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Eight Thoughts On Biosimilars

SCB Biosimilars Conference Call

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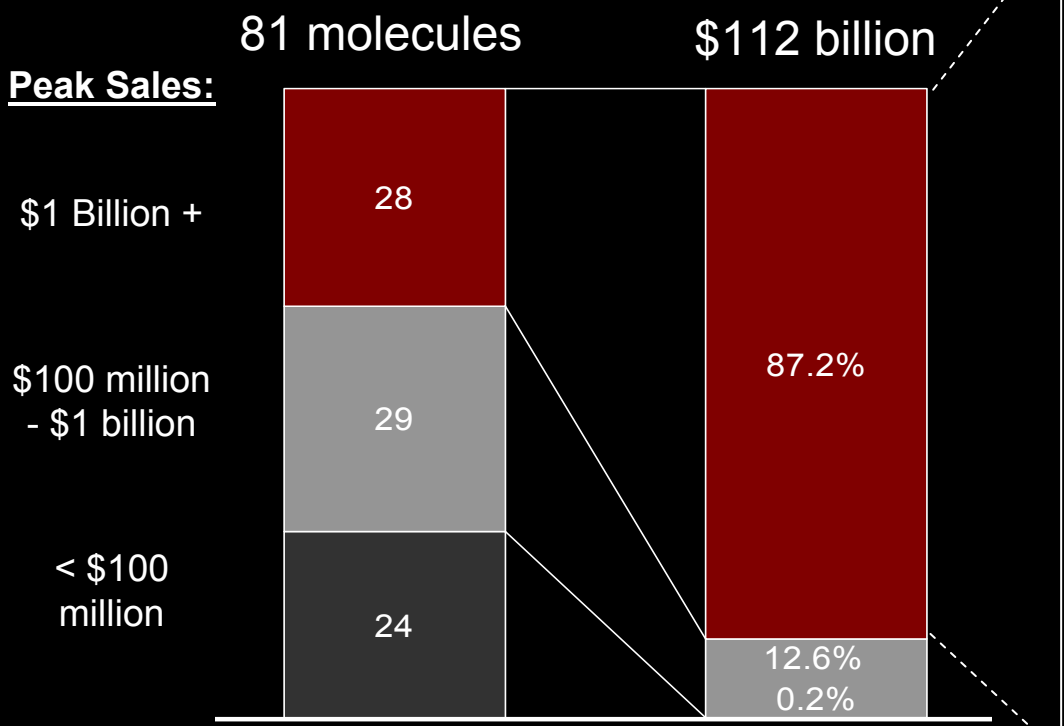
Biologics: Too Big To Ignore

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/Procri	5.1	Tysabri	1.4
Neulasta	4.2	Neupogen	1.3
Novolog	3.8	Synagis	1.3
Erbitux	3.6	Betaseron	1.2
Aranesp	3.2	Humulin	1.1
Recombinate	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

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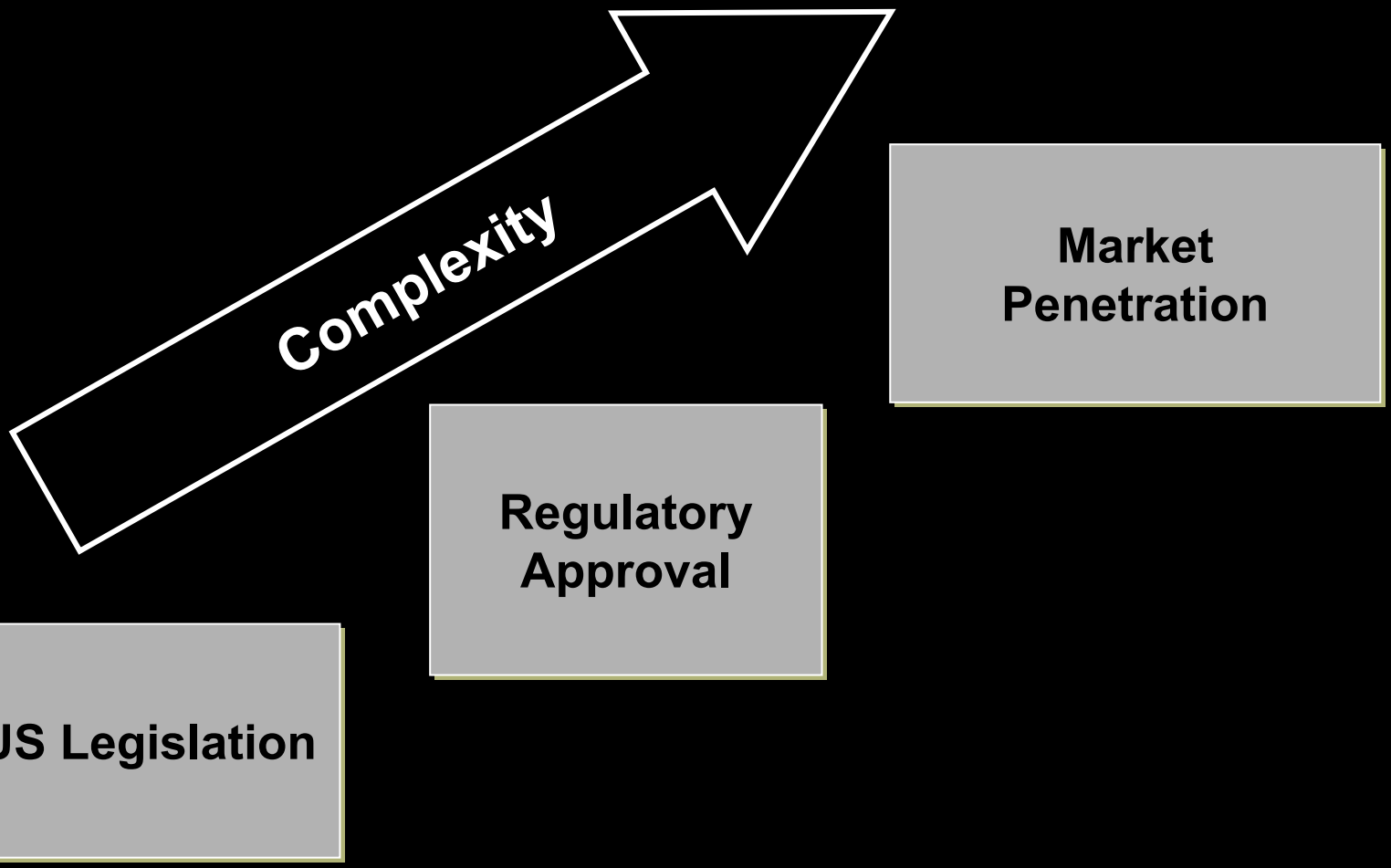
Ready, Set…For A Marathon, Not A Sprint



