**THE NEUROFIBROMATOSIS RESEARCH INITIATIVE (NFRI)**

**AT BOSTON CHILDREN’S HOSPITAL**

**GENOMICS OF MPNST (GEM) CONSORTIUM MASTER PARTICIPATION AGREEMENT**

This **MASTER PARTICIPATION AGREEMENT** (“Agreement”) is by and between \_\_\_\_\_\_\_\_\_\_\_\_ (“Participating Site”) and **THE NEUROFIBROMATOSIS RESEARCH INITIATIVE** (“NFRI”) directed by Dr. David Miller at Boston Children’s Hospital. Throughout this Agreement, the parties will be referred to as “\_\_\_\_\_\_\_\_\_\_\_” and “NFRI”. This Agreement shall become effective as of \_\_\_\_\_\_\_\_\_\_ (the “Effective Date”).

**RECITALS**

**WHEREAS**, NFRI is an independent, not-for-profit organization focused on accelerating the pace of advances in Malignant Peripheral Nerve Sheath Tumor (MPNST) pre-clinical research and serves as the coordinating center for the GeM Consortium; and

**WHEREAS**, the “Participating Sites” are U.S. and international academic centers or hospitals with substantial patient volume that are committed to contribute bio-specimens and clinical data for research purposes, and to participating through Steering Committee representation in the Genomics of MPNST Consortium (“GeM Consortium”); and

**WHEREAS**, the GeM Consortium will form a single, searchable database, including clinical data (medical history, pathology reports, imaging results) on individuals with MPNST (a rare tumor) which will be pulled from the a Clinical Registry (see below), and genomic data (e.g., DNA and RNA sequencing on tumor specimens from the same individuals), which together will be called the “International Genomics of MPNST Consortium Database” (“GeM Consortium Database”). This GeM Consortium Database is the primary deliverable of the GeM Consortium, a group that seeks to identify and validate genomic biomarkers relevant to treatment of NF1-related and sporadic MPNSTs by linking tumor genomic data from clinical sequencing and pathology efforts (the “GeM Project”) and;

**WHEREAS,** the GeM Consortium Database will be created with data submitted by the Participating Sites and specimen-derived data produced by the Consortium and administered by NFRI; and

**WHEREAS**, clinical data submitted by Participating Sites will be hosted in a “Multi-Institutional Registry for Malignant Peripheral Nerve Sheath Tumors” (the “Clinical Registry”) directed by Dr. Angela Hirbe at Washington University in St. Louis, a RedCap database housing clinical data on NF1 patients with Malignant Peripheral Nerve Sheath Tumors (MPNST); and

**WHEREAS**, specimen-derived and Participating Site submitted genomic data will be hosted in a secure, cloud-based GeM Consortium Database a third party with access to Participating Sites; and

**WHEREAS**, the Parties are entering into this Agreement to set forth the terms and conditions on which they will take part in the GeM Project, and by which the GeM Project will be initiated, implemented, and governed.

**NOW, THEREFORE**, in consideration of the mutual promises below, and intending to be legally bound, the undersigned agree as follows:

**AGREEMENT**

1. **GENERAL**

A. The GeM Consortium will develop, disseminate and apply approaches to integrate DNA sequence data with clinical outcomes data for cancer genomics research across large populations of patients treated at the Participating Site. To achieve this result, the Participating Sites will contribute bio-specimens for centralized pathology review (i.e., unstained FFPE tumor slides) and comprehensive molecular testing (i.e., fresh frozen tumor tissue and paired normal specimen), including Whole Genome Sequencing, with associated clinical data generated at each Participating Site for use by the GeM Consortium. NFRI and WU agree that all data contained in the GeM Consortium Database shall be accessible to Participating Sites and others as may be agreed upon by the GeM Consortium Steering Committee.

B. NFRI, directed by Dr. David Miller, shall oversee and manage the GeM Project and serve as the Genomics of MPNST (GeM) Consortium Coordinating Center (“Coordinating Center”) for the collection and analysis of data, the distribution of reports and the coordination of activities with the Participating Sites. NFRI will be responsible for locating and contracting with a strategic partner with expertise in database platform development and user interface to develop the GeM Consortium Database.

