

Starting or Expanding a Pharma/Biotech Business in the U.S.:  
*New Legal and Regulatory Issues*

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Stephen Paul Mahinka, Esq.  
Morgan Lewis, Washington, DC  
smahinka@morganlewis.com

**Morgan Lewis**  
C O U N S E L O R S   A T   L A W





## Japanese Entry and Expansion in the U.S.: *Substantial Opportunities*

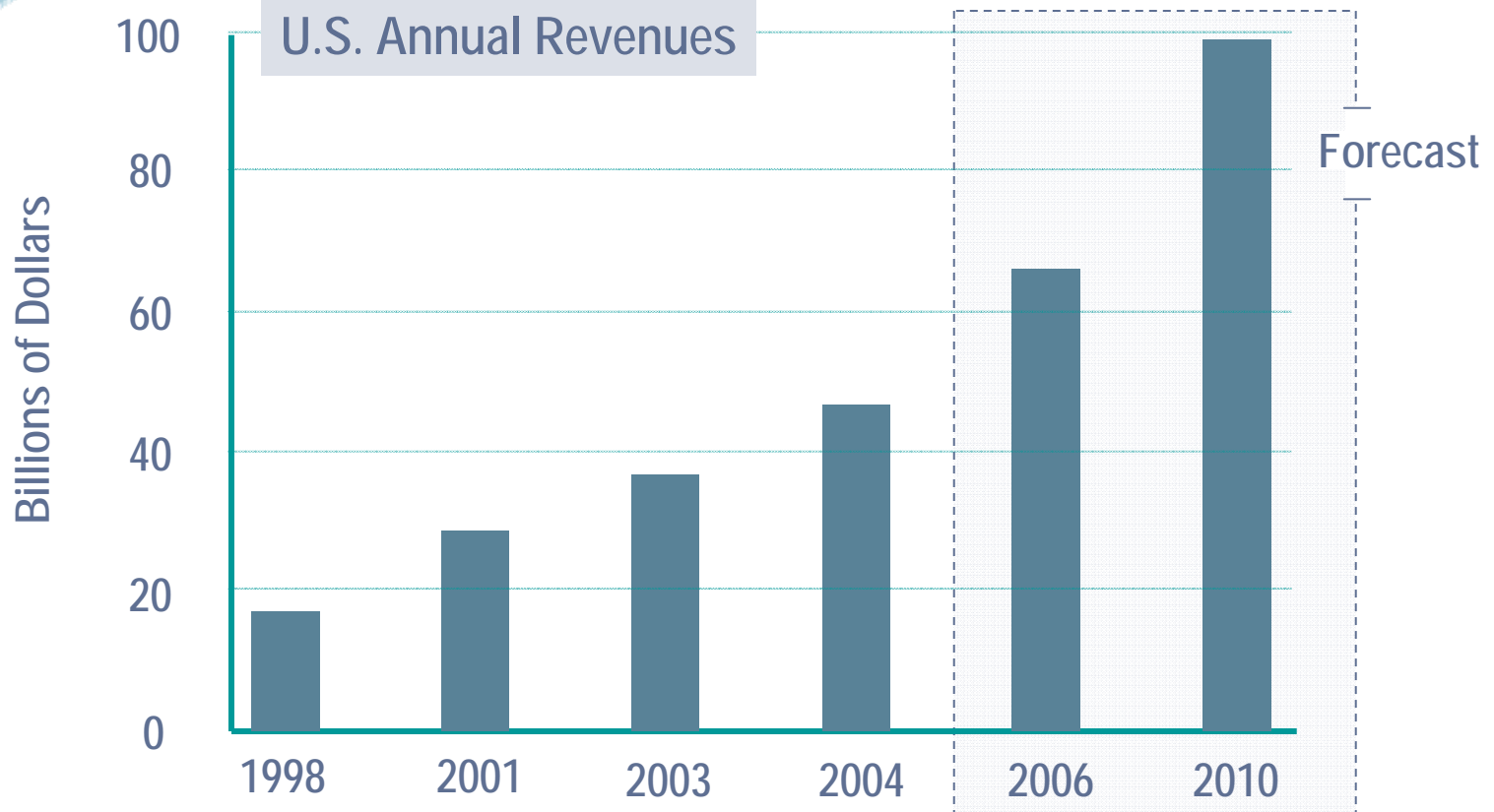
- Demand from changing U.S. population demographics (aging)
- Demand by big pharma for licensing/acquisitions/alliances for pipeline purposes
- Demand for new drug/biologic products for underserved/unaddressed indications



## Japanese Entry and Expansion in the U.S.: *Substantial Opportunities (cont'd)*

- Substantial expansion of funding available for prescription drugs
  - Medicare Prescription Drug, Improvement, and Modernization Act of 2003
    - > new act provides for an estimated \$750 billion of additional funding for government purchases of prescription drugs over first decade of operation
    - > will alter competitive landscape for pharma/biotech companies
  - New bioterrorism funding: Project BioShield (2004)
    - > provides \$5.6 billion in funding for development of defense-related vaccines and antidotes

# Japanese Entry and Expansion: Opportunities *Biotech Growth . . . And Promise*



Source: Data: Ernst & Young in *Business Week*, June 13, 2005, p. 35.



