Today's presentation is made possible in partnership with Stealth BioTherapeutics, UMDF, MitoAction, BSF and the mitochondrial disease patient community.

Goals for today's discussion:
Patient Perspectives

- Explore patient perspectives on deciding to participate in a clinical trial
- Demystify patient advocacy
- Learn ways to search, find, prepare and get involved in clinical trials
- Know the benefits and challenges of clinical trials for people with rare diseases

Goals for today's discussion:
Regulatory Perspectives

- Gain insights into the FDA and drug developer's perspective on clinical trials for rare diseases
- Capture ways rare disease clinical trials differ from other diseases
- Understand the process of bringing a drug to market for a rare disease
- Discover rare disease clinical trials influence beyond drug approval
- Learn your rights as a patient

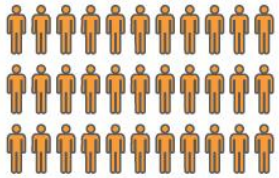
SEIZING A RARE OPPORTUNITY

Rare diseases are classified as those that affect 200,000 Americans or less.
How are patients of rare diseases and the people who care for them creating a network?

DIAGNOSIS & TREATMENT CHALLENGES

THERE ARE ALMOST 7,000 RARE DISEASES

Patients are frequently
MISDIAGNOSED
or
UNDERDIAGNOSED



30 MILLION

More than 30 million Americans are affected by these diseases

DRUG DEVELOPMENT CHALLENGES

- CLINICAL TRIAL TIMELINES ARE COMPRESSED
- FINDING CLINICAL TRIAL PARTICIPANTS
  Clinical trials often occur far from a patient's home
- KEEPING PARTICIPANTS IN CLINICAL TRIALS ADHERENT TO TREATMENT PROGRAMS AND PLANS

ABOUT 400 approved treatments exist for these patients

Patient populations are small and geographically dispersed

- Rare diseases tend to be serious, making travel difficult
- More than half of patients are children

PAVING THE ROAD TO ACCESS

How individuals are uniting the rare disease community:

BUILDING RELATIONSHIPS

- With patient organizations
- With KOLs (Key Opinion Leaders)
- Between patients, their HCPs (Health Care Professionals), and their treatment providers

BUILDING PATIENT COMMUNITIES

- Using social media can raise awareness of rare diseases and boost clinical trial enrollment
- Of rare disease patients who were asked to participate in a research study online, 84% of all responses came from social media

NORD® National Organization for Rare Disorders

From bench to bedside:
Nuances of Rare Disease Drug Development

Opportunities

- Greater potential to learn about the rare disease
- Save or extend lives
- Improve quality of life
- Greater global collaboration
- Potential for expedited process and partnership with the FDA

Challenges

- Fewer patients available
- Geographically dispersed
- Lack of awareness of available trials in remote communities or to isolated patients
- Variations within the same disease
- Genetic diagnosis
- Less basic science research
- Little to no prior clinical trial experience

