

Operational Risk:

Adapting an existing risk assessment process to better capture and manage operational uncertainties

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Discussion Topics



- What are the risk elements for a pharmaceutical new product development project?
- How do we routinely account for and manage these at Centocor?
- A need has been identified to better quantify the impact of operational risks
- Case study of pilot project
- Conclusions and future steps

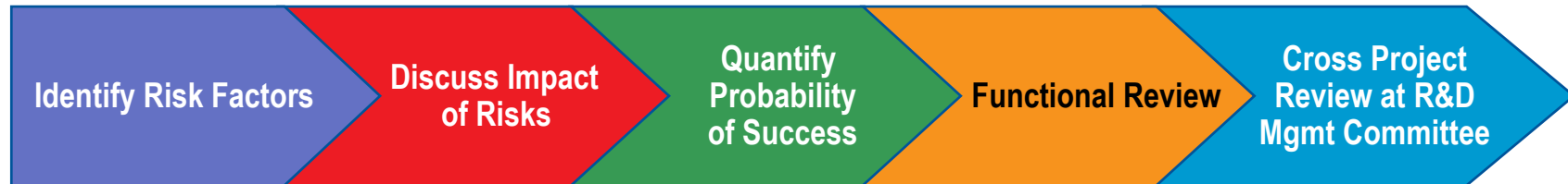
Key Elements of Project Risk/Uncertainty



- Technical & Regulatory Risk
 - Probability that a project will not advance through successive phases of development and therefore not achieve registration
- Commercial Risk
 - Risk that commercially-important elements of the TPP will not be achieved, or that the competitive environment will be different from the current forecast expectations
- Operational Risk
 - Probability that the project cannot be executed as planned
 - Unexpected data requirements
 - Resource availability
 - Task execution
 - Changed strategy/regulatory requirements
 - Thus leading to budget and or timeline overruns



Project Team Risk Assessment Process



- Overview of development plan to understand objectives and potential outcomes
- Identify issues and risks that could influence the success of the project
- Review each of the risk factors to hypothesize and understand potential implications on successful project completion as well as on the commercial forecast
- Identify mitigation strategies for risks
- Quantify the probability of success (probability of moving to next phase of development) associated with each phase of development and registration process
- Review risk assumptions defined by CDT (level set within function)
- Ensure mitigation strategies are supported/funded
- Review risk assumptions defined by CDT in context of other projects (level set across function)
- Ensure mitigation strategies are supported/funded

The risk assessment process assumes that a project will be completed within a specific timeframe and risks are evaluated against a specific development plan.

Project Team Qualitative Assessment of Project Risks by Category



Category	Project Specific Risk	Mitigation Strategy
Efficacy	<ul style="list-style-type: none"> Refer to the TPP What criteria do we need to meet to show that the drug is efficacious? What must we see to know we should continue? What are our concerns? 	<ul style="list-style-type: none"> Can we do anything about our concerns?
Safety	<ul style="list-style-type: none"> Refer to the TPP What criteria do we need to meet to show that the drug is safe? What must we not see? What are our concerns? 	<ul style="list-style-type: none"> Can we do anything about our concerns?
Alignment with TPP	<ul style="list-style-type: none"> Are there areas where we may not meet the TPP? If so, what would be their impact? 	<ul style="list-style-type: none"> Can we do anything about these areas or their impact?
Pharm Dev	<ul style="list-style-type: none"> Can we make the drug in the form needed? 	<ul style="list-style-type: none"> Can we use another form of the drug? If so, what would be the impact?
Regulatory	<ul style="list-style-type: none"> Are there concerns around a successful filing? 	<ul style="list-style-type: none"> Can we do anything about those concerns?
Operational Risks (Timing, Budget)	<ul style="list-style-type: none"> Are the projected timings realistic? How far off might they be? What factors would impact our timing? Is our budget realistic? What might change it? By how much? 	<ul style="list-style-type: none"> Can we do anything about these potential impacts?

