

# *Life Cycle Management as a Portfolio: A Case History*

Premise:

A combination of decision analysis project and portfolio tools can be used to provide insight and gain alignment for a Life Cycle Management strategy.

A couple of innovations improvisations developed along the way are discussed.



We'll call our company "DAAGPharmCo" and our product "DAAGira."

We'll use common body parts (head, arm, leg, foot) and cleaning functionality (shampoo, deodorize, preserve) as surrogates for the indications and uses...sort of an Armor All® for the human!



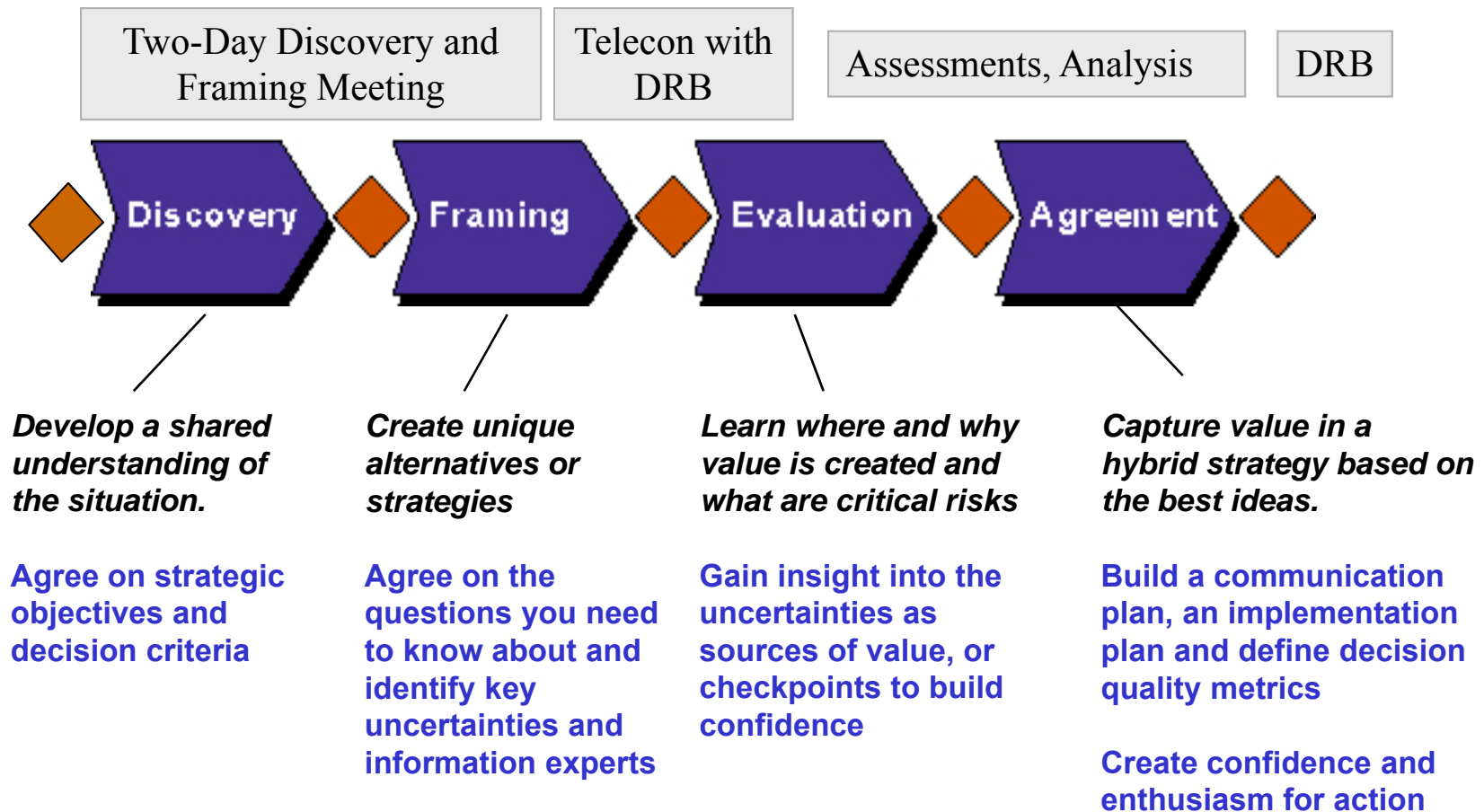
# Scenario

- A new product, “DAAGira®,” has just been introduced. The launch has gone well. The Team cannot agree within themselves and cannot agree with management as to which of a plethora of Life Cycle Management options should be pursued.
  - There are more options than the Team has money or people to complete.
  - The Team has never used a Decision Analysis (DA) process before and isn’t sure that it is a good idea to do so now. No time for training...
  - The Team has a 2-week deadline to complete the entire process and gain alignment with their management (hereafter referred to as the “DRB”).
- Project Manager’s Problem Statement: The primary objective of this exercise is to identify and assess the options to maximize the value of DAAGira®, and will include assessment of the new indication program (including “Trial 409”), along with other options for the program.

