

# Follow-On Biologics: Data Exclusivity and Related Policy Issues



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# Follow-on Biologics also Referred to as:

- Biogenerics
- Generic biologics
- Bio-similars
- Follow-on proteins

# Important Questions – Follow-on Biologics

- Congress and FDA currently considering a regulatory pathway for follow-on biologics
- How do we balance incentives for innovators and follow-on biologic firms?
- What is the appropriate length of data exclusivity, if any, for innovators?

# Data Exclusivity Versus Patents

- Data exclusivity and patents are complementary forms of intellectual property
- Patents reward innovation based on criteria of novelty, utility and non-obviousness
- Data exclusivity recognizes substantial R&D investment is necessary after invention occurs

# Balancing Innovation and Price Competition

- U.S. legislative proposals give new biological entities (NBEs) from 0 to 14 years of data exclusivity
- Hatch-Waxman gives innovators 5 years data exclusivity for new chemical entities (NCEs)
- European Union has 10 year data exclusivity for both NBEs and NCEs

# Why is Data Exclusivity Important?

- Core patents may have expired or be limited in scope for many new biological entities
- Legislative proposals reward the first follow-on biologics firm to successfully challenge a patent
- Without data exclusivity, one can expect an explosion of patent litigation after FDA approval

# Strategic Uses of Hatch-Waxman Act by Generics

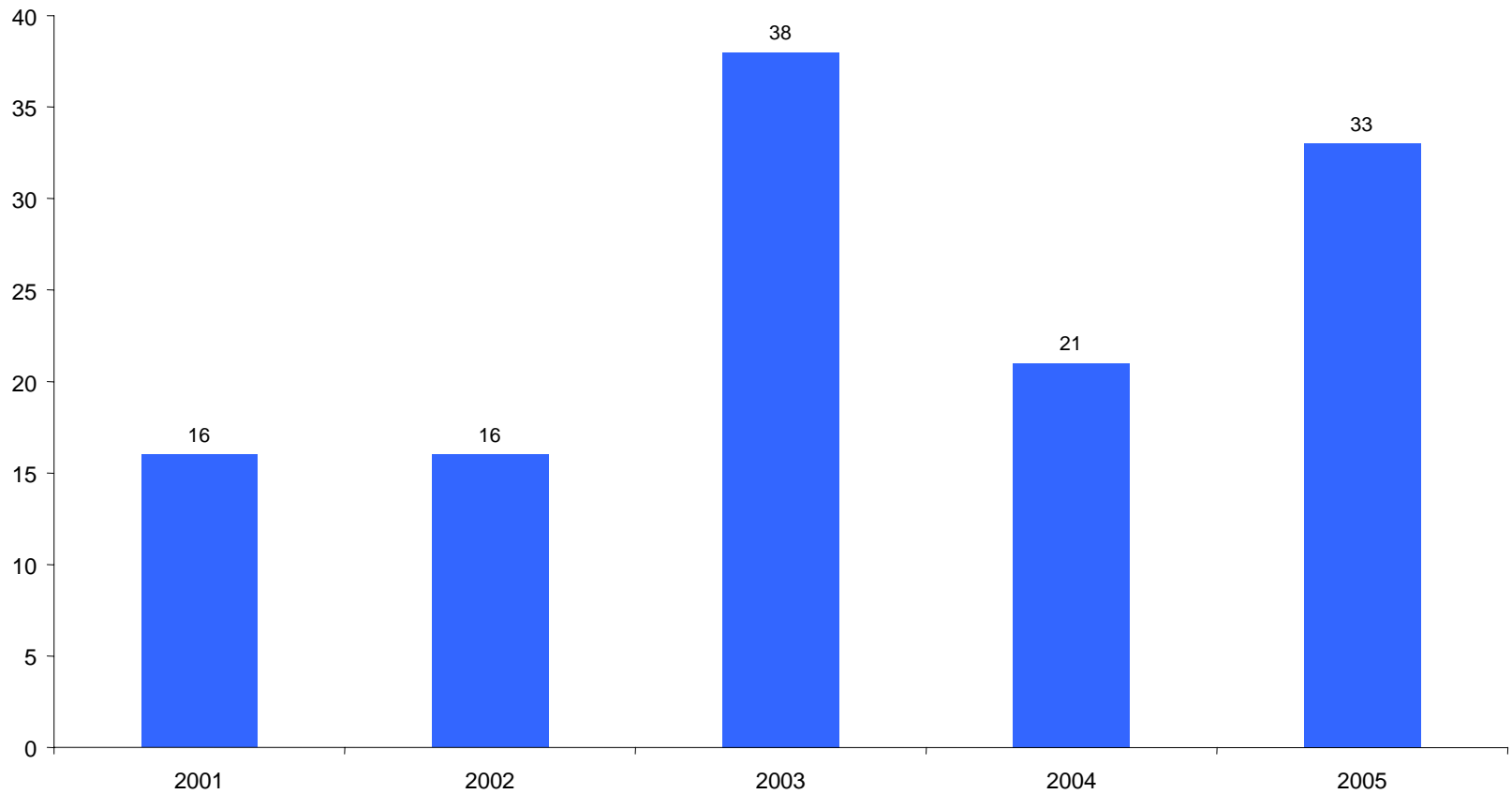
- Generics compete to be the first firm to challenge patents for 180 day exclusivity
- Almost all major brands are now subject to patent challenges four years after launch
- Patent suits create significant uncertainty about R&D returns prior to breakeven point

