
BURRILL & COMPANY
Life Sciences: Venture Capital, Private Equity, Merchant Banking, Media

Agenda

- About Burrill & Company
- State of the World – Adapting for Success
- "Idea to IPO…and Beyond" and Lessons Learned
- Q&A

Burrill & Company–Exclusively Focused on Life Sciences

- Human Healthcare (Rx, Dx, devices, services, informatics) from innovation to delivery
- Nutraceuticals/Wellness
- Agbio/Food
- Industrial/Bioenergy (biofuels)
- Enabling Technologies, including bionanotechnology

Burrill & Company

Venture Capital Group

- Investing across the entire spectrum of the life sciences/biotechnology…over $1 billion under management
- Funds in development
  - Burrill Capital Fund IV,
  - Burrill BioGreenTech Fund
  - Burrill Regional Funds:
    - India
    - Korea/Pan Asia
    - Latin America
    - Middle East/North Africa
    - Scandinavia/Europe
    - Burrill/Tower Healthcare (Elk Run)

Private Equity Group

- Raising $500 million Private Equity fund (Burrill Healthcare Opportunities Fund) focused on buyouts and PIPES in the healthcare sector

Merchant Banking

- Investment banking, financings and merger & acquisitions across life sciences
- Strategic Partnering (corporate development including licensing, research and other collaborations)
- Spin-outs ranging from products to research divisions to disease area franchises
- Strategic Advisory Services including new company formation

Media

- Conferences
- Publications

Burrill & Company U.S. & International Operations

Burrill & Company Platform

Burrill Venture Capital

- $980M Under Management
- 91 Investments
- 15 VCs (most w/MD/PhD/MBAs)
- 150+ Years of Industry Experience Among Managing Directors
- Access to Burrill Merchant Banking and Media

Global Experience

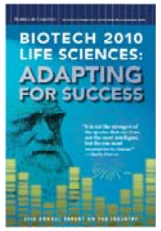
Strategic Partners

P&G Pharmaceuticals, Mitsubishi Tanabe Pharma, NOVARTIS, ADM, Bayer CropScience, IBM, Celgene, KRAFT, MONSANTO, Lundbeck, novo

…25+ in total

Significant Visibility

Burrill Merchant Banking and Burrill Media



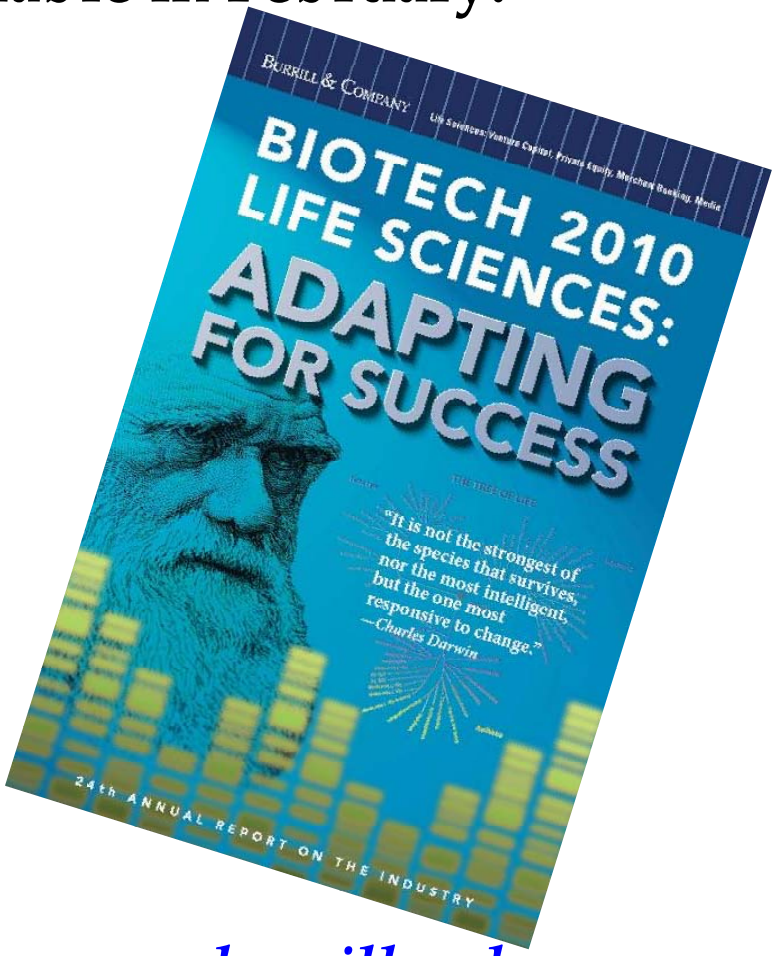
Annual Industry Book

Numerous Periodicals

The Burrill Consumer Digital Health Meeting

G. Steven Burrill's Annual Book

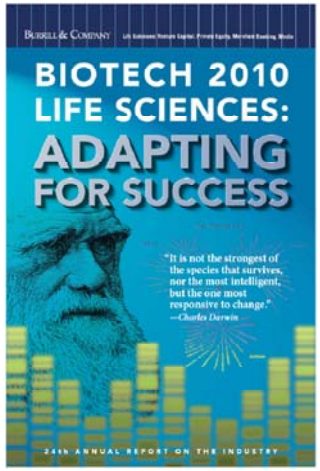
Order our 24th annual book available in February!



For ordering information go to www.burrillandco.com

Burrill & Company Publications

Biotech 2010: Life Sciences: Adapting For Success

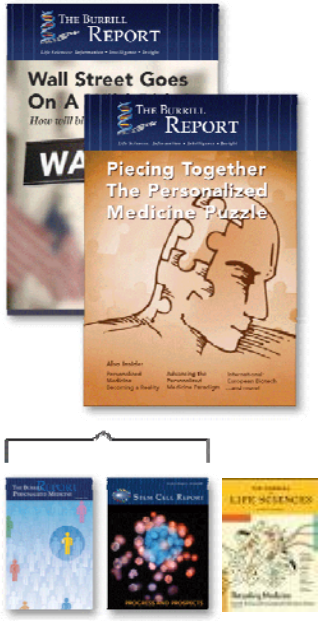


Annually for 24 years

The Journal of Life Sciences

Periodically

The Burrill Report*



* The Personalized Medicine Report and the Stem Cell Report will be included in the monthly Burrill Report

6x per year

The Burrill Weekly Brief

Weekly

The BurrillReport.com
http://www.burrillreport.com

Daily

Biotech 2010 Life Sciences: Adapting For Success

It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to change

—Charles Darwin

University of Illinois at Urbana-Champaign

March 12, 2010

G. Steven Burrill

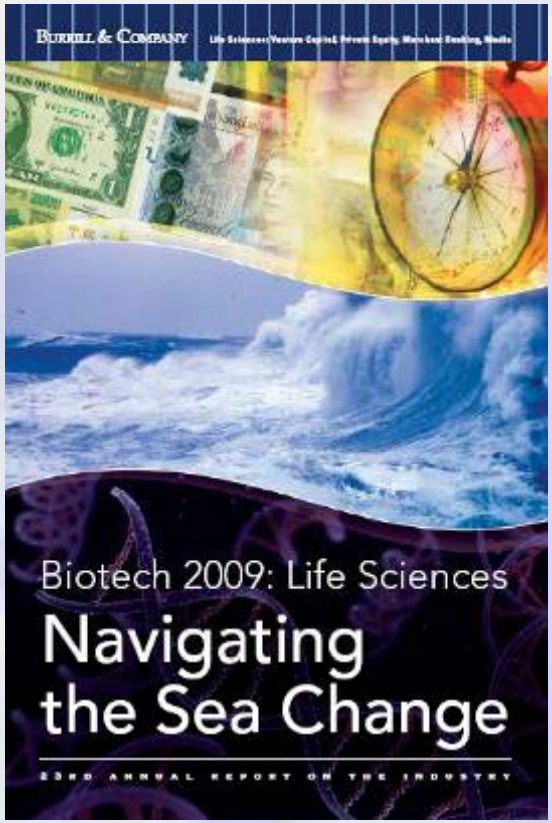
Chief Executive Officer
Burrill & Company

Adapting For Success: Four Biggest Problems in the World Today (Ignoring Terrorism)

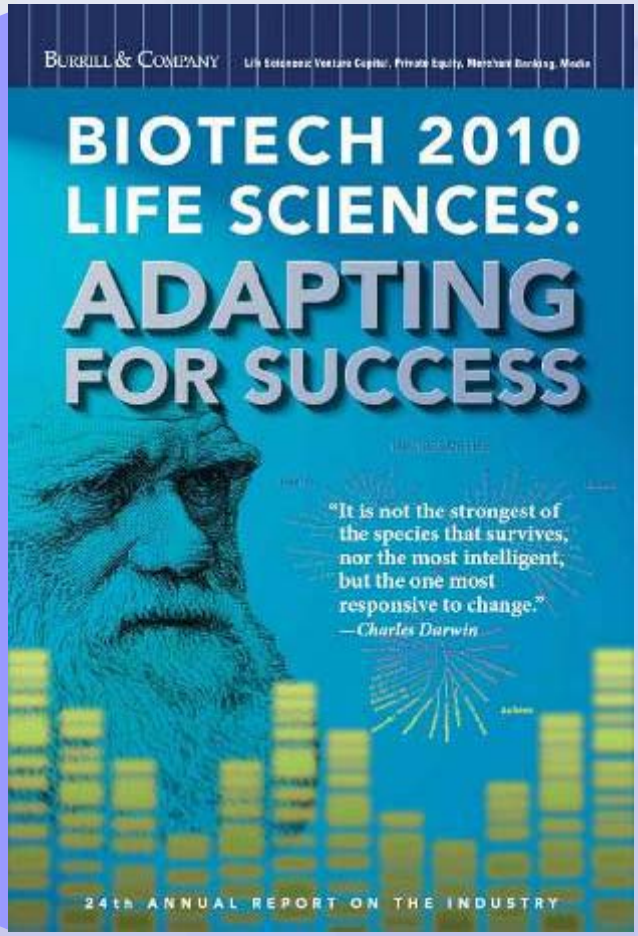
- Global Climate Change, Sustainability of the Planet
- Energy Security, Energy Self-Sufficiency
- Food Security & Food Production
- Healthcare and Healthcare "Reform"

…and, Biotech will solve/tackle all of them

Last Year's Book – Focused on the Sea Change…



This Year's Book – Focuses on adapting…



…but, what was that Sea Change?

- Imploded capital markets and financial services industry restructuring
- Global economic chaos/recovery
- The 3 "R's" of healthcare…and its implications
  - Healthcare **R**eform – is it happening? impact?
  - **R**eimbursement – who is going to pay for healthcare
  - **R**egulation
    - Approval vs. pharmacovigilence
    - Comparative effectiveness (cost, quality)
- Pharma industry blockbuster model has run its course, industry restructures and refocuses
- Emerging markets (BRIC plus MENA) trump traditional markets (US/Europe/Japan)
- Technology & what it is enabling – the world in 2020

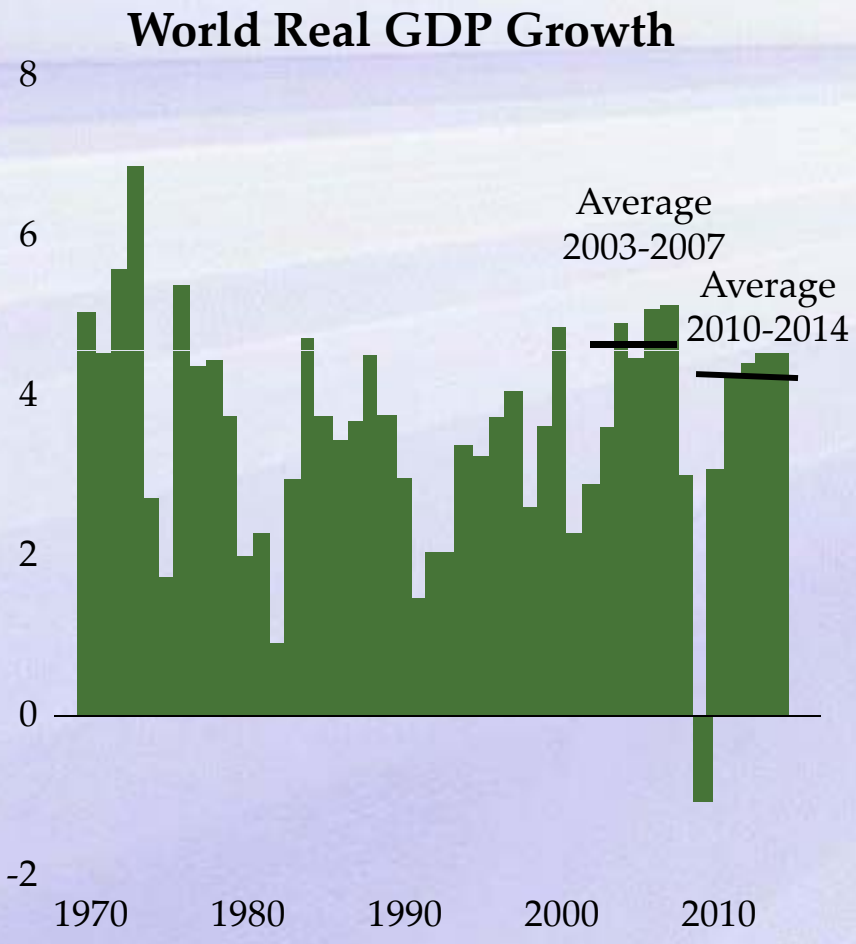
Optimism/Pessimism (half full/half empty)?

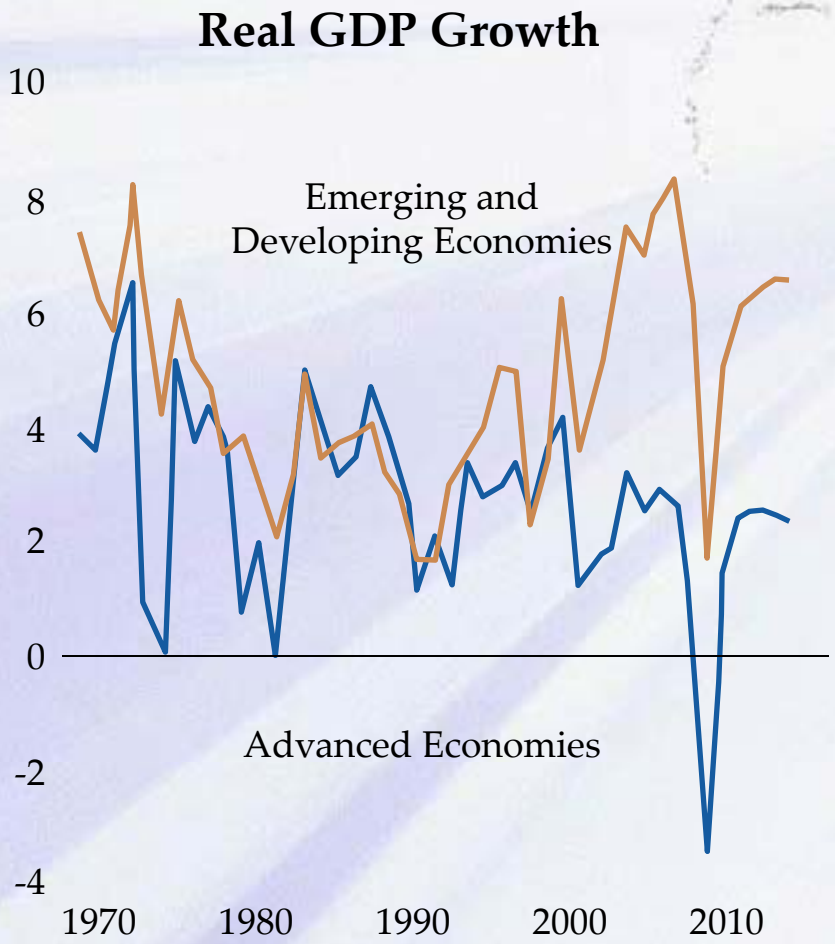
- "New normal" ?
  - World economy returns to pre-crisis rate of growth

    - OR -

  - Growth stays at a permanently lower rate – investment, employment and productivity growth all slowed down
- Stock market growth at all time highs, way ahead of economic indicators

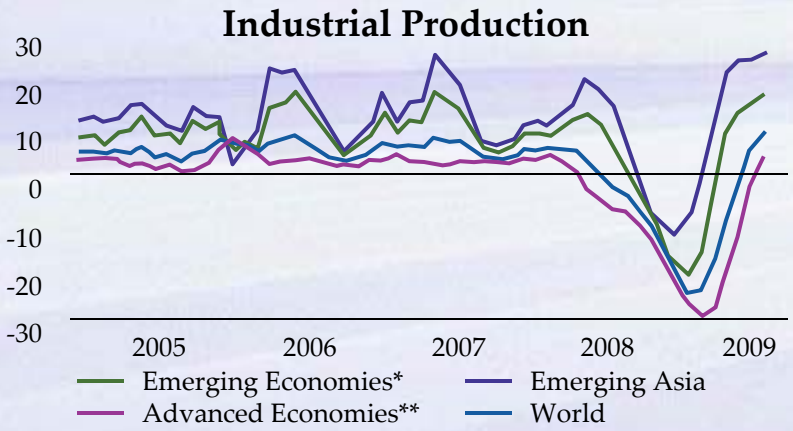
Financial crisis triggered largest contraction in activity since World War II

