Return on Investment in Discovery Chiral Separations

Averica Discovery Services

A lot of people believe that any important concept can be sketched on a cocktail napkin…

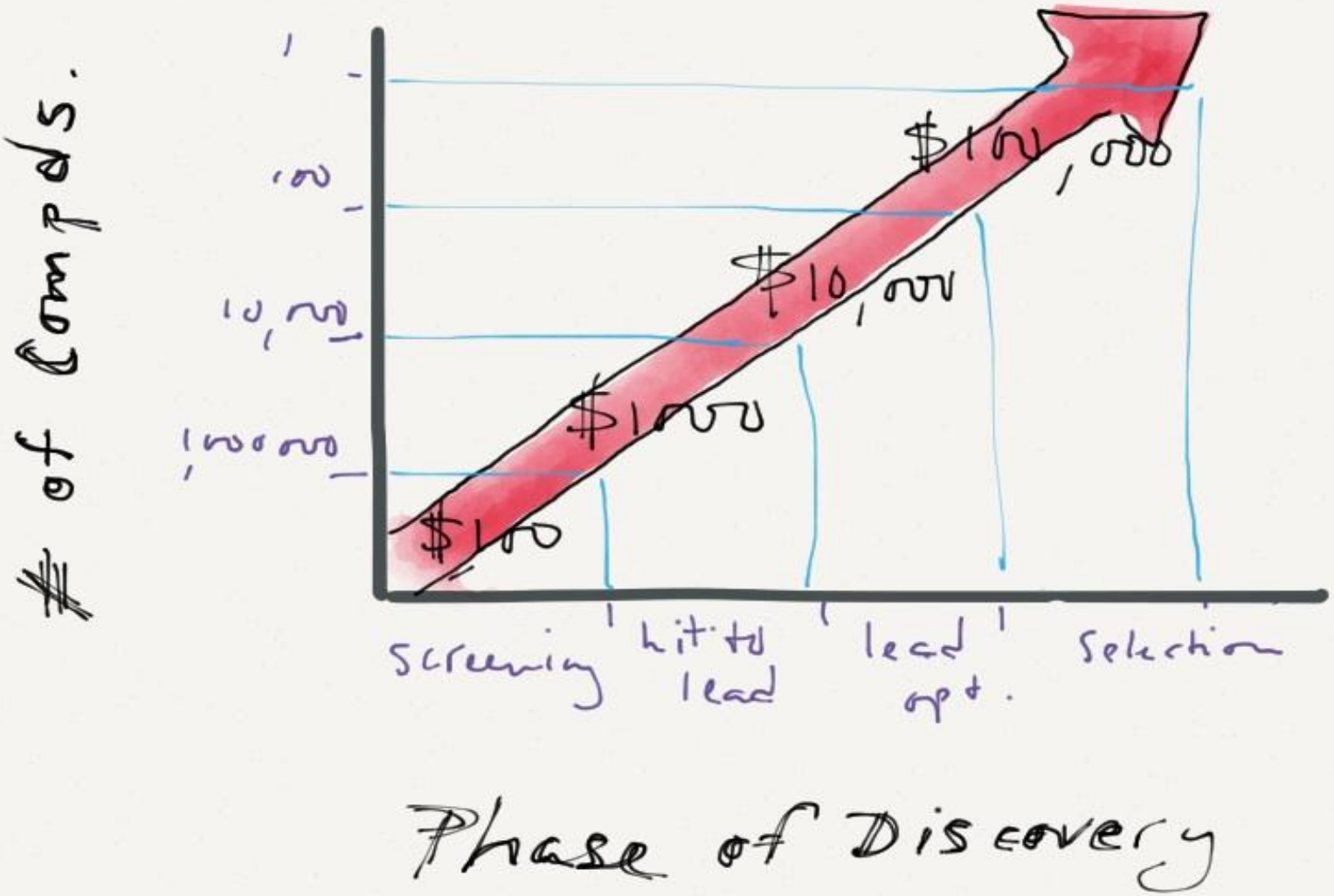
AVERICA

How Do I Rationalize What I Should Spend?

