Case Study:
Strategy Evaluation for a Pharmaceutical Oncology Asset

Erik C. Johnson
Bristol-Myers Squibb Company
February 25, 2004

Background

Oncology drug development differs from other disease areas in a few key areas:

- Phase I multiple ascending dose (MAD) study is proof of principle (PoP)
- Opportunity to file with Phase II data
- Sales in the U.S. are generated through both agency-approved indications and published Phase II data (compendia)
- Nearly all oncology assets show activity in multiple tumor types and therefore pursue multiple indications to maximize return on investment
- Key market drivers are efficacy followed by safety
- Therapy is administered through regimens

Situation Assessment

- Oncology asset has completed preclinical work without major safety issues
- Asset may work in any solid tumor
- Unmet medical need allows for accelerated filing options in certain lines of therapy and tumor types
- Sales generated through approval of indication or compendia published in 2 approved journals

Next decision point is to initiate Phase I first in human (FIH) studies to determine dose and identify potential efficacy

Analysis includes subsequent decision point to commence registrational trials

Generate Alternatives

Tumor Type		Population	Design	Regulatory Objective	Endpoint 1°	Endpoint 2°
Breast	Metastatic	Taxane refractory	Polytherapy	Accelerated	TTP	OS
		1st line chemo	Polytherapy	Full approval	OS	TTP
		1st or 2nd line hormonal	Polytherapy	Compendium	TTP	
Ovarian	Metastatic	3rd line	Monotherapy	Accelerated	RR	
		2nd line	Mono/Poly	Full approval	TTP	OS
		1st line	Polytherapy	Full approval	OS	
Bladder	Metastatic	2nd line	Monotherapy	Accelerated	RR	
		2nd line Her2 IHC +, ++ or +++	Polytherapy	Full approval	TTP	OS
		1st line	Polytherapy	Full approval	OS	
Pancreatic	Metastatic	2nd line	Monotherapy	Accelerated	OS	
		1st line	Polytherapy	Full approval	OS	
Head & Neck	Metastatic or unresectable	Not eligible for XRT	Polytherapy	Compendium	RR/TTP	
Colorectal	Metastatic	3rd line	Monotherapy	Accelerated	RR	
		2nd line	Polytherapy	Full approval	OS	
NSCLC	Metastatic	3rd line	Monotherapy	Compendium	RR	
		2nd line	Polytherapy	Compendium	RR/TTP	
		1st line	Polytherapy	Compendium	RR/TTP	

