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# Eight Thoughts On Biosimilars

SCB Biosimilars Conference Call

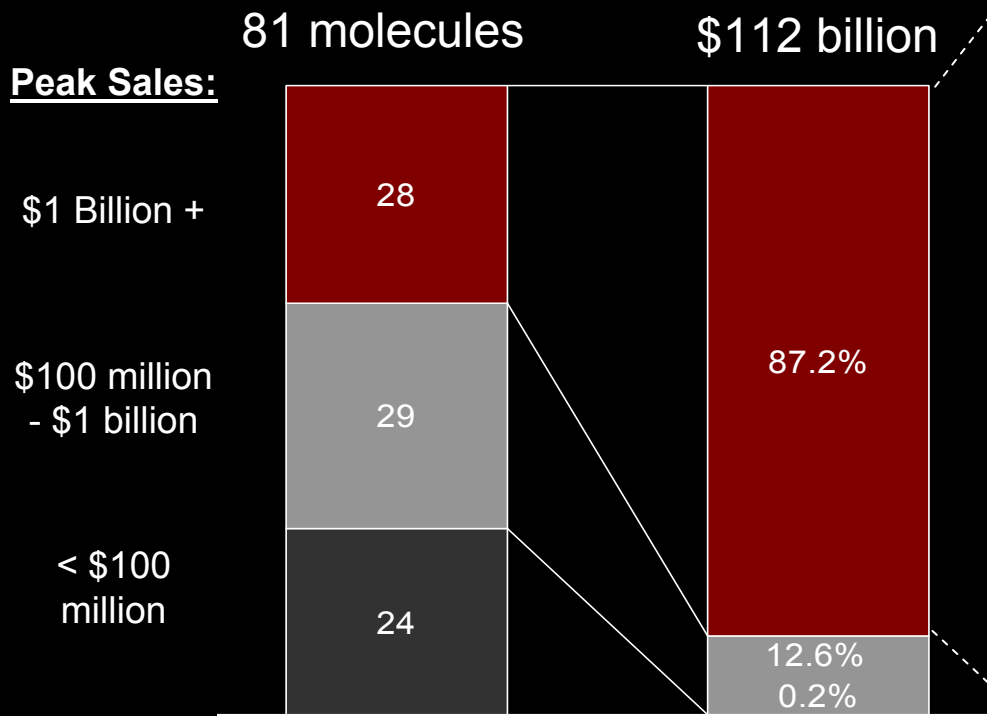
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DISCLOSURES AND ANALYST CERTIFICATIONS**

# Biologics: Too Big To Ignore

28 Molecules make up 87.2% of value of biologics



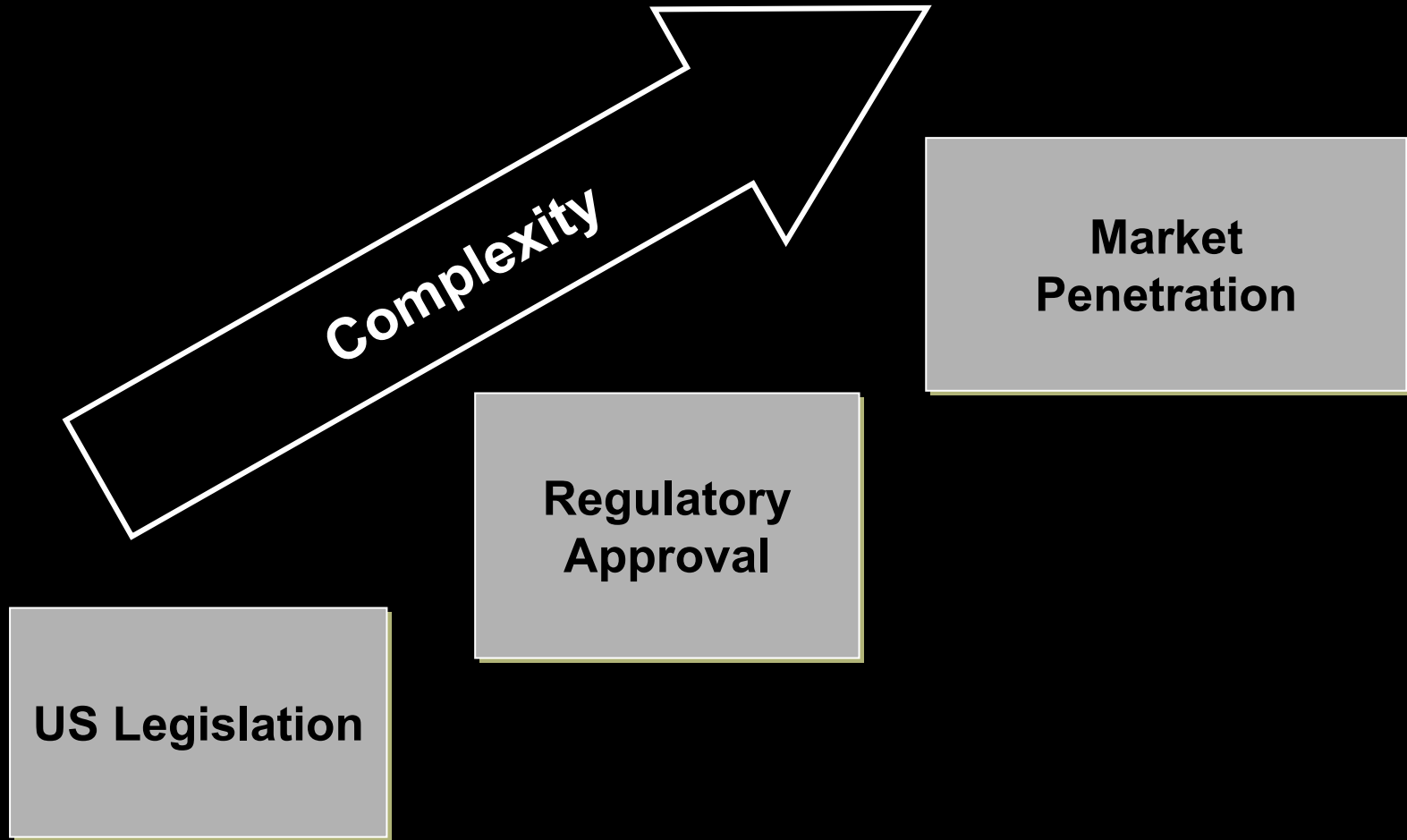
Peak Sales Potential			
Brand Name	Global Peak Sales > \$1 Bil	Brand Name	Global Peak Sales > \$1 Bil
Avastin	9.2	Avonex	2.6
Enbrel	8.0	Novolin	2.5
Remicade	7.9	Humalog	2.2
Humira	7.3	PEGasys	2.0
Rituxan	7.3	Rebif	1.7
Herceptin	5.7	Cerezyme	1.5
Lantus	5.1	NovoSeven	1.4
Epogen/Procrit	5.1	Tysabri	1.4
Neulasta	4.2	Neupogen	1.3
Novolog	3.8	Synagis	1.3
Erbix	3.6	Betaseron	1.2
Aranesp	3.2	Humulin	1.1
Recombinant	2.9	Kogenate FS	1.1
Lucentis	2.7		

