JENNIFER A. TEGFELDT, ESQ.

Jennifer has a Bachelor of Science degree in Biological Sciences from the University of California, Davis. Following a several year career as an analytical chemist, Jennifer graduated from Pierce Law in 1985 with the goal of practicing intellectual property law. The IP program, back then, was substantially different than now – Jennifer was the only woman in a class of eight men. She served as an editor to "Idea, the Journal of Law and Technology" almost from the beginning of her legal education. She counts among her most important mentors and guides (as do a number of IP students of Pierce Law), the irreplaceable Professor Bob Shaw, who never saw obstacles, only opportunities.

Jennifer was the first alumnae to be appointed law clerk to a judge of the Court of Appeals for the Federal Circuit. Jennifer served as law clerk to Circuit Judge Pauline Newman from 1985-1987, and assisted in such proceedings as Pennwalt, Texas Instruments, In re Thorpe, and the FAA air controller cases.

When her clerkship ended in 1987, Jennifer entered private practice with a small boutique patent law practice and was later recruited to join Fitzpatrick, Cella, Harper and Scinto in the firm's Washington D.C. offices. Her practice focused on patent prosecution and enforcement, appeals, trademarks, copyrights, licensing, and opinion work of all types. Jennifer has been very active in the Federal Circuit Bar Association, AIPLA, ITC Trial Lawyers Association, American Bar Association, including gaining Delegate status in the ABA's House of Delegates for the Federal Circuit Bar Association, and the American Inns of Court, Giles S. Rich Inn.

In 1994, Jennifer left private practice to join Genzyme Corporation as one of four attorneys supporting the company. Since that time, the legal team has grown to over twenty patent and corporate lawyers. For nearly seven years, Jennifer maintained a patent practice, while working closely with the corporate legal team in transactional matters, and in leading legal efforts to develop and put in place collaborations. In 2001, Jennifer has expanded her "Transactional IP" role in taking on a strategic position in the Business Development team for the Therapeutics business unit of Genzyme. In 2004, she joined the Corporate Development group, and as Director, Business Initiatives and Strategy, she continues to pursue her business knowledge as a logical and necessary component of intellectual property portfolio management and corporate growth.

Jennifer lives in the Boston area, and her friends know that when the winter weather breaks and she's not on a plane to visit a collaborator, she'll most likely be out on the water exploring the coast in her sailboat.

BIOTECHNOLOGY LICENSING

A View From the Inside

FOURTEENTH ANNUAL ADVANCED LICENSING INSTITUTE
PIERCE LAW
CONCORD, NEW HAMPSHIRE
JULY 11-15, 2005

Jennifer A. Tegfeldt, Esq.
Director, Business Initiatives and Strategy
Genzyme Corporation
Cambridge, Massachusetts

Discussion Points

- The Business of Biotechnology
- Forms of Collaboration
- Developing the Process
- Contractual Considerations
- Additional Thoughts in Crafting a Successful Collaboration

I. THE BUSINESS OF LIFE -- BIOTECHNOLOGY
An Historical Perspective

Source: 2004 Biotechnology Industry Association, www.bio.org, Time Line of Biotechnology

8000 B.C.	Humans domesticate crops and livestock
4000-2000 B.C.	Production of cheese and fermentation of wine (Sumeria, China, and Egypt)
	Babylonians control date palm breeding by selectively pollinating female trees with pollen from certain male trees
500 B.C.	First antibiotic made of moldy soybean curds to treat boils (China)
A.D. 100	First Insecticide made of powdered chrysanthemums (China)
1590-1675	1590-Janssen invents the microscope
	1663-Hooke discovers the cell
	1675-Leeuwenhoek discovers bacteria
1797	Jenner inoculates a child with a viral vaccine against smallpox
1830-1855	1830-Proteins discovered
	1833-First enzyme discovered and isolated
	1835-1855 Schleiden and Schwann propose that all organisms are made of cells
1859	Darwin publishes the theory of evolution by natural selection
1865	Genetics begins with Austrian monk Gregor Mendel studying garden peas and discovering that genetic traits are passed from parents to offspring in a predictable way -- the laws of heredity
1877-1879	1877-Koch develops a technique for staining and identifying bacteria
	1878-The first centrifuge is developed by Laval
	1879-Fleming discovers chromatin, the rod-like structures in the nucleus that became known as chromosomes
1902-1915	1902-The term “immunology” first appears
	1906-The term “genetics” is introduced
	1915-Phages, or bacterial viruses, are discovered

I. THE BUSINESS OF LIFE -- BIOTECHNOLOGY

An Historical Perspective *Continued*

1920	Human growth hormone discovered by Evans and Long
1928	Penicillin discovered as an antibiotic by Alexander Fleming
1930	U.S. Congress passes the Plant Patent Act, enabling plant breeding products to be patented
1944	Avery et al. prove DNA carries genetic information
1946	Discovery that genetic material from different viruses can be combined to form a new type of virus, an example of genetic recombination
1949	Pauling shows that sickle cell anemia is a "molecular disease" resulting from a mutation in the protein molecule hemoglobin
1953	"Nature" publishes James Watson and Francis Crick's manuscript describing the double helical structure of DNA
1956	Kornberg discovers the enzyme DNA polymerase I, leading to an understanding of how DNA is replicated
1966	The genetic code is cracked, demonstrating that a sequence of three nucleotide bases (a codon) determines each of 20 amino acids
1969	An enzyme is synthesized in vitro for the first time
1971	First complete synthesis of a gene
1973	Stanley Cohen and Herbert Boyer perfect genetic engineering techniques to cut and paste DNA (using restriction enzymes and ligases) and produce the DNA in bacteria
1976	First time the sequence of base pairs for a specific gene is determined (A, C, T,G)
1977-1979	First expression of a human gene in bacteria
	Recombinant human insulin first produced
	Human growth hormone first synthesized
1980	U. S. Supreme Court, in Diamond v. Chakrabarty, approves the patenting of genetically engineered life forms
1981	Scientists at Ohio University produce the first transgenic mice

