating the scientific and technical conduct of this project on behalf of their employers.
- 3.2 **Research Plan.** The Parties recognize that the Research Plan describes the collaborative 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 an NIH license agreement and in which Collaborator had an NIH 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 **Protocol Submission and Compliance.** The Protocol Steering Committee will be required to submit, or to arrange for submission of, each Protocol associated with this CRADA to the Central IRB which will track IRB approvals at the Clinical Research Sites. The research will be done in strict accordance with the Protocol(s) and no substantive changes in a finalized Protocol will be made unless agreed to by the Protocol Steering Committee. 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, the Central IRB or the Protocol Steering Committee, has been integrated in a way acceptable to the Parties, submitted to the FDA (if applicable) and approved by the appropriate IRBs.
- 3.7 **Investigational New Drug Applications.**
- 3.7.1 Collaborator will prepare and submit a related IND. All Extramural Investigators must have completed registration documents on file (1572 forms) with the CCC.
- 3.7.2 Collaborator may sponsor its own clinical trials and hold other INDs 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.
- 3.7.3 Whereas U.S. research sites are preferred, in the event that Collaborator would like non-U.S. institutions to participate in NeuroNEXT trials, Collaborator will need



to process the regulatory documents to allow for such participation.

### **3.8 Investigational Agent Information and Supply.**

- 3.8.1 Collaborator agrees to provide 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 Investigational Agent (and, as required by the Protocol(s), Placebo) to complete the clinical trial(s) agreed to and approved under this CRADA. Investigational Agent should be suitable for shipment to all participating Clinical Research Sites. Collaborator will provide a Certificate of Analysis to the CCC for each lot of the Investigational Agent provided. It is understood that the CCC on behalf of IC shall take responsibility for and reasonable steps to maintain appropriate records and assure appropriate supply, handling, storage, distribution and usage of these materials in accordance with the terms of this Agreement, the Protocol(s) and any applicable laws and regulations relating thereto.
- 3.8.2 Collaborator agrees to supply sufficient inventory to ensure adequate and timely supply of Investigational Agent for mutually agreed upon Protocol(s). The CCC will provide updated forecasts of amounts of Investigational Agent anticipated for ongoing and anticipated studies. Collaborator further agrees to utilize Investigational Agent labels that comply with applicable labeling requirements.
- 3.8.3 If Non-Clinical Studies are included in the Research Plan, Collaborator agrees to provide without charge Investigational Agent or unformulated analytical grade Investigational Agent or metabolites, if available, to Extramural Investigators for the development of mutually agreed upon Non-Clinical Studies such as analytical assays and ancillary correlative studies conducted in conjunction with NeuroNEXT trials. These studies will be approved by the NeuroNEXT Executive Committee and conducted according to mutually approved clinical Protocols.
- 3.8.4 If Non-Clinical Studies are included in the Research Plan, Collaborator agrees to distribute or to allow Investigational Agent to be distributed to Extramural Investigators for mutually agreeable Non-Clinical Studies designed to enhance the basic understanding and development of Investigational Agent. These may include non-clinical studies designed to support clinical trials in pediatric patients; non-clinical combination studies to provide data in support of a clinical trial and other pertinent requests.
- 3.8.5 Collaborator agrees to provide to the CCC the Investigator's Brochure (IB) for Investigational Agent and all subsequent revisions/editions. The IB will be on file with the CCC and will be distributed to all investigators participating on a clinical trial using the Investigational Agent. Distribution will be accompanied by a statement about the confidentiality of the document and it is anticipated that

distribution will be electronic. All electronic distribution will be done using Adobe Acrobat PDF. Any IB received by the CCC that is not in this format will be converted before distribution.

3.9 **Investigational Agent Delivery and Usage.** Collaborator will ship the Investigational Agent and, if required, Placebo to the CCC or its designee in containers marked in accordance with 21 C.F.R. § 312.6. IC agrees that the Clinical Research Sites will keep appropriate records and take reasonable steps to ensure that the Investigational Agent is used in accordance with the Protocol(s) and applicable FDA regulations. In addition, IC agrees that the Investigational Agent (and all Confidential Information supplied by Collaborator relating to the Investigational Agent) will be used solely for the conduct of the CRADA Research Plan. Furthermore, IC agrees that no analysis or modification of the Investigational Agent will be performed without Collaborator's prior written consent. At the completion of the Research Plan, any unused quantity of Investigational Agent will be returned to Collaborator or disposed as directed by Collaborator. The contact persons for the CCC and Collaborator are identified on the Contacts Information Page.

