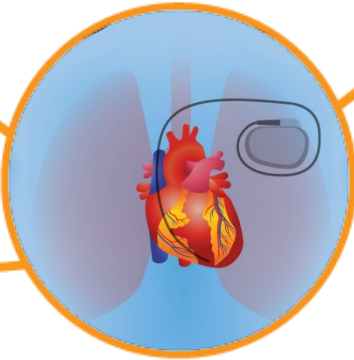


# BRINGING THERAPEUTICS, MEDICAL DEVICES, AND DIAGNOSTICS TO MARKET

Terri Butler, PhD  
ITHS Drug & Device  
Advisory Committee



# The Institute of Translational Health Sciences

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## **The Institute of Translational Health Sciences**

is dedicated to speeding science to the clinic for the benefit of patients and communities throughout Washington, Wyoming, Alaska, Montana, and Idaho.

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ITHS promotes this translation of scientific discovery to practice by fostering innovative research, cultivating multi-disciplinary research partnerships, and ensuring a pipeline of next generation researchers through robust educational and career development programs.



# ITHS Research Resources



Biomedical  
Informatics



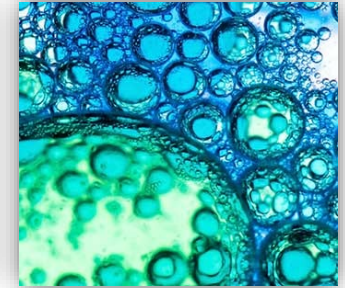
Biostatistics  
SCH & UW



Data and Safety  
Monitoring



Education and  
Training



GMP Production  
Facility



Research  
Navigation



Preclinical  
Consulting



Research  
Coordination



Regional  
Collaboration



Adult, Pediatric,  
Dental Translational  
Research Units

# Connecting with ITHS

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Contact the ITHS Navigator for guidance

[ithsnav@uw.edu](mailto:ithsnav@uw.edu)

206.221.1234



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ACCELERATING RESEARCH. IMPROVING HEALTH.

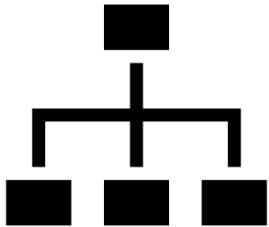


# Learning Objectives



## Steps To Market

- ▶ Define and validate the need
- ▶ Phases of development



## Expertise and Organizational Structures Needed

- ▶ Types of expertise needed along the development path
- ▶ How organizational structure will change over time



## Complications and Challenges

- ▶ Expect the unexpected
- ▶ Real-world rates of success and failure

# Categories of regulated products

## Drugs



*Therapeutics:  
small molecule,  
repurposed*

## Biologics



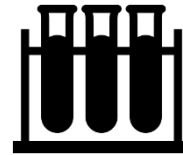
*Antibodies,  
vaccines*

## Medical Devices



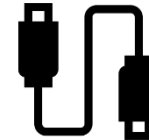
*Implanted  
devices,  
external devices*

## Diagnostics



*Laboratory,  
point-of-care, or  
home-based kits*

## Digital Health Tools



*Monitoring,  
therapeutic,  
control systems*

## Clinical Decision Support Tools



*In clinic  
standard of care  
information  
systems*

## Primary concerns: Safety and Efficacy

# FDA History

- 1820 First pharmacopeia
- 1848 Inspections to stop adulterated drugs from overseas
- 1912 Sherley Amendment prohibits false therapeutic claims
- 1912 Mrs. Winslow's Soothing Syrup for teething is laced with morphine and kills many babies
- 1938 Federal Food, Drug, and Cosmetic Act
  - New drugs must be shown to be safe
  - Must provide safe tolerances
  - Authorized factory inspections
- 1962 Thalidomide, birth defects in thousands of babies in Western Europe, FDA lauded for keeping off US market



# Steps To Market: Discovery!

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Discovery



Patient  
Gets the  
Product!