I. THE BUSINESS OF LIFE -- BIOTECHNOLOGY

An Historical Perspective *Continued*

1983	Conception of polymerase chain reaction (PCR), in which heat and enzymes are used to make unlimited copies of genes and gene fragments
1985	Genetic markers found for kidney disease and cystic fibrosis
1986	First genetically engineered vaccine for humans: hepatitis B
	First anticancer drug through biotechnology: interferon
1988	Harvard molecular geneticists receive first U.S. patent for genetically altered animal -- a transgenic mouse ("the onco-mouse")
1990	Human Genome Project -- an international effort to map all the genes in the human body -- is launched
	First transgenic dairy cow used to produce human milk proteins for infant formula
1994	First breast cancer gene discovered
	FDA approved food produced through biotechnology: FLAVSAVR™ tomato
1997	First animal cloned from an adult cell: a sheep named Dolly
1998	Embryonic stem cells used to regenerate tissue and create disorders mimicking diseases
2000	Rough draft of the human genome sequence is announced
2002	Scientific journals publish complete human genome sequence
2003	U.S. Environmental Protection Agency approves the first transgenic rootworm-resistant corn
	An endangered species (the banteng) is cloned for the first time (mules, horses and deer are also cloned)
2004	Korean researchers report the first human embryonic stem cell line produced with somatic cell nuclear transfer (cloning)
	FDA approves the first anti-angiogenic drug for cancer, Avastin (bevacizumab)

"…anything under the sun that is made by man." Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)

- The Possibilities of Biotechnology
  - Agriculture
    - Higher producing and drought and insect resistant plants
    - Better tasting and longer lasting vegetables and fruits
    - Higher productivity animals

"…anything under the sun that is made by man." Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)

Continued

- The Possibilities of Biotechnology
  - Therapeutics
    - Gene Therapy
    - Protein Therapies
    - Diagnostics, including genetic testing
    - Improved patient therapy monitoring
    - Cell Therapies
    - Combination Therapies
    - Synergies with "chemical" therapies

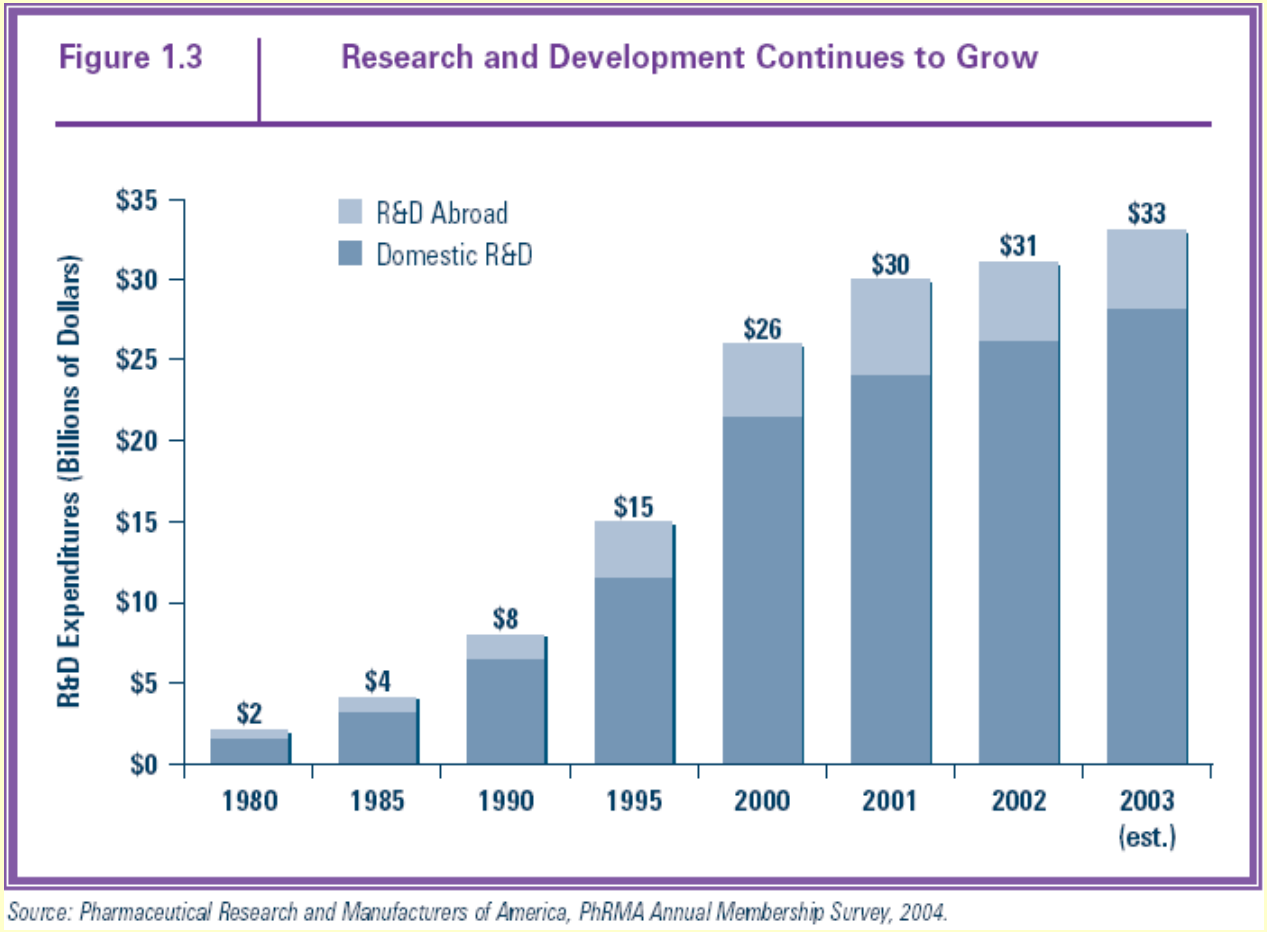
"…anything under the sun that is made by man." Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)