Source: Bernstein estimates and analysis

Eight Thoughts On Biosimilars

- 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? • Sill 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

Source: Bernstein estimates and analysis

The FDA – Mixed Signals

Agency is clearly interested in Biosimilars

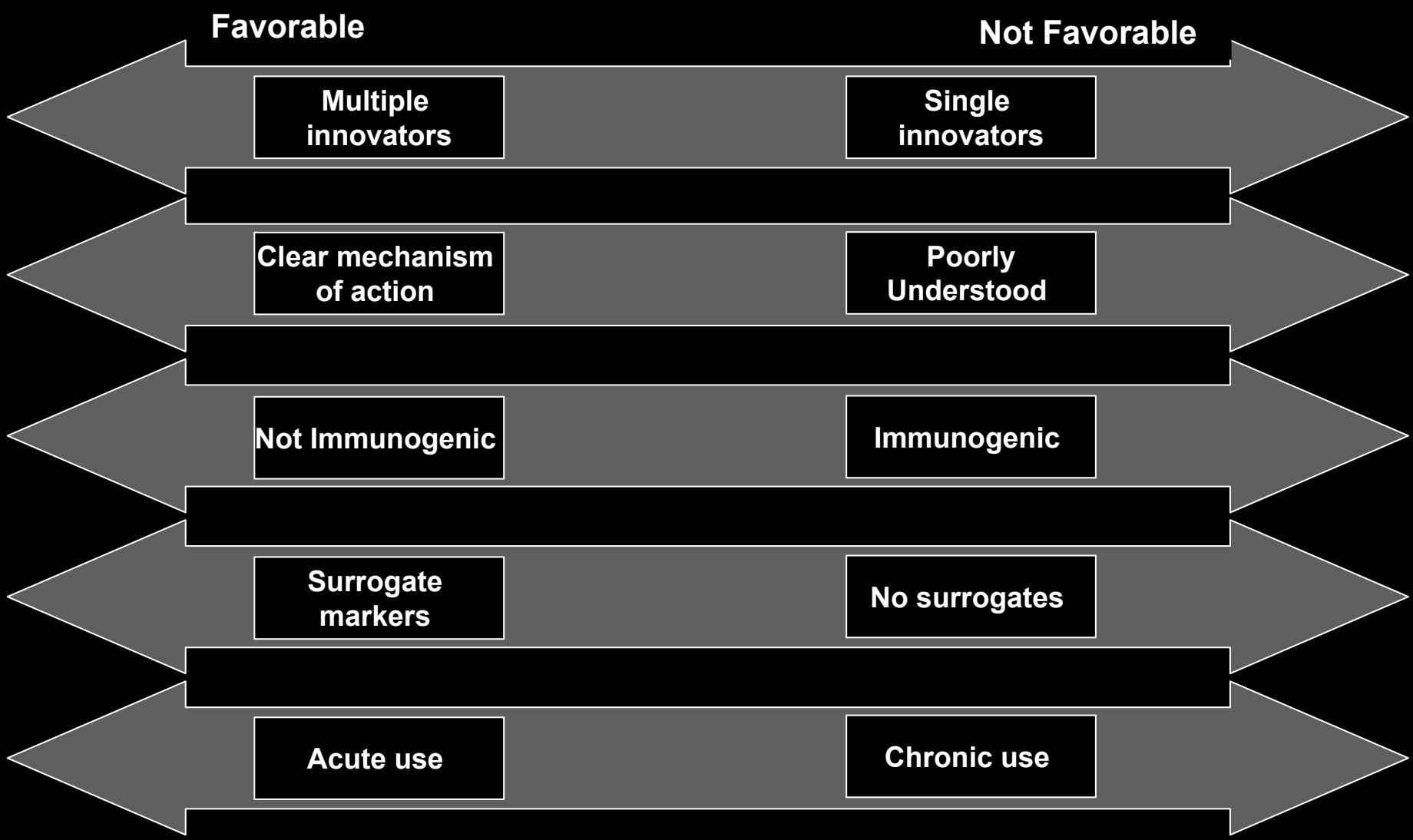
Engaged	• Involved in debate • Proactively divided reviewing responsibilities
hGH	• Approved under 505j, may have received interchangeability (Sandoz never requested)
LMWH	• FDA may approve without pivotal trials, EMEA regulate as biosimilar
mAb	• FDA staffers do not see big difference from other molecules, 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