## Issues Regarding Japanese Entry and Expansion *Into U.S. Pharma/Biotech Markets*

- New changes in U.S. FDA drug development regulatory focus
- New economic issues: cost/valuation/reimbursement
- Evolving issues in big pharma/biotech cooperative relationships
- New issues regarding pricing/marketing/distribution/patient data



## Issues Regarding Japanese Entry and Expansion *FDA Drug Development Regulation*

- New focus on product safety
  - increased use of Phase 4 marketing studies as a condition of approval
  - new FDA draft guidances on premarketing risk assessment, risk minimization action plans, and pharmacovigilance practices/ pharmacoepidemiologic assessment (March 2005)
  - new draft FDA Drug Watch program (web-based drug safety reporting system) (May 2005)
    - > likely consequences for potential product liability litigation



## Issues Regarding Japanese Entry and Expansion *FDA Drug Development Regulation*

- Costs of approval substantial and increasing
  - Tufts University Center for the Study of Drug Development estimates (2003) approximately \$897 million per approved drug (including post-approval R&D costs)
    - > affects therapeutic categories selected for clinical trials
    - > affects location of clinical trials (e.g., in Europe rather than U.S.)
- New focus on manufacturing/product quality
  - recent FDA consent settlements regarding manufacturing issues (GlaxoSmithKline; Schering-Plough)



## *New Economic Issues*

- Increased focus on cost of the drug/biologic
  - new Medicare Act will result in U.S. government paying for approximately 45% of drugs/biologics (up from current 16%)
  - significantly enhanced role of Centers for Medicare and Medicaid Services (CMS) in determining whether – and at what level – drugs/biologics will be reimbursed
  - development of administrative cost control mechanisms by CMS
    - > determinations of what therapeutic reimbursement category in which new drugs/biologics are placed
    - > determinations as to whether to reimburse for off-label use
    - > consideration of “pay for performance” models (linking reimbursement to clinical outcomes)
    - > determinations as to whether or not to reimburse new drugs/biologics as novel therapies (e.g., Amgen’s Aranesp)



## *New Economic Issues (cont'd)*

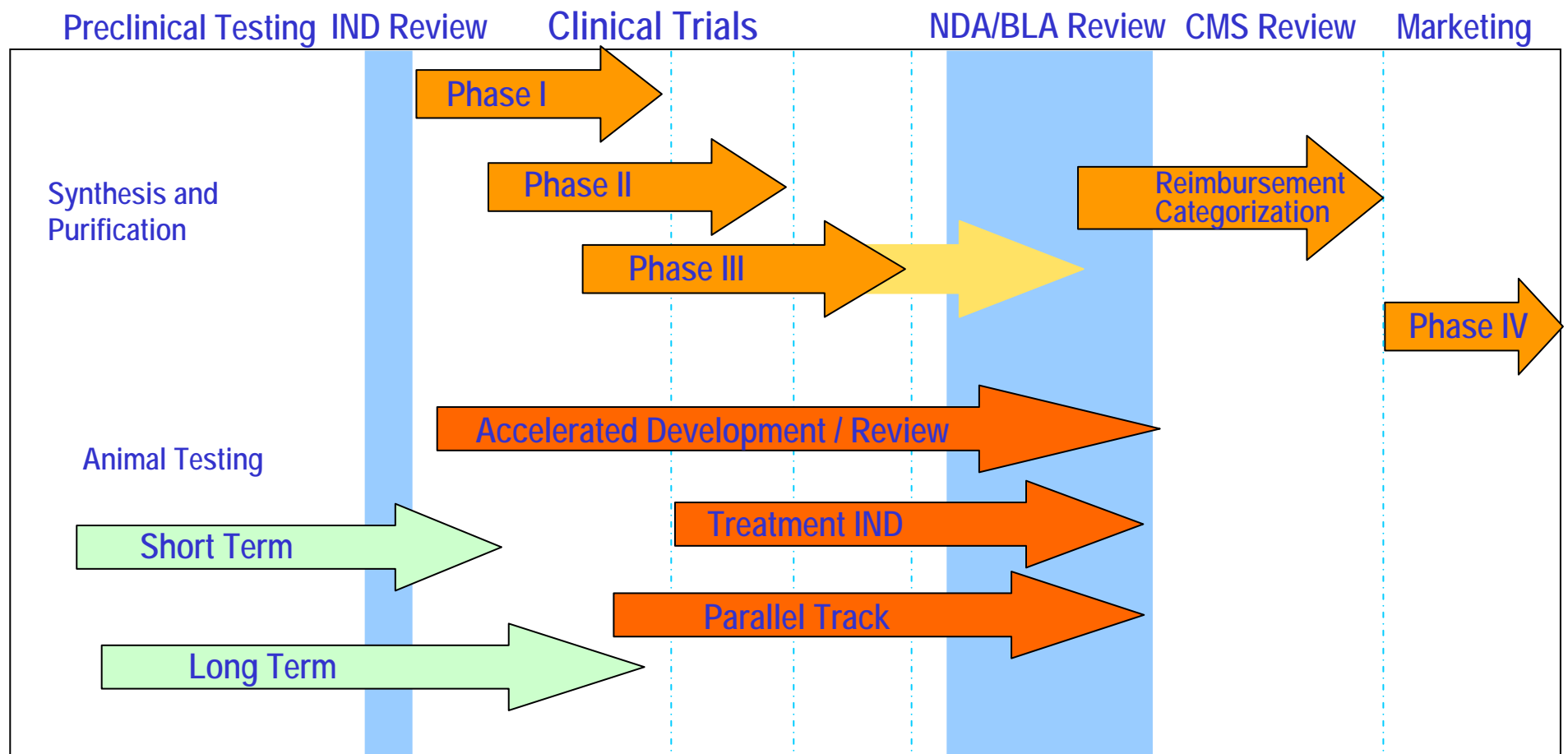
- Potential for legislation creating a regulatory pathway for approval of generic biologics to deal with cost concerns
  - FDA deferral of action (Aug. 31, 2004) on Sandoz' generic biologic application following Pfizer Citizen Petition
- CMS proposed draft guidance on factors in making a determination of reimbursement "coverage with evidence development" of safety and efficacy (April 7, 2005)
  - CMS coverage determinations also affect private managed care decisions on reimbursement and pricing



