Return on Investment from Patient Input on Development

Forum on Drug Discovery, Development, and Translation
Roundtable on Genomics and Precision Health
Enabling Precision Medicine

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Pfizer
OPERATIONS CENTER OF EXCELLENCE
Global Product Development

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CLINICAL
INNOVATION

Patient Group Engagement Across the Clinical Trial Continuum

Building a model to evaluate impact

- Direct funding and fund raising for research or product development
- Natural history database/registry support
- Help define eligibility criteria within the study protocol
- Feedback on meaningful clinical endpoints
- Assist in creating the informed consent form
- Advise on study recruitment
- Accompany sponsor to FDA to advocate study design

- Direct funding and fund raising for trial operations support
- Network recruitment / outreach
- Serve on a Data Safety Monitoring Board
- Report on patient feedback regarding sites, investigators, and study participant experience
- Serve in preference studies for benefit-risk assessment

- Natural history database / registry support
- Provide feedback on how the patient community views results
- Help return study results to participants
- Write newsletter articles or blog about results
- Co-present results
- Serve on post-market surveillance initiatives

Pre-Discovery → Pre-Clinical → Phase 1 → Phase 2/3 → FDA review & approval → PAS/Outcomes

- Interest of research question to patient community
- Provide data on unmet need and therapeutic burden
- Direct funding and fund raising for research or product development
- Understanding mechanisms of action relevant to disease and symptom burden

- Network recruitment / outreach
- Direct funding and fund raising for research or product development
- Infrastructure support
- Provide input on study design (barriers to participation)
- Support trial awareness and recruitment
- Peer advocate during informed consent procedure

- Serve on FDA advisory committees
- Provide testimony at FDA hearings
- Feedback on meaningful clinical endpoints

Provided by CTTI

**Adapted from Parkinson's Disease Foundation materials for CTTI's Patient Groups & Clinical Trials Project*

CTTI

Conceptual Approaches to Valuing Patient Centric Initiatives

Value Proposition

- Prospective
- Modeling
- Program level/Portfolio Level

(CTTI Working Group)

Return on Engagement

- Retrospective
- Case studies and historical data
- Study level/ Portfolio Level

(DIA -TCSDD working group)

CTTI Patient Groups & Clinical Trials Project Members:

- Bennett Levitan, Janssen R&D
- David Leventhal, Pfizer
- Eric Eisenstein, Duke University
- Michelle Goldberg, Johnson and Johnson Pharmaceuticals
- Matthew Harker, Duke Clinical Research Institute
- Sharon Hesterlee, Bamboo Therapeutics (now Pfizer)
- Jamie Roberts, Clinical Trials Transformation Initiative
- Joseph DiMasi, Tufts Center for the Study of Drug Development
- Kenneth Getz, Tufts Center for the Study of Drug Development

CTTI Patient Groups & Clinical Trials Project Methods Overview:

- Applied commonly used method for modeling financial value based on project development cost, time and risk

- Base cases: Typical phase II and III oncology development programs
- Comparisons: base case programs impacted by patient engagement initiatives:
  - Assumed reduction in the number of protocol amendments
  - Assumed improvement in enrollment and retention

- Data used to populate model based on published benchmark and source data in the literature