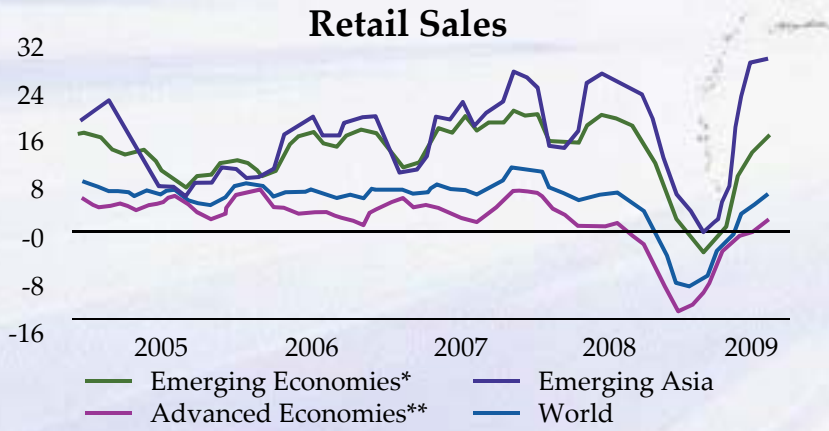


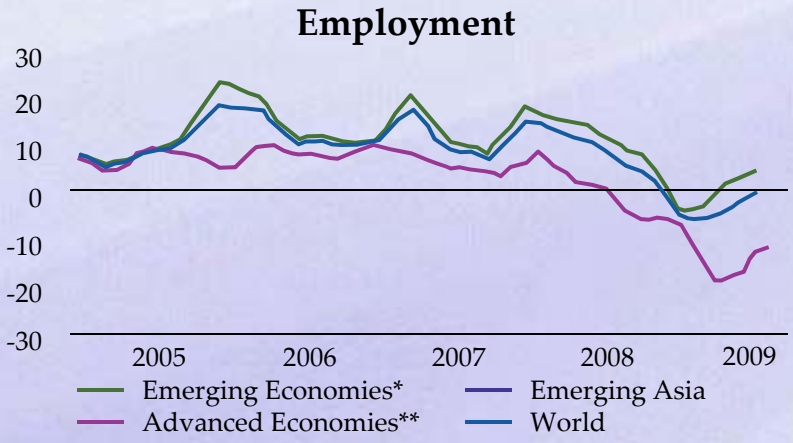


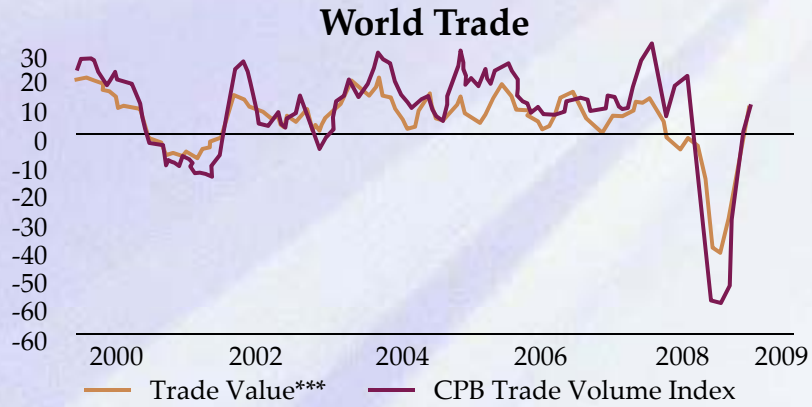
Source: IMF staff estimates

Recovery is evident…









* *Argentina, Brazil, Bulgaria, Chile, China, Colombia, Estonia, Hungary, India, Indonesia, Latvia, Lithuania, Malaysia, Mexico, Pakistan, Peru, Philippines, Poland, Romania, Russia, Slovak Republic, South Africa, Thailand, Turkey, Ukraine, and Venezuela.*

** *Australia, Canada, Czech Republic, Denmark, euro area, Hong Kong SAR, Israel, Japan, Korea, New Zealand, Norway, Singapore, Sweden, Switzerland, Taiwan Province of China, United Kingdom, and United States.*

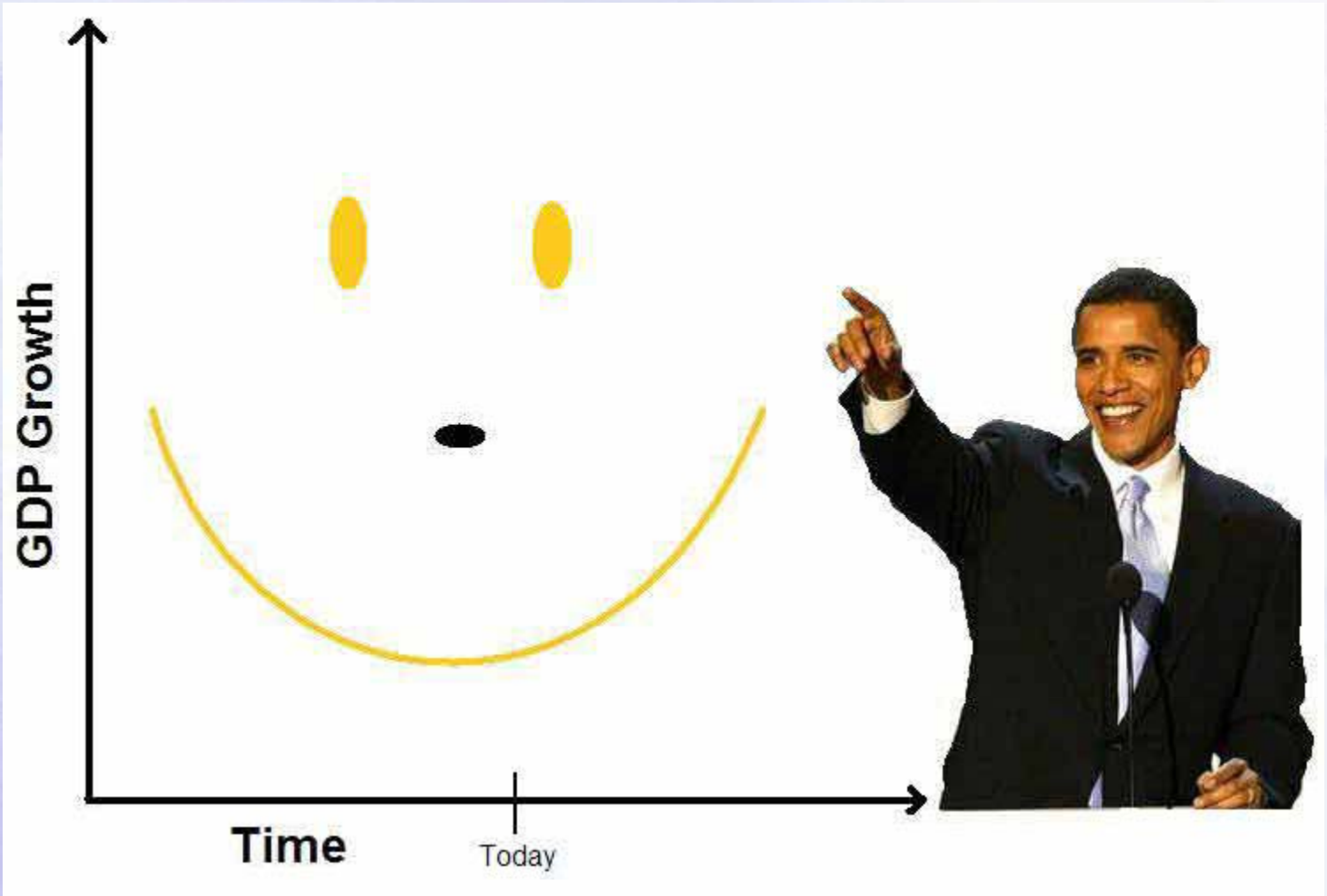
*** *In SDR terms*

Source: CPB Netherlands Bureau for Economic Policy Analysis for CPB trade volume index; for all others, NTC Economics and Haver Analytics

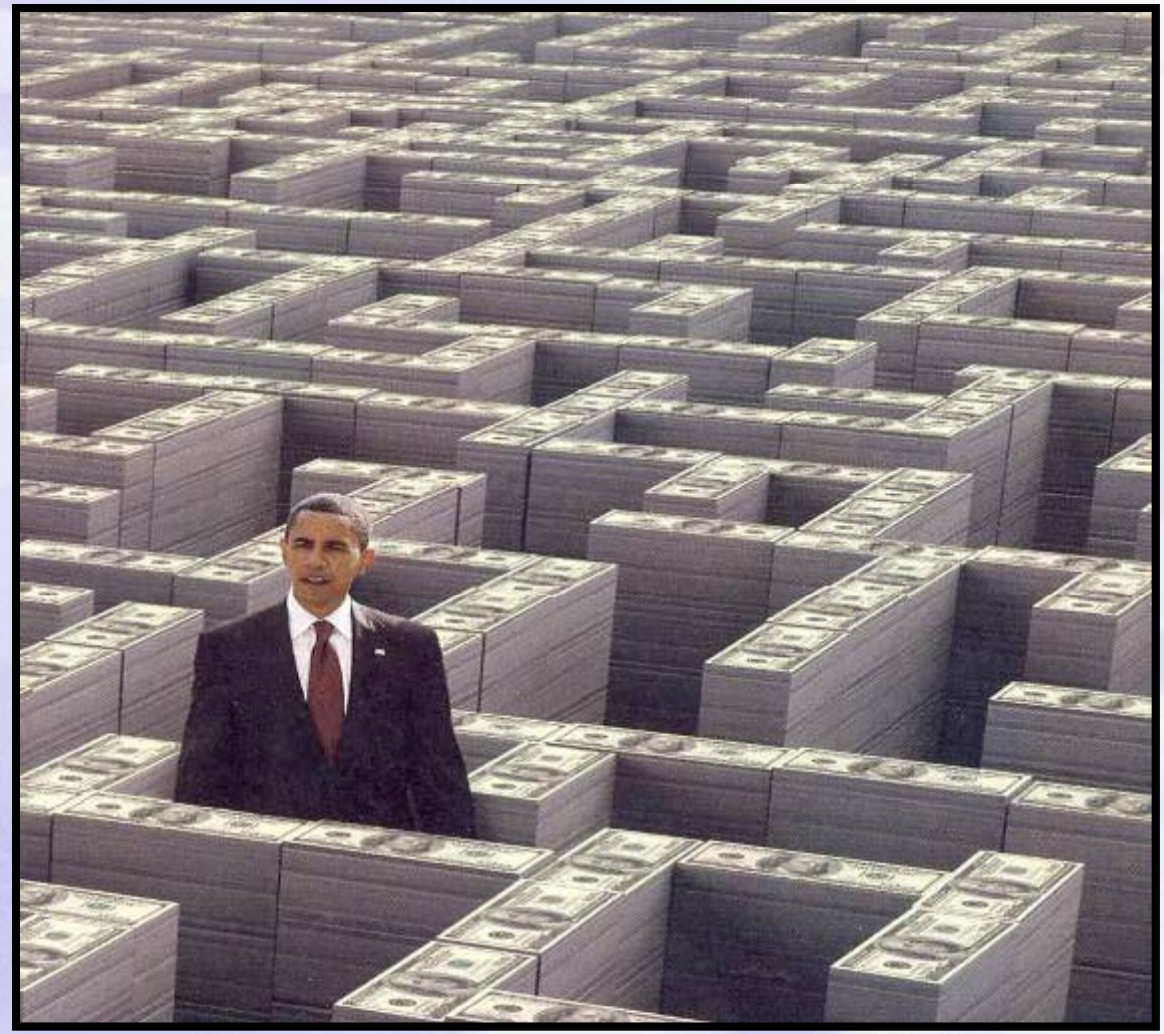
Is It Too Early To Celebrate?

- Unemployment still rising
- Manufacturing capacity remains idle
- Today's sources of growth
  - Temporary and precarious
  - Driven largely by global spending, by government largesse: stimulus continues
- World economy is far from returning to "normal" activity

Obamanomics



Obamanomics (cont.)



Source: George Poste and Burrill & Company

Underlying challenges remain…

- Healthcare reform – is it happening? insurance reform?
  - Conflict between more access, more coverage and reducing healthcare cost burden
- Congress will add power to Medicare to negotiate what it pays for drugs/devices/diagnostic…tough for industry
- Congress will reduce capital gains differential, tax rates will go up for the "rich;" "carry" for VCs to be taxed as ordinary income (all bad for capital raising, capital more expensive)
- Stricter regulatory oversight – Regulatory hurdle increases
  - Drug safety (pharmacovigilence) will trump approval
  - Comparative effectiveness – a third approval standard emerges
- Generic biopharmaceuticals, biosimilars, follow-on biologics

…and, on the positive side

- Stem cell funding increases, some restrictions removed
- Healthcare IT stimulus
- Biofuels/bioenergy stimulus
- Economy not getting worse
- Capital still available for good companies, good ideas
- …maybe everything just gets more complex!

Wall Street's Implosion…What did it mean to us?

- Capital Markets substantially restructured
  - Buy-side interest/resources reduced (hedge funds less interest, life sciences investors moved up)
    - VC/private investors (deep pockets/short arms) business challenging – and fundraising for VCs difficult
    - IPOs only for risk abated companies
  - Sell-side (investment banks) permanently restructured, reduced focus; new firms emerging
- Access to capital
  - Resources for micro-cap stocks (<$1B) dramatically decreased
  - Capital more difficult to find (more expensive)
- Big Pharma – not as eager (things will be cheaper if they wait), but focused across the value spectrum (early stage/pre-clinical to generics, orphan drugs, etc.)

Therefore...creativity in financing is an absolute requirement!

Some Interesting Facts

- When Roche bought Genentech, Genentech valued at $100B, Pfizer was $91B
- Today's market caps:

Biotech

- Roche – $142B
- Amgen - $56B
- Gilead - $43B

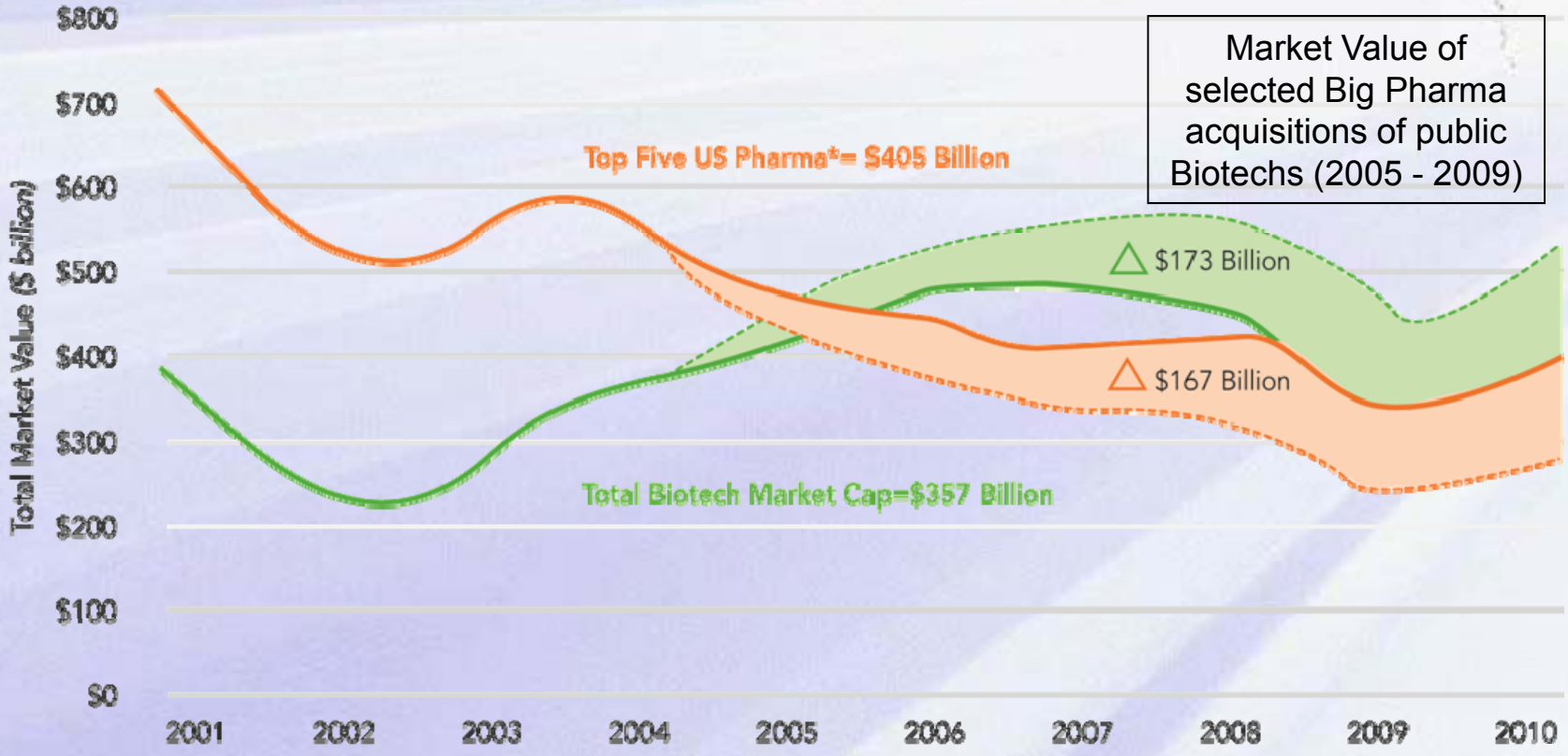
Pharma

- Pfizer - $145B
- Bristol-Meyers Squibb – $49B
- Eli Lilly - $40B/Bayer – $39B

- The top 5 pharma companies have lost 15% of their market capital in the last five years
- Biotechs have appreciated 22% from market lows in March