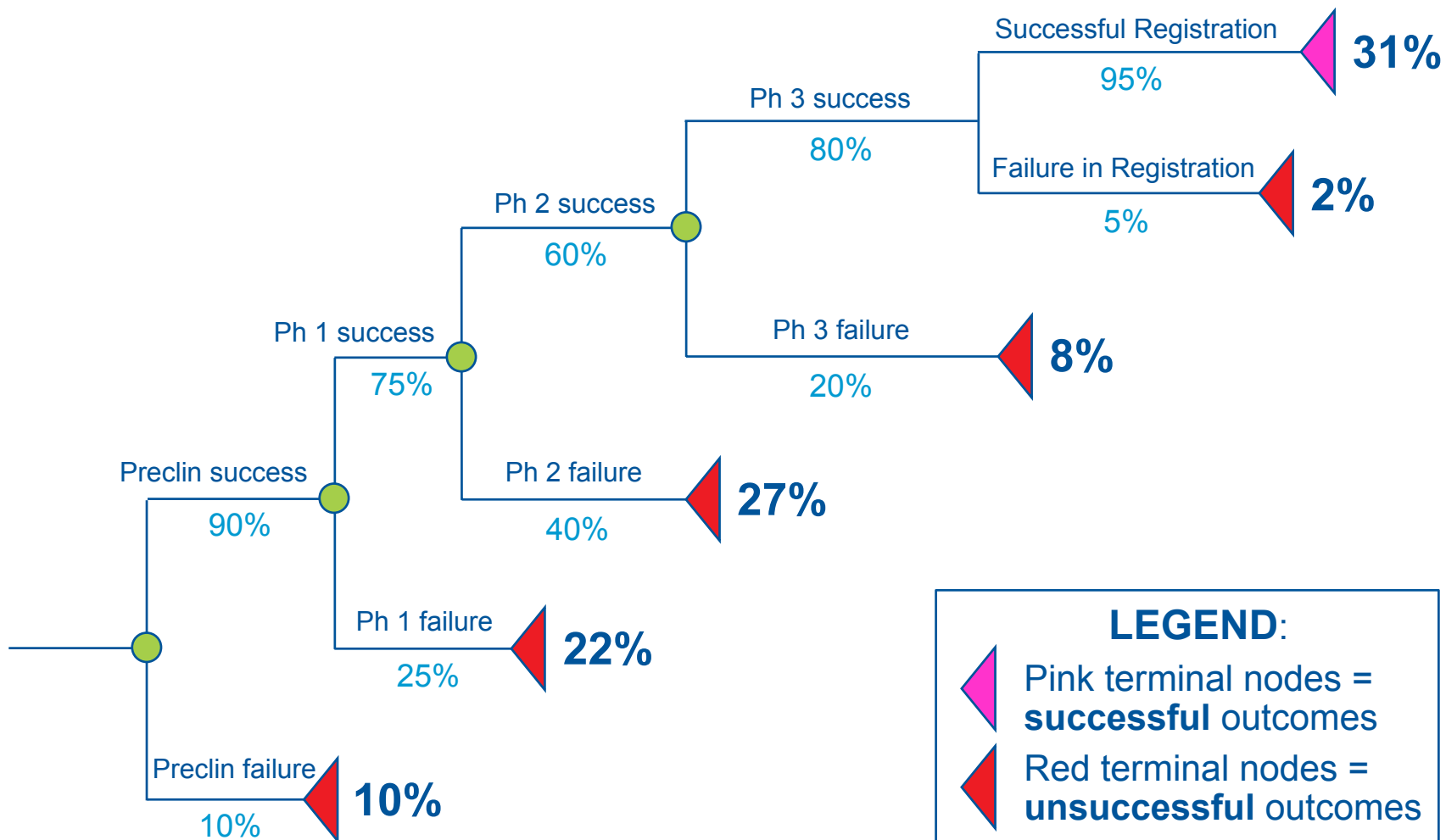
Team Identifies and Quantifies Risk by Stage Gate



Technical and Regulatory Risk Summary			
Phase	Go / No-Go Criteria (or critical success factors for phases beyond contract)	Risk Summary	POS for Phase
PreClin	<ul style="list-style-type: none"> What are we testing in this phase? What must we see to move forward to the next phase? What must we not see? 	<ul style="list-style-type: none"> What are our concerns in this phase? 	How confident, on a scale from 0 to 100, are we that we will meet the minimum criteria and move to the next phase?
1	<ul style="list-style-type: none"> Assuming that we met all the criteria in the prior phase, what are we testing in this phase? What must we see to move forward to the next phase? What must we not see? 	“	Assuming that we met all of the criteria in the previous phase, how confident are we, on a scale from 0 to 100, that we will meet the minimum criteria and move to the next phase?
2	“	“	“
3	“	“	“
Reg	<ul style="list-style-type: none"> What criteria must we meet to file for registration? 	“	Having met all of our criteria in all phases, how confident are we that our filing will lead to successful registration?
PTRS			Product of POSs for each phase

Note: If risk does not apply to the phase, enter N/A. If phase is complete enter 100%

Illustrative Example: Technical and Regulatory Risk – “PTRS”



How Is PTRS Used?

