

The Market for Follow-On Biologics

***David Ridley
February 2009***



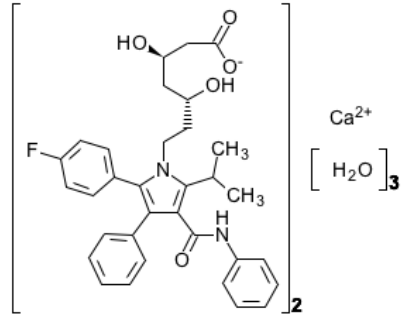
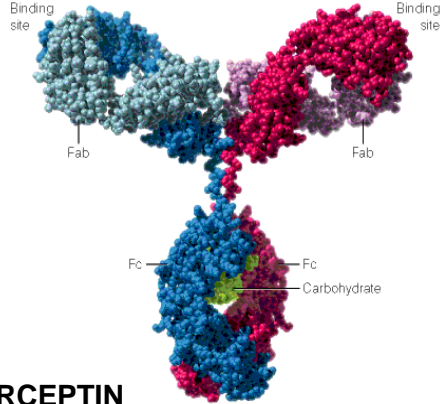
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Government creates 2 entry barriers for generic biologics

1. Clinical testing
 - New clinical trials not required for generic pharmaceuticals but likely required for some generic biologics
 - Because “process is product”
 - Tradeoff: safety vs. access to low cost
 2. Intellectual property protection
 - Patents
 - Data exclusivity
 - Tradeoff: innovation vs. access to low cost
- Cost reduction will be relatively “small”
 - Because competition limited by entry costs and differentiation
 - \$4-\$6 billion/decade for Federal (Avalere & CBO)

Pharmaceuticals vs. Biologics

	Pharmaceuticals	Biologics
Size (MW)	Small (<1000)	Large (>10,000)
Source	Chemical synthesis	Cultures of living cells
Form	Generally oral solids 	Often injected or infused 
Reimbursement	Pharmacy benefit	Often medical benefit
Generic Law	1984 Hatch-Waxman	No expedited provision for substances approved as biologics under Pub Health Services Act
Example	<p>Lipitor (anti-cholesterol)</p>  <p><small>D02258</small> LIPITOR MW = 559</p>	<p>Herceptin (breast cancer)</p>  <p>HERCEPTIN MW = 185,000</p>