TTP=Time to progression OS=Overall survival RR=Response rate

Note: Phase I MAD study results will confirm efficacy in the tumor type

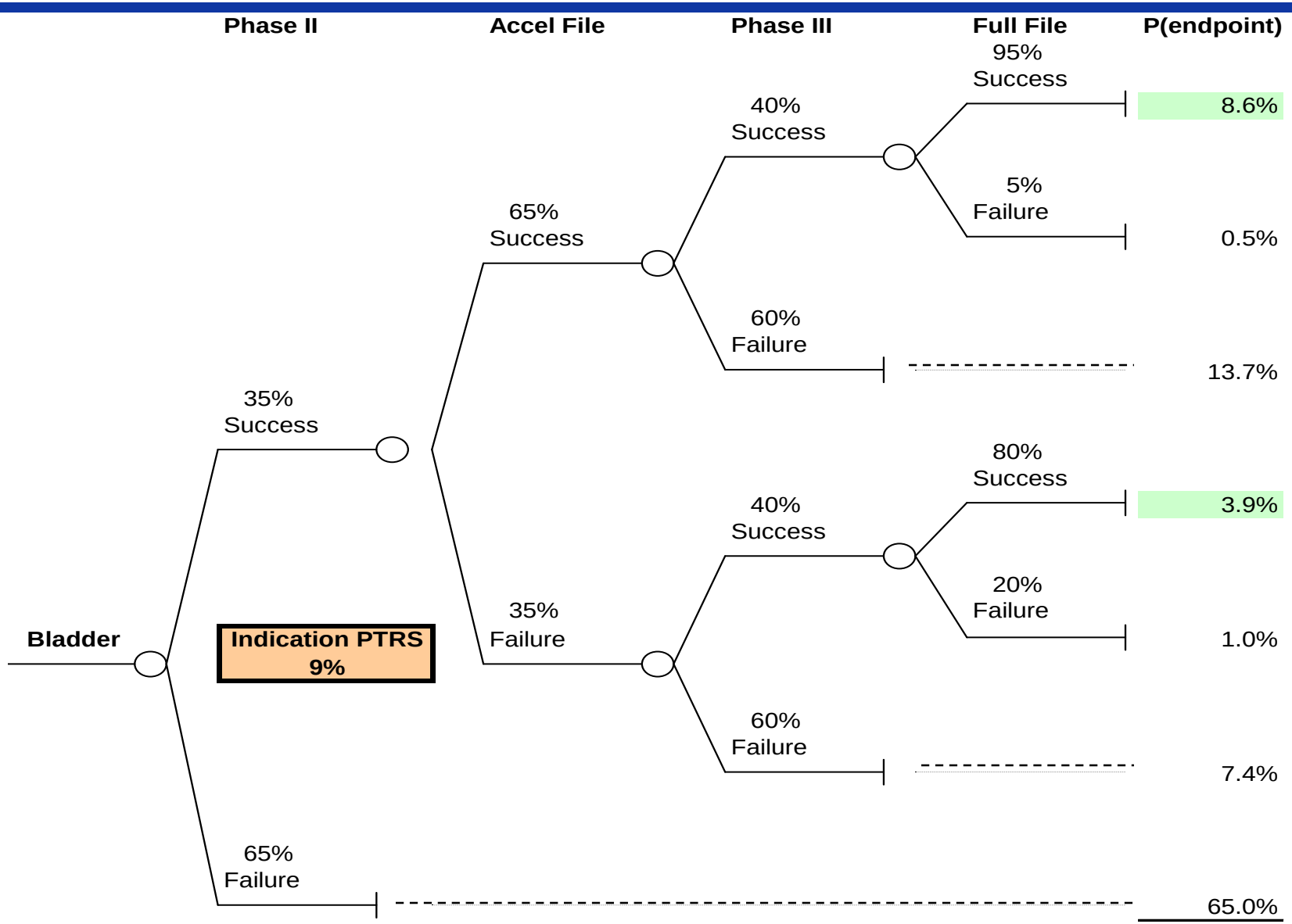
Uncertainties

- Use expert judgment grounded around industry benchmarks
- Considerations include:
  - efficacy
  - safety & tolerability
  - small molecule vs. biologic
  - novel or established mechanism of action
  - endpoint(s) - response rate, time to progression, overall survival
  - regulatory agency - FDA, EMEA, KIKO
  - regulatory goal - subpart H, accelerated review, full approval
- Objective senior management committee to review across portfolio