Continued

- The Possibilities of Biotechnology
  - Discovery
    - Models for disease, cell and animal
    - Screening techniques
  - Manufacture
    - Plant (such as tobacco and picchia)
    - Insect
    - Mammalian cells (human and CHO)
    - Transgenic animals
  - Environmental uses
    - Hazardous waste clean-up

Research and Development Investment

- In 2003, R&D investment worldwide reached $33 billion
- 26.9% increase in expenditures from 2000

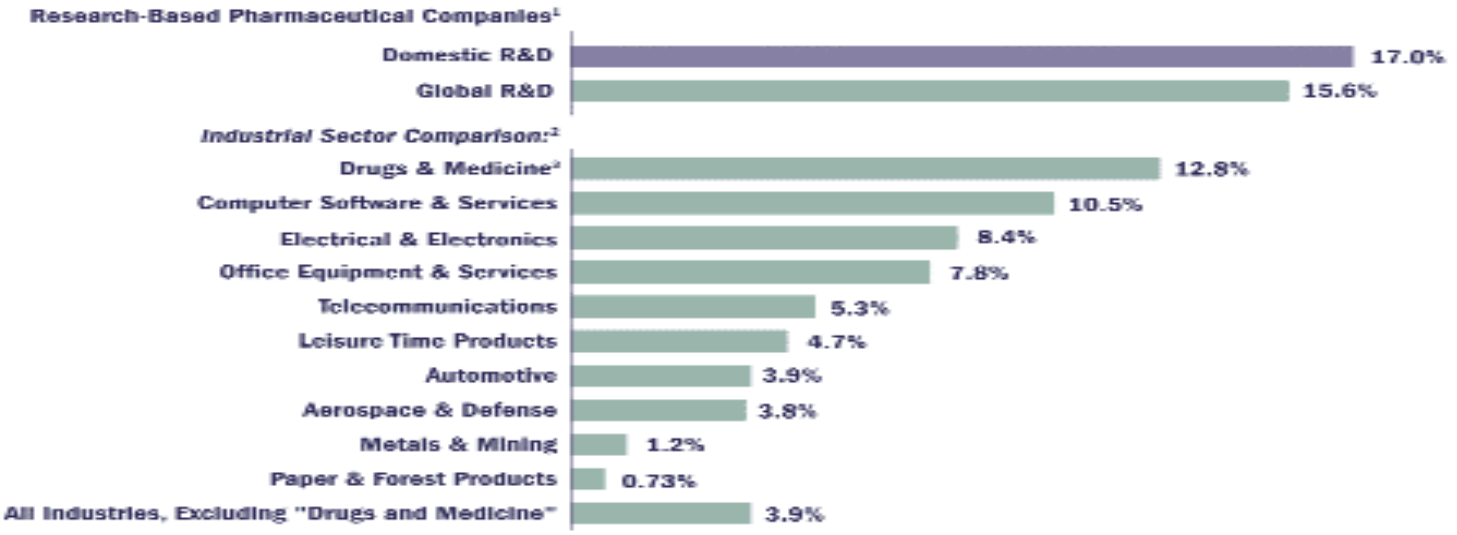


Source: Pharmaceutical Industry Profile 2004 (Washington, DC: PhRMA, 2004), Chapter 1, The Process of Innovation: R&D in America's Highest Technology Companies, page 7; www.phrma.org

Relationship of R&D to Sales

- Greater than three times the level of R&D investment in drugs and medicine

Figure 2-3
R&D AS A PERCENT OF SALES, RESEARCH-BASED PHARMACEUTICAL COMPANIES AND U.S. INDUSTRIAL SECTORS, 2000



1 "Researched-Based Pharmaceutical Companies" based on ethical pharmaceuticals sales and ethical pharmaceuticals R&D only as tabulated by PhRMA.

2"Standard and Poor's Compustat – 4 digit SIC codes.

3 "Drugs and Medicine" category based on total R&D and sales for companies classified within the "Drugs and Medicine" sector as tabulated by Standard & Poor's Compustat, a division of McGraw-Hill: (includes research- and non-research-based companies).

Source: PhRMA, 2001, based on data from PhRMA Annual Survey and Standard & Poor's Compustat, a division of McGraw-Hill.

Source: Pharmaceutical Industry Profile 2001, Chapter 2, Research and Development -- The Key to Innovation, pages 13,15; www.phrma.org

Where the Funding Goes

- 33.8% spent on preclinical studies
- 34.6% spent on Phase I, II, and III studies
- 12.4% spent on Phase IV studies, post approval by the FDA

Table 5
Domestic R&D By Function, PhRMA Member Companies: 2002

(dollar figures in millions)