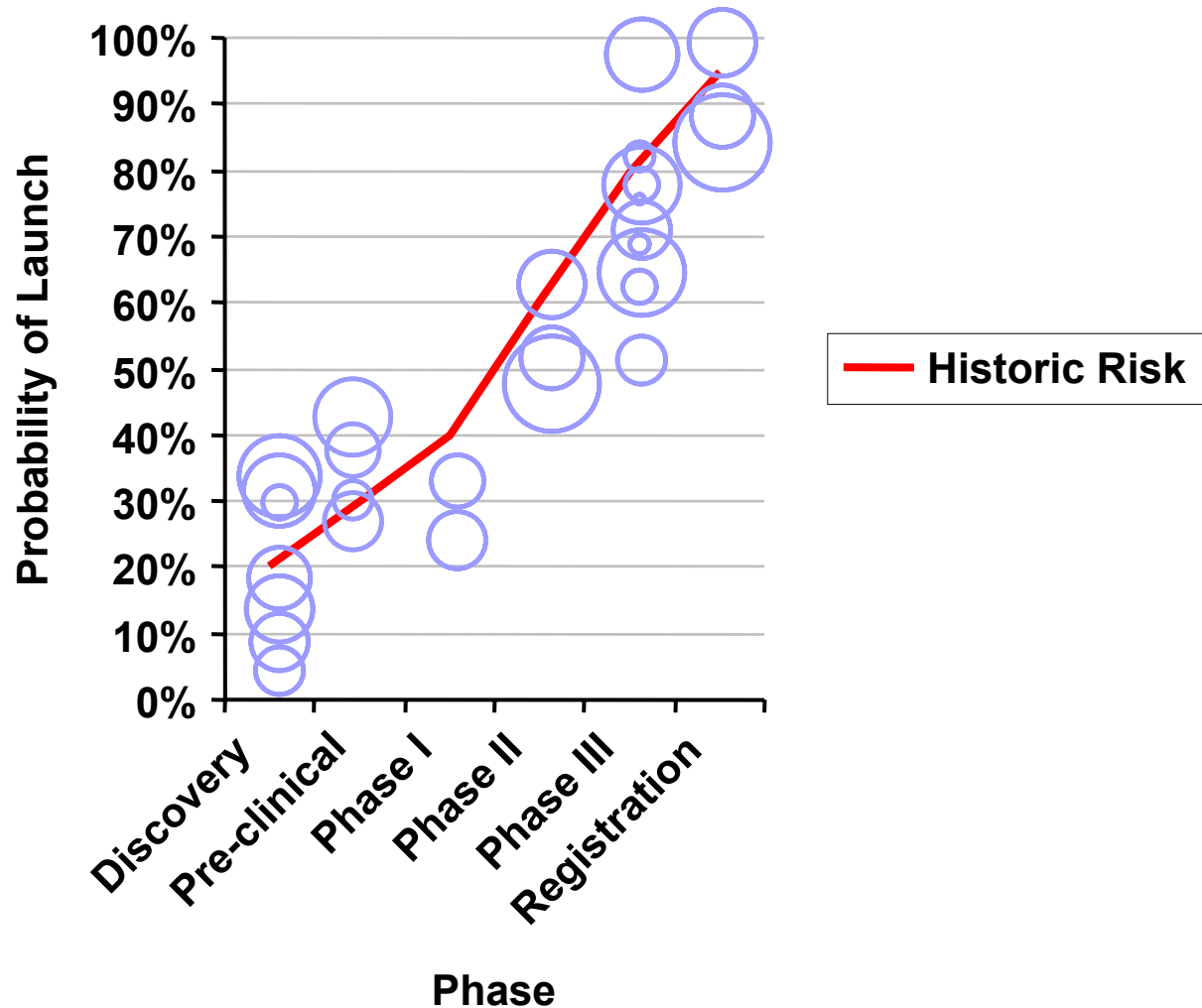


- By the CDT:
 - The process itself is helpful for the teams to identify where the risks are and to strategize how to manage/mitigate them
- By Management:
 - May be used as a metric in portfolio prioritization which attempts to balance risk, value, and flow of projects in the pipeline
 - To risk-adjust costs for budget planning by probability of spend
 - To risk adjust value metrics (such as NPV)