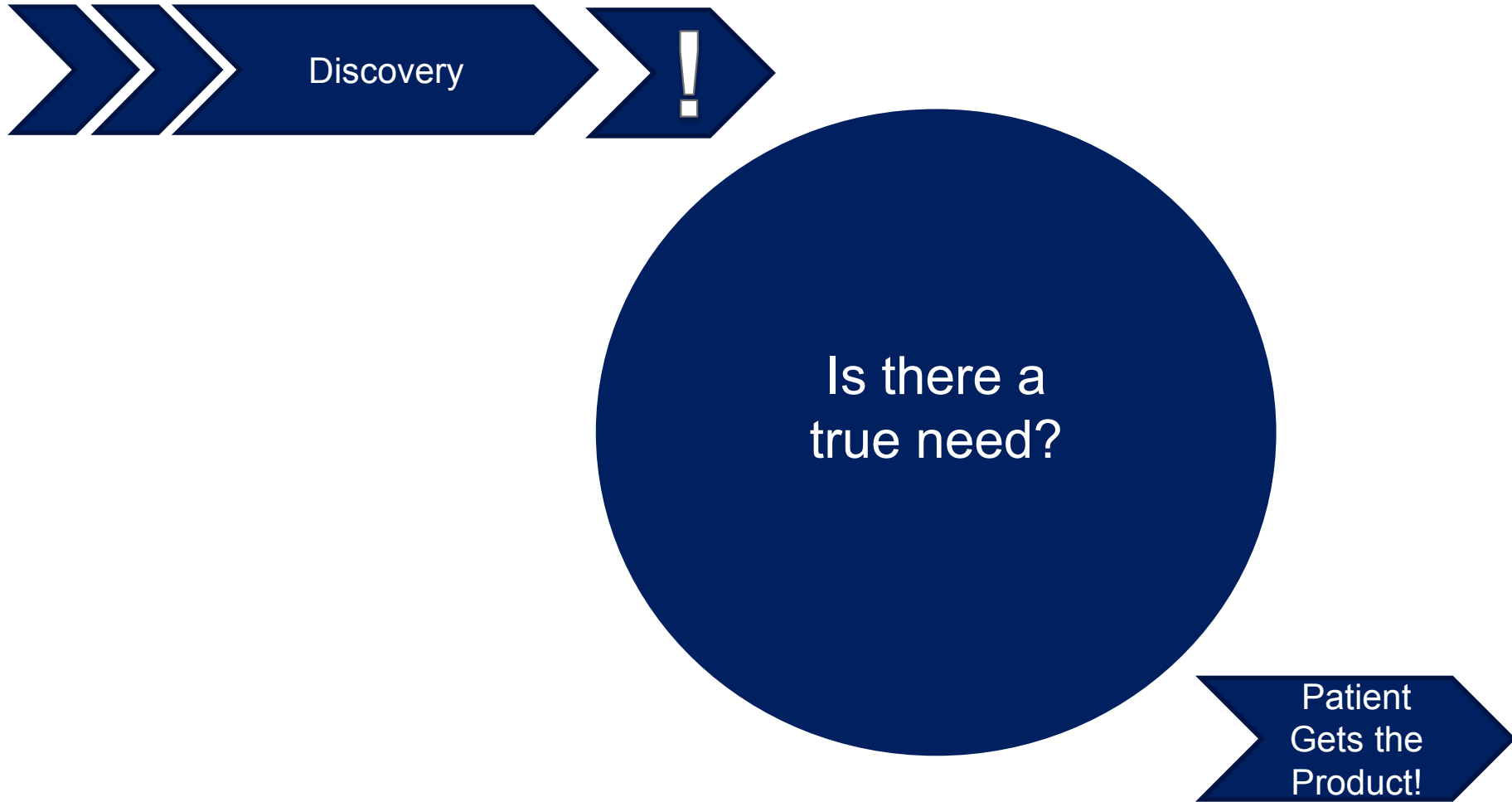


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# Steps To Market: Is there a need?

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# Steps to Market

---

---

Discovery



Possible New  
Product or  
Service

“Customer Discovery”  
Validate the need



# Steps To Market

---

## 1. Is there a true need?

# Steps to Market: Is there a true need?

---

“Customer Discovery”  
Validate the need

Who will benefit?



*Patient*  
*Physician*  
*Hospital*  
*Insurer/employer*

Current alternatives?



*Current practices*  
*“Do nothing”*  
*Side effects*  
*Cost issues*

Up and coming  
alternatives?



*Alternatives in the works*  
*Comparison to your approach*  
*Timing to market*



# Steps To Market

---

- ✓ **1. Is there a true need?**
- 2. Business model?**

# Steps to Market

Discovery



Possible New Product or Service

“Customer Discovery”  
Validate the need

Business Model



# Steps to Market: Business Model?

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Patentable?



*Novel*  
*Non-Obvious*  
*Useful*  
*Prior art*

Regulatory requirements?



*Category of product*  
*Risk*  
*Prior use in humans*  
*Clinical trial requirements*

Who will pay for it?



*Insurer*  
*Hospital or clinic*  
*Included in procedure*  
*Added cost*

# Steps to Market: Business Model?

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Business  
Model

Team members?



*Clinical expertise*  
*Regulatory expertise*  
*Product development expertise*  
*Business experience*  
*Legal advice*  
*...more*

Distribution channels?



*Large companies?*  
*Targeted distributors?*  
*Direct to patient?*

Development partners?