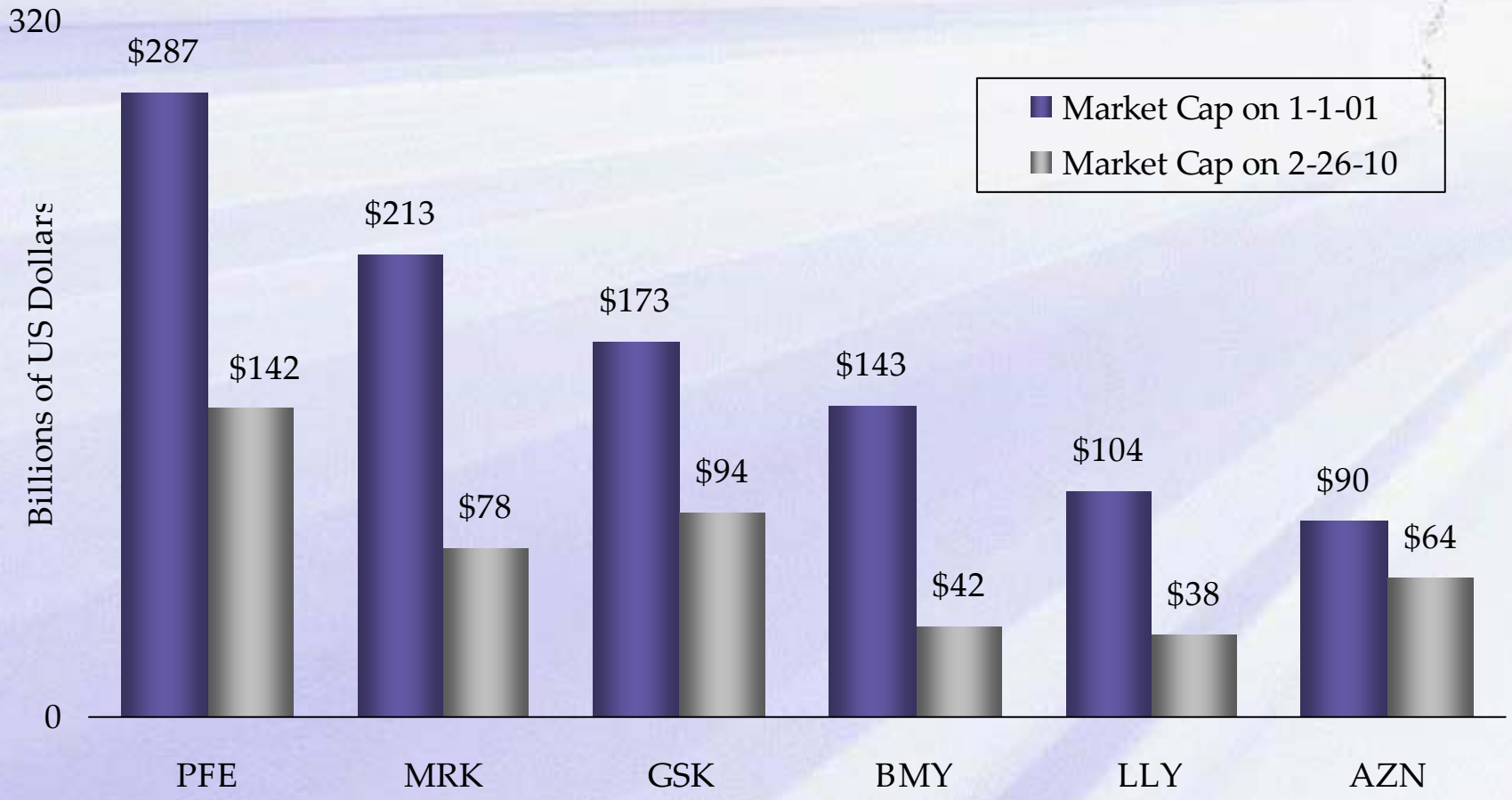
Biotech companies are becoming increasingly important as a source of value creation and innovation in the healthcare sector

Top US Pharma* vs. Total Biotech Market Cap



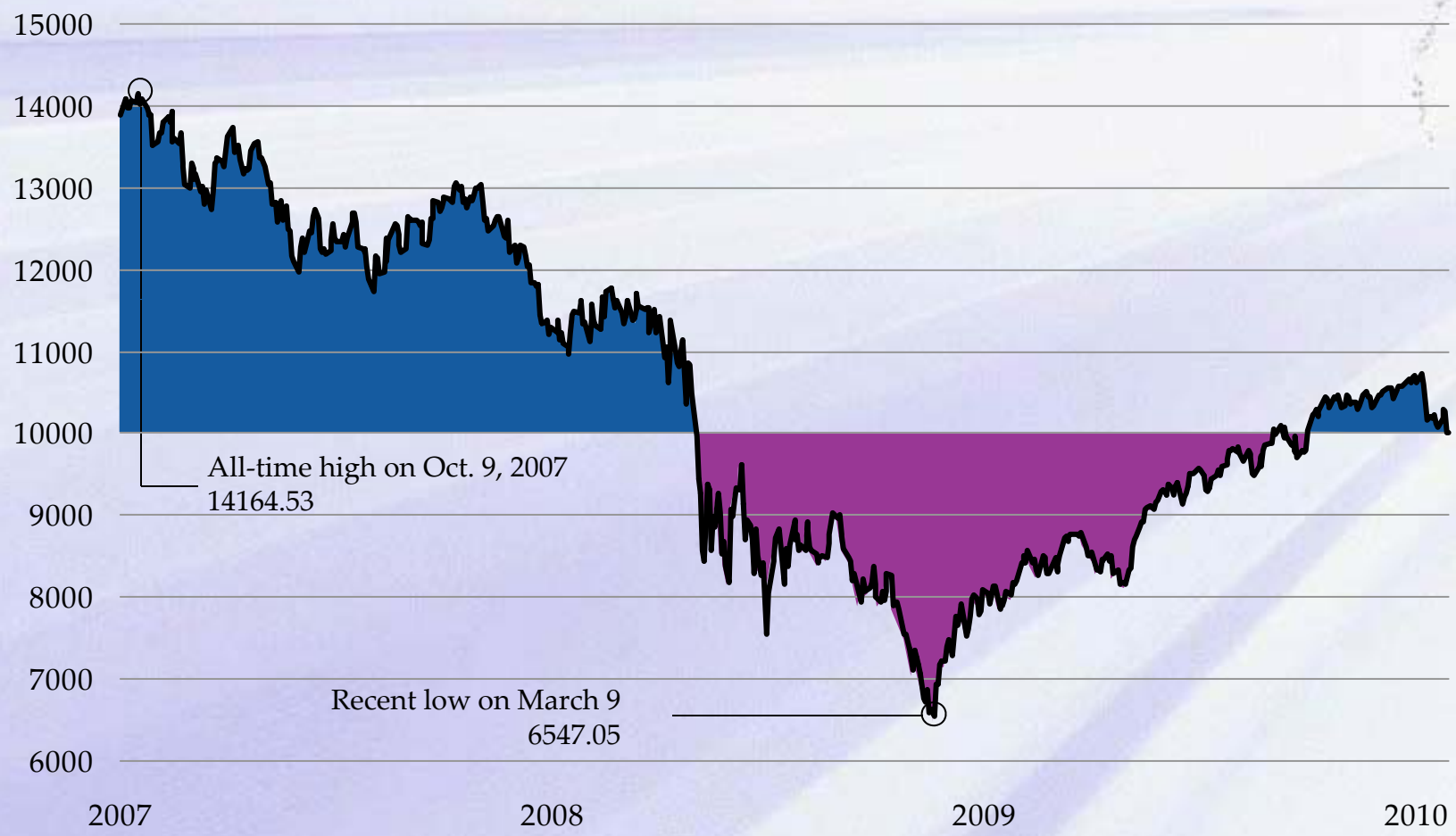
** Pfizer, Merck, Lilly, Bristol Myers Squibb, and Abbott*
Source: Capital IQ, Windhover, Burrill Analysis

Market Cap for Top-Tier Pharma Firms has Dropped $516B (51%) in 10 Years

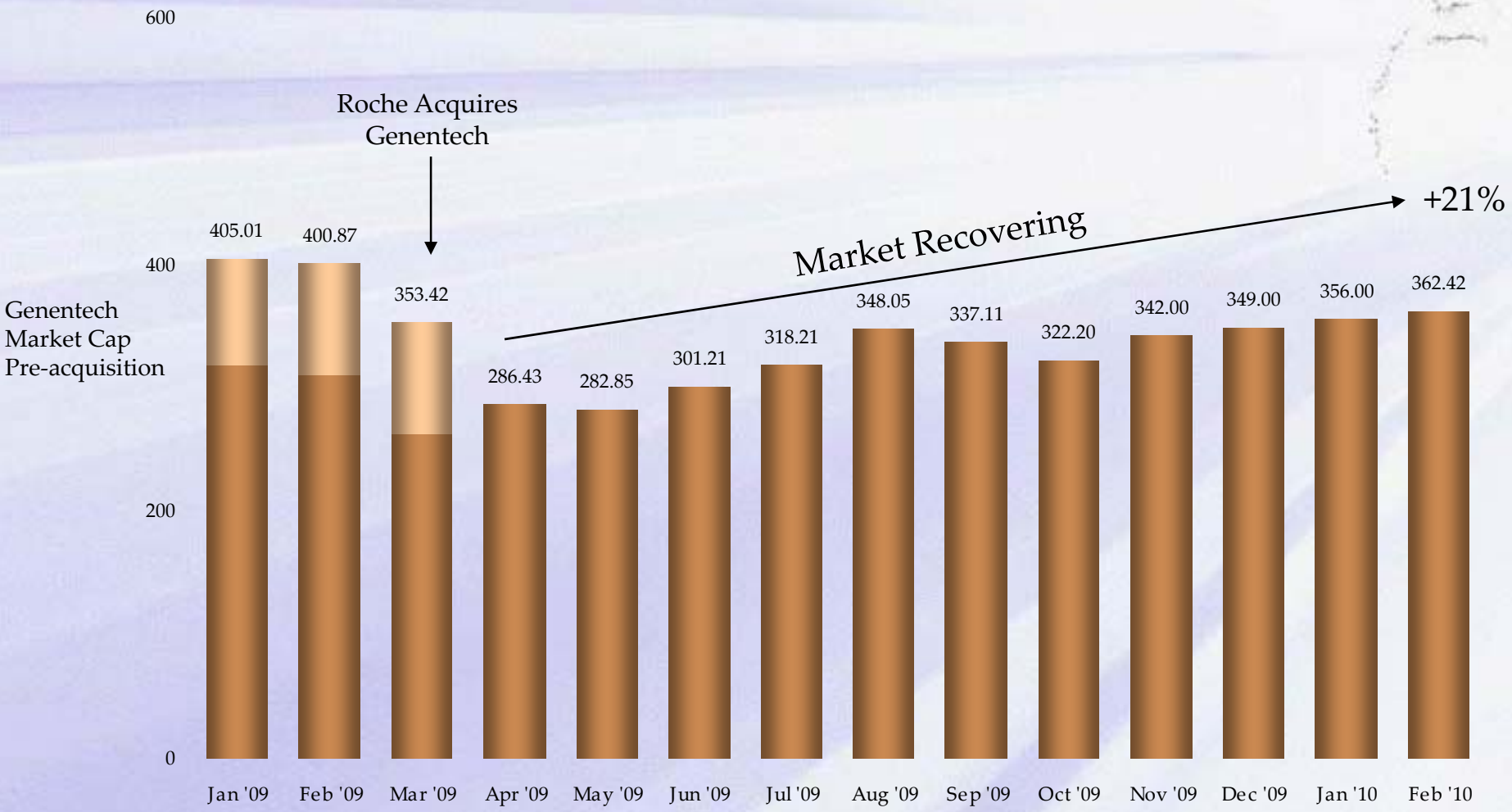


Source: Bloomberg

The Market's Comeback (DJIA since Oct 2007)



US Biotech Market Cap



…more interesting facts

- 312 biotechs are publicly traded on major US markets today with an aggregate market cap of $356 (In 2009, 356 companies, $391B market cap)
- 56 of those have market caps greater than $1B (2009 – 49)
- 10% are trading below their cash level (70 companies 12/31/08, ~20%)
- 40% have a market cap below $100M (2009 – 38%)
- In the last year, over 120 companies announced a corporate restructuring by slashing staff and putting promising projects in the refrigerator

…but the industry has raised over $55B in 2009 ($18B in financings and $37B in partnerships). It's a different world...

Is the IPO Window for Biotech Opening?

- IPO market for biotech remained closed for 12 quarters
- Three specialty pharmas successfully listed in 2009, all operating businesses with risk abated platforms, two in 2010

2009

$85,000,000

CUMBERLAND PHARMACEUTICALS

Initial Public Offering
August 11, 2009

IPO Price	$17/share
Y/E Price	$11.18
Δ in Price	↓52%

$1,064,000,000

Talecris BIOTHERAPEUTICS

Initial Public Offering
September 30, 2009

IPO Price	$19/share
Y/E Price	$22.82
Δ in Price	↑9%

$68,000,000

OMEROS

Initial Public Offering
October 7, 2009

IPO Price	$10/share
Y/E Price	$5.87
Δ in Price	↓72%

2010

$188,000,000

Ironwood

Initial Public Offering
February 3, 2010

IPO Price	$11.65/share
Current Price	$12.75
Δ in Price	↑9%

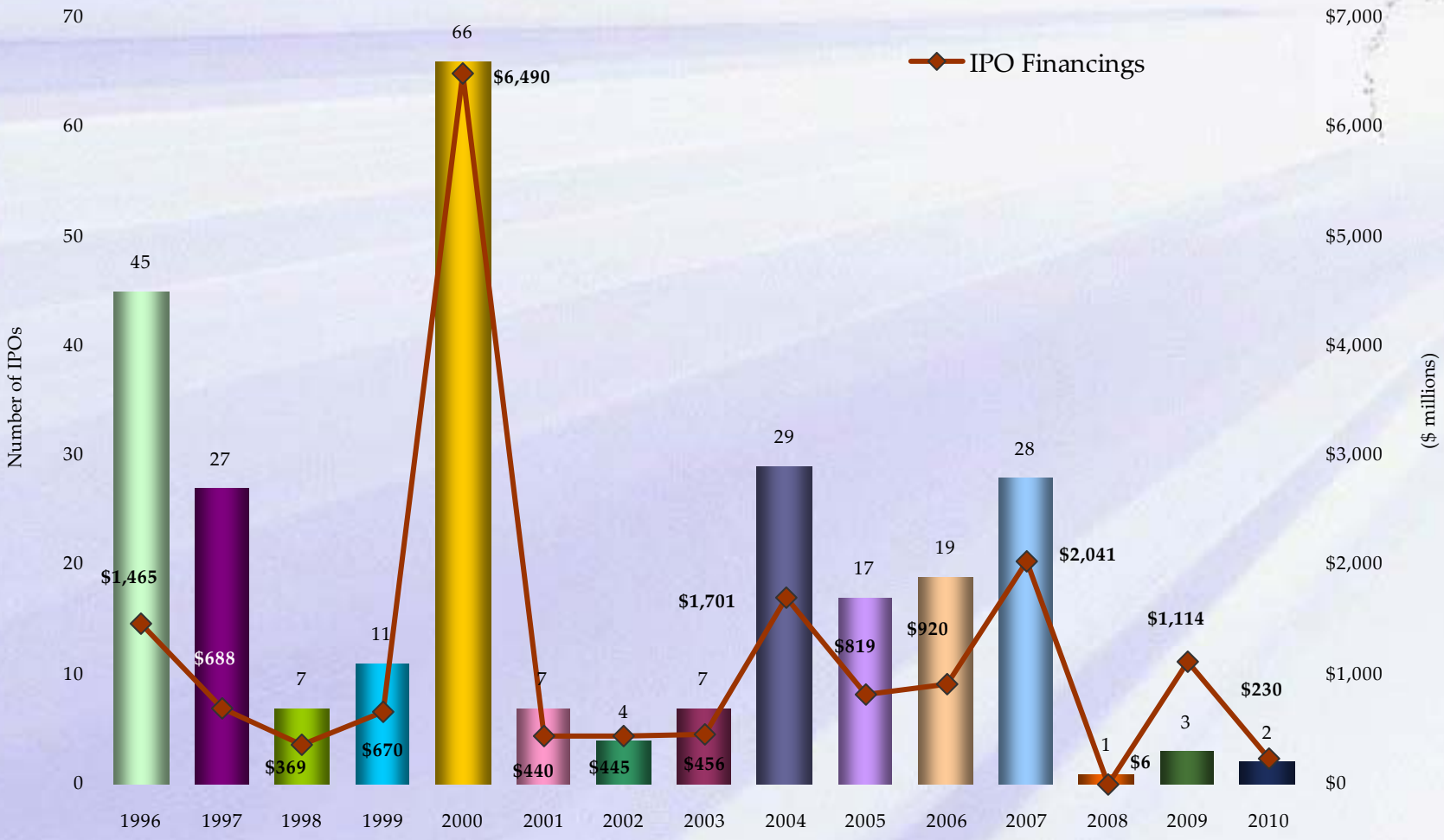
$42,000,000

Anthera PHARMACEUTICALS, INC.

