

## MATERIAL TRANSFER AGREEMENT

The NCI-supported Pediatric Preclinical Testing Program (PPTP) is a comprehensive program to systematically evaluate new agents against childhood solid tumor and leukemia models. The PPTP is supported through a National Cancer Institute (NCI) research contract (commencing from November 1, 2009) to Nationwide Children's Hospital (NCH with Dr. Peter Houghton as the Principal Investigator. Testing occurs both at NCH and also at subcontract sites that have expertise in specific childhood cancers, including: Children's Hospital of Philadelphia (John Maris), Albert Einstein Medical Center (Richard Gorlick), Duke University (Henry Friedman), Texas Tech University Health Sciences Center (C. Patrick Reynolds), Children's Cancer Institute Australia (Richard Lock) and St. Jude Children's Research Hospital (Jianrong Wu). The primary goal of the PPTP is to identify new agents that have the potential for significant activity when clinically evaluated against selected childhood cancers. The terms of this Material Transfer Agreement ("Agreement") are consistent with the above mentioned contractual agreements. This Agreement is effective as of November 1, 2009 ("Effective Date").

NCI: National Cancer Institute, Division of Cancer Treatment and Diagnosis

Institution: \_\_\_\_\_

Institution's PPTP Investigator: \_\_\_\_\_

1. NCI agrees to transfer to the Pediatric Preclinical Testing Program (PPTP) Investigator and Investigator's Institution Research Materials provided by NCI collaborators ("Collaborators"). The individual Research Materials are proprietary and confidential to NCI Collaborators. The Research Materials are provided to DCTD, NCI for the PPTP under a Material Transfer Agreement between NCI Collaborator and NCI. For purpose of Section 9 and Section 12 of this Agreement, if applicable, Collaborator shall also mean its affiliates, its agents, its licensee(s) of the Research Material and its business partner(s) co-developing the Research Material.

2. THE RESEARCH MATERIALS MAY NOT BE USED IN HUMANS. The Research Materials will only be used for research purposes by Institution's PPTP Investigator and staff members in his/her laboratory, for the research project described below, under suitable containment conditions. The Research Materials will not be used (i) for commercial purposes, including for screening, production or sale, for which a commercialization license may be required or (ii) in any research in which a for-profit company (other than Collaborator) has rights or an option to obtain rights, including the right to obtain access to the data or results. Institution agrees to comply with all Federal rules and regulations applicable to the research project described below and the handling of the Research Materials. Further, Institution and PPTP Investigator agree to comply with all applicable federal regulations and National Institutes of Health policies relating to the use and care of the laboratory animals.

3. The Research Materials will be used by Institution's PPTP Investigator solely in connection with the research project ("Research Project") described with specificity in Appendix 1: Pediatric Preclinical Testing Program (PPTP) Stage 1 and Stage 2 Research Procedures and Plans.

4. Institution, Institution's PPTP Investigator and other Institution staff members in PPTP Investigator's laboratory shall not (a) make any complements, analogs, conjugates, derivatives or modifications of the Research Materials or (b) sequence, analyze, or otherwise determine the chemical structure or physical properties of the Research Materials, to the extent such structures or properties are not already publicly known or expressly provided for in the

Research Project; and if Institution, Institution's PPTP Investigator or staff members in his/her laboratory does so in violation of the foregoing, then Institution hereby agrees that all such complements, analogs, conjugates, derivatives modifications, and sequences are Collaborator Inventions as defined in Section 12 hereof and shall be treated in accordance with the provisions of that section.

5. The Research Materials are proprietary and confidential to Collaborator. Collaborator has agreed to allow NCI to make its proprietary compound(s) available to Investigator and Institution solely for use in furtherance of this Research Project. No license grant to or assignment of interest in Research Materials, express or implied, by estoppel or otherwise is intended or shall be construed by Collaborator's agreement to provide Research Materials for the Research Project. Institution's PPTP Investigator agrees to retain control over the Research Materials and further agrees not to transfer the Research Materials to other people not under her or his direct supervision without advance written approval of NCI after consultation with Collaborator. NCI shall obtain Collaborator's consent for any such request. Collaborator reserves the right to distribute the Research Materials to others and to use it for its own purposes. When the Research Project is completed, Institution's PPTP Investigator will lawfully dispose of the Research Materials as directed by NCI (with certification of such destruction provided to NCI).

