OneIRB

Institutional Review Board (IRB) Reliance Agreement

Name of Institution or Organization Providing IRB Review (Designated IRB):

The University of Miami Institutional Review Board

IRB Registration #: IRB00005621, IRB00005622, IRB00006078, IRB00000260

Federalwide Assurance (FWA) #: FWA00002247

Name of Institution(s) Relying on the Designated IRB (Relying Institution):

Benaroya Research Institute at Virginia Mason (BRI)

IRB Registration #: 00000057 Federalwide Assurance (FWA) #: FWA00001994 and FWA00001995

The Officials signing below agree that Relying Institution may rely on the Designated IRB for review and continuing oversight of its human subjects research described below:

(Check one)

(___) This Agreement is limited to the following specific protocol(s):

Name of Research Project: _____
Name of Principal Investigator: _____
Sponsor or Funding Agency: _____
Award Number, if any: _____

(_X_) This Agreement applies to all human subjects research studies conducted at Relying Institution for TrialNet.

Terms of Agreement

I. Background

This Institutional Review Board Reliance Agreement ("Agreement") is to: (1) establish the Designated IRB as the IRB of Record for Relying Institution with respect to human subject research conducted through TrialNet and (2) to set forth the respective authorities, roles, and responsibilities of each party in such arrangement.

Both Designated IRB and Relying Institutions agree that review and approval of human subjects research under this Agreement shall be conducted in compliance with the federal regulations

as codified in 45 CFR 46 and 21 CFR 50 & 56 (as applicable), other pertinent federal regulations, state and local laws, and all applicable human research protection program (HRPP) policies at the Designated IRB's institution.

Both Designated IRB and Relying Institution agree to maintain effective communication and cooperation with the OneIRB Coordinating Center, referred to in this document as the Coordinating Center, as described in this Agreement to ensure adequate protections for human research subjects including providing relevant documentation and records as needed.

Both Designated IRB and Relying Institution agree they are primarily responsible for safeguarding the rights and welfare of research participants and that the rights and welfare of participants must take precedence over the goals and requirements of the research.

Both Designated IRB and Relying Institution agree that the liability of the Designated IRB is limited to its regulatory review and oversight of research covered by this Agreement and that Designated IRB will assure the protection of the rights and welfare of human subjects and will ensure its reviews and determinations are in accordance with all applicable federal regulations and human subjects protection requirements, state and local laws, and institutional policies and procedures.

Both Designated IRB and Relying Institution agree to develop or maintain standard operating procedures consistent with this Agreement.

This Agreement does not preclude Relying Institution or the researchers from taking part in research not covered by this Agreement.

This Agreement meets federal requirements for designation of another institution's IRB as the reviewing IRB, as set forth in the Office for Human Research Protections ("OHRP") document Terms of the Federalwide Assurance current as of June 2011. This Agreement will be kept on file at each signatory institution and will be provided to OHRP or other federal agencies upon request.

II. General Terms

Eligibility

Relying Institution's eligibility for participation in this Agreement is contingent on (i) its participation as a TrialNet Study Site and (ii) its maintenance of a current, OHRP-approved FWA.

The process for ceding IRB review of specific Research Projects is set forth in a document entitled "OneIRB Standard Operating Procedures." The purpose of these standard operating procedures (SOPs) is to set forth the requirements and otherwise provide guidance to Investigators, Designated IRBs, Relying Institutions, and Coordinating Center personnel about the processes for using a Single IRB of Record and Coordinating Center for multi-site research studies. For IRBs, these SOPs are intended to supplement, not replace, existing Human Research Protection Program (HRPP) policies and SOPs for the review of human subject research.

III. Roles, Responsibility, and Authority of Designated IRB

1. Federalwide Assurance. Designated IRB Institution will maintain a current, approved FWA with OHRP for the duration of this Agreement. Designated IRB will promptly notify Relying Institution via the Coordinating Center if its FWA is terminated or expires for any reason.

2. Designated IRB Review in Accordance with FWA. The Designated IRB will perform initial review and continuing oversight of the Studies included in this Agreement including review of informed consent forms, modifications to previously approved research, continuing reviews, and reportable events including unanticipated problems and noncompliance, in accordance with the human subjects protection requirements of Relying Institution's OHRP-approved FWA and the federal regulations and ethical principles referenced therein. Designated IRB will ensure proposed research funded in whole or in part by a federal entity are consistent with the grant provisions. Review by the Designated IRB will take into account the requirements of the local research context identified by Relying Institution.

3. Investigator Conflicts of Interest. The Designated IRB will review any financial conflicts of interest identified by Relying Institution and communicated to Designated IRB as part of the local context review, along with any resulting conflict of interest management plan. The Designated IRB has the authority to impose additional prohibitions or conflict management requirements more stringent or restrictive than what Relying Institution has implemented that are necessary for the Designated IRB to approve the Study.

4. Suspension or Termination of IRB Approval. The Designated IRB has the authority to suspend or terminate approval of all or part of a research study that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval includes a statement of the reasons for the IRB's action and is reported promptly to the investigator, appropriate institutional officials, department or agency head and regulatory agencies in compliance with 45 CFR 46.103(b)(5)(ii), 45 CFR 46.113, 21 CFR 56.108(b)(3) and 21 CFR 56.113.