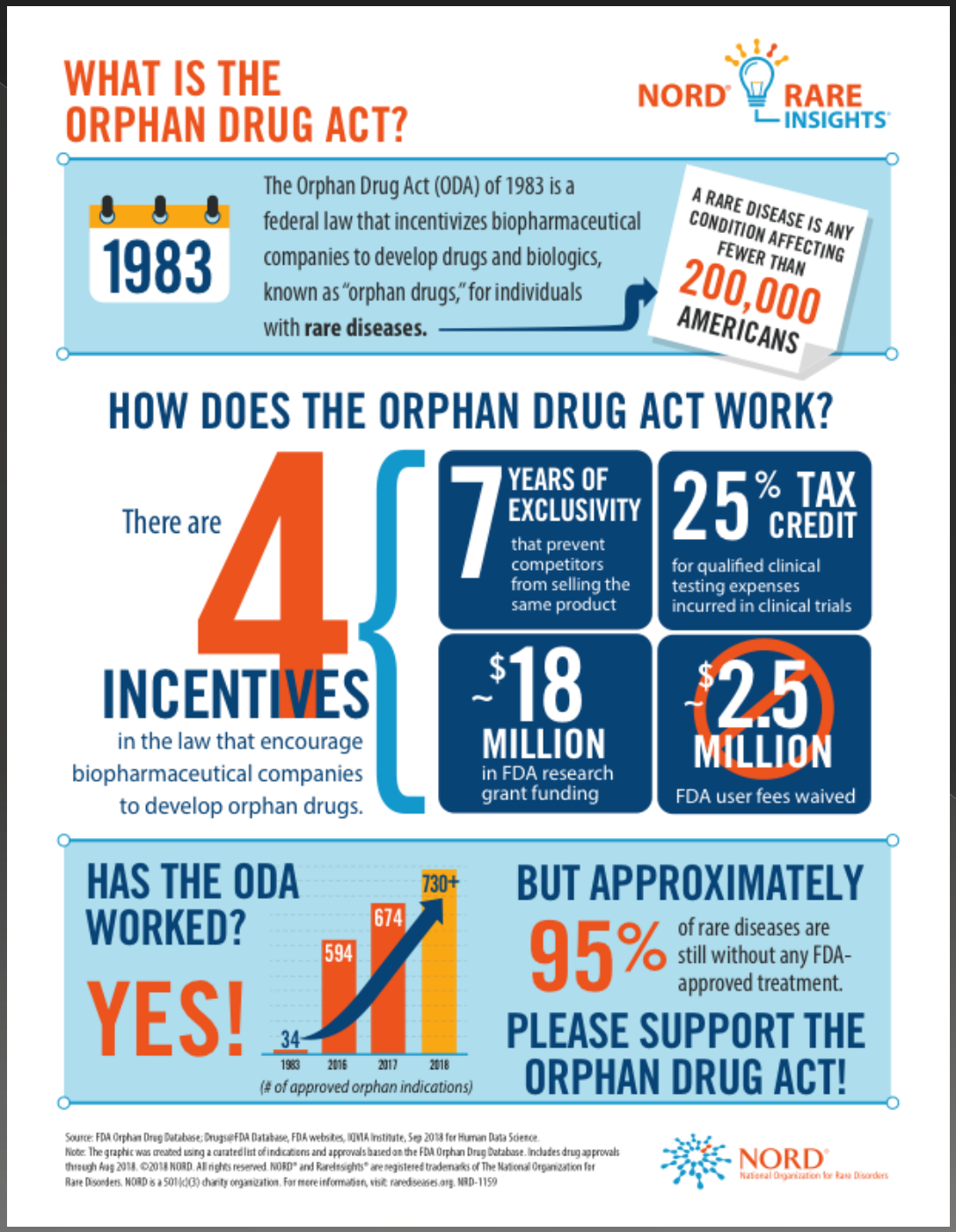
Clinical Trials 101

- Common Abbreviations
- The Orphan Drug Act
- From bench to bedside
- The FDA (aka regulatory agency)
- www.ClinicalTrials.gov

Common abbreviations

- FDA: Food and Drug Administration
- OLE: Open Label Extension *(also called expanded access)*
- IND: Investigational New Drug
- ADR/AE: Adverse Drug Reaction or Adverse Event
- PRO: Patient Reported Outcomes
- NDA: New Drug Application
- PFDD: Patient Focused Drug Development

https://www.fda.gov/ForPatients/ClinicalTrials/ucm410359.htm



What is the Orphan Drug Act?

Fact: The ODA provides incentives to develop "orphan drugs" for individuals with rare diseases.

Myth: The ODA grants or guarantees access to investigational drugs for patients with rare diseases.

Myth: The ODA expedites the process to approval

Phases of Clinical Trials

Pre-clinical: Animal models or basic research not in humans

Phase 1: Evaluating safety in humans

Phase 2: Evaluating safety AND efficacy in humans with the disease or issue being treated

Phase 3: Evaluating safety, effectiveness and dosing in a larger group using a randomized, double-blind, placebo controlled study design.

OLE (Open Label Extension): Gathering additional data, including patient-reported outcomes