Initial Public Offering
March 1, 2010

IPO Price	$7/share

IPOs – Are They Coming Back?



US IPOs – Not What They Used to Be

	Number of IPOs	Positive since IPO	Negative since IPO	Acquired or delisted	Amount Raised* ($ Million)	Average Δ % change Since IPO**
2003	7	0	0	7	$438	(100%)
2004	29	4	14	11	1,628	(22%)
2005	17	2	7	8	819	(41%)
2006	19	6	6	7	920	10%
2007	28	4	20	4	2,071	(33%)
2008	1	0	0	1	6	(100%)
2009	3	1	2	0	1,117	26%
2010	2	1	0	0	230	4%
Total	**105**	**18**	**49**	**38**	**6,082**	**(40%)**

* *Includes over-allotments*
** *As of 3/1/10*
Source: Burrill & Company

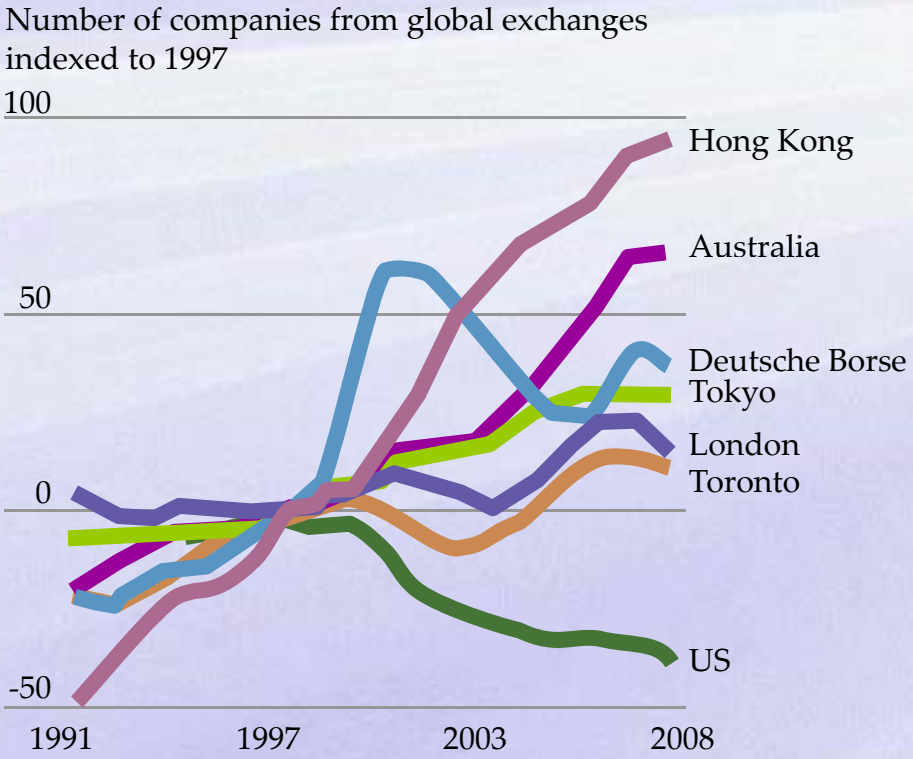
The Biotech IPO Queue (2/5/10)

Too early to announce window open for biotech

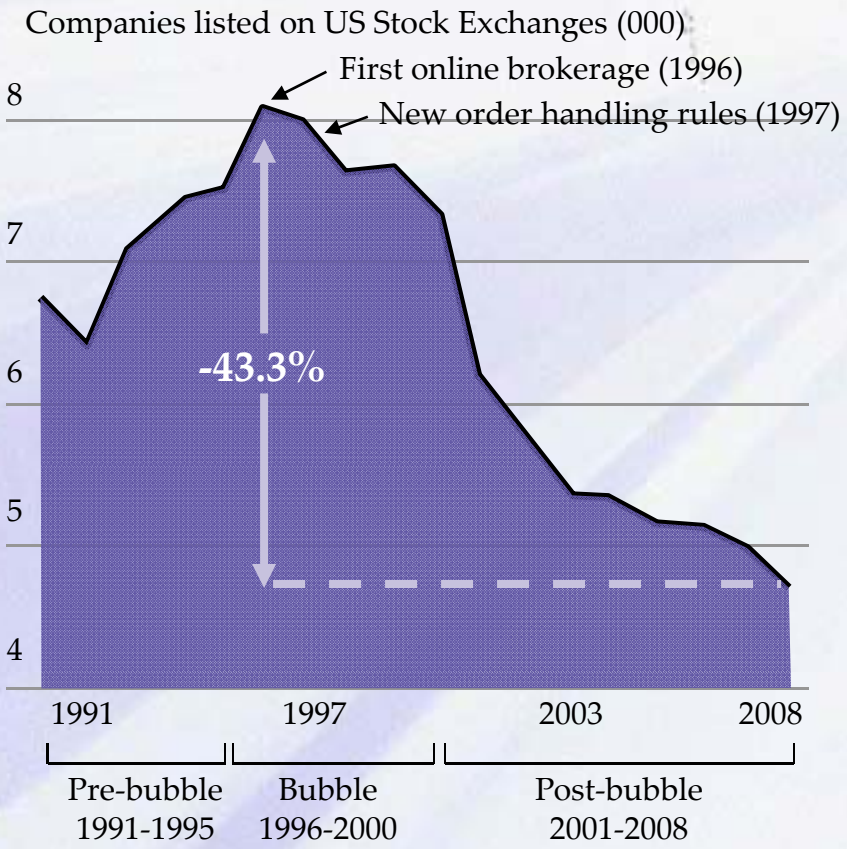
Source: Burrill & Company

Structural Problems in the IPO Market…US falling behind rivals in new listings

US listed markets in steady decline since 1997…



…starting with the advent of online brokerage and new order handing rules

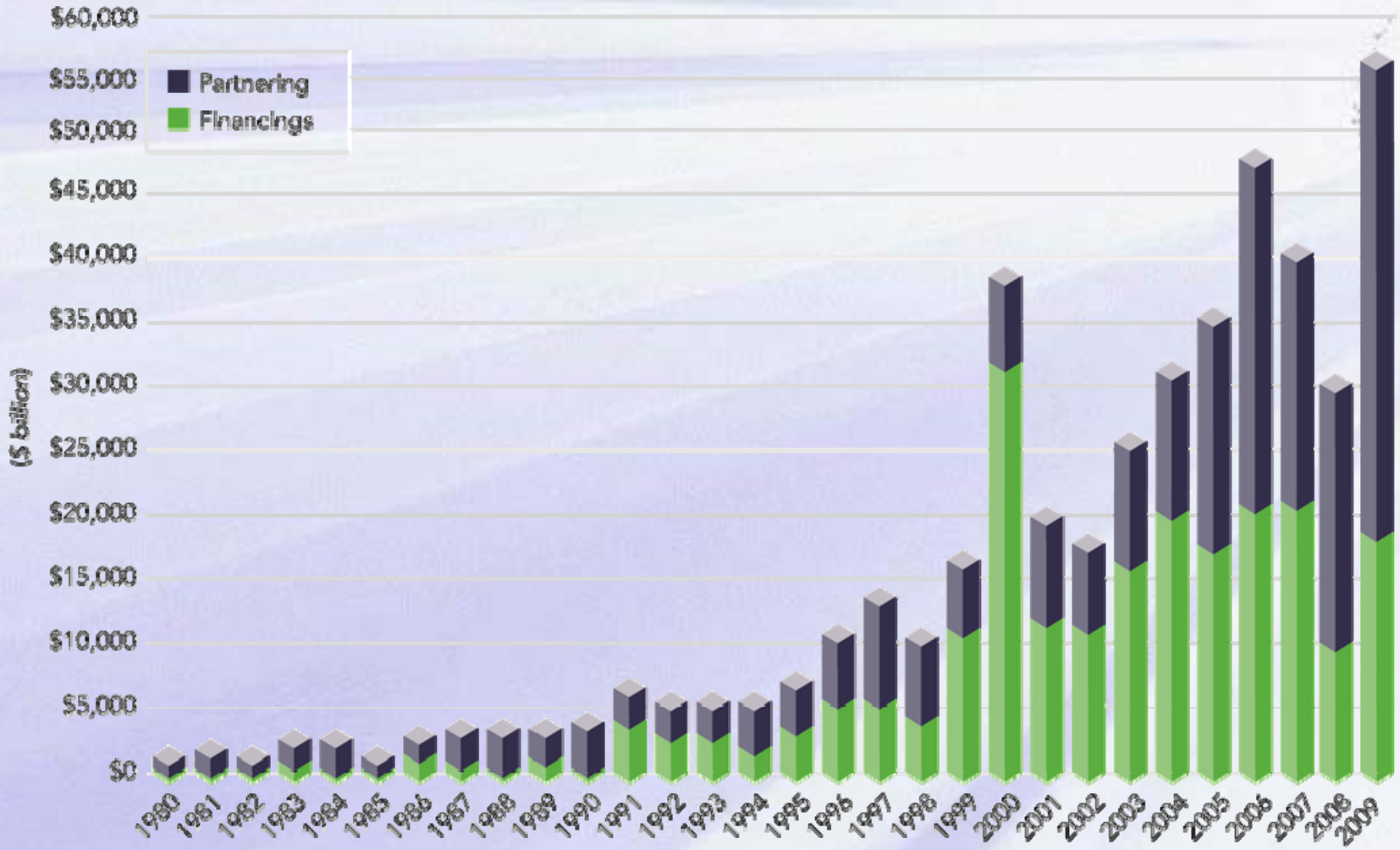


Source: Grant Thornton

US Biotech Financings ($M)

	2003	2004	2005	2006	2007	2008	2009	2010 YTD
Public								
IPO	$456	$1,701	$819	$920	$2,041	$6	$1,112	$216
Follow-ons	$3,536	$3,388	$4,194	$5,766	$6,311	$1,726	$5,619	$699
PIPEs	$2,051	$2,417	$2,376	$2,027	$1,818	$1,078	$1,632	$222
Debt	$7,170	$8,418	$5,565	$13,978	$6,569	$2,824	$6,306	$2,489
Private								
VC	$2,841	$3,733	$3,518	$4,236	$4,445	$4,175	$4,066	$1,082
Other	$294	$269	$1,114	$425	$611	$294	$158	$71
Subtotal	**$16,348**	**$19,927**	**$17,586**	**$27,352**	**$21,975**	**$10,103**	**$18,893**	**$4,779**
Partnering	$8,933	$10,933	$17,268	$19,796	$23,365	$20,023	$36,923	$3,552
Total	**$25,281**	**$30,860**	**$34,854**	**$47,148**	**$45,340**	**$30,126**	**$55,816**	**$8,331**

Capital Raised 1980-2009



Financing 2010: Adapting to a changed environment

- Governments/development authorities/research institutes providing capital
- Disease advocacy/charitable organization (active players in early stage R&D funding)
- Development stage (rounds now extending to E/F) available but still expensive…companies on track with progress financing at discounts to prior rounds
- Equipment/facility financing (even IP)
- IPOs – later stage operating companies (risk abated) with revenues/profits (Talecris 2008 sales - $1.4 billion)
- More follow-ons
- Reverse mergers into public companies, still happening
- Equity –lines of credit
- Shelf registration/registered direct/PIPES
- Global arbitrage – financing parts of business in non-local markets

Healthcare Reform

- What is our healthcare system?...(we don't have one!)
- It's really insurance reform, reallocating who pays for a dysfunctional "sickness" care system
- Enabling/requiring 30+M Americans to get healthcare insurance and receive healthcare services
- …but reducing aggregate healthcare costs (now $2.3T in US, going to $4T by 2015)

So what else is this "Adapting For Success" all about?

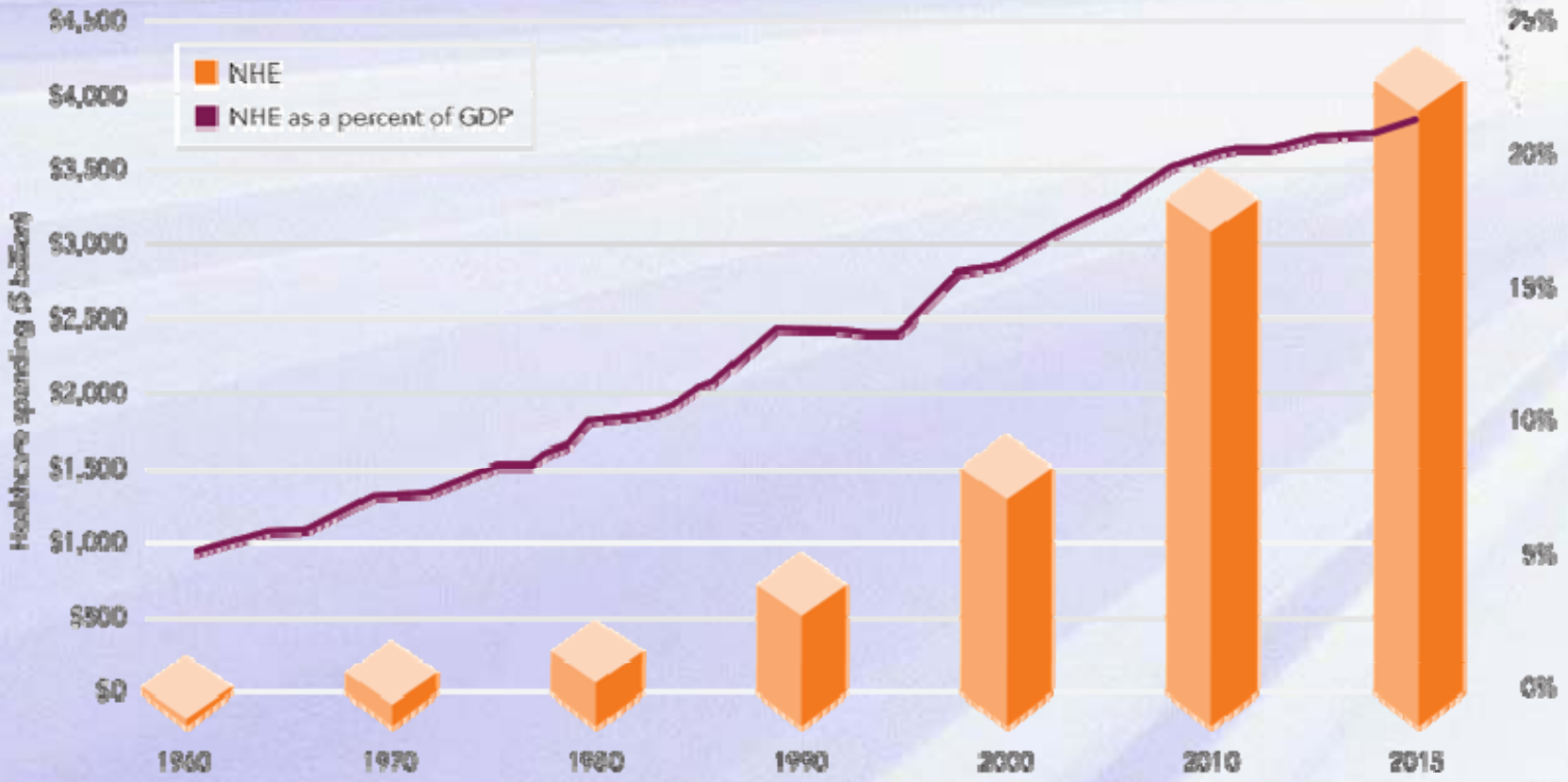
- Healthcare reform – what is really happening?
- Changed pharmaceutical environment – why; impact?
- Regulation – is genomics slowing us down?
- Reimbursement – who is really paying for what?
- Emerging markets (BRIC plus MENA) versus traditional markets (US/Europe/Japan)…changing global focus
- Technology – where is it taking us?

