Impact of Manufacturing Strategy On Portfolio Prioritization

DAAG Case Study

April 2010

A Decision Statement - Scope

Develop and value strategic options to achieve the optimal manufacturing strategy (including Ph3 clinical supply, licensure, and commercial supply) for three key portfolio products that maximizes the long-term value to patients and shareholders.

Out of Scope: Evaluate x-Company alternatives

Key Question

Baxter

Can the Existing Fill/Finish Facility meet the Phase 3 clinical requirements and Best Case launch timelines for the three clinical programs?

Constraints:

- ***T.O. Facility has only one fill line for animal protein-free products***
- ***Products 1, 2 and 3 have similar clinical and registration requirements and each anticipates BLA submissions at or near the same time.***
- ***To be competitive in the marketplace, each product will need multiple potencies***
- ***Each unique dosage/potencies will require a different vial size***
- ***Only one tech transfer can be conducted at a time***
- ***The Fill-Finish line will also need to be certified to fill the company's key marketed product***
- ***Any production schedule developed must allow for routine shutdowns for maintenance***

Methodology

- Workshop was held in WLV on Jan. 18 – 10 to frame the problem, solicit information from key functional leads and develop strategies for evaluation
- At the workshop, the each functional group demonstrated considerable flexibility and creativity in order to shrink implementation timelines to produce the BEST CASE production plan.
- The proposed production plan supports the goal of meeting all Phase 3 clinical product demand timelines while minimizing impact to the Best Case launch times and maximizing the product potencies at launch
- Providing adequate stability data at the time of regulatory submission proved to be the key driver of product sequencing, product profiles tradeoffs
- The following scenarios were evaluated
    1. Risk of Clinical delay to Best Case product timeline
    2. Commercial impacts of delay and changes to Best Case product profile
    3. Composite NPV was used as the decision variable

Strategy Summary Table

Product	Strategy #1 "Wish List"	Strategy #2	Strategy #3	Strategy #4
Implementation Sequence	Product 1, Product 2, Product 3	Product 1, Product 2, Product 3	Product 1, Product 2, Product 3	Product 1, Product 3, Product 2
Launch Delays (Months)	Product 1 – 0 Product 2 – 0 Product 3 – 0	Product 1 – 0 Product 2 – 0 Product 3 – 0	Product 1 – 0 Product 2 – 0 Product 3 – 9	Product 1 – 0 Product 2 – 12 Product 3 – 0
Potencies	Product 1 - 5 Product 2 - 3 Product 3 - 3	Product 1 – 5 Product 2 – 3 Product 3 – 2	Product 1 - 5 Product 2 - 3 Product 3 - 3	Product 1 - 5 Product 2 - 3 Product 3 - 3

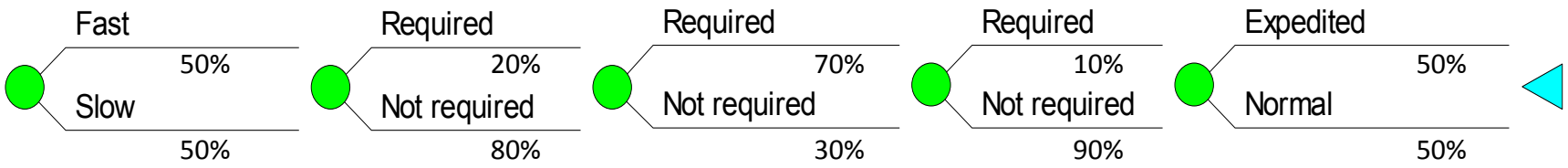
Assumptions/Observations:

