



# Translational Medicine and Therapeutics

**July 26, 2010**

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# Outline

- **New Charge to the SMRB: Translational Medicine and Therapeutics**
- **Impetus for Translational Medicine and Therapeutics Deliberations: A Changing Landscape**
- **Advancing Translational Medicine and Therapeutics Discovery: A Role for NIH**
- **TMAT Working Group: Next Steps**



**New Charge to the  
SMRB –  
Translational  
Medicine and  
Therapeutics**

# TMAT Membership

## Non- Federal

Arthur Rubenstein, MBBCh  
(*Chair*)

William Brody, MD, PhD

Gail Cassell, PhD

William Roper MD, MPH

Solomon Snyder, MD

Huda Zoghbi, MD

Norman Augustine (*ad hoc*)

## Federal

Josephine Briggs, MD

Anthony Fauci, MD

Stephen Katz, MD, PhD

Griffin Rodgers, MD MACP

Susan B. Shurin, MD

Harold Varmus, MD

Francis Collins, MD, PhD  
(*ex officio*)

# TMAT Charge

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

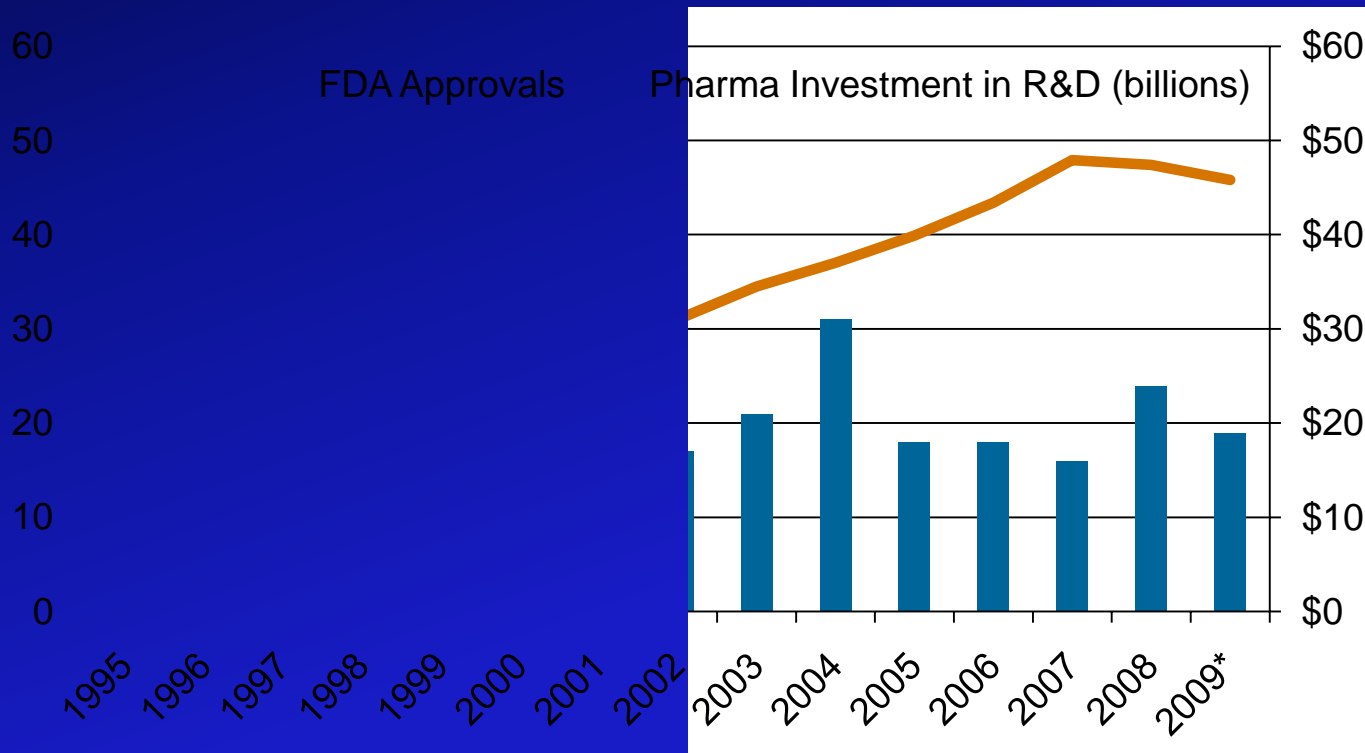