3.10 **Auditing and Monitoring.**

3.10.1 The DSMB will be primarily responsible for monitoring Clinical Research Sites and for assuring the quality of all clinical data, unless otherwise stated in the Research Plan.

3.10.2 Subject to the restrictions in Article 8 concerning IPI, and with reasonable advance notice and at reasonable times, IC will permit: (i) Collaborator or its designee(s) access to Clinical Research Sites to audit the conduct of the research and to obtain updates on ongoing clinical trials at times convenient to Clinical Research Sites; and (ii) Collaborator to make arrangements with IC to audit data and clinical source documents, at the completion of a Protocol and at Collaborator's expense, to the extent necessary to verify compliance with FDA Good Clinical Practice and the Protocol(s).

3.11 **FDA Meetings/Communications.** All formal meetings with the FDA concerning any clinical trial within the scope of the Research Plan will be discussed by Collaborator and IC in advance. Each Party reserves the right to take part in setting the agenda for and to participate in these meetings. The Collaborator will provide IC 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 IND(s) 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.

3.12 **NeuroNEXT Executive Committee and CRADA Research.** The NeuroNEXT

Executive Committee, including an IC representative, representatives from the Clinical Research Sites, the DCC principal investigator, and the CCC principal investigator, conduct and monitor the proposed and ongoing clinical studies and non-clinical research (if any) of the Investigational Agent in accordance with the CRADA Research Plan. Members of the NeuroNEXT Executive Committee shall continue to remain employed by their respective employers under their respective terms of employment.

Additional CRADA information, including NeuroNEXT Executive Committee meeting reports, Protocol Steering Committee records, Protocols, general regulatory information, and non-clinical and clinical data shall remain on file with either the CCC or the DCC.

- 3.13 **Extramural Investigator Meetings.** The Extramural Investigators may decide to meet in-person at various times throughout a NeuroNEXT clinical study. Collaborator may attend such meetings at its own expense.

#### **Article 4. Reports.**

- 4.1 **Interim Research Plan Reports.** The NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s) should exchange information regularly, in writing. This exchange may be accomplished through meeting minutes, detailed correspondence, circulation of draft manuscripts, NeuroNEXT Executive 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 Plan 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. Abstracts and publications provided to IC by investigators and further provided by IC to Collaborator will fulfill this final report obligation. With respect to clinical studies, a copy of the IND(s) Annual Report will also fulfill this reporting obligation.
- 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 Plan 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.** CCC on behalf of IC shall report all serious and unexpected possible,

probable and definite Adverse Events to FDA in accordance with the reporting obligations of 21 C.F.R. § 312.32 and will, within 24 hours of notification to FDA, forward all such reports to Collaborator. All other Adverse Event reports received by the CCC shall be reported to the FDA consistent with 21 C.F.R. §§ 312.32 and 312.33. In the event that Collaborator informs the FDA of any serious and unexpected Adverse Events, Collaborator must notify IC at the same time.

- 4.5 **Annual Reports.** Collaborator will provide IC 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 activities under this CRADA.
- 5.2 **IC Staffing.** No IC employees will devote 100% of their effort or time to the Research Plan. IC will not use funds provided by Collaborator under this CRADA for IC personnel or to pay the salary of any permanent IC employee.
- 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 Plan 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 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. An NIH contractor's or grantee's rights in data it generates will not be affected by this CRADA.
- 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 conduct of the Research Plan. 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 jointly owned CRADA Subject Inventions and will notify NIH 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 NIH of its decision within that time period or notifies NIH of its decision not to file a Patent Application, then NIH 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 in writing 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 for 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 patent office 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 jointly owned CRADA Subject Inventions. If Collaborator elects to file and prosecute Patent Applications on jointly owned CRADA Subject Inventions, then Collaborator agrees to use the U.S.P.T.O. Customer Number Practice and/or grant NIH a power(s) of attorney (or equivalent) necessary to assure NIH access to its intellectual property rights in these Patent Applications. NIH and Collaborator will cooperate with each other to obtain all 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 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 has been filed, NIH hereby offers to the Collaborator the following options and grants:

7.2(a). For CRADA Subject Inventions that would be described in Patent Applications that claim the use and/or the composition of the Investigational Agent(s): NIH hereby grants to Collaborator: (i) an option to elect a royalty-free (except for patent prosecution and maintenance fees for Patent Applications and Patents claiming such CRADA Subject Inventions, which will be pro-rated and divided equally among all licensees), worldwide, non-exclusive license for commercial purposes with the right to sublicense to Affiliates or collaborators working on behalf of Collaborator for Collaborator's development purposes; (ii) a time limited option to negotiate an exclusive, or co-exclusive, if applicable, world-wide, royalty bearing license for commercial purposes, including the

right to grant sublicenses, on terms to be negotiated in good faith by the Collaborator(s) and NIH; and (iii) an option to elect, at Collaborator's sole discretion, a paid-up, nonexclusive, royalty-free, world-wide license for research purposes only. NIH retains the right to make and use any CRADA Subject Inventions covered by this Paragraph 7.2(a) for all non-profit research, including for educational purposes and to permit other educational and non-profit institutions to do so, this license is in addition to the Government use licenses granted in Section 7.4 and 7.5 below.

7.2(b). For CRADA Subject Inventions pursuant to research under this CRADA not covered under Paragraph 7.2(a), including those that use non-publicly available CRADA Data or specimens from patients treated with Investigational Agent under the CRADA, (including specimens obtained from IC-funded tissue banks) NIH hereby grants to Collaborator: (i) an option to elect a paid-up nonexclusive, nontransferable, royalty-free, world-wide license for research purposes only; and (ii) an option to elect a nonexclusive, royalty-free, world-wide license to: (a) disclose such CRADA Subject Inventions to a regulatory authority when seeking marketing authorization of the Investigational Agent, and (b) disclose such CRADA Subject Inventions on a product insert or other promotional material regarding the Investigational Agent after having obtained marketing authorization from a regulatory authority. Notwithstanding the above, NIH is under no obligation to file a Patent Application or maintain patent prosecution for any such CRADA Subject Inventions.

7.2(c). In addition, for Inventions made by NIH's Intramural Investigator(s) or any other employees or agents of IC, which are or may be patentable or otherwise protectable, as a result of research utilizing the Investigational Agent(s), unreleased or non-publicly available CRADA Data or Investigational Agent-treated specimens outside the scope of approval granted by the IC (Unauthorized Inventions): NIH agrees, at Collaborator's request, to grant to Collaborator a royalty-free (except for all out of pocket Patent prosecution and maintenance costs for Patent Applications and Patents claiming such inventions, which will be pro-rated and divided equally among all licensees) exclusive or co-exclusive commercial license to Unauthorized Inventions. The NIH will retain a nonexclusive, nontransferable, irrevocable, paid-up license from the Collaborator to practice the invention or have the invention practiced throughout the world by or on behalf of the Government for research or other Government purposes.

7.2(d). In addition to the license options to CRADA Subject Invention(s) contained in Paragraphs 7.2(b) and 7.2(c) above, NIH hereby grants to Collaborator an exclusive option to CRADA Subject Inventions to elect an exclusive or nonexclusive commercialization license to such Inventions. The field of use of this license option will not exceed the scope of the Research Plan.