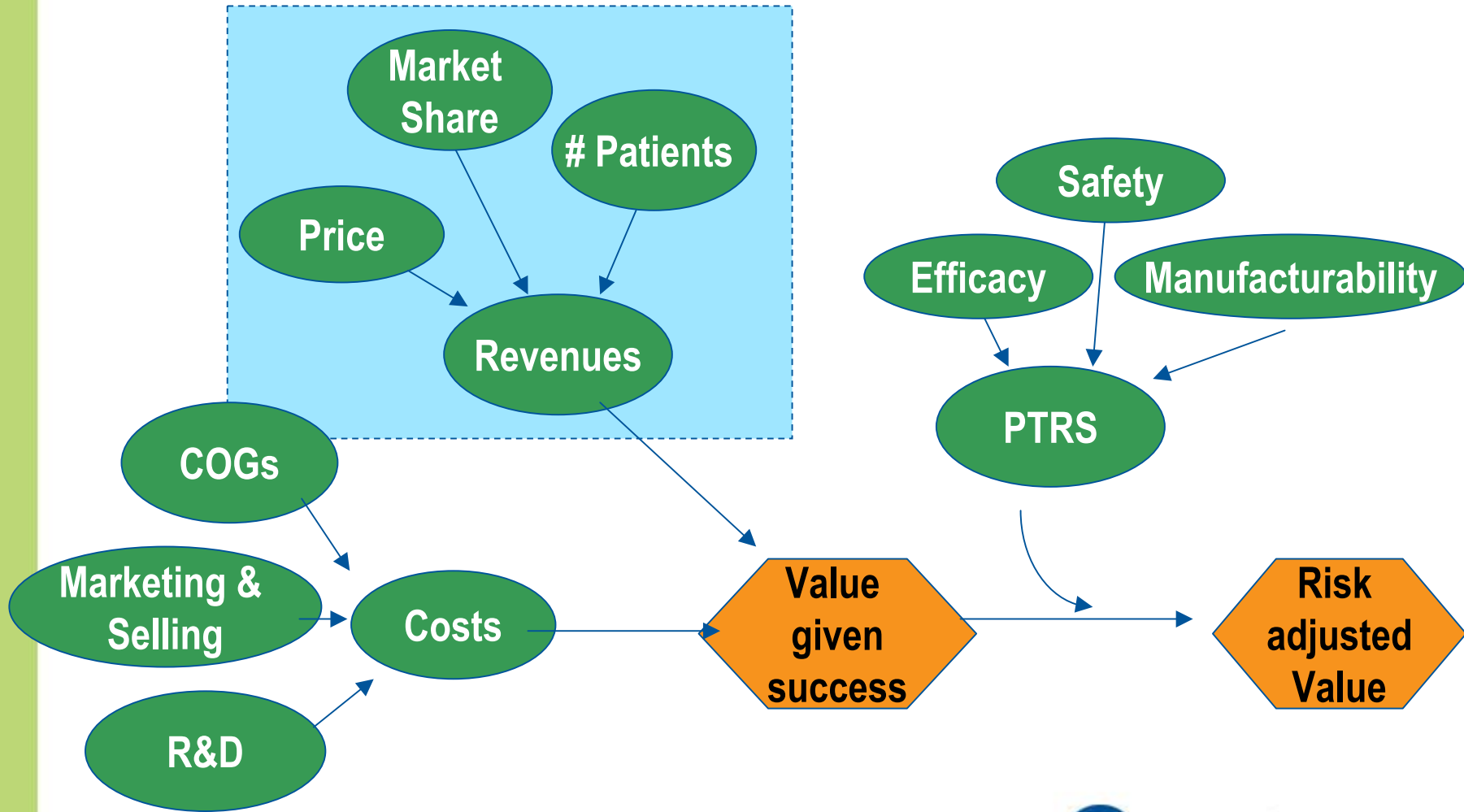
Balance PTRS Across Portfolio



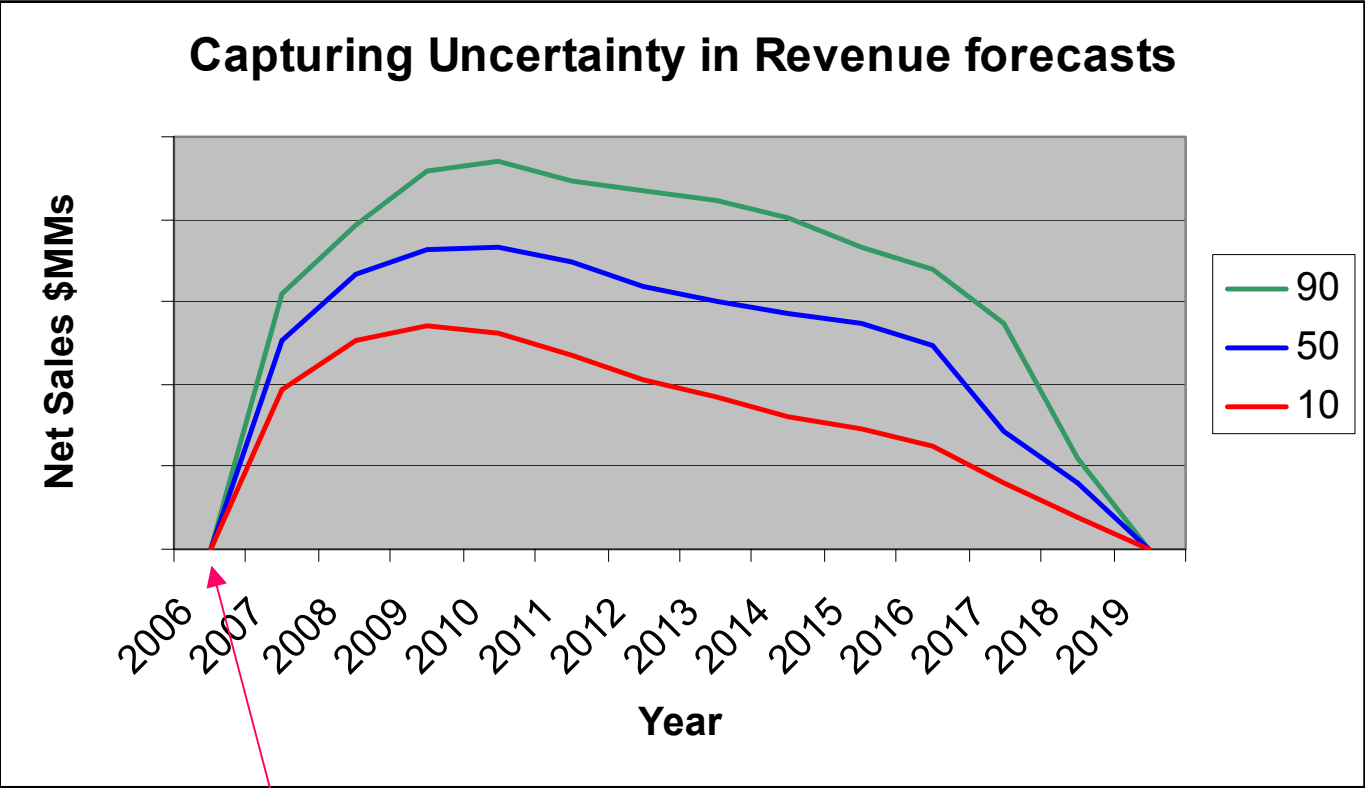
Compound Phase, Risk, and Value



Simple Influence Diagram of typical Pharmaceutical Product Value Model