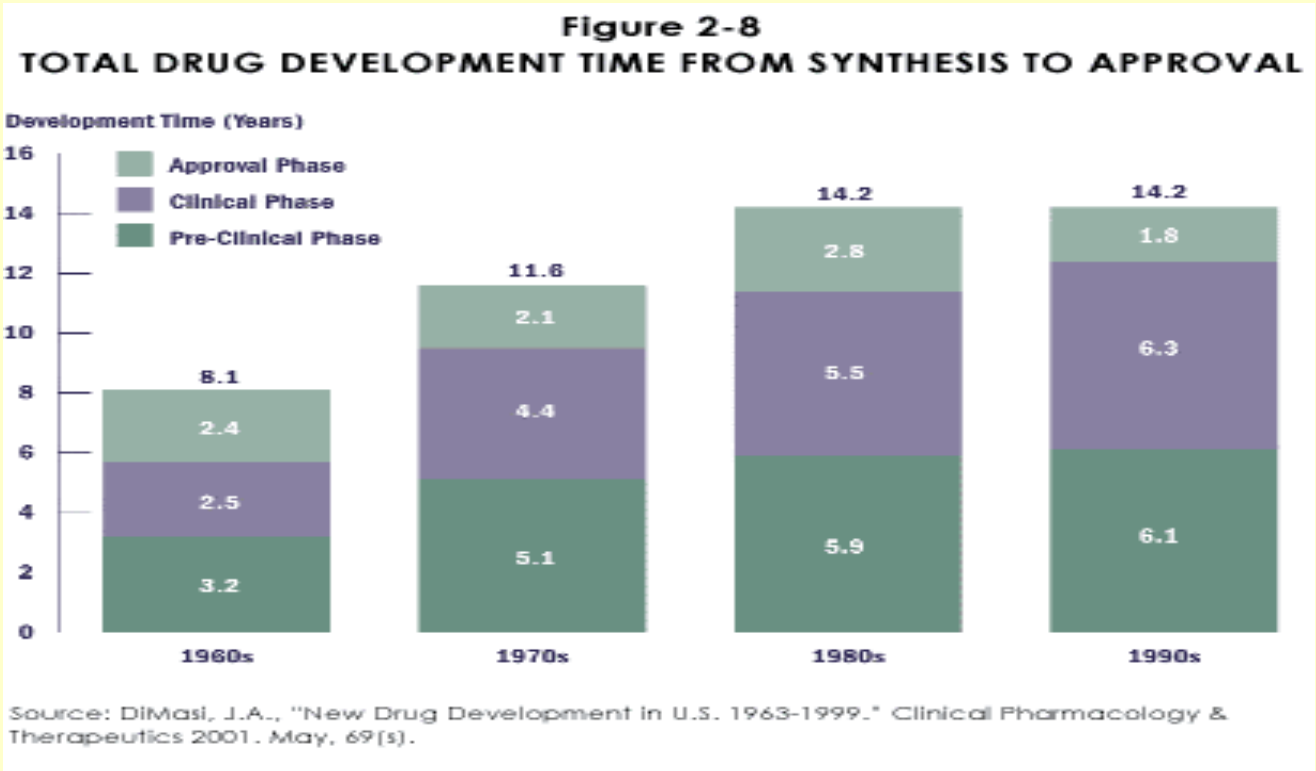
Function	Dollars	Share
Prehuman/Preclinical	$10,481.6	33.8%
Phase I	1,490.2	4.8
Phase II	2,968.1	9.6
Phase III	6,286.4	20.2
Approval	2,455.0	7.9
Phase IV	3,855.2	12.4
Uncategorized	3,493.7	11.3
TOTAL R&D	**$31,012.2**	**100.0%**

Notes: All figures include company-financed R&D only. Total values may be affected by rounding.
Source: Pharmaceutical Research and Manufacturers of America, PhRMA Annual Membership Survey, 2004.

Source: Pharmaceutical Industry Profile 2004 (Washington, DC: PhRMA, 2004), Appendix, page 43 ; www.phrma.org

Other Issues Bearing on Cost: Timeline for R&D

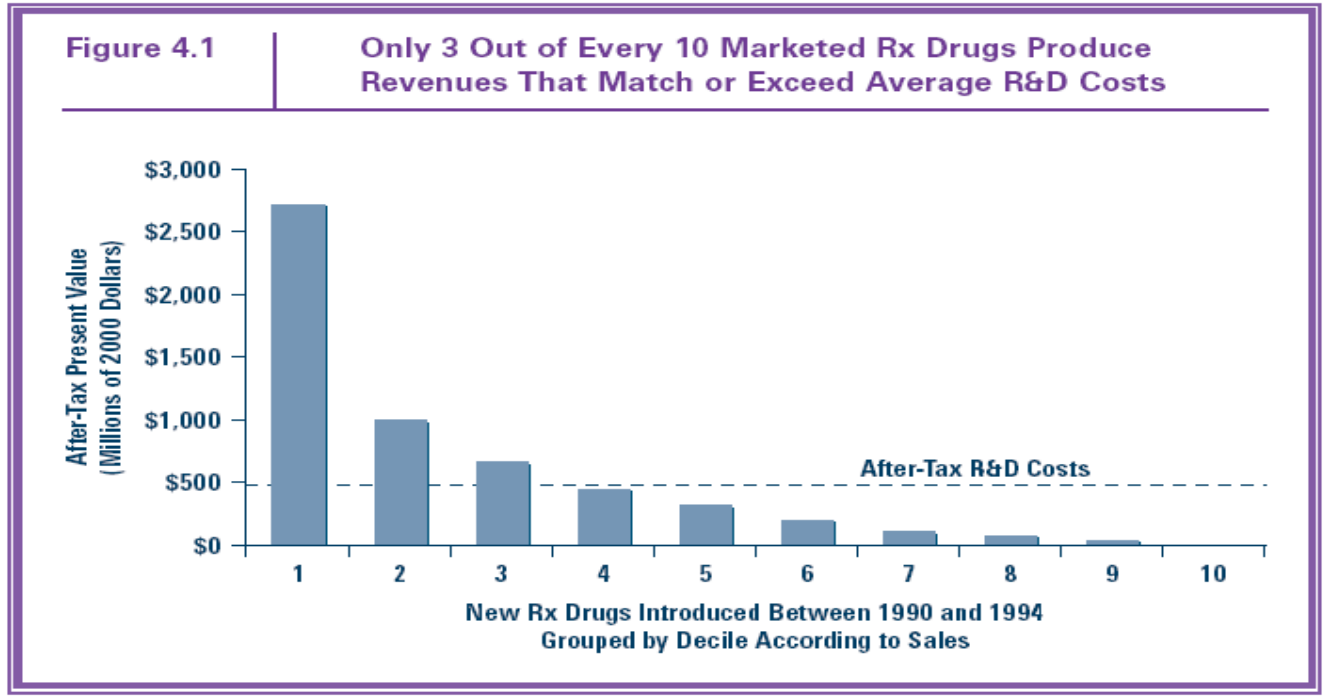
- The Developmental Timeline has increased
- 8 years to approval in the 1960's
- 14.2 years to approval in the 1990's



