Morgan Lewis

deskbook

Emerging Life Sciences Companies

second edition

Chapter 15

Expanding the Pharma/Biotech Business in the United States: Regulatory and Competition Issues

Chapter 15

EXPANDING A PHARMA/BIOTECH BUSINESS IN THE UNITED STATES: REGULATORY AND COMPETITION ISSUES

Substantial Opportunities

A. Demand from changing U.S. population demographics (aging)

B. Demand by biotech companies for licensing/acquisitions/alliances for funding purposes

C. Demand for new drug/biologic products for underserved/unaddressed indications

D. Substantial expansion of government funding available for prescription drug purchases

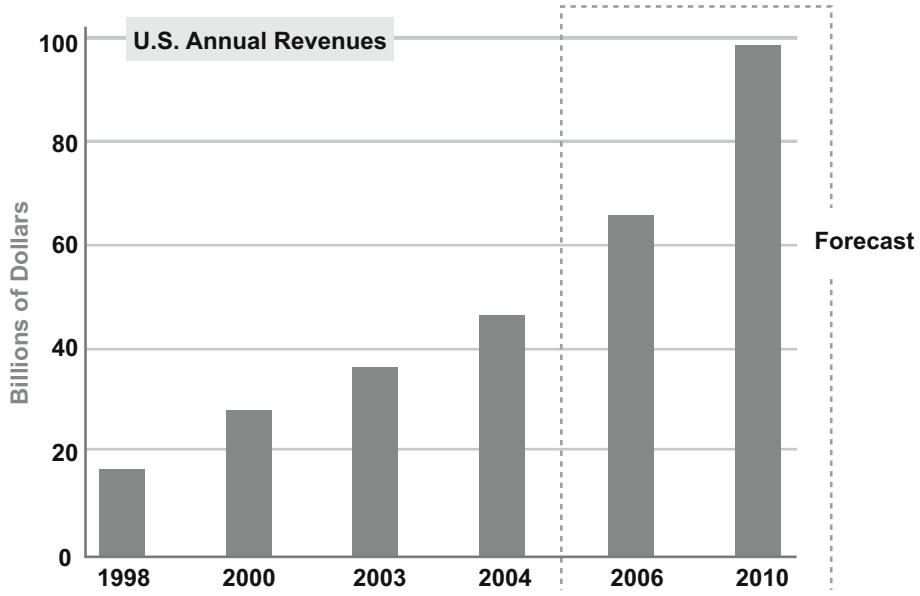
1. Medicare Prescription Drug, Improvement, and Modernization Act of 2003

   a. Provides for an estimated $750 billion of additional funding for government purchases of prescription drugs over the first decade of operation (beginning Jan. 1, 2006)

   b. Is altering competitive landscape for pharma/biotech companies

   c. Will result in U.S. government paying for approximately 45% of all prescribed drugs/biologics over the next decade

Biotech Growth . . . and Promise



Evolving Nature of Big Pharma/Biotech Relationships

A. Enhanced biotech bargaining position in view of demand for biologics products

   1. Greater interest in early-stage development products

   2. Willingness to consider broader partnering relationships (e.g., long-term involvement in drug's development; co-marketing and co-promotion agreements; co-manufacturing agreements; reservation of certain indications to the drug/biologic innovator)

Pharma/Biotech Markets

A. Changes in U.S. Food and Drug Administration (FDA) drug development regulatory focus

B. Economic regulatory issues: costs/valuation/reimbursement

C. Issues regarding pricing/marketing/distribution/patient data

D. Competition issues

FDA Drug Development Regulation

A. Sharper focus on product safety

   1. Increased use of Phase IV marketing studies as a condition of approval

   2. FDA draft guidances on premarketing risk assessment, risk-minimization action plans, and pharmacovigilance practices/pharmacoepidemiologic assessment (Mar. 2005)

   3. Emphasis on complete FDA regulation drug labeling (with preemption protection)

   4. Likely consequences for potential product liability litigation

   5. Voluntary industry code to limit direct-to-consumer (DTC) advertising

B. Costs of approval substantial and increasing

   1. Tufts University Center for the Study of Drug Development estimates costs of approximately $897 million per approved drug (including postapproval R&D costs) (2003) and $1.3 billion per approved biologic (2006)