# *Participants*

- Person A - Project Management
- Person B - Project Management
- Person C - Clinical Development
- Person D - Dave Charlesworth - Decision Analyst (DSI)
- Person E - Clinical Research
- Person F - Clinical Research
- Person G - Statistician
- Person H - Statistician
- Person I - Clinical
- Person J - Clinical Research
- Person K - Clinical Pharmacology
- Person L - Global Marketing
- Person M - Regulatory
- Person N - Regulatory

# *Process Flow to Develop Strategic Options*

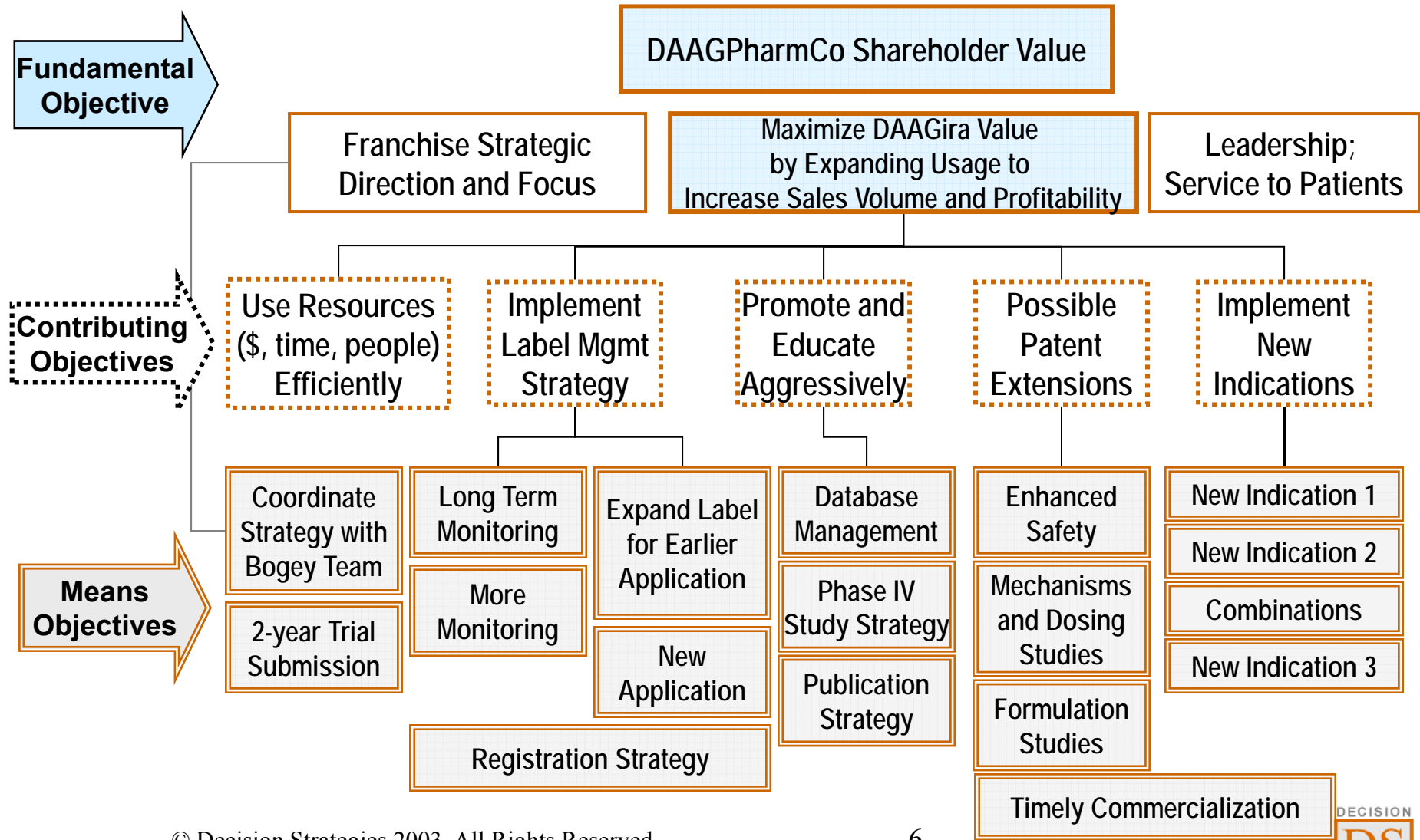


◆ *Decision Review Board Guidance and Endorsement of Next Steps*

# *Sequence of Activities*

- Day 1
  - ★ – “Rant” time: about 3 hours
  - ★ – “Trial 409” time: another 1-1/2 hours
  - Objectives Hierarchy
  - Closed Decisions
  - Strategic Decisions and Alternatives; Tactical Decisions
  - Strategic Themes
- Day 2
  - Qualitative Evaluation of Strategic Themes
  - Combine and Group
  - Influence Diagram
  - Teleconference with DRB to validate problem Frame
  - Preliminary Assessments
- Remainder of Week 1: Detailed Assessments and Modeling
- Week 2:
  - Analysis Feedback to Team
  - Advisory Panel
  - Updating of Assessments and Analysis
  - Decision Review Board
  - Implementation Schedule

# DAAGira® Objectives Hierarchy



# *DAAGira® Decision Hierarchy Update*

## **Closed (“Policy”) Decisions - already made**

- Submission of 2 year data ( this will happen)
- Trial 409 - This Trial can only be continued with revisions
- Must do Phase IV health authority mandates
- We are committed to additional DAAGira studies.
- No open label trials for registration

## **Strategic Decisions - focus for current evaluation**

### Trial 409

- Secondary decision - if salvage, target registration or publishing?

### New Uses

- Secondary decision - if New Indication 1, target registration or publishing?
- Secondary decision - if New Indication 2, alone or in combination with other drug?
- Secondary decision - if higher standard met...?

### Label Optimisation

### New Indications

- Secondary decisions - if publication only, open label or double blind? indication?

## **Tactical Decisions - for further investigation**

- Trial Design
- How to integrate / balance work with Bogey Team
- Publication trials: double blind strongly recommended - poorly designed trials can yield poor results
- New indication program - how to analyze data and build case to proceed?