New "Glossary" for Health Care Reform

- Bending the cure
- Bundling
- Comparative-effectiveness studies
- Defensive medicine
- Doughnut hole
- Employer mandate
- End-of-life care
- Guaranteed issue
- Health-insurance cooperative
- Individual Mandate
- Pooling
- Portability
- Public Option
- Rescission
- Single-payer

Source: Burrill & Company

U.S. Healthcare Costs Have Been Rising for a Long Time



Source: OECD FactBook, 2008

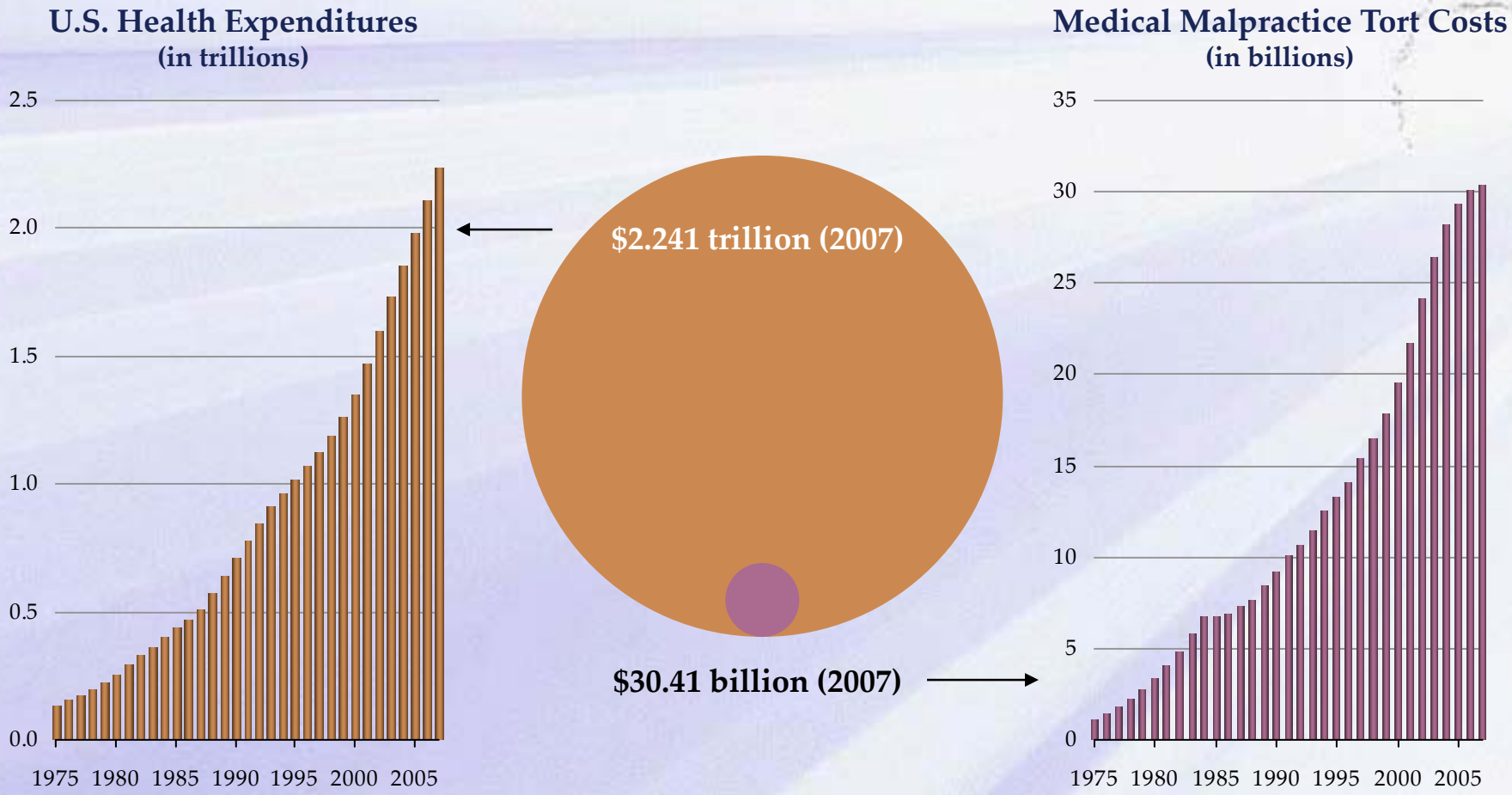
Market Distortions and Perverse Incentives in Modern Healthcare Delivery

- Focus on late-stage detection and intervention
  - High cost
  - Low reversibility
- Multiple reimbursements for fragmented (siloed) care versus integrated management of patient needs
- Medical professionals paid for illness versus wellness
- Inadequate social and economic incentives for wellness
- Inadequate medical training/understanding of genetics/genomics/proteomics

Source: George Poste / Burrill & Company

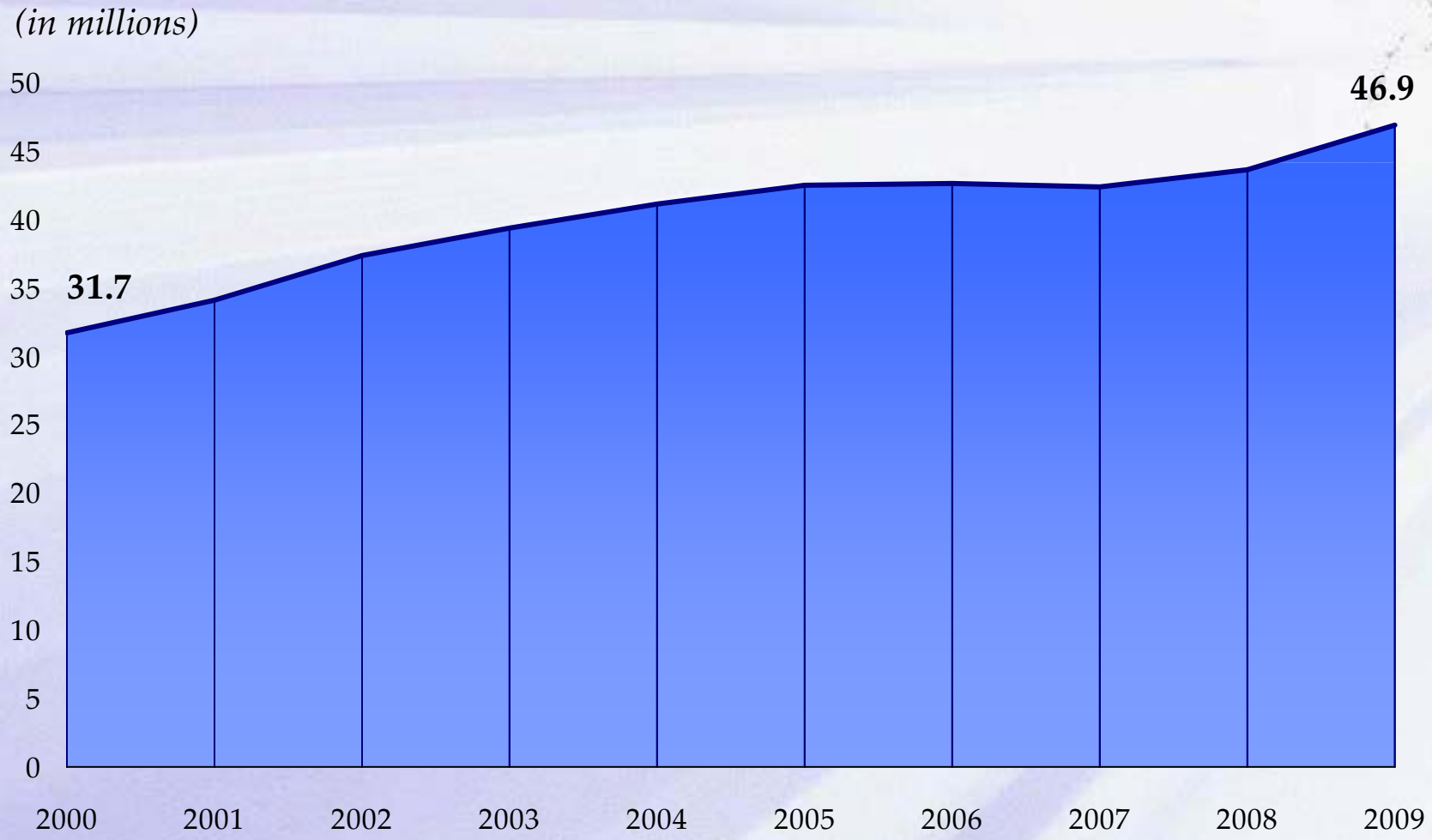
Tangible and Unseen Cost For Health Care

Malpractice costs are a small part of health spending, but could spur doctors to make costly choices



Note: U.S. Health expenditures include drug costs, nursing-home care and other spending, in addition to payments to doctors and hospitals. Malpractice costs don't include legal expenses incurred by pharmaceutical companies.
Source: Centers for Medicare and Medicaid Services; Towers Perrin

Medicaid Enrollment

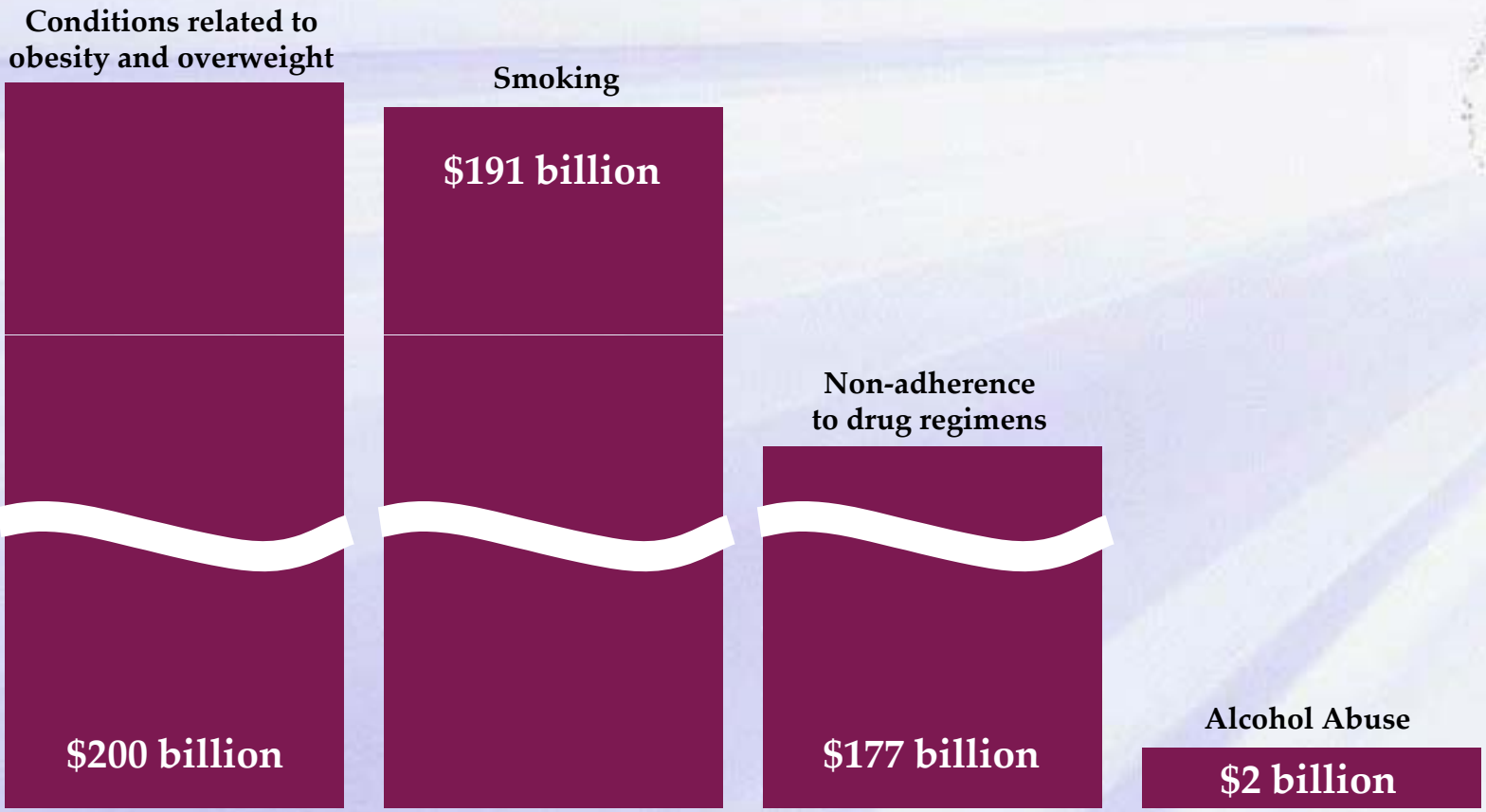


Source: Kaiser Family Foundation

Average annual premiums for employer-sponsored family health policies

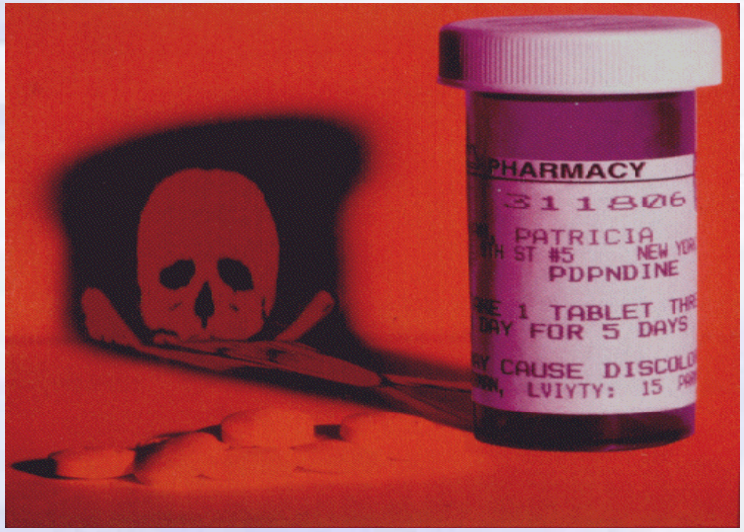
Source: Kaiser Family Foundation

Annual Excess Healthcare Costs Related to Consumer Behavior



Source: RTI International & Center for Disease Control and Prevention (200), Datamonitor (2007), Americas Health Insurance Plans (2007), Commonwealth Fund (2007), Agency for Health Research and Quality (2003), Analysis by PricewaterhouseCoopers' Health Research

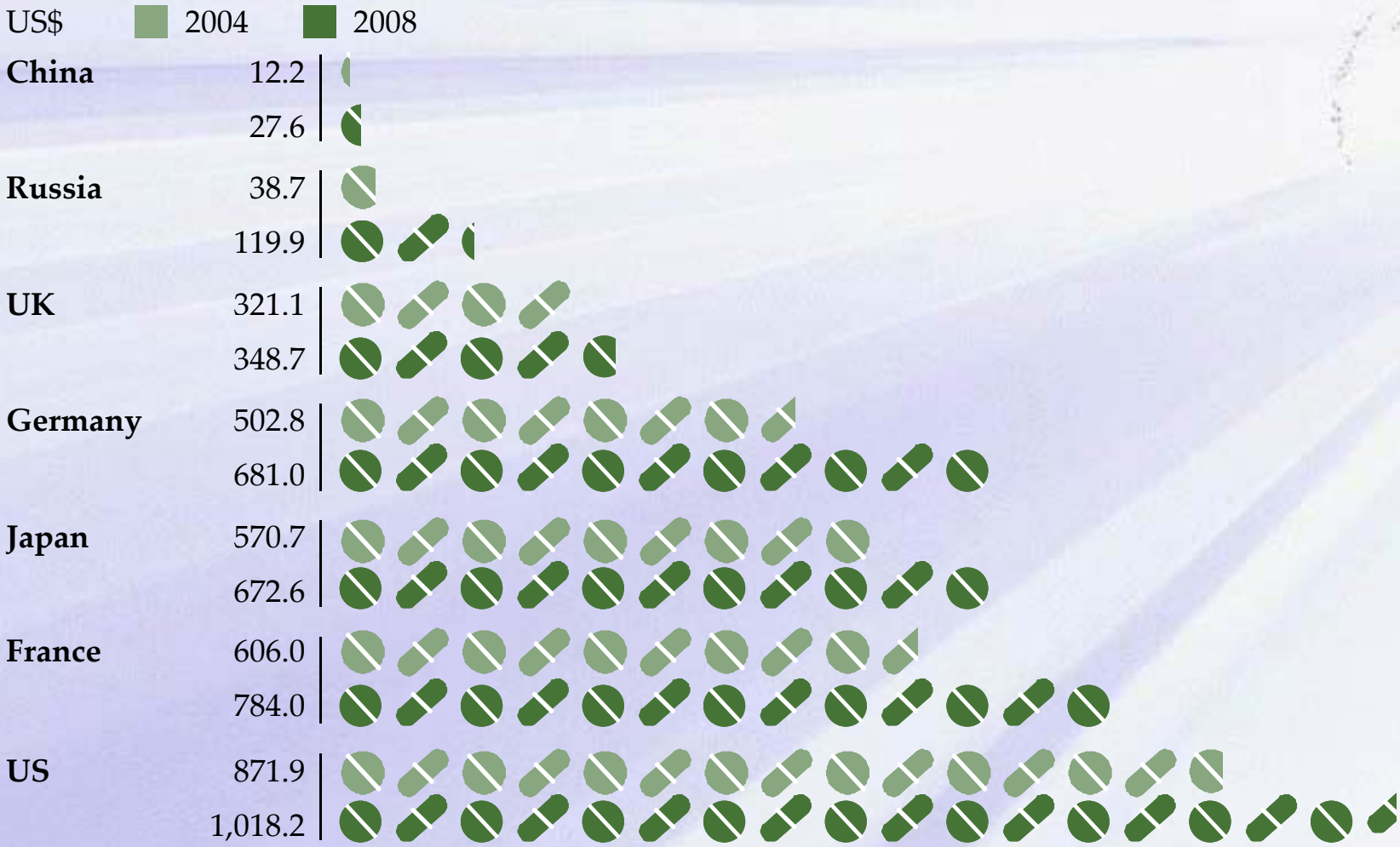
Pharmacogenetic Predisposition to Adverse Drug Reactions



