Presenting:

Modeling Ordered Uncertainties

by Jon Mauer

DAAG Conference 2016

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Modeling ~~Complex~~ Ordered Uncertainties

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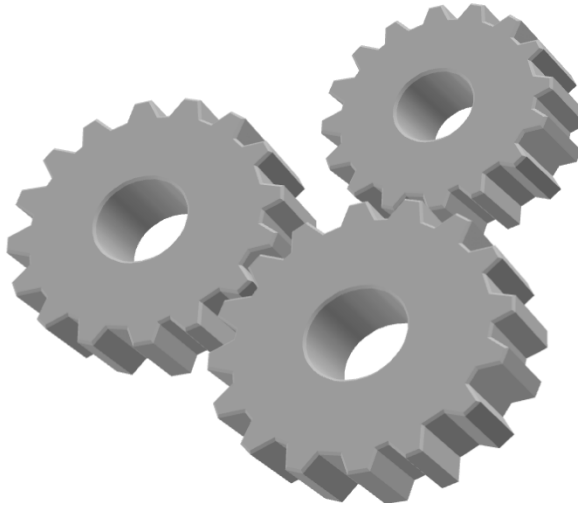

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Contents

- The Decision Problem
- The Geeky Stuff (for your amuzement)
- The Succinct, Solid Recommendation

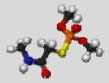
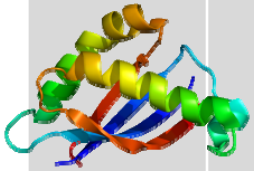
A Pfizer decision problem motivated this talk

How should 3 assets targeting one disease be developed?

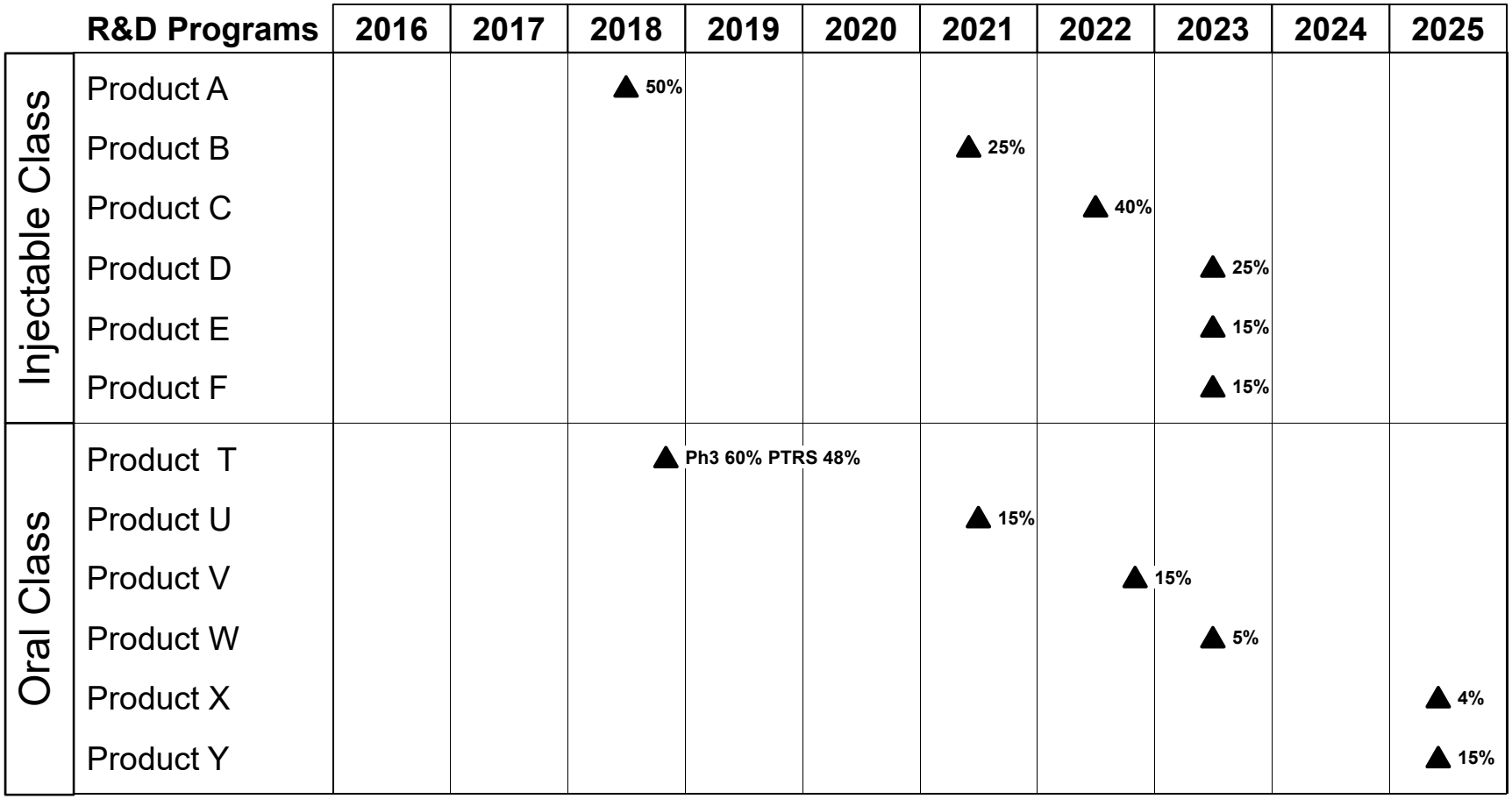
- All three assets…
  - Have completed P1 and some P2 development
  - Could benefit from add'l P2 development or proceed directly to P3
  - R&D risk: High
  - R&D cost: ~$1B each
  - R&D timelines: Long
  - Commercial opportunity: Large unmet medical need
  - Clinical trial environment: Competitive

