The Implications of Segmenting Disease Indications

PRESENTATION AT
SYMPOSIUM ON BEST PRACTICES IN CLINICAL STUDY DESIGN IN RARE DISEASE

30 APRIL, 2013

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Financial Acknowledgement

THIS WORK HAS BEEN SUPPORTED
IN PART BY:

ELI LILLY & CO.

THE MERCK FOUNDATION

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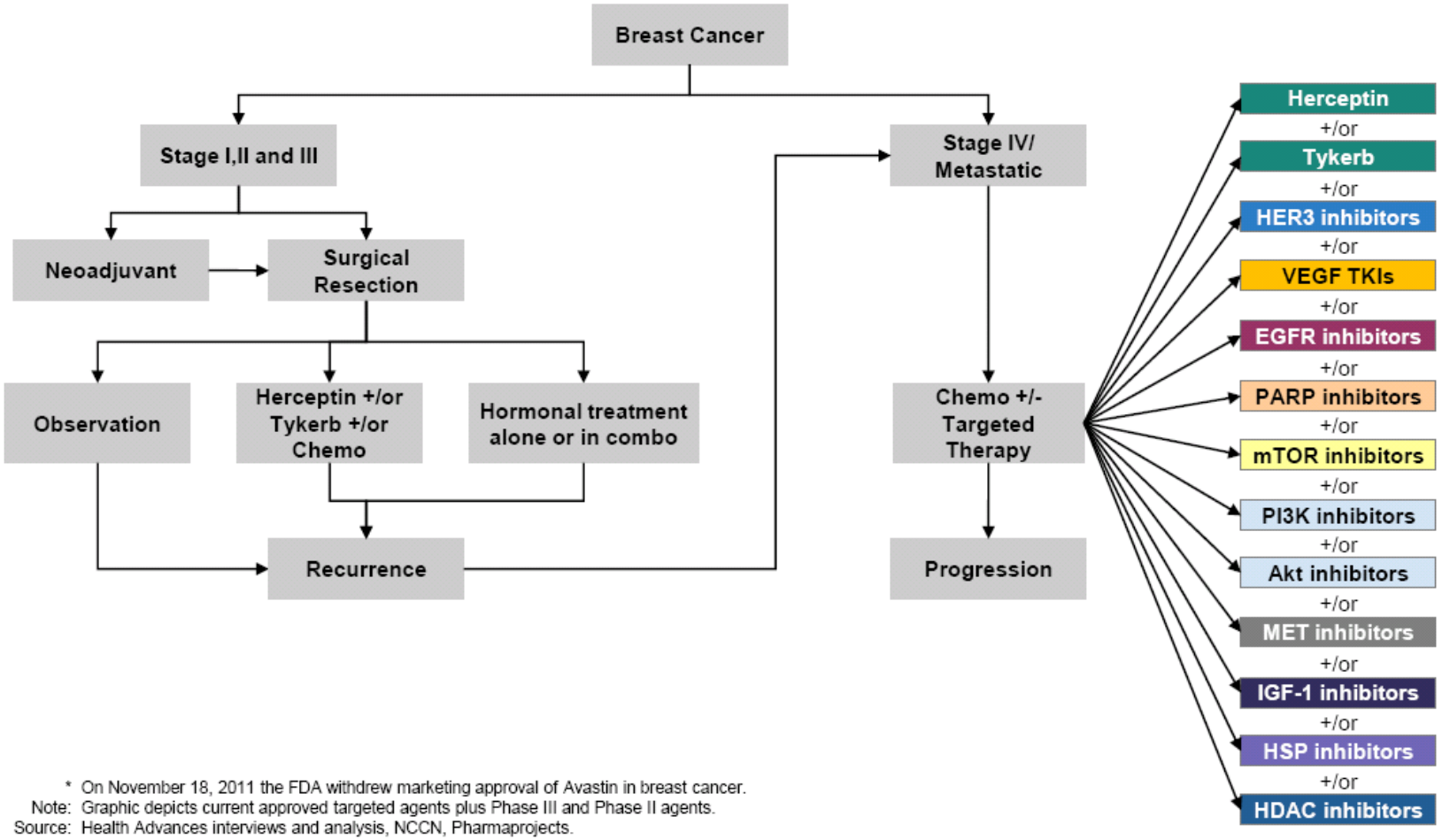
Diseases Fragmenting into Molecular Types



* On November 18, 2011 the FDA withdrew marketing approval of Avastin in breast cancer.
Note: Graphic depicts current approved targeted agents plus Phase III and Phase II agents.
Source: Health Advances interviews and analysis, NCCN, Pharmaprojects.