# Patent Challenges

- Generic firms have developed a business model involving prospecting in patent suit challenges
- Even if the odds of winning are long, the payoffs to being first can be huge (180 day exclusivity)
- Since costs of entry to generics are low relative to innovators', they can take a portfolio approach to patent challenges

# Number of Drugs Receiving Paragraph IV Filings for the First Time 2001-2005

Source: [www.paragraphfour.com](http://www.paragraphfour.com)



# Major Products with Recent Patent Challenges in the Courts

Lipitor

Taxol

Plavix

Risperdal

Celebrex

Zocor

Effexor XR

Fosamax

OxyContin

Paxil

Welbutrin SR

Neurontin

Norvasc

Imitrex

Allegra

Cipro

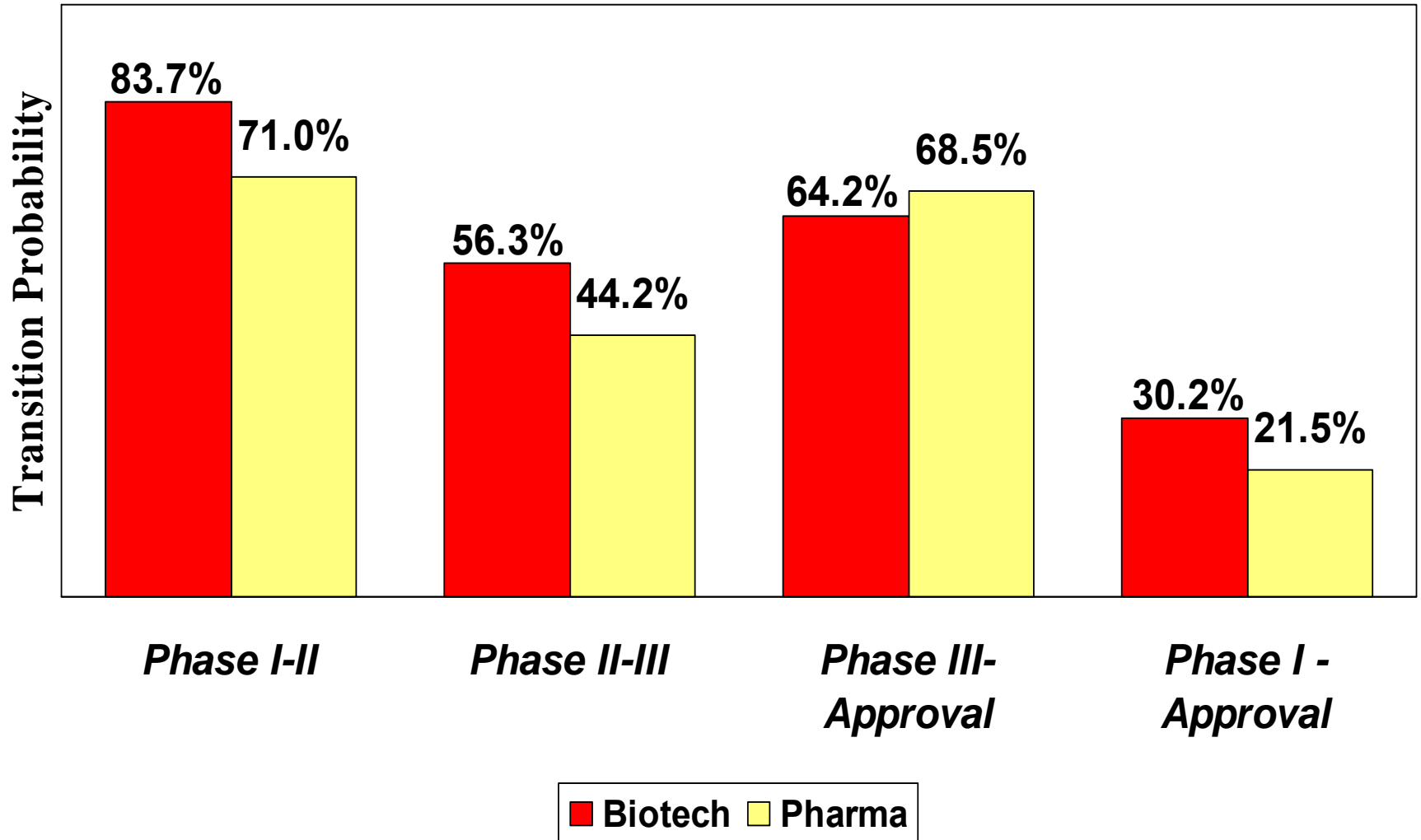
# What Industry Characteristics Support a Relatively Long Exclusivity Period?

