Public Summary
Investigational Drug Steering Committee (IDSC)
Tuesday-Wednesday, October 4-5, 2011

1) **Call to Order, Introductions and Review of Minutes**
   a) **Motion 1**: The IDSC meeting minutes from July 15th and August 8th call were approved.
   b) **Coordinating Center for Clinical Trials (CCCT) update** *(Reeves):*
      i) The new subject experts were introduced to the IDSC.
         (1) Steven Larson (Imaging)
         (2) Gary Rosner (Biostatistician)
         (3) Jedd Wolchok (Immunotherapy; not present)
      ii) Mario Sznol (immunotherapy), Don Berry (biostatistics) and Anthony Shields (imaging) will serve until the end of 2011. They were presented with letters of gratitude by James Doroshow.
      iii) Susan Groshen's (biostatistics) term will be extended until the end of 2012.
      iv) The next IDSC Winter meeting will be held on January 13, 2011 in Chicago, IL at the O'Hare Hilton.
   c) Amit Oza and Miguel Villalona are the new IDSC N01 co-chair nominees (*update: Miguel Villalona has been nominated and accepted the position as of 1/1/2012*). Dan Sullivan's term ends on 12/31/2011 (we thank him for his excellent service).
   d) **Cancer Therapy Evaluation Program (CTEP) update** *(Zwiebel):* James Zwiebel discussed the new OEWG IDB early phase trial monitoring/tracking and impact on U01 and N01 holders.
   e) **PI3K/Akt/mTOR (PAM) TF:** The hyperglycemia and hyperlipidemia PAM TF manuscript has been submitted to JCO.

2) **CTEP Drug Development Plan – TL32711 (Smac mimetic;** *Takebe)*
   a) CTEP is planning to add the Smac mimetic/IAP inhibitor, TL32711 to its portfolio (*further information is confidential*). A limited testing plan has been developed for this agent upfront.
   b) The IDSC endorsed the TL32711 CTEP drug development plan with modifications.
   c) Mass solicitation will be developed and distributed.

3) **CTEP Drug Development Plan – PCI-32765 (BTK inhibitor;** Pamela Harris*)*
   a) CTEP is planning to add the BTK inhibitor (PCI-32765) to its portfolio (*further information is confidential).* A limited testing plan has been developed for this agent upfront.
   b) The IDSC endorsed the PCI-32765 drug development plan.
   c) Mass solicitation will be developed and distributed.

4) **New IDSC categories for Subject Experts** (*please send Amy Gravell (agravell@emmes.com) nominees*):
   a) Pharmacogenomic/Pharmacometric Expert
   b) Preclinical Experimental Therapeutics Expert
   c) Genomics – Early Drug Development Expert
   d) Lymphoma Expert (for Liaison to IDSC)

5) NeXT Update *(Barbara Mroczkowski):*

a) Barbara Mroczkowski provided an overview of NExT and projects that are under review or approved. http://next.cancer.gov/. NExT is currently through Cycle 8 (*much of the information is confidential that was presented*).

b) Mission: The mission of the NExT Program is to advance clinical practice and bring improved therapies to patients with cancer by supporting the most promising new drug discovery and development projects. The NExT Program is not a grant mechanism; applications with exceptional science cannot be accepted without a clear path to the clinic or potential benefit to patients. Awardees will not necessarily receive direct funding; rather, the NCI may allocate various contracts and grant resources toward the implementation and development of submitted projects. The NCI will partner with successful applicants to facilitate the milestone-driven progression of new anticancer drugs (small molecules, biologics) and imaging agents towards clinical evaluation and registration.

c) The NCI's Experimental Therapeutics (NExT) Program, a partnership between NCI's Division of Cancer Treatment and Diagnosis (DCTD) and the Center for Cancer Research (CCR), consolidates NCI's anticancer drug discovery and development resources in support of a robust, balanced, goal-driven therapeutics pipeline. Combined, these resources are capable of supporting a discovery and development continuum from initial discovery through Phase II clinical trial evaluation. *The NCI is focused on moving high-priority discovery and development projects through to proof-of-concept clinical trials and, when warranted, will continue non-commercial research and development activities (up through and including clinical trials) on any discovery project in the NExT Program.*