Possible outcomes of a Phase 3 Clinical Trial

What Matters to Patients Also Matters to the FDA

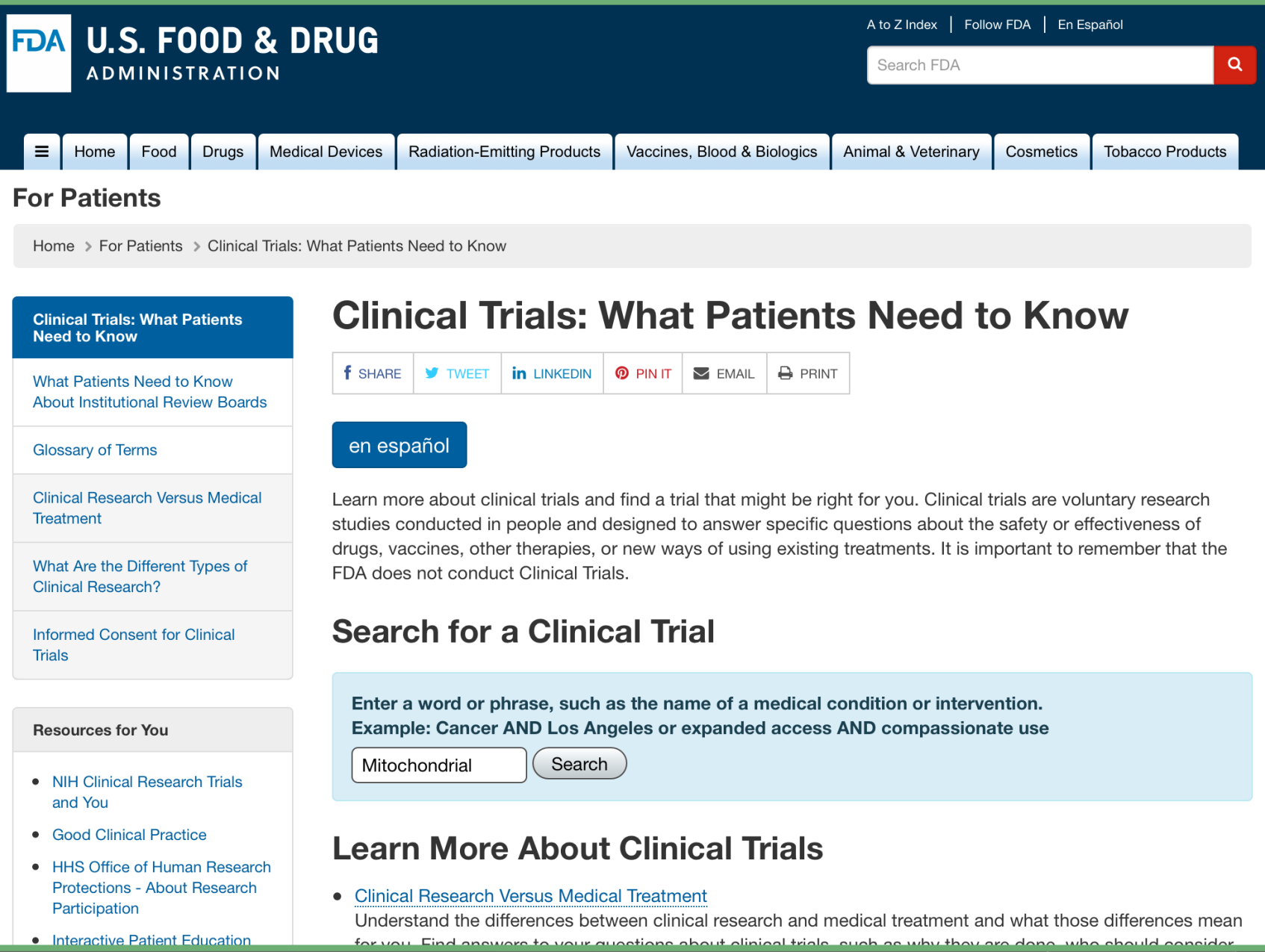
- Role of the FDA is to protect patients
- Need to demonstrate safety and efficacy, even for very small trials in very rare conditions
- Balance desires of patients with requirements of safety and efficacy
- What are “meaningful outcomes?”
- Opportunity to create new tools, such as scales to measure fatigue and other symptoms

FDA.gov and ClinicalTrials.gov

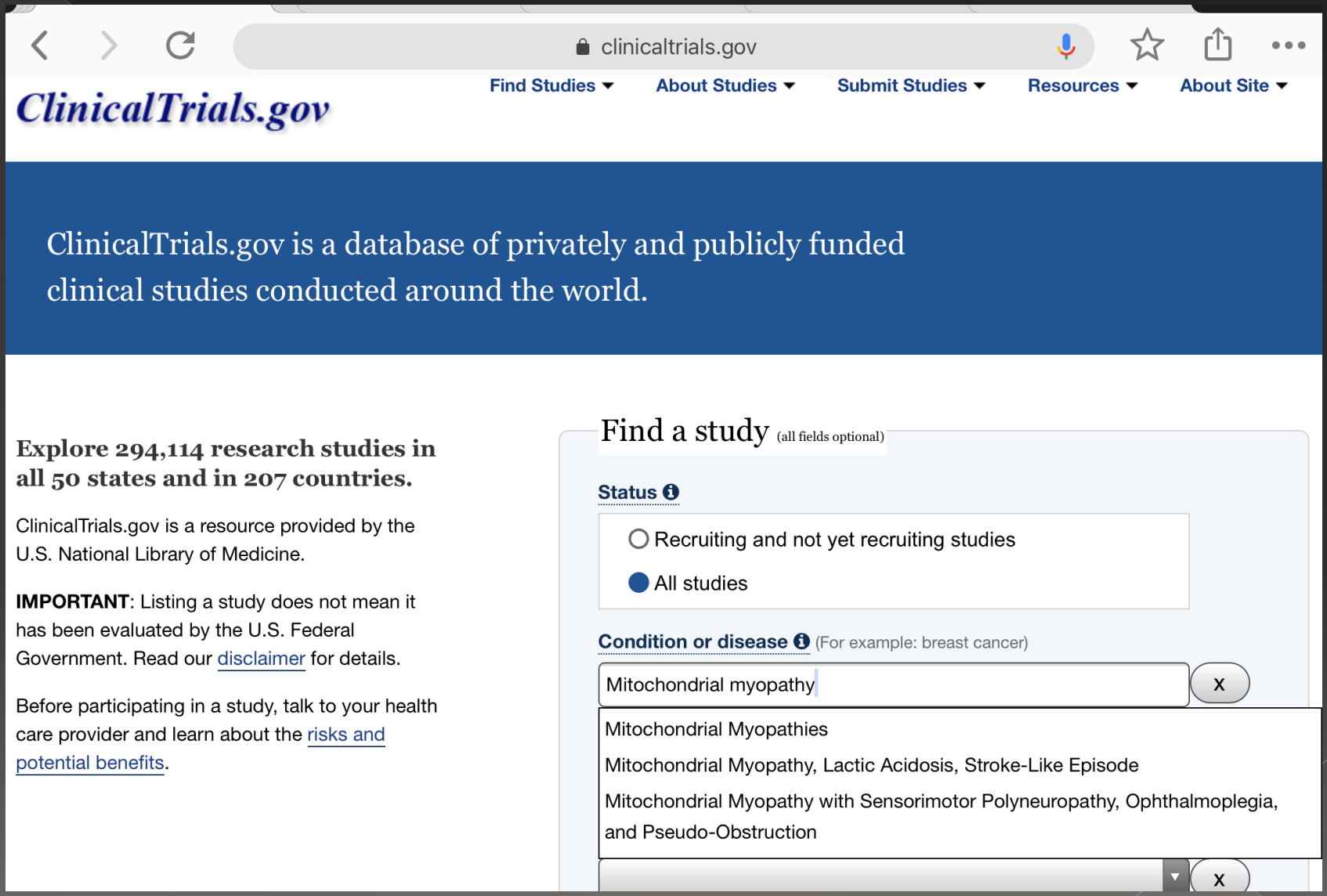
Resource pages exist for patients on the FDA and NIH websites