6. The Research Materials are provided as a service to the research community. THEY ARE BEING SUPPLIED TO INSTITUTION BY THE COLLABORATOR THROUGH NCI WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. NCI and Collaborator make no representations that the use of the Research Materials will not infringe any patent or proprietary rights of third parties. Collaborator has agreed to hold Institution and participating PPTP institutions harmless and to indemnify Institution and participating PPTP institutions for all liabilities, demands, damages, expenses and losses arising out of Collaborator's use for any purpose of the data resulting from the Research Project. Results of the Research Project disclosed by NCI to Collaborator are disclosed with no warranties, express or implied, including any warranty of merchantability or fitness for a particular purpose. Institution makes no representations that the use of the results will not infringe any patent or proprietary rights of third parties. Institution assumes sole responsibility for any liabilities, damages, losses and costs incurred in connection with Institution's use, handling, storage, transfer, or disposal of the Research Materials, except when such liabilities, damages, losses and costs arise from the gross negligence or willful misconduct of the Collaborator.

7. Subject to the rights set out in Section 12, Institution has the right to retain title to Institution Inventions as defined in Section 12. Institution agrees not to claim, infer, or imply endorsement by the Government of the United States of America (hereinafter referred to as "Government") of the Research Project, the institution or personnel conducting the Research Project or any resulting product(s). Unless prohibited by law from doing so, Institution agrees to hold the Government and Collaborator harmless and to indemnify the Government and Collaborator for all liabilities, demands, damages, expenses and losses arising out of Institution's use for any purpose of the Research Materials, except when such liabilities, demands, damages, expenses or losses arise from the gross negligence and/or willful misconduct of the Collaborator.

8. NCI and Institution expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

9. Institution agrees to inform NCI at least quarterly or more frequently as specified by contractual arrangements of the results of the Research Project using the Research Materials in

accordance with this section and will confidentially inform NCI promptly of any significant results that arise from such Research Project so that NCI may promptly forward such results and notification to Collaborator in confidence. Results of the Research Project shall be provided exclusively and in confidence to the NCI and the PPTP Steering Committee (NCI staff and selected childhood cancer experts who advise NCI staff concerning the Research Materials evaluated by the PPTP). From time to time, NCI will disclose the results to selected childhood cancer clinicians in order to assist their planning of clinical trials of anti-cancer agents. All selected childhood cancer experts and clinicians who need to have access to the Research Project results are under an obligation of confidentiality no less restrictive than in this Agreement. The Institution, PPTP Investigator, and NCI agree that, subject to publication rights under Section 11, they shall keep the research results confidential and that Collaborator is hereby granted the right to use, without further consideration, all data and results generated under this Research Project for any legitimate business purpose, including for Collaborator's own analyses and for use in regulatory or intellectual property filings.

10. The following will apply to all publications or presentations at the appropriate time for such disclosures. In all oral presentations or written publications concerning the Research Project, Institution's PPTP Investigator will acknowledge NCI's and Collaborator's contribution of the Research Materials unless requested otherwise. To the extent permitted by law, Institution agrees to treat in confidence, for a period of five (5) years from the date of its disclosure, any of NCI's or Collaborator's written information about the Research Materials that is/are stamped "CONFIDENTIAL" ("Confidential Information") except for information that Institution can clearly demonstrate by competent written proof was previously known to Institution or that is or becomes publicly available without breach of this Agreement by Institution or which is disclosed to Institution without a confidentiality obligation by a third party having a lawful right to do so or is independently developed by Institution's personnel who have not had access to Confidential Information as demonstrated by competent written proof, or is required to be disclosed by law. For the avoidance of any doubt, the identity or identification of the Research Materials, any non-public code number or designation associated with the Research Materials and any link between the Research Materials as identified in the Research Project and the Research Materials as they may otherwise be known or identified shall all constitute Confidential Information of the Collaborator. Any oral disclosures from NCI to Institution of Confidential Information shall be summarized in writing within thirty (30) days after the date of the oral disclosure and marked "Confidential". All Confidential Information shall be used solely in furtherance of the Research Project and not for any other purpose.

