ATTACHMENT 5

NIH SCIENTIFIC MANAGEMENT REVIEW BOARD

Translational Medicine and Therapeutics Working Group

CHARGE

BACKGROUND

Developing new therapeutics for human disease is a complex, challenging process. The outcome is often disappointing, as ninety-five percent of candidate drugs prove to be ineffective. Furthermore, efforts by biotech and pharmaceutical companies to develop new molecular entities have been reduced recently, due to lack of available venture capital and shrinking resources for research and development. Paradoxically, new molecular targets for therapeutics are appearing in unprecedented numbers, as a result of advances in genomics and molecular biology, but many of those new targets are being neglected. If the process of therapeutics development is to be accelerated, improved, and streamlined, a new paradigm of discovery will be required – ideally one that incorporates new and innovative strategies for research and development in addition to fostering new collaborations among government, academia, and industry – with the aim of more effectively bridging the translational divide.

The National Institutes of Health (NIH) possess scientific and technological resources to assist in the creation of this new paradigm, and extant and emerging programs at NIH are expertly equipped to catalyze its progress. For example, the Molecular Libraries Screening Center Network provides academic investigators with high throughput screening to obtain small molecule probes for modulating a given biological process or disease state. The NIH Chemical Genomics Center, part of this Network, deploys a robotic, high throughput screening system and a library of more than 350,000 compounds useful in basic discovery and as probes of cellular pathways. In addition, TRND – NIH's new program for Therapeutics for Rare and Neglected Diseases – provides resources for the preclinical phase of drug development, with a focus on disorders that have attracted minimal interest in the private sector. The NIH Clinical Center is well set up to carry out Phase I or II clinical trials for new molecular entities. Furthermore, the NIH has recently strengthened its relationship with the Food and Drug Administration to facilitate efficient and science-based regulatory review. Finally, the institutions that have received funding under NIH's Clinical and Translational Science Awards (CTSAs) offer a network of organizations with the infrastructure and the personnel to advance the cause of enhanced clinical investigation and therapeutics development.

With the recent passage of the Patient Protection and Affordable Care Act, NIH is even better poised to deploy these resources. The Act authorizes NIH to establish a Cures Acceleration Network (CAN) with the aim of advancing the development of "high need cures," particularly by reducing the barriers between research discovery and clinical trials in areas that the private sector is unlikely to pursue in an adequate or timely way. The CAN provisions of the Act grant

unprecedented flexibility to NIH to carry out therapeutic development projects and underscore the expectation, by Congress and the American public, that NIH is to play a catalytic role in realizing the promise of translational medicine and advancing human health.

CHARGE

The Translational Medicine and Therapeutics (TMAT) Working Group of the SMRB has a two-fold charge of:

1. Identifying the attributes, activities, and functional capabilities of an effective translational medicine program for advancing therapeutics development; and
2. Broadly assessing, from a high-level view, the NIH landscape for extant programs, networks, and centers for inclusion in this program and recommending their optimal organization.

In addressing its charge, the Working Group will consider how the Agency could leverage and organize a wide range of existing NIH resources and effectively implement the Cures Acceleration Network (CAN) (assuming appropriation of funds). Additionally, in executing its charge, the TMAT Working Group should consider the following:

- Infrastructure, initiatives, and resources with direct relevance to the therapeutic pipeline currently supported by the Agency, including, but not limited to, programs (e.g., TRND Program, Rapid Access to Interventional Development Program, CAN, etc.,) core facilities (e.g., Molecular Libraries Screening Center Network), and clinical research centers (e.g., NIH Clinical Center, CTSAs, etc.,)
- Methods to synergize with, and avoid competition with, resources in the private sector.
- Prior recommendations for strengthening the clinical and translational research enterprise at NIH, including recommendations of the IOM in its report *Enhancing the Vitality of the National Institutes of Health*, and relevant lessons learned from industry, academia, non-profit organizations, etc.;
- Metrics and methodologies that could be used for evaluating the impact of changes in the organization and management of the therapeutic development program.

PROCESS

The TMAT Working Group will:

- Seek input from experts and stakeholders, including, but not limited to, NIH leadership, NIH intramural researchers, NIH extramural grantees, representatives of the pharmaceutical and biotechnology industries, leaders of academic drug discovery units, representatives of venture capitalist firms, patient advocacy and consumer organizations, and other governmental organizations;

- Hold deliberations, including a roundtable session, open to the full SMRB; and
- Report its recommendations to the full SMRB.

DELIVERABLES AND TIMEFRAME

The TMAT Working Group will present to the full SMRB:

- Attributes, activities, and associated functional capabilities of a translational medicine program optimized to enhance therapeutics development;
- Recommendations for organizing the Agency's existing components to optimize a translational medicine and therapeutics program; and
- Metrics for evaluating successes and any untoward consequences of organizational and/or management change, in particular, consequences for the progress of research in the areas affected by the proposed changes.

The TMAT Working Group will present its findings and recommendations to the full SMRB in a timeframe that positions the full Board to complete its deliberations on this matter by December 2010.