The use of decision analysis for Phase 2 and Phase 3 drug development decisions

Elayne Ko — Manager, Deloitte Financial Advisory Services LLP
Charles Persinger — Sr. Research Scientist, Eli Lilly and Company

Decision Analysis Affinity Group Conference

May 2012

Agenda

- Brief overview of pharmaceutical drug development
- Characteristics of Phase 2 and 3 drug development
- Application of decision analysis process to Phase 2 and 3 decisions
- Connectivity between Phase 2 and Phase 3 decisions
- Example
- Implications on approach and value provided
- Summary
- Q&A

Brief overview of pharmaceutical drug development process

	Research	Development			Regulatory
	Pre-clinical	Phase 1	Phase 2	Phase 3	Registration
Primary objective	Progress compound to test in humans	Demonstrate safety in healthy subjects	Demonstrate efficacy in intend to treat population, dose finding	Demonstrate/ confirm safety and efficacy in larger population	Obtain regulatory and market approval from government agencies
Key risks and uncertainties	Animal studies, toxicology, PK/PD modeling	PK/PD, side effects and tolerability	Proof of concept study: explore possible efficacy of drugs	Confirmatory study: ability of compound to meet study endpoints	Regulatory review, 1st cycle review approval; market uptake and peak market share
Historical industry NME Success rates[1]	63%	47%	23%	59%	79%
Cost per project[2]	$20M	$15M	$40M	$150M	$40M
Number of molecules/ projects in development	LLY[3] PFE[4]	29 26	22 35	12 18	2 11

Decision analysis prior to Phase 3 starts is a major area of focus for the industry

1 – PBF 2011 R&D Performance Success Rates (2006-2010 Industry), KMR Group
2 – How to Improve R&D Productivity, SM Paul et. al, Nature Reviews Drug Discovery, Volume 9, March 2010
3 – www.lilly.com (molecules in development from website on 3/23/12)
4 – www.pfizer.com (projects in development as of 2/28/12)

Characteristics of Phase 2 and Phase 3 drug development

Characteristics	Phase 2 studies	Phase 3 studies
Uncertainties		
Technical	**High** (haven't tested efficacy)	**Lower** (endpoints, long-term safety)
Commercial	**High** (long way from market)	**Lower,** but key consideration (closer to market)
Regulatory	**High** (but likely resolved later)	**Lower** (End-of-Phase 2 discussions)
Decisions		
Influence on future value	**High** (outcome influences Phase 3)	**Limited** (influences life cycle, commercial)
Flexibility	**High** — many degrees of freedom (indication, endpoints, design)	**Limited** (regulatory requirements)
Perception of importance	**Lower** (less resources, many uncertainties remaining)	**Significant** (large costs, externally reported, more certain financial implications)