Is it worth it or are we too late?

The complex decision situation provoked anxiety

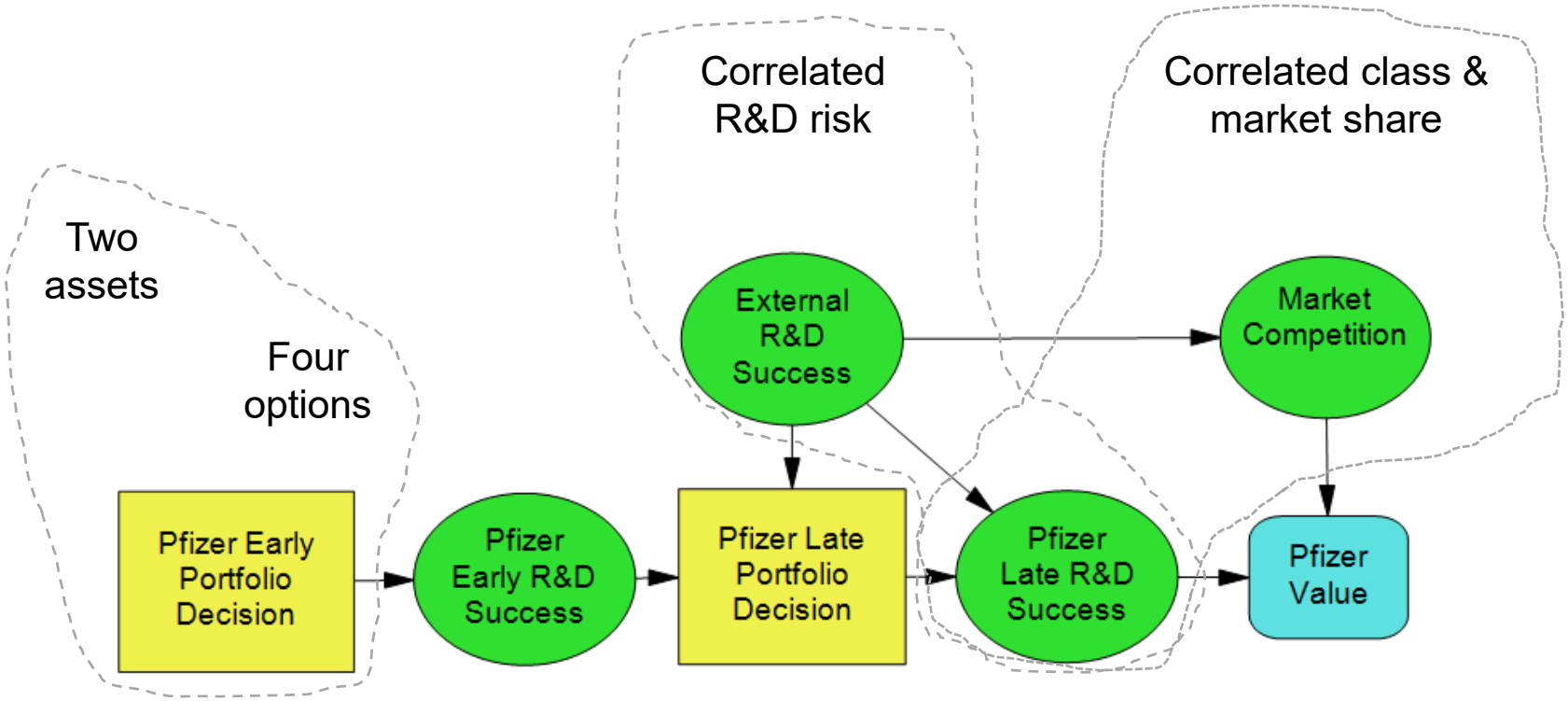
Molecule in R&D	MOA	Competitive Position	Anticipated Date for competitors' Ph3 Results	Impact of Competitors' Ph3 Success	Development Options			
					Learn	Choose A	Choose B	Catch-up
 Small molecule	A	3rd of 5 Potential Best-in-Class	2017 2018	Demonstration of clinical effect ↑PTRS & ↓CVGS with increasing competition	Staged Program	Accelerate Program	Stop	Accelerate Program
 Small molecule	B	1st of 1 Potential First-in-Class	N/A		Staged Program	Stop	Accelerate Program	Accelerate Program
 Protein	C	4th of 6 + potential advantages	2016		Initially included for combination potential, subsequently removed following policy decision to stop development - RELIEF -			