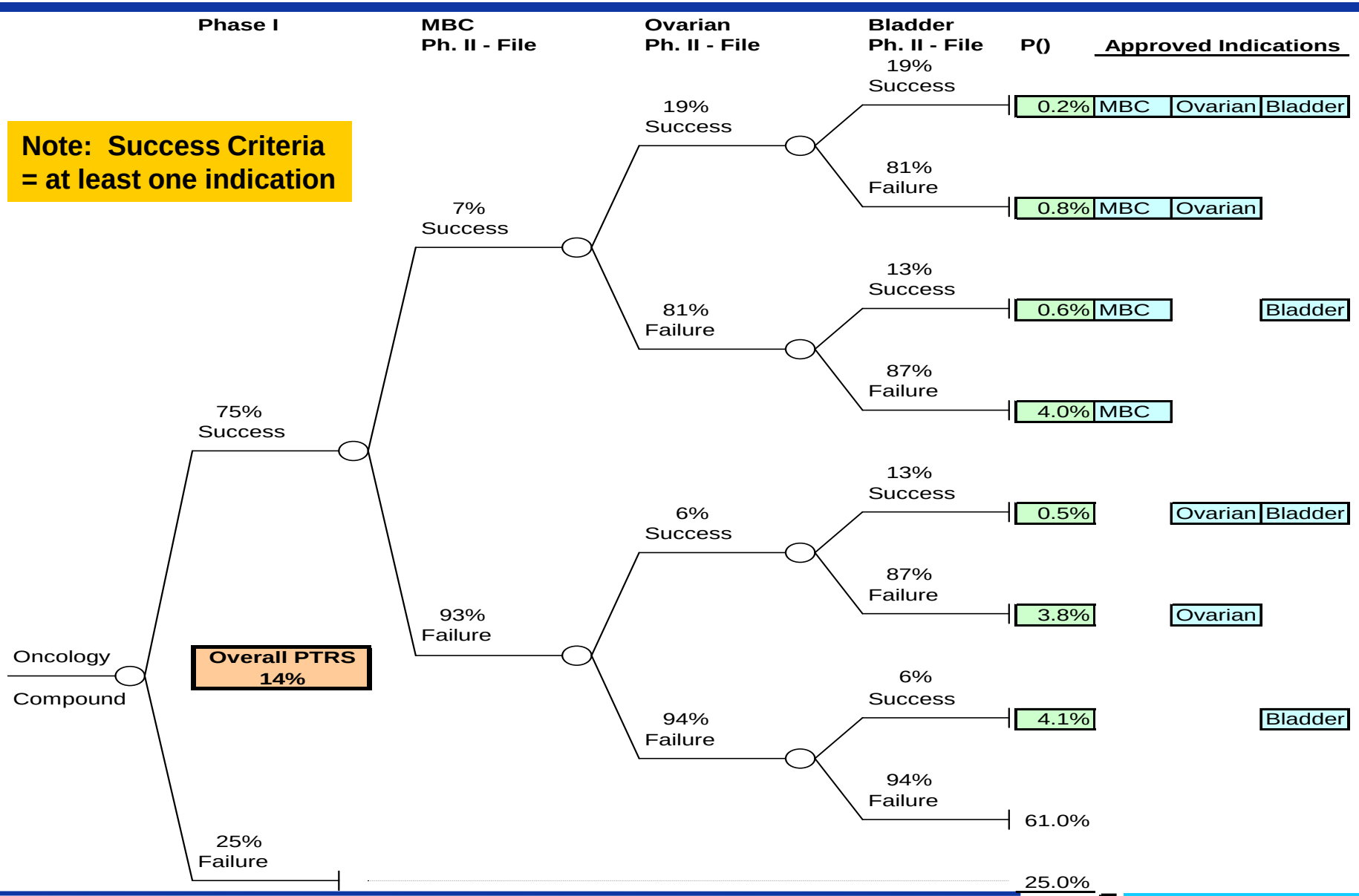
Uncertainties

Tumor Type	Population		Phase I	Phase II	Phase III	Accel File	Full File	Confirm File	Overall
Breast	Metastatic	Taxane refractory	75%	70%	30%	50%	65%	95%	
		1st line chemo			45%		85%		**20%**
		1st or 2nd line hormonal		70%					53%
Ovarian	Metastatic	3rd line	75%	35%		60%			
		2nd line			50%		85%	95%	**11%**
		1st line			30%		80%		6%
Bladder	Metastatic	2nd line	75%	35%		65%			
		2nd line Her2 IHC +, ++ or +++			50%		85%	95%	**11%**
		1st line			30%		80%		6%
Pancreatic	Metastatic	2nd line	75%	35%		60%		95%	
		1st line			25%		80%		5%
Head & Neck	Metastatic or unresectable	Not eligible for XRT	75%	35%					26%
Colorectal	Metastatic	3rd line	75%	35%		60%		95%	4%
		2nd line			30%		80%	95%	6%
NSCLC	Metastatic	3rd line	75%	70%					53%
		2nd line		60%					45%
		1st line							45%

Indication Decision Tree



Combined Decision Tree



Development Cost

- Development costs calculated for each opportunity
- Considerations include:
  - Study size (# of patients, # of sites)
  - Timing
  - Comparator(s), if any
  - Diagnostics to measure response, if any
  - In-house vs. CRO
  - Affiliated studies (food effect, ADME,etc.)
- Development costs include all studies needed for approval, regulatory fees and Phase IV commitments
- Several of the studies are required regardless of which indications are selected - the lead indication is burdened with these studies