# *DAA Gira® Strategic Decisions and Alternatives*

## "Trial 409" Study

- Revise and continue (Sample Size)
- Kill it
- Publication trial, not registration

## New Uses

- Shampoo trial using patients with low Preserving risk
  - target registration or publishing?
- Deodorizing (may be bigger risk)
  - alone or in combination with other drug?
- Preserving

## Label Optimisation

- Arm
- Top Secret
- Foot Monitor
- Early Head

## New Indication

- Registration
- Open label & Double Blind
  - open label or double blind?
  - indications (Head, Arm, Foot, Leg)?
- Head, Arm, Leg



# DAAGira® Original Strategy Table

	Theme and Objective	Decision 1: Trial 409	Decision 2: New Uses	Decision 3: Label Mgmt	Decision 4: New Indications
X	Momentum (no change)	Kill it (might revise)	Shampoo first	Top Secret	Pub. With some Coop
combine	Focus for the mostest sales quickly	Kill	Shampoo, Pub & enhanced Preserving	Top Secret	Reg 2 Leg trials & fall back pub - interim analysis point & open label 4B
X	High Success Strategy	revise and continue	None	Top Secret & early Head	Reg with 3 trials
X	Why stop at treatment - Grow	revise and continue	A pub C all	Top Secret	Reg with 3 trials
combine	Market Focused and Quick	Pub Trials quickly	Shampoo Pub	All	2 Quick reg: Leg/Leg
YES modified	Aggressive	revise and continue	Shampoo Pub C Rev	All	2 Leg, 1 Head, 1 Arm
YES modified	Publish Only	Pub Trials quickly	Shampoo Pub	None	Pub. With some Coop

## Aggressive Theme:

- Optimize Labeling
  - Top Secret
- new indication
  - Shampoo - built in
  - Foot Monitoring
- New Indications: all except Deodorizing

## Resource Conservation:

- Top Secret
- Publication focus - selected
- New Indications: use off-label

## Focused Hybrid

- Shampoo (Pub)
  - Combo Trials
- Top Secret - Label - Publication Strategy
- new indication Trials (2 Leg - Leg is faster but lower or no better than Head / Foot / Arm)

# *Strategic Theme: Momentum*

**Definition: Continue on current courses of action**

**Objective: Minimize changes**

**Positives:**

- **No risk**
- **Minimal resources required**
- **No negative outcomes**

**Negatives:**

- **Lower growth**
- **Negative outside perception (of DAAGPharmCo)**

**Hunches: Competition would love this; management split / ambivalent**

**Wins Big If: Something technical of which I have forgotten the significance**

**Loses Big If: Competitors take market leadership in these areas**

# Summary: Leadership Strategic Theme

## Resource Conservation

- "Trial 409" Registration Quality
    - Shampoo endpoint
    - Head population
  - Phase IV Study Strategy
    - Early Head
  - Top Secret Registration
    - Label Reg
  - Co-op new indication Group
- 
- Optimizing Use
    - Foot protective agents
  - Combination Therapy Preserving PreClinical
  - New Indication Phase III
  - Early Head Phase III
  - Deodorizing Phase III
  - Foot Monitoring ( Remove Label)