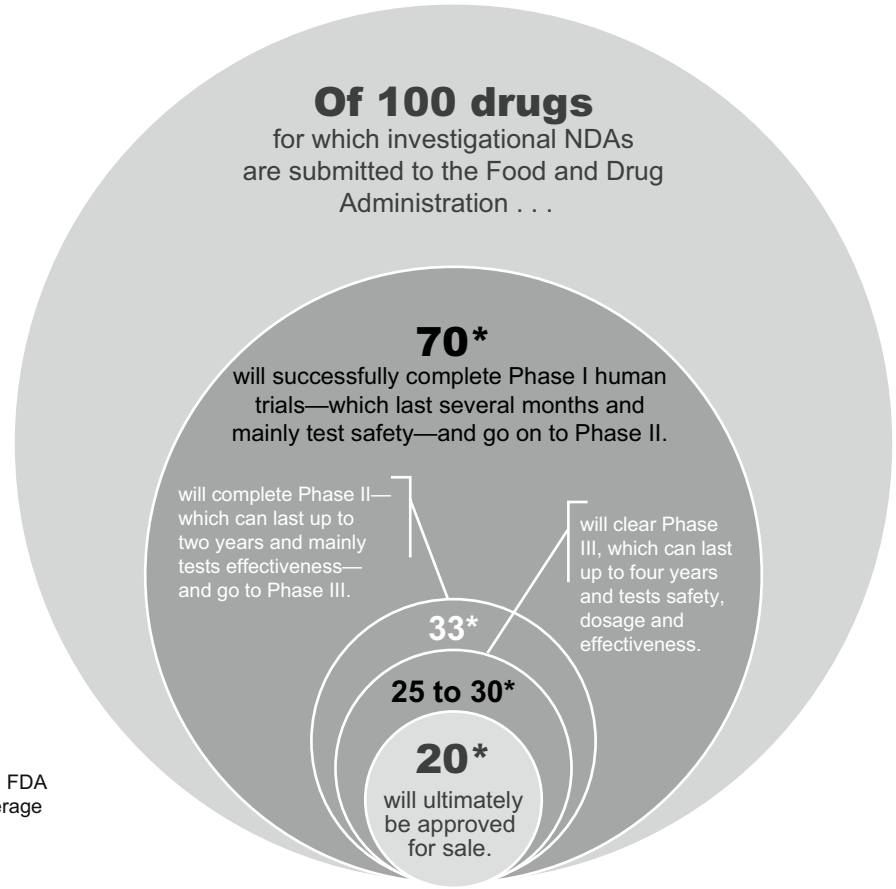
      a. Affects therapeutic categories selected for clinical trials

      b. Affects location of clinical trials

C. New focus on manufacturing/product quality

   1. FDA consent settlements regarding manufacturing issues (e.g., GlaxoSmithKline)

   2. FDA efforts to move to risk-based good manufacturing practice (GMP) compliance



Source: FDA
* On average

New Economic Issues and Challenges for Market Expansion

A. Increased focus on cost of the drug/biologic

1. The new Medicare Act will result in U.S. government paying for approximately 45% of drugs/biologics (up from current 16%)

2. The new Medicare Act also significantly enhanced the role of the Centers for Medicare and Medicaid Services (CMS) in determining whether—and at what level—drugs/biologics will be reimbursed

3. The development of administrative cost-control mechanisms by CMS

   a. Determination of the therapeutic reimbursement categories in which new drugs/biologics are to be placed

   b. Determination as to whether to reimburse for off-label use

   c. Consideration of "pay for performance" models (linking reimbursement to clinical outcomes)

   d. Determination as to whether new drugs/biologics should be recognized as new therapies for reimbursement (e.g., Amgen's Aranesp)

B. CMS's use of "inherent reasonableness" test for reimbursement

    1. CMS (and its carriers) have broad authority to adjust product and service payments found to be "grossly excessive or deficient" (effective Feb. 13, 2006, for Part B payments)

C. CMS's proposed draft guidance on factors in making a determination of reimbursement "coverage with evident development" of safety and efficacy (Apr. 7, 2005)

D. CMS may move drug reimbursement to medical device reimbursement model (including use of competitive bidding)

E. Potential for legislation creating a regulatory pathway for approval of generic biologics to deal with cost concerns

    1. FDA deferral of action (Aug. 31, 2004) on Sandoz's generic biologic application following Pfizer Citizen Petition

    2. Court order to FDA to act on Sandoz's application. *Sandoz Inc. v. Leavitt* (D.D.C. 2006)

F. Authorization to market generic biologics will adversely affect present market valuation levels of biotech companies by reducing exclusive life of products (e.g., EU regulatory approval of its first generic biologic, Sandoz's Omnitrope (Apr. 18, 2006))

