Public Summary
Investigational Drug Steering Committee (IDSC)
Friday, January 11th, 2013

1) Call to Order, Introductions and Review of Minutes

a) ***Proposed motion # 1****: The minutes from the October 16, 2012 IDSC meeting were approved.*

b) **Announcements**:

i) Elizabeth Garrett-Mayer has replaced Susan Groshen as an IDSC Biostatistician. We welcome Dr. Garrett-Mayer.

ii) Lillian Siu is the new IDSC U01 Co-chair replacing Pat LoRusso as of January 1, 2013. We thank Dr. LoRusso for her service.

iii) Antonio Jimeno has replaced Lillian Siu as a PAM (PI3K/Akt/mTOR) TF Co-chair as of January 1, 2013. Afshin Dowlati will remain the other TF co-chair.

c) **Thoracic Malignancies Steering Committee (TMSC) Update** (*David Gandara*):

i) A joint TMSC and FDA Workshop was held on February 2-3, 2012 in Bethesda, MD to discuss strategies for integrating biomarkers into the clinical development of new lung cancer therapies.

(1) **Development of Future Lung Cancer Trials**

(a) TMSC Master Protocol Task Force in NSCLC

(b) Biomarker-driven trial designs in both early stage adjuvant therapy & advanced stage NSCLC

(c) Account for inter-patient tumor heterogeneity & genomic complexity of NSCLC

ii) The TMSC Master Protocol Task Force has been working in a parallel effort with the Friends of Cancer (FOC) Task Force to finalize a Master Protocol design for NSCLC (*other information is confidential).*

d) **Task Force Updates:**

i) **Clinical Trial Design TF** (Mark Ratain): Drs. Rena Conti and Scott Ramsey (VOI Working Group Co-chairs) may come to an upcoming IDSC meeting to educate individuals on Value of Information – VOI.

(1) **Aim to provide the IDSC with:**

(a) Education and training in economic methods to prospectively evaluate clinical trials from a social perspective (VOI methods, Veenstra/Ramsey) and from a private perspective (Return on investment methods, Conti).

(b) Plan to discuss the complementary contexts in which the methods are currently applied, areas of agreement between the methods, and assumptions implicit in both strategies.

ii) **Pharmacology TF** (*Edward Newman*): The TF has revised the Drug-Drug Interaction Guidance (to make more global) and will pilot project with CTEP Pharmaceutical Management Branch (PMB) assistance. The group will come back to the IDSC after pilot is completed with results.

iii) **DNA Repair TF** (*Robert DiPaola*): Based on questions raised at the Task Force December 3rd call with ad hoc experts, TRC-102 has been postponed for IDSC presentation. Further information regarding its difference from Topoisomerase II will be pursued.

e) **The CTEP Spring 2013 Early Drug Development and IDSC meeting will be held on Monday-Tuesday, April 22nd and 23rd. The March 18-19th meeting has been canceled.**

2) **NCI Special Symposium**: **Using Team Science Approaches for the NCI Drug Program**

a) **Welcome/Introduction:** James Doroshow welcomed IDSC members and NCI staff to the Special Symposium.

b) **Overview of the Early Therapeutics – Clinical Trials Network** *(Percy Ivy):*

i) The NCI CTEP Early Experimental Therapeutics program has had a longstanding mission that is focused on the research and development of new treatments for cancer. To that end our program plays a number of roles. First, recognizing the importance of combination therapies, CTEP has succeeded in working with our collaborators to combine investigational new drugs. Our program also incorporates biomarker development and qualification for use in clinical trials. In addition, we seek a better understanding of cancer biology and how it relates to drug development. Drug development now requires new approaches, including the full molecular characterization of patients' tumors. To address these new challenges and opportunities, the NCI has initiated a full redesign of its early experimental therapeutics program, encompassing phase 0 through phase 2.

ii) The new Early Therapeutics – Clinical Trials Network (ET-CTN) will employ a team science approach for drug development, while integrating research resources and programs across the NCI. Teams will work together to define the best path forward for the development of a new drugs. This team science approach should allow NCI-sponsored investigators to perform high impact clinical trials enriched with molecular characterization of patients and sophisticated scientific research. The goal is to move toward the more precise selection of patients for participation on clinical studies. Along the way we hope to enhance interaction and collaboration as well as improving the training of the next generation of drug developers.

iii) The National Cancer Institute will build on its existing infrastructure including its grants and contracts for phase 1 and 2 clinical trials and plans to strengthen its collaborations with other NCI-sponsored agreements and programs. Many complex pieces will be cohesively brought together in a way that allows us to better understand patients' tumors and the best treatment for them.

c) **Team-Based Science Recommendations and Obstacles**:

(1) Ed Harlow introduced the esteemed group of speakers to participants and outlined the session for the symposium.

