

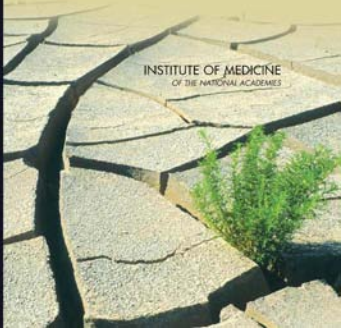


FORUM ON DRUG DISCOVERY, DEVELOPMENT, AND TRANSLATION

BREAKTHROUGH BUSINESS MODELS

Drug Development for Rare and Neglected
Diseases and Individualized Therapies

Workshop Summary



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

BREAKTHROUGH BUSINESS MODELS

Drug Development for Rare and Neglected
Diseases and Individualized Therapies

Workshop Summary

Theresa Wizemann, Sally Robinson, and Robert Giffin

Forum on Drug Discovery, Development, and Translation
Board on Health Sciences Policy

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

THE NATIONAL ACADEMIES PRESS 500 Fifth Street, N.W. Washington, DC 20001

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

Support for this project was provided by the American Diabetes Association; American Society for Microbiology; Amgen, Inc.; Association of American Medical Colleges; AstraZeneca Pharmaceuticals; Blue Cross Blue Shield Association; Burroughs Wellcome Fund; Department of Health and Human Services (Contract Nos. N01-OD-4-2139 and 223-01-2460); Doris Duke Charitable Foundation; Eli Lilly and Company; Entelos, Inc.; Genentech; GlaxoSmithKline; March of Dimes Foundation; Merck & Co.; Pfizer Inc.; and UnitedHealth Group. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the view of the organizations or agencies that provided support for this project.

International Standard Book Number-13: 978-0-309-12088-3

International Standard Book Number-10: 0-309-12088-8

Additional copies of this report are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet <http://www.nap.edu>.

For more information about the Institute of Medicine, visit the IOM home page at: www.iom.edu.

Copyright 2009 by the National Academy of Sciences. All rights reserved.

Printed in the United States of America

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The serpent adopted as a logotype by the Institute of Medicine is a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

Suggested citation: IOM (Institute of Medicine). 2009. *Breakthrough business models: Drug development for rare and neglected diseases and individualized therapies: Workshop summary*. Washington, DC: The National Academies Press.

*“Knowing is not enough; we must apply.
Willing is not enough; we must do.”*
—Goethe



INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the Nation. Improving Health.

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Ralph J. Cicerone is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Charles M. Vest is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Ralph J. Cicerone and Dr. Charles M. Vest are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

**PLANNING COMMITTEE FOR THE WORKSHOP ON
BREAKTHROUGH BUSINESS MODELS:
DRUG DEVELOPMENT FOR RARE AND NEGLECTED
DISEASES AND INDIVIDUALIZED THERAPIES¹**

NANCY SUNG (*Workshop Chair*), Burroughs Wellcome Fund
LINDA BRADY, National Institute of Mental Health
DENNIS CHOI, Emory University
TIMOTHY COETZEE, National Multiple Sclerosis Society
PETER CORR, Celtic Therapeutics Management, LLLP
ELAINE GALLIN, Doris Duke Charitable Foundation
MIKHAIL GISHIZKY, Entelos, Inc.
STEPHEN GROFT, Office of Rare Disease Research, National Institutes
of Health
MARLENE HAFFNER, Amgen
SUZANNE PATTEE, Cystic Fibrosis Foundation
WILLIAM THIES, Alzheimer's Association

IOM Staff

ROBERT B. GIFFIN, Director
SALLY ROBINSON, Program Officer
ANDREA KNUTSEN, Senior Program Assistant
REBECCA REY, Health Sciences Policy Intern
RONA BRIERE, Consulting Editor

¹IOM planning committees are solely responsible for organizing the workshop, identifying topics, and choosing speakers. The responsibility for the published workshop summary rests with the workshop rapporteur and the institution.