C. Dr. Angela Hirbe at Washington University and her research team (“WU”) will be responsible for generating and maintaining the Clinical Registry. To that end, WU will reach out to consortium Participating Sites to update clinical information at least annually for patients who are living. The Clinical Registry will maintain a contact for obtaining biospecimens for each Participating Site. The procedure for obtaining biospecimens will be defined by the GeM Consortium. For those tumors for which genomic information is obtained and hosted on the GeM consortium database, the clinical information will be transferred from WU to be paired with the genomic data.

D. The collection, receipt, use, maintenance, transmission and disclosure of data under the GeM Project shall comply with the requirements for the privacy and security of protected health information (“PHI”) under the Health Insurance Portability and Accountability Act of 1996, and its regulations, as amended by the Health Information Technology for Economic and Clinical Health Act of the American Recovery and Reinvestment Act of 2009, Pub. L. No. 111-5, Title XIII (2009) (all referred to as “HIPAA”), the Personal Information Protection and Electronic Documents Act (“PIPEDA”), the European Union Data Protection Directive, the Personal Health Information Protection Act (Ontario) of 2004, or other national equivalents (as appropriate and relevant to a particular Participating Site), if applicable, including any and all future amendments thereto.

E. All reference to “NFRI” or “Participating Site” herein shall include their employees, members, officers, directors, agents, subcontractors, and representatives.

## F. All data submitted to the GeM Consortium will be de-identified, and data transferred from the third party GeM Consortium Database will be free of IRB governance as a result. Each Participating Site will submit only de-identified data or limited data sets, as defined in 45 C.F.R. § 164.514(e) (“Limited Data Set”), to the GeM Consortium Database. PHI can/will be submitted to the Clinical Registry, but then a unique identifier would be generated to that PHI would not be transferred from the Clinical Registry to the GeM Consortium Database G. The GeM Consortium Database created by the Project is intended to be publicly available (wherever permitted by the original consent of the research subjects involved) for access by non-Participating Sites after initial periods of exclusive use by the Participating Sites, with the specific rules pertaining to such non-Participating Site access adopted by the Steering Committee.

**Now Therefore**, the Parties mutually agree as follows:

Background. The Genomics of MPNST (GeM) Consortium was founded in 2017 by Dr. David Miller (MD, PhD), a medical geneticist at Boston Children’s Hospital (BCH) and Director of the Neurofibromatosis Research Initiative (NFRI). The GeM Consortium aims to facilitate the collection of rare Neurofibromatosis-related malignancies and associated clinical data, promote data-sharing, and stimulate translational research to improve clinical outcomes.

Mission. The NFRI’s mission is to foster international, collaborative efforts towards translational and clinical research studies toward effective therapies for NF1-related MPNSTs. This encompasses the collection of 100 MPNSTs for whole genome sequencing and correlation with related clinical data in the cloud-based GeM Consortium database hosted by a third party. The intention is to promote efficient data-sharing to advance research on targeted therapies for NF-1 and related malignancies.

Membership. Institutional membership in the GeM Consortium is defined by agreement with the terms of this MPA by an authorized Participating Site representative and willingness to support the mission, goals and work of the Consortium. Participating Sites will provide recommendations for Principal Investigators or chosen member representative serve as Participating Site’s representative on the Steering Committee. Only individuals from Participating Sites may join the Steering Committee and the number of individual members from any Participating Site is limited to one representative. To remain a member, either Participating Site, in good standing requires active participation in the work of the Consortium and attendance at least 50% of the Consortium meetings (either in-person or as conference calls).

Steering Committee and Principal Investigators. The Steering Committee shall be established as the primary governing body of the Consortium and will initially consist of the Principal Investigators (or member representative) from each Participating Site.

