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A Return to Rational CNS Drug Development: De-Risking Phase 3 Investments Through Rigorous Early Phase Drug Evaluations

Part 2: Session Chairs

Gary Sachs/Atul R. Mahableshwarkar

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Designing the Right Series of Experiments

Part 2: Session Chairs

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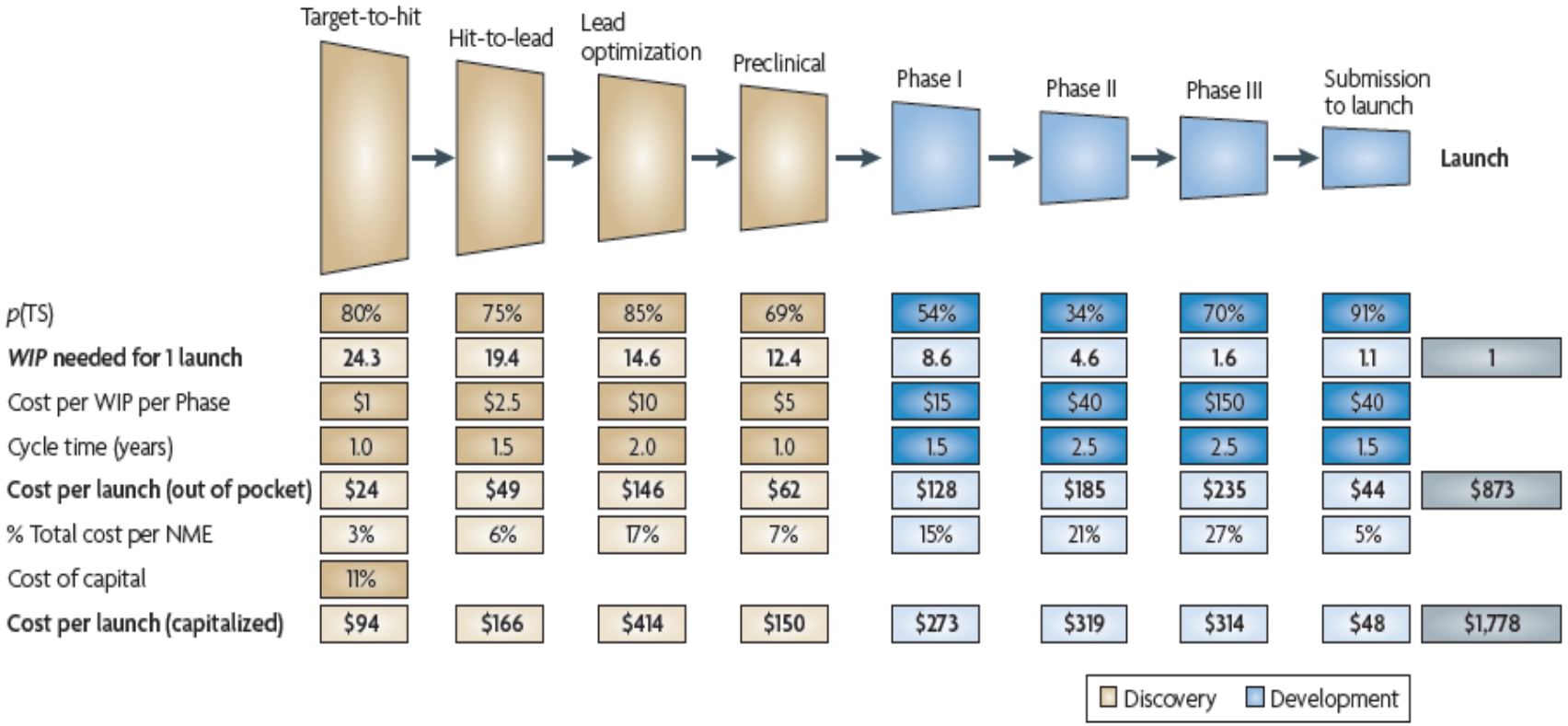
Standard R&D Model

Costs to Successfully Discover a Single New Molecular Entity



p(TS)	80%	75%	85%	69%	54%	34%	70%	91%	
***WIP* needed for 1 launch**	24.3	19.4	14.6	12.4	8.6	4.6	1.6	1.1	1
Cost per WIP per Phase	$1	$2.5	$10	$5	$15	$40	$150	$40	
Cycle time (years)	1.0	1.5	2.0	1.0	1.5	2.5	2.5	1.5	
Cost per launch (out of pocket)	$24	$49	$146	$62	$128	$185	$235	$44	$873
% Total cost per NME	3%	6%	17%	7%	15%	21%	27%	5%	
Cost of capital	11%								
Cost per launch (capitalized)	$94	$166	$414	$150	$273	$319	$314	$48	$1,778