- When R&D investment is difficult, risky, and lengthy
- When Innovation has important spillover benefits to society
- New biologicals satisfy these criteria

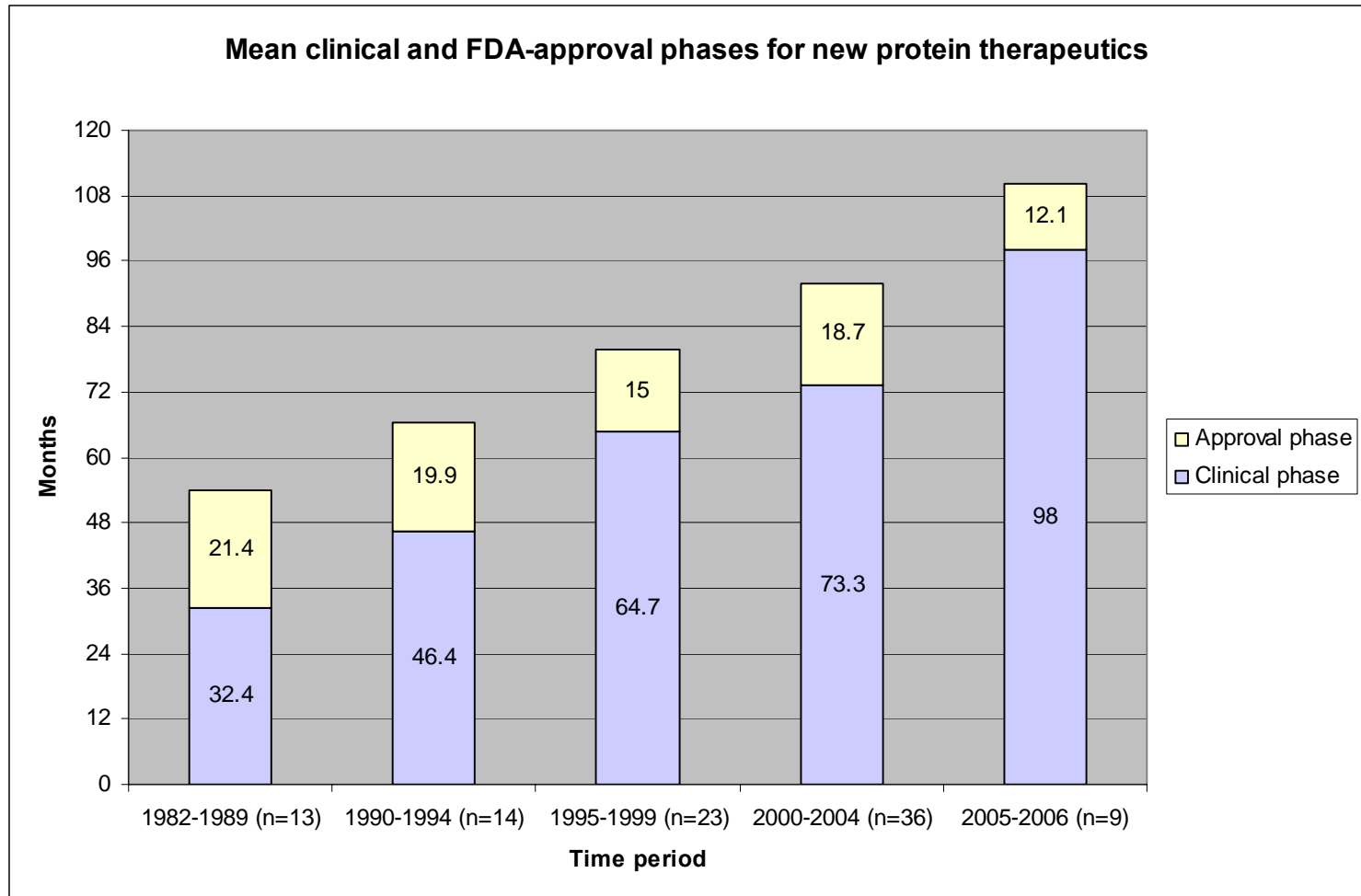
# Biological R&D Investments Currently Confront Many Risks