- www.FDA.gov/ForPatients

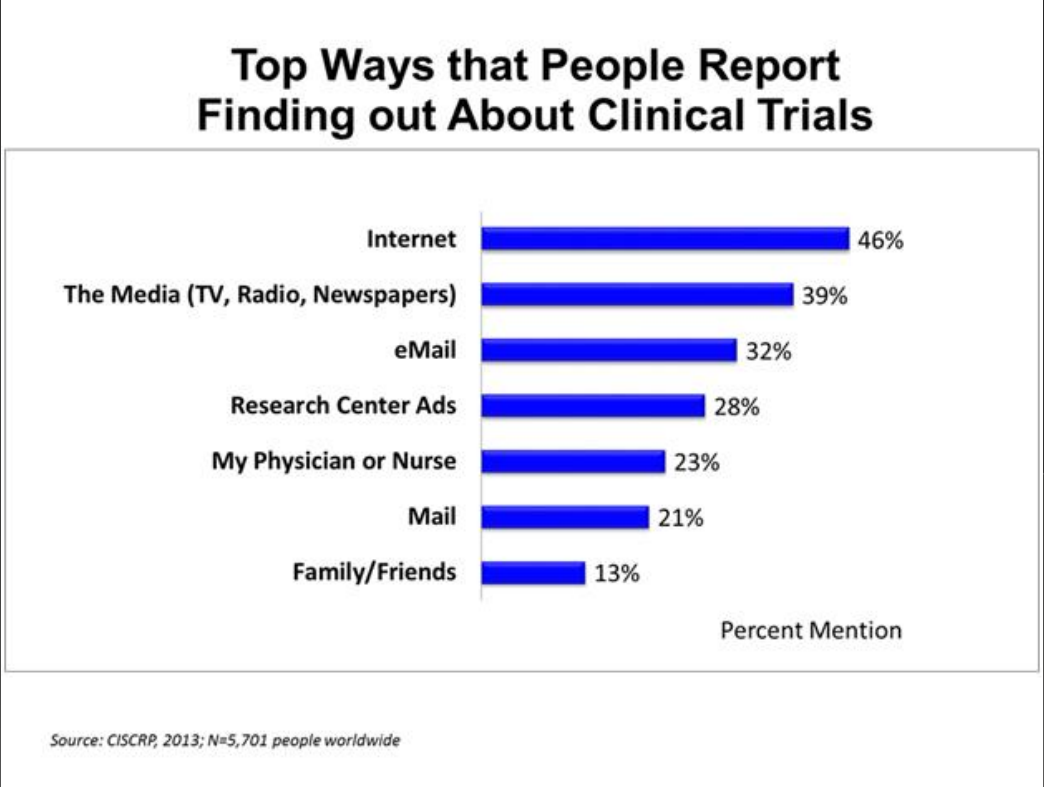
- www.ClinicalTrials.gov has advanced search options – free and open to the public
  - Updated regularly, so check periodically
  - Most comprehensive resource, but often difficult for patients and families to interpret



www.FDA.gov/ForPatients


clinicaltrials.gov
ClinicalTrials.gov
Find Studies
About Studies
Submit Studies
Resources
About Site
ClinicalTrials.gov is a database of privately and publicly funded clinical studies conducted around the world.
Explore 294,114 research studies in all 50 states and in 207 countries.
ClinicalTrials.gov is a resource provided by the U.S. National Library of Medicine.
IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.
Before participating in a study, talk to your health care provider and learn about the risks and potential benefits.
Find a study (all fields optional)
Status
Recruiting and not yet recruiting studies
All studies
Condition or disease (For example: breast cancer)
Mitochondrial myopathy
Mitochondrial Myopathies
Mitochondrial Myopathy, Lactic Acidosis, Stroke-Like Episode
Mitochondrial Myopathy with Sensorimotor Polyneuropathy, Ophthalmoplegia, and Pseudo-Obstruction

