The National Cancer Institute's Chemical Biology Consortium
Participants Agreement

Mission: The mission of the National Cancer Institute's ("NCI") Chemical Biology Consortium ("CBC") is to increase the flow of early stage drug candidates into NCI's drug development pipeline. By establishing an integrated network of chemical biologists and molecular oncologists from government, industry and academia, these CBC associate organizations and the NCI (collectively "Participants") can further address the unmet needs in therapeutic oncology focusing on areas such as "undruggable" targets and under-represented malignancies. Through the CBC and the interactions among the various Participants, the NCI's drug discovery and development pipeline can be enabled from target identification through proof-of-concept (POC) clinical trials. It is expected and understood that NCI will have the option to clinically develop successful compounds (NMEs) created by the CBC.

Description and Goals of CBC:

The CBC is a consortium designed to integrate chemical biology and molecular oncology research with governmental development resources. CBC Participants will:

a. Participate as an integrated network of chemical biologists and molecular oncologists to support lead development of promising new molecular entities

b. Focus on unmet needs in therapeutics not adequately addressed by the private sector.

c. Enable a clear, robust NCI pipeline all the way from target discovery through NCI POC clinical trials for academic, small biotech, and pharma investigators.

Participant Entrance Criteria:

CBC Participants will initially consist of participating government entities (NCI and associated NIH programs including the NIH Roadmap) and CBC contract awardees. Other organizations may be added to the Consortium at the discretion of the Senior Management Committee described below. Such organizations agree to be signatories to this Agreement.

Participant Interactions: Drug discovery and development requires teams of experts in different fields to advance the candidate from the early stages of discovery through preclinical development to the clinic. Participants will comprise a network of knowledge and expertise crossing scientific disciplines. It is anticipated that through this interaction, Participants can identify potential collaborations, navigate scientific roadblocks and obtain essential research resources from other Participants. These interactions are expected to accelerate the discovery and development of novel therapeutics. To accomplish this effectively, Participants will manage all of the resources generated under this Agreement, including intellectual property (IP), in a manner which promotes the sharing of research resources, therapeutic and diagnostic candidates, and data among the CBC Participants. It is understood by the Participants that the primary goal is the development of cancer therapeutics and diagnostics through cooperation and communication among the CBC Participants

Management of the CBC:

A. Senior Management Committee:

Overall oversight and accountability of the NCI pipeline will be provided by the Senior Management Committee (SMC). The SMC consists of members of NCI's senior leadership, including the NCI Director and Directors of the Division of Cancer Treatment and Diagnosis (DCTD) and the Center for Cancer Research (CCR), Associate Directors of relevant programs including the Developmental Therapeutics Program (DTP), and ad hoc government participants, depending on their expertise, as determined by the NCI Director.

The SMC will perform evaluative functions and provide guidance, final conflict resolution, and resources for the fiscal stability of the NCI pipeline. It will also have final authority in establishing policies for the operations of the NCI pipeline.

B. NExT Senior Advisory Committee

The Senior Advisory Committee (SAC) will oversee governance and allocation of resources for all projects in the NCI pipeline. It will approve operational plans and execute projects for both the Discovery and Development Committees. The SAC will be responsible for implementing the scientific recommendations of the NExT Drug Discovery and Development Committees. The SAC will meet bi-weekly and will review the NCI portfolio to ensure that projects are on time and on budget. They will have the authority to re-allocate resources based on prioritization of projects in the portfolio by the NExT Drug Discovery and Development Committees (subject to final approval by the Division Director who manages any particular resource).

The committee will have representatives from the DCTD Office of the Director (OD), DTP (including Branch Chiefs), the Cancer Imaging Program (CIP), the Cancer Therapy Evaluation Program (CTEP), CCR, and the Pharmacodynamic (PD) Biomarker Group. The SAC committee voting membership shall be approved by the SMC and consist entirely of NCI staff. Other NCI staff may serve in an advisory role and contract employees may serve in a liaison capacity on the committee.

Other NCI staff and contract employees may serve on the committee in an advisory role.