d) The discovery engine of this program is the **Chemical Biology Consortium (CBC)**. The NCI has established this collaborative network comprising 12 of the top Specialized and Comprehensive Screening and Chemistry Centers with world-class capabilities covering high-throughput methods, bioinformatics, medicinal chemistry, and structural biology. Additionally, the highly successful Developmental Therapeutic Program (DTP) provides the resources needed to facilitate discovery and late-stage preclinical development through the final steps of development to first-in-human studies. Concurrent molecular imaging and/or pharmacodynamic assay development provided by the **Cancer Imaging Program (CIP)**, **National Clinical Target Validation Laboratory (NCTVL)**, and CCR allow early assessment of potential clinical biomarkers. These coordinated and focused R&D processes enable continued incorporation of new data and disease insights into every step of the discovery and development process, thereby increasing the potential for successful clinical evaluation of agents.

e) Clinical evaluation is supported by the **Cancer Therapy Evaluation Program (CTEP)**, NCI. The development program will be a collaborative effort between NCI and industry for agents in the late preclinical stage or early clinical stage to further develop the clinical program in the niche area that is outside the pharmaceutical industry's scope. Agents requiring IND-directed toxicology data or agents already in Phase I or II clinical trials are of interest. Companies seeking NCI collaboration are encouraged to apply to the NExT Program.

f) Recognizing the importance of an integrated approach to therapeutics development, NCI Senior Leadership has organized a unified governance structure for the NExT Program responsible for coordinating and integrating available resources. With a goal of reaching go/no-go decisions as efficiently as possible, the purpose of **NExT governance** is to ensure a pragmatic approach to drug discovery and development and a clear path to market. With the governance structure and unified **NExT Program Mission**, NCI will make data-driven decisions following NExT **Stage Gate** guidelines to maximize the potential for success at each consecutive stage. As such, the NExT Program is envisioned to streamline the development and testing of promising new anticancer drugs and expedite their delivery to bedside.

6) CTEP Drug Development Plan – XL-184 (c-Met and VEGFR2 inhibitor; John Wright*)*

a) CTEP is planning to add the c-Met and VEGFR2 inhibitor (XL-184) to its portfolio (*further information is confidential).* A limited testing plan has been developed for this agent upfront.

b) The IDSC endorsed the XL-184 CTEP drug development plan with some modifications.

c) Mass solicitation will be developed and distributed.

7) Cooperative Group Update *(Jeff Abrams):*

a) Reviews of NCI's Clinical Trials System

i) ***Emphasized need for public clinical trials system***

ii) ***Consensus achieved on 4 goals for transforming the system***

(1) Improve speed/efficiency of development & conduct
(2) Incorporate innovative science and trial design
(3) Improve trial prioritization, support, & completion
(4) Incentivize participation of patients & physicians

iii) ***In response, NCI is transforming its clinical trials system to create a highly integrated network to address rapid advances in cancer biology based on:***

(1) Recommendations from the IOM Report
(2) Previous reports (CTWG & Operational Efficiency)
(3) NCAB, BSA and CTAC
(4) Current stakeholder input

iv) Vision of Transformed Network

(1) System provides essential infrastructure for Group trials in treatment, control, screening, diagnosis, & prevention; and is major enabler of definitive confirmation of cutting-edge discoveries across all of NCI's clinical research programs
(2) Trials approved by Steering Committees open rapidly and complete accrual according to defined guidelines by leveraging an integrated national network of performance sites
(3) User-friendly system with harmonized processes is available to the extramural cancer community: investigators, patients, advocates, and industry

(4) New system provides an optimal platform to perform large scale testing of increasingly smaller subsets of molecularly-defined cancers, and efficiently answers critical questions not well supported in a commercial environment

v) The timeline should be July 2012 for new FOA release and November 2012 for receipt of applications.

8) Future Plans/Calls/Meetings:

a) Next call: TBD

b) **Winter 2012 IDSC Meeting:** Friday, January 13th, 2012 (Chicago, IL)

c) **Spring 2012 CTEP EDD/IDSC Meeting:** Monday-Wednesday, March 12-14th, 2012 (Bethesda, MD)

d) **Summer 2012 IDSC Meeting:** TBD

e) **Fall 2012 CTEP EDD/IDSC Meeting:** Monday-Wednesday, October 15-17th, 2012 (Bethesda, MD)