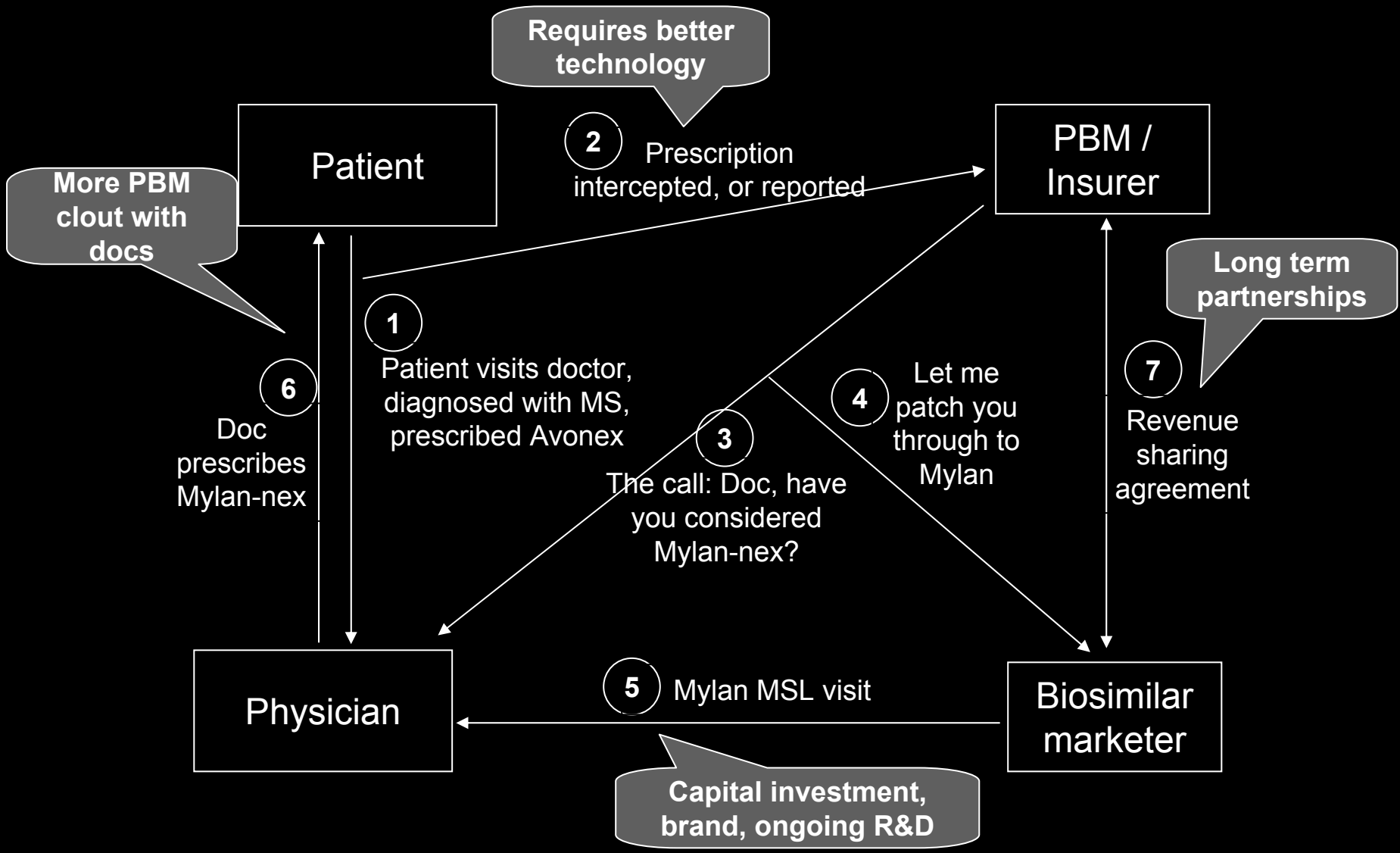
Source: Bernstein estimates and analysis

The FDA: What Will Influence Approvability?