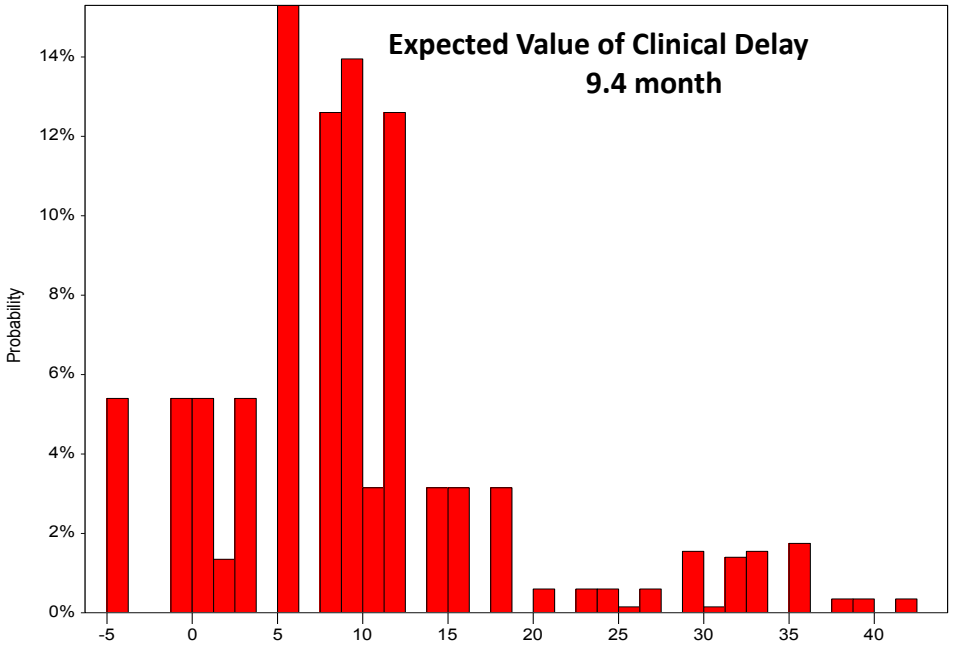
1. Product 1 is first in all cases (tech transfer already well under way),
2. Tech transfer capacity drives the need to establish a product implementation strategy immediately
3. The original goal of hitting **ALL** best case milestone to supply phase 3 clinical material is achievable,
4. Hitting product stability requirements to support best case launch timelines and product profiles is the key driver in determining product sequencing and tradeoffs,
5. In the absence of clinical delays, TO F/F must execute flawlessly (no significant mfg delays)
6. Submission of Product 2 may need to be delayed by one quarter due to availability of third and final potency

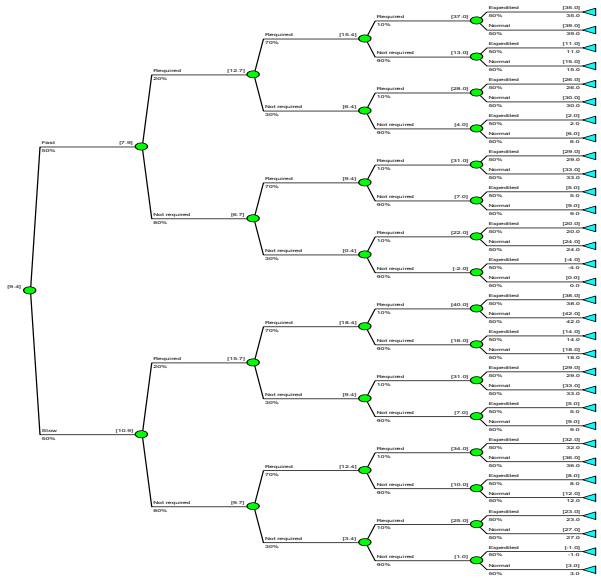
○ Indicates potential impact of strategy

