Clinical Trials and YOU

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Disclosure

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   Board of Directors

The content of this talk and the views expressed are those of JC and do not necessarily reflect the views or position of my employer GSK. This talk is about clinical trials and will not discuss GSK products or specific clinical research projects.

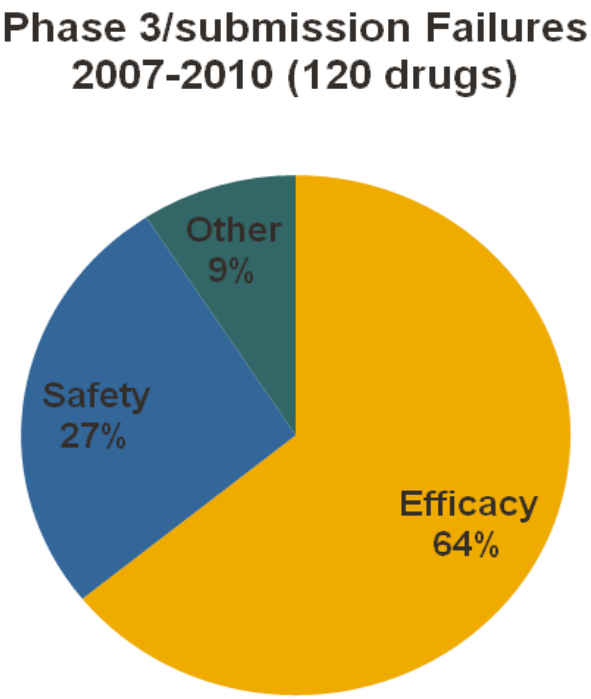
Introduction

- Thanks to the PBCers organization
- My objectives for this talk
  - Broad topic
  - Selected aspects with a patient focus
- Understanding clinical trials
  - The process of determining if a candidate medicine is safe and effective for the disease being treated
  - In many ways trials are the end-game
- Personal perspective
  - HUGE responsibility to many stakeholders
    - Patients waiting for a cure
    - Patients considering or have participated in earlier trials
    - Researchers who have worked tirelessly to advance candidate

Drug development is not for the faint of heart

Metric	Estimates*
Avg. time to develop a drug	10-15 years
Avg. cost to develop a new drug	1.2 to 2.6 billion USD
Est. success from discovery to human CTs	~1 in 5000 (~10%)
Est. success from early trials to approval	~1 out of 5 (~20%)