Source: Bernstein estimates and analysis

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

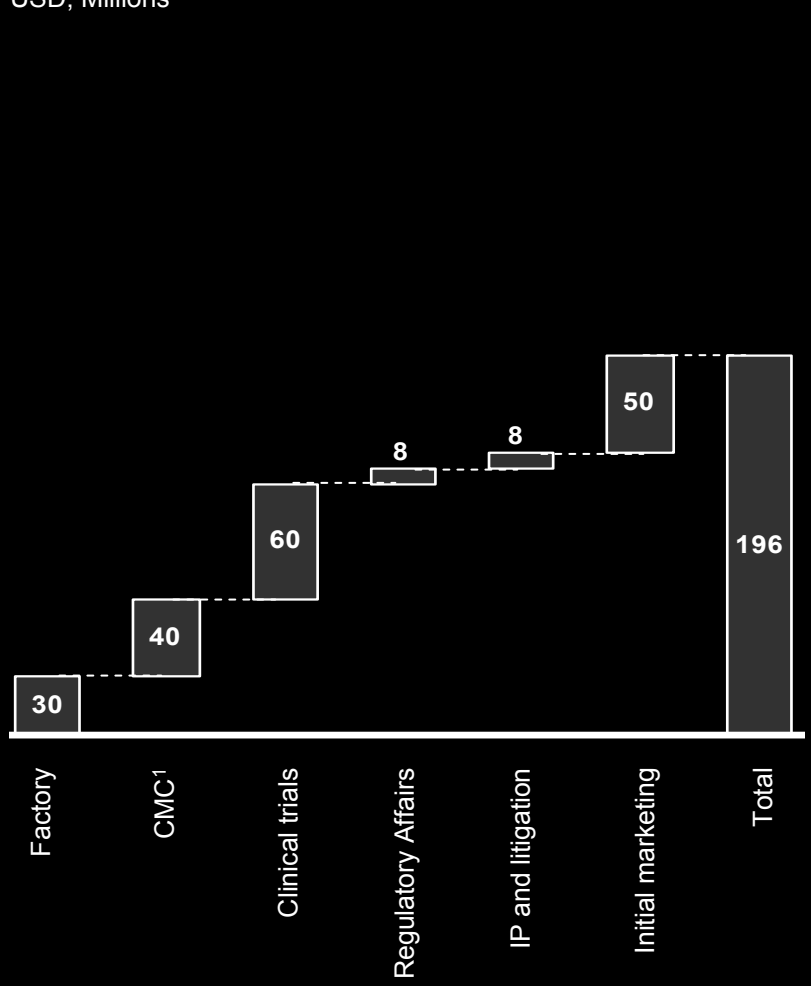


Note: conceptual example. Source: Bernstein estimates and analysis

Costs (I): Not A Low Cost Proposition

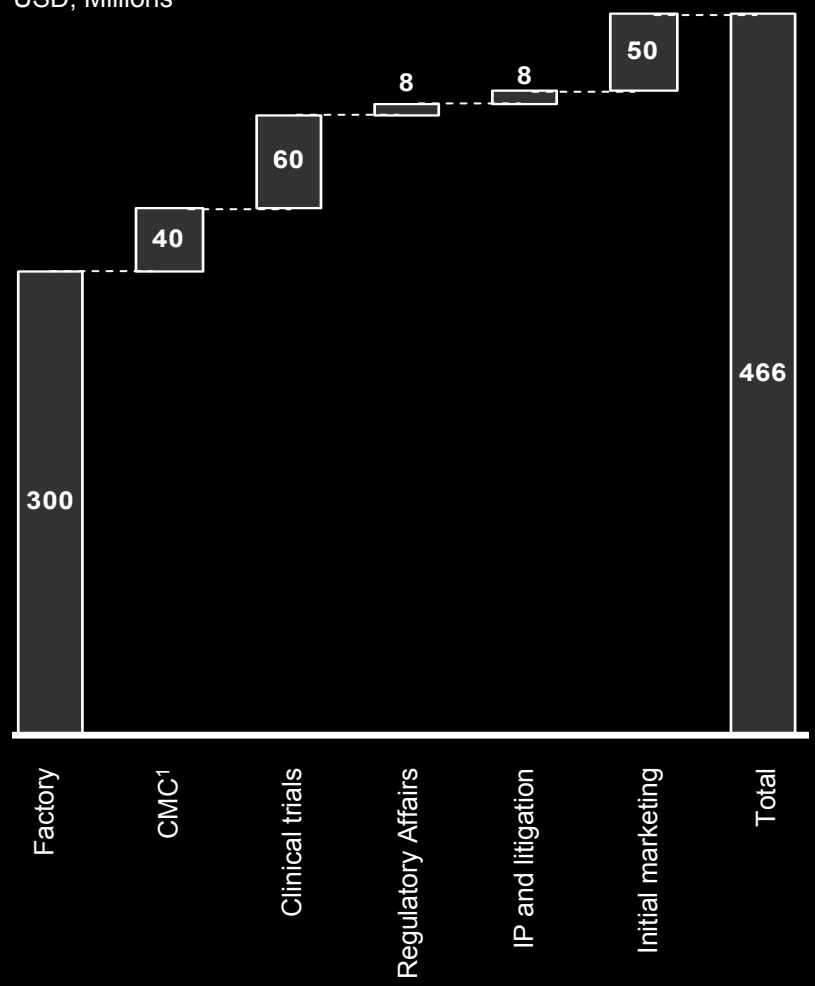
Bacterial facility

USD, Millions



Mammalian facility

USD, Millions



1 Chemistry, Manufacturing and Controls

Source: Corporate reports and Bernstein estimates and analysis

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)