It is understood that one Principal Investigator will be appointed to the Steering Committee from each Participating Site. Should a Principal Investigator leave the Participating Site with which s/he is affiliated, the Participating Site will remain a member of the Consortium and may replace that Principal Investigator with another individual capable of performing the duties related to the Consortium; such individual will require the consent of the Steering Committee. The Principal Investigator leaving the Participating Site, if he/she so wishes, may retain standing (at his/her new institution) in the Consortium if such institution is a Participating Site of the Consortium. If not already a member of the Consortium, the new institution may be invited to join the Consortium provided it meets the requirements of all Participating Sites and is approved by a majority of the Steering Committee.

Working Groups. Steering Committee Principal Investigators (or Participating Site representatives) will have the opportunity to serve on Working Groups.

The Steering Committee will develop Working Groups to address Consortium issues in specialized topic-areas, for example: oncology and pathology, genomics and informatics, data use and publications, etc. The major role of each Working Group member is to provide expertise and leadership in defining and accomplishing the goals set forth by the Steering Committee and GeM Consortium.

Should any of the members of a Working Group become unable or unwilling to continue in their role they shall promptly notify the Steering Committee in writing. The Steering Committee shall select a mutually acceptable replacement member of the Subcommittee within thirty (30) days of receipt of notice from the departing member of the Subcommittee.

Membership. The initial membership of the Consortium shall be the Parties to this Agreement. New members may join the Consortium upon majority consent of the Steering Committee and upon execution of the signature page to this Agreement. Upon execution of the signature page of this Agreement, an institution shall be deemed to be a Participating Site.

The work of the Consortium includes investigators from throughout the world with expertise in broad areas of the NF and sarcoma clinical and research community, including but not limited to: medical genetics, medical oncology, neurology and neuro-oncology, pathology, and surgical subspecialties. Preclinical and protocol studies will be collaboratively developed and institutes and centers will participate in protocols that fit within their disease-specific and scientific expertise and where patient populations are available to participate.

The Work of the Consortium. In furtherance of its mission, and under the direction of the Steering Committee, the Consortium may do any or all of the following:

* Review protocols designed by Consortium Members (“Research Projects”);
* Assist in developing site participation agreements with other institutions interested in participating in Research Projects;
* Assist Institutions and Investigators in applying for and accepting funding for Research Projects;
* Seek funding to support the work of the Consortium;
* Assist in the supervision and coordination of Research Projects;
* Coordinate multi-center publication of results of Research Projects in a manner consistent with a Consortium Publication Policy approved by the Steering Committee;
* Sponsor educational forums or educational reports in the area of MPNST and Neurofibromatosis-1;
* Form collaborations with other institutions and industry to further the work of the Consortium;
* Other activities that may further its mission.

Institutional Review Board (IRB). Each Participating Site agrees that it will consent research subjects using a protocol that allows the necessary sequencing and data sharing essential to the success of the GeM Consortium. Participating Sites enrolling under a local IRB protocol will make the details of that protocol available to the Coordinating Center (NFRI), which will track enrolment/consenting done at each Participating Site.

Submission of clinical data by Participating Sites to the MPNST Registry at Washington University, directed by Dr. Angela Hirbe, will require member institutions to implement and consent subjects under the Multi-Institutional Malignant Peripheral Nerve Sheath Tumors Registry protocol.

Participating Sites shall comply with all applicable laws and regulations governing the conduct of human subjects research.

Funding. Each Participating Site will be provided with a per specimen stipend to support tissue and data collection efforts. The NFRI will provide each Participating Site with a list of minimum requirements for specimen input for use by the Consortium. Stipend amount will be determined by number of eligible specimens provided and production of associated clinical data, and will be contingent upon upload of all Participating Site-generated data to the MPNST Registry (for clinical data elements) and upon receipt of required specimens for genomic analysis (fresh frozen tumor and paired normal sample) and pathology review (unstained FFPE slides).

Insurance/liability. Each Participating Site shall maintain in full force and effect general and professional liability coverage (or a program of self-insurance) at appropriate levels sufficient to cover all of its activities and the activities of its personnel working on a Research Project. Each Participating Site agrees to be responsible and assume the liability for its own wrongful or negligent acts or omissions or those of its officers, agents, or employees to the fullest extent allowed by law.