**Regulation Of Commoditization process Is Needed**

Note: 81 molecules include all products approved under BLA and biologics approved under NDA. Peak sales from analyst models (SCB or consensus, as available Source: FDA, Thompson, Zachs, Bernstein estimates and analysis

# Ready, Set...For A Marathon, Not A Sprint

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# **Eight Thoughts On Biosimilars**

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- US legislation: Details Matter
- The FDA: The unknown regulatory hurdle
- Market structure: PBM as the king-makers?
- Costs: Time and money, capacity at a premium
- Targets: Now, Later and Never
- Market share: Benchmarks and wrinkles
- Market participants: The usual and unusual suspects
- Impact on the Generic Group: Is It All Worth It?

# US Legislation: Watch For Details To Determine Market Structure

## Approval Requirements

- Agreement: FDA will determine requirements case-by-case
- Definition of Biologic still open (vaccines? DNA? mixtures?)
- Innovators want to tack on process requirements (guidance docs, clinical trial, all patent resolution)
- Generics want requirements for timely FDA actions (PDUFA dates, citizen petition)

## Approval Standards

- ‘*Biosimilar*’ standard largely agreed upon
- Will there be an *interchangeability* standard?
- Will there be *Bio-better* standard?
- Still unclear what approval means, exactly... (indications, naming)

## Data exclusivity periods

- More than 5 years, less than 12. call it EU-like 10?
- Fair exclusivity for second generation drugs?
- Will there be an exclusivity for first to file?

## Patent resolution pathway

- Both sides need patent resolution ahead of biosimilar launch
- BUT, topic is poorly understood
- Current ideas for pathway look very complex
- Could delay pathway creation

# The FDA – Mixed Signals

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## Agency is clearly interested in Biosimilars

### Engaged

- Involved in debate
- Proactively divided reviewing responsibilities

### hGH

- Approved under 505j, may have received interchangeability (Sandoz never requested)