**7.3 Exercise of Collaborator's License Option.** To exercise the option(s) or grant(s) set forth in Paragraph 7.2, Collaborator must submit a written notice to the NIH 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 NIH that a Patent Application has been filed or (ii) the date on which Collaborator files a Patent Application. The written notice exercising the option(s) will include a completed “Application for License to NIH Inventions” and will initiate a negotiation period that expires three (3) months after the date of exercise of the option. If NIH has not responded in writing to the last proposal by Collaborator within this three (3) month period, the negotiation period will be extended to expire one (1) month after NIH so responds, during which month Collaborator may accept in writing the final license proposal of NIH. If NIH and Collaborator fail to reach agreement within three (3) months, (or such additional period as described above) on the terms for an exclusive license for a particular Paragraph 7.2(a) Invention, then for a period of three (3) months thereafter NIH agrees not to offer to license the Paragraph 7.2(a) Invention to any third party on materially better terms than those last offered to Collaborator without first offering such terms to Collaborator, in which case Collaborator will have a period of thirty (30) days in which to accept or reject the offer. In the absence of Collaborator’s exercise of the option with respect to a CRADA Subject Invention, or upon election of a nonexclusive license to such Invention, NIH will be free to license the CRADA Subject Invention to others. These time periods may be extended at the sole discretion of NIH 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 NIH grants Collaborator an exclusive, or co-exclusive, license to a CRADA Subject Invention made solely by an IC employee or jointly with a Collaborator employee, the Government will retain the right to require Collaborator to grant to a responsible applicant a nonexclusive, partially exclusive, or exclusive sublicense to use the CRADA Subject Invention in Collaborator’s licensed field of use on terms that are reasonable under the circumstances;



or, if Collaborator fails to grant a license, to grant a license itself. The exercise of these rights by the Government will only be in exceptional circumstances and only if the Government determines (i) the action is necessary to meet health or safety needs that are not reasonably satisfied by Collaborator, (ii) the action is necessary to meet requirements for public use specified by federal regulations, and such requirements are not reasonably satisfied by Collaborator; or (iii) Collaborator has failed to comply with an agreement containing provisions described in 15 U.S.C. § 3710a(c)(4)(B). The determination made by the Government under this Paragraph is subject to administrative appeal and judicial review under 35 U.S.C. § 203(b).

- 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, NIH 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 Raw Data, CRADA Data and CRADA Materials.**

8.1.1 The DCC on behalf of IC will provide Collaborator with Raw Data as applicable throughout the Research Plan within a reasonable time after receipt from the Clinical Research Sites.

8.1.2 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 Raw Data, CRADA Data and CRADA Materials.** The Parties will be free to utilize Raw Data, CRADA Data and CRADA Materials internally for their own purposes, consistent with their obligations under this CRADA. IC may share Raw Data, CRADA Data or CRADA Materials with any contractors, grantees, or agents it has engaged to conduct the Research Plan, provided the obligations of this Article 8.2 are simultaneously conveyed. Collaborator may share Raw Data, CRADA Data or CRADA Materials with any contractors, Affiliates, development partners or agents it has engaged to conduct the Research Plan, provided the obligations of this Article 8.2 are simultaneously conveyed. Collaborator shall not transfer Raw Data or CRADA Data to any third party other than

those set forth in this section without the written permission of the IC; provided, however, that Collaborator may disclose Raw Data or CRADA Data to (1) the FDA, and (2) any third party with whom Collaborator is discussing a potential transaction provided that such third party executes a confidentiality agreement satisfactory to IC requiring the third party to keep all such information confidential. Following IC's permission, Collaborator and such third party shall enter into a Confidential Disclosure Agreement with confidentiality terms at least as stringent as those set forth herein. Collaborator can then transfer the data to such third party.

#### 8.2.1 **Data.**

Collaborator and IC will use reasonable efforts to keep Raw Data and 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 Raw Data and 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 NIH 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://ott.od.nih.gov/NewPages/RTguide\\_final.html](http://ott.od.nih.gov/NewPages/RTguide_final.html), following publication either Party may make available to third parties for further research those CRADA Materials made jointly by both NIH 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 activities under the Research Plan. However, Collaborator will not publish or publicly disclose any Raw Data or CRADA Data provided by IC or by Extramural Investigators under the CRADA without IC's permission or until after such data is made public. Before Collaborator or Extramural Investigators submit a paper or abstract for publication about a CRADA Subject Invention, Raw Data, 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. The obligation to provide advance review will extinguish once data from the NeuroNEXT trial is made public. Either Party may request in writing that a proposed publication be delayed for up to thirty (30) additional days as necessary to file a Patent Application. Manuscripts to be submitted for publication by Extramural Investigators will be sent to Dr. Elizabeth McNeil, NINDS, Neuroscience Center, Room 2215, 6001 Executive Blvd, MSC 9520, Bethesda, MD 20892 (ph: 301-496-9135; email: [mcneilde@ninds.nih.gov](mailto:mcneilde@ninds.nih.gov)) for forwarding to Collaborator for review as soon as they are received and in compliance with the timelines outlined above. Abstracts to be presented by Extramural Investigators will be sent to Dr. Elizabeth McNeil, NINDS, Neuroscience Center, Room 2215, 6001 Executive Blvd, MSC 9520, Bethesda, MD 20892 (ph: 301-