11. Collaborator agrees that Institution or PPTP Investigator may publish data and results generated under the Research Project in peer-reviewed scientific journals or present those data and results at academic symposia or similar professional meetings in accordance with the following provisions. Such public disclosure may be made only after Collaborator has had forty-five (45) days to review the proposed disclosure to determine if it includes any Confidential Information or patentable information, except when a shortened time period under court order or the Freedom of Information Act pertains. To ensure Collaborator's review of the proposed disclosure, Institution will provide a confidential copy of the proposed disclosure to NCI not less than sixty (60) days prior to submission of such proposed disclosure for publication. Abstracts and other presentations must be provided to NCI in sufficient time to allow Collaborator at least ten (10) days to review any planned submission. Institution agrees not to submit proposed disclosures for publication until written notification from NCI of approval to do so; Institution must check with NCI to confirm that the review period has elapsed before submitting proposed disclosures for publication. If NCI or Collaborator has provided comments, Institution must address comments prior to submission. If requested in writing by the NCI, pursuant to a request by the Collaborator, Institution shall delete, or cause to be deleted, any Confidential Information;

or withhold, or shall cause to be withheld, the proposed disclosure for an additional forty-five (45) days to allow the Collaborator to protect its confidential information or to cooperate with Institution in protecting the parties proprietary interests in the Institution Inventions. Failure by Institution to comply with the provisions of this Section 11 will constitute a violation of this Agreement and, at Collaborator's request to NCI, may result in termination of all rights under this Agreement. Institution agrees not to submit proposed disclosures for publication without written notification from NCI of approval to do so.

12. Institution agrees to abide by the following terms (the "Intellectual Property Option to Collaborator"):

Institution agrees to promptly and confidentially notify NCI in writing of any inventions, discoveries or innovations made by Institution's PPTP Investigator or staff members of his/her laboratory, whether patentable or not, which are conceived and/or first actually reduced to practice in the performance of the Research Project using the Research Materials or within six (6) months after completion of the Research Project (hereinafter together with any patent rights obtained thereon, the "Institution Inventions"). Institution agrees to notify NCI in writing upon the earlier of: (i) any submission of any invention disclosure by Institution's PPTP Investigator or his/her researchers to Institution relating to any Institution Invention, or (ii) the filing of any patent applications related to the research with the Research Materials and in either case will provide Collaborator, to the extent that Collaborator's identity is known based upon disclosure by the NCI, with a confidential copy of same. If Institution does not elect to file an intellectual property application on an Institution Invention, then Collaborator may elect to file and prosecute the intellectual property application appropriately naming Institution as an assignee, in a timely manner and at Collaborator's expense. Institution will cooperate in the preparation and filing of a patent or other intellectual property application.

Institution agrees to grant to Collaborator: (i) a fully paid-up, royalty-free, worldwide, non-exclusive, sub-licensable, license to use the Research Material under all Institution Inventions relating to the Research Material and resulting from the Research Project for any purpose, including commercial purposes; and (ii) a time-limited first option to negotiate an exclusive, world-wide royalty-bearing license for all commercial purposes, including the right to grant sub-licenses, subject to any rights of the Government of the United States of America to all Institution Inventions on terms to be negotiated in good faith by the Collaborator and Institution. Collaborator shall notify Institution, in writing, of its interest in obtaining an exclusive license to any Institution Invention within one (1) year of Collaborator's receipt of written notice of such Institution Invention(s). In the event that Collaborator fails to so notify Institution, or elects not to obtain an exclusive license, then Collaborator's option shall expire with respect to that Institution Invention, and Institution will be free to dispose of its interests in such Institution Invention in accordance with Institution's policies. If Institution and Collaborator fail to reach agreement within ninety (90) days of notification by Collaborator of its licensing interest (or such additional period as Collaborator and Institution may agree) on the terms for an exclusive license for a particular Institution Invention, then for a period of six (6) months thereafter Institution shall not offer to license the Institution 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 shall have a period of thirty (30) days in which to accept or reject the offer. Furthermore, Institution agrees to grant to Collaborator a non-exclusive, worldwide, royalty-free, fully paid-up, irrevocable right and license for research (including drug development) purposes to all research results and data and to any such Institution Inventions.