The SAC will develop clear strategic objectives for the portfolio/pipeline, clearly defining what type of DDD (Drug Discovery and Development) projects the organization is willing to invest in. The strategy should not only address global categories such as unmet need and novelty, but also provide prioritization guidelines for selection of therapeutic agents. The Strategic Plan is the most important element of this NCI implementation plan as it will provide clear focus to the organization and serve as a guideline for project solicitation, prioritization, and selection, and the selection of committee members and SEPs. The Strategic Plan should be developed through ad hoc meetings led by the SAC in a process that engages all stakeholders within the organization who may have relevant scientific expertise and control of key resources. This process will also help the SAC identify key individuals who can serve on committees. The SAC will revisit the Strategic Plan on a biannual or annual basis and modify it as necessary based on new knowledge.

a. Strategic Portfolio Management: The SAC will be responsible for approving investments in DDD projects and will provide global oversight and accountability over the entire NCI DDD portfolio.

b. Intramural and External Committee Coordination: The SAC will be responsible for approving membership to the NExT Drug Discovery, Drug Development, and SEPs.

c. High-Level, Program-Focused Decisions: The SAC will identify, recruit, and resource new high-impact initiatives, core technical facilities, and scientific experts to increase the efficiency and reduce the cost of bringing therapeutic agents into the clinic. This governing body will also be responsible for re-allocation of funds to ensure that high-priority projects can meet their milestones on time.

C. Drug Discovery Committee

The Discovery Committee will report to the SMC and oversee governance of all Discovery projects in the NCI pipeline. It will guide allocation of resources and develop strategic plans for individual projects in early discovery phase. Early discovery phase will encompass the following disciplines: in silico evaluations of pharmaceutics, pharmacology and toxicology; target discovery and validation; assay development and high throughput screening (HTS) assay development and screening; hit-to-lead chemistry, lead optimization (structural activity relationships incorporating structure-based drug design (SBDD) where appropriate); pharmaceutics; target pharmacology (selectivity, *in vitro* and *in vivo* pharmacokinetics (PK), *in vivo* PK and *in vitro* and *in vivo* pharmacodynamics (PD), biomarker discovery, assay development and validation) and early toxicology (*in vitro* human tissue assays, molecular toxicology and limited range-finding *in vivo* studies). Accordingly, the Discovery Committee is expected to provide input to the PTs in the following technical areas: synthesis, biopharmaceuticals, absorption, clearance, potency, distribution, metabolism, pharmaceutics, pharmacology (animal models and biomarkers), and safety. The Discovery Committee will perform risk-assessment at each stage-gate in the pipeline to ensure informed decision-making. Ideally, membership in this committee should include Participant representatives with expertise in each of the afore-mentioned discovery disciplines. The Discovery Committee will also be the steward of the CBC Drug Discovery Guidelines. These Guidelines will provide a consistent framework against which all clinical candidates will be measured. The Guidelines represent a living document modeled after biotech/pharma benchmarks. The Guidelines are an evolving set of quality attributes that will be updated and revised annually by the Discovery Committee. The Guidelines will serve as a tool for prioritization of projects in the NCI pipeline and will safe-guard the portfolio from having too many high-risk or duplicative projects.

On a quarterly basis PTs will provide information about the overall project status, activity and fiscal expenditures to the Discovery and Development Committees, and if necessary, the SAC. A key responsibility of the Discovery Committee will be to identify scientific gaps in the research plans and to ensure that the projects are moving toward completion. The Discovery Committee will be responsible for making decisions at each stage-gate.

The Discovery Committee will ensure that all the scientific objectives have been met to trigger nomination of a clinical candidate. Once a clinical candidate has been nominated by the PT and approved by the Discovery Committee it will be presented for review and endorsement by the Development Committee. At the point at which a clinical candidate is proposed for development, the PT will perform a risk assessment of the candidate to ensure informed decision-making by both Committees.

D. Drug Development Committee

The Development Committee will report to the SAC and endorse the critical transition of clinical candidates from Discovery phase to Development phase and oversee completion of all late-stage preclinical studies (e.g. Investigational New Drug (IND)-enabling toxicology studies, Good

Manufacturing Practice (GMP) manufacturing, validation of clinical biomarkers including imaging modalities; establishment of SOP-driven PK and PD assays) to support IND filing and first-in-human clinical trials. The Development Committee will assess eligibility of candidates for NCI Phase 0, I, II and make appropriate decisions at each phase. In addition, the development committee will be responsible for shepherding promising agents into NCI clinical development resources. The Development Committee will address issues related to: target patient population, dosing, clinical benefits, and basis of differentiation with FDA approved treatments to ensure that resources are focused on the most important and promising opportunities that match with the NCI vision of developing drugs to fill unmet needs, pediatric and niche indications and targeting natural products. Ideally, membership in this Committee should include Participant representatives with expertise in each of the afore-mentioned development disciplines.