**Impetus for  
Translational  
Medicine and  
Therapeutics  
Deliberations:  
A Changing  
Landscape**



# A Changing Landscape: Decline in Approved NMEs

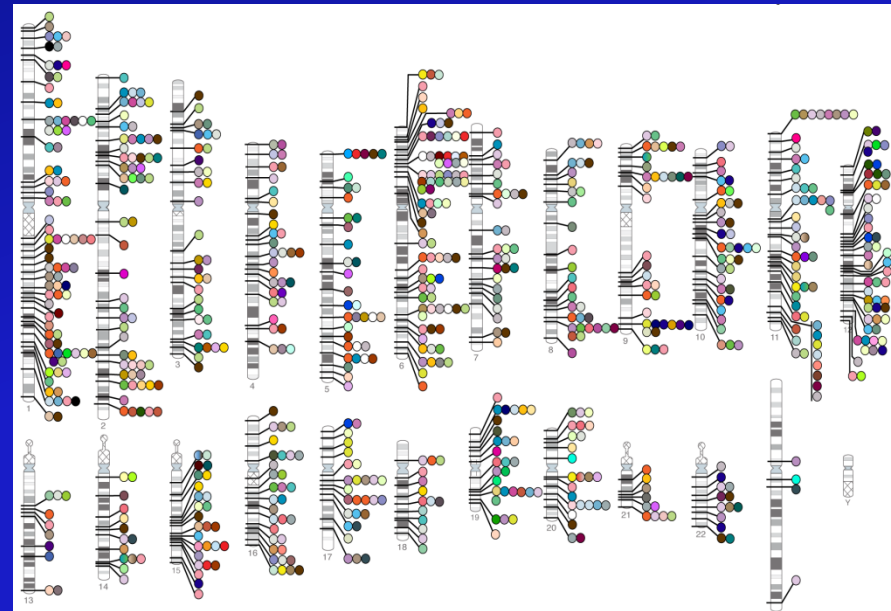
- Despite greater investments in R&D by Pharma, FDA approvals of new medical entities have declined



# A Changing Landscape: Increases in Potential Molecular Targets

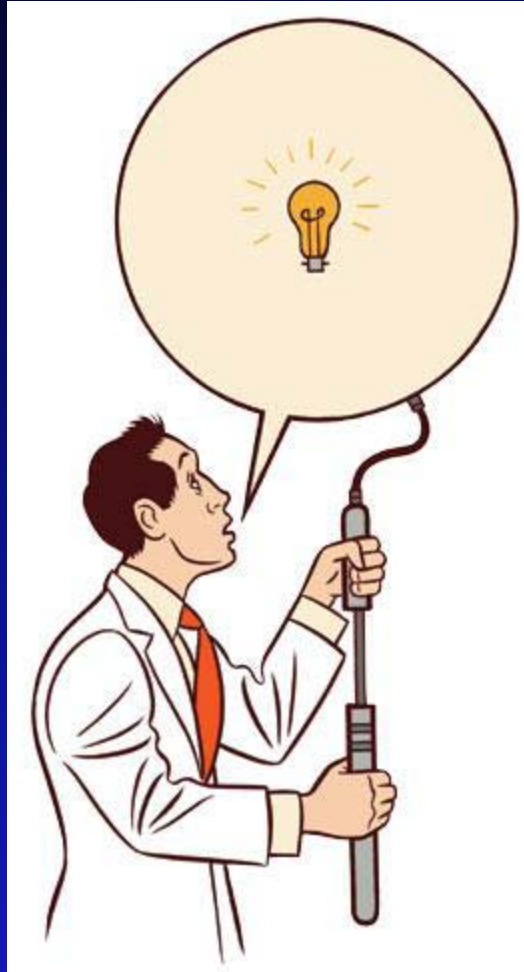
- Most recently, due to lack of available venture capital and shrinking resources for R&D, efforts have been reduced by biotech and pharmaceutical companies to develop new entities
- Paradoxically, new molecular targets for therapeutics are being discovered in unprecedented numbers as a result of advances in genomics and molecular biology

Validated GWAS hits 2010 1<sup>st</sup> Quarter





# A Changing Landscape: Need for A Paradigm Shift



*If the process of therapeutics discovery and translational medicine is to be accelerated, improved, and streamlined, a new paradigm of discovery will be needed*