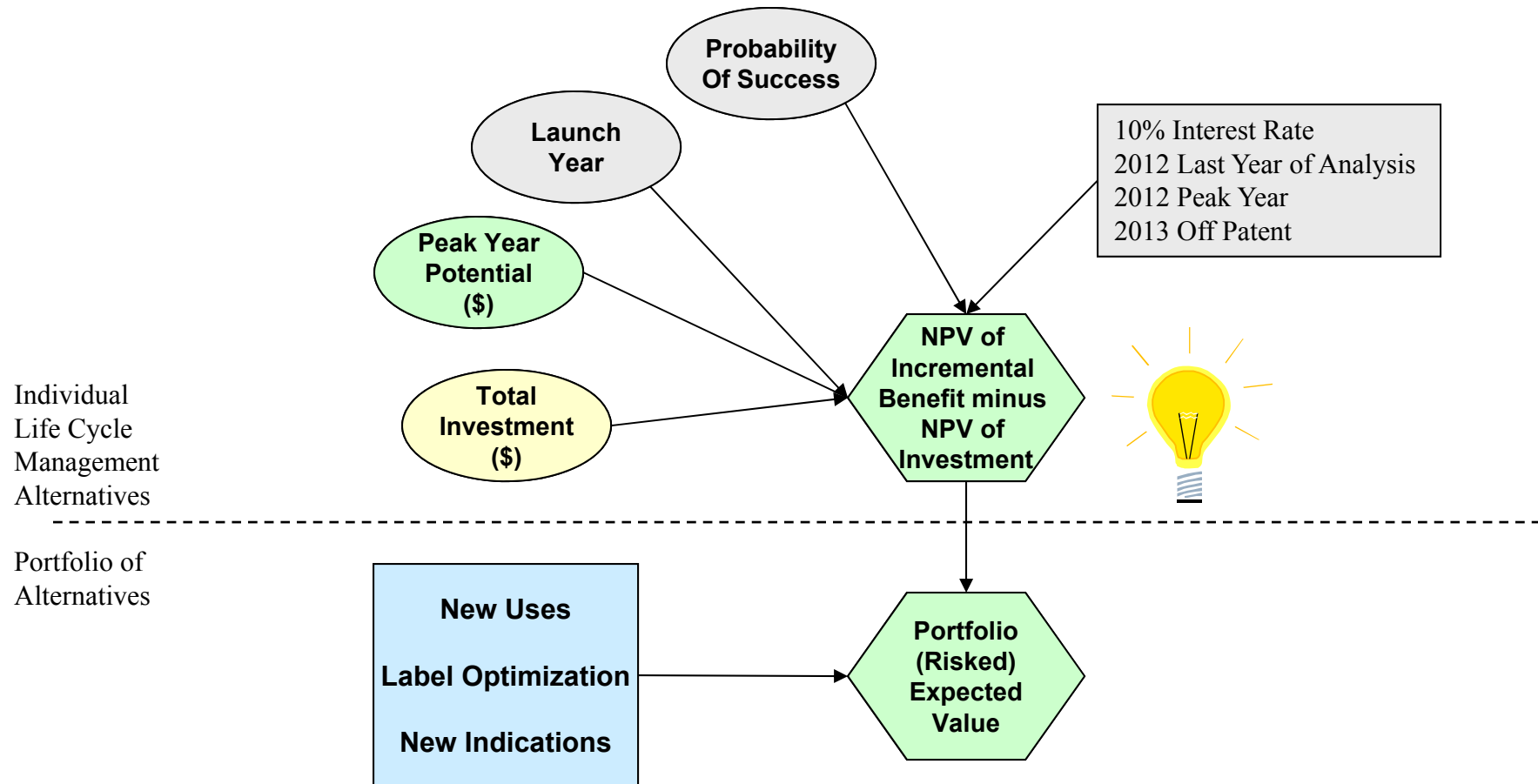
## Market Focused

- "Trial 409" Registration Quality
    - Shampoo endpoint
    - Head population
  - Phase IV Study Strategy
    - Early Head
    - Arm (?)
  - Optimizing Use
    - Foot protective agents
  - Top Secret Registration
    - Label Reg
  - New indication Phase III
    - One trial (Arm/Leg)
- 
- Different Group: Combination Therapy Preserving PreClinical
  - Early Head Phase III
  - Deodorizing Phase III
  - Foot Monitoring (Label)

## Leadership

- "Trial 409" Registration Quality
    - Shampoo endpoint
    - Head population
  - Phase IV Study Strategy
    - Arm
  - Optimize Use
    - Foot protective agents
  - Top Secret Registration
    - Label Reg
  - New indication Phase III
    - 1 to 3 trials (Arm/Leg)
- 
- Early Head Phase III and IV
  - Different Group: Combination Therapy Preserving PreClinical
  - Deodorizing Phase III
  - Foot Monitoring (Label)

# High Level Influence Diagram



## Qualitative Portfolio Assessment - New Uses



	<u>P(S)</u>	<u>Time</u>	<u>Size</u>	<u>Invest</u>
<b>Shampoo</b>	Hi	M (2-3)	Med	Big
<b>Deodorizing (reg)</b>	Lo	Long (5-7)	Big	Big
<b>Deodorizing</b> (pub, basis model work)	? (L-Med)	MF	Med	Small
<b>Enhance Treat Preserving</b> (comb therapy, new package)	M	Long	Med	Big



## Qualitative Portfolio Assessment - Label Optimization

	<u>P(S)</u>	<u>Time</u>	<u>Size</u>	<u>Invest</u>
<b>Arm</b>	Med	ML (4)	Med	Big
<b>Top Secret</b>	Hi	Quick (1)	Med-Small	Small
<b>Foot Monitor</b> (better)	Med	4	Small	Lo Incr with 1 other study
<b>Early Head (reg)</b>	Hi (based on prior analysis)	4	M-Small (already selling off- label)	Big
<b>Early Head (pub)</b>	Hi to Med (worried about quality)	2	Med-Small	Small

## Qualitative Portfolio Assessment - New Indication

	<u>P(S)</u>	<u>Time</u>	<u>Size</u>	<u>Invest</u>
<b>Head</b>	Med	Long	Med-Big	Big
<b>Arm</b>	Med	Long	Med-Big	Big
<b>Leg</b>	Med-Lo	4	M-Small	Big
<b>Foot</b>	Med-Lo	Long (recruit)	M-Small (off-label)	Big
<b>Combo (broaden claim, inferred)</b>	Med (2 indications) Lo (3 indications)	Parallel (Long)	Big	Big

