The Role of Non-Profit Organizations in Drug Development

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Patient groups are no longer content to be cheerleaders for research, they need to be involved at all stages

Nothing About Us Without Us

The Roles of the Patient Community In Drug Development Go Far Beyond Funding

Patients are uniquely equipped to identify unmet needs in their disease areas, and to develop and advocate for collaborative solutions to fill those gaps through

- Advocacy
- Infrastructure Support and Philanthropy
- Policy and Legislation
- Partnership Building
- Scientific Development

Promoting Research through Advocacy

Lead the scientific and clinical agenda for the field

- Focus funding for cutting-edge translational science on those projects that fill critical gaps in approaches to research and treatment
- Force collaboration and accountability of the research community

Priorities are driven by the needs of patient members, such as,

- Development of biomarkers for diagnosis/assessment of therapeutic efficacy
- Development of patient reported outcomes

Facilitate development of additional resources such as bio-banks and patient registries

Examples,

- Melanoma Research Alliance, The Leukemia & Lymphoma Society, Pancreatic Cancer Action Network, Cystic Fibrosis Foundation, and many, many more…

Promoting Research Through Infrastructure Support

Multiple Myeloma Research Foundation

- Sequenced the entire MM genome in collaboration with the Broad Institute and TGen
- Established the Multiple Myeloma Research Consortium to accelerate early phase clinical trials – a clinical network of 16 institutions which has advanced >20 compounds through trials
- MMRC also established a tissue bank and IT system to facilitate collaboration

Stand Up to Cancer (SU2C)

- Brings together brightest minds in different fields of cancer research in order to create "Dream Teams" - multi-institutional groups of scientists who work collaboratively, rather than competitively, to develop new treatments quickly. Innovative Research Grants support groundbreaking cancer research projects that are high-risk but could also be high-impact, and have the potential to significantly affect patient care.

Promoting Research Through Venture Philanthropy

Disease-focused non-profits can provide financial, intellectual, and human capital to for-profit biotechnology firms to help enable, de-risk, and ultimately accelerate the development of new therapies, particularly targeted therapies for rare diseases

Examples,

- **Cystic Fibrosis Foundation** – Vertex Pharmaceuticals collaboration led to discovery and approval of Kalydeco for rare subsets of cystic fibrosis
- **Alzheimer's Drug Discovery Foundation** – Pharmaceutical partners to fund early research that led to the FDA approval of Amyvid, a diagnostic test for Alzheimer's disease
- **Michael J. Fox Foundation for Parkinson's Research** – Provided funding, research tools, networking, and clinical trial recruitment assistance to nearly 225 pharmaceutical projects

Promoting Research through Legislation

Prescription Drug User Fee Agreement (PDUFA) – Re-authorized every 5 years, presenting an opportunity for the adoption of new legislation to improve/modernize components of the drug development and review process

- Food and Drug Administration Safety and Innovation Act (FDASIA), passed in 2012, included provisions developed by advocacy groups

21st Century Cures – A bi-partisan initiative of the House Energy & Commerce Committee led by Rep. Fred Upton (R-MI) and Rep. Diana DeGette (D-CO)

- Accelerate discoveries, streamline drug and device development process, and facilitate use of digital medicine and social media for treatment delivery
- Hosted US-wide meetings and roundtables to hear expert testimony, solicit ideas, and feedback from the patient community, an opportunity for patient groups to weigh in on legislation affecting NIH and FDA policies

Promoting Research Through Regulatory Policy

FDA's Patient Focused Drug Development Program

- Systematically gather patients' perspectives on their condition and available therapies
- Host disease-focused meetings that present an opportunity for patients and advocacy groups to have their voices heard on review of new drugs in their disease area

FDA Guidance

- Describe the Agency's interpretation of or policy on a regulatory issue
- Present an opportunity for non-profit patient groups to effect regulatory change
- Encourages the FDA and trial sponsors to engage patients and their families at all stages of trial development and to take into account what they consider acceptable risk in clinical trials
- Example: **Parent Project Muscular Dystrophy** – drafted guidance in 2014 to help accelerate development and review of potential therapies for Duchenne muscular dystrophy