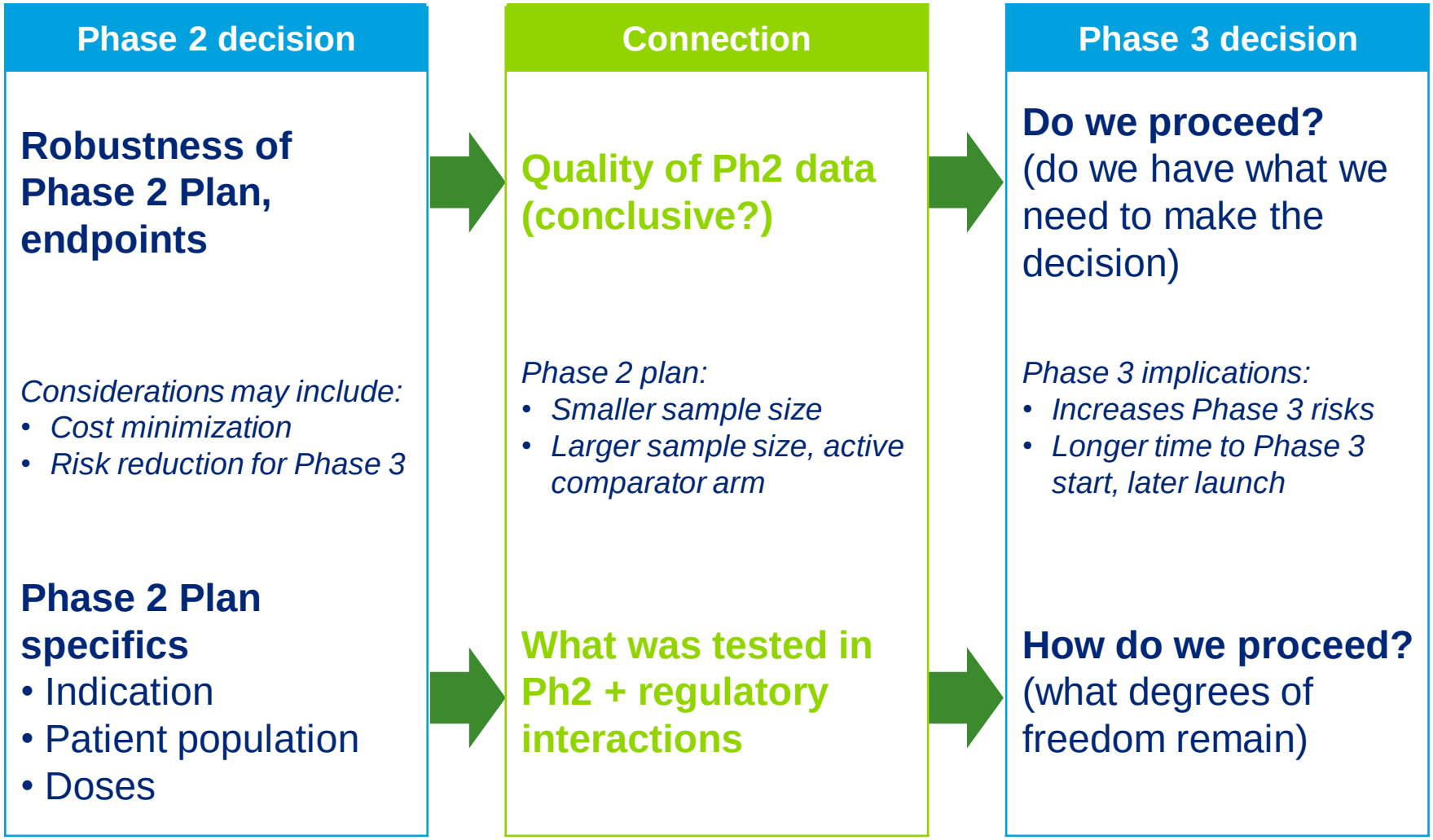
Applications of decision analysis process on Phase 2 and 3 decisions

DA process	Phase 2 studies	Phase 3 studies
Dec. maker	• R&D (with business unit input)	• Business unit + corporate level
Context	• Significant scientific uncertainties • Competing for funding	• Focus on getting drug to market • Highly visible (press releases and company-level financial implications)
Key decisions	• Do we proceed? • How do we proceed? • What do we need to learn?	• Do we proceed? • How big of a bet? • How do we compete in the market?
Alternatives/ degrees of freedom	• Robustness of plan — scientific • Development plan approach • Endpoints (biomarker vs. Clinical) • Indication, patient population • Statistical plan	• Robustness of plan — commercial • Geographies • (Limited) Patient population • (Limited) Endpoints
Value criteria	• Cost (limited resources) • Risk resolution/learning • Downstream implications	• Commercial value • Cost • Speed