Commercial risk is reflected in the Revenue forecast range



Note all assume same launch year

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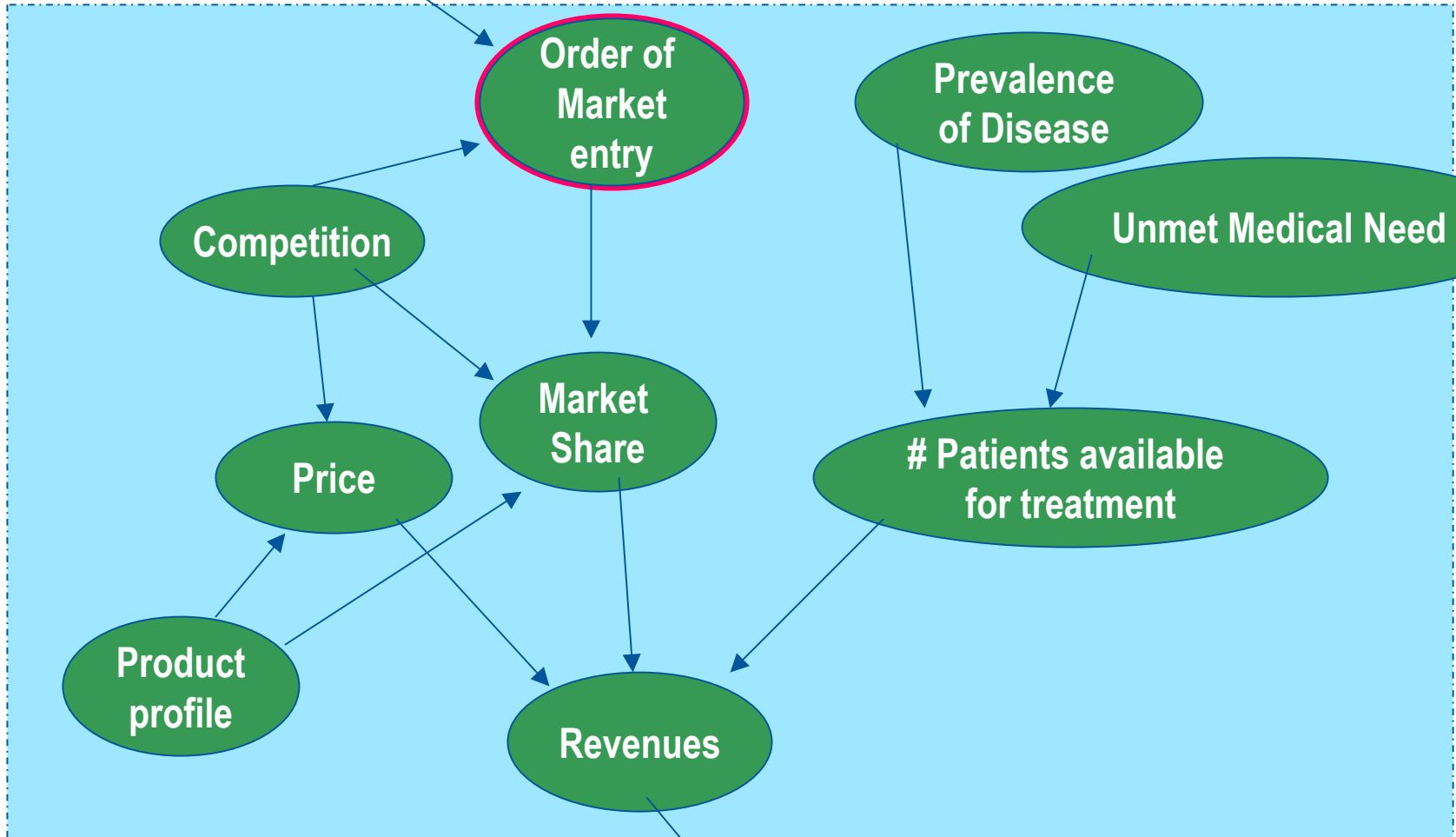