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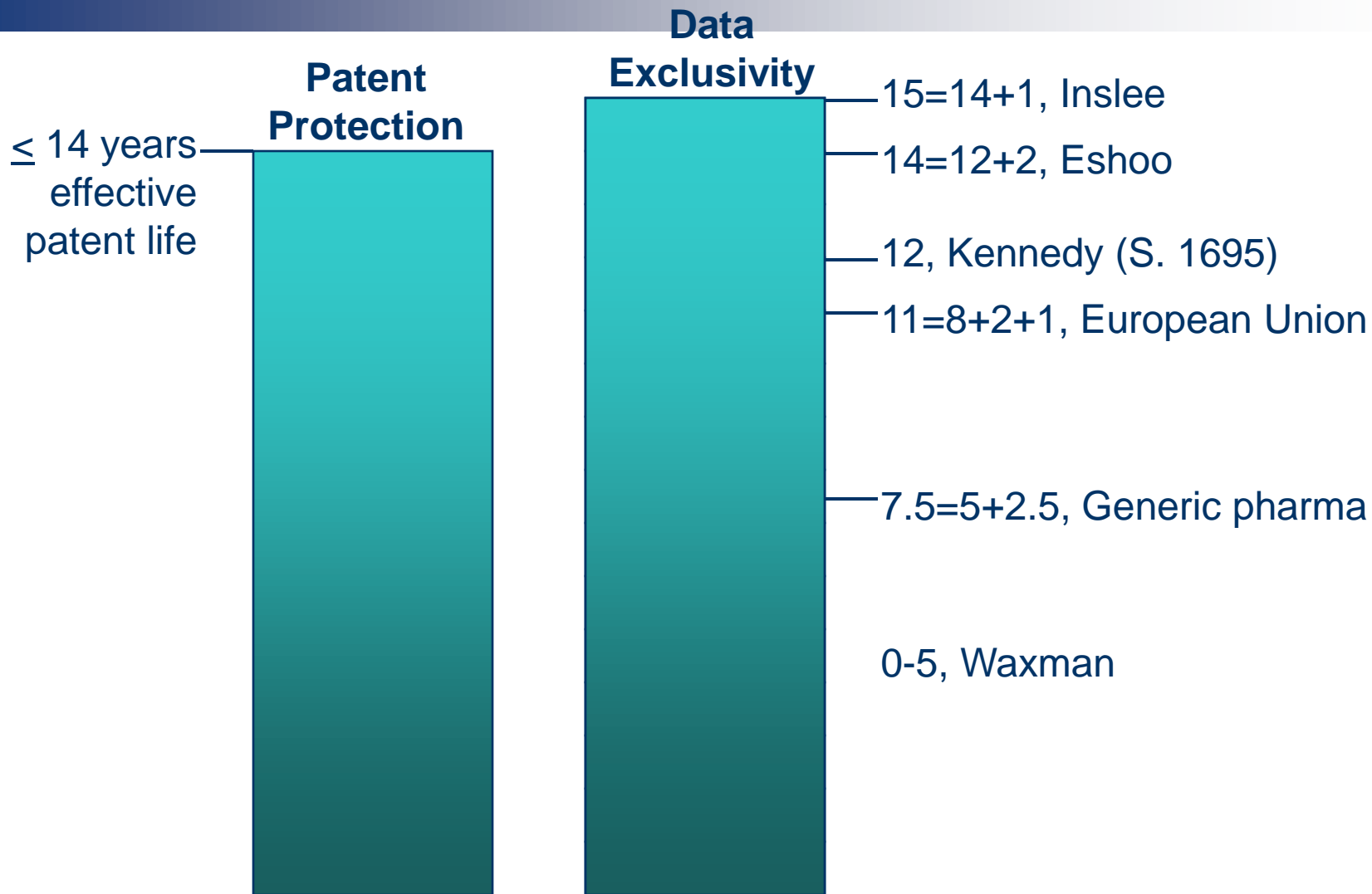
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Data exclusivity

- Cannot use innovator's clinical trials for specified time
- Concurrent with patent
- Ensures reward for clinical trials even if
 - Patent expired
 - Patent narrow (especially true for biologics where generics are “similar”)
- New indications
 - Ever-greening: new period of exclusivity? Proposed 1-2 years
- Economic analysis of optimal exclusivity
 - Buckley (BIO), Golec (UConn) and Vernon (UNC): break even > 17 years
 - Henry Grabowski (Duke): break even = 13-16 years
 - Not surprising 13-17 years because that’s probably what manufacturers expected when entered market
 - Alex Brill (AEI): optimal is 7 years (assumes continued branded sales, cost of capital 10%, contribution margin, i.e. revenue – variable cost, = 60%)
- If shorter data exclusivity then at the margin we will see less innovation
 - But really, really long not necessary because little value to dollars earned far, far in future

Patent Protection & Data

Exclusivity Run Concurrently



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Entry & Competition

- Paper we wrote in 2005/2006 and finally published in 2007
- Generics not inherently cheap
- Entry costs affect number of firms which affect prices

MANAGERIAL AND DECISION ECONOMICS
Manage. Decis. Econ. 28: 439–451 (2007)
Published online in Wiley InterScience
(www.interscience.wiley.com) DOI: 10.1002/mde.1352



Entry and Competition in Generic Biologics

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Patents for several blockbuster biological products are expected to expire soon. The Food and Drug Administration is examining whether biologics can and should be treated like pharmaceuticals with regard to generics. In contrast with pharmaceuticals, which are manufactured through chemical synthesis, biologics are manufactured through fermentation, a process that is more variable and costly. Regulators might require extensive clinical testing of generic biologics to demonstrate equivalence to the branded product. The focus of the debate on generic biologics has been on legal and health concerns, but there are important economic implications. We combine a theoretical model of generic biologics with regression estimates from generic pharmaceuticals to estimate market entry and prices in the generic biologic market. We find that generic biologics will have high fixed costs from clinical testing and from manufacturing, so there will be less entry than would be expected for generic pharmaceuticals. With fewer generic competitors, generic biologics will be relatively close in price to branded biologics. Policy makers should be prudent in estimating financial benefits of generic biologics for consumers and payers. We also examine possible government strategies to promote generic competition. Copyright © 2007 John Wiley & Sons, Ltd.