496-9135; email: [mcneilde@ninds.nih.gov](mailto:mcneilde@ninds.nih.gov)) for forwarding to Collaborator as soon as they are received, preferably no less than three days prior to submission, but prior to presentation or publication, to allow for preservation of U.S. or foreign patent rights.

- 8.8 **Clinical Investigators' Research and Non-Clinical Investigators' Development Activities.** In pursuing the development of Investigational Agent pursuant to this CRADA, IC will utilize Extramural Investigators at Clinical Research Sites that are not IC employees for part or all of the completion of the Research Plan, which will cover clinical studies and possibly Non-Clinical Studies through Funding Agreements. All Funding Agreements for the conduct of NeuroNEXT clinical trials and Non-Clinical Studies will include the Intellectual Property Option to Collaborator (including any updates) offering Collaborator first rights of negotiation to extramural Inventions (web site: [http://www.ninds.nih.gov/news\\_and\\_events/proceedings/IP\\_Options\\_to\\_CRADA\\_collaborators.pdf](http://www.ninds.nih.gov/news_and_events/proceedings/IP_Options_to_CRADA_collaborators.pdf)).
- 8.9 **Access, review and receipt of Identifiable Private Information.** Collaborator access to and review of Identifiable Private Information shall be only for on-site quality auditing. Collaborator will receive Identifiable Private Information only if necessary for purposes of satisfying FDA or other health authorities' reporting requirements, and for internal research purposes, directly related to obtaining regulatory approval of Investigational Agent. Collaborator is prohibited from access, review, receipt, or use of such information for other purposes. All IRB approved Protocols and informed consent documents related to this research project will clearly describe this practice. If the Collaborator will have access to Identifiable Private Information, the Protocol and the informed consent must clearly state (i) the existence of the Collaborator; (ii) the Collaborator's access to Identifiable Private Information, if any; and (iii) the extent to which confidentiality will be maintained. For clinical Protocol(s) involving a third party, the other party's access, review, receipt, or use of Identifiable Private Information shall be subject to the same limitations as described in this Article 8.9.

## **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 that would directly affect its performance of the CRADA. Should IC become aware that any of its personnel involved in this CRADA are debarred or suspended during the term of this CRADA, IC will

notify Collaborator within thirty (30) days.

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 become aware that any of its personnel involved in this CRADA are debarred or suspended during the term of this CRADA, Collaborator will notify IC within thirty (30) days.

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 Investigational Agent 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 Q7, 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 (see page \_\_\_ of this CRADA) unless it is extended in writing in accordance with Paragraph 13.6.

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

10.3 **Termination Upon DSMB Recommendation.** The Parties agree that study enrollment and/or this CRADA may be terminated for safety, futility or other concerns upon the final recommendation of the DSMB. In the case of terminated enrollment, continued follow-up of then-enrolled subjects is likely and the CRADA may still be in effect. DSMB concerns may arise during the conduct of the Research Plan or from information obtained about the Investigational Agent in a non-NeuroNEXT clinical trial. IC retains the option of posting a notice on its website regarding the termination or issuing an informational press release; IC will provide Collaborator with advance notice in accordance with Article 13.10.