- 1.5 to 3 million annual hospitalizations (US)
- 80 to 140 thousand annual deaths (US)
- est. cost of $30-50B

Source: George Poste

Pharmaceutical Expenditures Per Capita



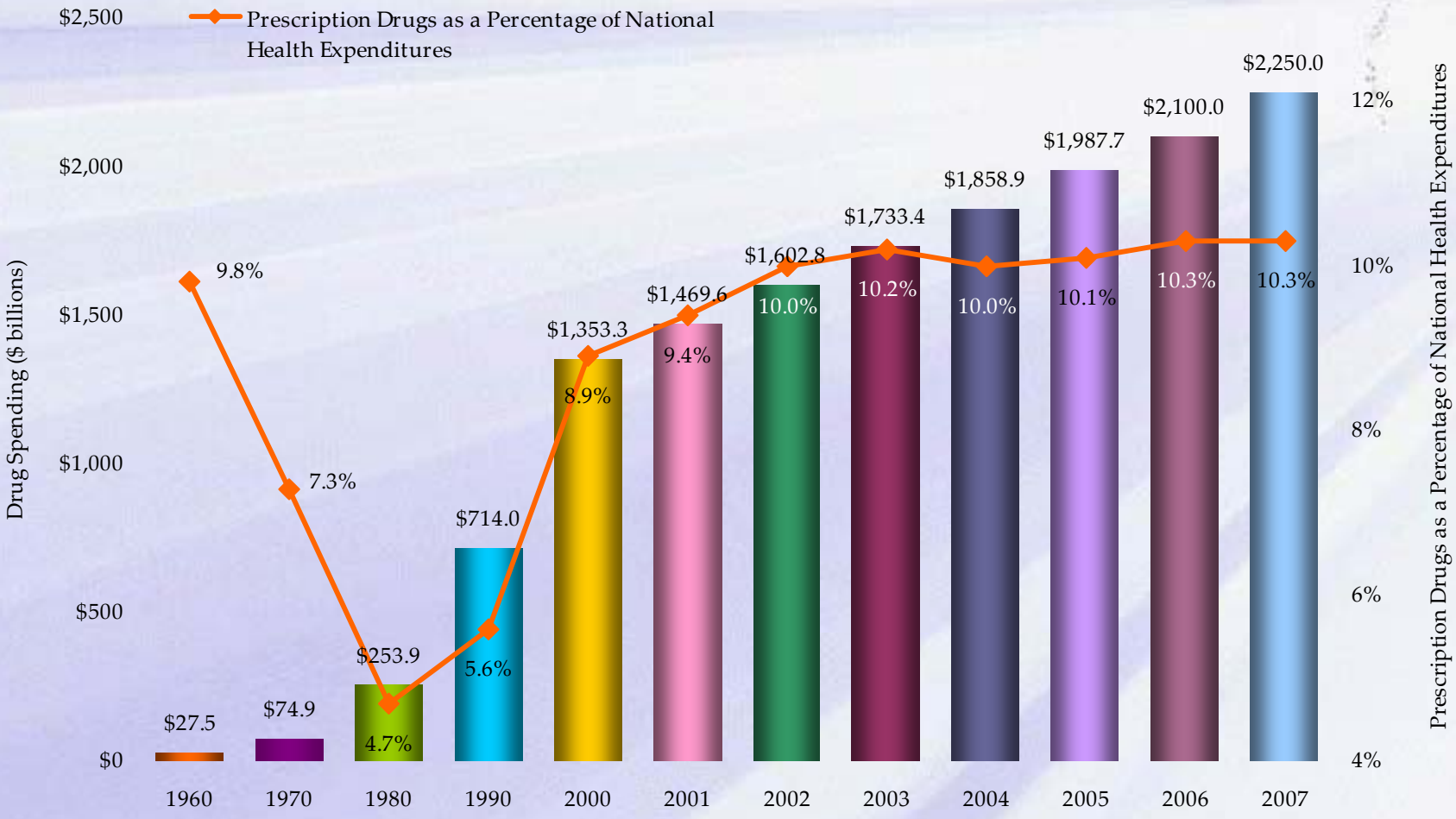
Source: Business Monitor International

Healthcare Costs are Unevenly Distributed

- 0.5% patients consume 25% of healthcare budget
- 1% consume 35%
- 5% consume 60%
- 10% consume 70%
- 50% consume 3%
- 75% of cost is for patients with chronic diseases

Source: G. Halvorson/George Poste

US Prescription Drug Costs as Percentage of Healthcare



US Healthcare Costs

- Administration 35%
- Personnel costs 35%
- Procedures 18%
- Drugs 12%
- In vitro diagnostics 0.01%

Diagnostic tests influence 85% of clinical actions

Source: George Poste

…but we have major challenges in healthcare

- Cost
- Demographics
- Access
- Variation in clinical practice
- Inefficient use of information
- Fragmented care versus integrated care
- Duplication, defensive medicine & waste
- Protracted adoption of innovation

Source: George Poste and Burrill & Company

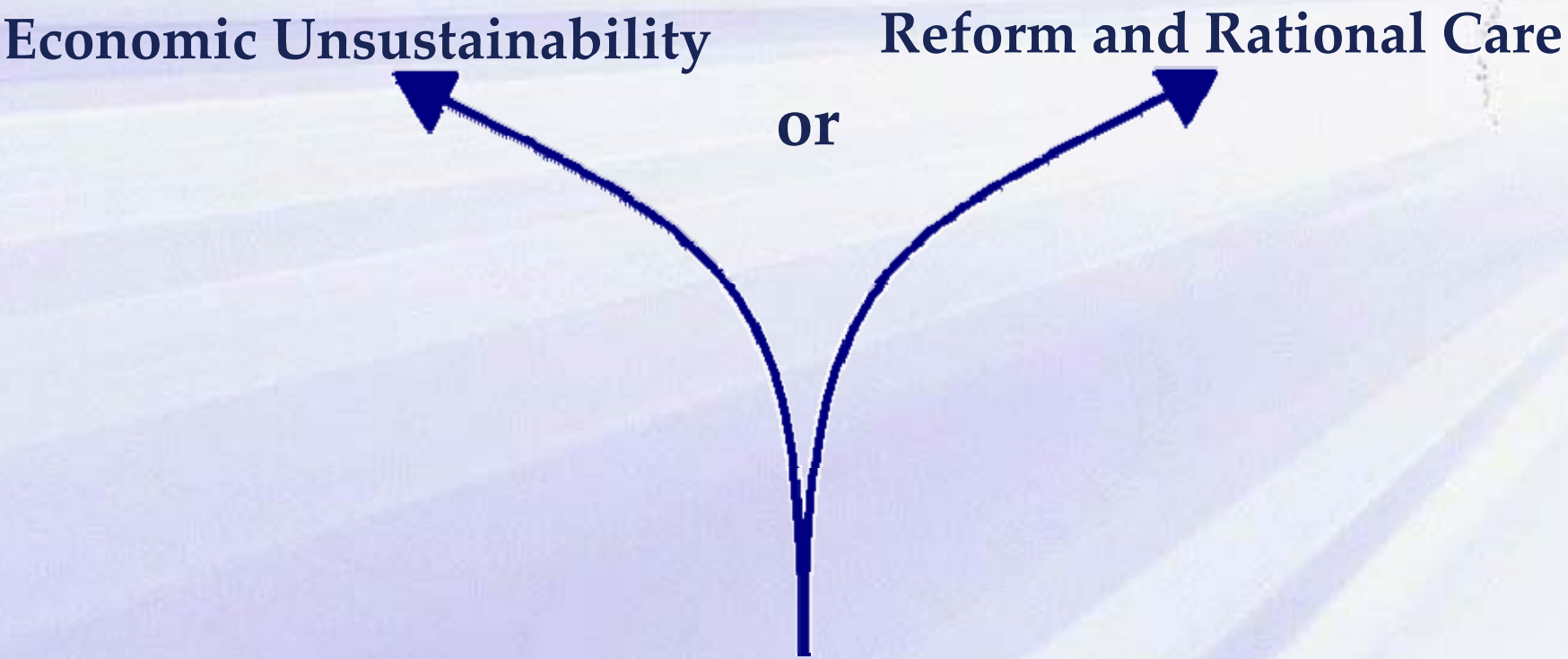
A Rational Healthcare System…

Value is created by:

• what works	→	• validated evidence
• why it works	→	• mechanism of action
• who it works for	→	• personalized medicine
• what works best	→	• comparative effectiveness
• when should it be used optimally	→	• best practice guidelines, standard-of-care and malpractice

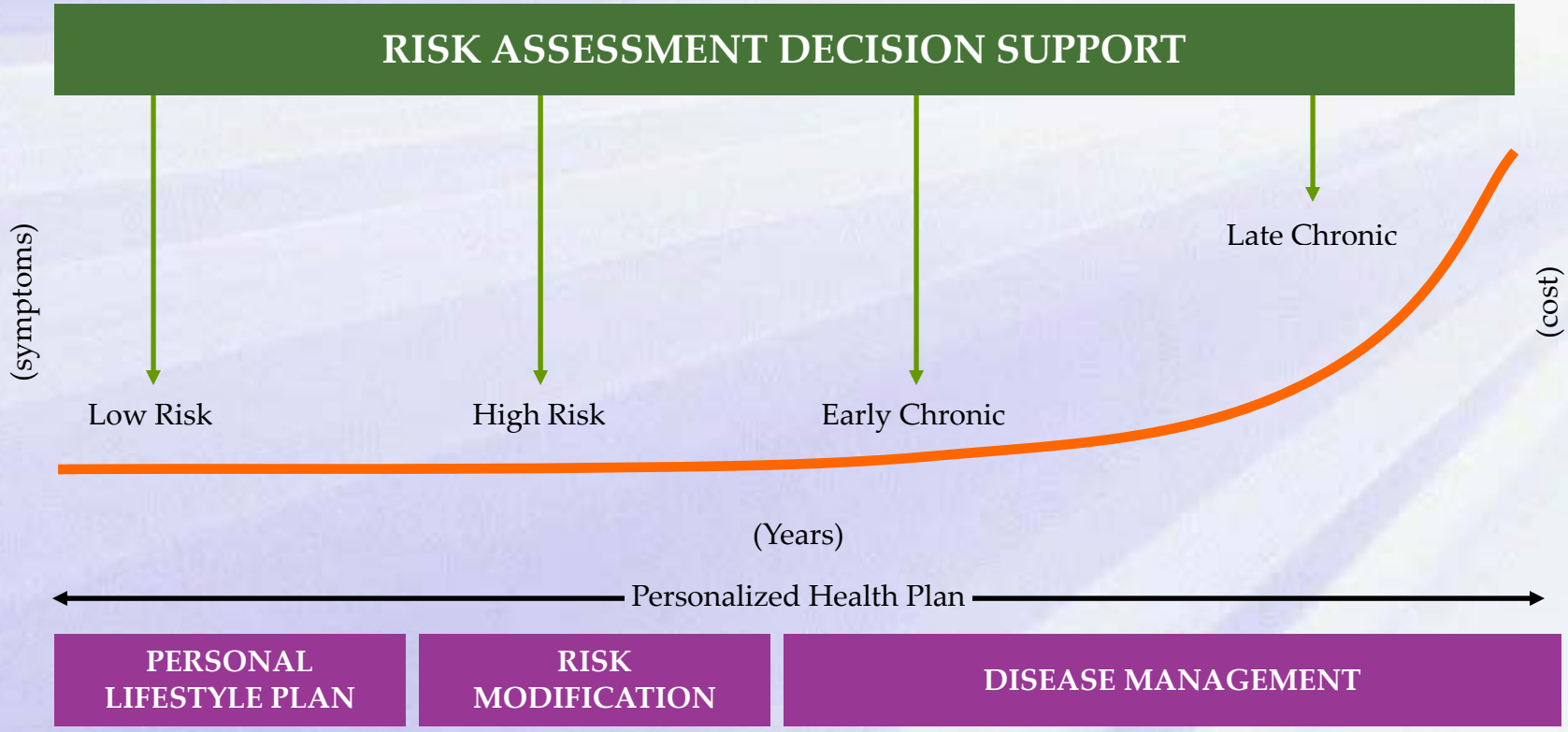
Source: George Poste and Burrill & Company

The Strategic Future of Healthcare



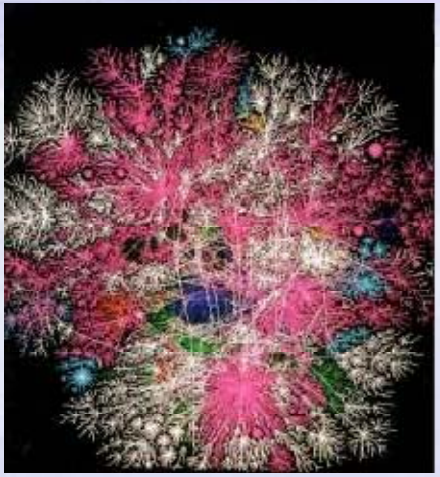
Source: George Poste

The Changing Focus of Healthcare

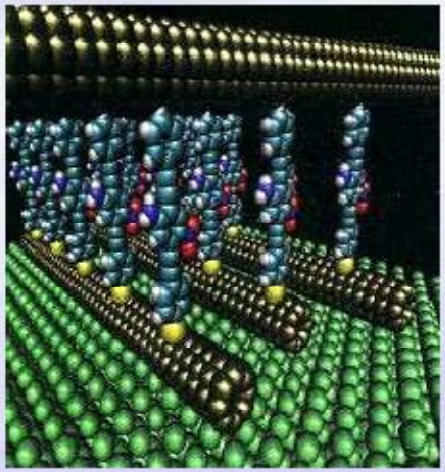


Source: Ralph Snyderman

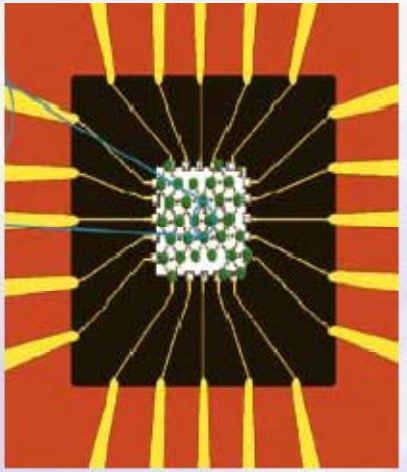
Technology Convergence: Integration of DX, Rx, and HIx



Biotechnology, Systems Biology and Synthetic Biology



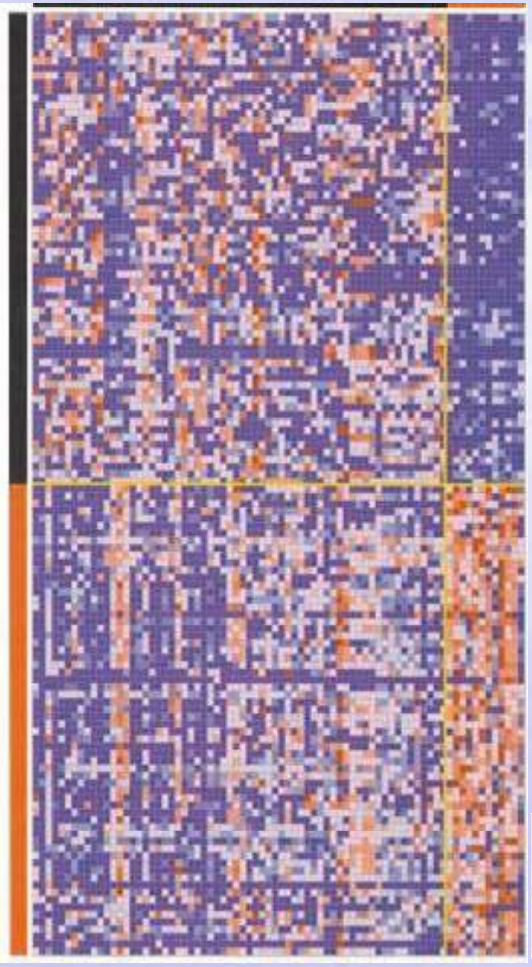
Nanotechnology Materials Science and Miniaturization Engineering