key on size:  
 Small = <200 \$ peak annual sales  
 Medium = 500  
 Big = 1000

# Summary of Outputs

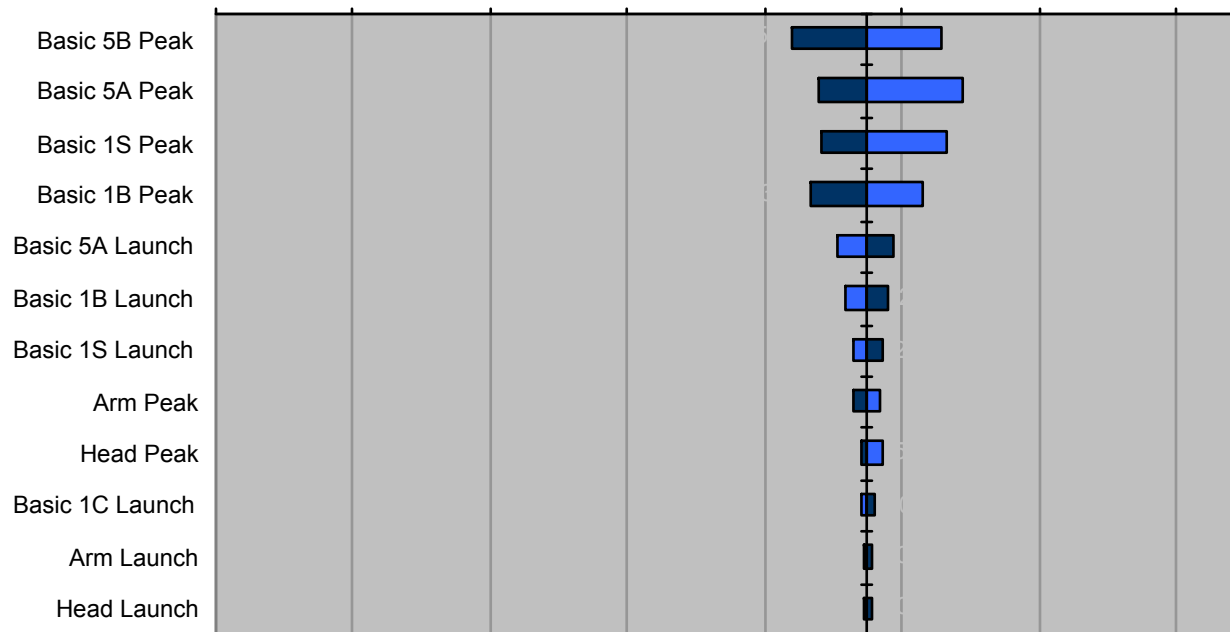
Time Series Calcs										© Decision Strategies 2002 All Rights Reserved										1	2	3
Name		Category	Goal	p(S)	Phs	Years to Launch	Launch Year	Peak (\$)	Invest (\$)	NPV Invest (\$)	Dur yrs	NPV Pot (\$)	rand	Suc-cess?	EV (Risked)	EV	eff	R C	M F	L		
1A	Basic 1S	NewUses	Reg	80%	3	3.5	2005.5				7.5	351	0.62	1.0	351	281	14.3					
1B	Basic 1B	Prevent	Reg	55%	3	5.5	2007.5				5.5	572	0.14	1.0	572	315	18.3					
1C	Basic 1C	Prevent	Reg	5%	3	8	2010.0				3	315	0.27	0.0	-15	16	1.1					
5A	Basic 5A	NewUses	Reg	80%	3	4.5	2006.5				6.5	590	0.86	0.0	-24	472	19.3					
5B	Basic 5B	Prevent	Reg	60%	3	6.5	2008.5				4.5	764	0.56	1.0	764	458	21.1					
5C	Basic 5C	Prevent	Reg	5%	3	8	2010.0				3	516	0.82	0.0	-19	26	1.3					
6	TopSecret	LabelOpt	Reg	95%	3B	1.7	2003.7				9.3	265	0.32	1.0	265	252	246.5					
9	Head	LabelOpt	Pub	65%	4	5	2007.0				6	45	0.19	1.0	45	29	9.6					
13	Optimizing Use	LabelOpt	Reg	0%	0																	
14	Arm	Promotion	Pub	40%	4	4	2006.0				7	233	0.59	0.0	-3	93	29.4					
14A	Arm 1A	LabelOpt	Reg	10%	3	2	2004.0				9	76	0.40	0.0	0	8	87.8					
Projects Not Supported																						
8	Head (Reg)	LabelOpt	Reg	60%	3	6	2008				5	162	0.21	1.0	162	97	2.7					
1E	Foot	LabelOpt	Pub	10%	4	2	2004				9	200	0.41	0.0	-3	20	5.8					
2	Deodorizing Reg	NewUses	Reg	10%	0	7	2009				4	341	0.14	0.0	-191	34	0.2					
3	Deodorizing Pub	NewUses	Pub	50%	4	3	2005				8	328	0.90	0.0	-3	164	49.4					
4	Combo	NewUses	Reg	50%	0	10	2012				1	217	0.18	1.0	217	108	0.6					
7	Foot	LabelOpt	Reg	5%	3	5	2007				6	199	0.41	0.0	-1	10	13.1					
Summary						Number		total invest		Potential		No. Success		Risk EV		EV	eff					
Resource Cons Strat						6																
Market Focused						10																
Leadership						11																

Note: *Success?* and *EV (Risked)* columns are affected by *rand* column, which changes with each iteration.



## Portfolio Sensitivity to Uncertainties - Focused Strategy

**Tornado (Sensitivity) Diagram (11) - Focused Strategy**  
Expected Value, NPV of Sales less NPV of Development Cos



The tornado graph shows the relative importance of the uncertainties and their relative contribution to upside potential and downside risk.

Peak Sales (Basic) are the most important uncertainties, followed by launch timing.

Expected value of the portfolio revenue for this strategy is about \$xxx.

(Optimizing use has not yet been assessed.)

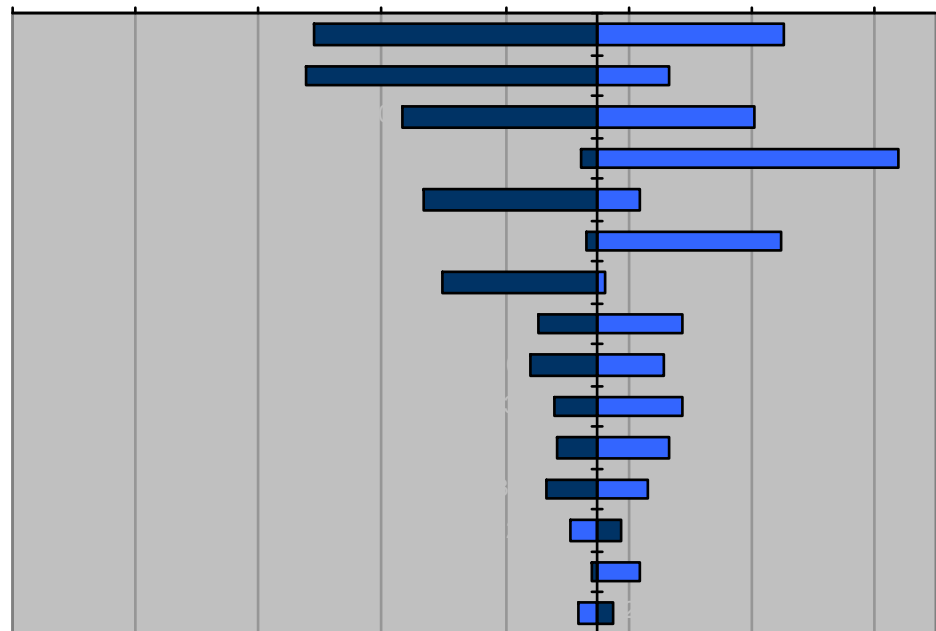
# Sensitivity Analysis Including Probability of Success

This graph is similar to the previous graph, except that it includes probabilities of success in order to show the relative importance of  $p(S)$  when compared with the other uncertainties.