### LMWH

- FDA may approve without pivotal trials, EMEA regulate as biosimilar

### mAb

- FDA staffers do not see big difference from other molecules, EMEA does

## But record shows agency usually takes conservative road, and it has plenty of room for conservative choices here

### AMPh / Premarin / LMWH

- The FDA has shown inability to resolve citizen petition on less complex issues

### Myozyme

- Significant requirements due to change in facility

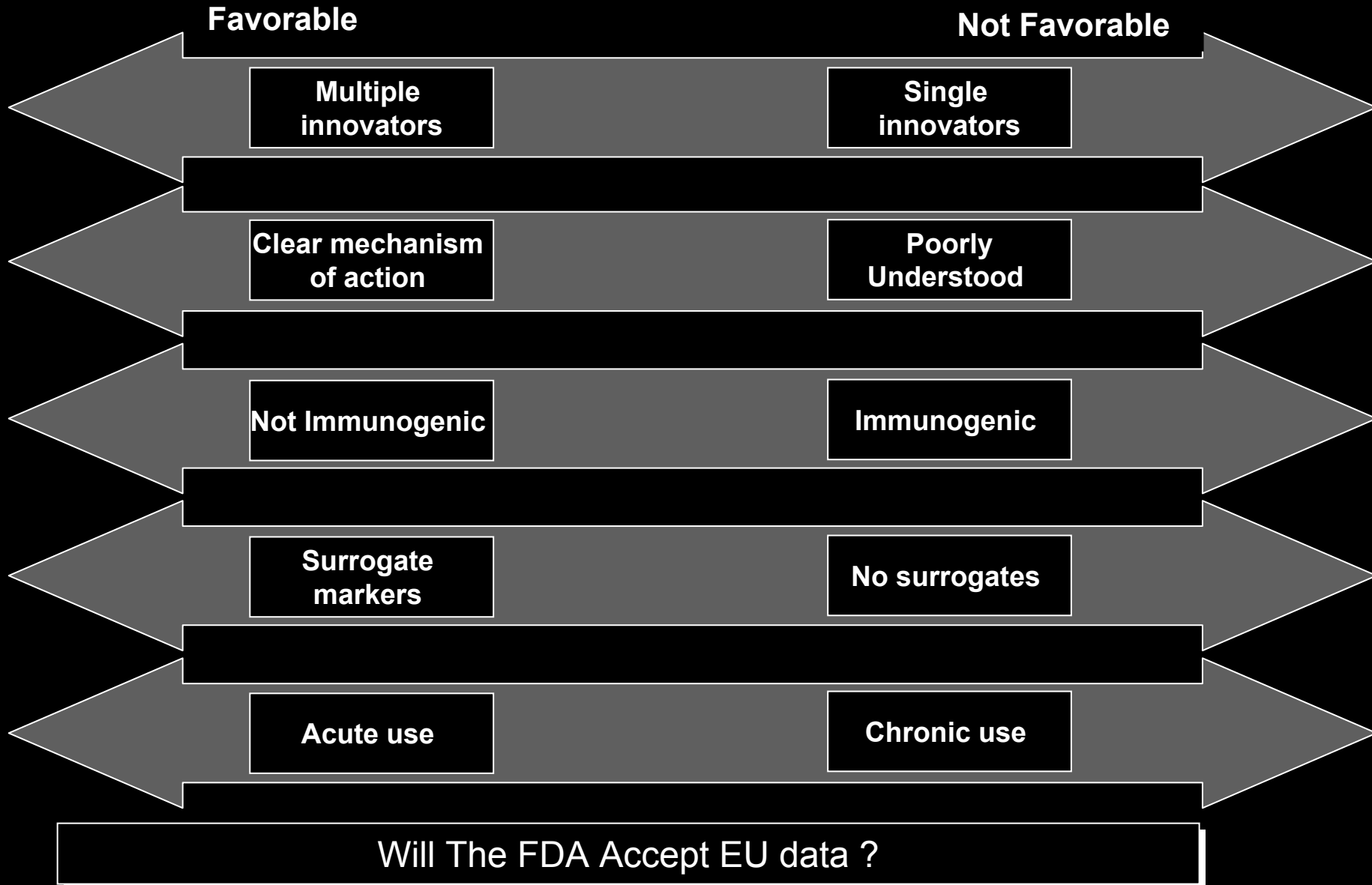
### Cautionary Stories

- Eprex
- Raptiva (Xoma to DNA facility)
- Insulin Merval (EU – PK/PD)