Commercial Forecast

- Commercial forecast is developed for each opportunity
- Considerations include:
  - Market share
    - Monotherapy vs. polytherapy
    - Line of therapy
  - Courses of therapy
  - Cost per course
  - Compliance rate
- Forecasts
  - include sales, COGS and direct marketing expenses
  - are estimated for compendia sales and indication sales
  - are developed for each major region (US, EU, Japan, ROW)
  - are developed for high, base & low scenarios

Analysis

Uncertainty, revenue and costs are all combined to evaluate each opportunity:

Opportunity		PTRS	Development Costs ($MM)		Peak Sales ($MM)	
			Indication	Compendia	Indication	Compendia
Breast	Taxane refractory	6%	$ 8	$ 3	$ 37	$ 8
	1st line chemo		$ 18	$ 4	$ 499	$ 27
	1st or 2nd line hormonal	53%	$ 21	$ 6	$ 50	$ 18
Ovarian	3rd line	9%	$ 8	$ 3	$ 31	$ 13
	2nd line		$ 8	$ 4	$ 26	$ 11
	1st line	6%	$ 18	$ 6	$ 54	$ 39
Bladder	2nd line	9%	$ 7	$ 3	$ 19	$ 6
	2nd line Her2 IHC +, ++ or +		$ 7	$ 4	$ 19	$ 7
	1st line	6%	$ 16	$ 5	$ 45	$ 32
Pancreatic	2nd line	7%	$ 12	$ 5	$ 2	$ 1
	1st line	5%	$ 13	$ 6	$ 2	$ 1
Head & Neck	Not eligible for XRT	26%	$ 18	$ 9	$ 12	$ 7
Colorectal	3rd line	4%	$ 21	$ 6	$ 88	$ 29
	2nd line	6%	$ 24	$ 8	$ 126	$ 53
NSCLC	3rd line	53%	$ 15	$ 4	$ 85	$ 23
	2nd line	45%	$ 18	$ 6	$ 35	$ 21
	1st line	45%	$ 23	$ 8	$ 50	$ 18

Tradeoffs

- Balance development risk vs. which indication will get the asset to market quickest
- Positioning relative to competitors may require entry in later stages of disease
- ROI to pursue approved indication vs. compendia listing
- Structure development plan to include contingency for lead indication failure vs. 2nd and 3rd indications as exclusively life cycle management opportunities
- Pursue Japan approvals
- Strategic considerations across oncology franchise and total portfolio

Recommendation

Opportunity		PTRS	Development Costs ($MM)		Peak Sales ($MM)		Maximum ROI		
			Indication	Compendia	Indication	Compendia	ENPV ($MM)	NPV Given	EIRR (%)
Breast	Taxane refractory	6%	$ 8	$ 3	$ 37	$ 8	$ 7	$ 256	26%
	1st line chemo		$ 18	$ 4	$ 499	$ 27	$ 19	$ 416	28%
	1st or 2nd line hormonal	53%	$ 21	$ 6	$ 50	$ 18	$ 3	$ 125	38%
Ovarian	3rd line	9%	$ 8	$ 3	$ 31	$ 13	$ 4	$ 185	14%
	2nd line		$ 8	$ 4	$ 26	$ 11	$ 4	$ 180	13%
	1st line	6%	$ 18	$ 6	$ 54	$ 39	$ 3	$ 85	12%
Bladder	2nd line	9%	$ 7	$ 3	$ 19	$ 6	$ 4	$ 163	15%
	2nd line Her2 IHC +, ++ or +		$ 7	$ 4	$ 19	$ 7	$ 4	$ 163	15%
	1st line	6%	$ 16	$ 5	$ 45	$ 32	$ 3	$ 108	12%
Pancreatic	2nd line	7%	$ 12	$ 5	$ 2	$ 1	$ 3	$ 50	16%
	~~1st line~~	~~5%~~	~~$ 13~~	~~$ 6~~	~~$ 2~~	~~$ 1~~	~~$ 2~~	~~$ 98~~	~~12%~~
Head & Neck	Not eligible for XRT	26%	$ 18	$ 9	$ 12	$ 7	$ 4	$ 115	19%
Colorectal	3rd line	4%	$ 21	$ 6	$ 88	$ 29	$ 12	$ 114	11%
	2nd line	6%	$ 24	$ 8	$ 126	$ 53	$ 18	$ 174	16%
NSCLC	3rd line	53%	$ 15	$ 4	$ 85	$ 23	$ 5	$ 78	44%
	2nd line	45%	$ 18	$ 6	$ 35	$ 21	$ 8	$ 102	58%
	~~1st line~~	~~45%~~	~~$ 23~~	~~$ 8~~	~~$ 50~~	~~$ 18~~	~~$ 6~~	~~$ 87~~	~~38%~~