Discovery Development

Paul SM et al. *Nature Reviews/Drug Discovery* 2010;9:203

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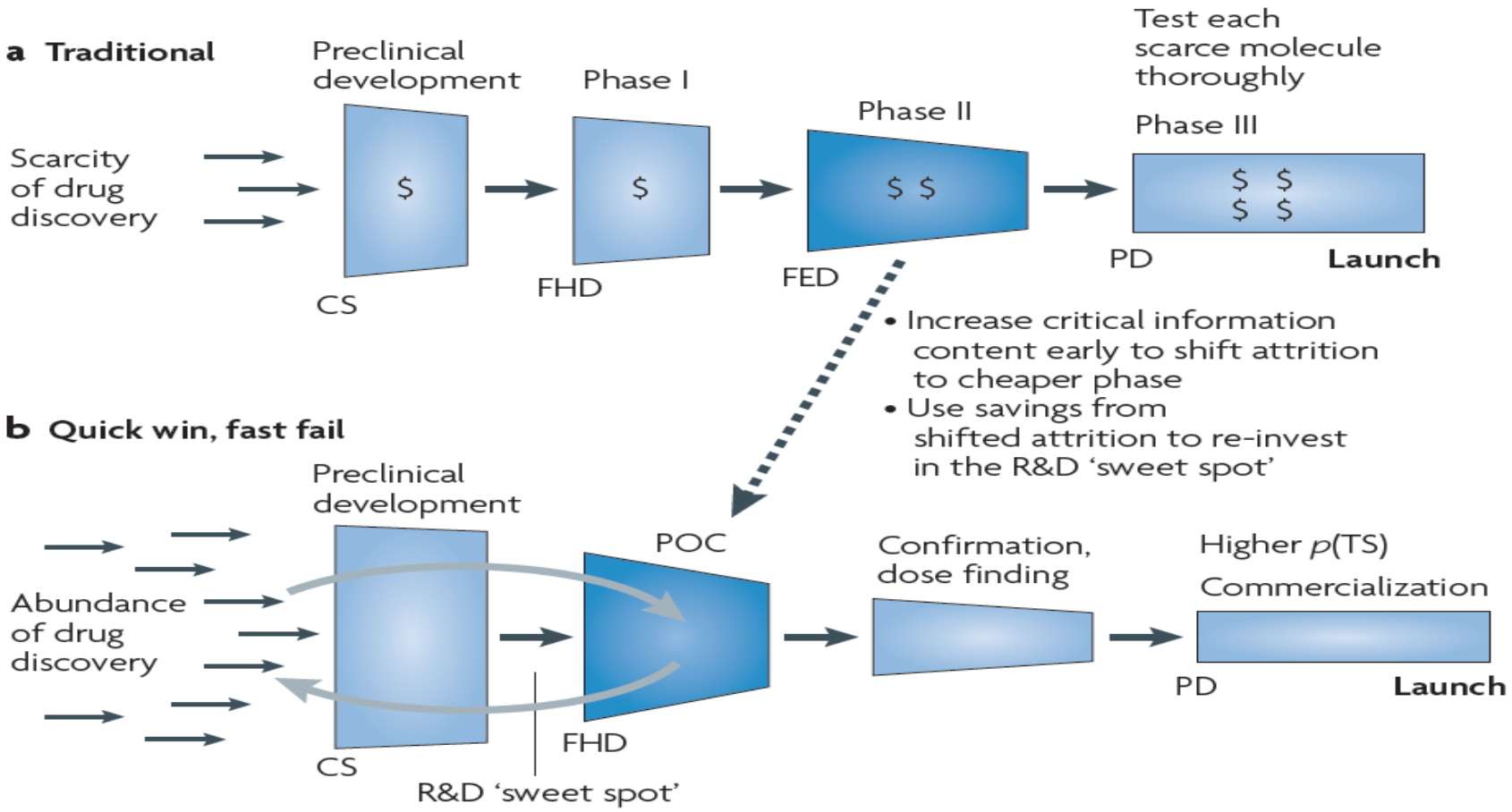
Alternative Models / Alternative Objectives



Paul SM et al. *Nature Reviews/Drug Discovery* 2010;9:203

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Traditional Development Paradigm

Trial → Learning → Trial → Learning → Trial → Learning

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Questions to be Answered

- Translation of pre-clinical safety and tolerability to humans
- Translation of PK and tolerability from healthy volunteers to patients
- Selecting dose for first in class compounds
- Establishing dose range
- Ensuring the right patient population

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Complications

- Resource constraints
- New hypotheses to understand diseases
- New regulatory guidances
- Inconsistent data

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New Questions

- How to combine steps and answer more questions from less/single trial
  - Ensure an enriched population
  - Appropriately sensitive instruments
  - Running a combo epidemiology/efficacy trial
- How to run trial to support new disease hypothesis and assess drug response
- How to incorporate new regulatory guidances in trial that are also sensitive to payer needs