# A Changing Landscape: Shifting the Paradigm for Therapeutics Discovery

## Growing “environmental” pressures on pharmaceutical industry



### How to improve R&D productivity: the pharmaceutical industry's grand challenge

Steven M. Paul, Daniel S. Mytelka, Christopher T. Dunwiddie, Charles C. Persinger, Bernard H. Munos, Stacy R. Lindborg and Aaron L. Schacht

**Abstract** | The pharmaceutical industry is under growing pressure from a range of environmental issues, including major losses of revenue owing to patent expirations, increasingly cost-constrained healthcare systems and more demanding regulatory requirements. In our view, the key to tackling the challenges such issues pose to both the future viability of the pharmaceutical industry and advances in healthcare is to substantially increase the number and quality of innovative, cost-effective new medicines, without incurring unsustainable R&D costs. However, it is widely acknowledged that trends in industry R&D productivity have been moving in the opposite direction for a number of years. Here, we present a detailed analysis based on comprehensive, recent, industry-wide data to identify the relative contributions of each of the steps in the drug discovery and development process to overall R&D productivity. We then propose specific strategies that could have the most substantial impact in improving R&D productivity.

**New molecular entity (NME)** is a medication containing an active ingredient that has not been previously approved for marketing in any form in the United States. NMEs are conventionally used to refer only to small molecule drugs, but in this article we use the term as a shorthand to refer to both new chemical entities and new biologic entities.

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The pharmaceutical industry is facing unprecedented challenges to its business model. Experienced observers and industry analysts have even predicted its imminent demise<sup>1</sup>. Over the past decade, serious concerns about the industry's integrity and transparency — for example, around drug safety and efficacy — have been raised, compromising the industry's image, and resulting in increased regulatory scrutiny<sup>2</sup>. This erosion in confidence in the industry and its products has resonated poorly with patients, health-care professionals, payers and shareholders. Indeed, the industry's price/cost/ratio, a measure of the current valuation of the industry, has decreased below that of the S&P 500 index and has remained more or less flat, as have share prices for the past 7 years.

The industry's profitability and growth prospects are also under pressure as healthcare budgets become increasingly strained. Generic drugs, although clearly helping to keep drug prices in check, are currently approaching 70% of all prescriptions written in the United States<sup>3</sup>. Moreover, key patent expirations between 2010–2014 have been estimated to put more than US\$209 billion in annual drug sales at risk, resulting in \$113 billion of sales being lost to generic substitution<sup>4</sup>. Indeed, for every dollar lost in declining product revenues due

