NEURONEXT MASTER CLINICAL TRIAL AGREEMENT

Clinical Coordinating Center ("CCC"): The The General Hospital Corporation dba Massachusetts General Hospital 55 Fruit Street Boston, MA 02114	**NeuroNEXT Site ("NNS"):**
CCC Principal Investigator ("CCC PI"): Merit E. Cudkowicz, M.D.	**NNS Principal Investigator ("NNS PI"):**
CCC Administrative Contacts: Krista Valladares kvalladares@mgh.harvard.edu 617-643-8251 Raji Bhat rbhat@mgh.harvard.edu 617-726-6266	**NNS Administrative Contact:**
CCC Agreement Contact: Paul Whitty pwhitty@partners.org	**Clinical Study Site ("CSS"):**

The General Hospital Corporation d/b/a Massachusetts General Hospital as the Clinical Coordinating Center (referenced above and hereinafter referred to as "CCC"), _____ (referenced above and hereinafter referred to as "NNS"), and Clinical Study Site (referenced above and hereinafter referred to as "CSS"), all hereinafter individually refered to as "Party" and collectively as "Parties," enter into this Master Clinical Trial Agreement ("Agreement") for the purpose of establishing the relationship among the CCC, NNS and CSS as participating in the Network for Excellence in Neuroscience Clinical Trials ("NeuroNEXT") funded by the National Institutes of Health ("NIH"). The Parties agree to the terms and conditions herein, as follows:

Article 1: TERM.

This Agreement shall be effective only through the duration of the NNS's Cooperative Agreement with the National Institute of Neurological Disorders and Stroke ("NINDS") ,Grant no. _____ ("NNS Cooperative Agreement"). The anticipated period of performance of the NNS Cooperative Agreement is _____through_____ ("Period of Performance").

Article 2: NeuroNEXT MEMBERSHIP.

NeuroNEXT provides a robust, standardized, and accessible infrastructure to facilitate the rapid development and implementation of protocols in neurological disorders, in both adult and pediatric populations. The network includes Network Member Sites, Clinical Study Sites, a Clinical Coordinating Center, and a Data Coordinating Center ("DCC"). As a Network Member Site, the NNS provides data for use by the NeuroNEXT leadership team to determine feasibility of conducting proposals submitted to NIH and participates as an enrolling site in NeuroNEXT clinical trials approved for funding by NIH ("Study" or "Studies"). When NNS/CSS is selected as a performance site in a Study, NNS/CSS conducts the Study as outlined in the central Institutional Review Board ("cIRB") approved protocol ("Protocol" or "Protocols") and submits data through the Study-specific electronic data capture system ("EDC System").

CCC will make payments directly to sites (NNS/CSS) for data entered into the EDC system as outlined in the schedule of activities for individual studies. All terms and conditions herein applicable to NNS also apply to CSS when participating in network funded studies.

Article 3: PROTOCOL DEVELOPMENT AND PARTICIPATION.

NINDS solicits applications for Protocols to be implemented through NeuroNEXT. Protocol submission guidelines are publicly available at https://neuronext.org/ ("NeuroNEXT Website") to assist investigators interested in collaborating with NeuroNEXT. Investigators interested in using NeuroNEXT submit a protocol concept form for initial consideration by NINDS and subsequent consideration by the NeuroNEXT Executive Committee ("NEC"), who assesses NeuroNEXT capacity and project feasibility and provides a recommendation to NINDS. NINDS notifies requesting investigators ("Protocol PIs") of approval to work with the CCC and DCC on protocol development. The Protocol PI works with the Protocol Working Group ("PWG") to develop the protocol and budget prior to submitting the pre-proposal to the Extramural Scientific Committee ("ESC"). Once the concept and initial budget are approved by ESC, The Protocol PI continues to work with the Protocol Working Group ("PWG") to advance the protocol's development and budget in preparation for a full grant submission to the NINDS for funding. Following submission, applications will be peer-reviewed by a Special Emphasis Panel ("SEP") at NINDS. Selection of protocols to go forward in NeuroNEXT will be made by the NINDS with approval of the NINDS Advisory Council based on their scientific merit. Following approval by the NINDS Advisory Council, the protocol will be finalized by the Protocol Steering Committee ("PSC"). Sites with approved protocols are referred to as Protocol PI Sites ("PPI").

CCC will distribute approved NeuroNEXT Protocols to all Network Member Sites to determine which sites elect to participate. When the Parties mutually determine that the NNS will participate in a NeuroNEXT Protocol, the CCC will send a NeuroNEXT Protocol Award Letter ("Protocol Award Letter") outlining the Study name, Protocol PI Site name, Protocol PI Site, NIH Grant Number, budget and payment schedule. A sample Protocol Award Letter is attached hereto as Appendix A.