FORUM ON DRUG DISCOVERY, DEVELOPMENT, AND TRANSLATION¹

GAIL H. CASSELL (*Co-chair*), Eli Lilly and Company, Indiana
EDWARD W. HOLMES (*Co-chair*), National University of Singapore
BARBARA ALVING, National Center for Research Resources, Maryland
NAOMI ARONSON, Blue Cross and Blue Shield Association, Illinois
HAL BARRON, Genentech, California
LESLIE Z. BENET, University of California–San Francisco
CATHERINE BONUCCELLI, AstraZeneca Pharmaceuticals, Delaware
LINDA BRADY, National Institute of Mental Health, Maryland
ROBERT M. CALIFF, Duke University Medical Center, North Carolina
SCOTT CAMPBELL, American Diabetes Association, Virginia
C. THOMAS CASKEY, University of Texas–Houston Health Science
Center
PETER B. CORR, Celtic Therapeutics, New York
JAMES H. DOROSHOW, National Cancer Institute, Maryland
JEFFREY M. DRAZEN, *New England Journal of Medicine*, Massachusetts
JOSEPH M. FECZKO, Pfizer Inc., New York
GARRET A. FITZGERALD, University of Pennsylvania School of Medicine
ELAINE K. GALLIN, Doris Duke Charitable Foundation, New York
STEVEN K. GALSON, Office of the Surgeon General, U.S. Department
of Health and Human Services, Maryland
MIKHAIL GISHIZKY, Entelos, Inc., California
STEPHEN GROFT, Office of Rare Disease Research, National Institutes
of Health, Maryland
MARLENE HAFFNER, Amgen, Washington, DC
PETER K. HONIG, Merck & Co., Inc., Pennsylvania
RICHARD JUSTMAN, UnitedHealth Group, Minnesota
MICHAEL KATZ, March of Dimes Foundation, New York
DAVID KORN, Association of American Medical Colleges, Washington, DC
RONALD L. KRALL, GlaxoSmithKline, Pennsylvania
JOHN R. MARLER, National Institute of Neurological Disorders and
Stroke, Maryland
MUSA MAYER, AdvancedBC.org, New York
MARK B. McCLELLAN, Brookings Institution, Washington, DC
SUZANNE PATTEE, Cystic Fibrosis Foundation, Maryland
JOANNE L. RHOADS, National Institute of Allergy and Infectious
Diseases (retired), Maryland

¹IOM forums and roundtables do not issue, review, or approve individual documents. The responsibility for the published workshop summary rests with the workshop rapporteurs and the institution.

JANET SHOEMAKER, American Society for Microbiology,
Washington, DC
LANA SKIRBOLL, National Institutes of Health, Maryland
NANCY S. SUNG, Burroughs Wellcome Fund, North Carolina
JORGE A. TAVEL, National Institute of Allergy and Infectious Diseases,
Maryland
JANET WOODCOCK, U.S. Food and Drug Administration, Maryland

Reviewers

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

Russell L. Bromley, Myelin Repair Foundation
Scott Campbell, American Diabetes Association
Mikhail L. Gishizky, Entelos, Inc.
Greg Simon, FasterCures

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the final draft of the report before its release. The review of this report was overseen by **Hellen Gelband**, Resources for the Future. Appointed by the Institute of Medicine, she was responsible for making certain that an independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of this report rests entirely with the authors and the institution.

Preface

The research and development process for new drug and biologic products has become extraordinarily expensive and time-consuming. Even for large pharmaceutical companies working to develop potential blockbuster drugs, many consider the current model to be unsustainable. While developing drugs to treat rare and neglected diseases can be just as expensive and time consuming as it is for blockbuster drugs, the products are often far less commercially viable to certain sectors of the pharmaceutical industry. Recognizing that patient advocacy groups can play a vital role in the development of new drugs to treat rare and neglected diseases, the Forum held a workshop in September 2007 entitled “From Patient Needs to New Drug Therapies: Can We Improve the Pathway.” The workshop featured the work of four patient-focused organizations: the National Breast Cancer Coalition, the Cystic Fibrosis Foundation, the Arthritis Foundation, and the American Diabetes Association.