35% of the time Product 3 experiences a clinical delay of 9 months or more

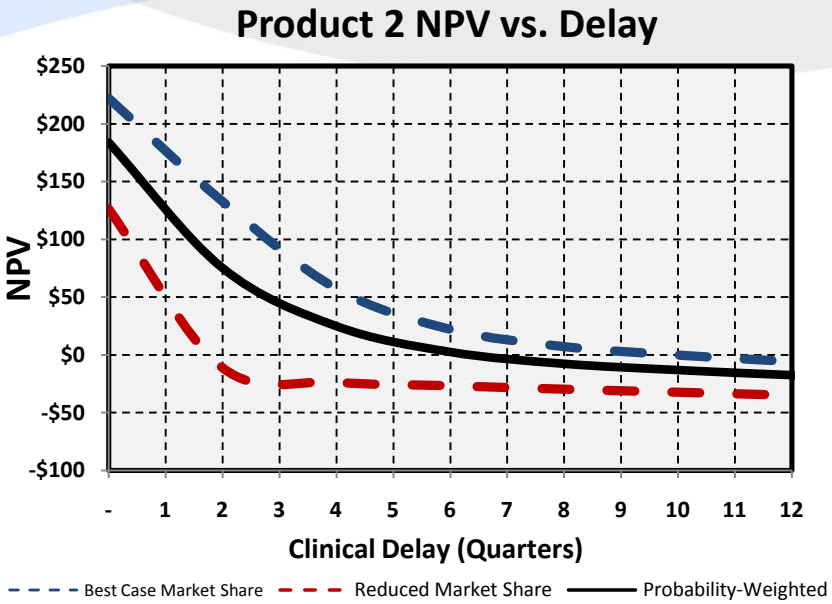
Phase 1 Recruitment	Phase 1 Cohort 5	Add'l Patient Phase 3	Phase 2 REQUIRED	Expedited Review
+3 months	+6 months	+9 months	+24 months	-4 months