Applications of decision analysis process on Phase 2 and 3 decisions

DA process	Phase 2 studies	Phase 3 studies
Data	• Technical uncertainties (significant, limited clinical data) • Commercial — high level (market size, peak sales) • Regulatory uncertainties • Development Costs	• Technical uncertainties (remaining based on Ph2 data) • Commercial — detailed revenue forecasts (market, payers, competition) • Regulatory uncertainties • Development Costs
Model	Multiple criteria with focus on: • Total remaining development cost • Risk resolution/learning • Development/launch timing	Multiple criteria with focus on: • eNPV (commercial value) • Costs, e.g., commercial, COGS • p(TS) • Development/launch timing
Analyze and evaluate	• Sensitivities to technical inputs (potential efficacy, adverse events)	• Sensitivity to commercial inputs (competitors, label, access and reimbursement)
Decision	• Made by R&D budget holder with input from Business Unit	• Made by Business Unit leadership and/or Corporate-level leadership

Connectivity — Phase 2 and Phase 3 decisions



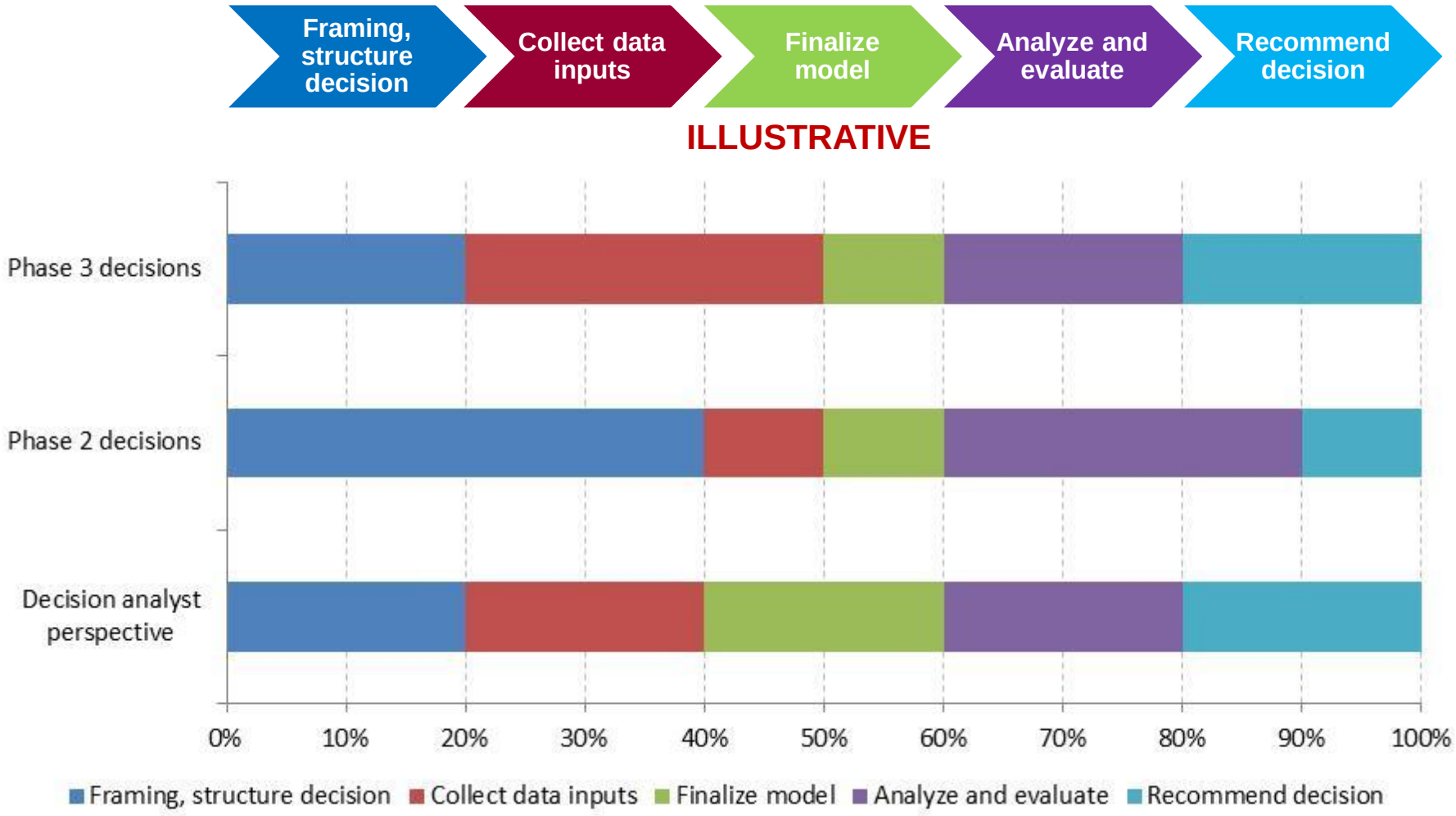
Example — Decision analysis for Phase 2 and 3 decisions