Confidentiality. During the term of this Agreement and for a period of five (5) years thereafter, each Participating Site shall cause all Confidential Information that is disclosed to it and accepted by its Principal Investigator to be treated according to the same internal security procedures and with the same degree of care regarding its secrecy and confidentiality as the party receiving the disclosure treats similar information of its own within its organization, and shall not use any such Confidential Information except for the purpose of performing its obligations related to the Consortium.

Confidential Information means information (i) that is in written form and marked confidential, or (ii) that is disclosed orally, is reasonably construed as confidential and proprietary, and is summarized in a writing marked confidential and delivered to the receiving party by the disclosing party within thirty (30) days of disclosure. Confidential Information does not include information that: (i) is or later becomes available to the public through no breach of this Agreement; (ii) is obtained from a third party who had the right to disclose the information; (iii) as of the date of disclosure, is already in the possession of the party to whom disclosure is made as evidenced by prior written records; or (iv) is independently developed by the receiving party.

This provision notwithstanding, if any Participating Site obtains any health or medical information of any patient or research subject of a Participating Site the receiving party will hold in confidence the identity of such patient or research subject and his/her health/medical information and will comply with all applicable laws regarding the confidentiality of such information.

In the event that any Confidential Information is required by law, regulation, administrative or court order to be disclosed, the party required to make disclosure shall promptly notify the other party to allow such other party the opportunity to assert whatever limitations, exclusions or exemptions may be available to protect its interests in such Confidential Information.

Results and Inventions. All tangible property provided to Principal Investigator, and their Participating Site in connection with the Consortium, shall be and remain the exclusive property of the providing Participating Site. All aggregated data and reports, or other information generated under the auspices of the Consortium (and any inventions or other results of such data, reports, or other information) shall be and remain the exclusive property of the Participating Site(s) generating the data and reports. Ownership of inventions shall be determined in accordance with federal law. Each Participating Site shall be granted by the owning Participating Site a non-exclusive, royalty-free license to use data first generated in connection with the Research Projects and the subject of the Consortium, including rights to use and reproduce copyrighted works for education and research purposes, publications, and for use in furtherance of the goals of the Consortium as expressed in this Agreement. Aggregated data will be maintained by each Participating Site over the lifetime of the Consortium, but not greater than ten (10) years. Data from individual Participating Sites will remain the sole property of that Participating Site to be utilized in anyway the Participating Site sees fit.

It is recognized and understood that the existing inventions and technologies of each Participating Site are each Participating Site’s separate background intellectual property and no other Participating Site shall have any claims to or rights in such existing inventions and technologies. Ownership of any new intellectual property developed during the course of a Research Project shall follow inventorship or authorship as determined in accordance with the U.S. law applicable to the type of intellectual property developed, the standard operating procedures developed by the Steering Committee and the terms of the relevant Research Project agreement.

Results. The Participating Sites agree that access to results generated by new Research Projects (“Results”) will be managed in accordance with standard operating procedures developed by the Steering Committee and the terms of the relevant Research Project agreements. The Participating Sites agree that such Results will be used solely by each Principal Investigator and those under his/her direct supervision and that he/she will not distribute or transfer Results to any other investigator at his/her institution or to any third party for any reason without the prior written consent of the Steering Committee. Further, the Participating Sites agree that Results may be used solely for non-profit research purposes.

Publications and other Public Disclosure. The Steering Committee will approve a Consortium Publication Policy, developed by a Working Group made up of members of the Steering Committee or member representatives appointed by the Steering Committee.

It is anticipated by the Participating Sites that Results from collaborative projects will be jointly published as determined by the Steering Committee. Nonetheless, each Participating Site separately reserves the right to publish its own institutional information and data generated by such Participating Site in the course of any Research Project, subject to any conditions imposed by funding sponsors or collaborators or the terms of the Research Project agreement. In a manner consistent with the Consortium Publication Policy, authorship of publications or public disclosures of Results will be determined by contributions to the Results being published or otherwise disclosed, in accordance with authorship standards of the International Committee of Medical Journal Editors (See: http://www.icmje.org/ethical\_1author.html), academic standards and custom. Authorship of such publications will be determined at the outset of the project, proposed by the Steering Committee and approved by majority of the Steering Committee. Proper acknowledgment will be made for the contributions of each Participating Site to the Results being published.