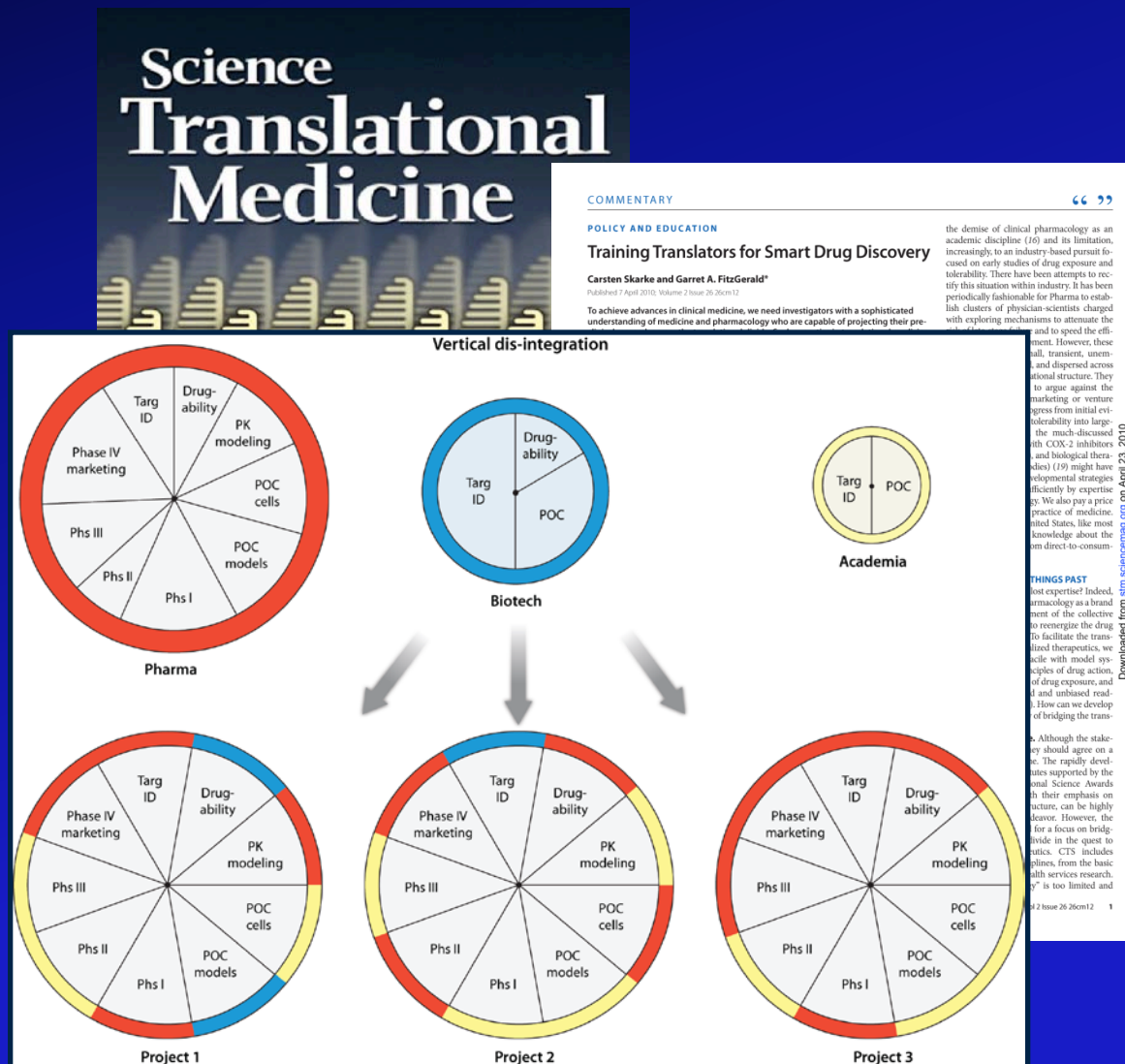
to patent expirations by 2012, it has been estimated that large-cap pharmaceutical companies will only be able to replace on average 26 cents with new product revenues<sup>5</sup>.

Simply stated, without a dramatic increase in R&D productivity, today's pharmaceutical industry cannot sustain sufficient innovation to replace the loss of revenues due to patent expirations for successful products. A key aspect of this problem is the decreasing number of truly innovative new medicines approved by the US Food and Drug Administration (FDA) and other major regulatory bodies around the world over the past 5 years (in which 50% fewer new molecular entities (NMEs) were approved compared with the previous 5 years<sup>6</sup>). In 2007, for example, only 19 NMEs (including biologics) were approved by the FDA, the fewest number of NMEs approved since 1983, and the number rose only slightly to 21 in 2008. Of the 21 new drugs approved by the FDA in 2008, only 6 were developed by the 15 largest pharmaceutical companies and only 29% would be considered first-in-class medicines. In 2009, 24 new drugs were approved, 10 of which were developed by large pharmaceutical companies and only 17% of which could be considered first-in-class. Some have argued that the number of approved “mechanistically

- Search for ways to increase # and quality of cost effective new medicines w/o unsustainable R&D risks and costs
- Traditional drug development paradigm → proposed alternative paradigm “quick win- fast fail”

# A Changing Landscape: Shifting the Paradigm for Therapeutics Discovery (cont.)

- Shift from silo approach to highly collaborative model that distributes risk
- Need innovative models for R&D partnerships that transcend sectors and international boundaries
- Need for training and incentives for investigators who pursue careers in clinical and translational research