To better understand the innovative approaches being used by these organizations to help advance drug development, the Forum hosted a public workshop on June 23, 2008, titled “Breakthrough Business Models: Drug Development for Rare and Neglected Diseases and Individualized Therapies.” Investors, policy makers, and companies seeking to develop therapies for smaller markets came together to discuss innovative strategies being implemented to expedite the development of products for these less commercially viable conditions. The intent of the workshop was first to raise awareness of these new models. Additionally, participants discussed approaches for reducing the risk of such investments by both filling critical

funding gaps along the drug development pathway and pursuing highly targeted approaches to early-phase development.

The workshop had several objectives. The first was to lay a foundation for the discussions by describing the changes that have taken place in the translational research process over the past 10 years, such as the 10-fold increase in investment by philanthropic organizations since 2000. The second objective was to discuss successful “venture philanthropy” models for funding translational research. Beyond new funding models, some philanthropic organizations and for-profit groups have undertaken innovative strategies to help expedite the development of safe and effective drugs for rare and neglected diseases by, for example, funding trials directly, supporting resources such as tissue banks, and negotiating intellectual property. A third objective was to explore whether such strategies are successful and could be implemented more broadly. Finally, workshop participants were asked to examine regulatory, legislative, and institutional policy tools currently in place to help advance the development of therapies for rare or neglected diseases.

The workshop provided an opportunity for participants to share ideas and identify potential collaborative activities. It is our hope that this workshop summary will serve as a resource for all organizations interested in advancing the drug development process for rare and neglected conditions, as well as individualized therapies.

Nancy Sung
Workshop Chair and Member
Forum on Drug Discovery, Development, and Translation

Stephen Groft
Member
Forum on Drug Discovery, Development, and Translation

Contents

1 INTRODUCTION AND OVERVIEW	1
Scope of the Workshop, 3	
Key Themes, 4	
Organization of the Report, 5	
2 CURRENT MODEL FOR FINANCING DRUG DEVELOPMENT: FROM CONCEPT THROUGH APPROVAL	7
Investors in Drug Development, 7	
Current Status of Investments, 9	
Ways to Facilitate Drug Development, 11	
3 THE FOOD AND DRUG ADMINISTRATION'S ORPHAN DRUG PROGRAM	12
Strategies, 15	
4 DIVERSE FUNDING MODELS	19
Institute for OneWorld Health: A Not-for-Profit Pharmaceutical Company, 19	
Cystic Fibrosis Foundation Therapeutics, Inc. (CFFT): A Virtual Company for Managing Drug Discovery and Development Alliances, 24	
Genzyme: Surviving and Thriving as a For-Profit Company in the Rare Disease Arena, 29	

	Celtic Therapeutics, LLLP: A Private-Equity Model for Addressing Global Health, 32	
	Panel Discussion, 37	
	Open Discussion, 39	
5	STRATEGIES FOR FACILITATING SHARING OF RESEARCH MATERIALS AND DATA	42
	Finding and Bargaining for Research Materials and Data, 42	
	The Alzheimer's Disease Neuroimaging Initiative (ADNI): A Public-Private Partnership, 45	
	Genetic Alliance BioBank, 51	
6	STRATEGIES FOR NAVIGATING INTELLECTUAL PROPERTY	55
	Overview: Creating an Enabling Intellectual Property Environment for Rare and Neglected Diseases, 55	
	Innovation in Alliances and Licensing: Vertex Pharmaceuticals Transforming Now for the Future, 64	
	The Myelin Repair Foundation: Accelerating Intellectual Property Sharing to Facilitate Translation, 67	
	The University of California at Berkeley's Approach to Management of Intellectual Property, 71	
	Open Discussion, 78	
7	STRATEGIES FOR FACILITATING CLINICAL TRIALS	82
	FDA Review and Regulation of Small Clinical Trials: Successes, Barriers, and Directions for the Future, 83	
	Approaches to Accelerating Clinical Trials, 91	
	Muscular Dystrophy Association's Approach to Maximizing Assets in Clinical Trials, 94	
	Open Discussion, 97	
8	SUMMARY	98
	Scientific and Regulatory Elements of the Translational Research Process, 98	
	Diverse Funding Organizations, 99	
	Sharing of Materials and Data, 100	
	Intellectual Property Strategies, 101	
	Approaches to Facilitating Clinical Trials, 101	
	Areas for Further Discussion, 102	
	REFERENCES	104