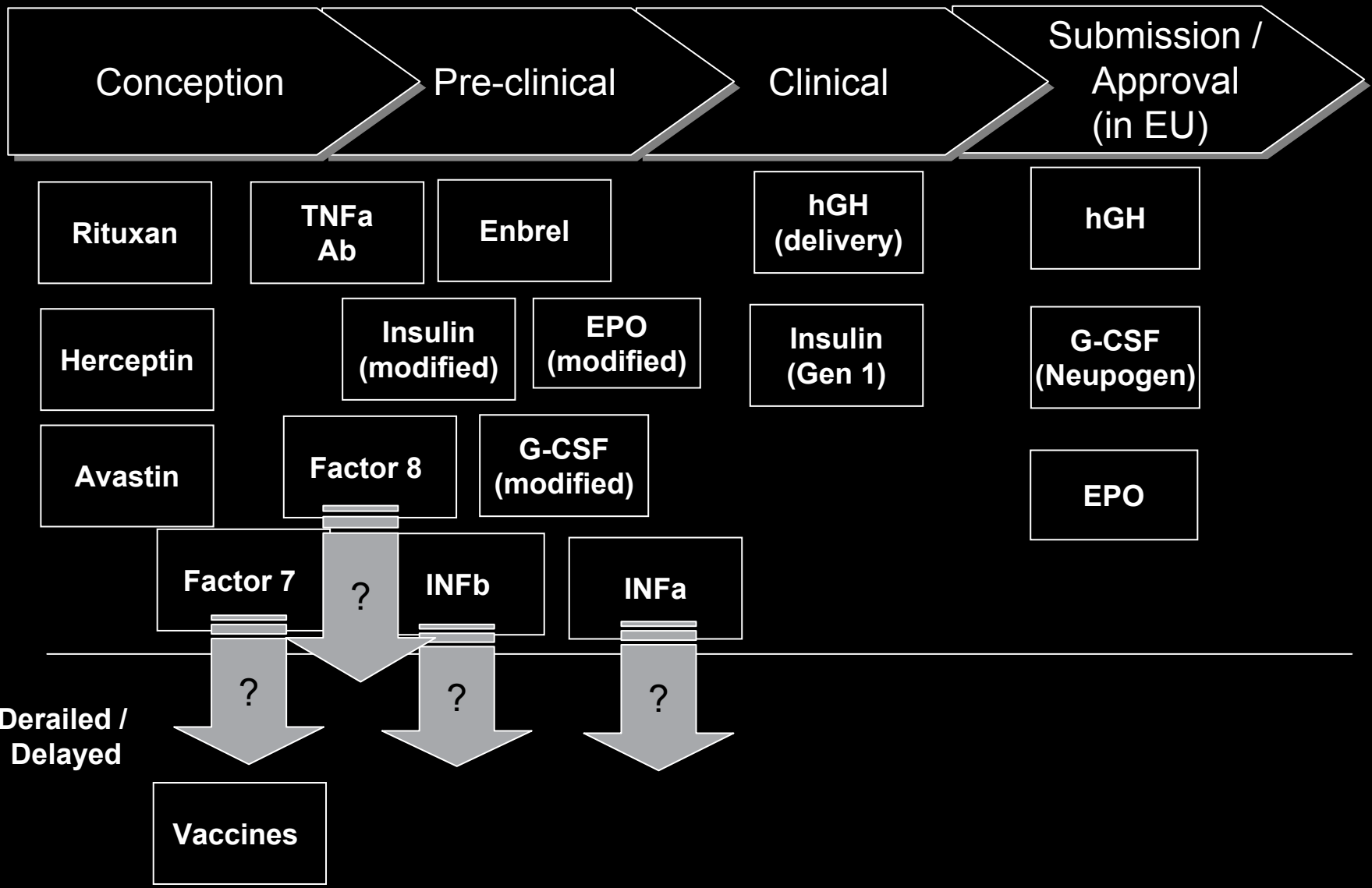
Outsourcing or sharing capacity is relatively attractive

- **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

Source: Lonza; industry experts, SCB estimates and analysis

Targets: Where Are They In Development



Source: Market discussions, SCB estimates and analysis

Targets: Antibodies On The Horizon

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**

EMEA seeking industry consultation to establish guidelines
- **“there is a reason we are doing it”**