Development	Phase 2 studies*		Phase 3 studies*
Target indication	• Mild to moderate Alzheimer's Disease (AD)		• Mild to moderate (AD)
Dosing/ formulation	• 0.15, 0.5, 1.0, or 2.0 mg/kg IV once every 13 weeks	• 3 different doses given subcutaneously monthly	• 0.5mg/kg, 1.0mg/kg once every 13 weeks
Number of subjects	• 234/196	• 120	• 1000/1300
Timeframe	• 78 weeks	• 78 weeks	• 78 weeks
Primary endpoint	• Safety and tolerability: treatment-emergent adverse events, clinically important changes in safety assessment results	• To evaluate effect on cerebral amyloid burden	• Cognitive and functional (ADAS-COG, DAD)
Secondary endpoint	• Efficacy: Cognitive and functional measurements (ADAS-COG, DAD, MMSE, dependency scale, RUD lite)	• Safety and effect on cognitive and functional endpoints	• Imaging and biochemical biomarkers of disease status (e.g., brain amyloid burden, CSF p-tau, vMRI, CDR-SoB)
Commercial	• Limited primary market research to estimate physician, patients/caregivers, payer preferences • High-level revenue forecast estimates in selected major markets		• In-depth market research with detailed revenue forecasts for all major markets

Alzheimer's Disease Assessment Scale (ADAS-COG), Disability Assessment for Dementia (DAD), Mini Mental State Examination (MMSE), Resource Utilization in Dementia (RUD), cerebrospinal fluid (CSF), volumetric magnetic resonance imaging, Clinical Dementia Rating Sum of Boxes (CDR-SoB)

* Source: www.clinicaltrials.gov

Implications on approach and value provided



Summary, Q&A

Benefit of DA: Pharmaceutical companies benefit from decision analysis on drug development decisions, in particular, Phase 2 and 3 investments where uncertainties are plentiful and costs are significant

Ph2 and Ph3 are different: Differences in the characteristics of Phase 2 and 3 drug development programs influences the practical application and focus of the decision analysis process

Importance of Ph2 decisions: The consequences and impact of Phase 2 decisions on the Phase 3 program necessitate an increased focus on the use of decision analysis for Phase 2 decisions

Approach to Ph2 decisions: Due to numerous degrees of freedom, significant uncertainties, multiple stakeholders (R&D and the Business Units) and the downstream consequences of Phase 2 decisions, these decisions require an increased emphasis on the first step of the DA process (framing and structuring)

This presentation contains general information only and Deloitte Financial advisory Services LLP ("Deloitte FAS") and Eli Lilly and Company ("Eli Lilly") are not, by means of this presentation, rendering accounting, business, financial, investment, legal, tax, or other professional advice or services. This presentation is not a substitute for such professional advice or services, nor should it be used as a basis for any decision or action that may affect your business. Before making any decision or taking any action that may affect your business, you should consult a qualified professional advisor.

Neither Deloitte FAS nor Eli Lilly shall be responsible for any loss sustained by any person who relies on this presentation.