INTRODUCTION

The Food and Drug Administration (FDA) is examining whether biological products can and should be treated like pharmaceuticals with regard to generics. The focus of the debate on generic biologics¹ has been on legal and health concerns, but there are important economic questions. How will differences in development and manufacturing costs and associated regulations affect the market for generic biologics? Will generic biologics be as competitive and provide the substantial financial savings provided by generic pharmaceuticals? We analyze market entry and prices in the generic biologic market using a theoretical model of generic biologics and regression estimates from generic pharmaceuticals.

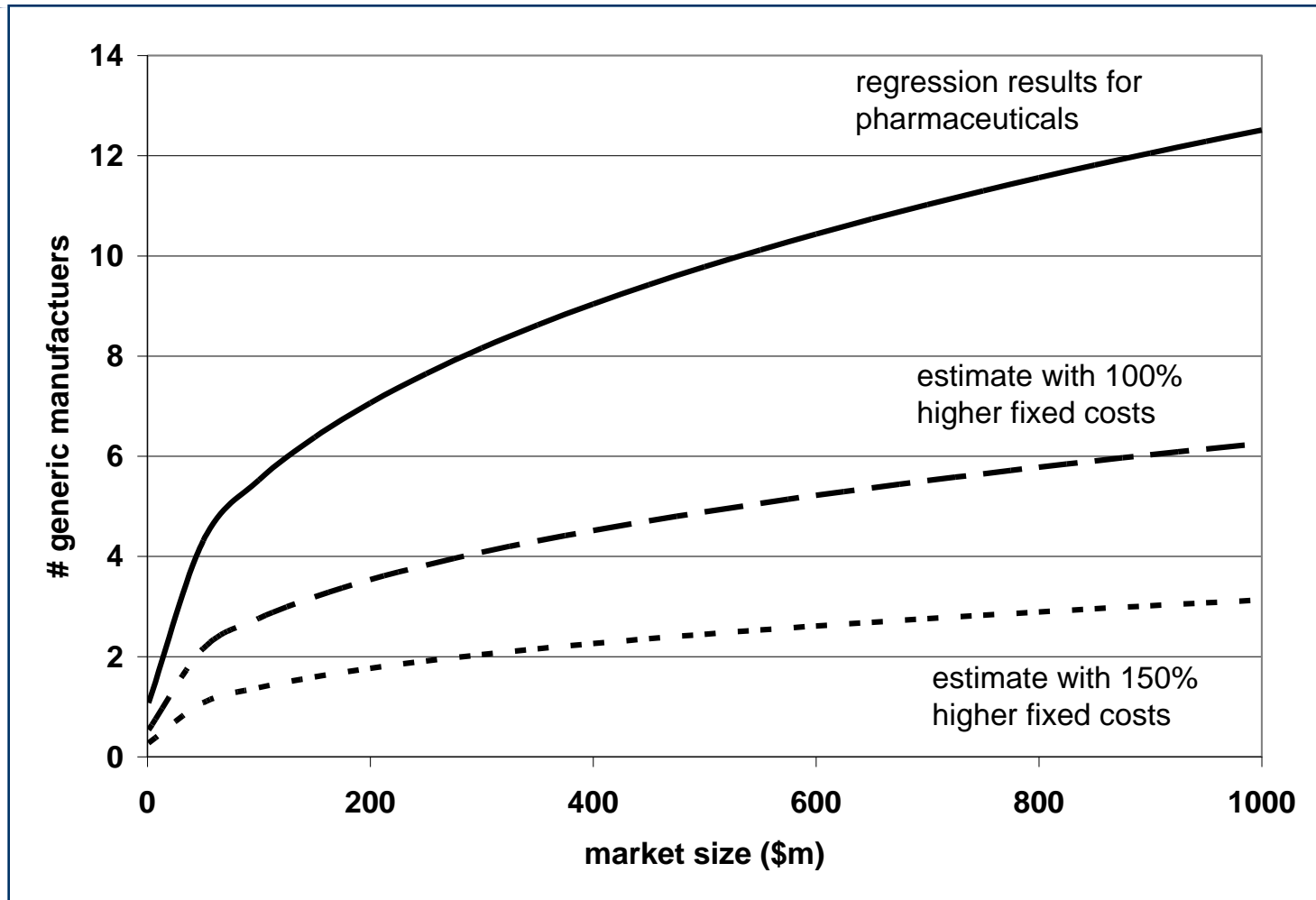
There have not yet been any major market approvals of generic biologics due to three barriers. First, the biotechnology industry is young, so few patents have expired for major biologic products. Second, the regulatory framework for generic biologics has not been settled. Third, biologic products are complex and have high costs of establishing scientific and manufacturing capabilities (Humphreys, 2004).