Drivers of Pharmaceutical Project Value

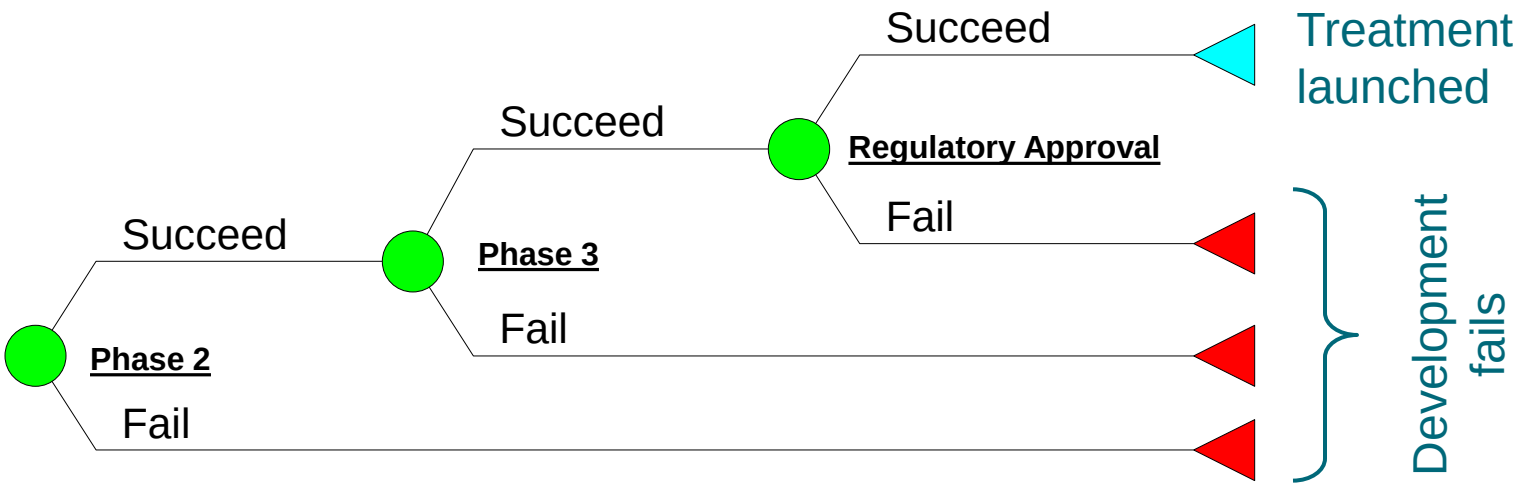
- Revenue
  - What financial benefits accrue from project success?
- Cost
  - Resource: What resources are expended developing the project?
  - Opportunity: What is not done while resources are committed?
- Time
  - When do the costs, revenue and risks occur?
  - Can risks be resolved before a major resource commitment?
- Risk – Tangible and Intangible

Numerous Risk Factors Impacting Value

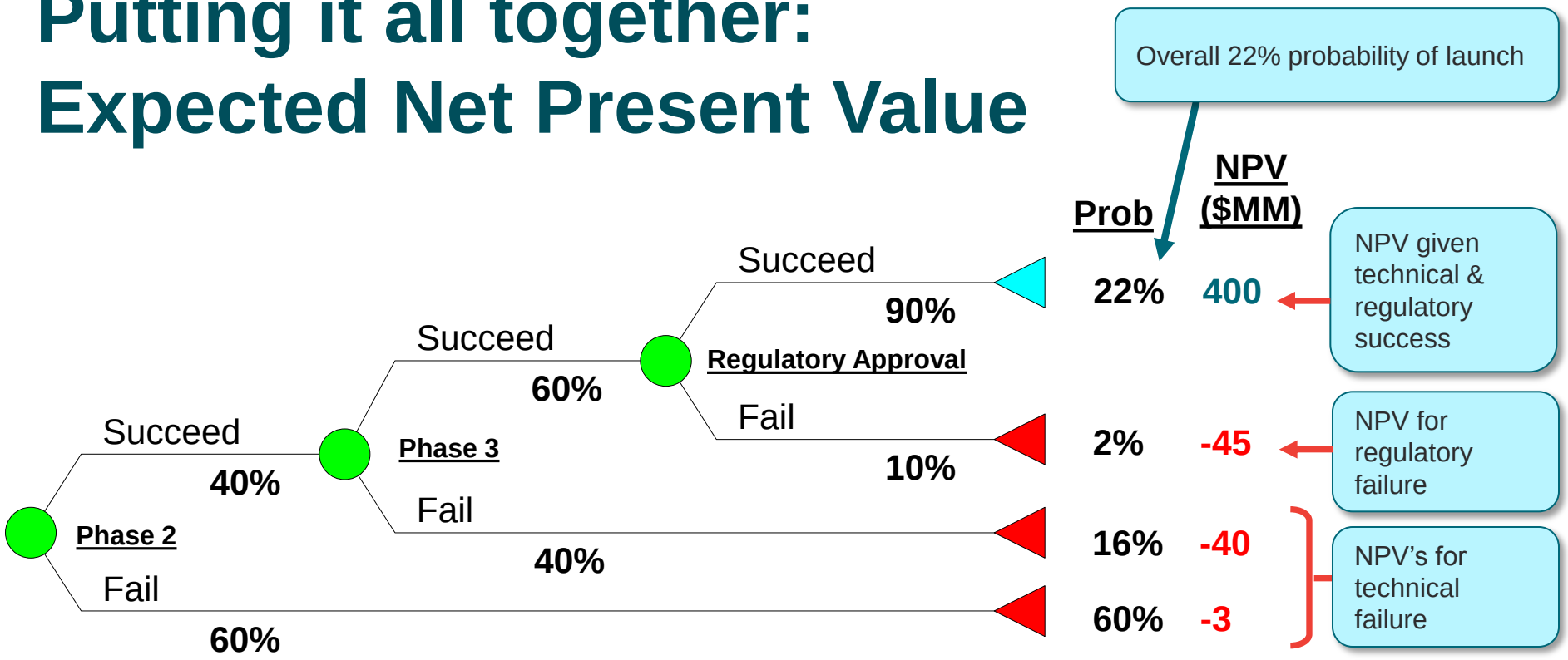
- Scientific and technical risks driving whether to advance development
  - Efficacy, safety, competitors, comparative effectiveness and economics
- Regulatory risk ultimately driving approval and launch
- Operational risk driving timely, efficient and compliant development activity
- Resource risk driving the accuracy of capacity and resource allocation
- Forecasting risk driving accuracy of predicted development performance and investment
- Intangible risks (e.g., Patient health and satisfaction; Strategic relevance; precedents) influencing development decisions