Promoting Research Through Public-Private Partnerships

Non-profit organizations funded and operated through a partnership of government and the private sector

Examples,

- **Foundation for the NIH** – identifies and develops opportunities for innovative collaborations between industry, academia, and the philanthropic community to support the NIH mission
- **Critical Path Institute** – develop pre-competitive drug development tools to accelerate the pace and reduce the cost of drug development
- **Reagan-Udall Foundation** – modernize medical product development at FDA, accelerate innovation, and enhance product safety

Roles of Non-Profit Groups Evolve Over Time

Friends of Cancer Research

- Founded in 1996 to increase public awareness and support for cancer research and for increased scientific capacity across all federal health agencies
- Began by holding educational “town halls” across the US, with leaders from science, industry, academia and key members of Congress in order to educate lawmakers and create new champions for biomedical research
- Worked with Congress and Federal agencies to establish the Office of Oncology Drug Products at FDA – focusing reviewers by disease type rather than molecule type

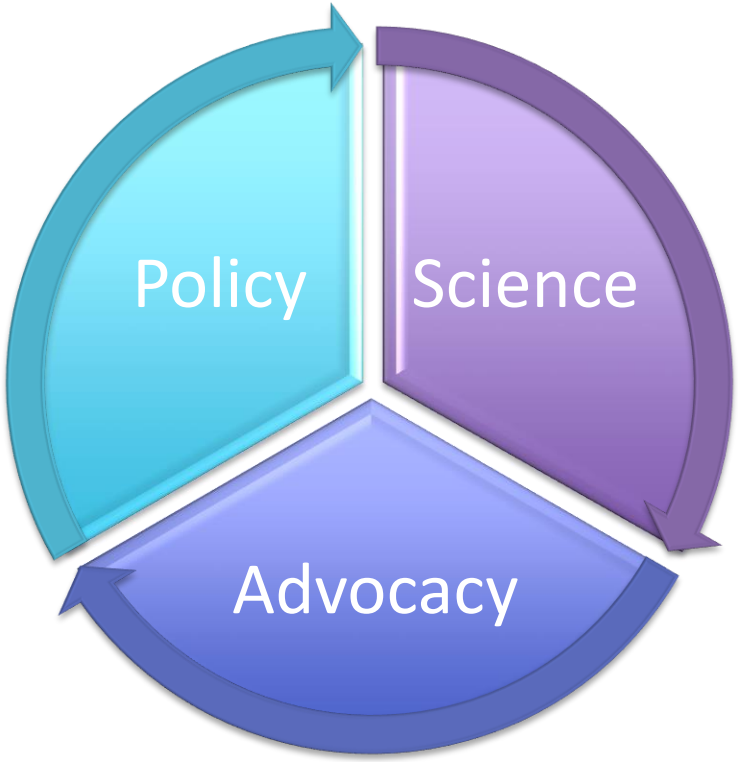
Where are we now?

Accelerating the Pace of Innovation

Washington, DC-based Think Tank & Advocacy Organization developing groundbreaking partnerships:

- Federal Agencies (FDA, NIH, NCI)
- Academic Research Centers
- Professional Societies
- Industry
- Advocacy Organizations

Create a path to better drug development and approval through scientific, regulatory, and legislative solutions



Modernizing Clinical Trial Designs

Developing a Master Protocol registration trial for Non-Small Cell Lung Cancer (NSCLC)

Challenges to traditional trial design:

- Each potential new therapy is typically tested independently from other therapies seeking to treat the same condition
- For every new trial, the protocol must be reviewed by a number of oversight entities
  - New phase III trials require an average of 36 administrative or regulatory approvals and averages more than 2 years
- Approximately 4% of adult cancer patients enroll in clinical trials
  - Inability to meet accrual goals is a frequent factor causing trials to close - wasting time, money, and limited patient resources
- New therapies molecularly targeted against specific mutations may be present in only a fraction of the patient population

Benefits of a Master Protocol

Enrollment Efficiency – Grouping these studies under a single trial reduces the overall screen failure rate

Operational Efficiency – single master protocol can be amended as needed as drugs enter and exit the study

Consistency – every drug entered into the trial would be tested in the identical manner

Predictability – if pre-specified efficacy and safety criteria are met, the drug and accompanying companion diagnostic will be approved

Patient Benefit – offers the advantage of bringing safe and effective drugs to patients sooner than they might otherwise be available

FNIH
Foundation for the National Institutes of Health

FRIENDS of CANCER RESEARCH

NIH NATIONAL CANCER INSTITUTE

SWOG
Leading cancer research. Together.