Commercialising Personalised Medicine
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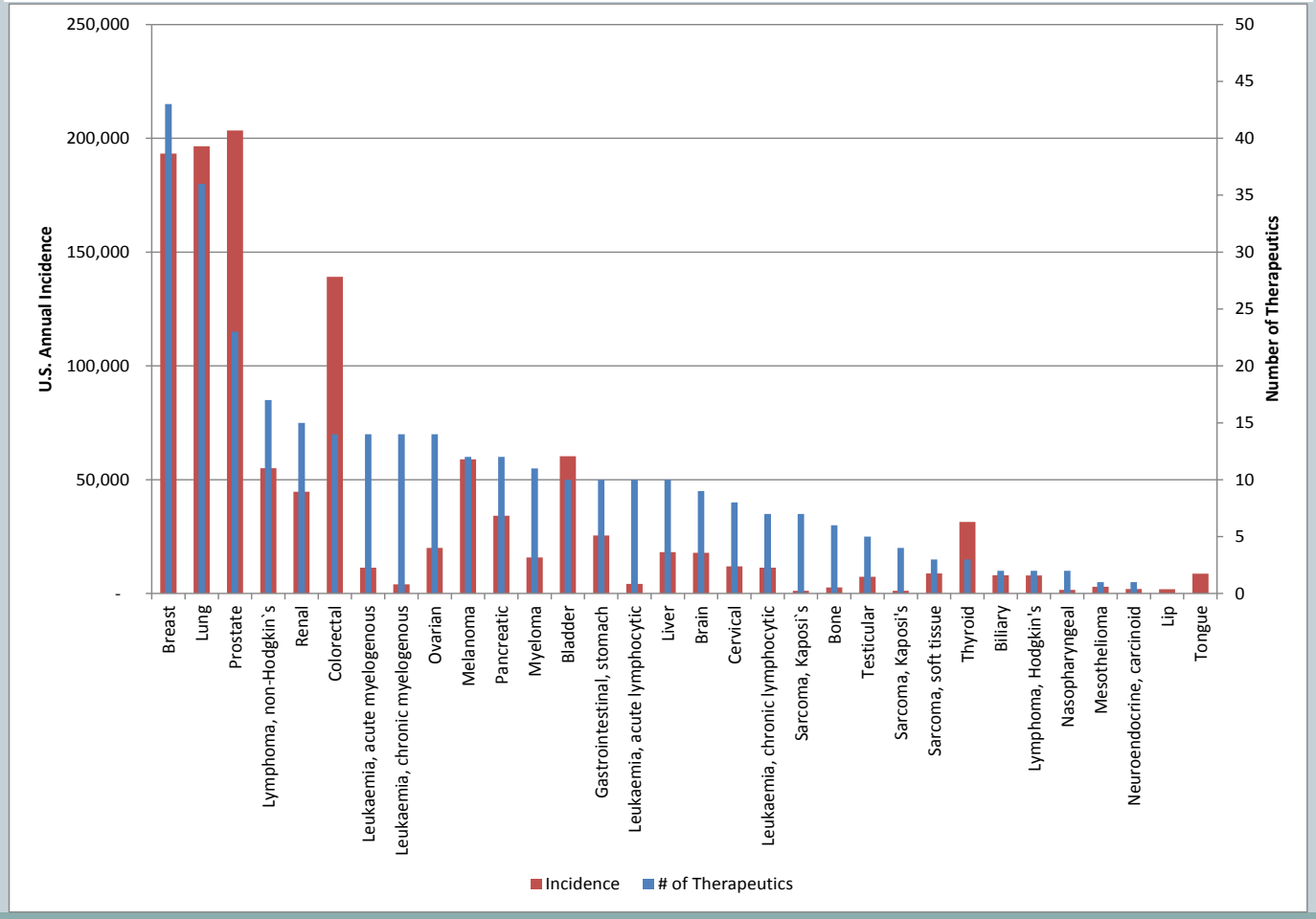
HEALTH ADVANCES