Source: Pharmaceutical Industry Profile 2001, Chapter 2, Research and Development – The Key to Innovation, pages 17, 19; www.phrma.org

Success Factor for Drug Candidates and Funding of Development Efforts

- Only three out of ten new drug products or new drug entities (introduced 1990-1994) had returns higher than average after tax R&D costs
- Companies rely on the success of a few products to support their product development pipeline



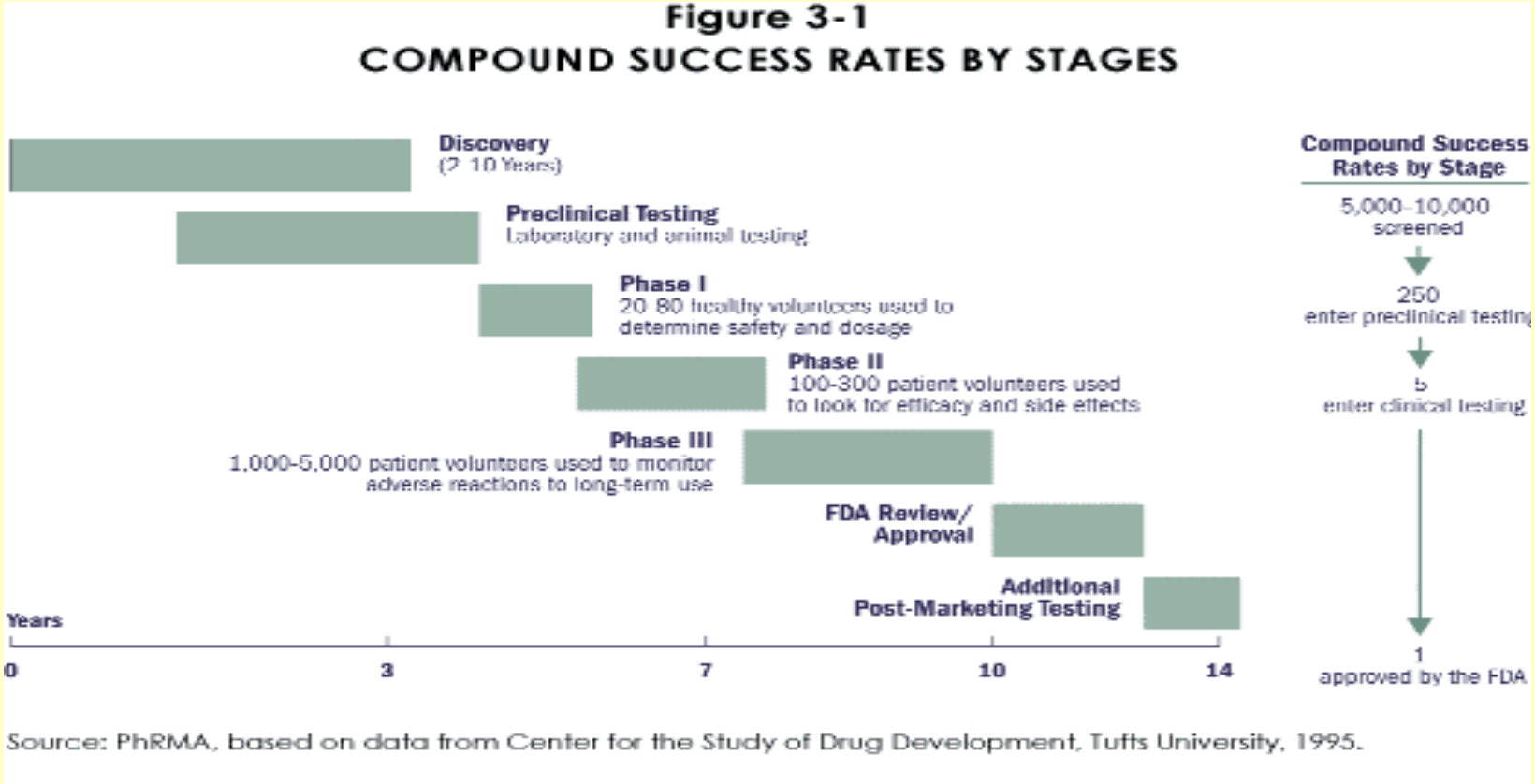
Note: The drug development costs cited in this chart are out of pocket after tax in 2000 dollars for drugs introduced between 1990 and 1994. The same analysis found that the total cost of developing a new drug was $802 million.

Source: H. Grabowski, J. Vernon, and J. DiMasi, "Returns on Research and Development for 1990s New Drug Introductions," Pharmacoeconomics 20, suppl. 3 (2002): 11–29.