Modeling Value and Impact

- Circles represent studies or other key risky milestones
- Assign probabilities based on scientific, operating and regulatory risk
- Each development path has an associated cost or reward expressed as cash flow in net present value terms



Putting it all together: Expected Net Present Value



ENPV = "Expected Net Present Value"

= Average NPV adjusted for risk

= 0.22 x 400 – 0.02 x 45 – 0.16 x 40 – 0.60 x 3 = $77 MM

Two Assumed Areas of Impact from Patient Centric Initiatives

1. May lead to avoiding one or more protocol amendments
   - ~70% of phase 2 and 3 trials have at least one amendment*
   - ~22% of amendments are due to recruitment difficulty or feedback from sites or investigators*
   - A single amendment adds 3 months of time and as much as half a million in direct costs to implement

2. May improve feasibility and ultimately the patient experience
   - Make the informed consent form easier to understand
   - Simplify eligibility criteria
   - Reduce participation burden for patients
   - Accelerate study cycle time (e.g., start-up, enrollment and completion)

* Getz K, et al,. Measuring the incidence, causes, and repercussions of protocol amendments. *Drug Inform J*. 2011;45:265-275.
Getz K, et. al. The impact of protocol amendments on clinical trial performance and cost. *Ther Innov Regul Sci* 2016; 50(4):436-441.

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Results

	Avoid One Amendment			Improve Patient Experience	
Millions of Dollars	**Phase II**	**Phase III**		**Phase II**	**Phase III**
NPV Impact	+ $24.5	+$32.0		+$38.2	+$30.9
ENPV Impact	+$3.8	+$15.0		+$30.1	+$57.0

OVERALL

Phase 2 Impact
- ➔ 10x benefit in cost
- ➔ 700x benefit in ENPV
- ➔ 1240x benefit in NPV

Phase 3 Impact
- ➔ 42x benefit in cost
- ➔ 1500x benefit in ENPV
- ➔ 1300x benefit in NPV

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Summary

- Main drivers of drug valuation are cost, revenue, timing, risk and intangibles -- patient engagement impacts on them all
- Expected net present value (ENPV) modeling can account for most drivers in a clear and well-accepted summary metric
- For engagement activities resulting in avoiding an amendment and/or an improved patient trial experience, the benefits in cost and ENPV vastly outweigh the resources spent on engagement
- ENPV modeling and similar approaches can support sponsor decisions to increase patient engagement throughout development