Institution agrees, and NCI agrees that Institution is authorized to agree, that notwithstanding anything herein to the contrary, any inventions, discoveries or innovations,

whether patentable or not, which are not Subject Inventions as defined in 35 USC 201(e),\* arising out of any unauthorized use of the Collaborator's Research Materials and/or any modifications to the Research Materials, shall be the property of the Collaborator that provided the Research Materials (hereinafter "Collaborator Inventions"). Institution will promptly notify the NCI and Collaborator in writing of any such Collaborator Inventions and, at Collaborator's request and expense, Institution will request permission from the National Institutes of Health (NIH), if necessary, to cause to be assigned to Collaborator all right, title and interest in and to any such Collaborator Inventions and provide Collaborator with reasonable assistance to obtain patents (including causing the execution of any invention assignment or other documents). Institution may also be conducting other more basic research using the Research Materials under the authority of a separate Material Transfer Agreement (MTA), or other such agreement with the NCI or Collaborator. Inventions arising thereunder shall be subject to the terms of the separate MTA or other such agreement, and not to this clause.

*\* 35 USC 201 (e): The term "subject invention" means any invention of the contractor conceived or first actually reduced to practice in the performance of work under a funding agreement: Provided, That in the case of a variety of plant, the date of determination (as defined in section 41(d) (FOOTNOTE 1) of the Plant Variety Protection Act (7 U.S.C. 2401(d))) must also occur during the period of contract performance.*

13. The failure of Institution or Institution's PPTP Investigator to comply with Sections 2, 3, 4, 5, 9, 10, 11 or 12 shall authorize NCI to terminate Institution's rights under this Agreement and shall require Institution's PPTP Investigator to return immediately any Research Materials provided under this Agreement to NCI.

14. This Agreement constitutes the entire agreement and understanding of the parties and supersedes any prior agreements, promises or understandings, written or verbal, relating to the subject matter hereof. This Agreement may not be changed or supplemented, nor may any provision or the benefit thereof be waived, except by a writing duly signed by all parties.

15. Each party represents to the other that (a) it has the full power and authority, and has taken all necessary actions and has obtained all necessary authorizations, licenses, consents and approvals required, to execute and perform this Agreement, (b) is not bound by or subject to any law that would conflict with, prohibit or interfere with the performance of its obligations hereunder, and (c) neither party is nor shall become party during the term of this Agreement to any agreement, arrangement, joint venture, collaboration, competitive project, or other dealing whatsoever with any other person or body that would or might affect, conflict with or prejudice this Agreement or the rights of either party under it.

16. This Agreement shall terminate six (6) years from the Effective Date. Sections 4, 5, 6, 7, 11 and 12 shall survive the termination. Section 10 shall survive the termination for the period provided therein.