Source: Pharmaceutical Industry Profile 2004 (Washington, DC: PhRMA, 2004), Chapter 4, Incentives for Innovation, page 31; www.phrma.org

Likelihood of Success in Development

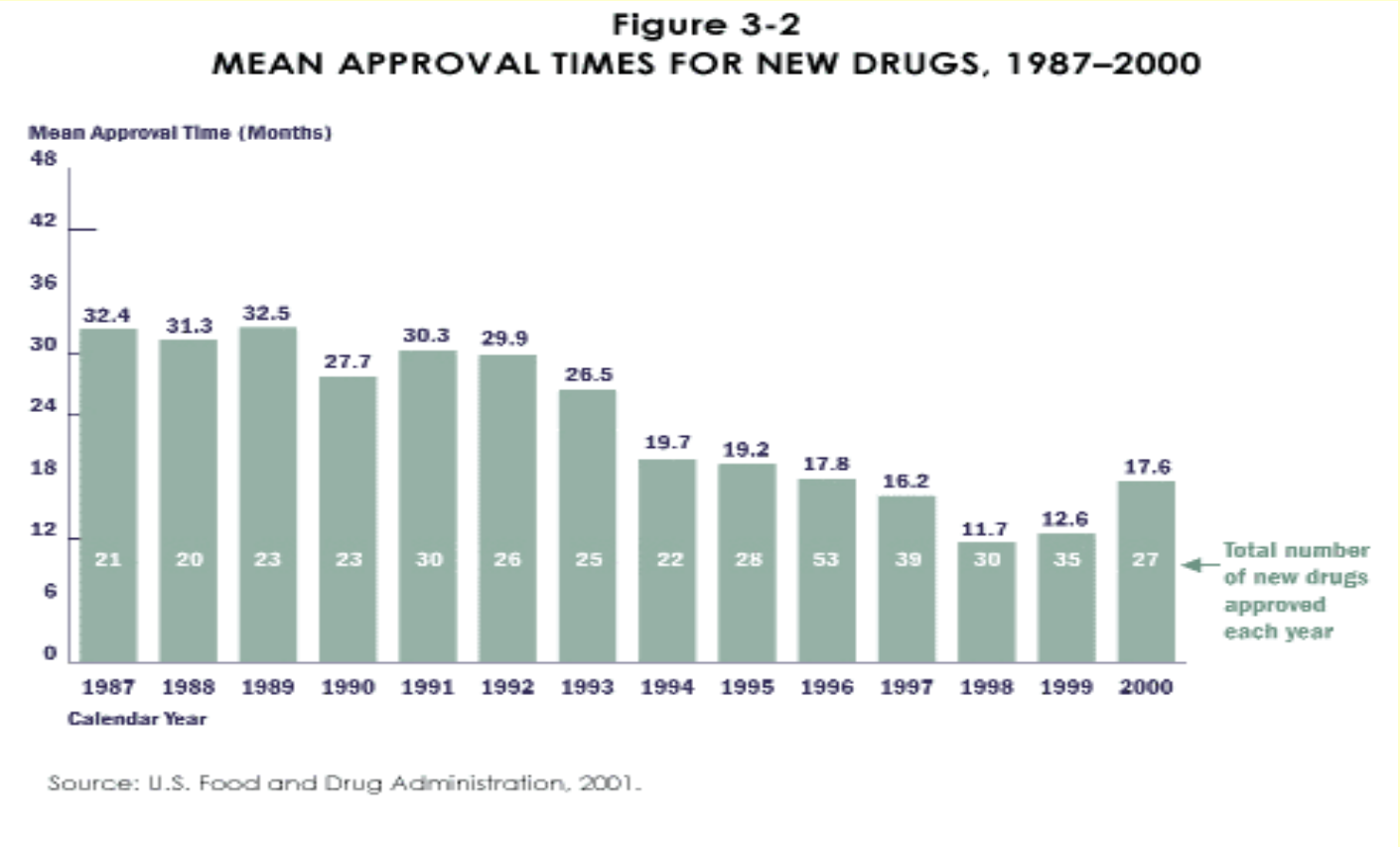
- One in up to 10,000 compounds ultimately becomes a marketed drug
- Rigorous science at the early stages of development is critical to improving the odds of success



Source: Pharmaceutical Industry Profile 2001, Chapter 3, Regulatory and Legal Aspects of Drug Development, page 24; www.phrma.org