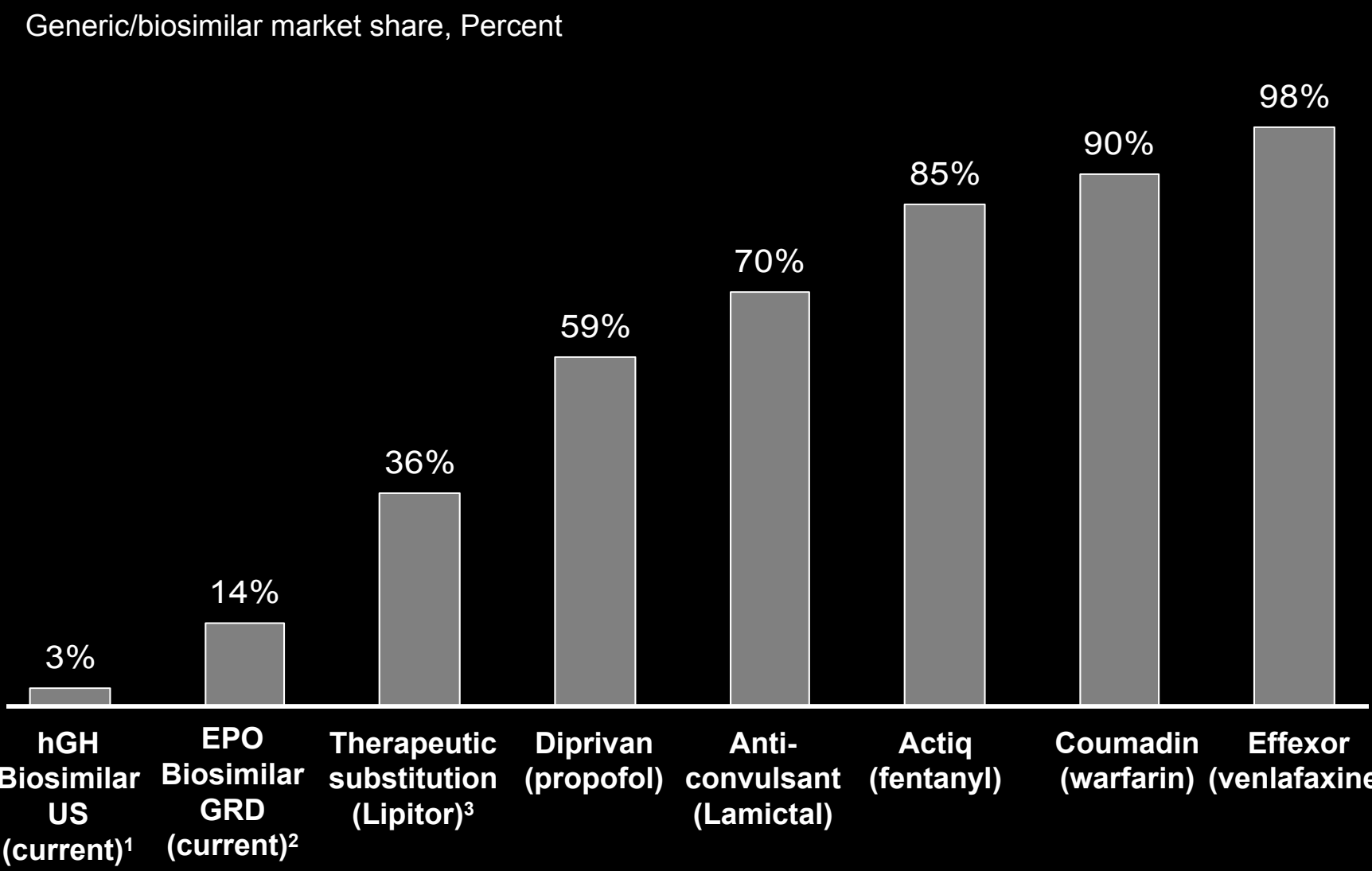
Regulatory experience with antibodies expanding
- **Bulky, complex but..**
- **Both industry and regulatory gathering experience**

Match innovators process or go for a breakthrough?... Or Both
- **The Biosimilar dilemma**

Development for ’15-’20 window begins now

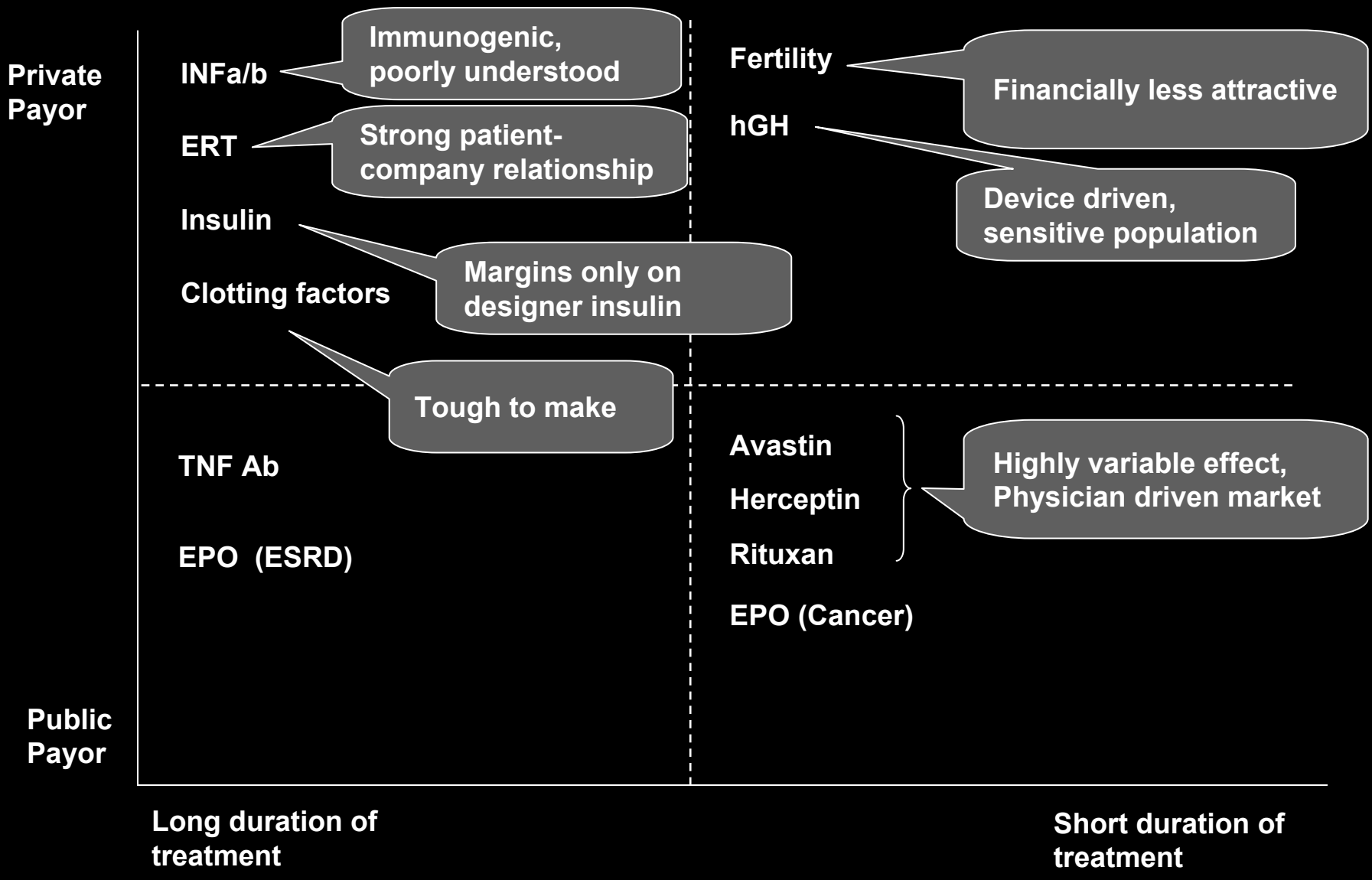
Source: Bernstein estimates and analysis

