Presenting:

Assessing Technical Success Probabilities in Pharma: A "Cap & Trade" Approach

by Chris Dalton

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Assessing Technical Success Probabilities in Pharma: A "Cap & Trade" Approach

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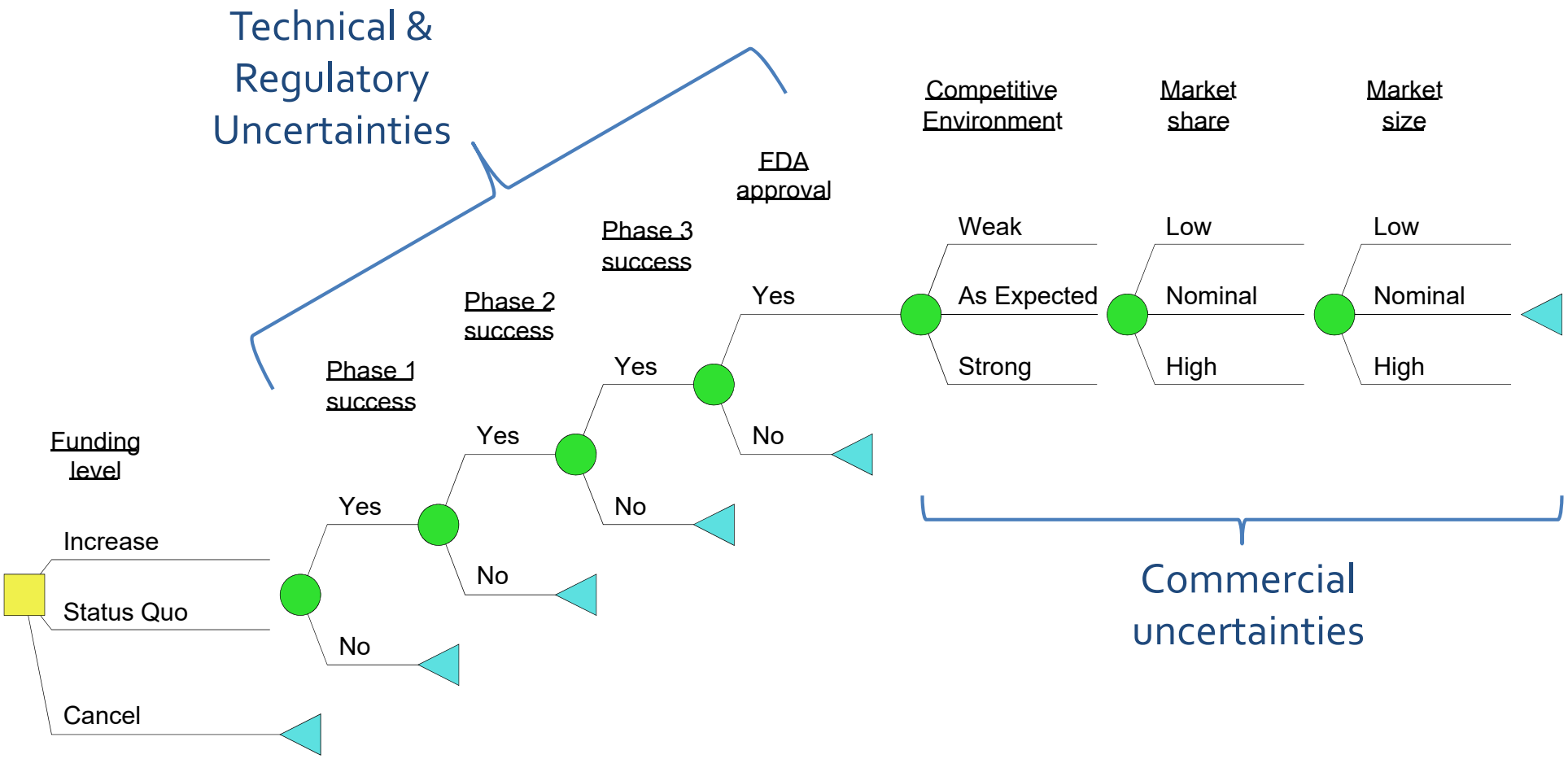
Agenda

- TALK: Probability assessment in the decision analytic approach to evaluating pharma R&D projects
  - The classic drug development decision tree
  - Probability assessment in the Pharma R&D context
  - Subjectivity and the "pain scale"
  - Approaches to balancing "objectivity" with the use of the best available information
- GAME: Group probability assessment exercise
  - The portfolio
  - The rules
- QUESTIONS/DISCUSSION
  - Your assessment of this assessment process

A typical pharma drug development decision tree

- Regulation imposes a structure, so pharma R&D models usually share certain characteristics



Technical and regulatory success ("PTRS") in pharma R&D portfolio management

- A project can fail for a variety of reasons
  - Serious safety issues
  - Insufficient or non-existent efficacy
  - Side effects that are not tolerable for the therapeutic area

- The good news is we have some information
  - Deep in-house knowledge about the particular molecule
  - In-house experience with other molecules, both generally and in the same therapeutic area
  - Commercial databases (IMS, etc.)