Article 4. POLICIES AND PROCEDURES.

The CCC and DCC have developed NeuroNEXT Standard Operating Procedures ("NeuroNEXT SOPs") and Policies ("NeuroNEXT Policies") that pertain to collaborative activities of NeuroNEXT and the CCC, DCC and each NNS. NeuroNEXT SOPs and Policies are found on the NeuroNEXT Website: https://neuronext.org/neuronext-standard-operating-procedures. By signing this Agreement, NNS agrees to follow NeuroNEXT SOPs and Policies in the conduct of NeuroNEXT Protocol(s) and administration of this Agreement.

Article 5. INDEPENDENT CONTRACTOR.

NNS hereby acknowledges that all employees hired by it, under or as a result of this Agreement, shall, during the Period of Performance, be deemed to be employees of NNS and, therefore, not entitled to any retirement or other fringe benefits from CCC.

Neither Party shall have authority to make any statements, representations, or commitments of any kind, or to take any action which shall be binding on the other Party, except as may be explicitly provided for herein or authorized by the other Party in writing.

NNS shall pay all debts for labor and materials contracted for by it, and for the rental of appliances and equipment hired by it, for and on account of, the responsibilities to be performed hereunder. NNS shall conform to all requirements of law and all other public authorities, state or local, relating to the methods or materials to be used or to the persons to be employed in the performance of this Agreement.

Article 6. PROFESSIONAL RESEARCH.

In the conduct of NeuroNEXT Protocols and administration of this Agreement, the NNS will observe the following provisions:

a. **Conduct of Clinical Trials**. The NNS agrees to assume all responsibility to treat and follow research participants according to NeuroNEXT Protocols, the NNS Cooperative Agreement, and applicable federal regulations. The complete NeuroNEXT Protocol List is posted to the NeuroNEXT Website. Updates to the NeuroNEXT Protocol List are made each time a new Protocol is appproved. In the event the NNS PI leaves the NNS institution, the NNS is responsible to make arrangements for continuity of treatment, follow-up, and data collection for patients already entered into NeuroNEXT studies and shall promptly notify the CCC of such arrangements. Such notice shall include the name of a new NNS Principal Investigator.

b. **Human Subjects Protection.** The NNS agrees to comply with 45 CFR Part 46, Subpart A, "Basic HHS Policy for the Protection of Human Subjects"("HHS Regulations"). An OHRP-approved Federal Wide Assurance ("FWA") of compliance with HHS Regulations (45 CFR 46.103) for the protection of human subjects must be submitted to the CCC and renewed every five years. The NNS shall also be responsible for carrying out all Protocol activities in accordance with the NeuroNEXT Central Institutional Review Board ("Central IRB") Authorization Agreement signed between the CCC and NNS.

c. **Research Participants Accrual Requirements.** The NNS shall participate in at least four different NeuroNEXT Protocols. Research Participant accrual requirements shall be in accordance with the individual Protocol.

d. **Scientific Misconduct Policy.** The NNS certifies that it has established administrative policies as required by 42 CFR 50, Subpart A, "Responsibilities of PHS Awardee and Applicant Institutions for Dealing with and Reporting Possible Misconduct in Science," and will comply with the policies and requirements set forth therein.

e. **Conflict of Interest.** The NNS shall be responsible for compliance with 42 CFR Part 50, Subpart F & 45 CFR Subtitle A, Part 94 ("FCOI Regulations"). If a financial conflict of interest as defined by the Regulations ("FCOI") is identified by the NNS during the period of any Award Letter made under this Agreement, the NNS will be responsible for the timely reporting of the FCOI and submission of all accompanying information required by the FCOI Regulations directly to the Grants Management Specialist identified in the NNS Cooperative Agreement. Furthermore, the NNS shall provide the Central IRB (via the CCC IRB Liaison) with a copy of said report together with such additional information concerning the reported FCOI as is specified in the NeuroNEXT Central IRB Authorization Agreement.

   It is the expectation of the parties that the IND/IDE holder for each NeuroNEXT Protocol is responsible for compliance with the Food and Drug Administration ("FDA") regulations regarding Financial Disclosure by Clinical Investigators, 21 CFR Part 54, and is responsible for obtaining and maintaining documentation of financial information from clinical investigators in compliance with 21 CFR 312.53 and 21 CFR 812.43, as applicable. The CCC may, upon request, assist IND/IDE Sponsors with their implementation of these requirements.

f. **Confidentiality**. "Confidential Information" shall mean any business or proprietary information provided by one party to the other and clearly identified as "Confidential" by appropriate marking by the transmitting party at the time of disclosure. If such transmittal

occurs orally, the transmitting party will within thirty (30) days reduce such transmittal to written form, mark and identify it as confidential, and provide such record to the other party. In the event that a Party discloses Confidential Information to the other during the Project, the receiving Party agrees to disclose the Confidential Information only on a need-to-know basis to its employees, directors or other advisors or representatives who are subject to confidentiality obligations, to use the Confidential Information only for the purposes contemplated by this Agreement and to use reasonable efforts to prevent its disclosure to third parties.