*Pharma companies*  
*Contract research orgs*  
*Manufacturing partners*  
*Device companies*



# Steps to Market: Business Model Canvas










## The Business Model Canvas

Designed for:

Designed by:

Date:

Version:

<p><b>Key Partners</b> </p> <p>Who are our Key Partners? Who are our key suppliers? Which Key Resources are we acquiring from partners? Which Key Activities do partners perform?</p> <p><b>MOTIVATIONS FOR PARTNERSHIPS</b> Optimization and economy Reduction of risk and uncertainty Acquisition of particular resources and activities</p>	<p><b>Key Activities</b> </p> <p>What Key Activities do our Value Propositions require? Our Distribution Channels? Customer Relationships? Revenue streams?</p> <p><b>CATEGORIES</b> Production Problem Solving Platform/Network</p>	<p><b>Value Propositions</b> </p> <p>What value do we deliver to the customer? Which one of our customer's problems are we helping to solve? What bundles of products and services are we offering to each Customer Segment? Which customer needs are we satisfying?</p> <p><b>CHARACTERISTICS</b> Newness Performance Customization "Selling the Job Done" Design Brand/Status Price Cost Reduction Risk reduction Accessibility Convenience/Usability</p>	<p><b>Customer Relationships</b> </p> <p>What type of relationship does each of our Customer Segments expect us to establish and maintain with them? Which ones have we established? How are they integrated with the rest of our business model? How costly are they?</p> <p><b>EXAMPLES</b> Personal assistance Dedicated Personal Assistance Self-Service Automated Services Communities Co-creation</p>	<p><b>Customer Segments</b> </p> <p>For whom are we creating value? Who are our most important customers?</p> <p>Mass Market Niche Market Segmented Diversified Multi-sided platform</p>																		
	<p><b>Key Resources</b> </p> <p>What Key Resources do our Value Propositions require? Our Distribution Channels? Customer Relationships? Revenue Streams?</p> <p><b>TYPES OF RESOURCES</b> Physical Intellectual (brand, patents, copyrights, data) Human Financial</p>		<p><b>Channels</b> </p> <p>Through which Channels do our Customer Segments want to be reached? How are we reaching them now? How are our Channels integrated? Which ones work best? Which ones are most cost-efficient? How are we integrating them with customer routines?</p> <p><b>CHANNEL PHASES</b> 1. Awareness How do we raise awareness about our company's products and services? 2. Evaluation How do we help customers evaluate our organization's Value Proposition? 3. Purchase How do we allow customers to purchase specific products and services? 4. Delivery How do we deliver a Value Proposition to customers? 5. After sales How do we provide post-purchase customer support?</p>																			
<p><b>Cost Structure</b> </p> <p>What are the most important costs inherent in our business model? Which Key Resources are most expensive? Which Key Activities are most expensive?</p> <p><b>IS YOUR BUSINESS MORE:</b> Cost Driven (Minimal cost structure, low price value proposition, maximum automation, extensive outsourcing) Value Driven (Focused on value creation, premium value proposition)</p> <p><b>SAMPLE CHARACTERISTICS</b> Fixed Costs (salaries, rents, utilities) Variable costs Economies of scale Economies of scope</p>	<p><b>Revenue Streams</b> </p> <p>For what values are our customers really willing to pay? For what do they currently pay? How are they currently paying? How would they prefer to pay? How much does each Revenue Stream contribute to overall revenues?</p> <table border="0"> <tr> <td><b>TYPES</b></td> <td><b>FIXED PRICING</b></td> <td><b>DYNAMIC PRICING</b></td> </tr> <tr> <td>Asset sale</td> <td>List Price</td> <td>Negotiation (Bargaining)</td> </tr> <tr> <td>Usage fee</td> <td>Product feature dependent</td> <td>Usage Management</td> </tr> <tr> <td>Subscription Fees</td> <td>Customer segment dependent</td> <td>Real-time Market</td> </tr> <tr> <td>Licensing</td> <td>Volume dependent</td> <td></td> </tr> <tr> <td>Franchise fees</td> <td></td> <td></td> </tr> <tr> <td>Advertising</td> <td></td> <td></td> </tr> </table>	<b>TYPES</b>	<b>FIXED PRICING</b>	<b>DYNAMIC PRICING</b>	Asset sale	List Price	Negotiation (Bargaining)	Usage fee	Product feature dependent	Usage Management	Subscription Fees	Customer segment dependent	Real-time Market	Licensing	Volume dependent		Franchise fees			Advertising		
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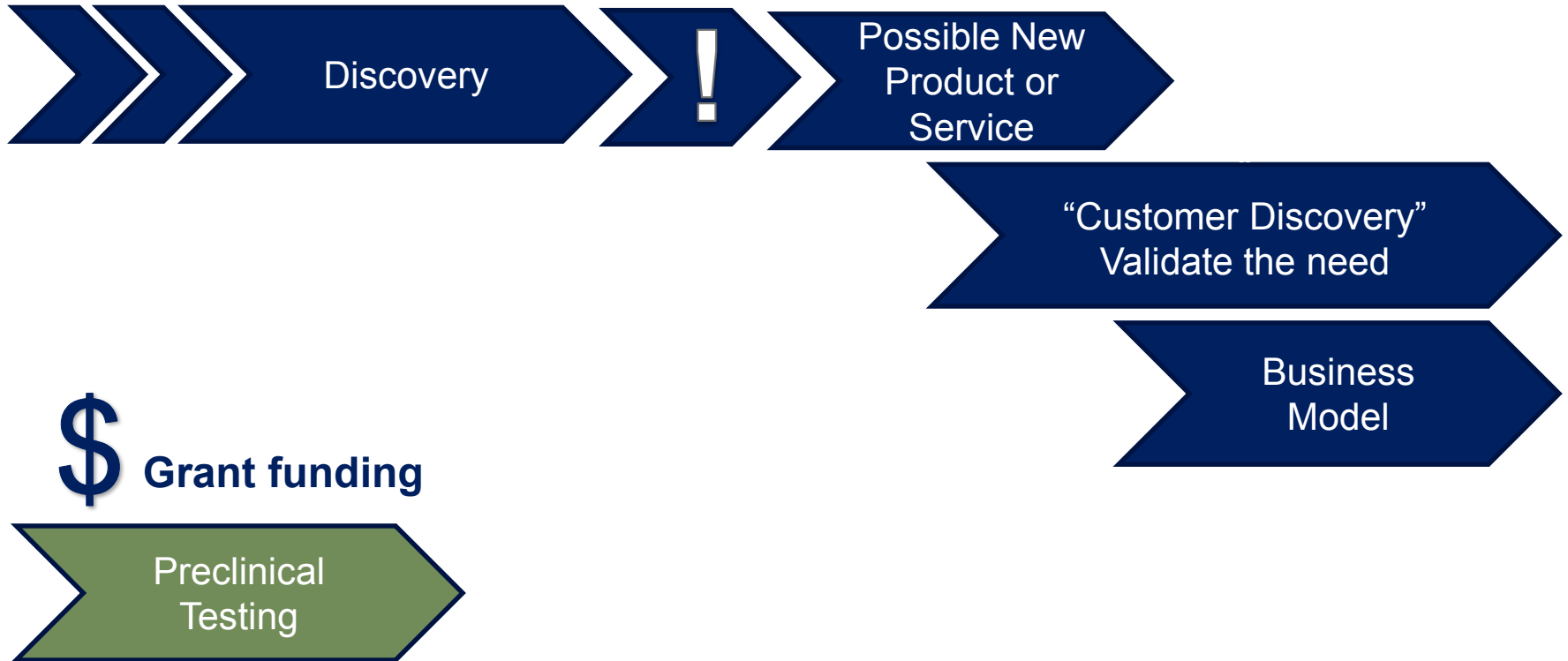
# Steps To Market