Stopping research to calculate costs and explain them can add an extra burden to scientists. This presentation takes business school concepts to understand and calculate Return on Investment (ROI) and makes them easy enough to use on scratch paper at the bench.

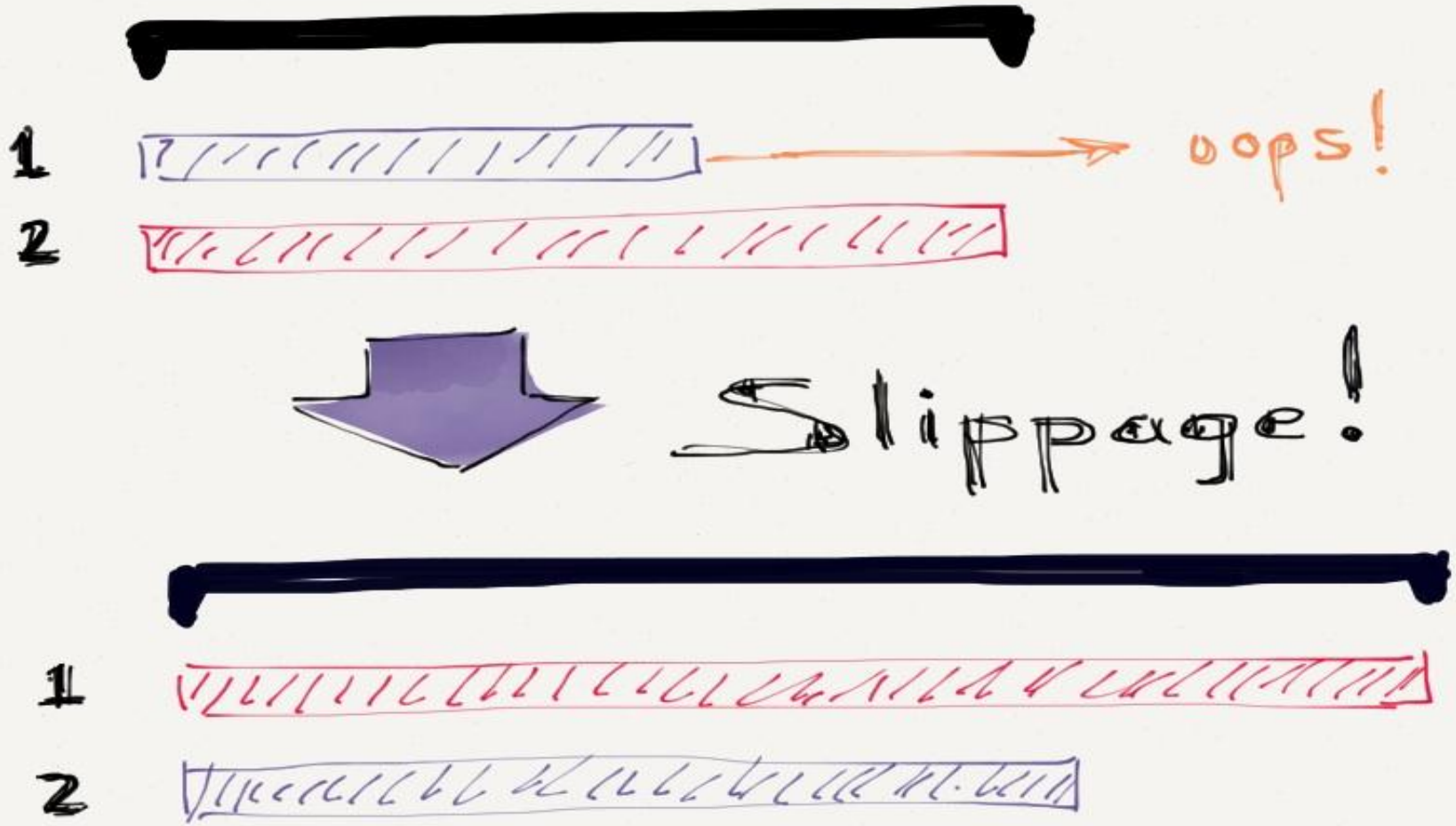
We will explore offer four fast and simple methods. Which method you use depends on both your goals and on your program's progress.