- Many product candidates fail at pre-clinical stage based on *in-vivo* or *in-vitro* screens
- Many products taken into human testing fail due to safety, efficacy, manufacturing, competitors' actions, reimbursement, etc.
- The increased uncertainty arising from early stage patent challenges would lower expected payoffs relative to risks

# Transition Probabilities for Clinical Phases

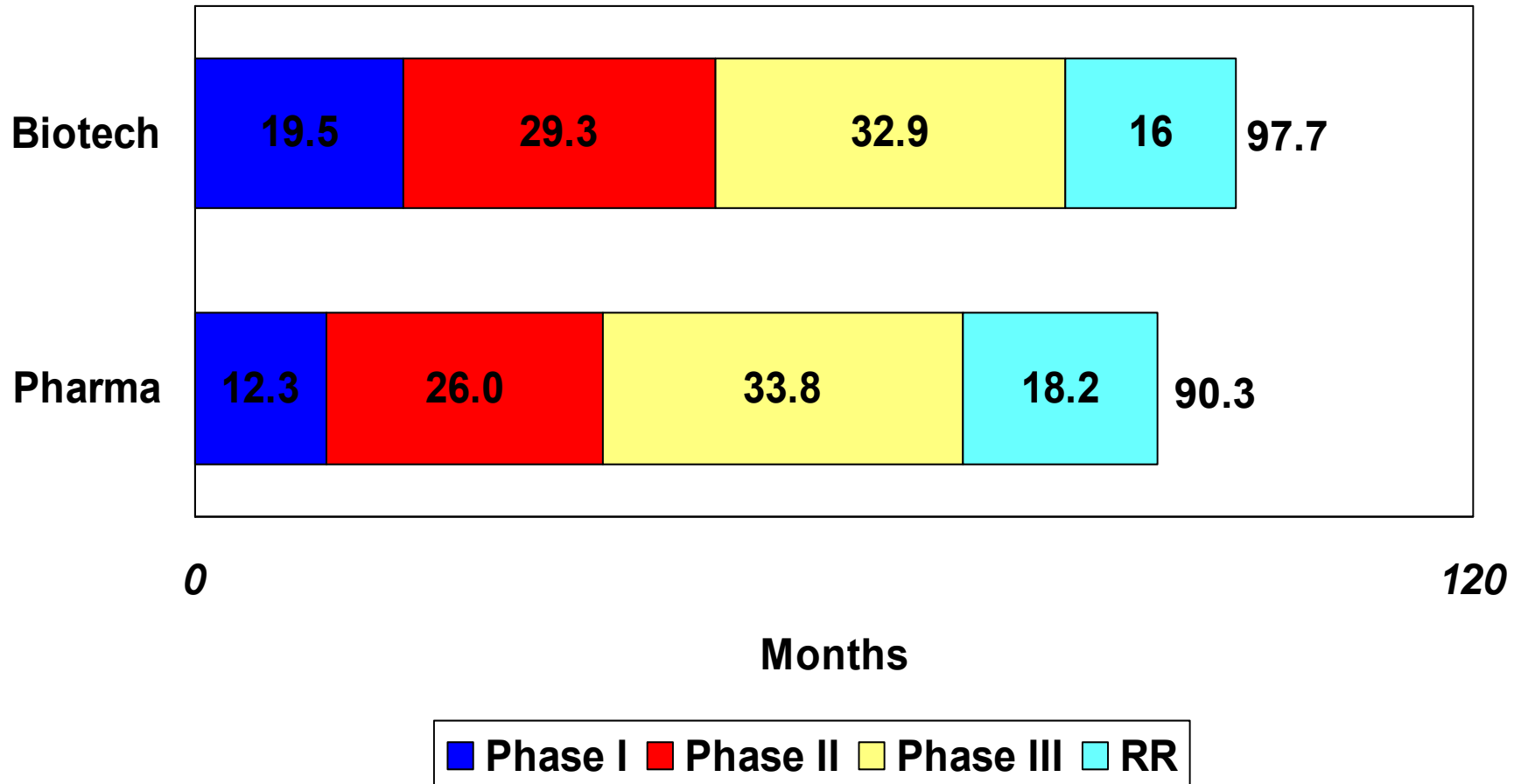


# Development Times for New Protein Therapeutics

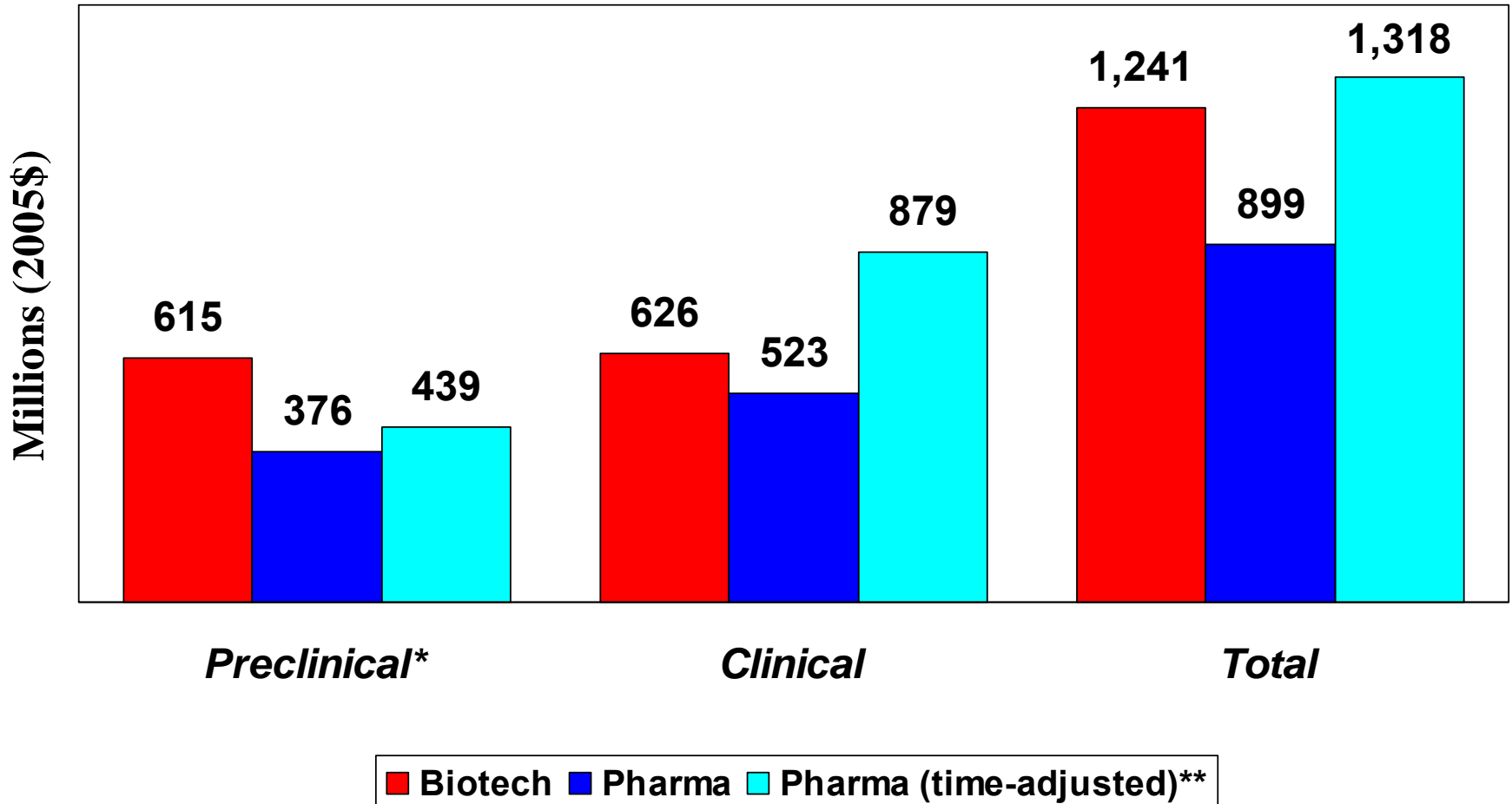


Note: Development times include only clinical phases and regulatory review (RR) periods. Pre-clinical times are not included.