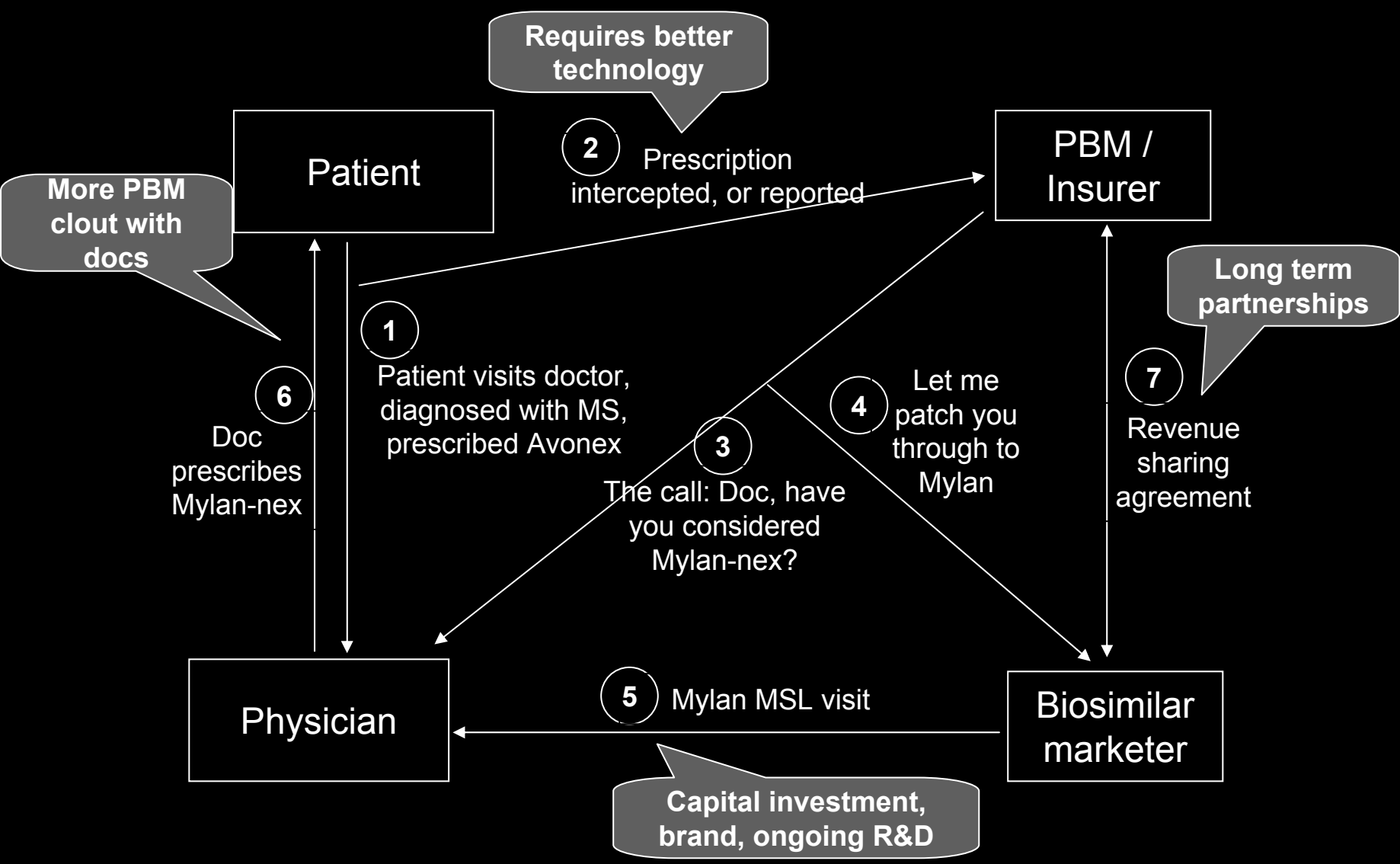
### Complex mechanisms

- What you don't know
- Multiple effects

# The FDA: What Will Influence Approvability?



# Market Structure – PBM As The King-Makers? Winner Takes All Markets?



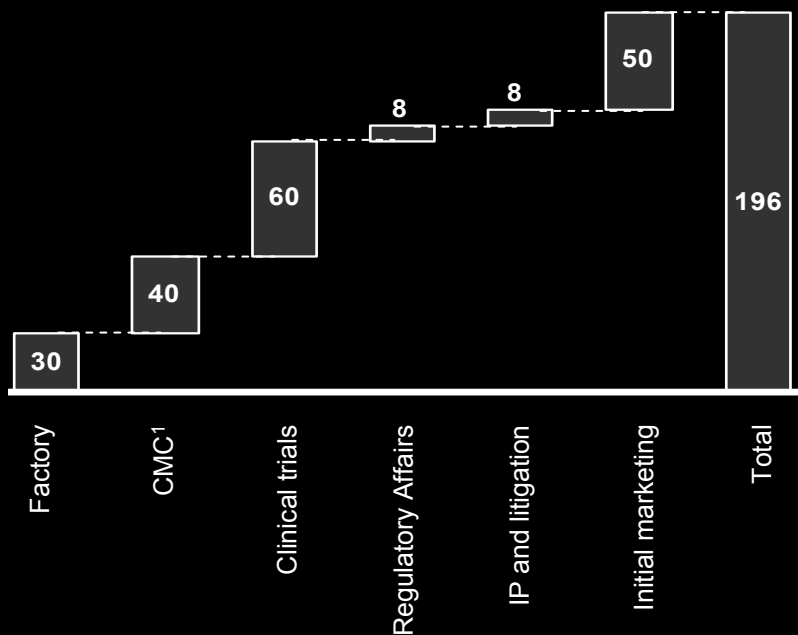
Note: conceptual example. Source: Bernstein estimates and analysis