Example- How operational risk can impact value: A deeper dive into revenue drivers...



Launch Date assumption

Often taken for granted in the revenue forecasts as a single deterministic value, despite the sophistication in accounting for uncertainty of the other drivers

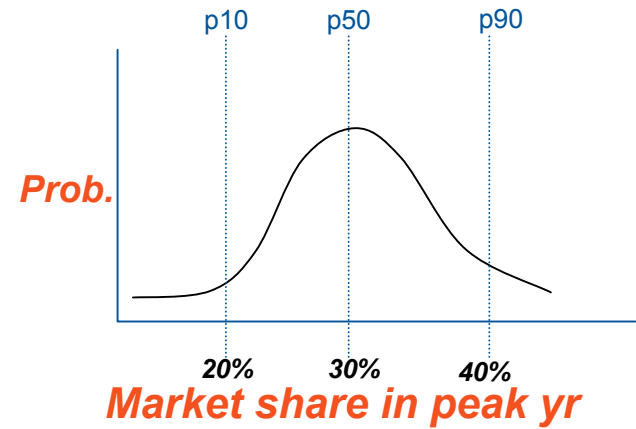
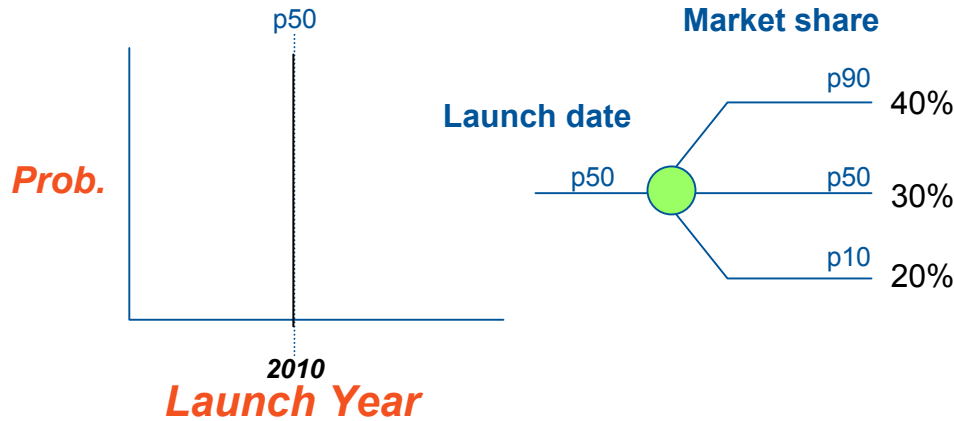


Why is Launch date so important?