However, the receiving Party may disclose the Confidential Information if such information (i) was already in the public domain or becomes publicly available through no wrongful act of receiving Party, (ii) was previously known or developed by the receiving Party without any violation of existing confidentiality obligations, (iii) was known by receiving Party prior to disclosure by disclosing Party, as evidenced by tangible records; (iv) becomes known to receiving Party after disclosure from a third party having an apparent bona fide right to disclose it; (v) is independently developed or discovered by receiving Party without use of disclosing Party's Confidential Information, as evidenced by tangible records; or (vi) was required to be disclosed by operation of law. These obligations of confidentiality shall be effective for a period of seven (7) years from the date of disclosure.

g. Data. Study Data is data first developed and delivered by the NNS to the DCC in the conduct of a NeuroNEXT Study. The NNS may use its own Study Data for non-commercial research and educational purposes in accordance with the restrictions listed herein including but not limited to the Study subjects' Central IRB-approved informed consent, the data sharing plan approved by NINDS as specified in the NeuroNEXT Proposal for the NNS Cooperative Agreement, the Health Information Portability and Accountability Act of 1996 ("HIPAA"), NeuroNEXT SOPs and Policies, and any other applicable federal, state or local government laws or regulations.

h. Publication. Each NeuroNEXT Study is a multi-site study and a collaborative publication is anticipated. NNS agrees that it shall delay publication using its own Study Data until such time as the collaborative publication is released or eighteen (18) months after the conclusion of the Study and Study Data lock, whichever occurs first.

Publication and Data Sharing Committees have been appointed by the NEC and shall be responsible for developing and disseminating scientific and medical knowledge derived from the NeuroNEXT Network, with due regard for the scientific merit of each proposed publication. A NNS PI who participated in the Study may apply to the Data Sharing Committee for access to the multi-site Study Data. If the NNS Investigator desires to publish independently, he/she shall submit proposed manuscripts to the Publication Committee for review and comment at least thirty (30) days prior to submission for publication, and shall consider in good faith all comments provided by the Publication Committee during that review period. In the event that the Publication Committee identifies Confidential Information, the NNS agrees that such Confidential Information shall be removed from the publication. In the event that the Publication Committee determines that the manuscript contains patentable information, the NNS shall delay publication for a period of not longer than an additional sixty (60) days to allow for patent protection to be sought.

Authorship and other matters relating to publications shall be determined in accordance with academic standards. All publications shall comply with the NNS Cooperative Agreement, HIPAA, NeuroNEXT Policies and the NIH Public Access Policy (http://publicaccess.nih.gov/).

In the event the NNS PI independently publishes in accordance with this Article, the NNS agrees that the support of the NIH and NINDS shall be acknowledged, whenever research findings funded in whole or in part by this Agreement are published.

i. **Copyright.** The NNS grants to CCC an irrevocable, royalty-free, non-transferable, non-exclusive right and license to use, reproduce, make derivative works, display, and perform publicly any copyrights or copyrighted material (including any computer software and its documentation and/or databases) first developed and delivered under this Agreement solely for the purpose of and only to the extent required to meet CCC's obligations to the Federal Government under its NeuroNEXT Cooperative Agreement from NINDS ("CCC Cooperative Agreement").

j. **Intellectual Property Rights.** Intellectual Property terms and conditions can be found within NNSthe NNS Cooperative Agreement.

Article 7. TERMINATION.
This Agreement may be terminated before its expiration by the CCC with written notice provided to the NNS at least thirty (30) days prior to the termination date. Termination includes termination for convenience.

Notwithstanding, the Parties hereby agree that this Agreement immediately terminates upon expiration or early termination of the NNS Cooperative Agreement or Authorization Agreement.

Article 8. LIABILITY AND INSURANCE.
The NNS shall be responsible for its own negligent acts or omissions and the negligent acts of its employees, officers, or directors, to the extent allowed by law.

The NNS agrees to maintain, for the duration of this Agreement, insurance, or a program of self-insurance, in an amount that will be adequate to cover its respective obligations hereunder, and, upon request, will provide CCC proof of insurance showing that such insurance is in place.