Finding a clinical trial



- Your doctor may not know all the trials available
- Rely on patient advocacy organizations, support groups, social media

Additional Resources for Mito Patients

www.umdf.org/current-clinical-trials/

www.mitoaction.org/trials

www.barthsyndrome.org/research/clinicaltrials

www.mitochondrialdiseasenews.com/clinical-trials-2/

www.mitotrials.com/

Patients as Partners Case Study: Duchenne's Muscular Dystrophy

F.D.A. Approves Muscular Dystrophy Drug That Patients Lobbied For

Stacie Al-Chokhachi, second from right, and her son, Dalton, who has Duchenne, at an F.D.A. meeting in April. Eric Kruszewski for The New York Times

By Sabrina Tavernise

Sept. 19, 2016

WASHINGTON — The Food and Drug Administration approved the first drug to treat patients with the most common childhood form of muscular dystrophy, a vivid example of the growing power that patients and their advocates wield over the federal government's evaluation of drugs.

https://www.nytimes.com/2016/09/20/business/fda-approves-muscular-dystrophy-drug-that-patients-lobbied-for.html

Patient Perspectives:
Rare Disease Clinical Trials

PATIENT PERSPECTIVES

"Should I participate in a clinical trial?"
"What about side effects?"
"There isn't a study site in my city."
"How do I know if I'm eligible?"
"I don't like being in the hospital"
"Should I ask my doctor first?"
"Will I have to pay?"
"How do I know if I get drug or placebo?"

Rare Disease Clinical Trials:
Unique challenges

- Geographic limitations
- Evolution of a diagnosis
- No 2 patients are alike
- Awareness – healthcare providers
- Awareness – patients
- Risks and perceived risks
- Disease progression and uncertainty

JAMA Network Open

Source: JAMANetwork.org

October 5, 2018

Global Public Attitudes About Clinical Research and Patient Experiences With Clinical Trials

Annick Anderson, MBA[1]; Deborah Borfitz, BS[1]; Kenneth Getz, MBA[1,2]

» Author Affiliations | Article Information

JAMA Netw Open. 2018;1(6):e182969. doi:10.1001/jamanetworkopen.2018.2969

Most important Participation Factors Reported by Patients

Participation Factor
Potential risks and benefits
Purpose of the clinical research study
Types of medical procedures required[c]
If my confidentiality would be protected
Physical location of the research study center
Potential costs and reimbursements
Length of participation
Receiving a summary of the study results after my participation ended
Being provided with supporting information on the clinical research study
Provided with information on managing my health condition in general
Duration of each study visit
No. of study visits[c]
If I would have access to the study drug after my participation ended