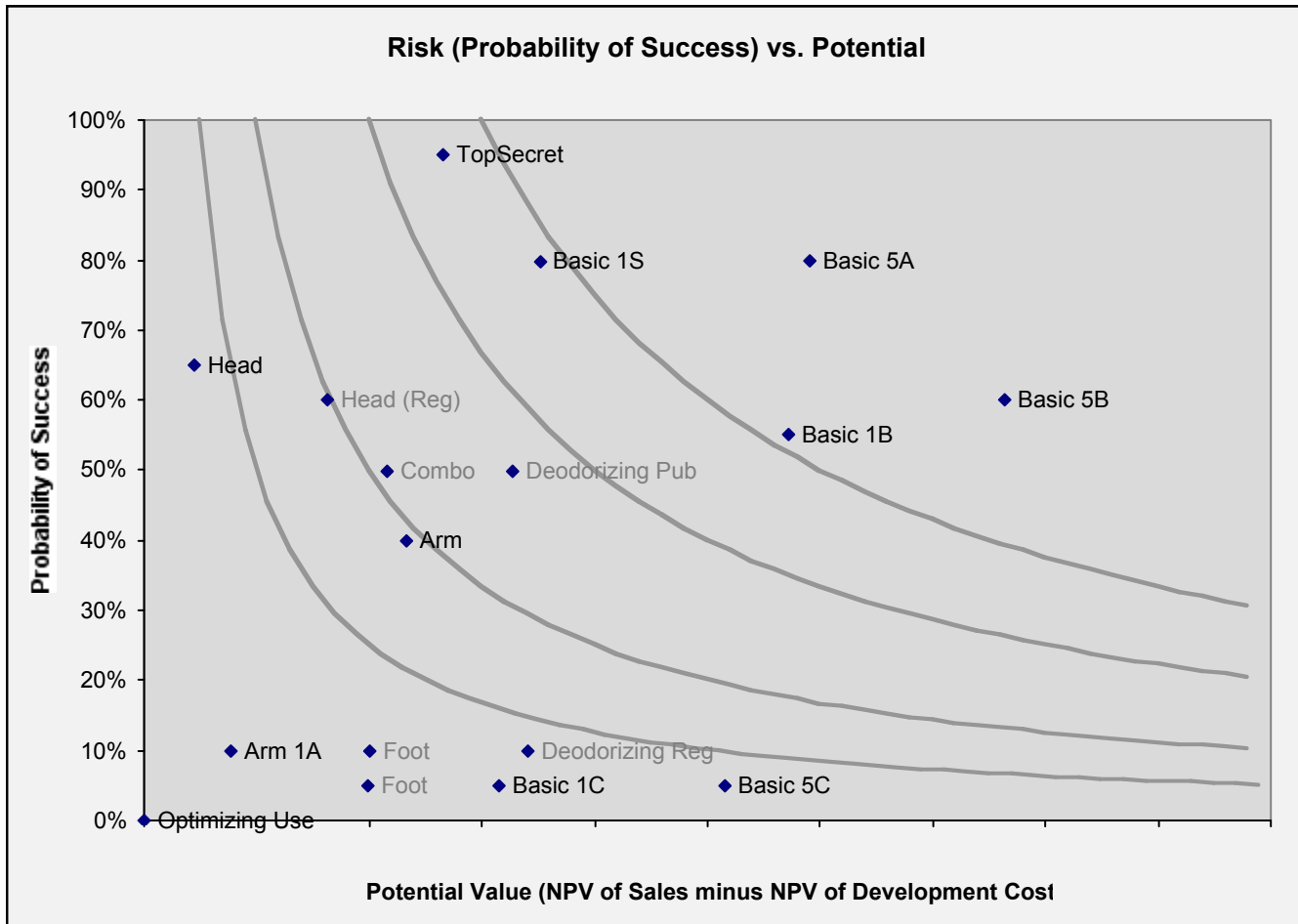
The potential benefit of obtaining a low-probability event can be clearly seen, as can the downside associated with *not* achieving and expected event (e.g. Top Secret approval).

Expected value of the portfolio revenue for this strategy is about \$xxx.

**Tornado (Sensitivity) Diagram (8) - Focused Strategy**  
**Expected Value (risked), NPV of Sales less Development Costs**