Responsibilities. Each Participating Site is responsible for its own acts and omissions relating to this MPA and the Consortium and its use of Results. In no event shall any Participating Site be liable for any indirect, special, incidental or consequential damages (including, without limitation, damages for loss of profits or expected savings or other economic losses, or for injury to persons or property) arising out of or in connection with this MPA or its subject matter, regardless of whether such Participating Site knows or should know of the possibility of such damages.

NO PARTY MAKES ANY WARRANTIES, EXPRESS OR IMPLIED, AND EACH PARTY EXPRESSLY DISCLAIMS ANY SUCH WARRANTIES, AS TO ANY MATTER WHATSOEVER, INCLUDING WITHOUT LIMITATION: (A) ANY MATERIAL, TANGIBLE RESEARCH PROPERTY, INFORMATION OR DATA PROVIDED TO THE OTHER PARTY; (B) THE CONDITION, ORIGINALITY OR ACCURACY OF THE RESEARCH CONDUCTED BY SUCH PARTY; (C) ANY INVENTION(S) OR PRODUCT(S) CONCEIVED, DISCOVERED OR DEVELOPED PURSUANT TO THIS AGREEMENT; OR (D) THE OWNERSHIP, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE OR NON-INFRINGEMENT OF THE RESEARCH OR ANY INVENTION OR PRODUCT

Compliance with Laws and Regulations. All research done in connection with the Consortium, will be done in compliance with all laws, governmental regulations and guidelines of the country in which the research takes place, including without limitation, in the United States, current NIH guidelines.

Term of Agreement and Termination. This Agreement shall go into effect on the Effective Date and shall expire three (3) years thereafter, renewable for successive three year terms if agreed to by a majority vote of the Steering Committee. The term of this Agreement may be extended by mutual written consent of the parties. Any party may terminate its participation in the Consortium, at any time and for any reason, on 60 days notice to the other parties. If the Steering Committee determines that there is insufficient funding for completion of the Consortium Mission or if a scientific or academic dispute among Participating Sites cannot be resolved to the satisfaction of the Steering Committee, the Steering Committee, in consultation with the Consortium Members and NFRI’s Scientific Advisory Committee may elect to terminate this Agreement.

Participating Site Withdrawal. A Participating Site may withdraw from the Consortium at any time provided that such Participating Site provides sixty (60) days prior written notice to the Steering Committee and provided that such Participating Site and its personnel agrees to complete all work on Research Projects pending at the time of such withdrawal in full compliance with applicable law and the terms of any Research Project agreements.

Participating Site Termination. Any Participating Site which becomes debarred, suspended, excluded, or otherwise sanctioned by the any federal governmental agency shall be excluded from further participation in the Consortium.

Assignment. This Agreement is not assignable by a party, whether by operation of law or otherwise, without the prior written consent of the other parties.

Publicity. Any publicity regarding the Consortium shall be agreed upon by the Steering Committee. Other than agreed upon statements regarding the Consortium, no party will use the name of any other party, or of any affiliate of that party, in any manner without the prior written approval of the other party.

Notice. Any notices required or permitted under this Agreement shall be in writing and addressed to addresses or facsimile numbers of the parties as shown on the signature page.

Notices shall be delivered by hand, recognized national overnight courier, confirmed facsimile transmission, confirmed electronic mail, or registered or certified mail, postage prepaid, return receipt requested and shall be given or made as of the date received. A party may change its contact information immediately upon written notice to the other party in a manner provided in this Section.

Survivorship. The terms of the following sections shall survive termination of this MPA: Confidentiality, Results; Inventions; Publication and other Public Disclosures; Responsibilities; Compliance with Laws; Publicity; Governing Law.

Headings. All headings are for convenience only and shall not affect the meaning of any provision of this MPA.

Entire Agreement. In Witness Whereof, the Parties have caused this Agreement to be executed by their respective duly authorized representatives as of the Effective Date.

**Boston Children’s Hospital NFRI Director**

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Title: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

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Phone: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_Facsimile: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Participating Site Principal Investigator**

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