# Costs (I): Not A Low Cost Proposition

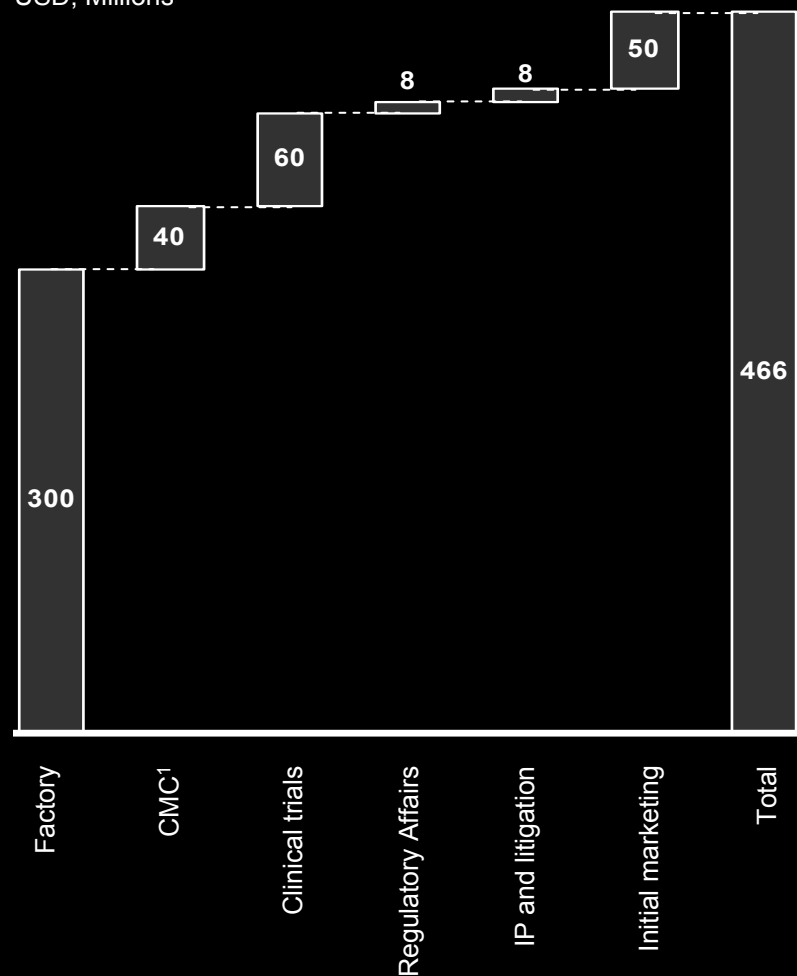
## Bacterial facility

USD, Millions



## Mammalian facility

USD, Millions



## Costs (II): The CapEx Dilemma

Building mammalian capacity makes CFO uneasy

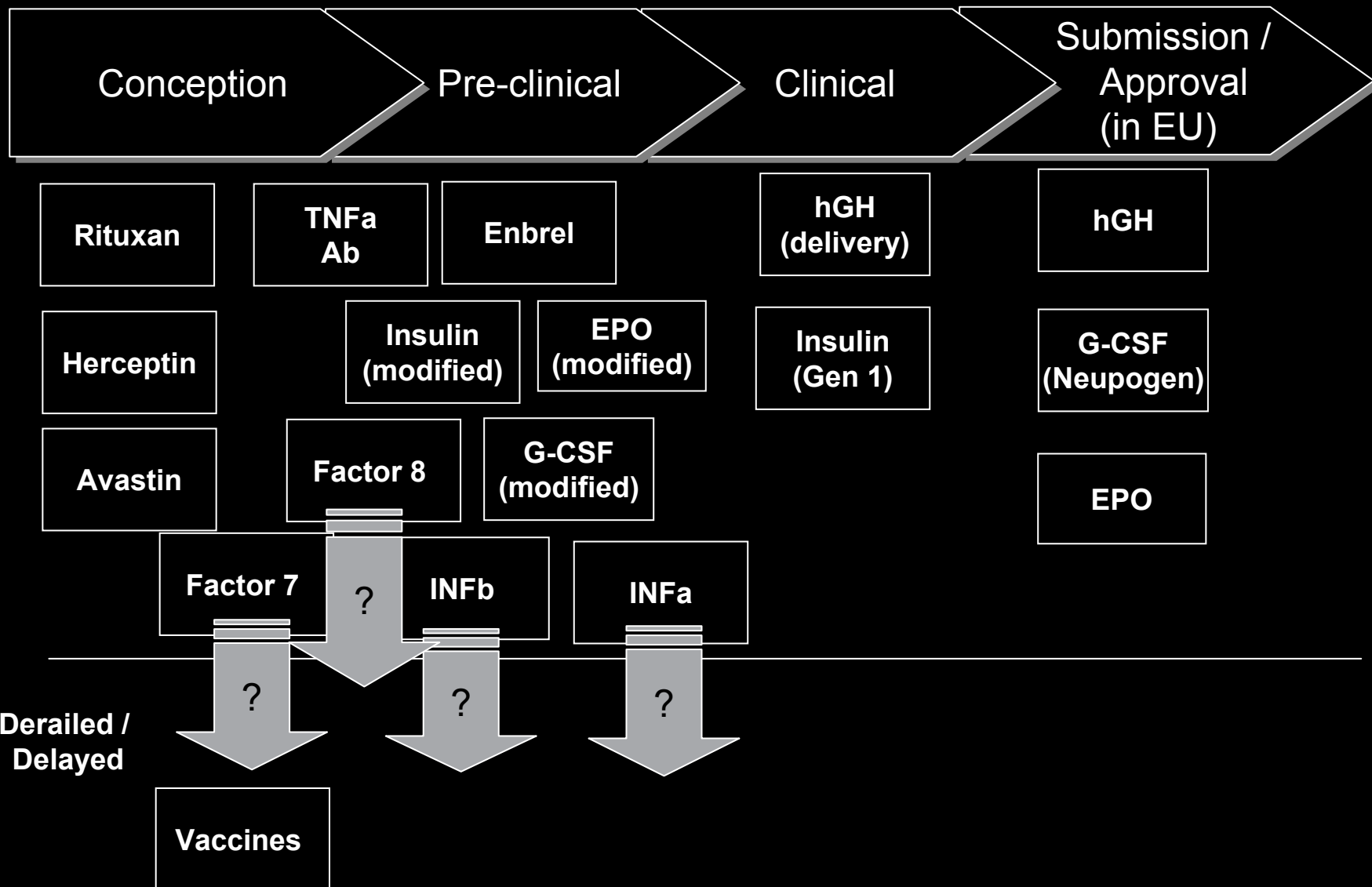
- \$420M upfront: \$300M to build, \$30M/yr while in trials \* 4 years  
 X (risk of approval)  
 + (risk of FDA or court delay\*\$30M/yr)

Outsourcing or sharing capacity is relatively attractive

- Global peak demand for Herceptin: 500kg/yr, Enbrel: 400kg/yr
- Can be achieved in ~20,000L production facility
- Modern facilities at 80,000L

	Current	2010	2015	2020
Large Scale (20,000L* 6 batches / Yr)	180 kg (1.5 mg /L /Batch)	300 kg (2.5 mg /L /Batch)	720 kg (6 mg /L /Batch)	1,200 (10 mg /L /Batch)
Mid Scale (late clinical)	2-3 g/L	5-7 g/L	10 g/L	20 g/L
Small Scale (early clinical)	5-7 g/L	10 g/L	20 g/L	> 20 g/L

# Targets: Where Are They In Development



# Targets: Antibodies On The Horizon

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**Development products take seven years**