# Life Cycle Management Portfolio - Risk (Probability of Success) vs. Potential Value (NPV)



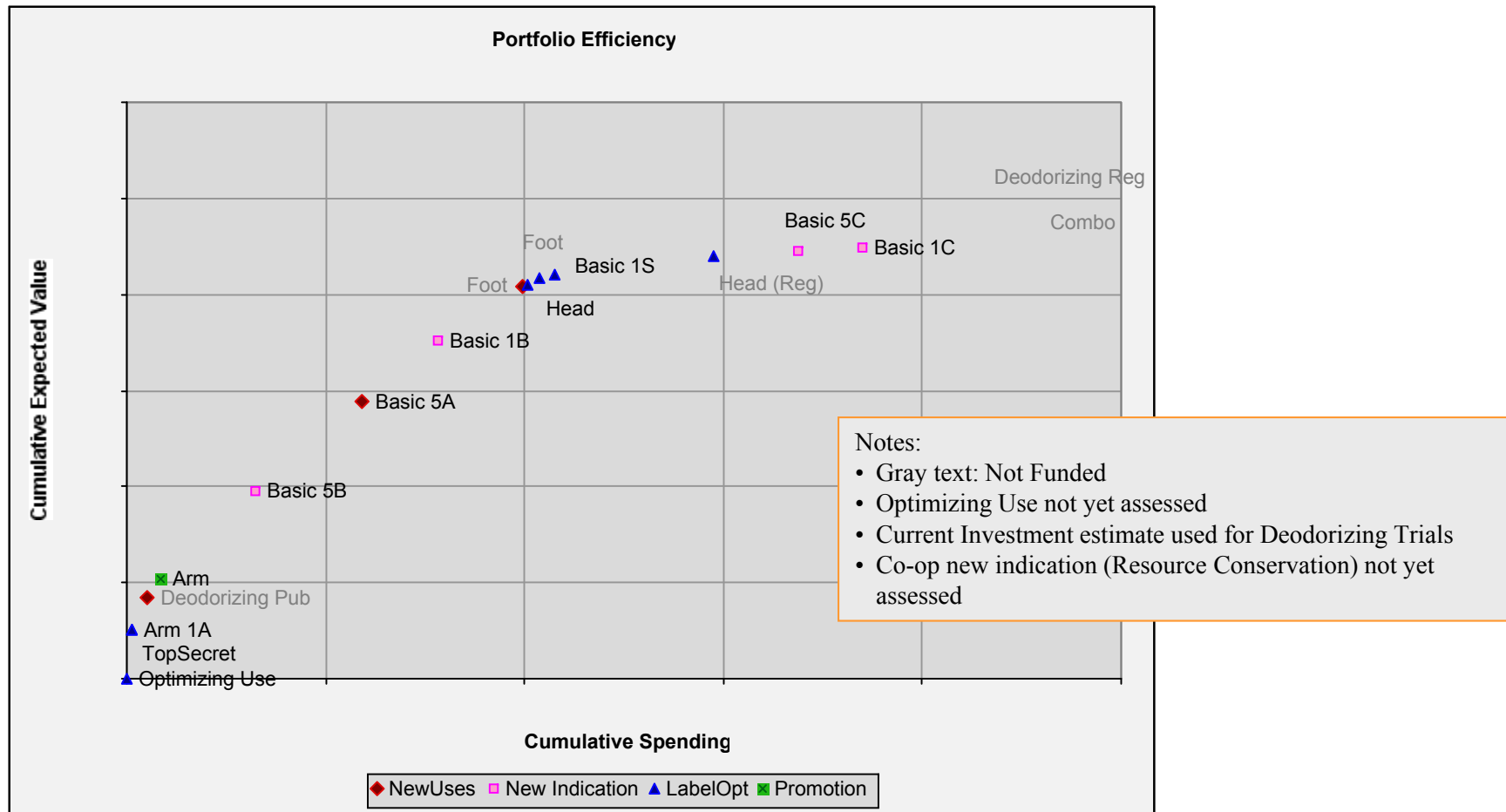
## Notes:

- Gray text: not funded
- “Optimizing Use” not yet assessed

Interpretation: Projects in the upper right quadrant large and likely to succeed and would be of highest priority.

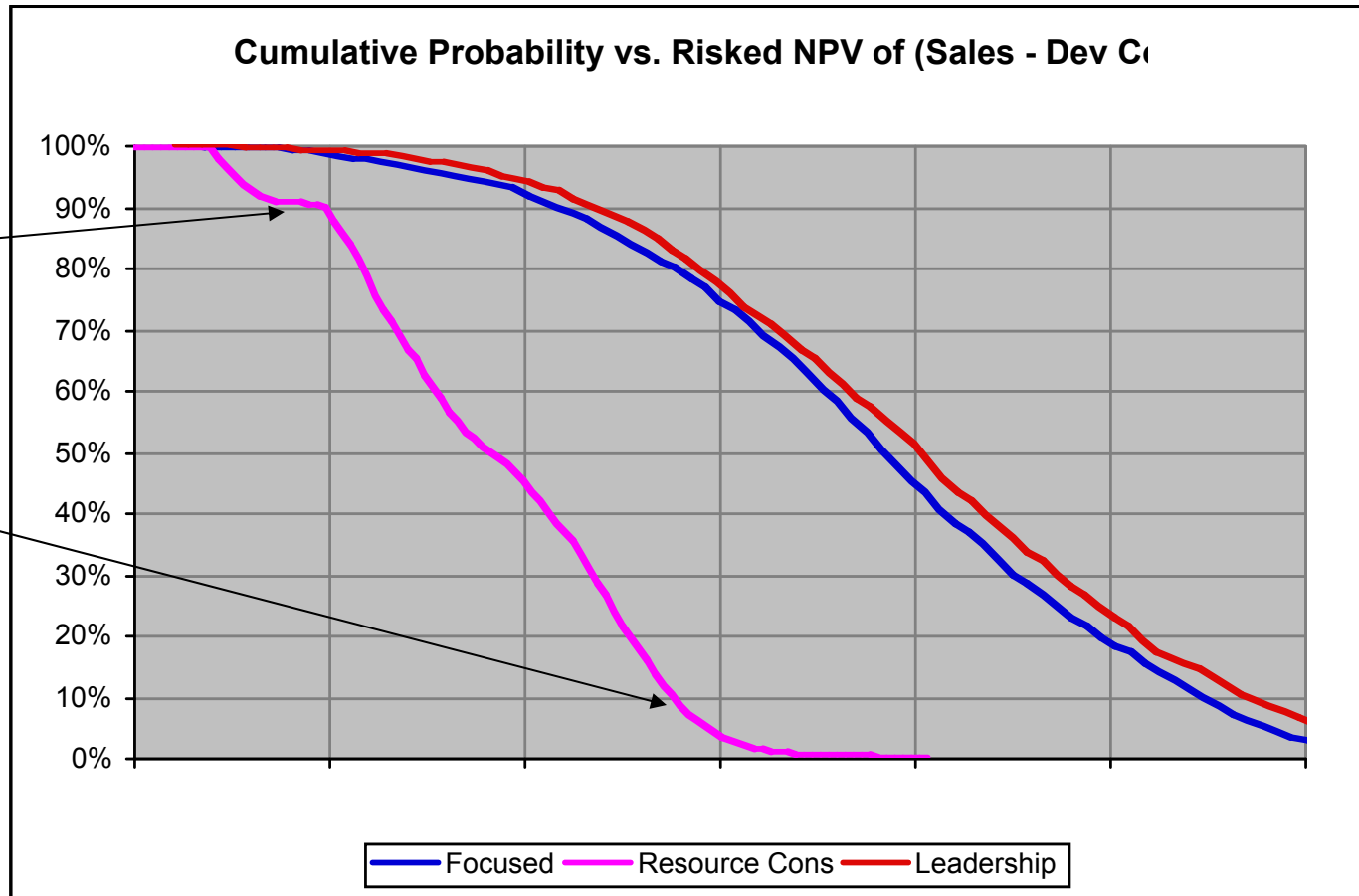
The light gray lines are lines of indifference. For example, a project with 100% chance of success with 100 NPV would have the same expected value as a 200 NPV project with a 50% chance of success.