The first two barriers might fall soon. First, by 2007 patent expirations are expected for blockbuster biologics such as Procrit, Epogen, and Intron A (Humphreys, 2004). Second, FDA is considering guidelines for the approval of generic biologics.² The third problem of complexity and high costs will likely limit but not blockade entry of generics.

Biologics differ from pharmaceuticals in many respects. Pharmaceuticals are small molecules, can be chemically synthesized, and are orally available. Biologics are large molecules, are created through

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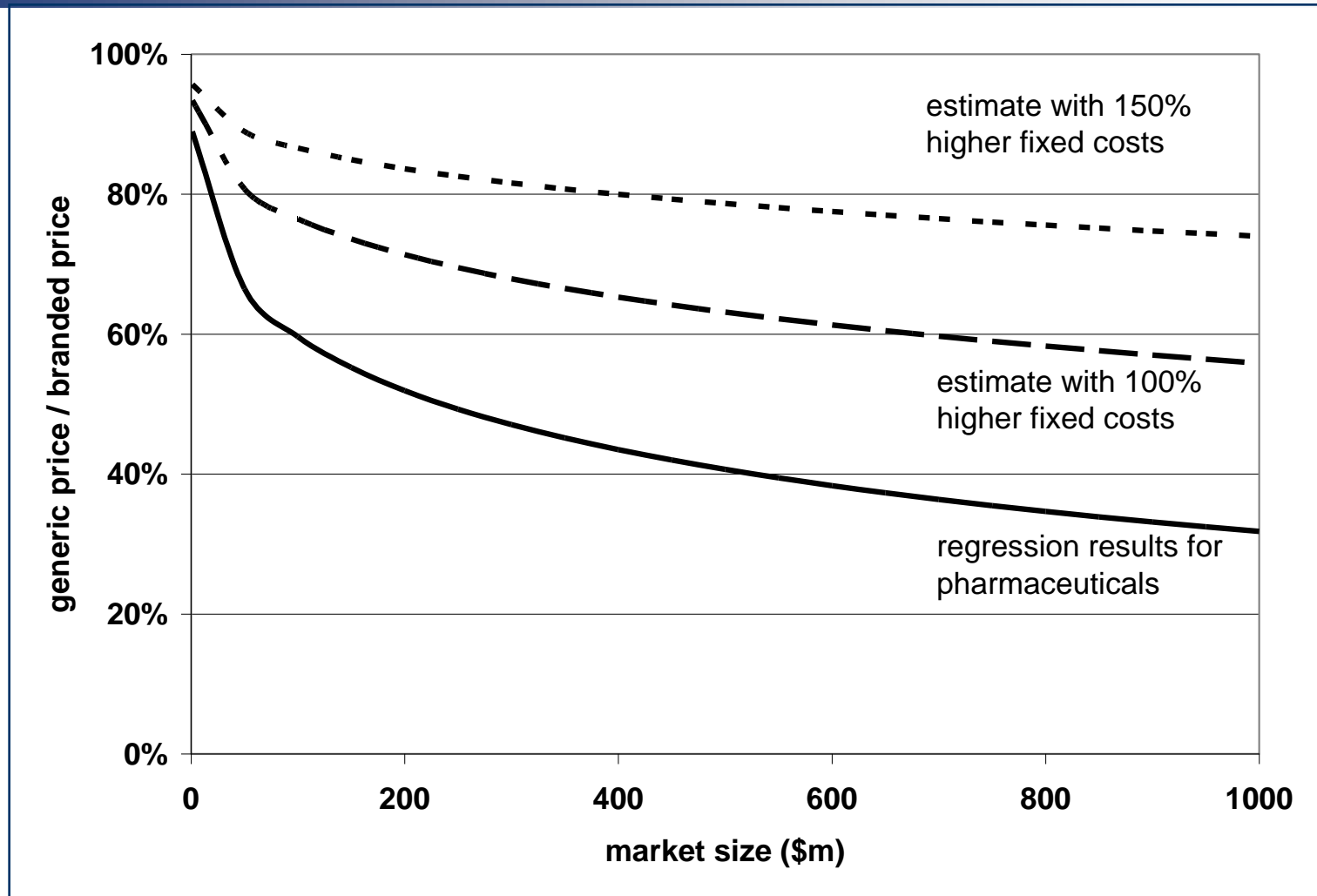
Generic biologics: **↑ fixed costs → ↓ entry**