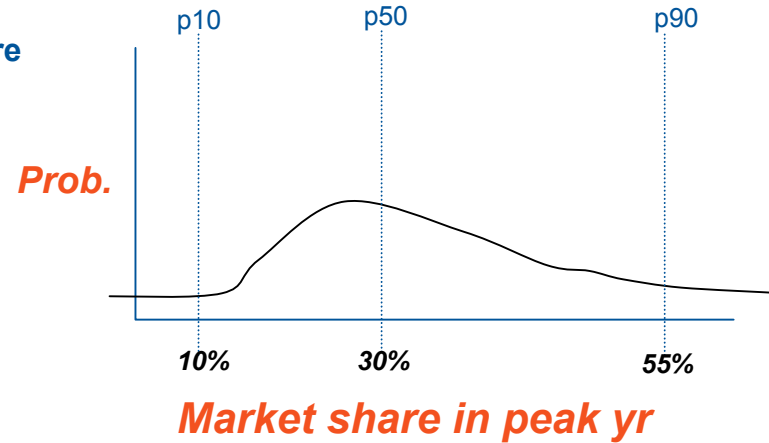
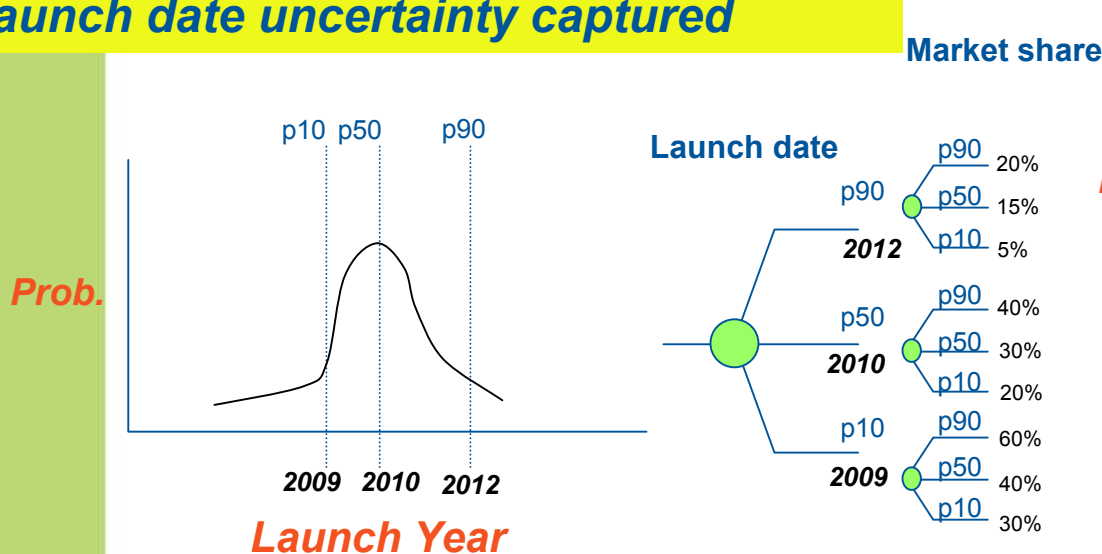
Hypothetical illustration: Effect of timing



Launch date uncertainty not captured



Launch date uncertainty captured



Case Study- Project “X”