**Advancing  
Translational  
Medicine and  
Accelerating  
Therapeutics  
Discovery:  
A Role for NIH**



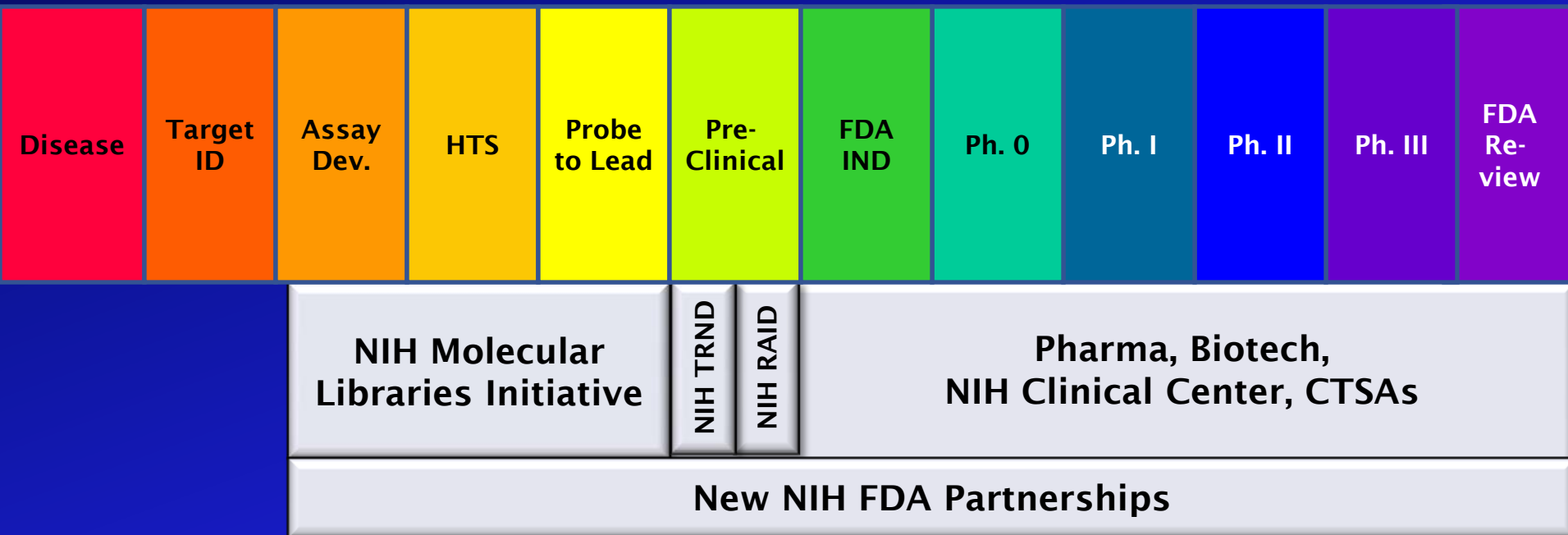
# A Role for NIH: Areas of Opportunity

- Applying high throughput technologies to understand fundamental biology, and to uncover the causes of specific diseases
- Translating basic science discoveries into new and better treatments
- Putting science to work for the benefit of health care reform
- Encouraging a greater focus on global health
- Reinvigorating and empowering the biomedical research community



# A Role for NIH: Areas of Expertise

- 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.





# A Role for NIH: Health Care Reform

## An Act

Entitled The Patient Protection and Affordable Care Act.

*Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,*

### SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) **SHORT TITLE.**—This Act may be cited as the “Patient Protection and Affordable Care Act”.

(b) **TABLE OF CONTENTS.**—The table of contents of this Act is as follows:

Sec. 1. Short title; table of contents.

#### TITLE I—QUALITY, AFFORDABLE HEALTH CARE FOR ALL AMERICANS

##### Subtitle A—Immediate Improvements in Health Care Coverage for All Americans

Sec. 1001. Amendments to the Public Health Service Act.

##### “PART A—INDIVIDUAL AND GROUP MARKET REFORMS

##### “SUBPART II—IMPROVING COVERAGE

“Sec. 2711. No lifetime or annual limits.

“Sec. 2712. Prohibition on rescissions.

“Sec. 2713. Coverage of preventive health services.

“Sec. 2714. Extension of dependent coverage.

“Sec. 2715. Development and utilization of uniform explanation of coverage documents and standardized definitions.

“Sec. 2716. Prohibition of discrimination based on salary.

“Sec. 2717. Ensuring the quality of care.

“Sec. 2718. Bringing down the cost of health care coverage.

“Sec. 2719. Appeals process.

Sec. 1002. Health insurance consumer information.

Sec. 1003. Ensuring that consumers get value for their dollars.

Sec. 1004. Effective dates.

##### Subtitle B—Immediate Actions to Preserve and Expand Coverage

Sec. 1101. Immediate access to insurance for uninsured individuals with a pre-existing condition.

Sec. 1102. Reinsurance for early retirees.