Intense competition may threaten commercial viability



Organizational momentum favored urgent development

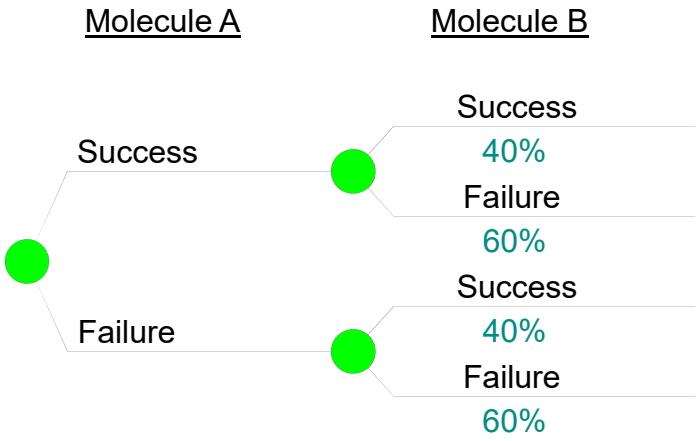
The solution is complicated by multiple options with correlated technical and commercial uncertainties



R&D risk correlation is reflected in probability trees

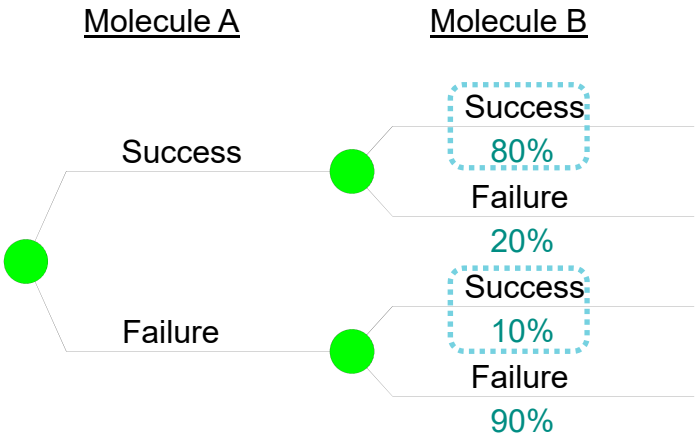
Independent Risk

Molecule B probability of success is the same regardless of Molecule A outcome



Dependent Risk

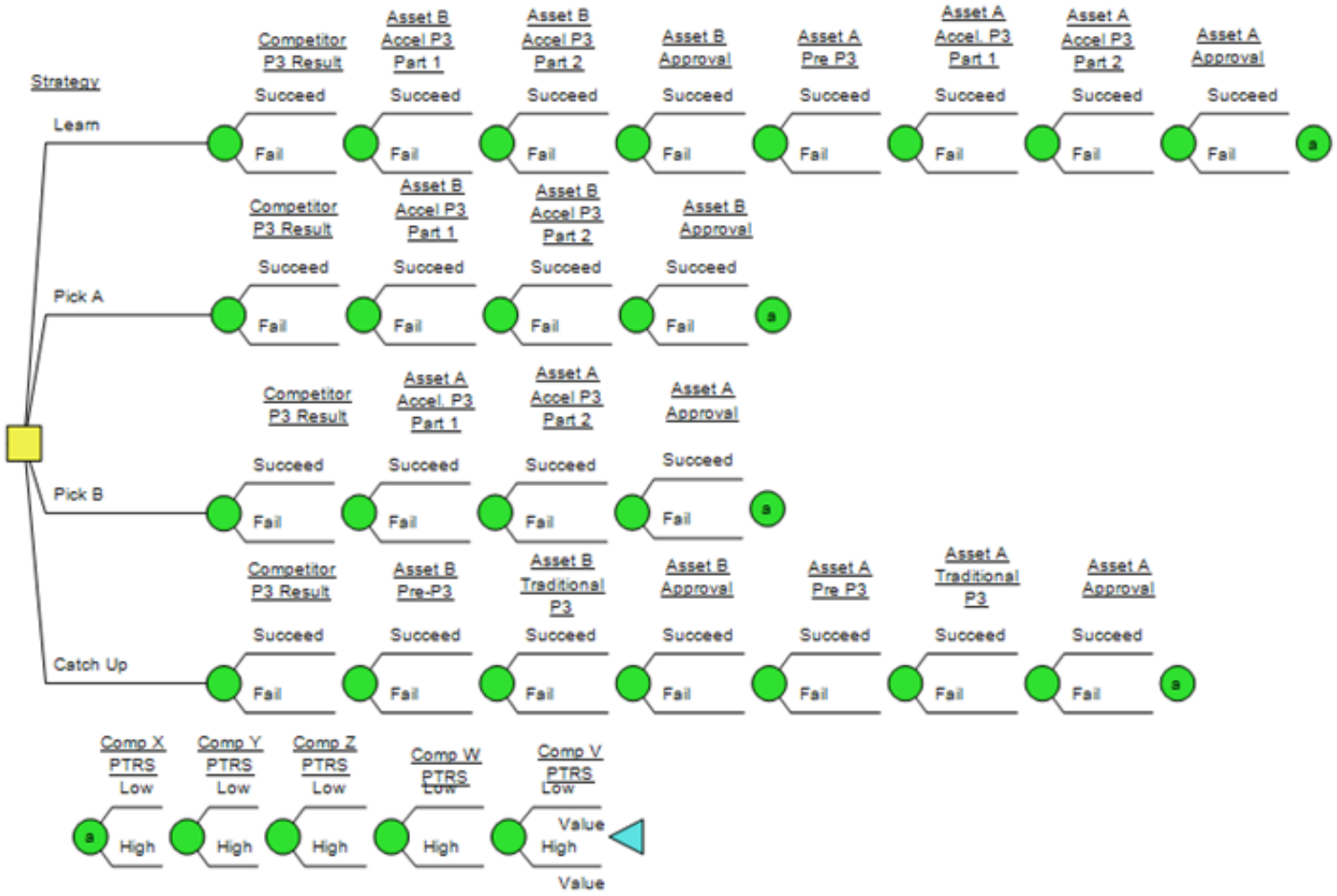
Molecule B probability of success changes depending on Molecule A outcome



- √ Molecules targeting same indication
- √ Molecules with same MOA*
- ? Material impact

* MOA: mechanism of action

Numerous uncertainties make the math difficult



Simulation helps avoid difficult math

Market share correlates with entry-order and competitive intensity*

Competitive Intensity – assuming undifferentiated assets										
EO Rank	1	2	3	4	5	6	7	8	9	10
1	1.00	0.58	0.44	0.36	0.31	0.27	0.25	0.23	0.21	0.20
2		0.42	0.31	0.25	0.22	0.19	0.18	0.16	0.15	0.14
3			0.25	0.21	0.18	0.16	0.14	0.13	0.12	0.11
4				0.18	0.16	0.14	0.12	0.11	0.11	0.10
5					0.14	0.12	0.11	0.10	0.10	0.09
6						0.11	0.10	0.09	0.09	0.08
7							0.09	0.09	0.08	0.08
8								0.08	0.08	0.07
9									0.07	0.07
10										0.06