- **hGH: Sandoz project started 1996, clinic in 2000, submitted 2003**
- **EPO: Sandoz project started 1998, clinic in 2002, ready for submission 2005**

**Start now to support '15-'20 products**

- **Assuming multi-year litigation**
- **Enbrel programs running, turning to antibodies**

**EMA seeking industry consultation to establish guidelines**

- **“there is a reason we are doing it”**

**Regulatory experience with antibodies expanding**

- **Bulky, complex but..**
- **Both industry and regulatory gathering experience**

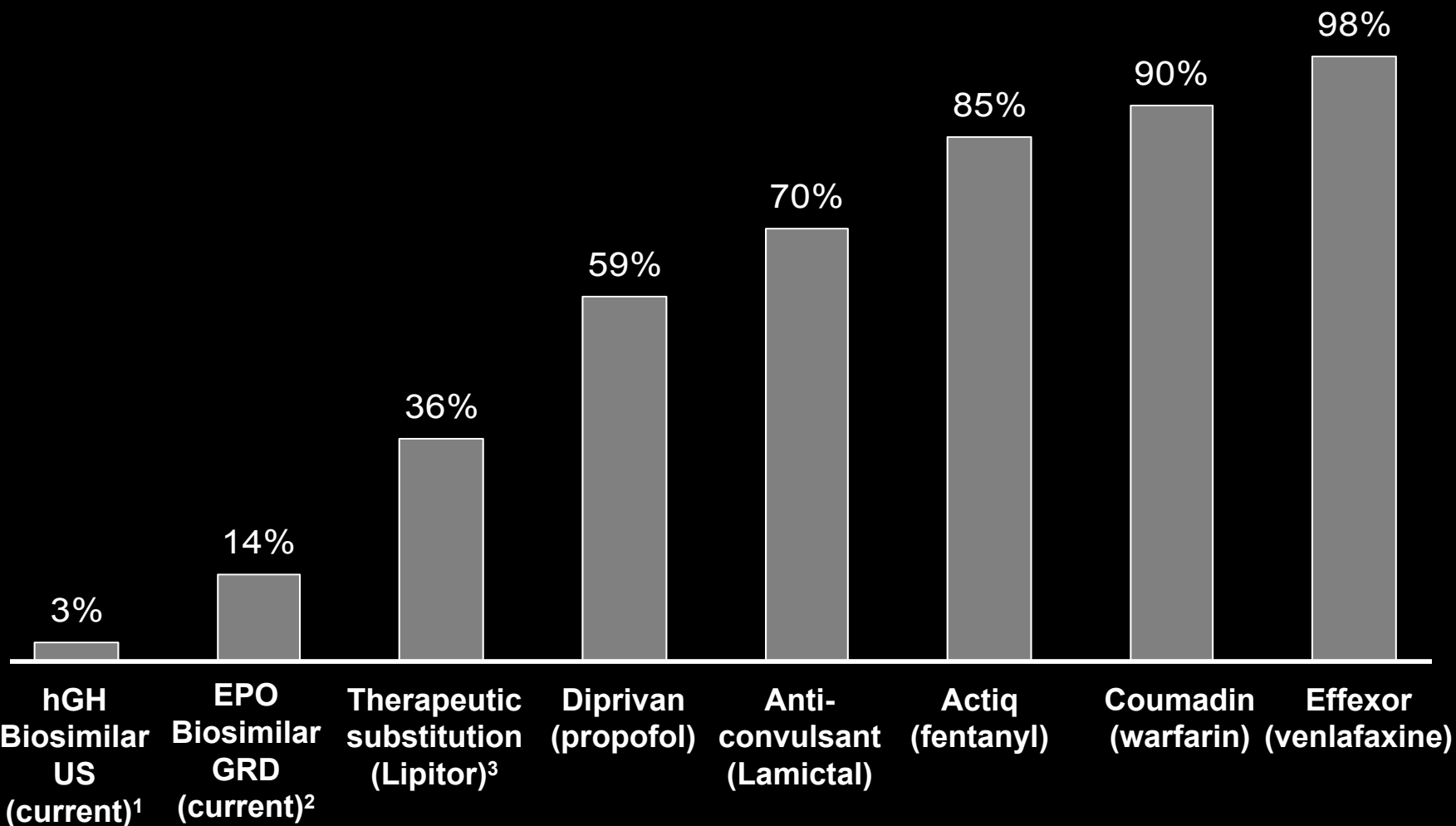
**Match innovators process or go for a breakthrough?... Or Both**