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- ✓ 1. **Is there a true need?**
- ✓ 2. **Business model?**
- 3. **Is it safe?**

# Steps to Market

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# Steps to Market: Preclinical Testing

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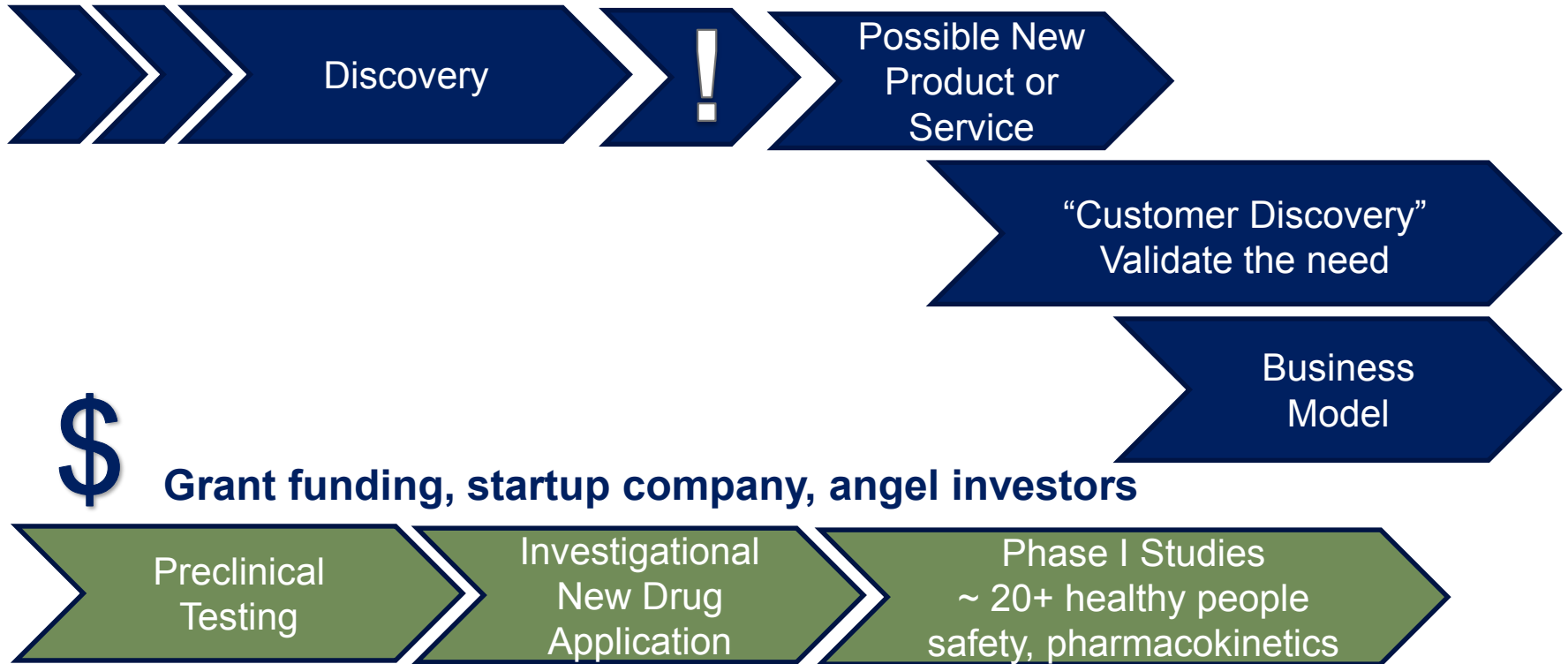