Historically, Larger Incidence Organ Types Receive Most Therapeutic Options

Cancer organ of origin incidence with number of approved therapeutics for each



Stratified Medicine Development Rapidly Becoming Uneconomic

SCENARIO

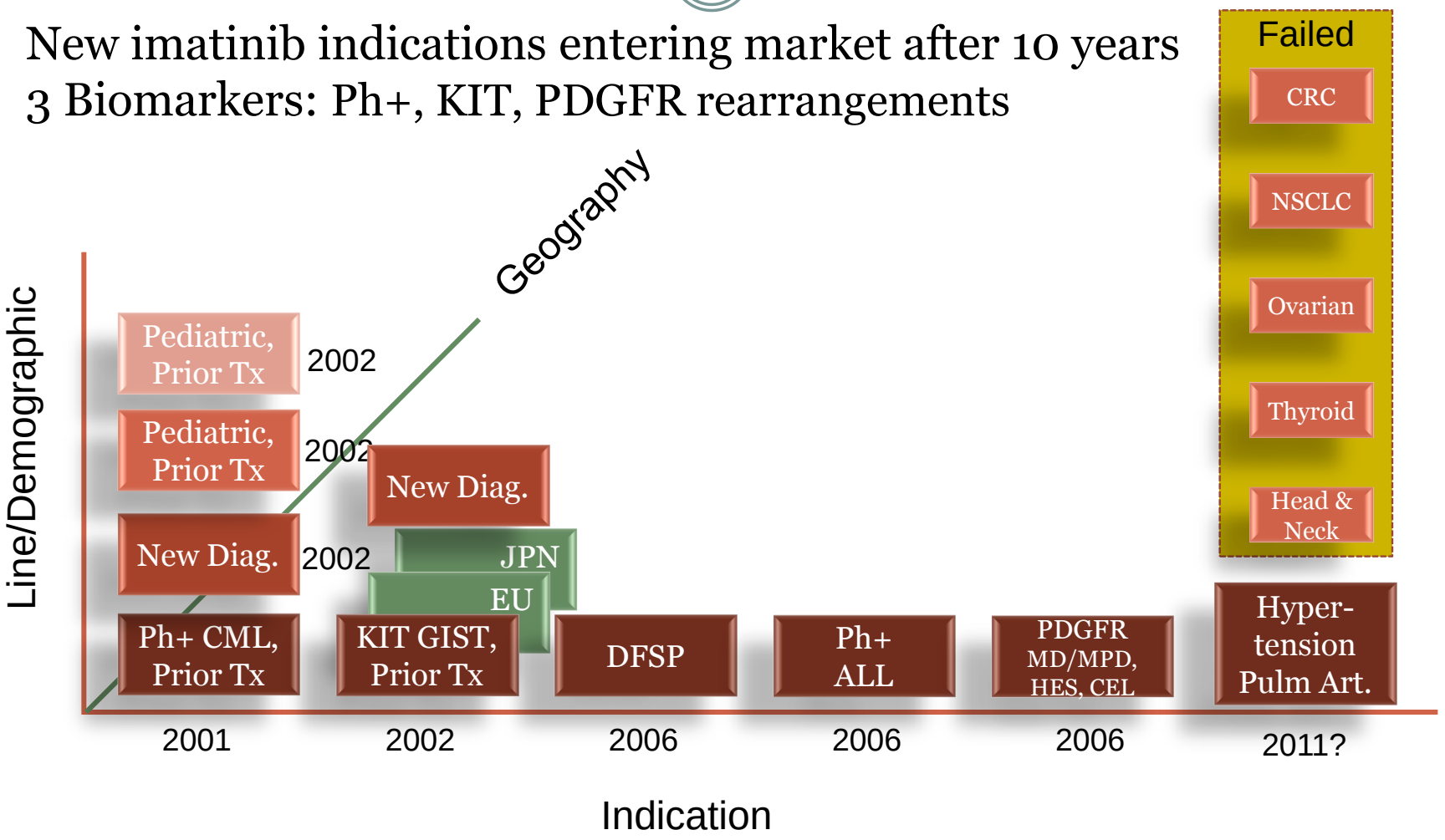
	S1: Empiric, Large Cancer
Cost of Development ($M)	$400
Years of Development	7
Net Patent Life	13
# of Eligible Patients/ Year	200,000
Revenue per Patient	$20,000
Peak Market Share (of Eligible)	40%
Peak Patients Treated	80,000
Peak Revenue ($M)	$1,600
Years to Reach Peak	6
Costs as % of Revenue	40%
Taxes	35%
After Tax Margin	39%
Peak Year Net Income	$624
Discount Rate	11%
NPV	**$1,166**

Inputs in **bold red** differ from Empiric, Large Cancer base case, Scenario S1

Trusheim, Berndt: Economic Challenges and Possible Policy Actions to Advance Stratified Medicine, *Personalized Medicine*, 9(4)413-427June 2012

Extending a Therapeutic to Molecularly Similar Diseases Not Always Effective

- New imatinib indications entering market after 10 years
- 3 Biomarkers: Ph+, KIT, PDGFR rearrangements



Making Stratified Medicines Attractive for Investment (Public or Private)

SCENARIO

	S7: Empiric, Small Cancer, Extend Exclusivity
Cost of Development ($M)	$400
Years of Development	7
Net Patent Life	**33**
# of Eligible Patients/ Year	**20,000**
Revenue per Patient	$20,000
Peak Market Share (of Eligible)	40%
Peak Patients Treated	8,000
Peak Revenue ($M)	$160
Years to Reach Peak	6
Costs as % of Revenue	40%
Taxes	35%
After Tax Margin	39%
Peak Year Net Income	$62
Discount Rate	11%
NPV	**($64)**

Inputs in **bold red** differ from Empiric, Large Cancer base case, Scenario S1 in Table 1

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Increasing Pressures on Economic Incentives Moving towards Pharmageddon Scenarios

Regulatory
CLIA lab restriction
Multi-variate test guidance
Rejection of retrospective data

Product Exclusivity
Biosimilar 7-12 year period
Diag Patent restrictions
Unclear Orphan designation

Drug Reimbursement
Asymmetric post-launch adjustment
4th Tier formulary

Provider Adoption
Poor Adherence to EBM
Restricted product education/detailing

Diagnostic Reimbursement
Remains 'cost plus' rather than value
No payer investment in R&D

Academic Research Standard Assymetry
New biomarker claims often statistically underpowered
Retrospective, Meta analysis not confirmed prospectively (KRAS)