- **The Biosimilar dilemma**

**Development for '15-'20 window begins now**

# Market Share (I) – What Is The Right Benchmark?

Generic/biosimilar market share, Percent



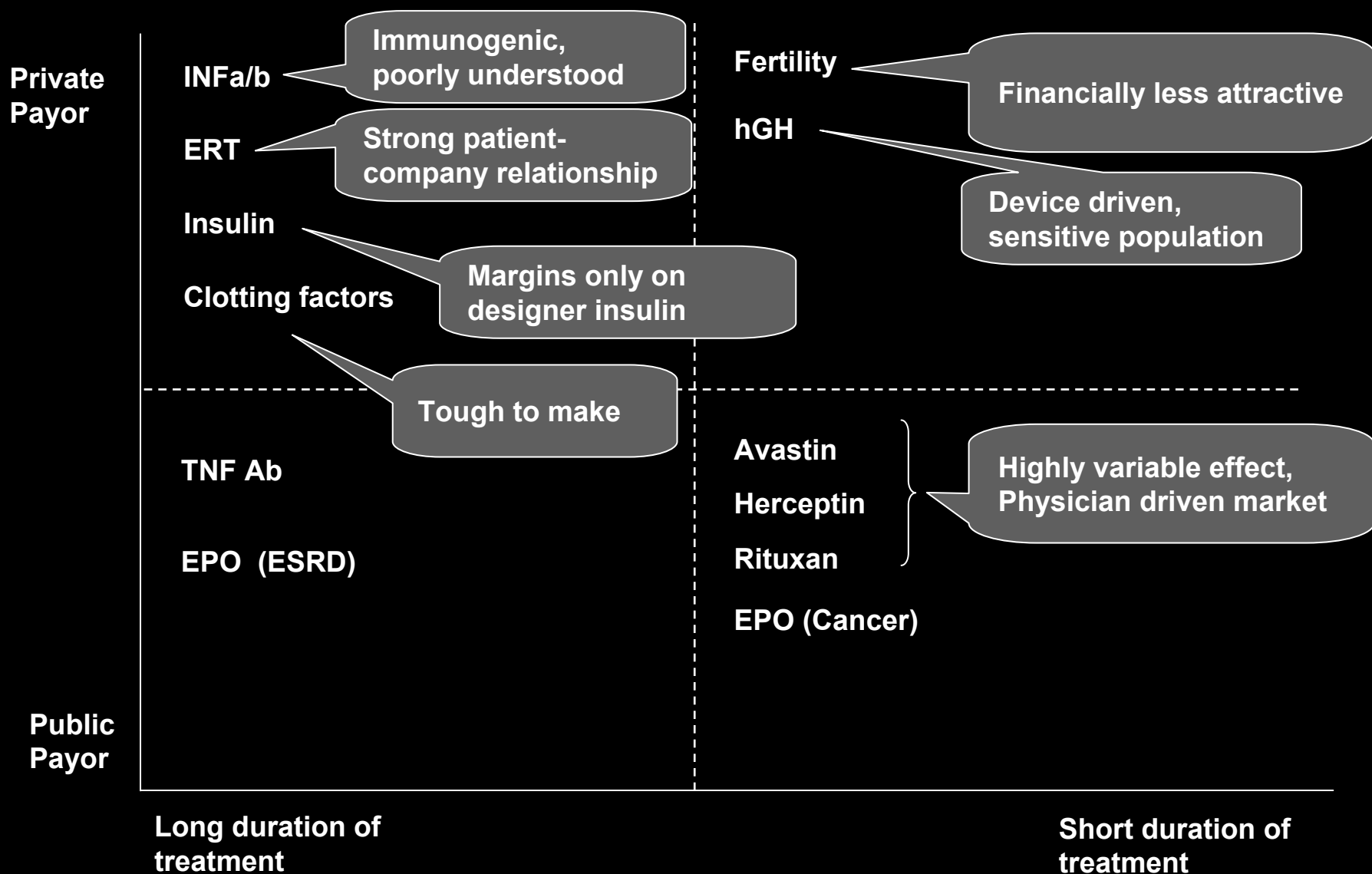
1 Market share for Omnitrope and Tev-tropin

2 Market share for Binocrit, Abseamed, Epoetin alfa Hexal, Retacrit/Silapo in the ESA market

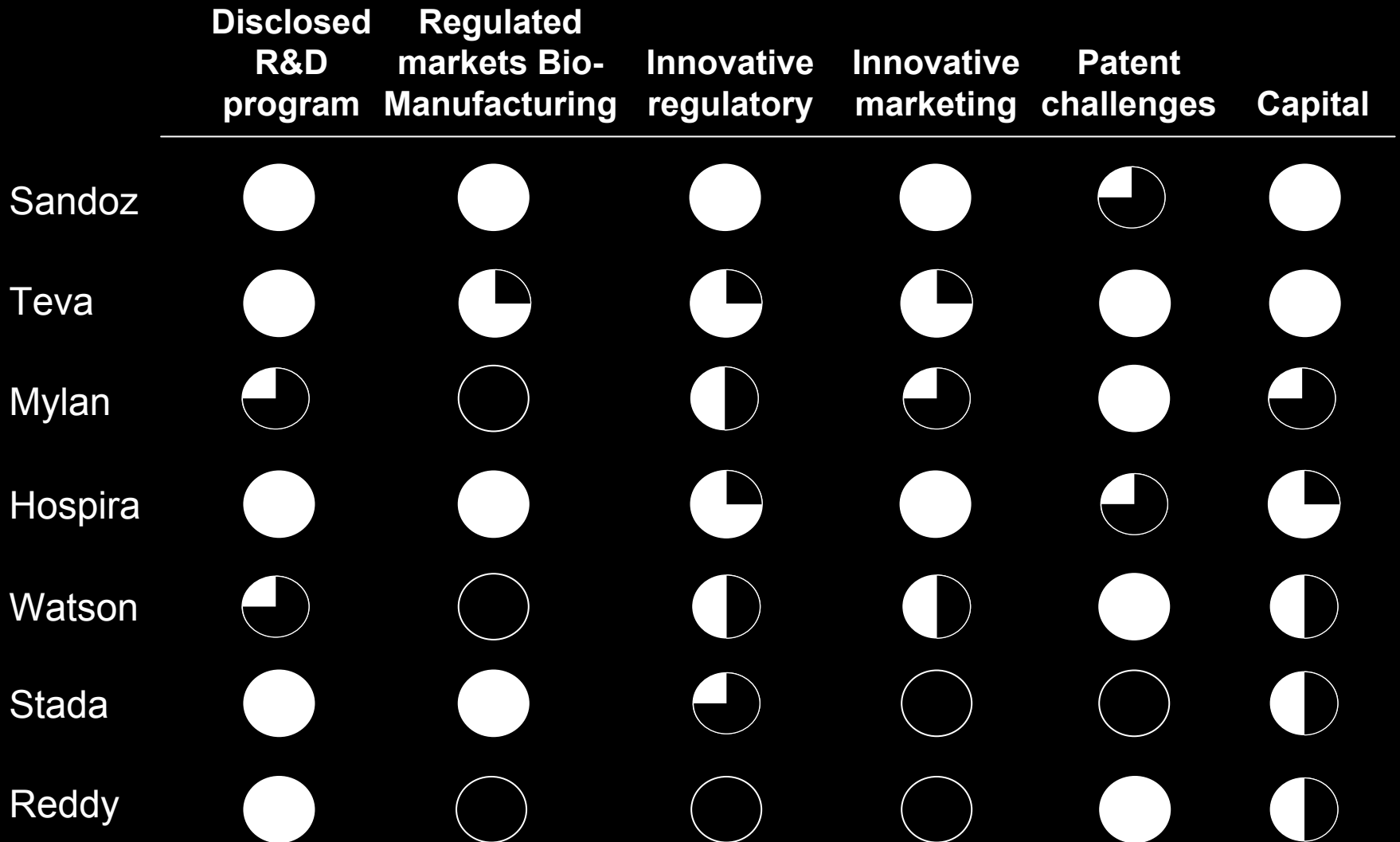
3 Therapeutic substitution impact from pravastatin and simvastatin