# Clinical Development and Approval Times



# Pre-Approval Capitalized Cost Per Approved New Molecule



\* All R&D costs (basic research and preclinical development) prior to initiation of clinical testing

\*\* Based on a 5-year shift and prior growth rates for the preclinical and clinical periods

Source: DiMasi and Grabowski, *Managerial and Dec Econ* 2007, in press

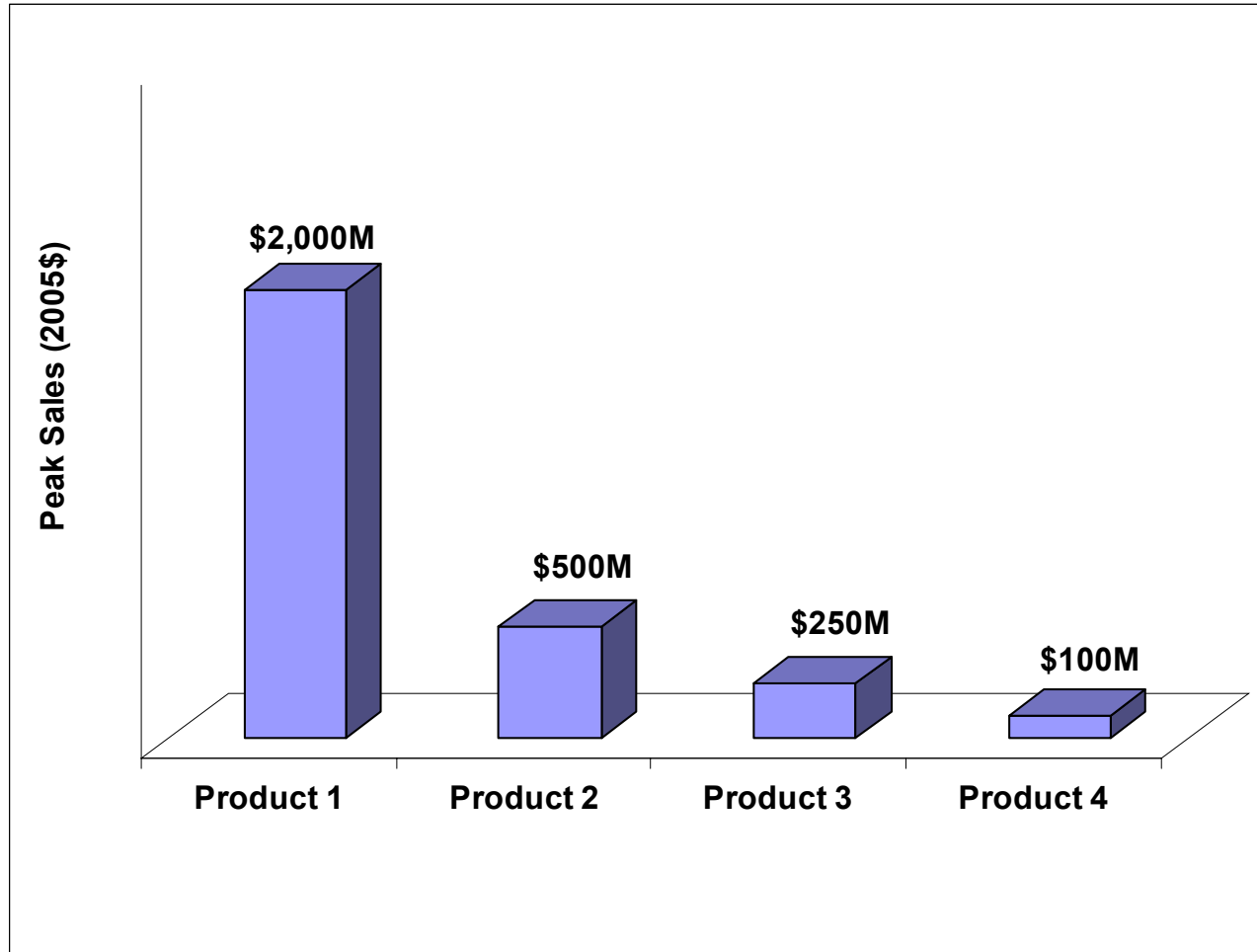
# What Other Factors Support a Lengthy Data Exclusivity Period for Biologicals?