Pfizer Clinical Innovation Patient Engagement Framework

Pre-Study

Pfizer.com Find-a-Trial
Study Pages

PfizerLink PRO Data

Social Media
Policy/Guidance/Strategy

epharmasolutions Referral+

ePatient Finder
& Stimulating Referrals

Walgreens Recruitment
Collaboration

Live Protocol
Simulations

Patients in Global Product
Development Patient Insights

During Study

BYOD ePRO
Drug intake diary

Sensor

eConsent

Education materials (trial,
drug, disease, etc.)

Scheduler, reminders and
alerts (basic)

Participant dashboard

eVisit/video conferencing
& Home visits

EHR integration
eSource

Post-Study

PfizerLink

Blue Button Clinical
Data Return

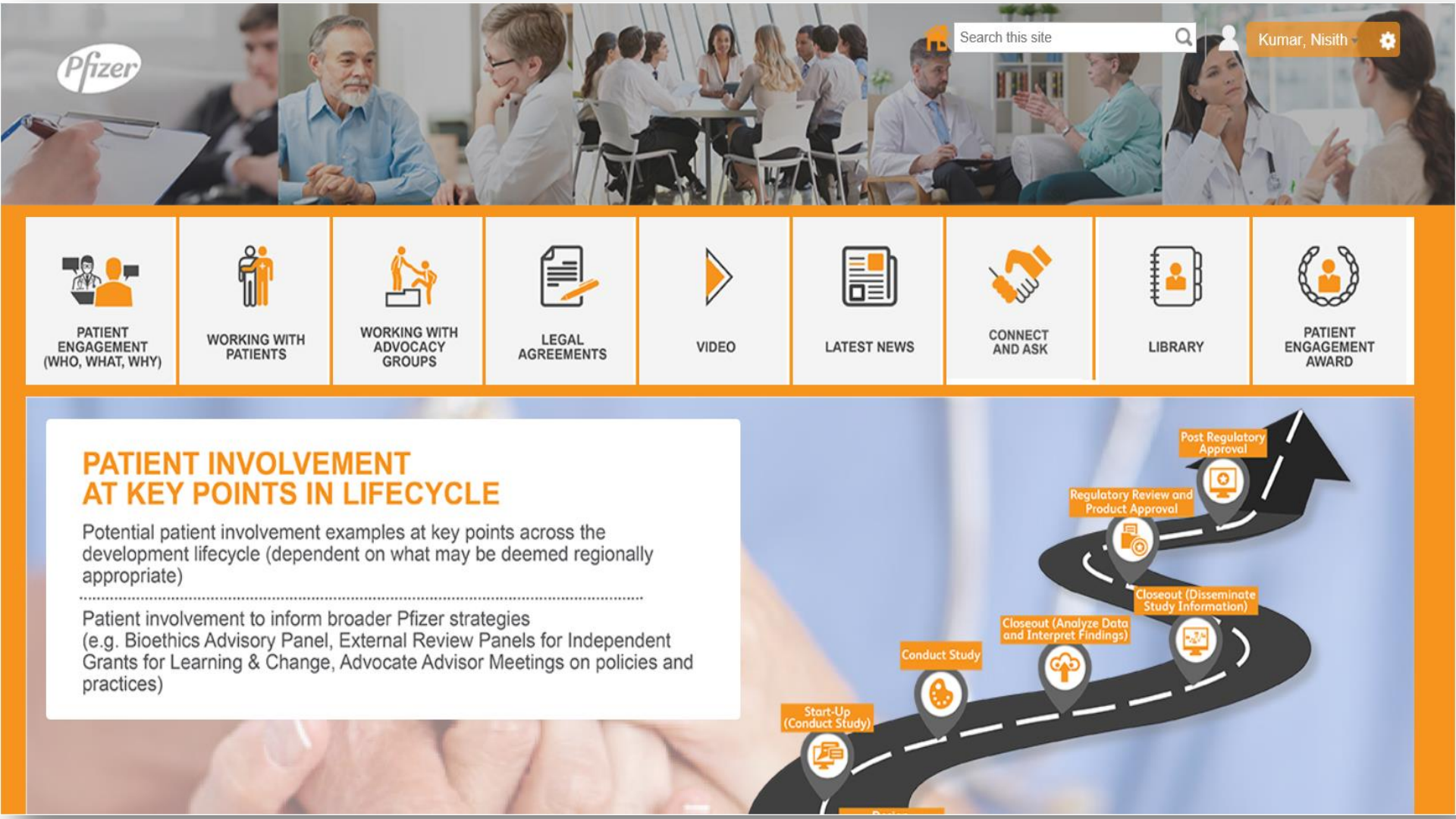
Return of Patient
Lay-Summary Results

P. E. Playbook / Toolkit / Policy / Guidance / Ext. Collab.

Patients in GPD Initiative at Pfizer

- Deliverables
  - Communicate Existing Resources for GPD Teams
    - Key colleagues, tools & platforms
  - Demonstrate Impact of Patient Engagement/Advocacy
    - Dare to Try with 2-3 assets with required GPD patient engagement to measure study impact
  - Identify Gaps & Make Recommendations for the Best in Class Capability to Engage Patients in Development
    - Build list to test & prioritize with patients
- What success looks like
  - Teams know when & how to engage patients in development
  - GPD colleagues lead teams in consistently engaging patients [codified]
  - Teams know how to incorporate feedback to realize value
  - Fewer protocol revisions, improved recruitment, retention and compliance
  - Improved patient experience

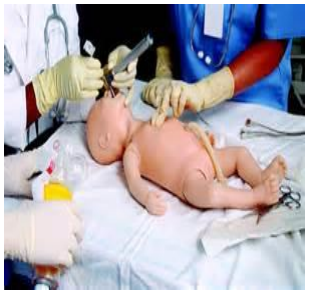
Patients in GPD: Making Patient Insights Accessible



Simulation for Clinical Protocol Optimization

What is "Simulation"?

- Use of Patients, Clinical Staff and Hi-Def Mannequins (sophisticated, computerized human "functioning" mannequins) to simulate "Real World" clinical settings & activities