## Preclinical Testing

- ▶ Source of drug: **cGMP manufacturer**
- ▶ Pharmacodynamics – drug action
- ▶ Pharmacokinetics – metabolism of the drug
- ▶ Toxicity
- ▶ Efficacy
- ▶ In vitro: **Test tube or cell culture with documentation**
- ▶ In vivo: **Two-species animal testing in specialized lab**
- ▶ Devices: Biocompatibility testing
- ▶ **CAN TAKE 2-5 YEARS!**



# Steps to Market



# Steps to Market: IND and Phase I Studies

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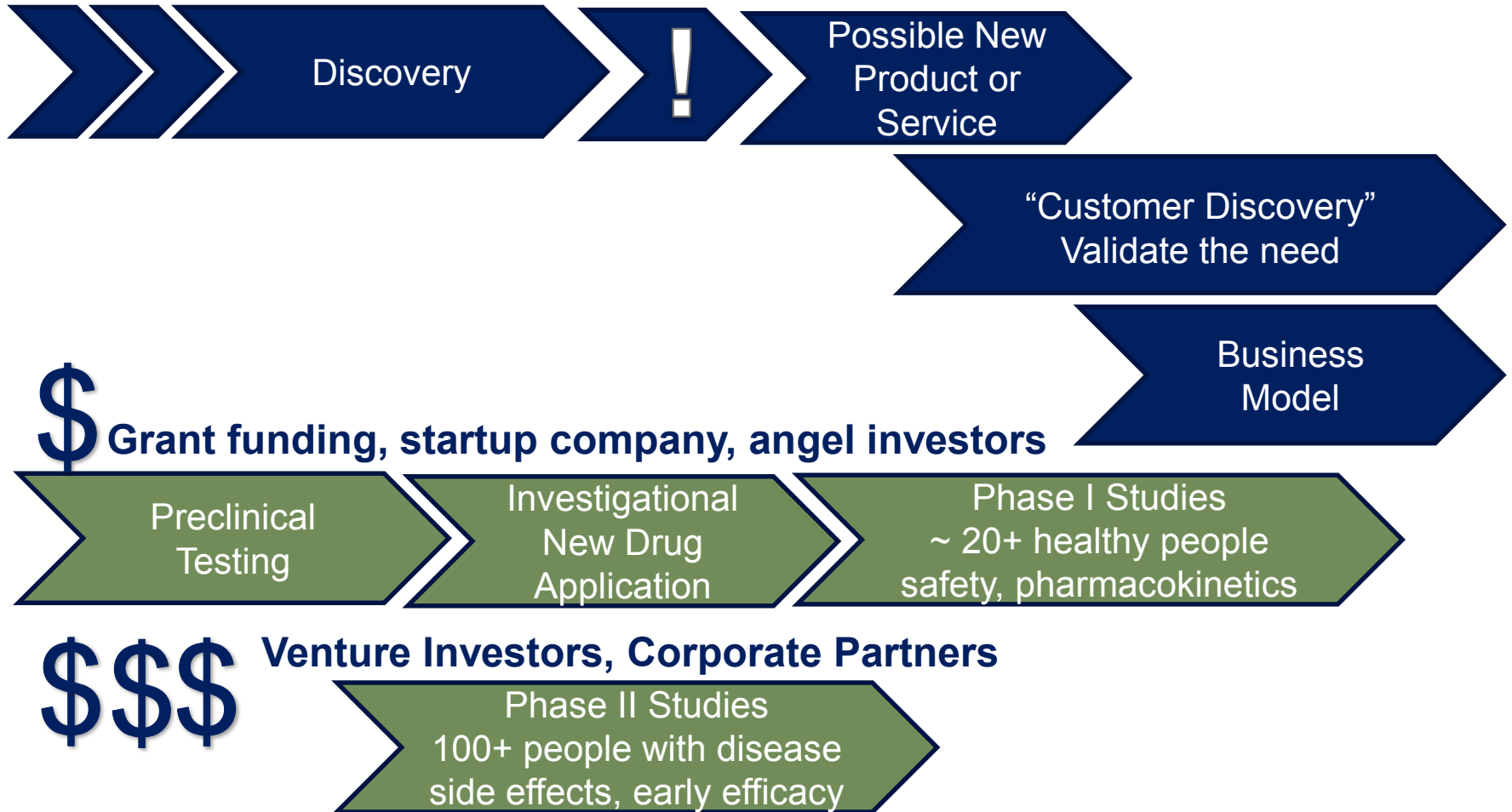
- ▶ "First-in-humans" studies
- ▶ Investigational New Drug Application to get FDA permission
- ▶ 20-100 healthy volunteers
- ▶ **Clinical study setting**
- ▶ Safety, absorption
- ▶ Dose ranging
- ▶ Success rate ~ 70%
- ▶ 2-4 MORE YEARS!