1. Changing Value
2. Negative Impact of Gantt Chart Slippage
3. Rough Calculation of Running Costs
4. Relative Costs of Alternatives


# of Compds.
1
100
10,000
1,000,000
$100
$1,000
$10,000
$100,000
Screening
Hit to lead
Lead opt.
Selection
Phase of Discovery

Changing Value

- *As the candidate advances, the reasons to spend money increase faster*
- In hit-to-lead or lead optimization:
  - How fast is the program moving – impact of delay?
  - Are there ancillary benefits: validation of mechanism? Better assay results?
- In candidate selection:
  - How much material is needed to finalize lead selection? How many compounds are potential candidates?
  - Can you source the active enantiomer in increasing amounts?
  - What are the costs of a delay or quality problem?



When Gantt chart slippage forces a new critical path.

Gantt Chart Slippage

- Discovery
  - Compound profiling determines timeline - supply should not slow things down
  - Chromatography is a quick source of chirally pure material
  - Validate mechanism, improve assay signal/noise, and speed decision making
- Development
  - Availability of larger scale supply determines timeline
  - Chromatography is a just-in-time supply strategy
  - Long term supply will require a production process, with an expensive (time, $$) development timeline

Program Run Rate

1. Assume 8 months to candidate selection
   - 6 months lead discovery
   - 2 months profiling & de-risking
2. FTE costs:
   - 2 internal @ $280,000 fully loaded cost
   - 5 external @ $100,000
3. Ancillary costs (program overhead) = $750,000
   - assays, scale-up, de-risking
   - 2/3 of this cost accrues during last two months of program!

∴ Costs:

Months 1-6 = ~~$113,000/month~~

Months 7-8 = $322,000/month

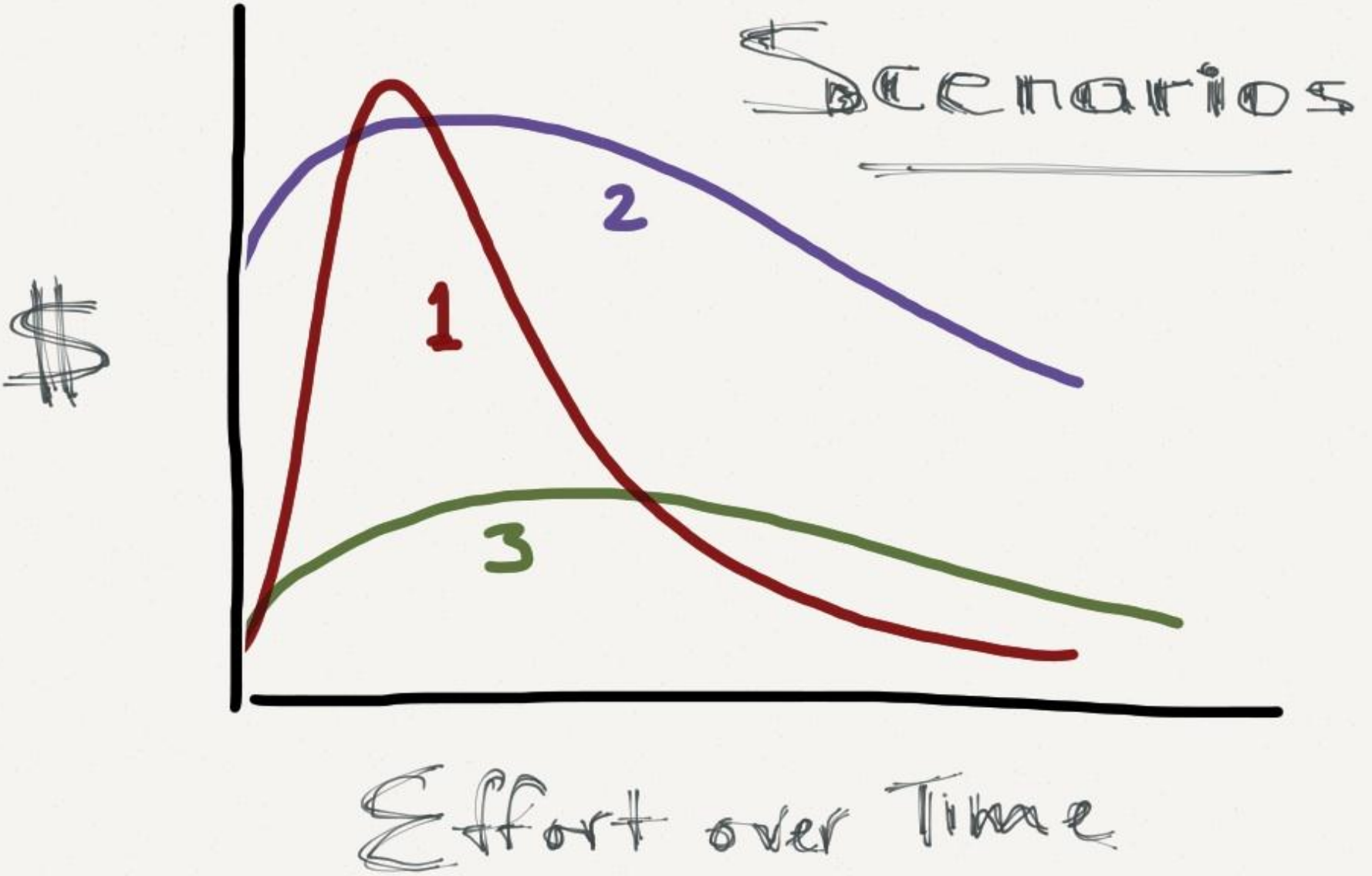
Running Cost : Common Conclusions

- Simple assumptions can lead to a fairly accurate calculation of running costs, esp. time and resources in “per unit” bites
- Weekly Discovery program costs are in the tens of thousands of $, increasing as the program progresses
- Even if you shift chemists off the program, overhead costs continue to escalate
- No matter what your absolute costs, the DIY approach makes sense only when outsourcing = delays

Decisions Based on Relative Costs

- Suppose you want 50 grams of 98% ee material for assays. Put alternatives into **time and resource** terms, and use a Program Run Cost Model. Then figure the chances of success.
  - 1-6 weeks of chemist effort to develop an asymmetric synthesis (90% chance of success)
  - 2-4 weeks of chemist effort to develop a diastereomeric crystallization (75% chance of success)
  - 1-2 weeks to resolve material chromatographically (100% chance of success)

Scenarios



Relative Cost Scenarios

Imagine a program exploring three chiral late stage leads. To nominate any one requires 200 grams for profiling and de-risking. Internal medicinal chemistry can make racemic at the 50 gram scale.

- Choices:
  1. Develop an asymmetric process and transfer it to CRO. Have them make 250-500 grams of each compound.
  2. Beg, borrow or steal internal Process Chemistry resources. Have them do it.
  3. Have medicinal chemist make 50 g at a time, and resolve it chromatographically.
- Choice 3 has limited chance of delay, and is less wasteful – it's unlikely that 200 grams will be needed for all three compounds

Averica Discovery Services

- <u>We are a boutique CRO:</u> Contract chemistry services, small molecule pharmaceutical sector, non-GMP focus
- Massachusetts corporation established 2007
- Services Include: Purification, Impurity Isolation, Analytical Method Development
- Clients in pharma, agricultural chemicals, veterinary medicine, and flavor/fragrance industry

Our strength is in speed and problem solving, with success rates that far surpass our competition

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