# Life Cycle Management Portfolio - Efficiency

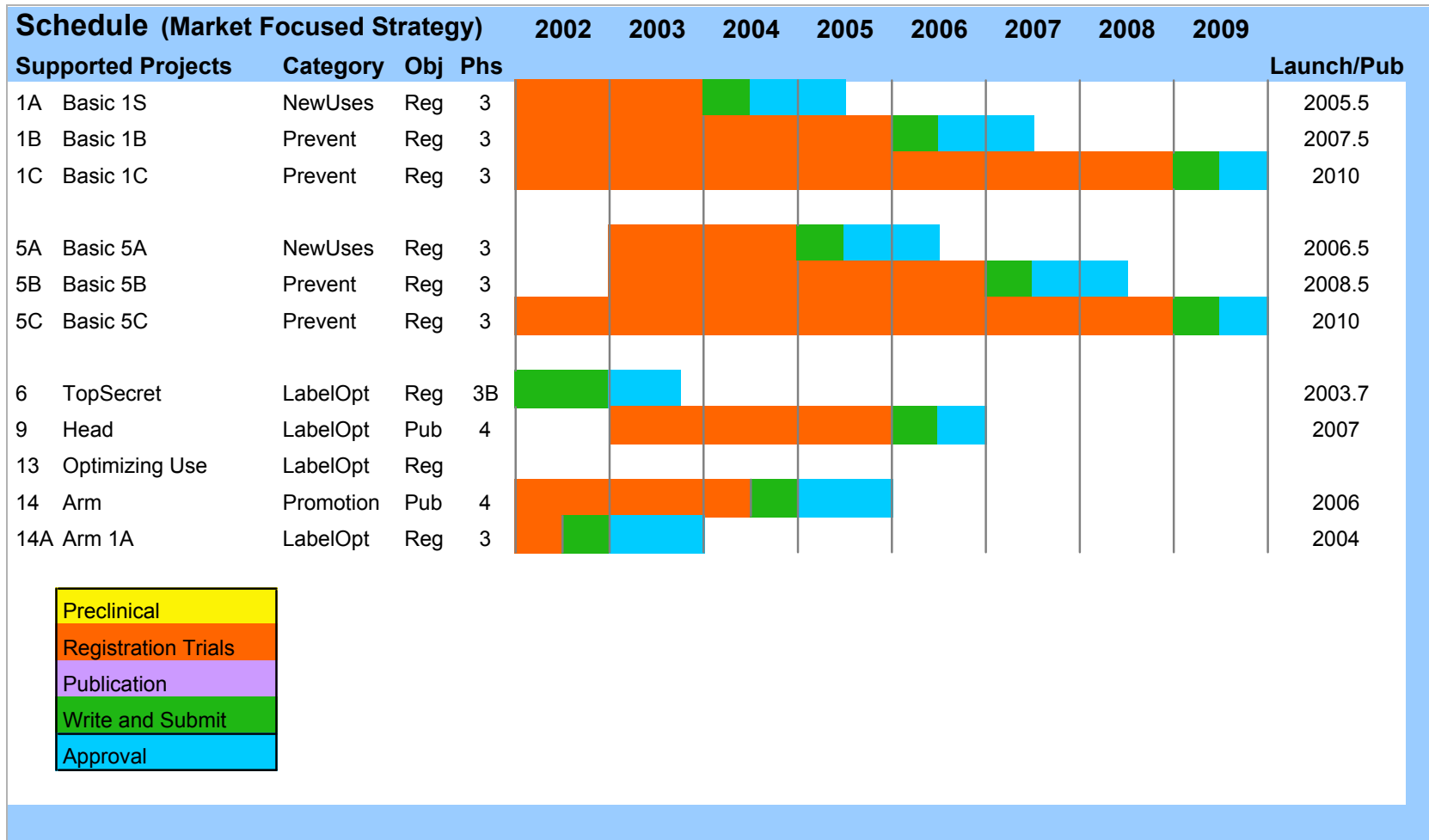


# Cumulative Probability (Risked)

Interpretation: for the Resource Conservation Strategy (violet line), there is a 90% chance that the value of the portfolio for this strategy will be at least \$xxx (NPV). There is only a 10% chance that it will exceed \$yyy.



# Schedule



## *Summary (for DRB)*

- Relative to the “409” Trial, the Team agreed that: Clinical team will develop a proposal for adding Shampoo end points and Foot endpoints.
  - Uncertainty: FDA response
  - address 2nd Trial
- The “Market Focused” strategy, given the current state-of-knowledge, has the highest efficiency of the three strategies investigated and offers significant potential for increased sales.
- Short-term analysis needs to develop more detailed information concerning dosing, schedule, potential sales, timing, and cost uncertainties for Phase III Trial 409 trials.

## *Summary (for DAAG)*

- For LCM projects, a combination of DA Project and Portfolio analysis tools can yield insight and help a Team and their DRB reach consensus around a business strategy.
- DA Hints:
  - Facilitation – Allow for lots of “Rant” time and be prepared to handle non-strategic issues if necessary.
  - Use the *simplest possible* measure-of-value which will allow distinctions between strategies to be made.
  - Obtaining qualitative group assessments at the end of the Framing stage can help prevent a non-analysis event.
  - Build the calcs in the model with a 1-line orientation so that strategy switches can easily be built into the model.