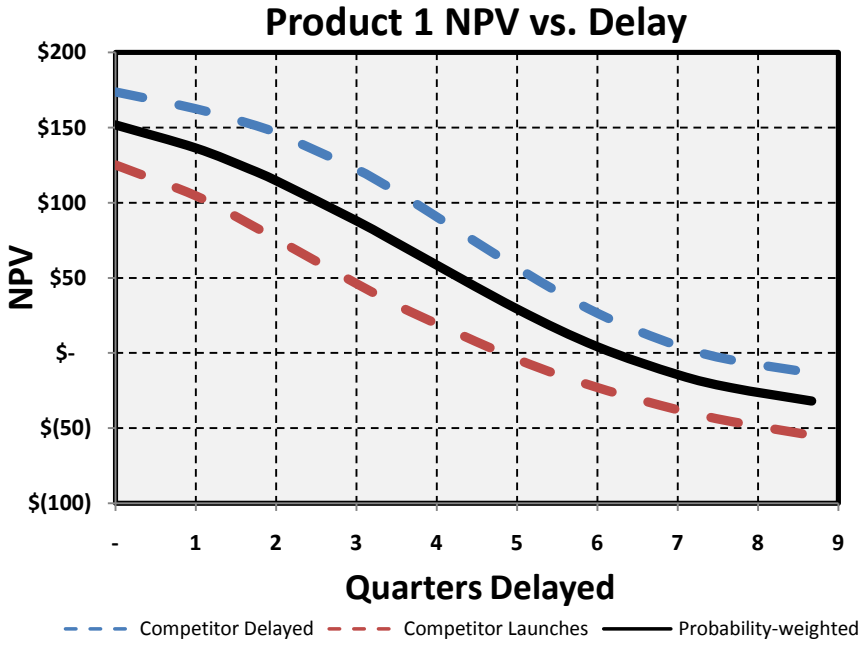


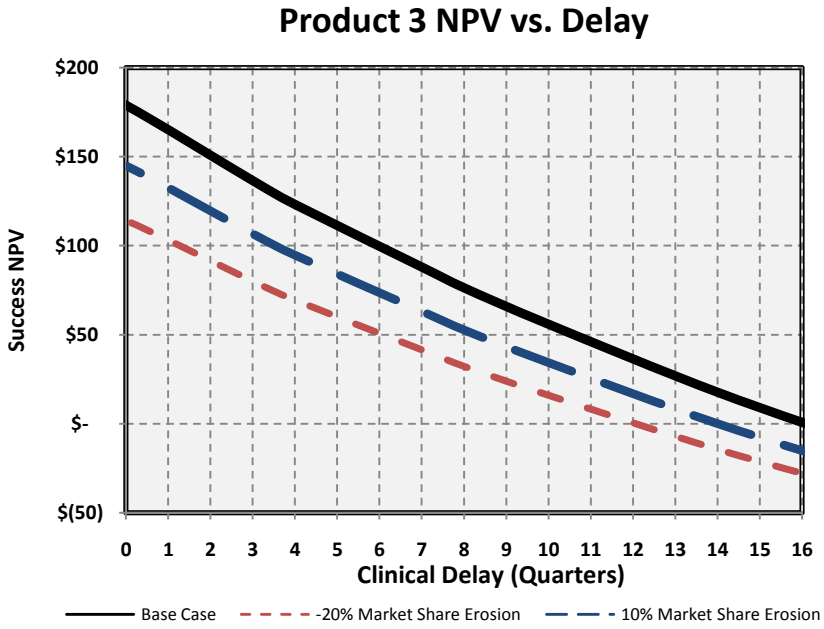




The impact of delay on peak market share is the key driver for of NPV







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Project NPV	Product 1 – $130 Product 2 - $150 Product 3 - $130	Product 1 –$130 Product 2 - $150 Product 3 -$125	Product 1 –$130 Product 2 - $150 Product 3 -$125	Product 1 –$130 Product 2 - $ 20 Product 3 -$130
Composite NPV	**$410**	**$405**	**$405**	**$280**

1. Small changes in the Market Share Penalty for launching Prod #3 with only 2 potencies can flip the optimal strategy from Strategy #3 to Strategy #2.
   - However, it does **not** change the priority of product implementation in TO.
   - That order remains Prod #1, Prod #2 and Prod #3.
2. Probabilities of clinical and regulatory delays have been factored into analysis.
3. Probability of manufacturing delays are negligible relative to clinical and regulatory
4. Product #3 will possess highest risk of delay due to cumulative effect of any previous production delays

○ Indicates potential impact of strategy

3 Strategies were developed at the workshop

	Delay	No of Potencies Product 2	No of Potencies Product 3	Concentration Product 1
Wish List	Product 3	Two	Two	Four
No Delay Product 3 - 2 potencies				
Delay Product 3 - 9mo				
Delay Product 2 - 12 mo with3 potencies	Product 2	Three	Three	FIve
	No Delay			
	Shared Delay			

Detailed planning at workshop allowed us to accomplish the goal of hitting best case milestone for 1st clinical material, but it is **not** sufficient to support best case launch dates for the target product profile. Tradeoffs will be necessary in either launch timing or product profiles.

When will project uncertainties be resolved?

Project	Uncertainty	When is Outcome Known?
Product 3	Recruitment Delay	March 2010
Product 3	Cohort in Phase 1	April 2010
Product 3	Patient Increase	Q4 2010
Product 3	Need Phase 2	Q4 2010
Product 3	Review Time	Q4 2012
Product 1	Regulatory Agency Accept Protocol	Q2 2010 (March– June)
Product 1	Recruitment Delays	Q4 2010
Product 1	EMEA Needs Pediatric Data	Q2-Q4 2010 (unknown)
Product 2	Phase 1 Recruitment Delay	Q4 2010
Product 2	Additional Study Required	April 2011

Preliminary Recommendation

- **Under the revised production plan for TO, the initial decision is the sequence for tech transfer and should be made as soon as possible**

- **The optimal product implementation strategy is:**
  - ✓ 1st Product
  - ✓ 2nd Product
  - ✓ 3rd Product