FDA Review Process—Timeline

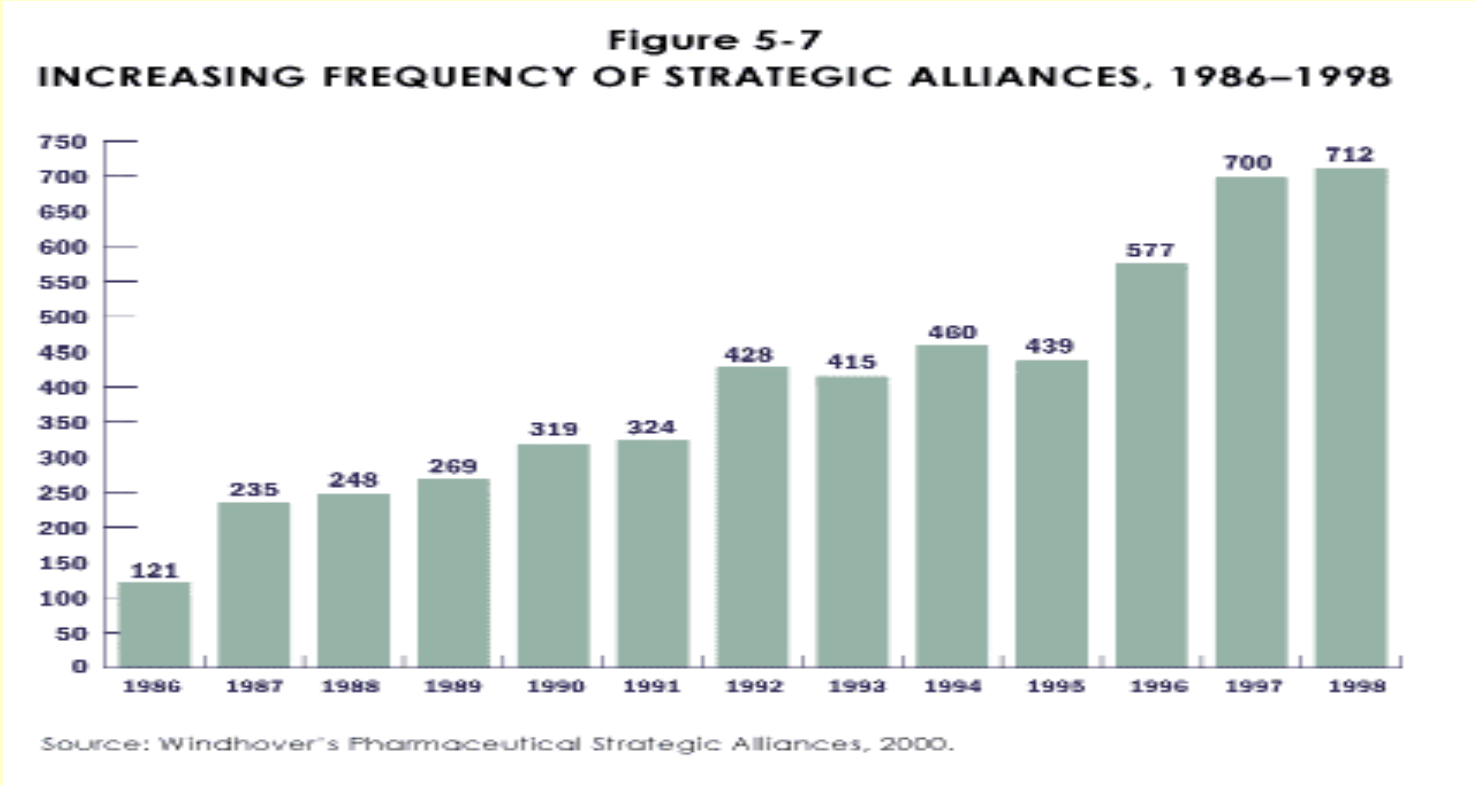
- FDA review period reduced by almost half since 1987 due to increased pre-clinical efforts and clinical trials supporting more comprehensive regulatory filings, and FDA efficiency
- Safety is a paramount concern throughout



Source: Pharmaceutical Industry Profile 2001, Chapter 3, Regulatory and Legal Aspects of Drug Development , page 25; www.phrma.org

Options for Meeting the Financial Challenge

- Opportunities of success optimized through collaborations
  - •Development expertise
  - •Regulatory support, national and international
  - •Marketing expertise, national and international
  - •Capital
- The impetus to form strategic alliances has built nearly seven fold in the twelve year period from the mid 1980's to the late 1990's
- The frequency of mergers and acquisitions have grown annually, and have included larger transactions



Source: Pharmaceutical Industry Profile 2001, Chapter 5, pages 62-63; www.phrma.org

Mergers and Acquisitions in the Pharmaceutical Industry

2000	G.D. Searle and Pharmacia & Upjohn › Pharmacia Corporation
2000	Warner-Lambert and Pfizer Inc. › Pfizer Inc.
2000	Rhone-Poulenc and Hoechst Marion Roussel › Aventis AG
2000	SmithKline Beecham and Glaxo Wellcome › GlaxoSmithKline
2000	Centecor and Johnson & Johnson › Centecor acquired
2000	Knoll Pharmaceuticals acquired by Abbott Laboratories
2000	Alza Corporation anticipated to be acquired by Johnson & Johnson (subject to Board approval)
2000	The Liposome Company acquired by Elan Pharmaceuticals
2000	Pasteur Merieux Connaught › Aventis Pasteur
2000	Pathogenesis Corporation acquired by Chiron Corporation (non-member)
1999	Monsanto and Pharmacia & Upjohn
1999	AHP/Warner-Lambert and Pfizer/Warner Lambert (pending)
1999	Roche and Genentech
1999	Warner-Lambert and Agouron
1998	Hoechst AG and Rhone-Poulenc Rorer
1998	Sanofi SI and Synthelabo
1998	Zeneca and Astra
1997	Hoffmann-La Roche and Boehringer Mannheim
1997	Nycomed and Amersham
1996	CibaGeigy and Sandoz
1996	Elan and Athena Neurosciences

Mergers and Acquisitions in the Pharmaceutical Industry *Continued*

1995	Knoll and Boots
1995	Glaxo and Burroughs Wellcome
1995	Gynopharma and Ortho-McNeil
1995	Hoechst-Roussel and Marion Merrell Dow
1995	Pharmacia and Upjohn
1995	Rhone-Poulenc Rorer and Fisons
1995	Schwarz Pharma and Reed & Carnrick
1994	American Home and American Cyanamid
1994	Hoffmann-La Roche and Syntex
1994	Pharmacia and Erbamont
1994	Sanofi and Sterling (prescription drug operation)
1994	SmithKline Beecham and Sterling (over-the-counter pharmaceutical unit)
1991	SmithKline and Beecham
1990	Boots and Flint
1990	Pharmacia and Kabi
1990	Rhone-Poulenc and Rorer
1989	American Home and A.H. Robins
1989	Bristol-Myers and Squibb
1989	Dow and Marion
1988	Kodak and Sterling
1986	Schering-Plough and Key
1985	Monsanto and Searle
1985	Rorer and USV/Armour

Source: Windhover's Health Care Strategist, 2000.

II. Forms of Collaboration

The relationship begins...

- Intentions and objectives are paramount
- Ensure the agreement matches the intentions of both sides—ask questions!