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



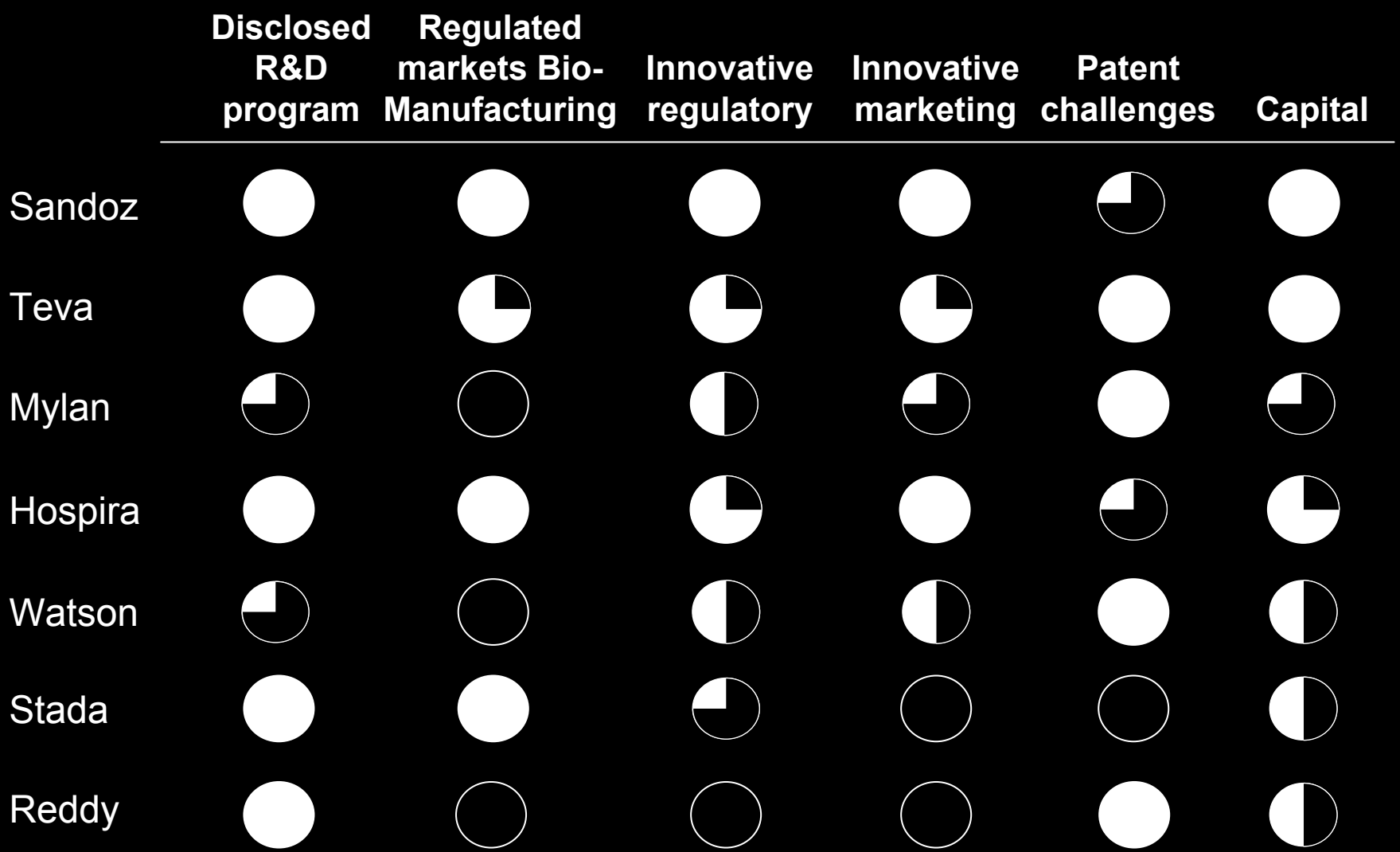
1 Market share for Omnitrope and Tev-tropin
2 Market share for Binocrit, Abseamed, Epoetin alfa Hexal, Retacrit/Silapo in the ESA market
3 Therapeutic substitution impact from pravastatin and simvastatin
Sources: IMS Health; Potomac Research; Bernstein estimates and analysis