## *New Economic Issues (cont'd)*

- Consequent new focus on pharmacoeconomics at early development stages
  - e.g., Johnson & Johnson's recent decision to train its drug discovery scientists in pharmacoeconomics, to incorporate cost-effectiveness at an early stage of the R&D and development process
  - need to incorporate pharmacoeconomics into the clinical trial process for data development


# Drug/Biologic Development Timeline





## *New Economic Issues (cont'd)*

- Expanded involvement by CMS regarding categorization and levels of reimbursement for drugs/biologics will significantly affect valuation of developmental drugs/biologics
  - importance of monitoring CMS policies and actions
  - importance of assessing potential indications of a proposed product and the likely relative reimbursement levels among them in deciding on focus of clinical trials
  - importance of early discussions with CMS on categorization of a developmental product
  - new Medicare Act formulary system allows exclusion of products to reduce pricing levels and reimbursement



## *Evolving Nature of Big Pharma/ Biotech Relationships*

- Enhanced biotech bargaining position in view of demand for biologics products
  - greater interest in early-stage development products
  - 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
- Potentially enables biotech/new entrant to enter and expand as an operating company, rather than solely through licensing or by acquisition

## Biotech Deal Making Activity 1997 - 2004



Legend:

- All deals
- Biotech deals

Source: PharmaDeals Agreements published in *Biopartnering Today*, p. 6 (2005)



## *Challenges for Market Entry and Expansion*

- Cost and complexity of developing a detail force for marketing
  - analysis of scope and type of market coverage needed
  - need for careful training in FDA promotional compliance
    - > including pre-approval and off-label promotion
  - need for careful training in healthcare pricing, marketing and distribution compliance
    - > increasing focus on healthcare fraud and abuse and anti-kickback investigations and prosecutions by Office of Inspector General, Department of Health and Human Services
    - > see, *OIG Compliance Program Guidance for Pharmaceutical Manufacturers* (April 2003)
    - > see, *Pharmaceutical Research and Manufacturers of America (PhRMA) Code on Interactions with Healthcare Professionals* (July 2002)



## *Challenges for Market Entry and Expansion*

- Increased focus by state governments on drug marketing and promotion
  - see, e.g., California marketing compliance law (effective July 1, 2005)
    - > requires pharmaceutical firms to implement compliance programs in accordance with the OIG guidance and the PhRMA code
    - > requires adoption of limits on promotional spending directed to physicians, and annual declarations of compliance
  - other state price reporting statutes
- Enhanced FDA focus on manufacturing/quality/safety
- New focus on clinical trials integrity and reporting
  - e.g., new voluntary public reporting of all completed clinical trials



## *Challenges for Market Entry Expansion (cont'd)*

- New focus on protection of patient data — and interest in use of such data
  - importance of familiarity with Healthcare Insurance Portability and Accountability Act (HIPAA) privacy restrictions on use of patient data
- Potential effect on product marketing of development of e-prescribing and electronic health information networks
  - formation of advisory panel and request for proposals for contracts to develop electronic health records architecture, by Dept. of Health and Human Services (June 2005)

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