- **The NPV difference for prioritizing Product 2 over of Product 3 is over $100 million**

- **The major decision impacting program NPVs is the scheduling sequence of the 3rd potencies for Product 2 and Product 3 sometime in 2011**

- **Key drivers of the strategy are:**
  - ✓ Impact of delay on respective project NPVs
  - ✓ Expected delay in clinical programs (delays offset impact of manufacturing timing)
  - ✓ Adequate stability data is key to achieving desired product profiles
  - ✓ Financial impacts of forfeiting potencies and launch delays

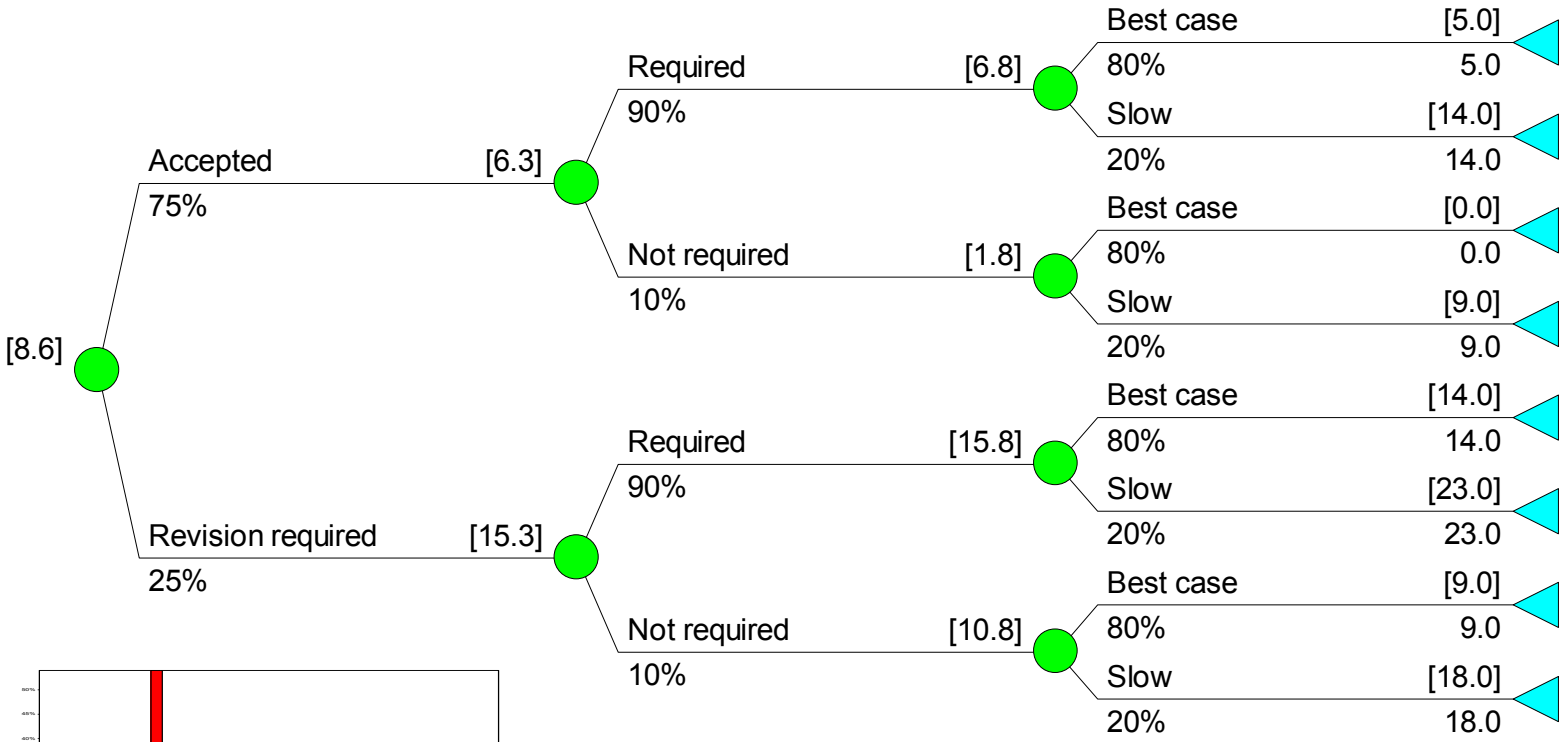
Backup

Product 1 - Clinical Delay

Regulatory Acceptance of Protocol Q2 2010

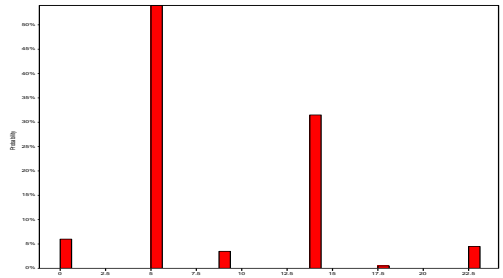
EMEA Pediatric Study Required Q2-Q4 2010

Phase III Recruitment Q4 2010



Most Likely
54%

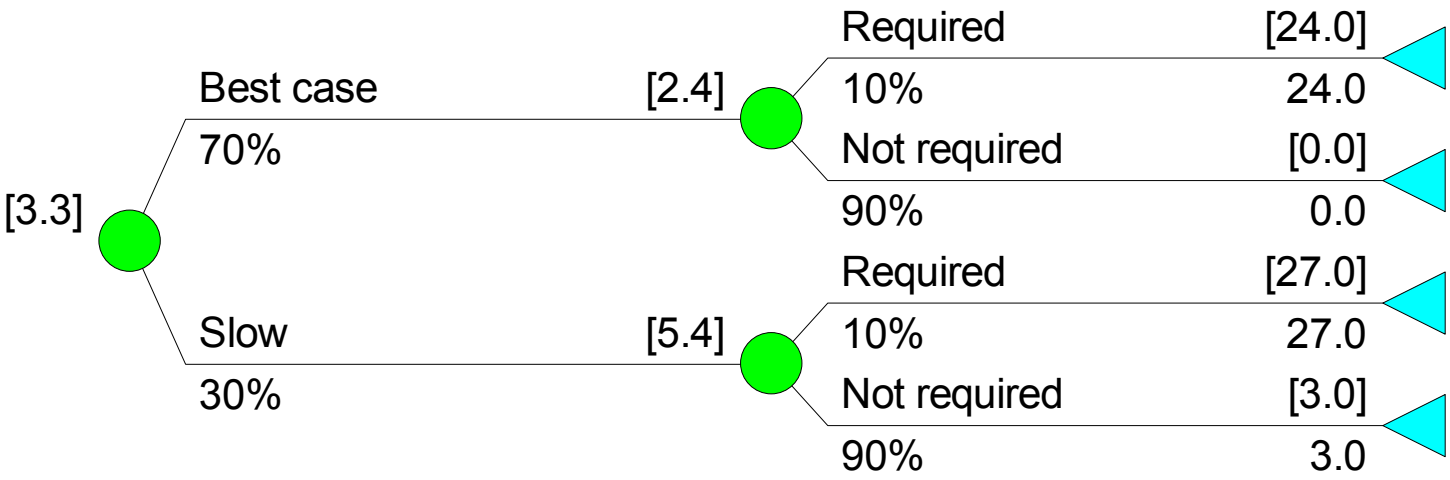
Best Case



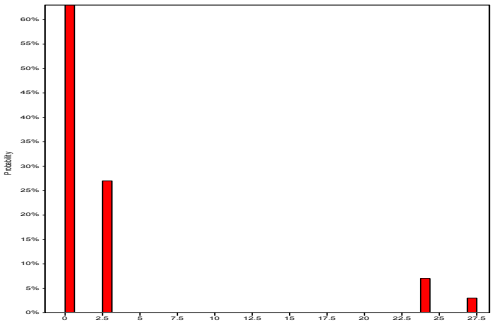
Product 2 Clinical Delay – Probability Assessment