- Can be done in Simulation Center OR at PI sites
- Used in Medical Training for years; *(residency training, nursing, new procedures, models of care***)**



Exploring Use of Simulation in Clinical Research Protocol Optimization:

- **Opportunity to run protocols in "real world setting"**
  - ❑ Does it work? Is what we've written Feasible to execute? What are the challenges for patients, sites? Can we reduce protocol amendments, create efficiencies & reduce costs related to amendments, improving patient experience?
  - ❑ How can we improve the patient experience while still in protocol development stage?
  - ❑ Develop a "What's it like to be a patient in X trial" video to help in patient recruitment & education

Gain learnings for Protocol Optimization to create efficiencies, improve patient/PI experience; Gain "Post-mortem leanings" to inform future studies"

- ❑ Reduce Amendments
- ❑ Improved Investigator Training
- ❑ PI, Patient Insights

Patients Insights Across the Portfolio

- **Oncology**
  - Non-small cell Lung Cancer – Partnered with Bonnie Addario Lung Cancer Foundation & Lungevity.org on Protocol Review and ICF Design
  - Breast Cancer – Partnered with Breastcancertrials.org and the Metastatic Breast Cancer Network on ICF Design and Schedule of Activities Review
  - ALK+ NSCLC - Partnering with Bonnie Addario Lung Cancer Foundation & Lungevity.org on Protocol Review and ICF Design
- **Neuroscience**
  - Parkinson's Disease - D1 team patient participation in study simulation (Drug Packaging), feedback on study logistics
- **Vaccines**
  - Clostridium Difficile Stool Collection Simulation and Patient Feedback at Pfizer New Haven PCRU
- **Inflammation & Immunology**
  - Rheumatoid Arthritis – Partnership with Arthritis UK on Protocol design and ICF
- **CV/Met**
  - Non-Alcoholic Steatohepatitis – Partnership with the Global Liver Institute to provide feedback on Protocol Design and ICF