- New biological entitles constitute many novel therapies for diseases with high unmet needs
- Many start-ups in the life science area depend on VC funding and partnerships
- VC funding in partnerships are quite sensitive to risks versus pay-offs.

# What Is the Breakeven Lifetime for a Portfolio of Biotech Products?

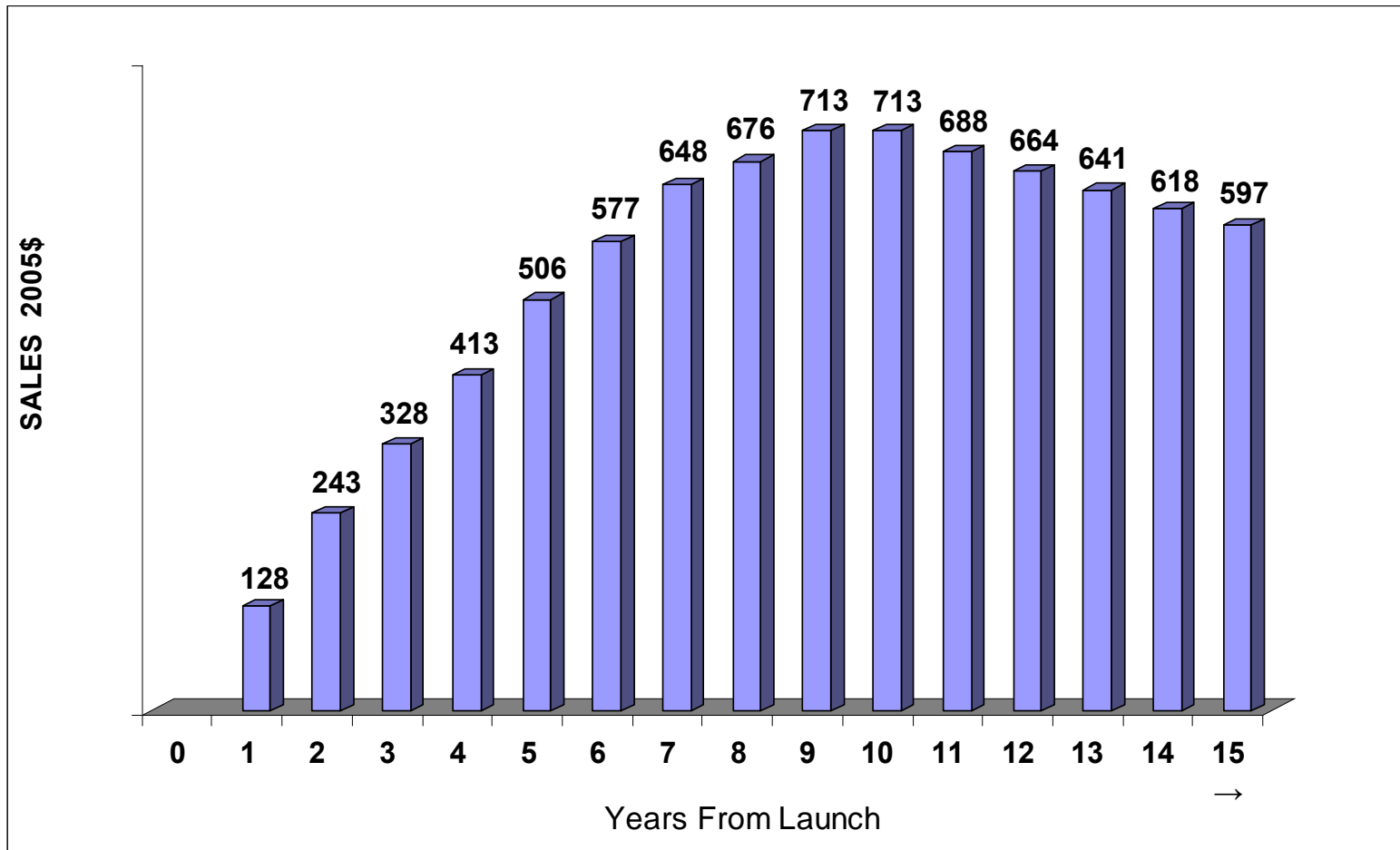
- Representative data utilized on R&D costs and returns for a portfolio of biotech products
- Peak product revenues range from \$2 billion to \$100 million in value
- Breakeven lifetimes ranged from 12.8 to 16.2 years for this model portfolio