Phase I Recruitment Q4 2010

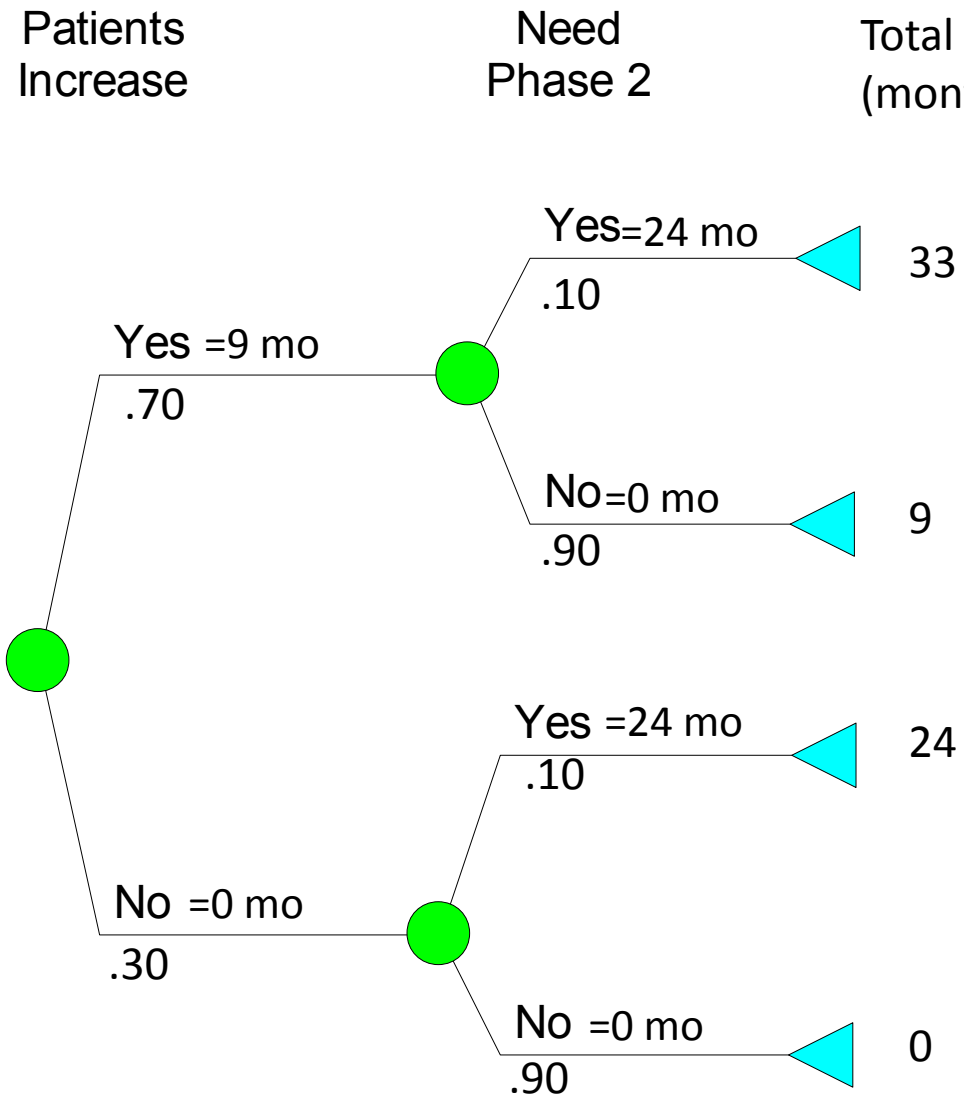
Additional Study Required Q2 2011



Best Case and Most Likely
63%



Product 3– Duration of Ph 3 Uncertainties



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