5. Informed Consent Form. The Designated IRB will review informed consent forms for each study included under this Agreement. The forms will be consistent among sites except for site-specific language included by Relying Institution. Designated IRB will provide approved informed consent forms for each site to the Coordinating Center to distribute to Investigators for use at their sites.

6. HIPAA Authorization. The Designated IRB will perform the determinations required by the Health Insurance Portability and Accountability Act of 1996, the Health Information Technology for Economic and Clinical Health Act of 2009, and their implementing regulations (collectively, "HIPAA") with respect to the mechanisms for permitting the use and disclosure of Protected Health Information ("PHI") for the Studies included in this Agreement, namely authorization and waivers of authorization for use and disclosure of PHI as applicable. When an authorization will be used, the Designated IRB will also provide as part of the approved informed consent form authorization for use and disclosure of PHI. Such authorization shall explicitly permit PHI to be

used and shared by and with the Designated IRB, the Designated IRB's Institution, the Rare Disease Clinical Research Network Data Management and Coordinating Center, the Relying Institution, and all Study Sites and their investigators participating in a Study as necessary for conducting, reviewing, and overseeing the Study (including investigation and evaluation of events) as contemplated by the protocol and this Agreement.

Each party shall be independently responsible for its own HIPAA compliance and obligations (for example, minimum necessary requirements, or accounting of disclosures of PHI made pursuant to a waiver of authorization) in connection with the Studies included in this Agreement other than the initial determinations regarding mechanisms for use and disclosure of PHI referenced in this Agreement.

7. Reports to Sponsors and Oversight Authorities. Designated IRB will report to sponsors/funding agencies, OHRP, FDA, and/or other oversight authorities of unanticipated problems involving risks to subjects or others, serious or continuing non-compliance, and suspension or termination of IRB approval in connection with the Studies included in this Agreement, and will provide a copy of the report to the Coordinating Center. The Designated IRB will provide the Relying Institution the opportunity to review and comment on the report before it is sent. Submission of such report by the Designated IRB does not preclude Relying Institution from submitting report.

8. Designated IRB Decisions; Minutes. Determinations made by the Designated IRB will be communicated to the Coordinating Center in writing. Designated IRB will maintain IRB records in accordance all applicable federal, state, and local regulations including 45 CFR 46.115, and will make records available when and as required by law. Relevant minutes of the Designated IRB's meetings pertaining to an included Study will be made available to the Coordinating Center upon request.

9. Post-Approval Monitoring. The Designated IRB reserves the right to conduct post-approval monitoring of Studies included in this Agreement. Designated IRB agrees that Relying Institution may also conduct post-approval monitoring of Studies included in this Agreement either in addition to, or in conjunction with the Designated IRB. Designated IRB and Relying Institution will notify Coordinating Center of such post-approval monitoring.

10. Coordinating Center. The Designated IRB agrees to accept IRB submissions from and communicate with the Coordinating Center for all studies included in this Agreement. The Designated IRB agrees that the Coordinating Center serves the role of collecting information from sites, completing IRB submissions, responding to IRB queries, and distributing notifications of IRB determinations to participating Investigators and relying Institutions.

IV. Roles, Responsibility, and Authority of Relying Institution

1. Local Research Context: State/Local Law; Conflicts of Interest; Other Local Ancillary Committee Reviews. The role of the Relying Institution is to conduct a review of the protocol for local context issues and to provide documentation of such review to the Coordinating Center. The Coordinating Center will provide Relying Institution with the protocol and Certification of Local

Context Review form to complete. Relying Institution may also use own form to document local context review as long as all issues noted below are addressed. The Relying Institution will document the review and will submit the form to the Coordinating Center for submission to the Designated IRB.

The local context issues to be assessed by the Relying Institution include but are not limited to the following:

- Specific state or local laws, regulations, or policies applicable to Relying Institution or the study
- Qualifications and human subject protection training of Investigators and study staff
- Financial conflicts of interest of Investigators related to the research
- Ethical concerns pertaining to the study population to be included in the research
- Radiation safety review
- Biosafety Review
- Insertion of institution-specific language into the model informed consent

It shall be the sole responsibility of Relying Institution to identify, interpret, and ensure compliance with the requirements of its applicable state or local laws, regulations, policies, and ancillary review processes as are relevant to specific Studies, and to communicate such requirements to the Designated IRB.

2. Federalwide Assurance. Relying Institution will maintain a current, approved FWA with OHRP for the duration of this Agreement. Relying Institution will notify the Designated IRB promptly in writing if its FWA is terminated or expires for any reason.

3. Acceptance of and Cooperation with Designated IRB Decisions. Relying Institution will accept the decisions and requirements of the Designated IRB with respect to the Studies included in this Agreement.

4. Notification of Investigator Status. The Relying Institution and site Investigator(s) and study team agree to promptly inform the Coordinating Center of suspension or termination of Investigator duties or privileges pertaining to the studies included in this Agreement.