- Judgement is required, but most people agree that relevant benchmarks can be useful

The probability assessment "pain scale"

- Methods of obtaining probabilities are often categorized as either
  - Objective: repetitive events, statistics -- the uncertainty is "in nature"
  - Subjective: expert judgement -- the uncertainty is "in your head"
- Actually, it's always in your head …
  - The deep and heterogeneous information (~data) in your head is why you're an expert
  - Somebody has to use judgement to select and use relevant data
- … but sometimes your head hurts!
  - How hard do you have to think?

Less hard thinking

More hard thinking

"Look it up in an engineering manual"

"Wish we had more *recent* data"

"Yeah, OK, but this product is different"

"Very novel mechanism of action"

"Totally new product category"

How should benchmarks be integrated into the assessment process?

- "Thou shalt use the benchmarks!"
  - "Always remember you're special, just like everyone else."
  - Feels good ("objective"), but this is way is not best for decision quality!
- "FYI, here are some benchmarks"
  - "Just so you know, we're batting 300 in this therapeutic area in Phase x …"
- Due process for deviation
  - Like FYI, but specific reasons must be given for deviating from the benchmarks
  - "We know a lot about this compound, it's really just a pegalomophicateified …"
- Cap & Trade benchmarks (or grading on a curve, etc.)
  - The set of N projects in this therapeutic area must meet the benchmark *on average*
  - "If this one is unusually safe, which one is unusually dangerous?"

The Game (1 of 2): Introducing the portfolio of "assets"

- Consider the elections for the US House of Representatives in November, 2016
- In all US congressional elections the vast majority of incumbents who seek reelection are victorious
- Even in races considered competitive*, the incumbent wins **72%** of the time (this is your benchmark probability)
- Your portfolio consists of six randomly selected members of congress who were seeking re-election in competitive districts
- Names and states/districts have been masked (**no online research**)

* I used Ballotpedia ratings of "Battleground" and "Competitive"; see https://ballotpedia.org/United_States_Congress_elections,_2016

The Game (2 of 2): Rules and scoring

- Your table is your group (tables with 1-3 people please consolidate)
- Each group will have one game board and some poker chips
  - Before you start, write your names on the back of the game board
- Chip values: white 10%, red/green/blue 25%, black 50%
- The chips add up to N times the benchmark (6 * 72% ~= 435%)
- Start with 70 or 75% on each square
- Read the information supplied about the races and move chips as per the success probabilities you infer
- Don't put more than 100% on any square
- When you're done, write your probabilities on the blanks

Scoring:

- I will tell you which squares are winners; chips on losing squares are lost
- The team with the most probability value left wins
  - Tiebreaker: team with the fewest DA "old pros"
- In the interest of time, we may determine the winning table offline

Game Board -- DAAG PTRS

Member #1
- Republican
- West Coast
- First elected in 2000
- One poll says he leads 48-46 (+/- 4.5%)
- Cook Political Report calls this race a "toss-up"

p = _____ %

Member #2
- Republican
- Midwest
- One-term incumbent
- Election is a rematch (same opponent as 2014)
- Polls are mixed
- Out fundraised his opponent

p = _____ %

Member #3
- Republican
- Rust Belt
- 4-way race (D, R, Libertarian, Green)
- Cook Political Report says this race "leans R"

p = _____ %

Member #4
- Democrat
- Great Plains
- Has a "commanding" lead in fundraising
- One-term incumbent
- $1m fundraising advantage over opponent

p = _____ %

Member #5
- Republican
- Northeast
- One-term incumbent
- Unchallenged in primary
- Opponent supported by Emily's List

p = _____ %

Member #6
- Republican
- Deep South
- One-term incumbent
- Defeated a primary challenger 82-18
- Election is a rematch (same opponent as 2014)
- Declined to endorse Trump

p = _____ %

Achtung!

- Answers follow ....
- don't
- spoil
- the
- fun

Game Board -- Results

Member #1 • Darrell Issa • California 49th • RE-ELECTED	Member #2 • Robert Dold • Illinois 10th • DEFEATED	Member #3 • Tim Walberg • Michigan 7th • RE-ELECTED
Member #4 • Brad Ashford • Nebraska 2nd • DEFEATED	Member #5 • Lee Zeldin • New York 1st • RE-ELECTED	Member #6 • Will Hurd • Texas 23rd • RE-ELECTED

Wrap up

- Was it easier or harder than if I'd just stated the benchmark?
- Was granularity (5% epsilon, other constraints) a help or a hindrance?
- Was there enough information that you felt comfortable your probability was better than just using the benchmark?
  - The "objective" approach would have scored 290%
- Did you incorporate knowledge you have of last fall's election other than what was given on the game board?

- Did you write your probabilities on the blanks and your names on the back of the board?