- 10.4 **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. If Collaborator unilaterally terminates this CRADA before the completion of all approved or active Protocol(s) and IC wants to complete the Research Plan, then:
- (1) Collaborator will supply enough Investigational Agent (and Placebo, if applicable) to complete the Protocol(s);
  - (2) IC may, at its option, retain Collaborator funds transferred to IC before unilateral termination by Collaborator for use in completing the Research Plan;
  - (3) if IC determines it necessary to file an investigator IND in order to complete the Research Plan, Collaborator agrees to execute such documents as may be reasonably required to support an investigator IND, including a cross-reference to existing regulatory documentation;
  - (4) Collaborator will not receive Raw Data, CRADA Data or CRADA Materials and will not receive advance review of proposed manuscripts or abstracts; however, foregoing items received prior to unilateral termination must be kept confidential or as otherwise restricted under this CRADA;
  - (5) upon the date of the unilateral termination, Collaborator will be excluded from the Protocol Working Group, the Protocol Steering Committee, and the investigator meetings; and
  - (6) the Parties will continue to exchange information concerning serious and unexpected possible, probable and definite Adverse Events.
- 10.5 **New Commitments.** Except as may be required to fulfill the terms of Article 10.4, 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 five (5) years subsequent to the expiration or termination date to cover any unpaid costs obligated during the term of the CRADA in undertaking the activities set forth in the Research Plan.
- 10.6 **Collaborator Failure to Continue Development.** If Collaborator suspends development of the Investigational Agent without the transfer of its active development efforts, assets, and obligations to a third party within one hundred eighty (180) days of discontinuation, Collaborator agrees that IC may continue developing the Investigational Agent. In that event, Collaborator agrees to transfer to IC all information necessary to enable IC to contract for the manufacture of the Investigational Agent and, unless abandoned for reasons relating to safety as determined by the data safety monitoring board, to provide the Investigational Agent (and Placebo, if any) in Collaborator's inventory to IC or arrange for an independent contractor to manufacture and provide Investigational Agent to IC for two years or until the completion of ongoing mutually agreed to Protocols.

**Article 11. Disputes.**

- 11.1 **Settlement.** Any dispute arising under this CRADA which is not disposed of by agreement of the NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s) 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 Article 11 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 Research Plan 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 and Corporate Integrity Policy. 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 NIH CRADA Extramural Investigator/Officer(s) and CRADA Collaborator PI(s). Substantial changes to the Research Plan (Appendix A of this CRADA) and any changes to the CRADA including extensions of the term 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 CRADA. 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. If Collaborator elects to perform any portion of the Research Plan through a contractor(s) or consultant(s), Collaborator agrees to incorporate into such contract all provisions necessary to ensure that the work of such contractor(s) or consultant(s) is governed by the terms of the CRADA, including, but not limited to a provision for the assignment of inventions of the contractor(s) or consultant(s) to the Collaborator.
- 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 or complete Summary Page (all on page \_\_\_ of this 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, including 21 U.S.C. 382 and 21 C.F.R. Part 312.110. 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, including (add other related agreements).
- 13.14 **Survivability.** The provisions of Paragraphs 3.3, 3.4, 3.8, 4.2, 4.3, 4.4, 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 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:

\_\_\_\_\_  
Walter J. Koroshetz, M.D.  
Acting Director  
National Institute of Neurological Disorders and Stroke

\_\_\_\_\_  
Date

FOR COLLABORATOR:

\_\_\_\_\_

\_\_\_\_\_  
Date

**CONTACTS INFORMATION PAGE**

**CRADA Notices**

For IC:

For Collaborator:

**Patenting and Licensing**

For IC:

For Collaborator:

**Delivery of Materials Identified In Appendix B (if any)**

For IC:

For Collaborator:

N/A

N/A

**Investigational Agent Delivery**

For IC:

For Collaborator:

**Investigator's Brochure**

For IC:

For Collaborator:

**Press Releases**

For IC:

For Collaborator:

**Review of Manuscripts and Abstracts**

For IC:

For Collaborator:

**Adverse Events, Safety Reports**

For IC:

For Collaborator:

**Protocol Issues**

For IC:

For Collaborator:

## SUMMARY PAGE

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

TITLE OF CRADA:

NIH IC Component:

National Institute of Neurological Disorders  
and Stroke

NIH CRADA Extramural Investigator:

Elizabeth McNeil, M.D., M.Sc.

NIH CRADA Extramural Officer:

Collaborator:

CRADA Collaborator Principal Investigator:

Term of CRADA:

\_\_\_\_ ( ) years from Effective Date

ABSTRACT OF THE RESEARCH PLAN:

**APPENDIX A: RESEARCH PLAN**

*(NINDS has information about appropriate language and proper formatting for this appendix.)*

## **APPENDIX B**

### **Financial and Staffing Contributions of the Parties**

*(NINDS has information about appropriate language and proper formatting for this appendix.)*