G. Consequent focus on pharmacoeconomics at early development stages

    1. For example, Johnson & Johnson's decision to train its drug discovery scientists in pharmacoeconomics, to incorporate cost-effectiveness at an early stage of the R&D process

    2. Need to incorporate pharmacoeconomics into the clinical trial process for data development

H. Consequent greater emphasis on breakthrough drugs/biologics, targeted therapies, and comparative safety/efficacy

    1. Comparative effectiveness reviews by the Agency for Healthcare Research and Quality (AHRQ)

I. Cost and complexity of marketing in new regulatory environment

    1. Need for enhanced training in FDA promotional compliance

        a. Including preapproval and off-label promotion

        b. Including increased training of physicians and other healthcare providers

    2. Need for enhanced training in healthcare pricing, marketing, and distribution compliance

        a. Increasing focus on healthcare fraud and abuse and antikickback

investigations and prosecutions by the Department of Health and Human Services (DHHS)

b. *See* OIG Compliance Program Guidance for Pharmaceutical Manufacturers (Apr. 2003)

c. *See* Pharmaceutical Research and Manufacturers of America (PhRMA) Code on Interactions with Healthcare Professionals (July 2002)

J. Expanded involvement by CMS regarding categorization and levels of reimbursement for drugs/biologics will significantly affect the valuation of development drugs/biologics

1. Importance of monitoring CMS policies and actions

2. Importance of assessing potential indications of a proposed product and the likely relative reimbursement levels among them in deciding on focus of clinical trials

3. Importance of considering the principal purchasers (e.g., hospitals, physicians)

4. Importance of early discussions with CMS on categorization of a developmental product/CMS due diligence with potential biotech partners

5. New Medicare Act formulary system allows exclusion of products to reduce pricing levels and reimbursement

K. Increased focus by state governments on drug marketing, promotion, and training

1. California marketing compliance law (effective July 1, 2005)

a. Requires pharmaceutical firms to implement compliance programs in accordance with the OIG guidance and the PhRMA code

b. Requires adoption of limits on promotional spending directed to physicians, and annual declarations of compliance

2. Vermont law (effective Jan. 1, 2006) requiring annual reports of anything valued over $25.00 given to any Vermont physician

3. Several state price reporting statutes

L. Increased price transparency in commercial arrangements leading to further price pressures

1. State of Maine pharmacy benefit manager (PBM) disclosure law (fees, educational grants, rebates) upheld, *PCMA v. Rowe* (1st Cir. Nov. 2005)

M. New focus on protection of patient data—and interest in use of such data

1. Importance of familiarity with Healthcare Insurance Portability and Accountability Act's (HIPAA's) privacy restrictions on use of patient data

N. Potential effect on product marketing of development of e-prescribing and electronic health information networks

1. Formation of advisory panel and request for proposals for contracts to develop electronic health records architecture, by the DHHS (June 2005)

Current Competition Issues

A. The Federal Trade Commission (FTC) is challenging the resurgence of pioneer company patent litigation settlement agreements with generic companies that provide compensation in return for an agreement to restrict market entry

   1. FTC petition to Supreme Court to review and reverse *Schering-Plough Corp. v. FTC* (11th Cir. 2005); petition opposed by the Solicitor General

   2. *See* Summary Report by FTC Bureau of Competition of FY 2005 pharmaceutical company settlement agreements (Apr. 24, 2006)

B. FTC plans to study impact of authorized generics in the market (announced Mar. 29, 2006)

   1. FTC will assess effects on market entry by generic drug companies

   2. FTC anticipates preparing a final report in 2008

C. Court affirmed FDA's view that it lacks legal authority to delay marketing of authorized generics solely to protect 180-day exclusivity under the Hatch-Waxman Act (*see Teva Pharmaceutical Industries, Ltd. v. Crawford* (D.C. Cir. 2005))

D. Legislation enacted in 2006 mandating that the price of authorized generics must be included by pioneer manufacturers in the calculation of their average manufacturer's price and "Best Price" for reimbursement purposes (*see* Pub. L. No. 109-171 (Feb. 8, 2006))