

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

*A Collaboration between the Forum on Drug Discovery, Development, and Translation
and the Roundtable on Genomics and Precision Health*

**Enabling Precision Medicine:
The Role of Genetics in Clinical Drug Development –
A Workshop**

March 8, 2017

Keck Building of the National Academies
500 Fifth Street NW, Room 100
Washington, DC 20001

Statement of Task:

The current drug development process faces challenges of efficiency and overall sustainability due in part to high research costs, lengthy development timelines, and late-stage drug failures. Novel clinical trial designs that target genetically identified participants represent a potentially disruptive paradigm shift that could reduce overall health care costs associated with drug development, improve patient outcomes, and further realize the goals of precision medicine. An ad hoc committee will plan and conduct a one-day public workshop that will examine and discuss successes, challenges, and best practices for effectively utilizing genetic information in the design and implementation of clinical trials to support the development of precision medicines, including exploring the potential advantages and disadvantages of such trials across a variety of disease areas. Topics covered could include strategies for including genetically focused populations in clinical trial design, logistical challenges in conducting genetics-based clinical trials, and mechanisms for engaging with and educating potential trial participants. Discussions will be held among a broad array of stakeholders, which may include patients, academic researchers, health care providers, and representatives from the biopharmaceutical sector.

Objectives:

- To explore how clinical trials with genetically identified participants can enable more efficient and effective drug development and advance precision medicine.
- To highlight ongoing genetics-based clinical trials across a variety of diseases, examining best practices and lessons learned.
- To learn about the logistical challenges and successes associated with genetics-based clinical trial design.
- To examine possible mechanisms to engage participants and improve enrollment into clinical trials based on genetic characteristics.

The planning committee will develop the workshop agenda, select and invite speakers and discussants, and may moderate the discussions. Proceedings of the workshop will be prepared by a designated rapporteur in accordance with institutional policy and procedures.

8:00 a.m. *Breakfast available outside Keck 100*

8:30 a.m. **Opening Remarks**

STEVEN GALSON, *Co-Chair of the Forum on Drug Discovery, Development, and Translation*
Senior Vice President, Global Regulatory Affairs and Safety
Amgen Inc.

GEOFFREY GINSBURG, *Co-Chair of the Roundtable on Genomics and Precision Health*
Director, Duke Center for Applied Genomics and Precision Medicine Professor of
Medicine, Pathology, and Biomedical Engineering
Duke University Medical Center

8:35 a.m. **Charge to the Speakers and Participants**

LAURA NISENBAUM, *Workshop Co-Chair*
Advisor, Chorus Clinical Development
Eli Lilly and Company

**SESSION I: OVERARCHING CONSIDERATIONS FOR IMPLEMENTING
SUCCESSFUL GENETICS-BASED DRUG DEVELOPMENT**

Session Objectives:

- Discuss the perspective of patients with regard to the use of genetic data in clinical drug development.
- Consider challenges and possible solutions associated with the development and use of biomarkers or genetic tests for molecularly-targeted therapies.
- Explore issues that pertain to the regulatory pathway for genetic tests and biomarkers used in clinical drug development.

Moderator: LAURA NISENBAUM, Advisor, Chorus Clinical Development, Eli Lilly and Co.

8:45 a.m. **Accelerating the Pace of Progress in Genetics-Based Drug Development: The Perspective of a Patient and Patient Advocate**

JANE PERLMUTTER
President and Founder
Gemini Group

9:00 a.m. *Clarifying Questions*

9:10 a.m. **Clinical Development and Use of Biomarkers for Molecularly Targeted Therapies: Recommendations from a National Academies' Consensus Study**

ROBERT NUSSBAUM
Chief Medical Officer
Invitae

9:30 a.m. *Clarifying Questions*

9:40 a.m. **Navigating the Regulatory Pathway for Genetic Tests and Biomarkers for Clinical Drug Development**

MICHAEL PACANOWSKI
Associate Director for Genomics and Targeted Therapy
Center for Drug Evaluation and Research (CDER)
U.S. Food and Drug Administration

10:00 a.m. *Clarifying Questions*

10:10 a.m. **BREAK**

SESSION II: CASE STUDIES IN PRECISION DRUG DEVELOPMENT

Session Objectives:

- Explore recent examples of precision drug development in order to identify lessons that can be applied across disease fields.
- Examine clinical development plans for precision medicines, including:
 - using our understanding of the underlying biology to inform trial design and product development;
 - effects on research costs and timeline; and
 - patient recruitment and stratification.