# Model Portfolio Based on Sales Distribution for Established Biological Products



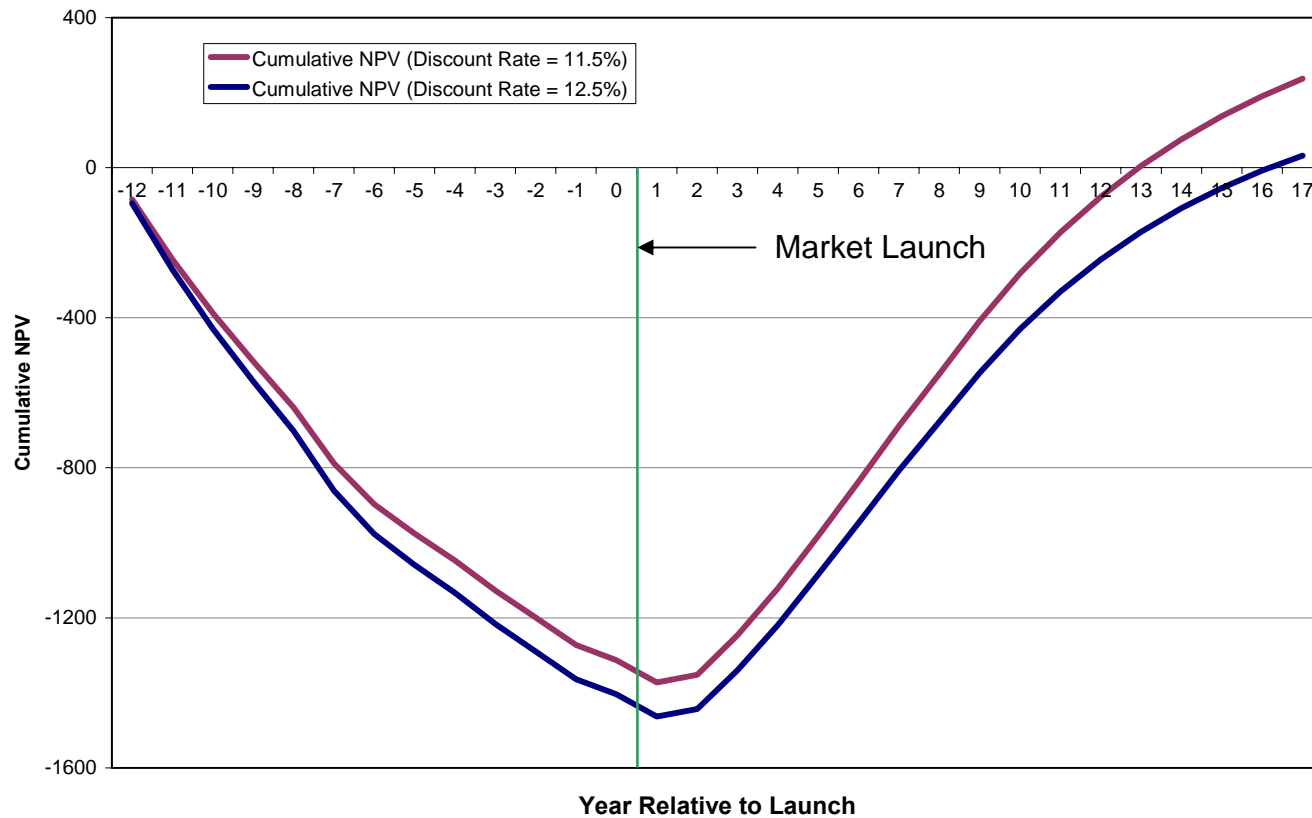
Source: Grabowski (2003) and (2007)

# Life Cycle Profile for Mean Product in Model Biologics Portfolio



Source: Author's analysis

# Estimated Cumulative Net Present Value for Average Biological Drug



Source: Author's analysis

# Summary

- Basic characteristics of R&D process for new biologicals support a lengthy exclusivity period
- Legislation without data exclusivity, or with only nominal periods of exclusivity, would have significant adverse effects on innovation