Market share (II) – There is always a wrinkle



Source: Bernstein estimates and analysis

Market Participants (I) – The Usual Suspects



Source: Bernstein estimates and analysis

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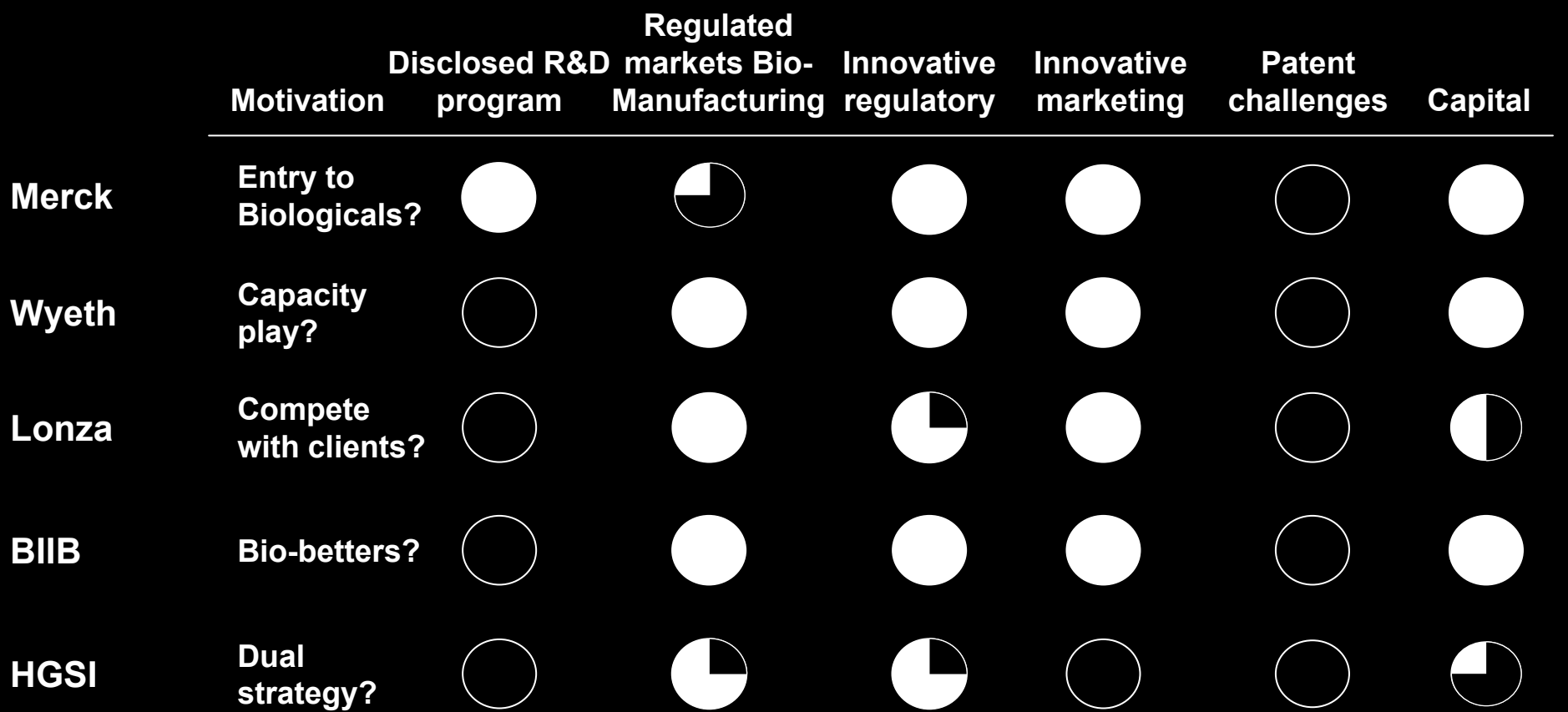
Market Participants (II) – The *Un*usual Suspects



Bio-betters as tie breakers ?

Source: Bernstein estimates and analysis

EXAMPLE

Is It All Worth ? (I)

Contribution to generic EBITBA per $1B branded sales

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

Source: Bernstein estimates and analysis; A 'back of the envelope' analysis

Is It All Worth It? (II)

Contribution to generic EBITBA

	Conservative scenario	Moderate scenario	Aggressive scenario
Branded sales[1]			
-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	$30.56B
Biosimilar share (%)	20%	50%	75%
Biosimilar price (% of BRx)	80%	70%	55%
Biosimilar revenue ($B)	**$4.89B**	**$10.69B**	**$12.61B**
Biosimilar COGS (% rev)	12.5%	14%	18%
Marginal SG&A/R&D (% rev)	25%	27.5%	30%
Biosimilar EBITDA ($B)	**$3.06B**	**$6.25B**	**$6.56B**
Generic industry EBITDA ($B)[2]	$10.65B	$10.65B	$10.65B
Percent industry EBITDA	**29%**	**59%**	**62%**

1 SCB 2015 estimates
2 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

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BRL - O (UG) 5/9/2007
CEPH - M (DG) 8/15/2006
FRX - O (UG) 10/16/2008, M (IC) 3/2/2006
MYL - O (UG) 11/15/2007
SEPR - M (IC) 3/2/2006
TEVA - O (IC) 3/7/2006
WPI - M (IC) 3/7/2006

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