E. Overall Project Management

The Discovery and Development Committees will assign "Projects" that will focus on a target, agent, compound or class of compounds determined by the SAC to be of high priority. The Discovery and Development Committees will each assign a PL to a specific Project. The PT will be made up of Participants with interest and expertise related to the specific Project. The PL will provide day-to-day direction, including organizing meetings and directing project work-flow. Oversight of the individual Projects will be the responsibility of the Discovery and Development Committees, which will monitor progress and identify problems with implementation, both by regular monthly meetings and by electronic communication.

Discovery PTs will also make recommendations to the Discovery Committee and SAC regarding the development status of therapeutic technology, and whether that technology is ready to be transferred to the Development Committee.

Monitoring will occur via quarterly reports submitted by the PTs to the Discovery, Development and Senior Management Committees. These reports will be prepared by Discovery and Development PTs and will encompass updates on the entire CBC endeavor. These reports will be made available for the quarterly meetings of the SMC.

F. Special Emphasis Panels

The Discovery Committee and the Development Committee each will have an external Special Emphasis Panel. These Special Emphasis Panels will provide information in the form of evaluations to their NCI counterparts who will be responsible for overseeing the scientific direction of the CBC consortium. Membership of these external committees will consist of key thought leaders in therapeutic discovery and development chosen by the SMC and SAC (in conformity with NIH guidelines and FACA) and will be subject to appropriate confidentiality and conflict of interest requirements to ensure any confidential information is kept proprietary. Both Special Emphasis Panels will be tasked with portfolio prioritization that will be tied into a fiscal appropriation for each project. Quarterly Meetings will be held for the Discovery and Development Special Emphasis Panels coincident with the NExT application cycle.

G. CBC Steering Committee

The Chemical Biology Consortium (CBC) represents the early discovery engine for the identification and advancement of new chemical entities. The CBC will be most effective if the collective insight, experience, and expertise of its Centers and Participants can be shared with senior NCI officials. The CBC Steering Committee will meet on a quarterly basis to provide intellectual contributions on

operational strategy and suggestions for improving CBC operations, as many of the PIs have been instituting similar programs in academia. Creating this body of expertise within the CBC will provide far-ranging benefit for all Participants, enhancing the therapeutic significance of new scientific findings and the recognition of unexpected opportunities. The CBC Steering Committee will consist of Participants, most notably, PIs from the Specialized and Comprehensive Screening and Chemistry Centers. **Access to the Central CBC Database:**

Central CBC Database access will be limited to Participants approved by the SAC with molecular oncology and drug discovery/development expertise that are signatories to this Agreement. Participants that have left the CBC will no longer have access to the Central CBC Database.

Project Leaders will be responsible for ensuring that Project Team data is entered into the database in a timely fashion. In general, members will be able to enter their data remotely, and will be expected to do so in a timely fashion once appropriate allowances are made for filing of necessary patent applications (described below).

Participants will have access to all data contained in the database, subject to the confidentiality terms in this Agreement.

Technology Transfer Committee

Each Participant is expected to assign one Technology Transfer Representative (TTR) to the CBC. A Technology Transfer Committee (TTC) will be established for the CBC and will be made up of the CBC TTRs. The purpose of the TTC is to maintain lines of communication related to the IP developed from the CBC and to share best practices for commercial development of their respective technologies and establish common guidelines for the management of CBC-related partnership and other technology transfer agreements.

THIS AGREEMENT sets forth the framework for cooperation among the Participants for pursuing collaborative projects. It is understood by the Participants that separate agreements among the individual Participants, which compliment the spirit of this Agreement, may be required to implement the NIH Research Tools Policies, maintain this cooperative framework and reach commercial endpoints.

Therefore, in support of these goals and objectives of the CBC, Participants agree to the following:

Article 1 Participation

1.1 Participants agree to participate in the CBC in good faith under the terms of this Agreement.

1.2 Participants acknowledge that to become a Participant under this Agreement the membership criteria described above must be met as determined by NCI at its sole discretion.

1.3 Nothing in this Agreement will be construed to limit the freedom of a Participant from engaging in research with other parties consistent with its obligations under this Agreement.

1.4 It is anticipated and encouraged that Participants will enter into separate agreements with one another to accomplish specific projects or tasks. The terms of these separate agreements will be consistent with and complement the spirit of this Agreement and follow the NIH Guidance for Government-funded research including the NIH Research Tool Policy at http://ott.od.nih.gov/policy/research_tool.html.

1.5 Each Participant represents to the best of its knowledge that it has no conflicts of interest or relationships that would preclude it from entering into this Agreement or participating in the CBC.