Source: Grabowski, Ridley, & Schulman, 2007

Generic biologics:

↑ *fixed costs* → ↓ *entry* & ↑ *prices*



Source: Grabowski, Ridley, & Schulman, 2007

Limits on Competition

- Entry costs
 - Clinical trials
 - Costly manufacturing
- Product differentiation
 - “Bio-similars”
 - “Bio-betters”
 - Like “me-too” drugs

Analog: Generic Cancer Treatment

- “On Feb. 3, Joyce Elkins filled a prescription for a 2-week supply of nitrogen mustard, a decades-old cancer drug used to treat a rare form of lymphoma. The cost was \$77.50.
- On Feb. 17, Ms. Elkins... returned to her pharmacy for a refill. This time... the cost was \$548.01
- ... emblematic of an industry trend of basing drug prices on something other than the underlying costs.”
- Source: NYT Mar12, 2006

Analog: Omnitrope

- Omnitrope = generic human growth hormone
- Europe: ~20% cheaper than branded
- U.S.: small market share (<5%?)

Generics reduce Federal costs \$4-6 billion over decade, say Avalere & CBO

- Estimated cost reduction from follow-on biologics:
- Avalere Health
 - 2007
 - Federal save **\$3.6b** over 10 years
 - <http://www.avalerehealth.net>
- Congressional Budget Office (CBO)
 - December 2008
 - USA save **\$25b** (Federal **\$6b**) over 10 years (< 1% of drug spending)
 - Assumes 12 years data exclusivity (S. 1695) and insurers encourage switch to generics
 - <http://www.cbo.gov>
- Biotechnology Industry Organization (trade group for biotech)
 - Buckley (BIO), Golec (UConn) and Vernon (UNC)
 - January 2009
 - Federal save < **\$1.4b** over 10 years
 - Assumes data exclusivity < 14 years
 - Average (mean or median?) takes 17 years to cover costs
- ExpressScripts (PBM)
 - 2007
 - USA save **\$71b** over 10 years
 - <http://www.expressscripts.com>

Avalere Health: Projected Federal Gov't Savings

2008, 2009, 2010	2011, 2012	2013	2014	2015	2016	2017	Total
Write regs	Review	Brand incr price					
\$0b	\$0b	\$0.1b	\$-0.4b	\$-1b	\$-1.1b	\$-1.2b	\$-3.6b

- But net present value is even smaller since far in future
- \$1 billion per year and growing after gets going
- In contrast, ExpressScripts (PBM) projects 20 times that
- Questions: How quickly? What price discount (10-35%)? Will branded respond with price decrease? Will branded respond with incremental innovation? What market share (50-75%)?

Conclusions

- Intellectual property
 - Data exclusivity 0-15 years
 - Harmonize with EU? 8+2+1 years
- Cost savings
 - Generic ≠ cheap, unless many competitors
 - Generic biologics will have higher costs of entry than generic pharmaceuticals which will limit entry and limit price discounts
 - Also “bio-betters” like “me-too” drugs
 - Federal government savings of \$1b+ per year beginning 2015 (Avalere)