**Signatures Begin on the Next Page**

## SIGNATURES

### INSTITUTION

\_\_\_\_\_  
Date

\_\_\_\_\_  
PPTP Investigator

\_\_\_\_\_  
Date

\_\_\_\_\_  
Authorized Signature for Institution and Title

Institution's Official and Mailing Address:

(please provide contact information)

### NATIONAL CANCER INSTITUTE

\_\_\_\_\_  
Date

\_\_\_\_\_  
Laurie Whitney, Ph.D.  
Unit Supervisor  
Technology Transfer Center, NCI

\_\_\_\_\_  
Date

\_\_\_\_\_  
Sherry Ansher, Ph.D.  
Associate Chief, Research and Development Agreements

Please address all correspondence related to this agreement to Dr. Zhang at the following address:

Jianqiao Zhang, Ph.D.  
Regulatory Affairs Branch  
Cancer Therapy Evaluation Program  
DCTD, NCI, NIH  
Executive Plaza North, Suite 7111  
6130 Executive Blvd  
Rockville, MD 20852  
301-496-7912

Any false or misleading statements made, presented, or submitted to the Government, including any relevant omissions, under this Agreement and during the course of negotiation of this Agreement are subject to all applicable civil and criminal statutes including Federal statutes 31 U.S.C. ' ' 3801-3812 (civil liability) and 18 U.S.C. ' ' 1001 (criminal liability including fine(s) and/or imprisonment).

**APPENDIX 1: PEDIATRIC PRECLINICAL TESTING PROGRAM (PPTP)  
STAGE 1 AND STAGE 2 RESEARCH PROCEDURES & PLANS**

Testing for the PPTP’s tumor panels occurs both at Nationwide Children's Hospital (NCH) and also at subcontract sites that have expertise in specific childhood cancers as shown in the table below:

<b>Site</b>	<b>Tumor Types Tested</b>
Nationwide Children's Hospital	Sarcoma (rhabdomyosarcoma, Ewing), Renal (Wilms, Rhabdoid), Brain tumor (medulloblastoma, ependymoma)
Children’s Hospital of Philadelphia	Neuroblastoma
Children’s Cancer Institute Australia	Acute lymphoblastic leukemia
Duke University	High-grade gliomas
Albert Einstein Medical Center	Osteosarcoma
Texas Tech University Health Sciences Center	<i>In vitro</i> panel

Research Materials obtained from NCI Collaborators will be supplied to the PPTP Operations Center at NCH, which will then distribute Research Materials in a blinded fashion to sites for Stage 1 testing and generally in a non-blinded manner for Stage 2 testing. Complete instructions for drug storage, formulation and administration will be provided to sites by the PPTP Operations Center.

Stage 1 testing will evaluate the Research Materials against panels of pediatric tumors comprised of neuroblastoma, brain tumors, osteosarcoma, soft tissue sarcomas, Ewing family tumors, Wilms tumor, Rhabdoid tumor and models of acute lymphoblastic leukemia, in SCID or athymic nude mice. The *in vivo* primary screen comprises various tumor models and represents many of the cancer types that occur in children. Additional studies will determine the sensitivity *in vitro* of cell lines representing many of these same tumor types.

Stage 2 testing at PPTP testing sites may occur for Research Materials that demonstrate sufficient activity (either broad-spectrum or histiotype specific) in Stage 1 testing or for which there is a biological rationale for further testing. Detailed plans for Stage 2 testing are prepared following a comprehensive evaluation of the Stage 1 results by NCI, PPTP Steering Committee, PPTP Investigators, and NCI Collaborators providing the Research Materials.

Stage 2 testing for the *in vivo* panels may include, but not limited to:

- *In vivo* testing to determine dose response relationships using tumor models in which activity was observed in Stage 1.
- *In vivo* combination testing using the Research Materials in combination with other agents selected by the PPTP and approved by NCI Collaborators.
- Pharmacokinetic analysis for those Research Materials that have not been adequately characterized previously, which may include timed collection of blood and/or tissue specimens and which may include assaying these specimens for the presence of Research Materials.
- Studies evaluating pharmacodynamic endpoints that may require the timed collection of blood or tissue and/or the conduct of laboratory studies to evaluate a specific cellular or physiological effect that is associated with drug treatment or to determine the extent of target modulation associated with anti-tumor activity.
- Evaluating appropriate secondary models (e.g., orthotopically implanted tumors or models of disseminated disease) to confirm or refute results obtained using subcutaneous tumors. Genetically engineered mouse models may be utilized when relevant during Stage 2 testing.