Sec. 1103. Immediate information that allows consumers to identify affordable coverage options.

Sec. 1104. Administrative simplification.

Sec. 1105. Effective date.

##### Subtitle C—Quality Health Insurance Coverage for All Americans

##### PART I—HEALTH INSURANCE MARKET REFORMS

Sec. 1201. Amendment to the Public Health Service Act.

##### “SUBPART I—GENERAL REFORM

“Sec. 2704. Prohibition of preexisting condition exclusions or other discrimination based on health status.

“Sec. 2701. Fair health insurance premiums.

“Sec. 2702. Guaranteed availability of coverage.



# A Role for NIH: Health Care Reform *(cont.)*

- The Patient Protection and Affordability Act authorizes the NIH to establish a Cures Acceleration Network. **Functions include:**
  1. Conduct and support revolutionary advances in basic research, translating scientific discoveries from bench to bedside;
  2. Award grants and contracts to eligible entities to accelerate the development of high need cures;

# A Role for NIH: Health Care Reform *(cont.)*

- **Functions include:** *(cont.)*

3. Provide the resources necessary for government agencies, independent investigators, research organizations, biotechnology companies, academic research institutions, and other entities to develop “**high need cures**”;
4. Reduce the barriers between laboratory discoveries and clinical trials for new therapies; and
5. Facilitate review in the FDA for the high need cures funded by the CAN

# A Role for NIH: Health Care Reform *(cont.)*

- A **“High Need Cure”** is defined as a drug, biological product, or device that, in the determination of the Director of NIH:
  - A. is a priority to diagnose, mitigate, prevent, or treat harm from any disease or condition; and
  - B. for which the incentives of the commercial market are unlikely to result in its adequate or timely development.



# **TMAT Working Group: Next Steps**

# Next Steps: Deliverables

- 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.



# Next Steps: Process for Deliberations

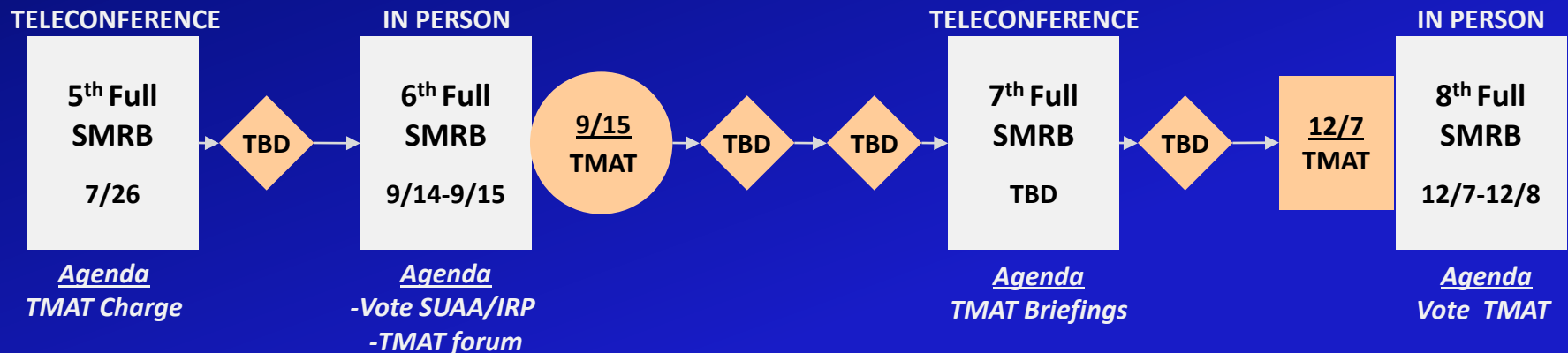
In addressing its charge, **the Working Group will consider** how the Agency could leverage and organize a wide range of existing NIH resources and effectively implement the CAN (assuming appropriation of funds)

# Next Steps: Process for Deliberations

- Additionally, in executing its charge, the **Working Group should consider** the following:
  - Infrastructure, initiatives, and resources with direct relevance to the therapeutic pipeline currently supported by the Agency;
  - Methods to synergize, 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.; and
  - Metrics and methodologies that could be used for evaluating the impact of changes in the organization and management of the therapeutic development program.

# Next Steps: Time Frame for Deliberations

The TMAP 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





## Discussion

*What questions and issues should the working group consider as it undertakes this task?*