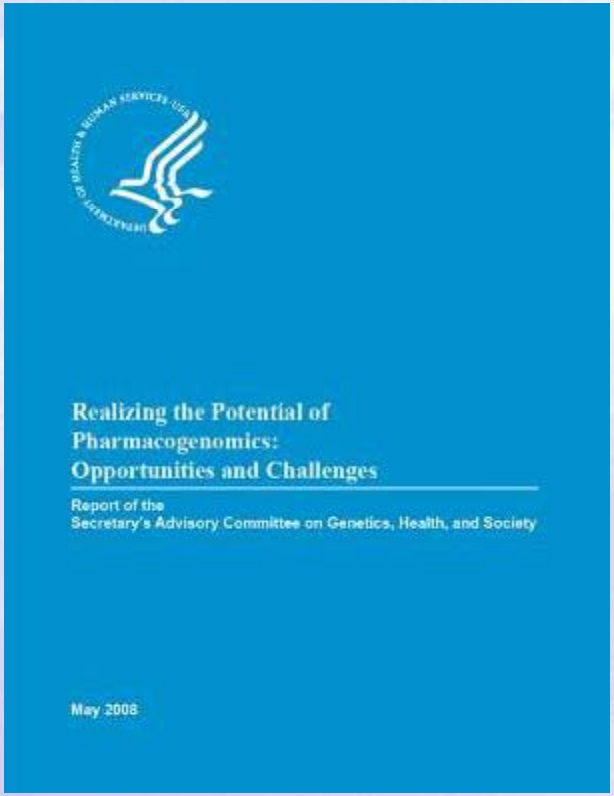


Advanced Computing and Knowledge Management

Source: George Poste and Burrill & Company

Personalized Medicine: Key Drivers





Science **Policy** **Cost and Outcomes**

Source: George Poste and Burrill & Company

Molecular Medicine and Rational Therapeutics

- opening era in linking disease molecular pathology to rational Rx
- increasing payor, regulatory and public pressures for reliable ID of Rx-responsive patients
- Rx/Dx combination will become an obligate element of NDA/BLA submission and product labeling
- development of Rx/Dx combinations as intrinsic components of R&D programs for investigational Rx

Source: George Poste and Burrill & Company

Deriving Value from "-Omics"

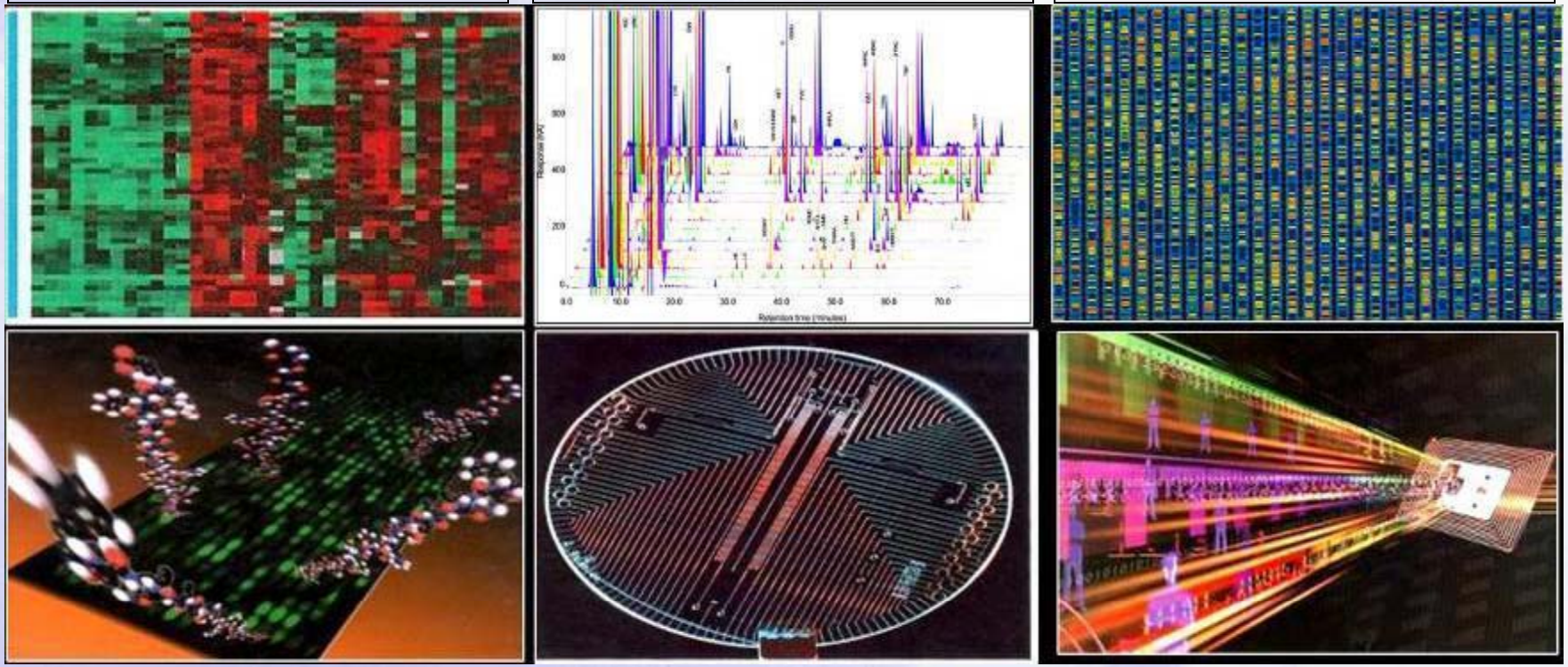
- useful only when correlated with additional parameters
  - clinical outcomes
  - clinical utility
  - actionable information
  - demonstrable economic value

Standards are critical!

Development of Molecular Diagnostics and Biomarkers for Personalized Medicine: The Need for End-to-End R&D Solutions

Complex Biosignature Profiling

Genomics	Proteomics	Immunosignature



Signature Detection, Deconvolution and Multivariate Analysis

multiplex assays	novel test devices (POC)	new algorithms

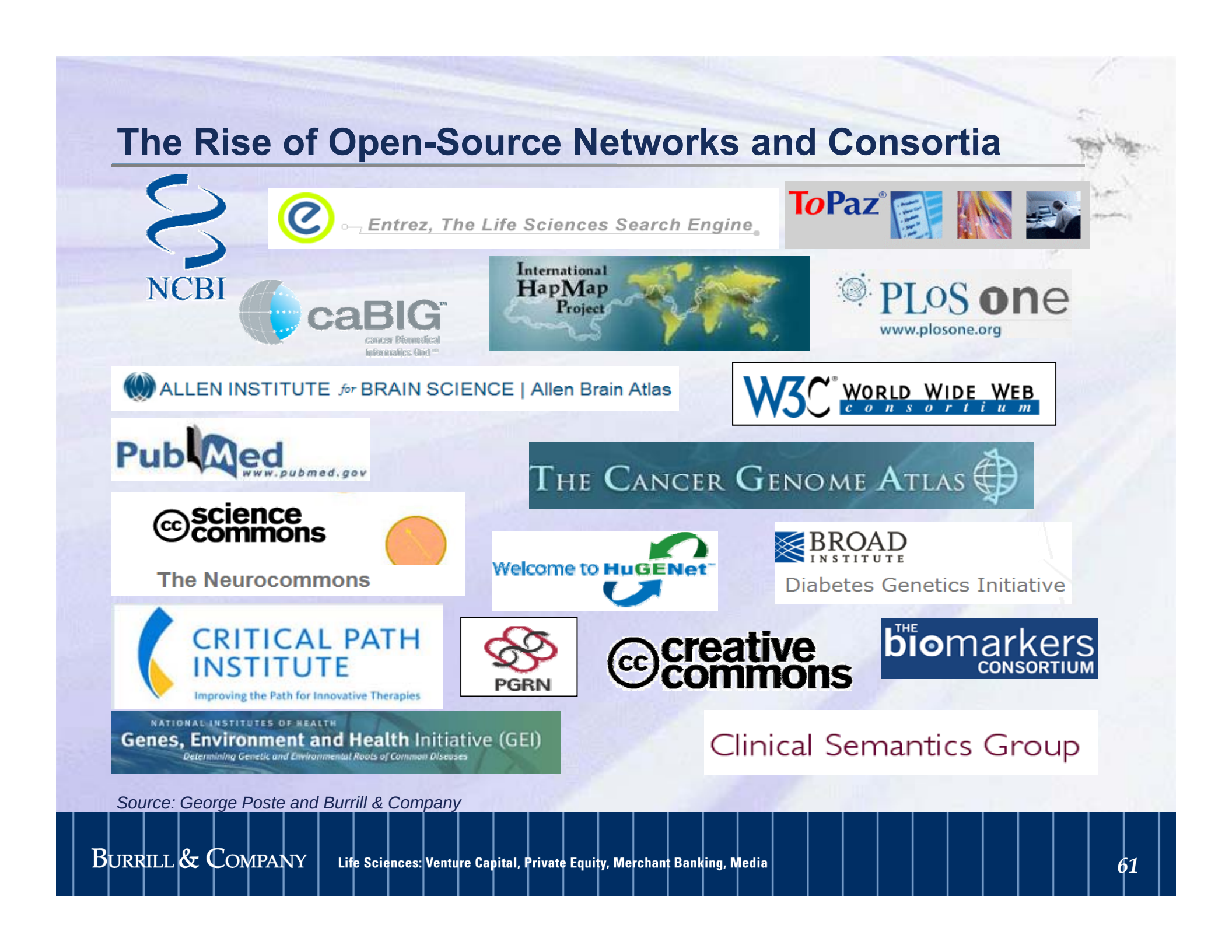
Source: George Poste and Burrill & Company

Increased Legislative Interest in Standards, Oversights and Regulation of Molecular Diagnostic Testing

- (2008) In Vitro Diagnostic Multivariate Index Assays (IVDMIAs)
- (2009) Quality, Regulation and Clinical Utility of Laboratory-Developed Tests
- (2009) Good Laboratory Practices for Molecular Genetic Testing for Heritable Diseases and Conditions
- (2009) Secretary's Advisory Committee on Genetics, Health and Society (SACGHS)
- (2009) SB 42: Post-CLIA Bioinformatics Services

Source: George Poste and Burrill & Company

The Rise of Open-Source Networks and Consortia



Source: George Poste and Burrill & Company

If You Build It, Will They Pay?
Adoption of Disruptive Innovation

- new technology/service that simplifies a complex/costly problem
- business model that allows market adoption of the simplified solution at low(er) cost
- incentivized supply and demand to networks to reinforce the disruption

Source: George Poste and Burrill & Company

Reimbursement for Diagnostic Tests

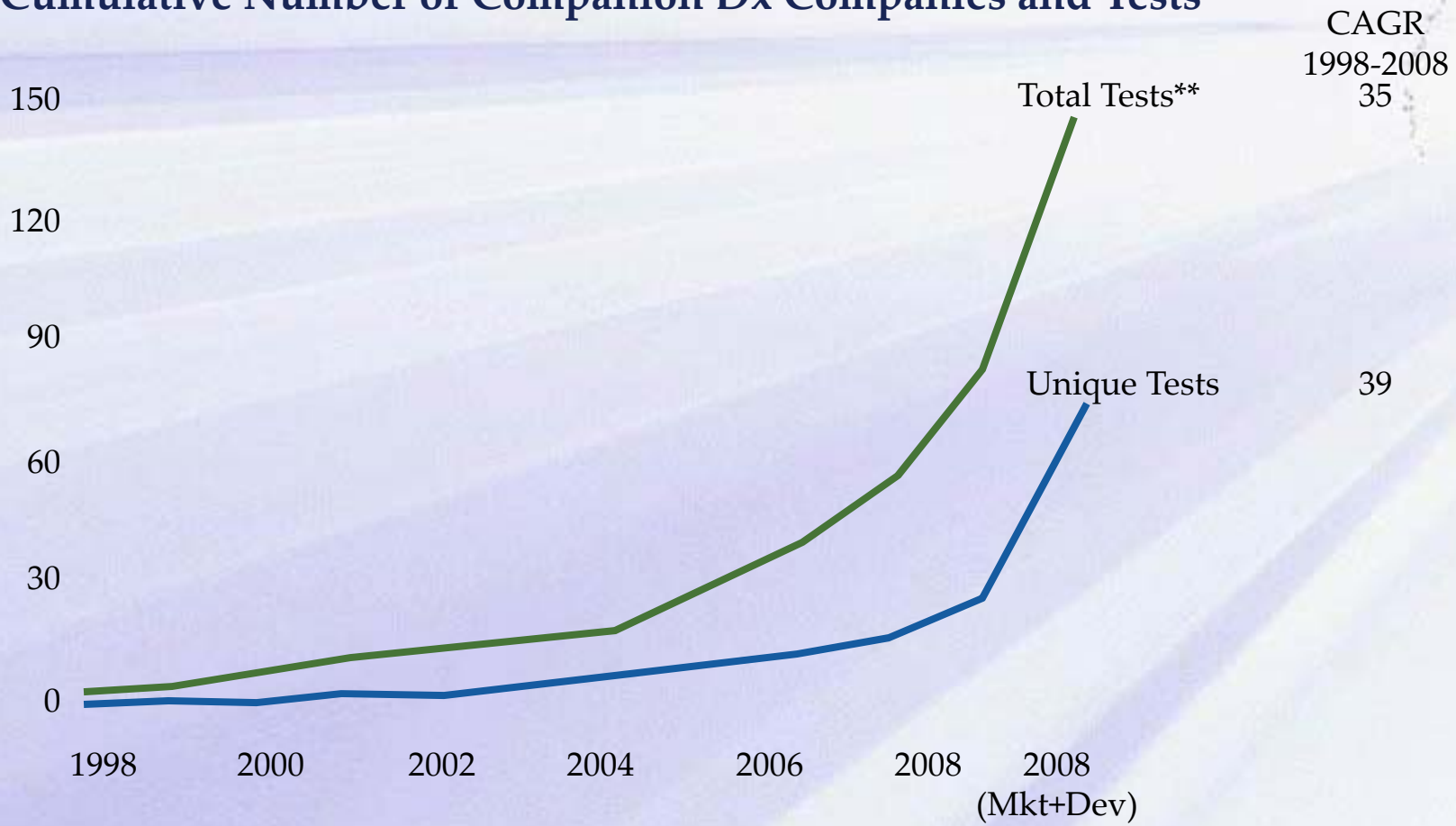
The Imperative for Value-Based Pricing versus Current Cost-Based Models

- inadequate US Medicare coding and payment mechanisms
  - out moded, out-dated, lacking in transparency, inconsistently applied
- inappropriate assignment of existing CPT codes to new tests
- engagement of third party payers who derive economic/clinical value from new Dx

Source: George Poste and Burrill & Company

Companion diagnostics tests have surged

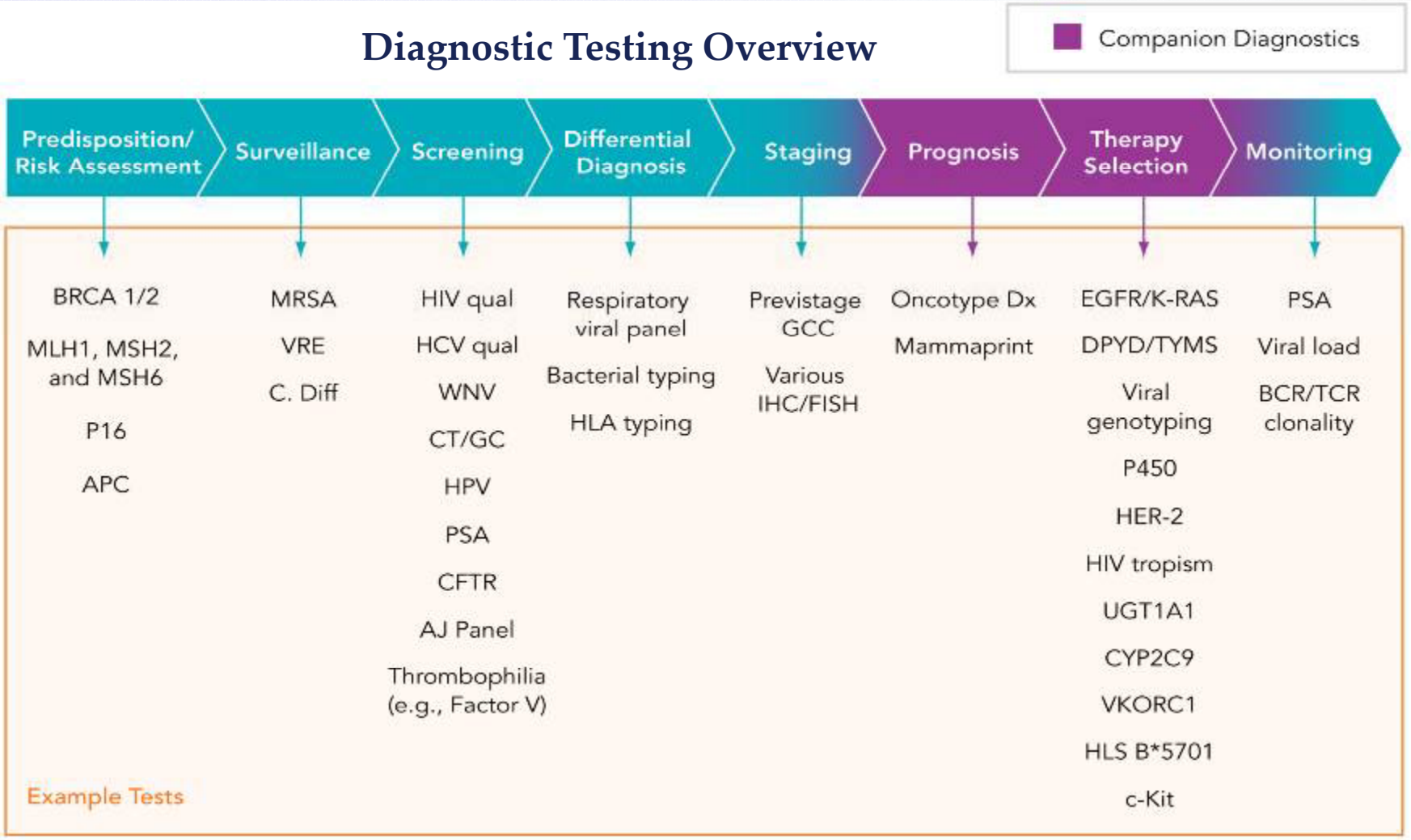
Cumulative Number of Companion Dx Companies and Tests