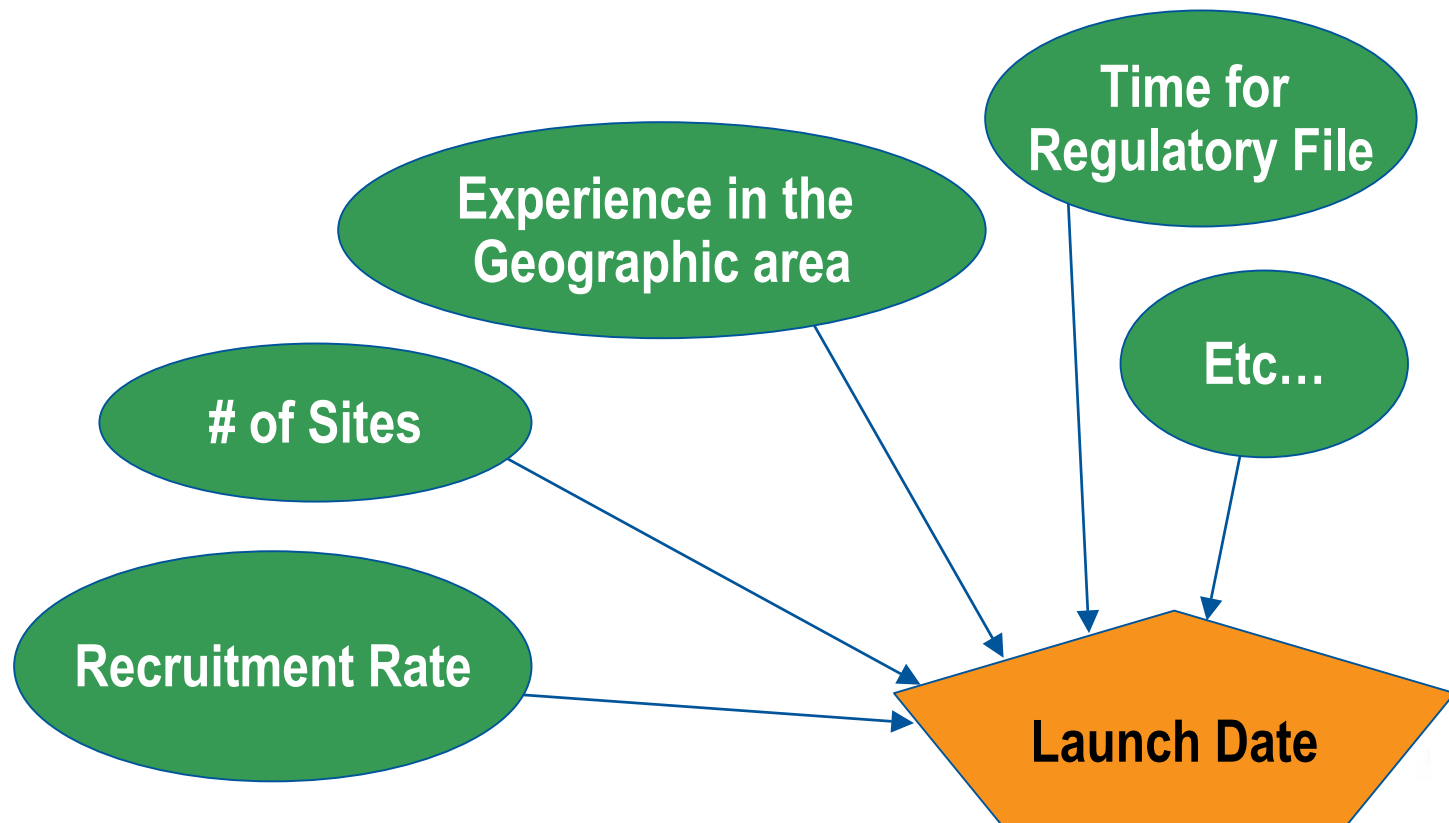


- Background
 - Strong competition in this marketplace
 - Competitor product anticipated to launch in similar timeframe to our own
 - Order of market entry often a strong determinant of market share
 - Strong pressure for project team to deliver high quality product to market as soon as possible
 - Timelines very aggressive, would require flawless operational execution to deliver

Uncertainties That Have an Influence on Launch Timing



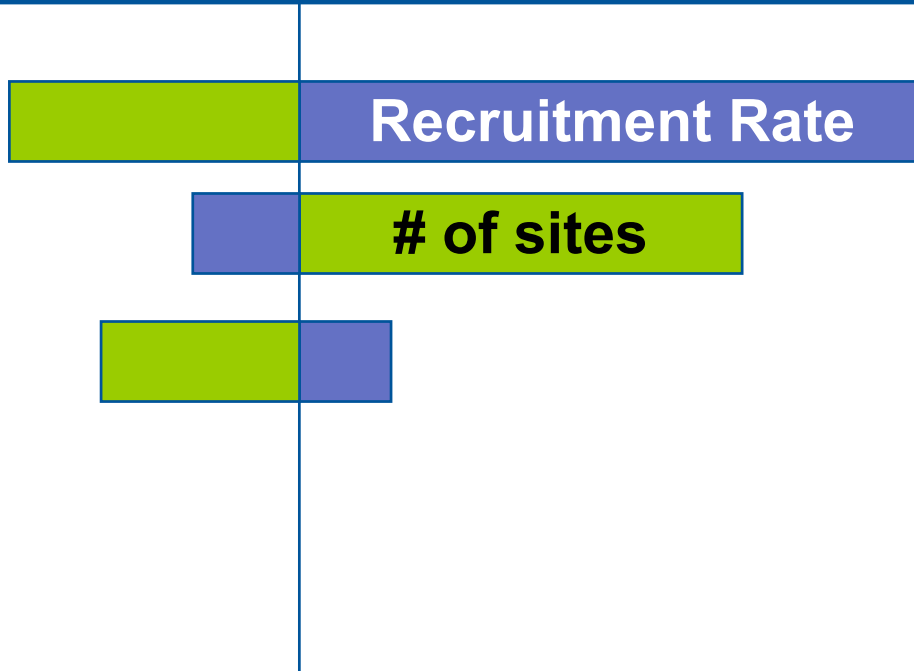
- Need to ID experts that can estimate a range around each of these (10-base-90) and consequence for critical path timeline



Sensitivity Analysis Around Launch Timing



2011	2012	2013	2014	2015
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10	50	90
Green	White	Purple
Green	White	Purple
Green	White	Purple
Green	White	Purple
Green	White	Purple
Green	White	Purple

Visual to show consequence of each on timeline. **Could also do a simulation that would select combinations of these at random and do a distribution curve around the launch date.

Other examples of Operational Risks



- Additional trials demanded by FDA
- Changes in global currency rates
- Changes in cost or availability of supplies from vendors
- Yield of drug substance lower than expected\
- Etc...

Conclusions

- We have well-established processes for assessing project risk
 - PTRS
 - Qualitative Operational Risk
- Operational risks can have a significant impact on project value
 - These risks need to be understood and managed
 - Quantifying these risks aids decision making
 - *i.e.*: Is it worthwhile to invest more resources in Project X to ensure it meets its timelines?
 - If I can accelerate X or Y, but not both, where should I put the resources?
- We are in the process of improving upon existing methods and tools to better quantify operational risks