Sources: IMS Health; Potomac Research; Bernstein estimates and analysis

# Market share (II) – There is always a wrinkle



# Market Participants (I) – The Usual Suspects



# Market Participants (II) – The *Unusual Suspects*

		Motivation	Disclosed R&D program	Regulated markets Bio-Manufacturing	Innovative regulatory	Innovative marketing	Patent challenges	Capital
<b>Merck</b>	<b>Entry to Biologicals?</b>	●	◐	●	●	●	○	●
<b>Wyeth</b>	<b>Capacity play?</b>	○	●	●	●	●	○	●
<b>Lonza</b>	<b>Compete with clients?</b>	○	●	◐	●	○	◐	
<b>BIIB</b>	<b>Bio-betters?</b>	○	●	●	●	○	●	
<b>HGSI</b>	<b>Dual strategy?</b>	○	◐	◐	○	○	◐	

Bio-betters as tie breakers ?



# Is It All Worth ? (I)

Contribution to generic EBITBA per \$1B branded sales

	Conservative scenario	Moderate scenario	Aggressive scenario
Notional branded sales	\$1B	\$1B	\$1B
Biosimilar share (%)	20%	50%	75%
Biosimilar price (% of BRx)	80%	70%	55%
<b>Biosimilar revenue (\$M)</b>	<b>\$160M</b>	<b>\$350M</b>	<b>\$413M</b>
Biosimilar COGS (% rev)	12.5%	14%	18%
Marginal SG&A/R&D (% rev)	25%	27.5%	30%
<b>Biosimilar EBITDA (\$M)</b>	<b>\$104M</b>	<b>\$205M</b>	<b>\$215M</b>

# Is It All Worth It? (II)

## Contribution to generic EBITBA

	Conservative scenario	Moderate scenario	Aggressive scenario
Branded sales <sup>1</sup>			
-EPO	\$6.64B	\$6.64B	\$6.64B
-hGH	\$3.36B	\$3.36B	\$3.36B
-Interferon alfa	\$2.88B	\$2.88B	\$2.88B
-Interferon beta	\$3.74B	\$3.74B	\$3.74B
-Neulasta/Neupogen	\$5.99B	\$5.99B	\$5.99B
-Enbrel	\$7.95B	\$7.95B	\$7.95B
Total BRx sales (\$B)	\$30.56B	\$30.56B	\$30.56B
Biosimilar share (%)	20%	50%	75%
Biosimilar price (% of BRx)	80%	70%	55%
<b>Biosimilar revenue (\$B)</b>	<b>\$4.89B</b>	<b>\$10.69B</b>	<b>\$12.61B</b>
Biosimilar COGS (% rev)	12.5%	14%	18%
Marginal SG&A/R&D (% rev)	25%	27.5%	30%
<b>Biosimilar EBITDA (\$B)</b>	<b>\$3.06B</b>	<b>\$6.25B</b>	<b>\$6.56B</b>
Generic industry EBITDA (\$B) <sup>2</sup>	\$10.65B	\$10.65B	\$10.65B
Percent industry EBITDA	<b>29%</b>	<b>59%</b>	<b>62%</b>

<sup>1</sup> SCB 2015 estimates

<sup>2</sup> Estimated 2009 EBITDA for Teva (incl. Barr), Mylan, Watson, Sandoz, Ranbaxy, Reddy's, Actavis, Stada, Ratiopharm, Perrigo, Par, Sun, Hospira, GR

Source: Bernstein estimates and analysis

# Disclosure Appendix

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MYL - O (UG) 11/15/2007  
SEPR - M (IC) 3/2/2006  
TEVA - O (IC) 3/7/2006  
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