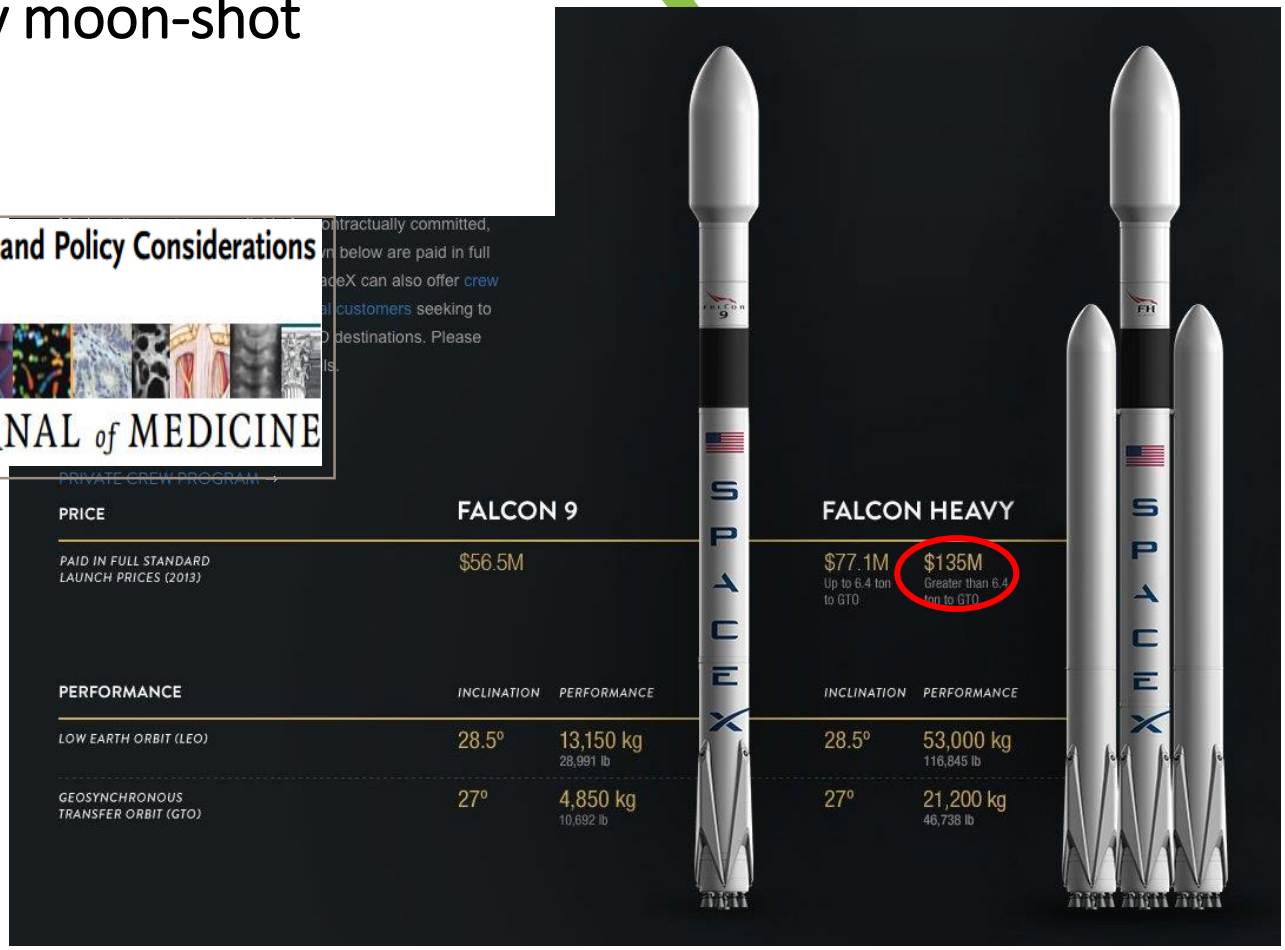
Cost and times depend on many variables



U. Nitin Kashyap et al *J Pharm. Sci. & Res.* 5(6), 2013, 131 – 136; *Pharma Profile 2013*
Tufts center for the study of drug development, 2014

Cost of Drug Development

The drug discovery moon-shot



We can fund 20 space missions for the cost of developing a single drug

Clinical trials (CT)

- Human research that determines if a drug is both safe and effective for its intended use
- A clinical trial almost never stands alone
  - Part of a clinical development program
  - Detailed pre-defined plan
  - Regulatory checks along the way
- Goal is to estimate **Risk/Benefit**
  - Risk/benefit is assessment of safety and efficacy
  - Other currently available treatments
  - Severity of the condition for treatment
- Rare disease presents special considerations that can impact risk/benefit
- It's (still) all about the data

Phases of CTs

Phase 1

- Safety focused; usually in **healthy volunteers** (without disease)
- Small # participants, dose-finding, first-time in human

Phase 2

- Safety and effectiveness in **patient population**
- Larger, dose-ranging and vs. comparator (placebo)

Phase 3

- Efficacy and safety in **intended** population
- Larger than Ph2, comparator (Standard of care and/or placebo)
- Pivotal

Phase 4

- Testing an **approved** drug for a different disease, populaton or dose, etc.

Key roles in a CT

- Patient/Participant/Subject/Volunteer
- Sponsor – commonly pharma
  - Multiple functions in concert
  - Sponsor is defined as ‘holder’ of the Investigational New Drug Application (IND)
- Principal Investigator (PI) – leads site team & medical oversight
  - Study Coordinator
  - Pharmacy
- Institutional Review Board (IRB)
- Regulatory Authority- FDA
- Personal Health Care providers
- Patient advocates
- Caregiver

Key CT elements

- Informed consent (ICF)
- Clinical protocol
  - Pre-specified instructions for clinical trial
  - Comprehensive
  - Part of a Clinical Development Plan (CDP)
- Investigational New Drug Application (IND)
  - Pre-IND meeting with FDA
  - End of Phase 2 meeting
- New Drug Application (NDA)
- Publication (Paper, Manuscript or other dissemination)

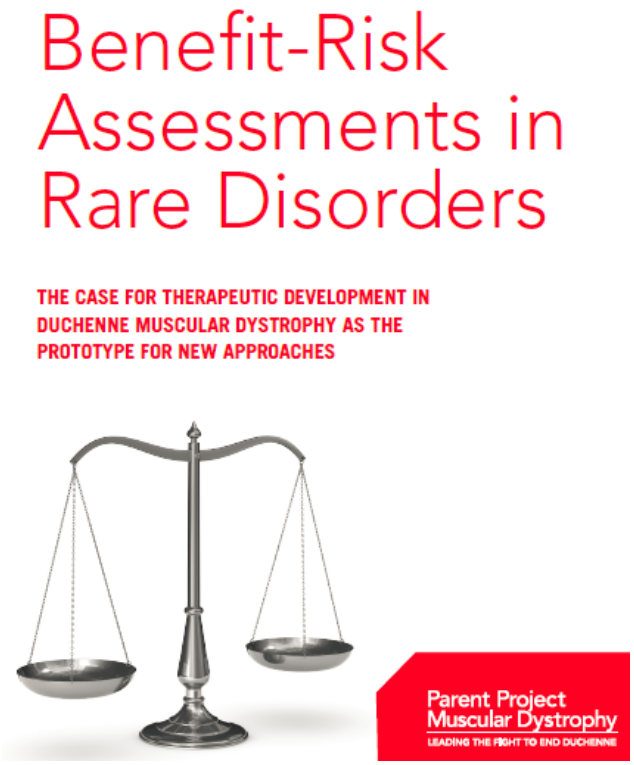
Informed consent (IC)