Top Perceived Benefits and Risks to Clinical Research Participation

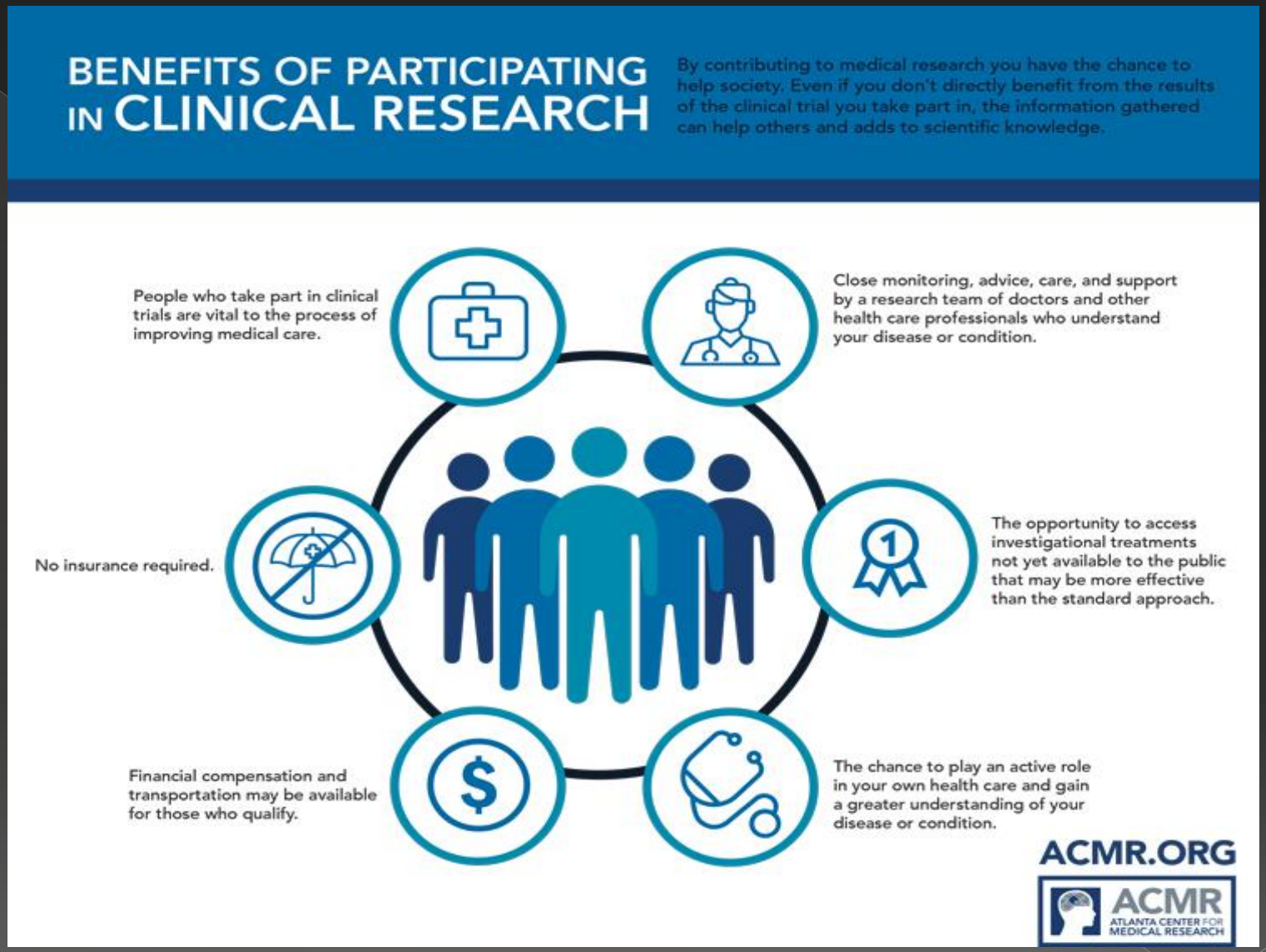
Benefits and Risks
Top Mentioned Benefits
May help advance science and the treatment of my disease or condition
May help save or improve the lives of other patients
May help improve my disease or condition
May represent the best treatment option
May provide monetary compensation for participation
May guide understanding of how available medications compare with a new treatment
May receive more care and attention from physicians and staff
Top Mentioned Risks
Possibility of adverse effects
Possible risks to my overall health
Possibility of receiving a placebo or inactive drug
Possibility of stopping treatments that may be providing some benefit
Possibility of making my private medical information public
Possibility of missing too much time at work

10 Reasons Patients Don't Enroll in a Clinical Trial

1. Lack of awareness
2. Fear of the unknown
3. Don't meet the requirements
4. Travel
5. Don't want placebo
6. Concerned about way drug is administered or by requirements of the trial (tests, diaries, injections, etc.)
7. Tests involved or required
8. Time requirements
9. Lack of family support or caregiver help
10. Safety concerns

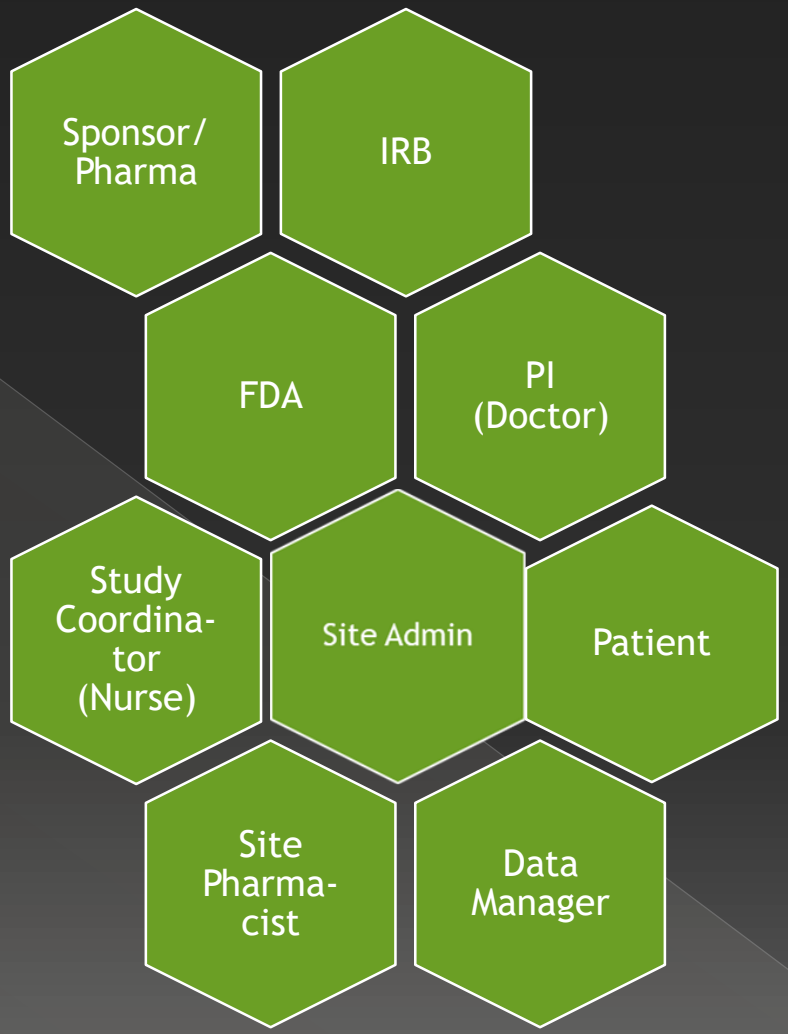
10 Reasons Patients Benefit from Clinical Trials