Highest ROI Lowest ROI

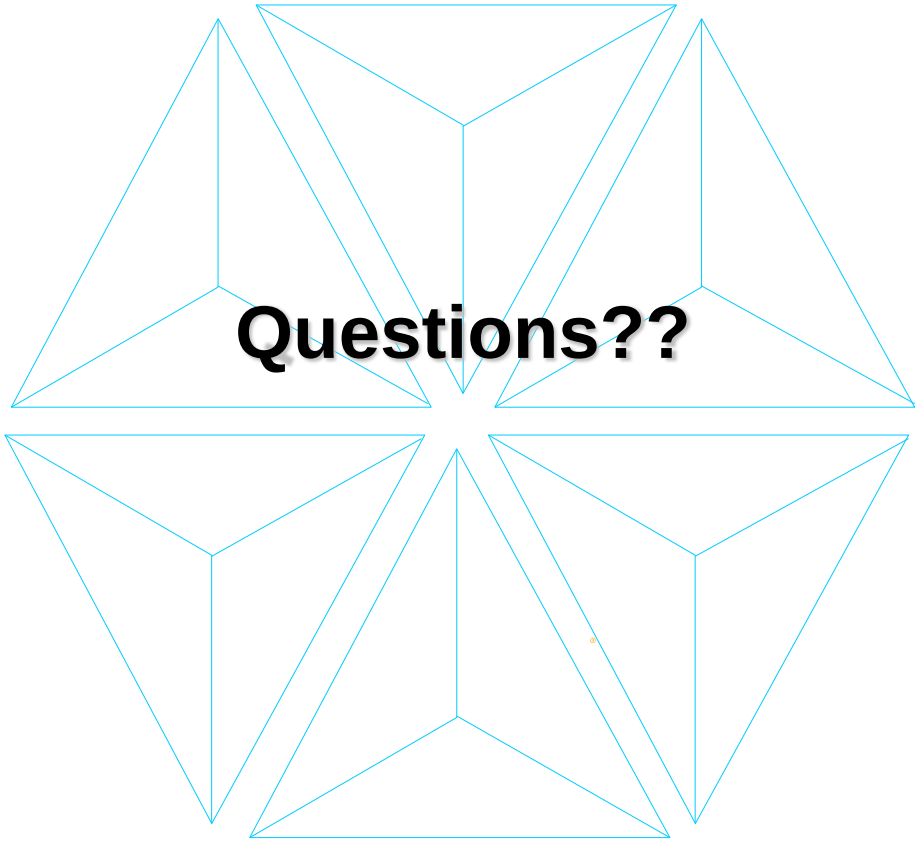
Opportunity removed for strategic reasons

Key Takeaways

- Initial clinical development plan included 14 Phase II trials and 10 Phase III trials with a total cost over $350MM and average ROI of 16%
  - Recommended plan includes 6 Phase II trials and 5 Phase III trials with a total cost less than $200MM and average ROI of 28%
  - Recommended plan allows for potential sales in all tumor types and most lines of therapy originally considered
- Accelerated filing opportunities are included for each of the 3 indications
  - “Multiple shots on goal” improves overall probability of success
  - Accelerated approval generates sales quicker and shortens the uptake curve

Key Takeaways

- Can’t simply choose the opportunities with the highest return
  - Opportunities have shared costs
  - Dependencies exist between tumor types and lines of therapy
  - Need to include contingency option(s)


Questions??