# Steps To Market

---

- ✓ 1. **Is there a true need?**
- ✓ 2. **Business model?**
- (✓) 3. **Is it safe?**
- 4. **Does it work in humans?**

# Steps to Market



# Steps to Market: Phase II Studies

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Phase II Studies  
100+ people with disease  
side effects, early efficacy

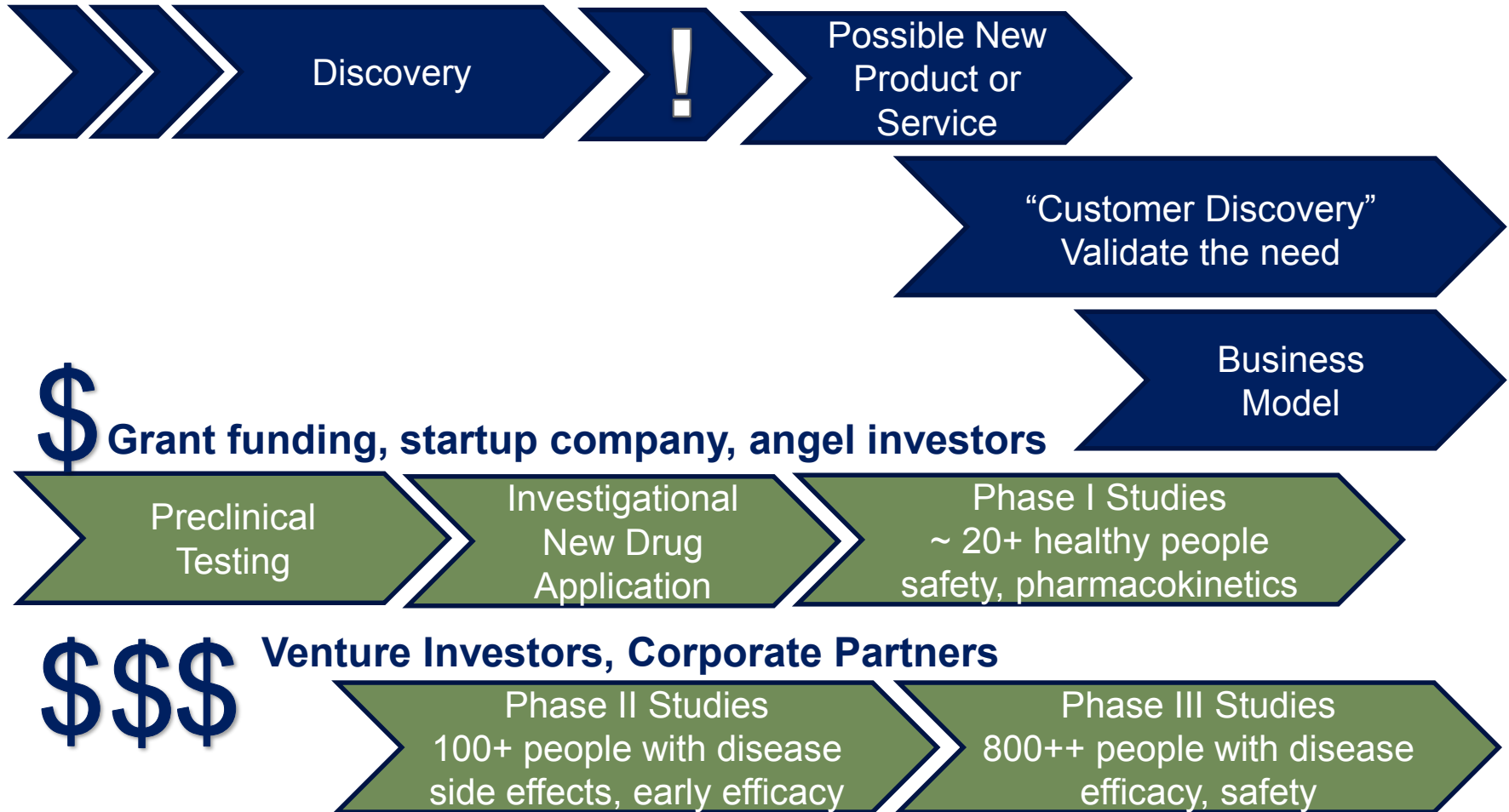
- ▶ Testing in patients with the disease at **clinical trial site**
- ▶ Explore efficacy
- ▶ Dose response
- ▶ Safety
- ▶ 100– 300 subjects
- ▶ Success rate ~ 33%
- ▶ **CAN TAKE 2-5 MORE YEARS!**