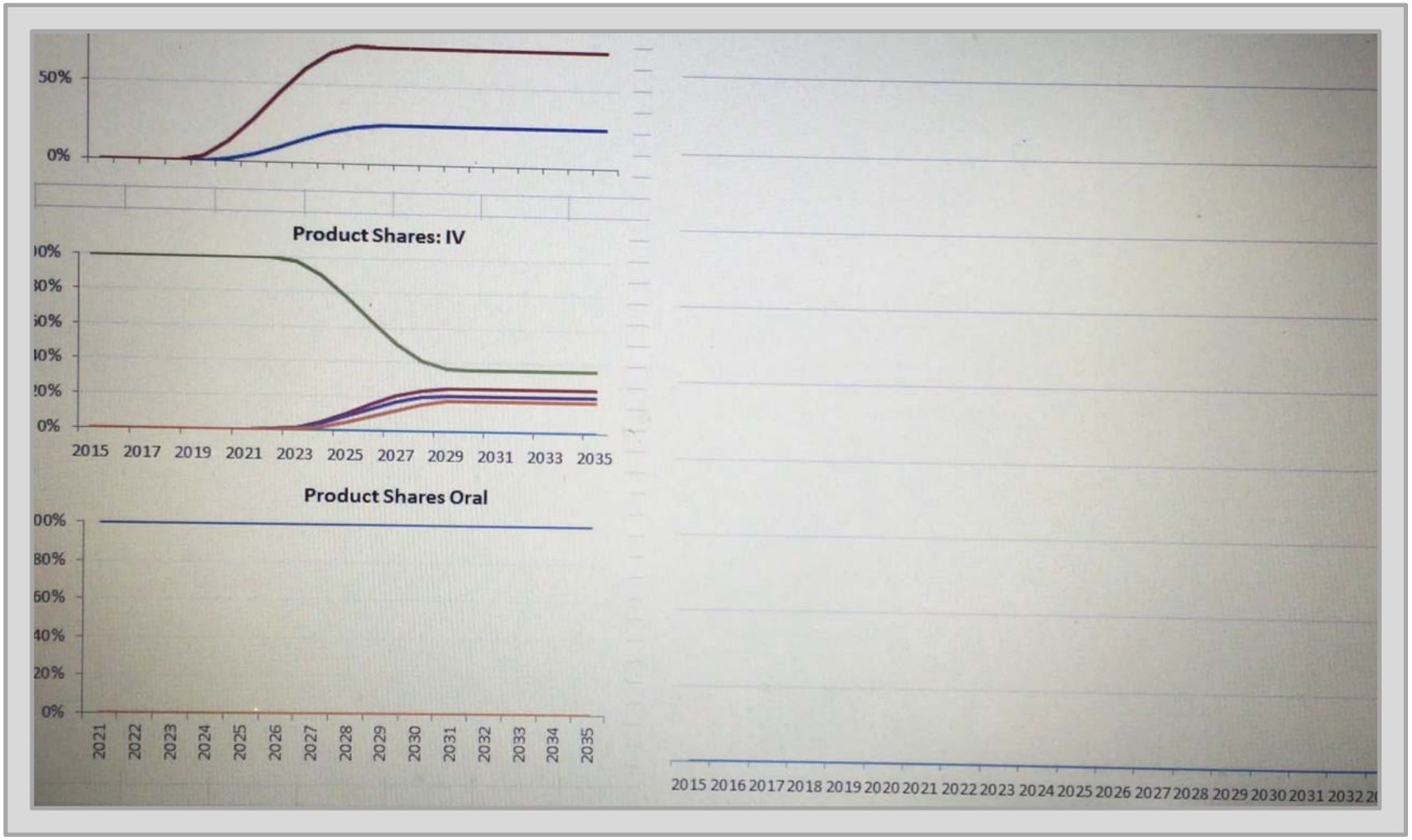
* BASES consumer industry

R&D outcomes and market dynamics are linked by logical equations

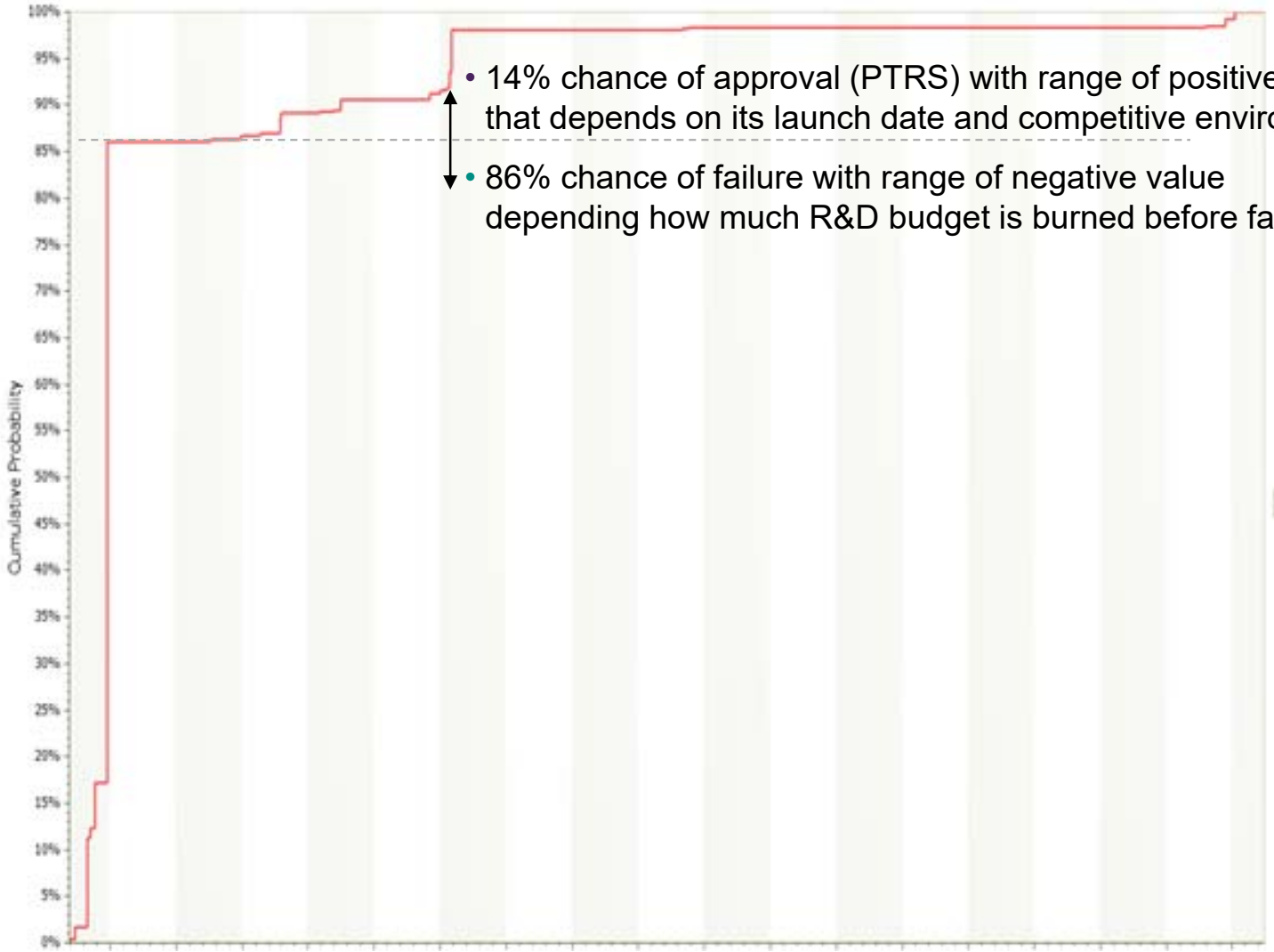
I. Input for all products:
   1. R&D attrition rates
   2. Launch dates
   3. Peak class share
   4. Time to peak class and product share

II. Calculate product share battle:
   1. Successful R&D programs' launch date determines entry order
   2. Entry order determines peak share for each marketed product
   3. Launch dates trigger share growth towards predicted peak share
   4. New product entries intensify competition and redefine peak shares between marketed products over time