1. Access to expert clinicians
2. Symptom improvement
3. Contribution to science
4. Help pave the way for other patients
5. Better connected to the community
6. Increase understanding of the disease
7. Possible continued treatment after the randomized part of the trial has ended
8. Tracking self-reported outcomes can help patients better manage symptoms
9. Development of new tools
10. Potential to be the first treated with a new drug



2016 NIH study found that 97% of patients who had been in a clinical trial would recommend participation to a family member or friend. Patients reported having received better care than they were receiving before enrolling in the trial.

Join the CT Research Team



Education before Participation: Be prepared to ask questions

- What is the main purpose of the study?
- Does the study involve a placebo?
- Do I have to discontinue my current medications, including vitamins and supplements?
- What has been learned about the investigational drug already?
- How is the study drug administered?
- Do I have to travel? If so, do I have to pay for travel expenses?
- What will happen to my medical care while I am in the study?

Education before Participation: Be prepared to ask questions

- Do I (or my insurance) have to pay for any part of the study, including any tests or routine visits while I am in the study?
- Can I find out the results of the study when it is finished?
- Will I know if I am receiving study drug or placebo?
- Does the study require hospitalization?
- How long does the study last and how often am I expected to visit the study site?
- What am I expected to do during the study on my own, such as completing daily or weekly assessments?

Medical Records

- Where is your medical record??
- Right to Access
- Create a medical binder with sections
- Responsibility of the PI to build a written medical history about every patient in a clinical trial
- Share prior symptoms, issues, surgeries, medications, etc. (Be honest!)

Top 3 Patient & Family Considerations when Evaluating a Clinical Trial

1. Eligibility
   - Am I right for this study?
   - What are the inclusion and exclusion criteria?
2. Safety
   - Has the drug been studied before?
   - What are the side effects?
3. Access
   - Where is the study site? Are there travel costs?
   - How often should I expect to visit the study site?
   - Who will be providing my care?
   - Will I be expected to change my current standard of care? (medications, therapies, supervision of other physicians, etc.)

Eligibility: Inclusion and Exclusion criteria

- Inclusion criteria – what you must meet to participate
  - Age requirement
  - Ability to provide consent as well as complete assessments
  - Specific diagnosis
- Exclusion criteria – factors that prohibit your eligibility
  - Co-existing medical conditions
  - Participation in other clinical trials
  - Type and stage of your disease

Genetic diagnosis – friend or foe?

- Rationale for requiring a genetic diagnosis in rare disease clinical trials
- Challenges exist around genetic diagnosis, especially for adult patients
- New standard of care, consider pursuing additional testing for your own information, as diagnostic technology has changed

Informed Consent

Components of Informed Consent

- You must have the capacity (or ability) to make the decision.
- The medical provider must disclose information on the treatment, test, or procedure in question, including the expected benefits and risks, and the likelihood (or probability) that the benefits and risks will occur.
- You must understand the relevant information.
- You must voluntarily grant consent, without coercion or duress.

You can discontinue the study drug (or placebo) and withdraw from the trial at any time for any reason.

Side Effects

- AE (Adverse Event)
  - Anything NEW
  - Anything WORSE
- SAE (Serious Adverse Event)
- Reporting AE or SAE
- Risk-benefit decisions as a team

Your safety is a priority. *The ethics and legalities that guide good medical practice also apply to clinical trials. Even more safeguards exist for CT!*

How are WE, the patients, PIONEERS?

- We define **meaningful outcomes** – what really matters to people with the disease
- We help researchers and clinicians **learn about the disease** as well as the investigational drug
- We cause **improvements in standards of care** and diagnostics
- We help **establish a global network**, by identifying patients outside of geographic hotspots, connecting community

How are WE, the patients PARTNERS?