- Purpose and elements
  - Explain the **reason** for the trial
  - Investigational medicine being studied
  - The **time commitment** involved (# of visits and duration)
  - Procedures that will be done at each visit
  - Chances of receiving the Investigational drug or comparator
  - Who may see your data and how it will be used
  - Potential risks and/or benefits of participation
  - Your rights pertaining to your participation and your data
- Important document to understand
  - PI or designee is required to make sure it is fully understood
  - The IC is also an agreement to participate and comply

Special topics

- Clinical trial controls – comparison?
  - Demonstrate Investigational Drug works as intended
  - Need to compare to something (Risk/Benefit)
  - FDA expectation
- Randomization & blinding – minimize bias & confounders
  - Single vs. double-blind
- Rare disease clinical trials
  - Differences – mostly on sponsor side
  - How they are not different
- Can a clinical trial be stopped?
  - Safety Monitoring Committee or Data Safety Monitoring Board
  - Interim analysis - futility
- Compensation
  - Personal expenses
  - Injury
- Dissemination of results
  - Regulatory, professional & public

Risk/Benefit



The risk/benefit equation differs

1. Regulators - FDA
2. Provider – patient welfare
3. Patient – quality of life
   - Especially true in rare disease
   - Emphasis on the patient perspective
   - Endpoints that are clinically meaningful
   - Endpoints that improve functional outcomes, reduce disease burden or improve quality of life

Online information sources

Source	Sponsor
Clinical trials.gov	FDA/NIH
CenterWatch	Corporate
FDA Websites	FDA
Patient Advocacy Groups	Private
Pharma websites	Corporate
NORD	National

- Critically read & compare
- Know source of information
- Access multiple sources
  - Look for differences
- Discuss with trusted family, friends & colleagues
- Talk with others who have participated
- Consult your PCP and specialist
- Research development drug and other options

Very important to consult your own physician(s) to discuss the risks and benefits of YOUR clinical trial participation

Key online resources

ClinicalTrials.gov - Official Site

https://clinicaltrials.gov

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

Search
Search Tips and Examples. You can enter a word or a phrase, such as the name of a ...

Home
ClinicalTrials.gov is a registry and results ...
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Find Studies
Find Studies. The Find Studies section of this site describes the options for finding studies ...

Why Register
Why Should I Register and Submit Results? Contents. What Is the Purpose of Trial ...

For Researchers
For Researchers. ClinicalTrials.gov is a registry and results database of publicly and ...

For Patients & Families
For Patients and Families. The ClinicalTrials.gov Web site provides current ...

Study Record Managers
For Study Record Managers. Clinical studies are registered on ClinicalTrials.gov via a ...

Learn About Studies
Learn About Clinical Studies Contents. What Is a Clinical Study? Clinical Trials; ...

Patient Advocacy Resources

Home - PBCers.org

The PBCers Organization is a wonderful source of education and support for those who suffer from Primary Biliary Cholangitis (originally Primary Biliary Cirrhosis) and other autoimmune liver diseases. Formed December 1, 1996, the PBCers is the largest PBC online support group worldwide.

We offer our members:

- **PBC E-mail Daily Digest**
- **Facebook & Twitter**
- **Family & Friends E-mail Group**
- **Find a Doctor**
- **Local PBC Groups**
- **Partners & Other Links**
- **Patient Registry**