Confidential Disclosure Agreements

- Purpose: To exchange proprietary information under obligations of confidentiality
- Limited term (often five years)
- Use of the exchanged information only for the purposes of evaluating the contemplated collaboration
- “Industry convention” format and terms

Materials Transfer Agreements

- Purpose: The exchange of materials to conduct specified experimentation
- Use of materials limited to specified uses
- Typically requires exchange of resulting data
- May include a provision permitting publication of results, subject to confidentiality provisions
- Materials cannot be transferred to third parties, and any unused materials must be returned or destroyed
- “Industry convention” format and terms; general IP provisions

Consulting Agreements

- Purpose: To engage a collaborator, often an individual, in the provision of services of mutual interest
- Term can be one or multiple years, depending on the objectives for the services
- Should clearly define:
  - The services to be provided by the consultant
  - The time commitment required
  - Payment terms
  - Ownership and use of the consultancy results, and any inventions
- Typically includes confidentiality provisions
- Can be used as an adjunct to other forms of agreement, such as licenses or sponsored research agreements
- If an academic collaborator, be aware of institutional restrictions on scope, time commitment, and rights in intellectual property
- If the consultant is an employee of an institution, seek institutional approval and sign off

More Comprehensive Forms of Agreement

- Sponsored Research Agreement
  - Performed under a Research Protocol and Budget
  - Provides for exchange of results obtained
  - Typically includes provisions of confidentiality, and rights to intellectual property developed
  - Often includes publication provisions, if an academic collaborator, subject to obligations of confidentiality
  - Be sure to include a scientific contact within the company to work with the research collaborator
  - Can be developed concurrent with a license or other strategic agreement

Agreements With Increasing Strategic Importance

- License Agreements
- Collaboration Agreements
  - Marketing, manufacture, product development, delivery and formulation
- Joint Venture Agreements
  - Focus is on a field defined by product or service
- Mergers and Acquisitions
  - Can involve companies of greater/lesser or approximately same size
  - Asset Acquisitions
  - Formation of a new business entity
  - Spin-outs of some or all technology

III. Developing the Process

A successful collaboration cannot be built without:

- Determining the intentions of the parties in working together, AND

- Clearly defining their objectives and the means to carry out those objectives in a work plan

Consider

- Relationship defined by Industry
  - Synergistic technologies
  - Service provider becoming collaborator
  - Advantage of broader collaboration to provide guidance for relationship in the future (such as Master Agreements)
  - Customer/Supplier

Consider *Continued*

- Relationship defined by Technology
  - Value of Intellectual Property held, and improvements
  - Anticipated future development of the technology field
  - What other technologies will offer alternatives
  - Is the value in patents, or driven by trade secrets, copyrights or trademarks

Consider

Continued

- Relationship between the Parties
  - On-going participation of seller
  - Allocation of responsibilities, such as R&D and manufacture, marketing
  - Is the collaboration an entry into a broader future collaboration/acquisition
  - Is “relationship building” a purpose for the collaboration
  - Alliance Management

Ask

- What does the client want at the end of the day?
- What is important to the deal, and what is not?
- What makes a good deal a great deal (and when does it go in the other direction)?

Client and Counselor Should Understand:

- How is the collaboration going to move forward, after execution?
- What is the effect of not thinking through all aspects of the collaboration?
  - Lengthy and difficult negotiations
  - Poor future relationships in the future
  - Project abandoned and investment lost

IV. Contractual Considerations

The agreement must clearly reflect the obligations and rights of the parties and what is important to each

- Cost
  - Research funding
  - Services funding
  - Option fees for improvements
  - Patent expenses
  - Royalties on earned sales
  - Minimum annual royalties
  - Milestones
  - Patent enforcement expenses
  - Options for fully paid up rights

IV. Contractual Considerations

Continued

The agreement must clearly reflect the obligations and rights of the parties and what is important to each

- Grant clause
  - Exclusive or non-exclusive
  - When can one shift to another
  - Buy-ups or Buy-downs

IV. Contractual Considerations

Continued

The agreement must clearly reflect the obligations and rights of the parties and what is important to each

- Term and Termination
  - Term and patents, pending applications, and trade secrets
  - Termination
    - Unwind Provisions
      - Financial considerations, effects of bankruptcy
      - Disposition of results
      - Disposition of intellectual property (solely or jointly owned)
      - On-going obligations (such as confidentiality, participation in intellectual property litigation)
    - Termination for cause
    - Termination for convenience

IV. Contractual Considerations

Continued

The agreement must clearly reflect the obligations and rights of the parties and what is important to each

- Due Diligence
  - Development and Milestone Timelines
  - What happens if technical events interrupt the timeline
- Confidentiality and Publications
  - Publications not often issue with companies, but a key issue for academic collaborators
  - Period allowed for removal of the disclosing party's confidential information and patent application filings
- Definitions
  - Test the definitions with a "lay person" reading of the agreement
  - Layering

Drafting Thoughts

- Don’t write an agreement you wouldn’t sign
- If the agreement requires a lawyer to understand it...

V. Additional Thoughts

- Reevaluate the collaboration positioning through the negotiation process
  - Have the goals or the objectives of the parties changed?
  - As discussions proceed, are there new opportunities for tailoring the collaboration (broadening or narrowing)?
  - Have outside events changed the needs/wants of the parties?
  - Have internal events changed what parties want/need or can afford?

V. Additional Thoughts

Continued

- Coordinate stacking provisions for royalties
- Consider tax implications
  - Joint ventures, spin-outs, wind-ups
  - International collaborations
    - Manufacture on one shore, fill-finish on another
    - Customs duties and COGS
  - The real cost to the collaborator
    - In management time
    - In consumption of R&D, manufacture, regulatory and marketing resources
    - In $$ outlay

Work toward a win-win collaboration even when negotiations seem difficult

Good relationships only get better