5. Investigator Responsibilities. The Relying Institution will ensure its Investigators are aware of the their responsibilities in the conduct of human subjects research including, but not limited to the following:

   a. Investigator is responsible for complying with the determinations and requirements of the Designated IRB.
   b. Investigator is responsible for record keeping and reporting, and for providing information requested by the Coordinating Center, should there be any, in a timely manner.

c. Investigator is responsible for disclosing to both Coordinating Center and Relying Institution any changes in financial conflicts of interest and abiding by the Conflict of Interest Management Plan, including additional restrictions as determined by Designated IRB, if applicable.
d. Investigator is responsible for obtaining IRB approval before implementing any changes to the research (including informed consent form), except where necessary to eliminate an immediate risk of harm to participants. Investigator is responsible for promptly reporting any such change and the perceived risk to the Relying Institution and Coordinating Center.
e. Investigator is responsible for maintaining human subjects protection education in accordance with Relying Institution's policies and procedures.
f. Investigator is responsible for reporting unanticipated problems to Coordinating Center promptly, in accordance with Designated IRB's policies.

6. Compliance with SOPs. The Relying Institution and its Researchers shall comply with the OneIRB SOPs. Only Research Studies for which both the Relying Institution and the Designated IRB have agreed that IRB review will be ceded to the Designated IRB in accordance with the SOP will be included in this Agreement.

7. Obligation to Update Information. Relying Institution will provide written notification to the Designated IRB (via the Coordinating Center) promptly upon any material changes to the information provided as part of its participation in the Research Study or otherwise about its site, its human research program, or the local research context in connection with this Agreement or any Research Study.

V. Notices and Primary Contacts. Any notices to the undersigned institutional officials or correspondence regarding IRB review and oversight must be addressed as follows:

Designated Institutional Review Board Primary Contact:

Name:	Khemraj Hirani, PhD, MPharm, MBA, RPh
Title:	Associate Vice Provost for Human Subject Research
Address:	1400 NW 10th Avenue (M-809), Suite 1200A, Miami, FL 33136
Email:	khirani@med.miami.edu
Phone:	305-243-3195

Relying Institutional Review Board Primary Contact:

Name:	Chris Weir CIP
Title:	Administrative Director, Research Protection Department
Address:	1201 Ninth Ave. IN-RC
Email:	cweir@benaroyaresearch.org
Phone:	206-342-6916

VI. Termination

1. Term. This Agreement shall become effective on the last date signed below and shall continue for the duration of and until the cessation of Relying Institution's participation as a TrialNet Study Site, provided that the Agreement is not earlier terminated as provided in Section VI.2 below.

2. Termination. Any parties to this Agreement may terminate this Agreement for cause upon fourteen (14) days prior written notice to the other party(ies) as provided in Section V. Cause may include, but is not limited to, breach of the Agreement by a party that is not cured to the reasonable satisfaction of the non-breaching party(ies) within said fourteen (14)-day notice period, and in the case of Designated IRB evidence of material changes in any information provided by Relying Institution . In the event that any party's FWA is threatened, terminated, or expires, the other party(ies) may terminate the Agreement immediately.

3. Effect of Expiration or Termination; Survival. In the event of any termination of this Agreement, the parties will work together to determine the effect of such termination on any Study(s) and associated research activities being conducted under the Agreement at the time of termination. In the event of any expiration or termination of this Agreement, Relying Institution will remove the Designated IRB from the list of designated IRBs on its FWA (if it had included the Designated IRB on this list) and will notify the Designated RB (via the Coordinating Center) that this has been done.

VII. Miscellaneous.

1. This Agreement may be amended only by a written Agreement signed by authorized representatives of all parties. If any provision of this Agreement shall be held to be invalid, illegal, or unenforceable, the validity, legality and enforceability of the remaining provisions of this Agreement shall not be affected thereby. The failure of a party to insist upon the performance of any of the terms of this Agreement shall not be construed to be a waiver or relinquishment of any of the terms of the Agreement or of the whole Agreement. All the titles and headings contained in the Agreement are inserted only as a matter of convenience and reference and do not define, limit, extend, or describe the scope of this Agreement or the intent of any of its provisions. This Agreement is not assignable in whole or in part, and any attempt to do so shall be void.

2. This Agreement is not intended to create nor shall be construed to create any relationship between the parties other than that of independent entities contracting for the purpose of effecting provisions of this Agreement. Other than as expressly set forth in this Agreement, no third persons or entities are intended to be or are third party beneficiaries of or under this Agreement. Nothing in this Agreement shall be construed to create any liability on the part of the parties or their respective directors, officers, trustees, faculty, employees or agents, as the case may be, to any such third parties for any act or failure to act of any party hereto.

oneIRB

Signature of Signatory Official (Designated IRB Institution):

_____ Date: 1/6/2017

Print Full Name: John L. Bixby PhD

Institutional Title: Vice Provost for Research

Signature of Signatory Official (Relying Institution):

_____ Date: 12/13/16

Print Full Name: Lynn M. Rose, PhD

Institutional Title: Director, Scientific Administration