Genentech
A Member of the Roche Group

Bristol-Myers Squibb

Pfizer

FOUNDATION MEDICINE

AstraZeneca

http://www.focr.org/events/design-lung-cancer-master-protocol
http://www.lung-map.org/

Development of Legislative Policy

- The 2011 Conference included a panel entitled: *Development Paths for New Drugs with Large Treatment Effects Seen Early*
- This panel proposed scientific strategies to ultimately expedite FDA approval for a drug showing dramatic responses in the early stages of development while maintaining drug safety and efficacy standards
- **Breakthrough Therapy Designation**
  - Goal 1: Expedite drug development process for products that show remarkable clinical activity early
  - Goal 2: Minimize the number of patients exposed to a potentially less efficacious treatment

Concept ⟶ Scientific Whitepaper ⟶ Legislation ⟶ FDA Tool

ISSUE BRIEF

Conference on Clinical Cancer Research

November 2011

PANEL 4

Development Paths for New Drugs with Large Treatment Effects Seen Early

Thomas Fleming, Professor, Biostatistics, University of Washington

Mikkael Sekeres, Director, Leukemia Program, Associate Professor of Medicine, Cleveland Clinic

Ed

ISSUE BRIEF

Conference on Clinical Cancer Research

November 2012

Developing Standards for Breakthrough Therapy Designation

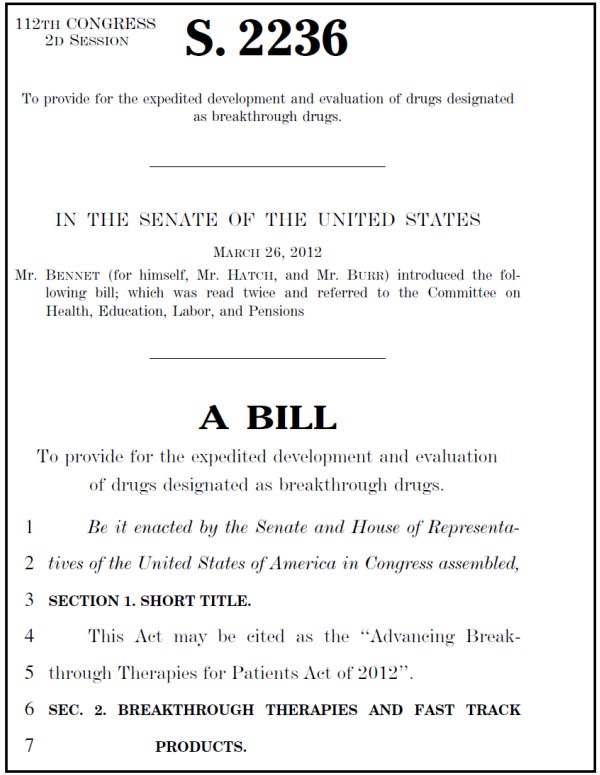
Charles L. Sawyers, Chair, Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center; Investigator, Howard Hughes Medical Institute

Daniel A. Haber, Director, Cancer Center, Massachusetts General Hospital; Investigator, Howard Hughes Medical Institute

Sandra J. Horning, Senior Vice President, Global Head, Clinical Development Hematology/Oncology, Genentech

S. Percy Ivy, Associate Branch Chief, Investigational Drug Branch, CTEP, NCI

Wendy K.D. Selig, President and CEO, Melanoma Research Alliance



112TH CONGRESS
2D SESSION

S. 2236

To provide for the expedited development and evaluation of drugs designated as breakthrough drugs.

IN THE SENATE OF THE UNITED STATES

MARCH 26, 2012

Mr. BENNET (for himself, Mr. HATCH, and Mr. BURR) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

A BILL

To provide for the expedited development and evaluation of drugs designated as breakthrough drugs.