2018 Clinical Trials

ClinicalTrials.gov (Search) ClinicalTrials PBC

Arena Pharmaceuticals

Genefit Corp

Target Pharma Solutions

Clinical Trials PBC

CymaBay Therapeutics

Genkyotex

Zydus Healthcare

Thank you

Acknowledgements

- PBCers
- GlaxoSmithKline
- Patients

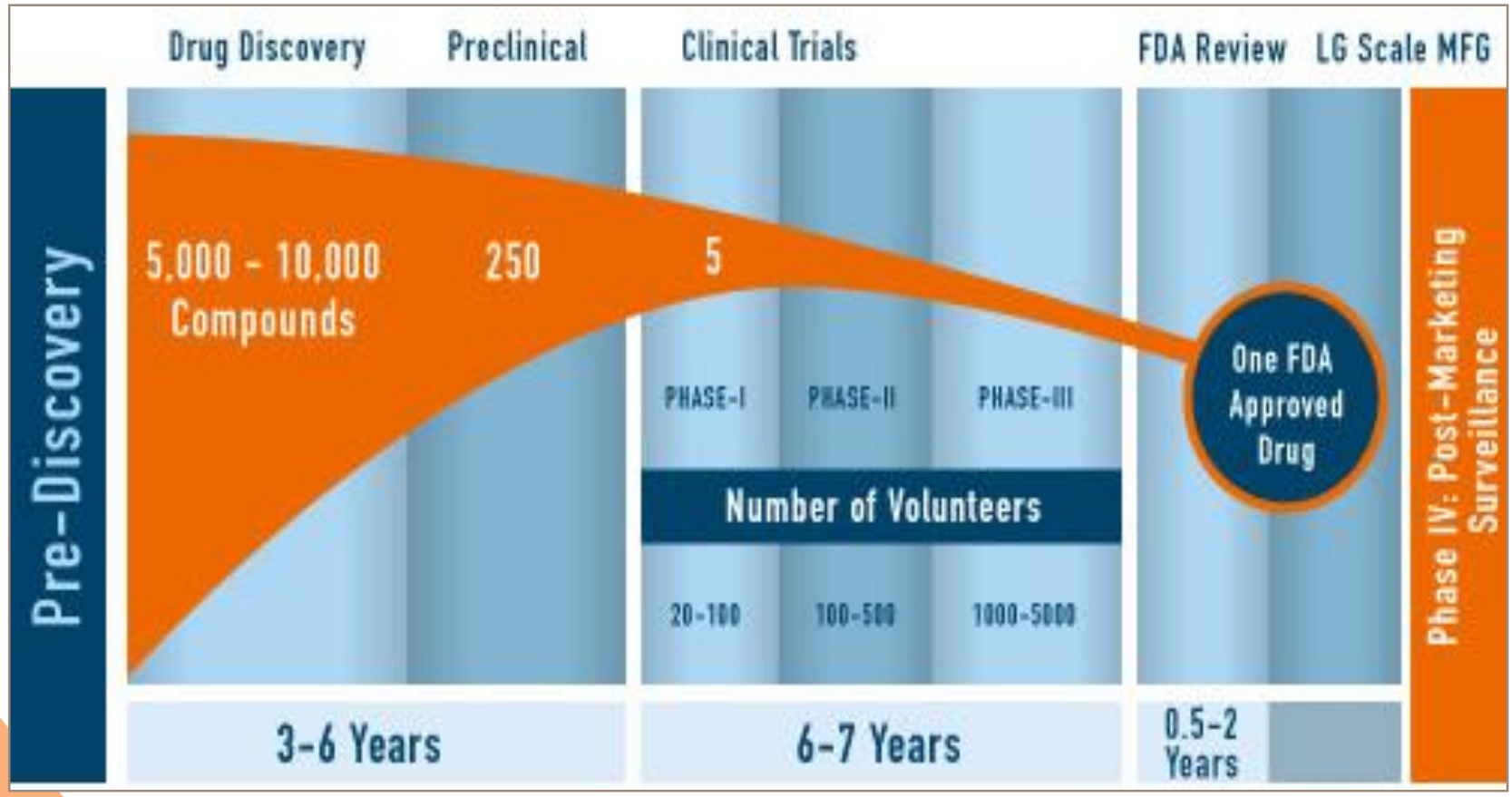
Questions & answers

Back-up

Key terms

Protocol	Comprehensive and detailed instructions for a clinical trial
Randomized	A way of removing bias in a trial by randomly assigning treatments and entry
Blinded vs. open-label	Double vs. Single-blind
Control (placebo vs. comparator)	RCT
Informed consent	Patient document that explains trial and agreement to participate
Phase	
Primary endpoint	Pre-defined in protocol
Sponsor	
Investigator (PI)	Medical oversight and responsible for conduct
Patient, participant, subject	
Investigational drug **Investigational New Drug Application (IND)**	
Regulatory Authority (In US –FDA)	
Biomarker	
Natural History	
New Drug Application (NDA)	
Standard of Care	The current best medical practice for treatment
Pivotal trial	A trial intended to support regulatory approval
Good Clinical Practice (GCP)	quality standard that is provided by ICH that govt.'s use to set clinical research standards
International Conference on Harmonization (ICH)	International harmonized guidelines for global drug development

Drug development takes a long time and is a process of attrition



Topics

- Clinical trials – nuts and bolts
  - The drug development journey
  - Types and phases of clinical trials
  - Its all about the data
- It takes a village
  - Pharma perspective
  - Patient perspective
  - Risk vs. Benefit
- Limitations and challenges
- Importance and benefits
- So you want to be in a clinical trial?
  - Consenting process
  - What to know & what to ask
- Information resources
  - Know the source
  - Prioritize
  - Consult you physician