1.6 The relationship of the Participants is that of independent contractors and not agents of each other or joint venturers or partners; thus, no Participant may act for or bind another Participant. Each Participant shall maintain sole and exclusive control over its personnel and operations.

Article 2 Confidentiality

2.1 Participants agree to keep information provided by another Participant(s) that is marked 'Confidential' ("Confidential Information") confidential for a period of five (5) years from the date the Confidential Information was provided and to employ all reasonable efforts to maintain the Confidential Information of the disclosing Participant secret and confidential, such efforts to be no less than the degree of care employed by each Participant to preserve and safeguard its own confidential information. Oral disclosures of confidential information will be reduced to writing within fifteen (15) days, marked 'Confidential" and provided to the receiving Participant by the disclosing Participant. The obligations of a Participant shall not extend to any part of the Confidential Information of the disclosing Participant that:

(a) can be demonstrated to have been in the public domain or publicly known at the time of disclosure; or

(b) can be demonstrated to have been in the possession of or that can be demonstrated to have been readily available to the receiving Participant from another source not subject to a confidentiality obligation prior to the disclosure; or

(c) becomes part of the public domain or publicly known by publication or otherwise, not due to any unauthorized act by the receiving Participant; or

(d) can be demonstrated as independently developed or acquired by the receiving Participant without reference to or reliance upon such Confidential Information;

(e) is disclosed by a receiving Participant(s) with the written approval of the disclosing Participant, or

(f) is or was disclosed by the disclosing Participant to a third party without restriction; or

(g) is required to be disclosed by law by a court order or regulatory body of competent jurisdiction, or by the Freedom of Information Act (FOIA).

2.2 All Participants acknowledge and agree that any information that may be obtained from any Central CBC Database to which a Participant may have access is included in the Confidential Information.

2.3 To the extent permitted by law, it is the intention of NCI to protect Confidential Information provided by Participants to the Central CBC Database under the exemptions provide in the Freedom of Information Act; however, the applicability of exemptions is determined solely by the NCI FOIA Office The party providing the Confidential Information will be given a 60 day notice of any said FOIA request for its Confidential Information to permit the necessary action to protect its Confidential Information.

Article 3 Intellectual Property

3.1 Each Participant will retain ownership of inventions made by its employees. Ownership of joint inventions made by two or more Participants will be determined by applicable patent law. It is expected that Participants with joint ownership of an invention will establish an appropriate agreement among them which establishes the rights and responsibilities of each Participant and reflects cooperation to efficiently develop such an invention to an appropriate commercial endpoint. Furthermore it is expected that groups of Participants which own individual inventions which collectively may produce a beneficial commercial product(s) will similarly cooperate to reach an appropriate commercial endpoint. Participants will report inventions made as part of the CBC to the Technology Transfer Committee on a semi-annual basis.

3.2 Consistent with the spirit of sharing resources and data within the CBC community, it is expected that each Participant will manage intellectual property in a manner which allows sharing of technology within the CBC for research purposes and also protects those inventions which may benefit from IP protection to facilitate downstream development (i.e., therapeutics, diagnostics).

3.3 Each Participant will license inventions according to its own institutional policies or applicable laws and regulations. Preference for nonexclusive licensing or limited exclusive licensing to facilitate broad commercial application and wide use of research resources by the research community is expected. When appropriate to encourage investment in and development of a technology, exclusive licensing might be considered. Participants that exclusively license a technology should retain the right to use the invention for research purposes for itself and the broader research community.

3.4 Each Participant will assign one Technology Transfer Representative (TTR) to the CBC. The TTRs will collectively establish a CBC Technology Transfer Committee (TTC) to maintain lines of communication related to the IP developed from the CBC and to share best practices for commercial development of their respective technologies and establish common guidelines for the management of CBC-related partnership and other technology transfer agreements.

3.5 The TTC will prepare CBC Technology Transfer Guidelines (“TT Guidelines”) and have the TT Guidelines ratified by Participants within twelve (12) months of execution this Agreement. The TT Guidelines will be considered ratified by approval of a two-thirds majority of the Participants and approval of the SAC.

Participants will operate according to the ratified TT Guidelines. By signing this Agreement, Participants joining the CBC following the ratification of the TT Guidelines agree to operate according to the TT Guidelines.

3.6 The TTC and TTRs will assemble for a face-to-face Technology Transfer meeting at least annually. The TTC and TTRs will participate in quarterly technology Transfer teleconferences.