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

SECTION 1. SHORT TITLE.

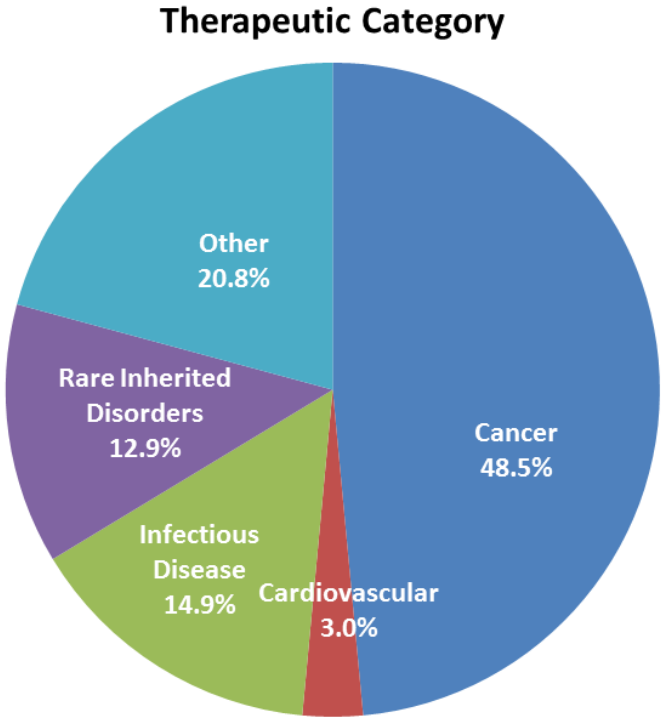
This Act may be cited as the "Advancing Breakthrough Therapies for Patients Act of 2012".

SEC. 2. BREAKTHROUGH THERAPIES AND FAST TRACK PRODUCTS.

Breakthrough Therapy Designation

Breakthrough Therapy, by the numbers,

- **337** Total requests for Breakthrough Designation
- **110** Designations granted
  - **38** Approvals for Breakthrough Drugs
- **49** Designations granted in Cancer
  - **17** Approvals in Cancer



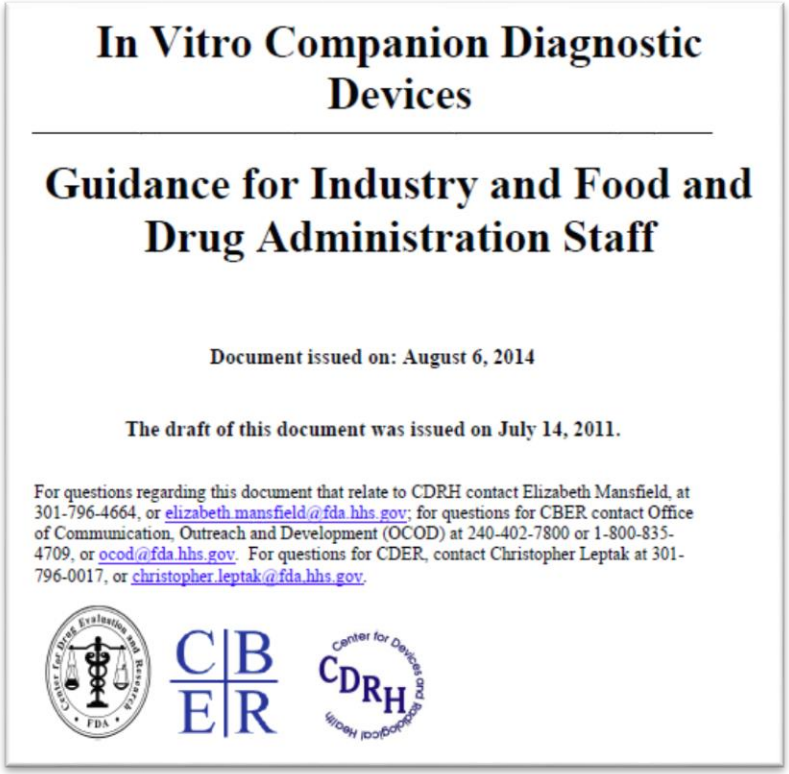
Blueprint for Breakthroughs

FRIENDS of CANCER RESEARCH

ALEXANDRIA
ALEXANDRIA CENTER™ FOR LIFE SCIENCE | NEW YORK CITY

A Risk-based Approach for In Vitro Companion Diagnostics Device FDA Approval Process Associated with Therapies that have Breakthrough Designation

Presented at the "A Blueprint for Drug/Diagnostic Co-development: Breakthrough Therapies" September, 2013



In Vitro Companion Diagnostic Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on: August 6, 2014

The draft of this document was issued on July 14, 2011.