Simulation illustrates dynamic market share battle

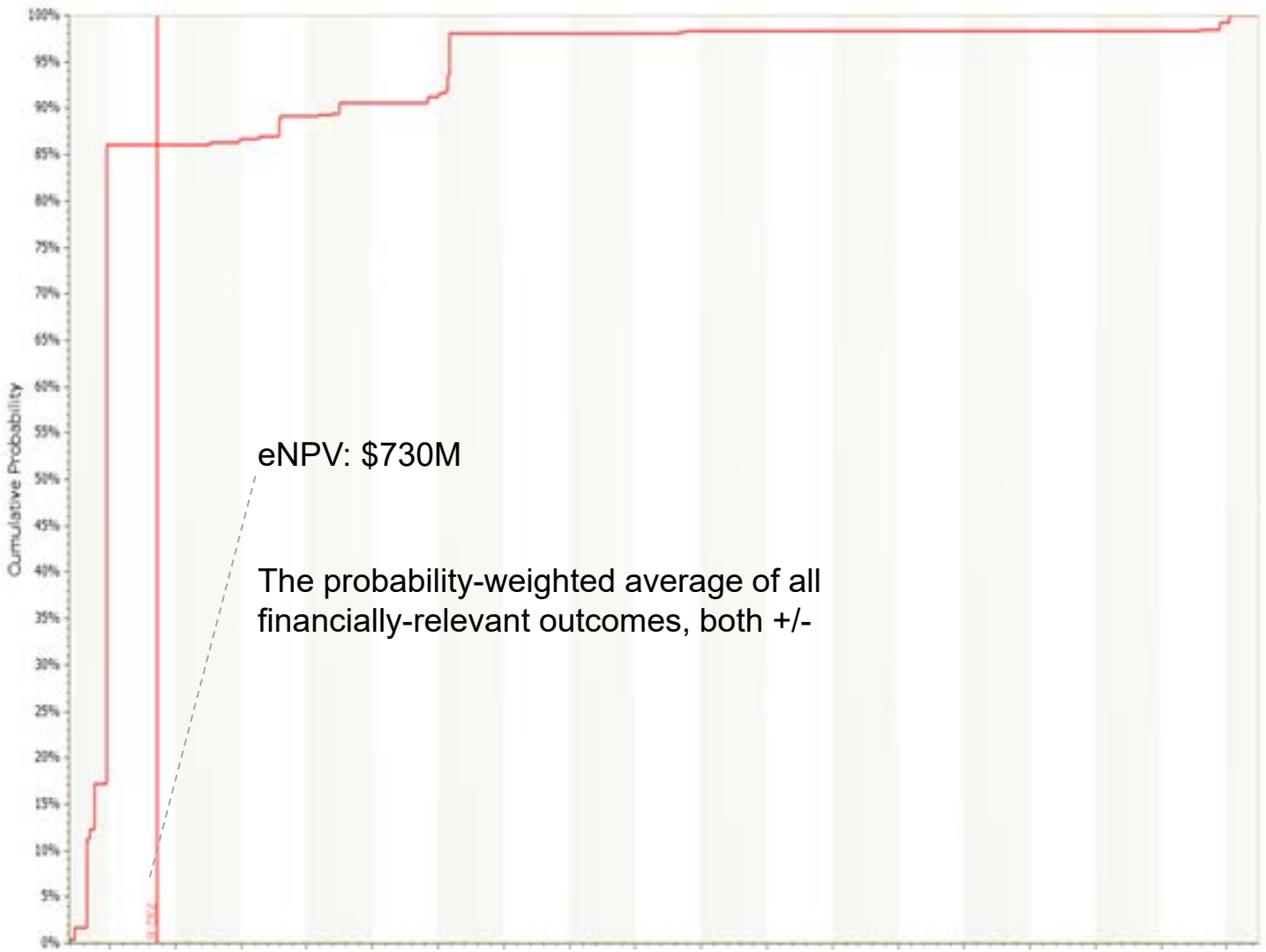


Simulation illustrates wide range of financial outcomes

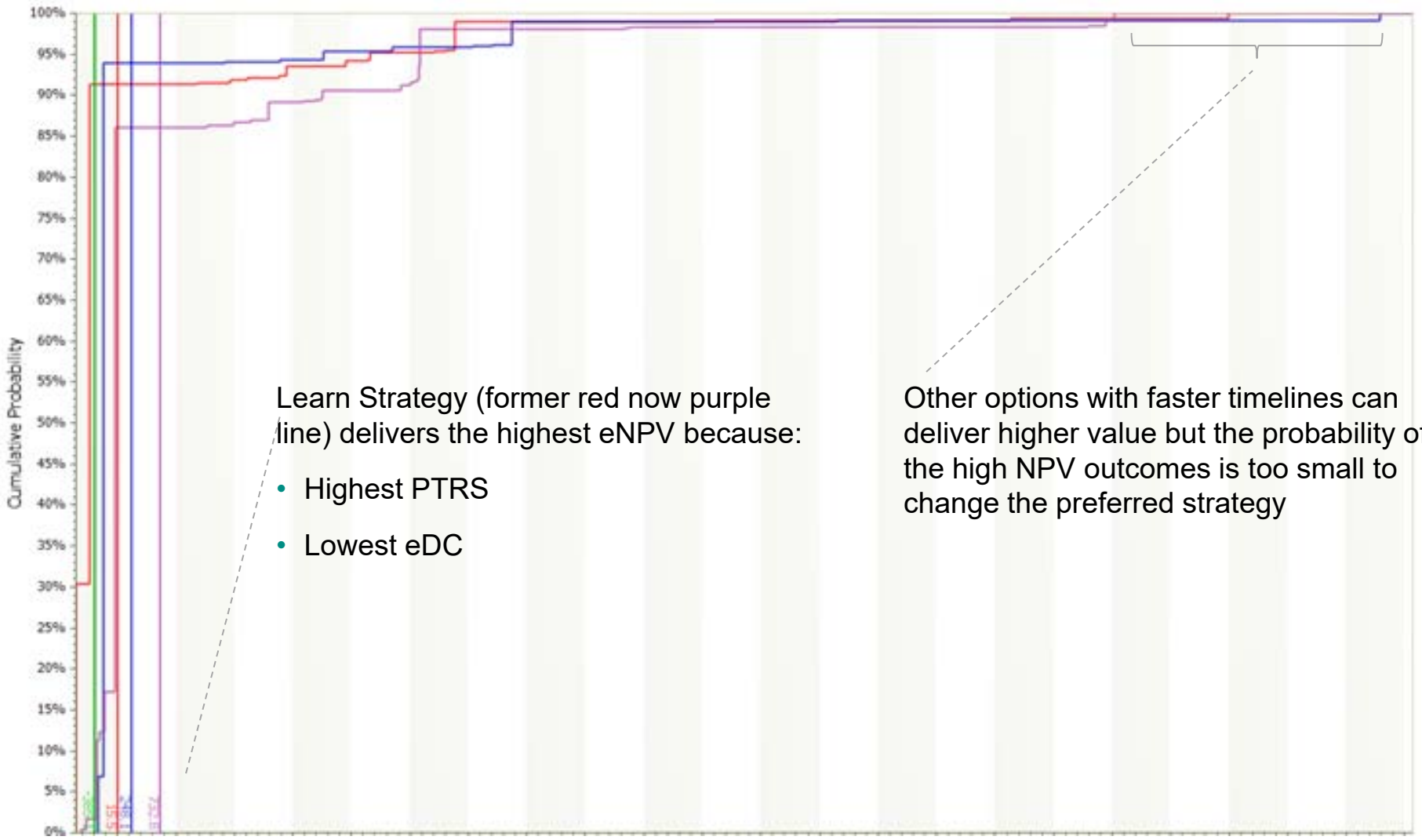


- 14% chance of approval (PTRS) with range of positive value that depends on its launch date and competitive environment
- 86% chance of failure with range of negative value depending how much R&D budget is burned before failure

Simulation Results



Simulation Results



Learn Strategy (former red now purple line) delivers the highest eNPV because:

- Highest PTRS
- Lowest eDC

Other options with faster timelines can deliver higher value but the probability of the high NPV outcomes is too small to change the preferred strategy

Strategy Recommendation

- Large market opportunity will support late product entrants
  - High unmet need,
  - Large growing market, and
  - Pricing rewards value proposition
- Continue staged development with both small molecules
- Prepare both for P3, then await competitors' results:
  - to inform our technical risk, program design, market direction & business opportunity prior to larger scale investments (P3)

Economics favor stage development to learn before making large P3 investment

Strategy	PTRS (≥1 Launch)	eNPV ($M)	Total Cost ($M)	eDC ($M)	Launch A	Launch B
Learn	High	High	High	Low	`23 (4th)	`25 (5th)
Only A	Low	Low	Low	Mid	`22 (3rd)	-
Only B	Low	Low	Low	Mid	-	`24 (4th)
Catch-up	Mid	Mid	High	High	`22 (3rd)	`24 (4th)

- **Economics favor the Learn Strategy**
  - Resolves risk at lower cost prior to major P3 resource commitment
  - Highest probability of ≥1 product launch and potential for two possible launches
- **Double asset strategies (Learn & Catch-up):**
  - Total cost is similar – twice the cost of single asset strategies
  - Higher PTRS from having two potential product launches
- **Single asset strategies:**
  - Both suffer from low probability of reaching market
  - Speed to market provides deterministic entry order advantage but commercial upside can't offset single asset risk

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