APPENDIXES

A	Agenda	106
B	Speaker Biographies	113
C	Resources	128

Tables, Figures, and Boxes

TABLE

- 5-1 Examples of Repositories of Materials and Data Supported by the National Institutes of Health, 43

FIGURES

- 3-1 The number of products that received orphan designation and the number of new drugs approved from 1983 to 2005, 14
- 3-2 Diseases treated by orphan drugs, 2000 to 2006, 15
- 4-1 Breadth and depth of the Cystic Fibrosis Foundation Therapeutics pipeline as of April 30, 2008, 26
- 4-2 The Therapeutics Development Network of cystic fibrosis clinical care centers, 28
- 4-3 Defining the gap in biomedical research, from idea to patent expiration, 35
- 5-1 Worldwide use of ADNI data, 50
- 5-2 Sources of applications for use of the ADNI database, 51
- 5-3 PXE International, Inc., biobank model, 53
- 6-1 Duke University concept of how a technology trust might create an enabling intellectual property environment for rare and neglected diseases, 63
- 6-2 Vertex approach to maintaining strategic research alliances, 67
- 6-3 The Myelin Research Foundation's collaborative research process, 70

- 6-4 Bridging the translational research gap between discovery and treatment, 71
- 6-5 UC Berkeley IPIRA intellectual property management models, 74

BOXES

- 4-1 Examples of Business Models for Funding the Development of Drugs to Treat Rare and Neglected Diseases, 20
- 5-1 Examples of Data Sharing Models for Biomedical Research, 46
- 6-1 Managing Strategic Alliances, Licensing, and Intellectual Property: Company, Foundation, and University Perspectives, 56
- 6-2 Examples of Serendipitous Dual Markets, 61
- 6-3 Gates Foundation Global Access Agreements, 62
- 6-4 Examples of Innovations Licensed and/or Funded Under the Socially Responsible Licensing Program (SLRP) at UC Berkeley, 76
- 6-5 Highlights of “In the Public Interest: Nine Points to Consider in Licensing University Technology,” 78
- 7-1 Examples of Disease Foundation Strategies for Facilitating Clinical Trials, 84
- 7-2 FDA Review: Opportunities to Facilitate the Drug Development and Approval Processes, 86

Introduction and Overview*

An objective look at current statistics characterizing the state of drug development paints a gloomy picture. The traditional process for developing a new drug or biologic product and bringing it to market has become exceedingly expensive and lengthy—estimated to cost between \$800 million and \$1.3 billion, and to take approximately 10–15 years. Only 8 percent of investigational new drugs entering Phase I clinical trials run the full course of development and receive U.S. Food and Drug Administration (FDA) approval, and of those, about 4 percent are eventually removed from the market. In addition, the number of new drug approvals has been slowly declining over the last 11 years—from 53 new molecular entities approved in 1996, to an average of 28 per year between 1999 and 2005, and to a mere 17 in 2007. A recent editorial outlines many of these issues and concludes that “the conventional business model appears fallible” and that “both industry and academia are poorly positioned to respond in the [current] financial landscape” (FitzGerald, 2008). Even considering the potential for blockbuster drugs, this lengthy, high-cost, low-success-rate model is likely to prove unsustainable; for those far less commercially attractive drugs used to treat rare and neglected diseases,¹ it is simply infeasible.

*The planning committee’s role was limited to planning the workshop, and this summary was prepared by the workshop rapporteur and the Drug Forum staff as a factual summary of what occurred at the workshop.

¹For the purposes of this report, rare diseases are defined as diseases that affect small patient populations, and neglected diseases are defined as diseases that are concentrated in poor or developing countries.