Article 4 Sharing of Research Resources and Data

4.1 Consistent with the intellectual property management described in Article 3, the Participants agree to share research materials among the other Participants for CBC research under an agreement that is consistent with this Agreement and no more restrictive than the NIH Material Transfer Agreement, the NIH Simple Letter Agreement or the Uniform Biological Material Transfer Agreement found at http://ott.od.nih.gov/forms_model_agreements/forms_model_agreements.html#MTACTA.
Such agreements would not include reach-through to future inventions or restrictions on the sharing of modified derivatives which may be produced using the research materials.

4.2 Participants will share data from CBC research in confidence pursuant to Article 2 to facilitate the efficient development of cancer therapeutics and diagnostics through cooperation and communication among the CBC community.

Article 5 Publications and Press Releases

5.1 Participants are encouraged to make publicly available the results of their research and development activities. Before a Participant(s) submits a paper or abstract for publication or otherwise intends to publicly disclose information, such Participant(s) will allow another Participant which has provided Confidential Information thirty (30) days to review the proposed publication or disclosure to assure that Confidential Information is not inappropriately disclosed. A Participant may request in writing that the proposed publication or other disclosure be delayed for up to thirty (30) additional days as necessary to file a patent application.

5.2 Participants agree to provide proposed press releases that reference the CBC or that rely on work from another Participant for review and comment by the NCI or other Participants as appropriate at least ten (10) days prior to its release.

5.3 Participants will provide the TTC with a list of its publications related to the CBC on a semi-annual basis.

Article 6 Liability

6.1 No indemnification for any loss, claim, damage or liability is intended or provided by any Participant under this Agreement. To the extent permitted by law, each Participant shall be liable for any loss, claim damage, or liability that said Participant incurs as a result of its activities under this Agreement. The NCI or any other agency of the federal or a state government assumes liability only to the extent provided by law.

6.2 THE PARTICIPANTS MAKE NO EXPRESS OR IMPLIED WARRANTY AS TO ANY MATTER WHATSOEVER RELATED TO THIS AGREEMENT INCLUDING THE MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE OF THE RESEARCH OR ANY INVENTION OR MATERIAL, OR THAT A TECHNOLOGY UTILIZED BY A PARTICIPANT UNDER THIS AGREEMENT DOES NOT INFRINGE ANY THIRD-PARTY PATENT OR OTHER INTELLECTUAL PROPERTY RIGHTS.

Article 7 Termination or Withdrawal

7.1 A Participant may withdraw from the CBC and this Agreement with thirty (30) days written notice.

7.2 The NCI may terminate this Agreement unilaterally with thirty (30) days written notice.

7.3 The provisions of Articles 2-7 will survive withdrawal by a Participant or the termination of this Agreement.

Article 8 General Terms

8.1 By entering into this Agreement, no Participant directly or indirectly endorses any product or service of another Participant whether directly or indirectly related to this Agreement. A Participant will not in any way state or imply that this Agreement is an endorsement of any product or service by another Participant or any of its organizational units or employees.

8.2 This Agreement may be amended by the NCI to reflect programmatic changes in the CBC or the addition or departure of Participants. The NCI may implement a substantive change to this Agreement to be applied prospectively thirty (30) days following an announcement by NCI. All amendments and changes to this Agreement must be approved by a simple majority of the SMC and approved by the NCI Director.

8.3 Participants acknowledge that there is no additional funding from any source associated with this Agreement. This Agreement does not prohibit Participants from otherwise submitting prospective targets, lead compounds and drug candidates to NCI for evaluation or possible access to additional resources; however, access to any future NCI resources or programs including the NCI pipeline or clinical resources will be only after approval by appropriate committees or NCI units not necessarily associated with the CBC. Participants acknowledge that the NCI, should it so decide has the express right to enter lead compounds into NCI's clinical development program.

8.4 Any dispute arising under this Agreement will be submitted jointly to the signatories or their designee of this Agreement. 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 Paragraph 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. Pending the resolution of any dispute or claim pursuant to this Article, the Parties agree that performance of all obligations will be pursued diligently.

8.5 As the Participants are part of institutions of higher education that have many foreign persons as employees and students, and conduct their activities under the fundamental research exclusion to the U.S. export control laws, the Participants agree that there will be no exchange of information that is subject to export control under the U.S. Export Administration Regulations and International Traffic in Arms Regulations.

8.6 Participants will operate in accordance with all appropriate federal, state and local laws and regulations including those related to safety, human subjects research and animal welfare.

(Signatures Begin on the Following Page)*By signing below the Participant agrees to the terms contained herein.*

NCI: _____
(Authorized Signature)

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(Authorized Signature)

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Title

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