Moderator: RICHARD SCHILSKY, Chief Medical Officer, American Society of Clinical Oncology

10:25 a.m. **Lung Master Protocol (Lung-MAP): A Biomarker-Driven Protocol for Accelerating Therapeutic Development for Squamous Cell Lung Cancer**

ROY HERBST
Professor of Medical Oncology; Associate Director for Translational Research
Yale Cancer Center

10:40 a.m. **STARTRK2 Clinical Trial: A Basket Study of Entrectinib for the Treatment of Solid Tumors with Specific Gene Rearrangements**

ZACHARY HORNBY
Chief Operating Officer
Ignyta

10:55 a.m. **Genetic Testing and Clinical Drug Development for Spinal Muscular Atrophy**

JOHN STAROPOLI
Associate Medical Director
Biogen

11:10 a.m. **Using Genetics in Clinical Trials for Mitochondrial Diseases**

MARNI FALK
Associate Professor of Pediatrics, University of Pennsylvania
Director, Mitochondrial Disease Clinical Center, Children's Hospital of Philadelphia

11:25 a.m. **Panel Discussion with Audience and Speakers**

12:10 p.m. **LUNCH**

**SESSION III: INTEGRATING GENETICS INTO THE DRUG DEVELOPMENT
PATHWAY FOR COMPLEX DISEASES**

Session Objectives:

- Illuminate novel ways to apply genetics/genomics discoveries into clinical development plans for complex diseases as a way to increase efficiency and improve outcomes.
- Survey innovative ways to engage participants in precision clinical trials, including communication, outreach, and education-based initiatives, with additional attention paid to increasing the diversity of such trials.
- Discuss additional logistical challenges associated with the execution of a successful genetics-based clinical trial for a complex disease, including:
 - techniques for patient stratification, including considerations for employing genetic risk scores; and
 - timelines for developing molecularly-targeted therapies, including trial execution.

Moderator: RUSS ALTMAN, Professor, Stanford University

1:00 p.m. **Patient Perspective on Genetics-Enabled Drug Development**

THERESA V. STRONG
Director of Research Programs
Foundation for Prader-Willi Research

1:15 p.m. *Clarifying Questions*

1:20 p.m. **Potential Advantages and Pitfalls to Using Genetics in Drug Development for Complex Diseases**

MATT NELSON
Head of Genetics
GlaxoSmithKline

1:35 p.m. *Clarifying Questions*

1:40 p.m. **Challenges in Leveraging GWAS Findings during Drug Development: A Case Study**

REBECCA BLANCHARD
Head of Clinical Pharmacogenomics and Operations
Merck

1:55 p.m. *Clarifying Questions*

2:00 p.m. **Updates and Strategies from the Tailor-PCI trial**

MICHAEL FARKOUH
Professor and Vice Chair Research, Department of Medicine
University of Toronto

2:15 p.m. *Clarifying Questions*

2:20 p.m. **Panel Discussion with Audience and Speakers**

Reaction Panelists:

G SCOTT CHANDLER
Vice President and Global Head Licensing and Early Development Safety
Genentech / Roche

JESSICA LANGBAUM
Principal Scientist
Banner Alzheimer's Institute

MARK TRUSHEIM
Visiting Scientist
MIT Sloan School of Management

L. KEOKI WILLIAMS
Professor of Medicine
Wayne State University School of Medicine

3:20 p.m. **BREAK**

**SESSION IV: FINDING INNOVATIVE WAYS TO INTEGRATE GENETICS
RESEARCH INTO THE DRUG DEVELOPMENT PROCESS**

Session Objective:

- Explore innovative, “outside-the-box” ideas for genetics-based clinical trials that could make the therapeutic development pathway more efficient.

Moderator: BRAY PATRICK-LAKE, Director of Stakeholder Engagement, Duke University CTSI

3:35 p.m. **Return on Investment from Patient Input on Development**

DAVID LEVENTHAL
Director, Clinical Innovation
Pfizer Worldwide Research and Development

3:55 p.m. **SaME Therapeutics: Grouping Rare Disease Patients by Shared Molecular Etiology to Accelerate Clinical Trials**

PJ BROOKS
Program Director, Division of Clinical Innovation
National Center for Advancing Translational Sciences

4:15 p.m. **New Targets, New Modalities, New Challenges – The Inconvenient Path of Human Genetics in Drug Discovery**

ROBERT PLENGE
Vice President and Head of Translational Medicine
Merck

4:35 p.m. **Panel Discussion with Audience and Speakers**

SESSION V: LOOKING FORWARD—RECAP AND CONCLUSIONS

Moderator: ESTEBAN BURCHARD, Professor, University of California, San Francisco

5:05 p.m. **Summary of Key Points – Session I**

LAURA NISENBAUM, *Workshop Co-Chair*
Advisor, Chorus Clinical Development
Eli Lilly and Company

5:10 p.m. **Summary of Key Points – Session II**

JOHN CARULLI
Director, Precision Medicine
Biogen

5:15 p.m. **Summary of Key Points – Session III**

RUSS ALTMAN, *Co-Chair of the Forum on Drug Discovery, Development, and Translation*
Professor of Bioengineering, Genetics, Medicine, and (by courtesy) Computer Science
Stanford University

5:20 p.m. **Summary of Key Points – Session IV**

BRAY PATRICK-LAKE
Director, Stakeholder Engagement
Duke University, CTSI

5:25 p.m. **Final Remarks**

ESTEBAN BURCHARD, *Workshop Co-Chair*
Professor and Vice Chair, Department of Bioengineering and Therapeutic Sciences and
Medicine
University of California, San Francisco

5:30 p.m. **ADJOURN**