- We support the critical role of **patient advocacy organizations**
- We must be **self-advocates**
- We have a voice… **Patient-reported outcomes** are very important
- **We help pave the road for the future.** Successful clinical trials→
  - improvements in diagnosis
  - support of specialty centers
  - potential for more future clinical trials

Knowledge is Power

- Contact the study coordinator, and take time to ask questions
- Include your tribe – your family, support system, and your physicians- but know that YOU are the ultimate decision-maker
- Embrace the opportunity to learn more about yourself and your disease

Homework

Check out current Mito Clinical Trials

www.ClinicalTrials.gov → Search "Name of condition" → Actively Recruiting

Showing: 1-12 of **12** studies 25 ▼ studies per page

Show/Hide Columns

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	Diagnostic Screening Tests and Potential Biomarkers in **Mitochondrial Myopathies**	• **Mitochondrial Myopathies**	• Diagnostic Test: Diagnostic screenings tests	• Copenhagen Neuromuscular Center, Rigshospitalet Copenhagen, Denmark
2	☑	Recruiting	A Trial to Evaluate the Safety and Efficacy of Elamipretide in Subjects With Primary **Mitochondrial Myopathy** Followed by an Open-Label Extension	• Primary **Mitochondrial Myopathy**	• Combination Product: elamipretide • Combination Product: placebo comparator • Combination Product: elamipretide open label treatment	• University of California San Diego La Jolla, California, United States • Stanford University Palo Alto, California, United States • Children's Hospital Colorado Aurora, Colorado, United States • (and 18 more...)
3	☐	Recruiting	Resveratrol Supplementation in Patients With **Mitochondrial Myopathies** and Skeletal Muscle Fatty Acid Oxidation Disorders	• **Mitochondrial Myopathies** • Fatty Acid Oxidation Defects	• Dietary Supplement: Resveratrol	• Copenhagen Neuromuscular Center Copenhagen, Denmark
4	☐	Recruiting	Oxidative Capacity and Exercise Tolerance in Ambulatory SMA	• Spinal Muscular Atrophy Type 3 • **Mitochondrial Myopathy**		• Columbia University Medical Center New York, New York, United States
5	☐	Recruiting	Nicotinamide Riboside and **Mitochondrial** Biogenesis	• **Mitochondrial** Diseases • **Mitochondrial Myopathies** • Progressive External Ophthalmoplegia • (and 6 more...)	• Dietary Supplement: Nicotinamide Riboside	• Cambridge University Hospitals NHS Foundation Trust Cambridge, United Kingdom
6	☐	Recruiting	Fat and Sugar Metabolism During Exercise in Patients With Metabolic **Myopathy**	• Metabolism, Inborn Errors • Lipid Metabolism, Inborn Errors • Carbohydrate Metabolism, Inborn Errors • (and 20 more...)	• Other: Sugar	• Neuromuscular Research Unit, 3342 Copenhagen, Denmark
7	☐	Recruiting	Fatty Acid Oxidation Defects and Insulin Sensitivity	• Very Long-chain Acyl-CoA Dehydrogenase Deficiency • Trifunctional Protein Deficiency • Long-chain 3-hydroxyacyl-CoA Dehydrogenase Deficiency • (and 3 more...)	• Drug: Intralipid/Heparin • Drug: Glycerol/Saline • Drug: Hyperinsulinemic euglycemic clamp	• Oregon Health & Science University Portland, Oregon, United States
8	☐	Recruiting	Natural History Study - **Mitochondrial** Disease	• MELAS or m.3243 A>G **Mitochondrial** DNA Mutation Carrier		• Columbia University New York City, New York, United States
9	☐	Recruiting	The Leigh Syndrome Registry	• Leigh Syndrome • Leigh Disease • Leigh's Necrotizing Encephalopathy • (and 2 more...)		• The University of Texas Health Science Center at Houston Houston, Texas, United States
10	☐	Recruiting	Genetic Studies of Strabismus, Congenital Cranial Dysinnervation Disorders (CCDDs), and Their Associated Anomalies	• Congenital Fibrosis of Extraocular Muscles • Duane Retraction Syndrome • Duane Radial Ray Syndrome • (and 23 more...)		• Boston Children's Hospital Boston, Massachusetts, United States
11	☐	Recruiting	Inherited Retinal Degenerative Disease Registry	• Eye Diseases Hereditary • Retinal Disease • Achromatopsia • (and 25 more...)		• Foundation Fighting Blindness Columbia, Maryland, United States
12	☐	Recruiting	North American **Mitochondrial** Disease Consortium Patient Registry and Biorepository (NAMDC)	• **Mitochondrial** Disorders • **Mitochondrial** Genetic Disorders		• University of California San Diego San Diego, California, United States

Questions? info@stealthbt.com Mito411@mitoaction.org UMDF Support Line 1-888-317-8633

YOU are a hero!

https://www.ciscrp.org/our-programs/medical-heroes-campaign/national-clinical-trial-outreach-and-awareness-initiative/

Externally-led Patient Focused Drug Development: Barth syndrome

PFDD for Mito: MARCH 29th

Externally-led Patient-Focused Drug Development Meeting

Come and Share Your Voice!

Connect with your Community

MDA

UNITED MITOCHONDRIAL DISEASE FOUNDATION
HOPE. ENERGY. LIFE.

MITO HOPE and HELP
Reaching out to individuals living with Mitochondrial Diseases

mitocanada

Miracles for Mito™

...Give a child Hope and Smiles

mito ACTION

Barth Syndrome Foundation®

RNE

KEEP CALM AND RAISE AWARENESS
FOR MITOCHONDRIAL DISEASE