(2) Ken Anderson (SPORE), Lewis Cantley (Stand Up to Cancer Dream Team), Levi Garraway (Broad Institute), Ken Turteltaub (Lawrence Livermore National Library), and L. Michelle Bennett (NHLBI) discussed team science strategies and obstacles. Recommendations from the session are listed below.

(a) <u>Recommendations for "Successful" Team Science</u>:

(i) Must have a clear goal that is achievable in the funding period.

(ii) Leverages multiple resources.

(iii) Trust must be established with all team members.

(iv) Fosters partnerships of academia, pharmaceuticals, NCI, regulatory agencies, and advocacy to fast forward progress.

(v) Mentors should be available for new Team members.

(vi) Able to resolve conflict swiftly and effectively (developing ways to circumvent conflict).

(vii) All members of the team believe that the goal is a worthy one **AND** that it is achievable with the technology, expertise and funds available to the team.

(viii) Each member of the team must understand her/his role in achieving the goal, and must feel that she/he will get credit for making this contribution.

(ix) There must be clear, achievable **milestones with a timeline.**

(x) Frequent teleconferences and/or face-to-face meetings are required to verify that the milestones are being met.

(xi) **The Leader is critical:** the Leader must be fully engaged in achieving the goal and must be willing to cede senior authorship on key papers to members of the team who achieve their assigned tasks (motivation). Ideally, the Leader should have a working knowledge of all aspects of technologies/disciplines utilized by the team (or be willing to learn these at a level that allows evaluation of quality).

(xii) **The Leader (or leadership team) must have the ability to re-distribute resources** in a timely manner to solve unanticipated problems that arise or replace team members who, for whatever reason, are not meeting their milestones.

(xiii) An escalating budget rather than fixed yearly budget is usually better. Some members of the team only become relevant at late stages of the project.

(xiv) There must be sufficient funds to achieve the goal(s).

(xv) Facilitates iterative bench to bedside and back research which has markedly improves patient outcome**.**

(xvi) Metric of success is improved patient outcome.

(xvii) Funds infrastructure for translational research and tissue banks.

(xviii) Deep and sustained collaborations are essential.

(xix) Model of team development includes: forming, storming, norming, and performing. This model is cyclical and arises each time the team is changed/altered.

(xx) May want to develop a "prenuptial" contract for scientist, which outlines what is expected of leadership, team members, and timelines.

(b) **<u>Reasons that Team Science can fail or underachieve</u>:**

(i) The goals are ambiguous, too broad, or premature with existing knowledge or tools.

(ii) Some members of the team are only there for the money (or fame).

(iii) A key technology needed for success is premature or oversold.

(iv) Success depends on making a highly unlikely "Discovery". Most members of the team twiddle their thumbs waiting for someone to make

the "Discovery" or perfect the technology needed for their role to become relevant.

(v) The funds are divided up at the beginning with no ability of the leader to shift funds from non-performers to performers.

(vi) There are insufficient funds to achieve the goal.

(vii) Poor leadership. Members don't like or trust each other and thus, don't exchange ideas or even attend meetings.

(viii) Bureaucratic and logistical delays.

(ix) Publication/authorship considerations – members don't feel valued.

ii) **Ed Harlow held an open discussion regarding the session and zoned in on a few areas that should be worked on or are concerns of the group**.

(1) Currently the process for the new ET-CTN is being structured by agent. There was some concern regarding using this approach by IDSC and other attendees. Target/pathway may be a better way to organize.

(2) Could drugs outside of the CTEP portfolio be studied with yearly ET-CTN funds that are set-aside? Reallocation of resources has to be discussed internally through CTEP.

(3) Several IDSC members were concerned that CTEP have the flexibility to bring in the "best" agents not just what comes through NCI NExT (NCI Experimental Therapeutics Program). A look at the NExT process is needed.

(4) Flexibility to change teams and leadership was discussed. More than one Team leader and one leader should select other.

(5) Finding the right team leader will be essential to the ET-CTN process (should be organized, unique, duel team leaders, timelines, milestones, etc),

(6) Communication process should encompass small groups, not 20-30 people on a teleconference line.

(7) Storming was a concern brought up by several IDSC members (conflict resolution).

(8) Need concise SOPs developed.

3) **Future Plans/Calls/Meetings:**

a) CTEP EDD/IDSC Spring 2013 Meeting: Monday-Tuesday, April 22nd-23rd (NIH Campus; Room/Building TBD)

b) IDSC Summer 2013 Meeting – Friday, July 26th (Bethesda, MD)

c) CTEP EDD/IDSC Fall 2013 Meeting: Monday-Wednesday, September 9-11th (Natcher; IDSC location TBD)