# Steps To Market

---

- ✓ 1. **Is there a true need?**
- ✓ 2. **Business model?**
- (✓) 3. **Is it safe?**
- (✓) 4. **Does it work in humans?**

# Steps to Market





# Steps to Market: Phase III Studies

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Phase III Studies  
800++ people with disease  
efficacy, safety

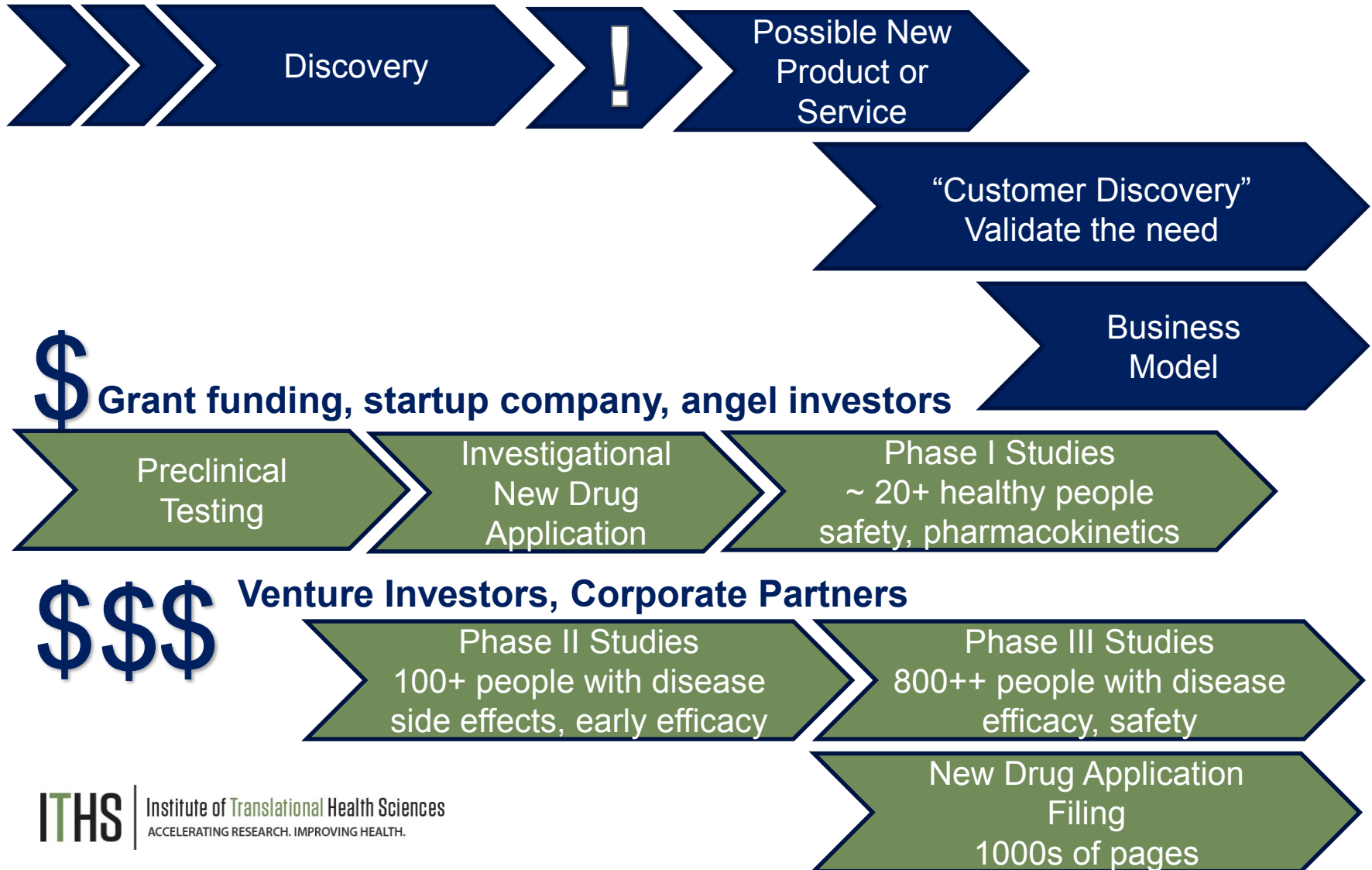
- ▶ Testing in patients with the disease
- ▶ Effectiveness
- ▶ Therapeutic dose
- ▶ Safety continues to be monitored
- ▶ 300– 3000 subjects
- ▶ Success rate ~ 25%
- ▶ WILL TAKE 3-5 MORE YEARS!