For questions regarding this document that relate to CDRH contact Elizabeth Mansfield, at 301-796-4664, or elizabeth.mansfield@fda.hhs.gov; for questions for CBER contact Office of Communication, Outreach and Development (OCOD) at 240-402-7800 or 1-800-835-4709, or ocod@fda.hhs.gov. For questions for CDER, contact Christopher Leptak at 301-796-0017, or christopher.leptak@fda.hhs.gov.

Blueprint for Breakthroughs

AAPS PharmSciTech (© 2016)
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White Paper

Examining Manufacturing Readiness for Breakthrough Drug Development

Earl Dye,[1,13] Annie Sturgess,[2] Gargi Maheshwari,[3] Kimberly May,[4] Colleen Ruegger,[5] Usha Ramesh,[6] Heow Tan,[7] Keith Cockerill,[8] John Groskoph,[9] Emanuela Lacana,[10] Sau Lee,[11] and Sarah Pope Miksinski[12]

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KEY WORDS: breakthrough therapy; CMC; FDA.

INTRODUCTION

In July 2012, Congress passed the Advancing Breakthrough Therapies for Patients Act as part of the Food and Drug Administration Safety and Innovation Act (FDASIA). Section 902 of FDASIA provides for designation of a drug as a breakthrough therapy "if the drug is intended alone or in combination with one or more other drugs, to treat serious or life-threatening diseases or conditions and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies (1)." Breakthrough designation is a mechanism that the U.S. Food and Drug Administration (FDA) can grant to sponsors to expedite the development of these promising therapies.

As part of the program, the FDA and sponsor collaborate in a dynamic, multi-disciplinary, resource-intensive process to determine the most efficient path using an "all hands on deck approach"

Key findings:

- Presents 2 small molecule and 4 biologic case studies
- Identifies flexibilities during development for accelerated products
- Highlights the benefits of open and transparent communication between sponsor and FDA

Ongoing Efforts – Modernization of Clinical Trial Eligibility Criteria

Category	Question for Consideration
Relationship to scientific objective	• Does the eligibility criterion support the scientific hypothesis? • Could the scientific goal be achieved without including this particular eligibility criterion?
Generalizability to the non-study population	• Will the results of the study be applicable to a patient not enrolled on the study? • Are the eligibility criteria too restrictive for practical clinical use?
Patient safety and drug toxicity	• Is patient safety being adequately protected and does this eligibility criterion contribute to this? • Are potential drug toxicities and mechanism of action being accounted for and does limiting or including this criterion support or hinder the scientific goal?
Continual review on a regular basis	• At what point should eligibility criteria be re-justified during protocol development and during enrollment? • Should a trial close due to poor accrual or be allowed to reduce/relax eligibility criteria as a first step?

Ongoing Efforts – Streamlining Regulatory Review Processes

Establish an **Oncology Center of Excellence at the US Food and Drug Administration (FDA)** - Leverage the skills of regulatory scientists and reviews across product categories and introduce efficiencies and expedite the development of novel combination products and support an integrated approach in:

– Evaluating products for the prevention, screening, diagnosis, and treatment of cancer

– Supporting the continued development of companion diagnostic tests, and the use of combinations of drugs, biologics and devices to treat cancer

– Developing and promoting the use of methods created through the science of precision medicine

Non-profit patient groups, no longer funders for, but partners in research

Keeps the patient voice in translational and clinical research to ensure that meaningful studies are designed to meet patient needs

Partnership is essential – only by working together can the promise of biomedical research be fully realized in the form of safe and effective treatments for patients