Article 9. REQUIRED ASSURANCES.
NNS certifies and assures the CCC that it is in compliance with all applicable federal regulations related to NNS' conduct of NeuroNEXT Protocols and the administration of this Agreement, including but not limited to the applicable regulations of the U.S. Department of Health and Human Services, ("DHHS" or "HHS"), the U.S. Public Health Service ("PHS"), the Code of Federal Regulations ("CFR"), the NIHGPS and Uniform Guidance.

Article 10. CONTINUING COMPLIANCE.
The NNS agrees that the terms of this Agreement entered into between the CCC and the NNS including the certification of compliance with all regulatory requirements in Article 9 above, shall apply to the NNS in the conduct of each NeuroNEXT Study. Compliance with Article 9 by the NNS will be evidenced by NNS' signature on this Agreement and NNS entering Study Data into the NeuroNEXT Website.

Article 11. PAYMENTS.
Per-Case Payment Program. The CCC will pay sites for work-performed in alignment with the applicable Study's schedule of activities and NNS/CSS' entry of complete and accurate data into the EDC System. These payments, made with funds provided by the PPI are to defray the costs incurred in treating and following research participants on selected NeuroNEXT Protocols. The CCC will prepare and pay

invoices, on a quarterly basis, using information obtained from the DCC regarding completed case report forms attributable to the NNS/CSS. Per-accrual payments will continue based on availability of funds for the designated Study in each fiscal year.

a. **Funding Sources.** The funding for each Protocol will be provided to the CCC by the PPI for distribution to participating NNS/CSSs. The source of funding, including the NIH Grant Number and Catalog of Federal Domestic Assistance ("CFDA") Number, will be indicating in each Award Letter.
b. **Facilities and Administration or Indirect Rates.** The CCC will distribute the per-patient cost to the NNS on a total fixed rate basis. As mandated by the CCC Cooperative Agreement, to take into account differences in indirect rates, the CCC has worked with the NINDS to determine a low, moderate and high indirect tier for the NNS and include a fixed percentage of indirect costs (uniform within that tier) in the total cost. The CCC will include applicable indirect rates in each Award Letter.

Article 12. NOTICES. All notices and demands required there under shall be deemed given upon personal delivery or next business day following sending by reputable overnight delivery carrier or three (3) business days following sending by United States Registered or Certified mail, postage prepaid addressed to the NNS and the CCC, at the address first above written.

Article 13. NO WAIVER. The failure of either Party at any time to enforce any right or remedy available to it under this Agreement with respect to any breach or failure by the other party, shall not be construed to be a waiver of such right or remedy with respect to any other breach or failure by the other party.

Article 14. SEVERABILITY. The presence in this Agreement of any clause, sentence, provision, paragraph or article held to be invalid, illegal or ineffective by a court of competent jurisdiction, shall not impair, invalidate or nullify the remainder of this Agreement. The effect of any such holding shall be confined to the portion so held invalid.

Article 15. HEADING. The headings used in this Agreement are for convenience only and are not intended to be considered in construing its terms. The use in this Agreement of the terms "include"; "includes"; and "such as" shall be deemed in all cases to be followed by the words "without limitation."

Article 16. LAW. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts and the United States.

If the NNS is prohibited by law from complying with the laws of the Commonwealth of Massachusetts, this Article is inapplicable.

Article 17. AMENDMENTS. This Agreement may be amended only by a written instrument signed by both Parties. The Parties anticipate that amendments may be necessary in circumstances where industry funding is being provided and such funding necessitates the incorporation of the additional legal terms to this Agreement.

Article 18. ENTIRE AGREEMENT. This Agreement, the NeuroNEXT Policies and Procedures, and any amendments mutually agreed upon in writing comprise the complete and entire agreement between the CCC and the NNS.

Article 19. SURVIVAL.
The following Articles of this Agreement shall survive the expiration or early termination of this Agreement, as allowed by law: *Article 6(b) Human Subjects Protection; Article 6(g): Data; Article 6(h):*

Publications; Article 6(i) Copyright; *Article 6(j): Intellectual Property Rights*; *Article 8: Liability and Insurance;* and this *Article 19.*

IN WITNESS WHEREOF, the parties have executed this Agreement in two (s) counterparts, each of which shall be deemed an original and do hereby warrant and represent that their respective signatory whose signature appears below has been and is on the date of this Agreement, duly authorized to execute this Agreement.

Clinical Coordinating Center (CCC)

_____
Name: Stephanie Stone
Title: Director-Contracting

_____
Date

NeuroNEXT Site (NNS)

_____
Name:
Title:

_____
Date

Clinical Study Site (CSS)

_____
Name:
Title:

_____
Date

Appendix A: Protocol Award Letter Sample

See attached