# Steps to Market

---

- ✓ 1. **Is there a true need?**
- ✓ 2. **Business model?**
- ✓ 3. **Is it safe?**
- ✓ 4. **Does it work in humans?**
- 5. **Permission to market**

# Steps to Market



# Steps to Market: New Drug Application

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New Drug Application  
Filing  
1000s of pages

- ▶ Submit all study data to the FDA
- ▶ Safety information
- ▶ Proposed labeling
- ▶ Directions for use
- ▶ Patent information
- ▶ Study data from outside the US
- ▶ IRB compliance information
- ▶ 60 days for FDA to respond yes, need more info, rejected

# Steps to Market

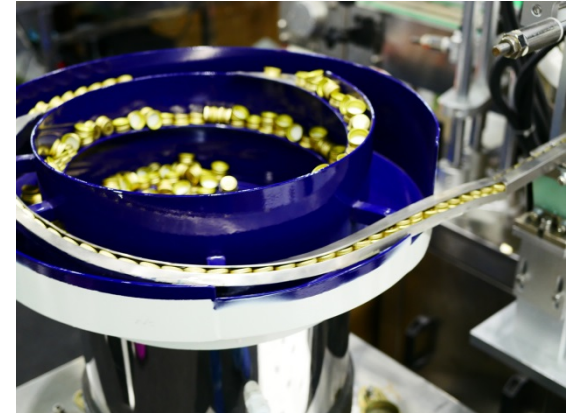
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- ✓ 1. **Is there a true need?**
- ✓ 2. **Business model?**
- ✓ 3. **Is it safe?**
- ✓ 4. **Does it work in humans?**
- (✓) 5. **Permission to market**
6. **Manufacturing?**

# Steps to Market: Manufacturing

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- ▶ Source of drug: **cGMP manufacturer**
- ▶ Assure consistent control over manufacturing
- ▶ Quality control procedures in place
- ▶ Documentation
- ▶ Trial runs and monitoring
- ▶ Inspection by the FDA
- ▶ Buildings, equipment, materials management, cleaning validation, packaging



# Steps to Market

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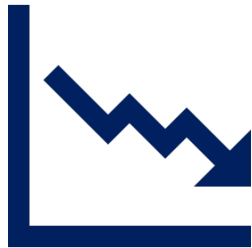
- ✓ 1. **Is there a true need?**
- ✓ 2. **Business model?**
- ✓ 3. **Is it safe?**
- ✓ 4. **Does it work in humans?**
- ✓ 5. **Permission to market**
- ✓ 6. **Manufacturing?**



# What can go wrong?



- ▶ Average cost to approval \$2.4B
- ▶ 9 out of 10 drug candidates fail!
- ▶ Alzheimer's drugs 99.6% failure!
- ▶ \$1.4B lost per drug program
- ▶ ~50% of Phase III trials fail



- ▶ AstraZeneca researchers concluded need:
  - Right target
  - Right tissue for target engagement
  - Right safety margins
  - Right patient
  - Right commercial potential

*2017 FDA white paper:*

## 22 Case Studies Where Phase II and Phase III Trials Had Divergent Results

- ▶ Biomarker data as predictors of clinical efficacy promising for Phase II trials, but **not in Phase III trials.**
- ▶ Drugs in study:
  - Heart disease (aliskiren, dafapladib, torcetrapib)
  - Staph infection (V710 vaccine)
  - Herpes infection (HSV-2 vaccine)

# Why???

# Drug and Device Advisory Committee

## REGULATORY REQUIREMENTS ADVISORY PROGRAM



**Supporting investigators who are taking their research from bench to bedside.**

- ▶ Contact Terri Butler, PhD, [TLButler@uw.edu](mailto:TLButler@uw.edu)
- ▶ Committee formed in 2008
- ▶ 11-15 members
- ▶ Industry experience
- ▶ Assisted 130+ teams in past 10 years
- ▶ Experience in:
  - National and international regulations
  - Preclinical requirements
  - Clinical study design
  - Manufacturing scale up
  - Marketing requirements
  - Partnerships

# Questions?

Terri Butler, PhD

[TLButler@uw.edu](mailto:TLButler@uw.edu)

[https://www.iths.org/investigators/  
services/prd/ddac/](https://www.iths.org/investigators/services/prd/ddac/)



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*Members can access a variety of workforce development and mentoring programs and apply for formal training programs.*

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## Funding

*Members can apply for local and national pilot grants and other funding opportunities. ITHS also offers letters of support for grant submissions.*

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## Collaboration

*Members can connect with collaborators across the CTSA consortium.*