* The launch date for 16 tests (out of 161) could not be identified
** Includes duplicates
Source: Company websites, SEC filings, Capital IQ, L.E.K analysis

Companion Diagnostics (Leading to "Companion therapeutics")

Diagnostic Testing Overview



Source: Company websites, L.E.K. analysis

Personalized Medicine and Lower Drug Cost

	Alzheimer's	Asthma	Pain	Rhumatoid Arthritis*	Schizophrenia
Patients who are are helped	30%	60%	80%	50%	60%
U.S. Prescriptions (billions a year)	$1.5	$8.0	$14.1	$13.6	$9.5
Estimated waste (billions)	$1.1	$3.2	$2.8	$6.8	$3.6

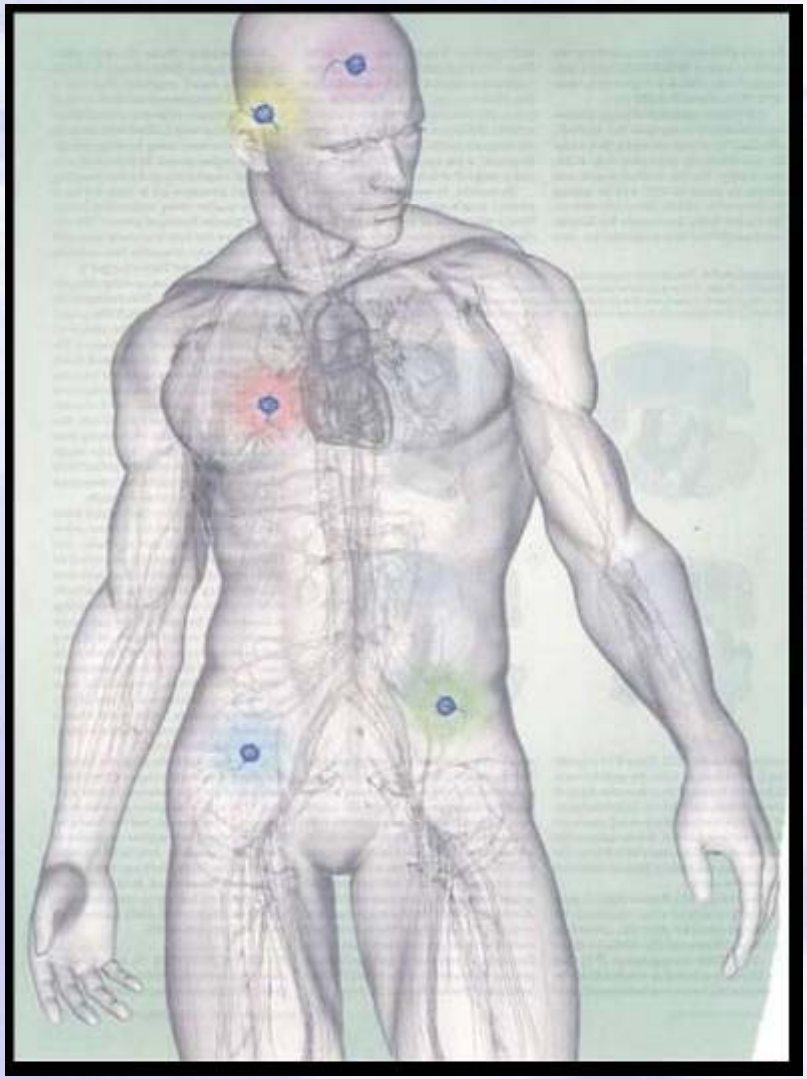
** Includes all autoimmune diseases, but RA is the most prevalent*
Source: Business Week, February 1 & 8 2010

Personalized Medicine: A Broader Perspective

Promotion of Wellness

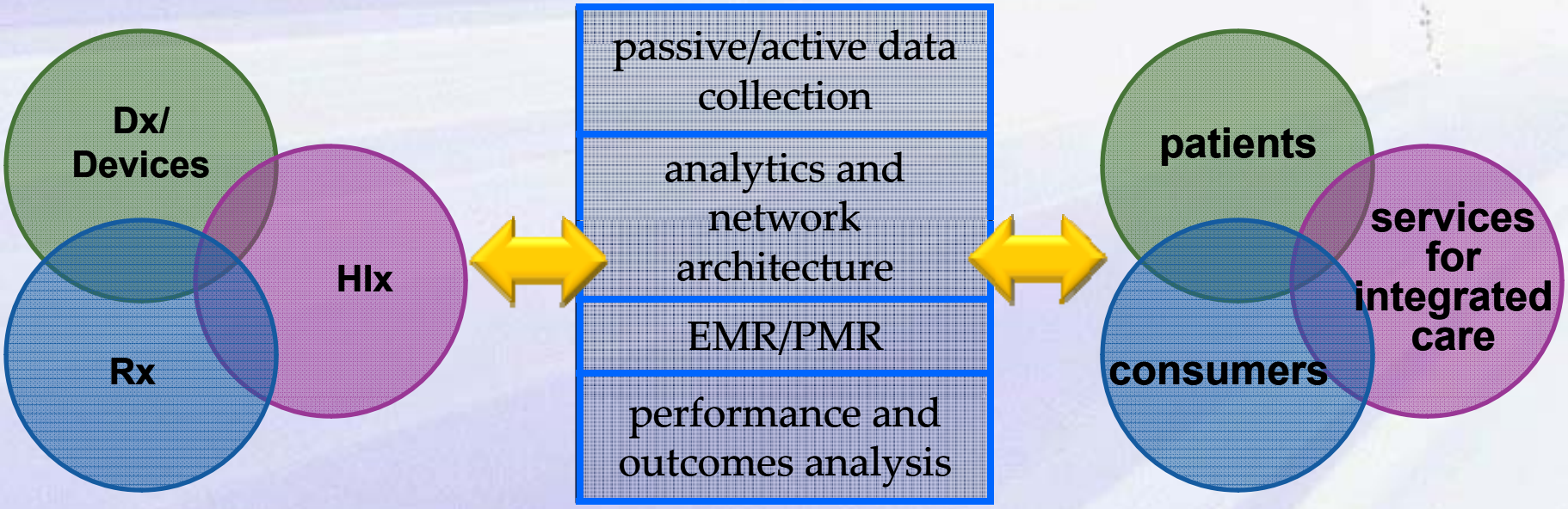
- increased consumer responsibility for wellness
- remote monitoring of individual health status
- crucial role of healthcare information systems
  - integrated Rx care for complex chronic conditions
  - outcomes and comparative effectiveness
  - earlier detection of disease episodes and risk mitigation
  - wellness versus illness

On Body: In Body Sensors/Devices
For Real Time and Remote Monitoring of Individual Health Status



Source: George Poste

A New Healthcare Ecosystem Arising From Technology and Market Convergence



Integrated Technology Platforms

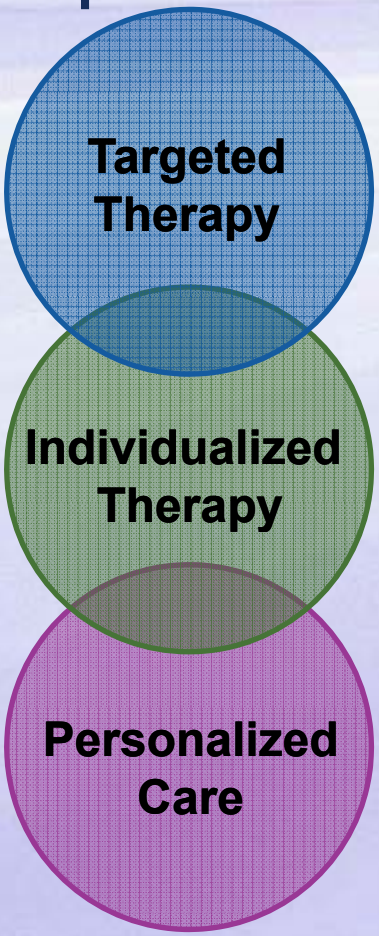
Data Mining and Integration Services

Increasingly Targeted Care and Efficient Use of Finite Resources

Source: George Poste

Personalized Medicine

Progressive Evolution Based on Increasingly Comprehensive Profiling of Disease Risk and Health Status



- Rational Rx based on profiling of underlying molecular pathology
- MDx and disease subtyping

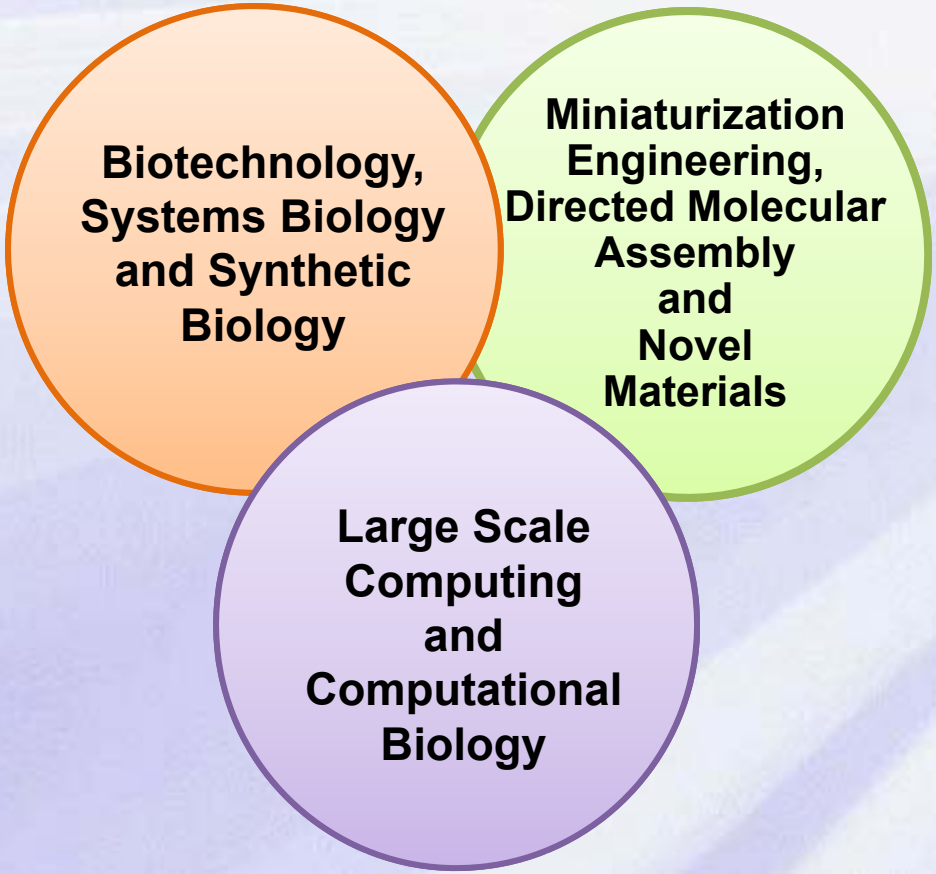
- Rational Rx based on comprehensive molecular profiling of individuals
  - disease subtypes and optimum Rx
  - Rx AE risk
  - disease predisposition risk and mitigation

- Integrated framework of longitudinal data on individual health status
- Real time remote health status monitoring
- Transition to disease prediction and preemption

Source: George Poste

21st Century Science: Comprehending Biological Design – "Systems and Synthetic Biology"

- the design principles of biological order and complexity
- the information content of biopathways and networks
- engineering bio-inspired novel functions and life forms



Source: George Poste

The Convergence in Healthcare Delivery

- Technologies
  - biotechnology, medicine, engineering, computing, telecommunications and social media
- Clinical Practice
  - molecular medicine and increasingly customized care
  - diagnostic, drug and device combinations
  - POC testing and remote monitoring
  - reduced error and improved compliance
  - improved outcomes
- Connectivity
  - integrated care networks for chronic disease
  - social media networks and informed consumers
  - new supplier networks of specialized turnkey expertise
  - value added 'content' services for clinical data mining
  - clinical decision-support systems

The Convergence in Healthcare Delivery (continued)

- Realigned Incentives
  - integrated care for complex chronic diseases
  - earlier disease detection and risk reduction
  - wellness versus illness
  - remote health status monitoring
- Consumers
  - increased personal responsibility for health
  - new incentives for wellness/compliance
  - health status monitoring

Healthcare will be…digitized

- Smart cards with electronic health records & sequenced DNA
- Consumer driven personal health planning
  - PHR
    - Microsoft -HealthVault™
    - Google Health
    - WebMD
    - Revolution Health
    - WalMart/Dell/eclinicalWorks
  - Note: Europe / Asia may be faster, more integrated than US

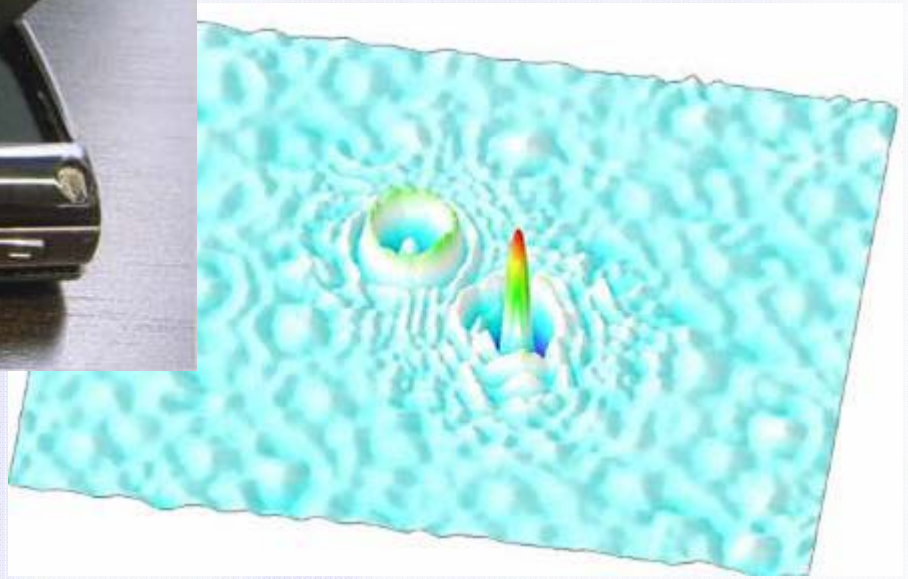
Need to Check Your Cholesterol?

There will be an app for that.

Smart-Phone Makers Call the Doctor

Monitoring Fitness (fitbit)… See How You Run, Walk and Sleep

Far From a Lab? Turn a Cellphone Into a Microscope



The process creates holograms that can show, for example, a stained white blood cell

Handheld Ultrasound – The New Stethoscope?

Interesting Facts

- 55% of consumers want to communicate with their Dr. via e-mail
- 57% want to schedule appointments via e-mail
- 57% want to buy prescriptions via e-mail
- 42% want personal health records (only 9% have them today)

Source: Deloitte's survey of 4,000 US consumers 18 years and older

Doctors & E-prescribing

- Only 12% of office based doctors e-prescribe (doubled in last year)
- 20% of prescriptions are never filled (patients don't bother taking them to pharmacy)
- CMS now pays a bonus of 2% on charges billed to medicare in 2009/2010, declines to .5% by 2013 (avg. is $2-4k per doctor)

Is there a doctor in the "mouse"?

- American Well, Inc. – a web service allowing patients to communicate via web/video/text/chat/phone with doctors (who can review PHR through Microsoft HealthVault)
- Swift MD, Inc. - $18 sign up/ $9 per month
  - Doctor's call/connect in less than 30 minutes ($59/consultation)
- TelaDoc, Inc. – online/phone consultations with doctors

Managing Health Online

- HazMap – federal government site for health & safety professionals
- EverydayHealth.com – (recently merged with RevolutionHealth)
  - Markets 24 separate sites catering to various interests
- HealthCentral.com
- Google Health
- Microsoft HealthVault
- WebMD.com
- VisualDxHealth.com
- QualityHealth.com
- Healthline.com
- Wellsphere.com
- RealAge.com

So, What are the Consequences for us of this Consumer Digital Healthcare World?

- Low margin ethical drugs will predominate
  - China/India/other low cost manufacturing sites will have an edge
- Theranostics – Rx tied to Dx
- Worldwide pricing/parallel pricing – direct importation from lowest priced country
- Pro-generics environment
- Patents devalued – increasing competition in marketplace
- Big pharma will become product distributors/disease managers – more value across the entire care spectrum, but more specialized

Stratified/Personalized Medicine will Profoundly Alter R&D and Business Strategies

- Increased reliance on biomarkers
- Greater reliance on Phase IV studies to verify clinical effectiveness and safety
- Emergence of new clinical development paradigm (phase 1-3 distinctions will become obsolete)
- New project management, business, and manufacturing models
- Increasing partnerships with diagnostics companies
- New regulatory framework
- Legal and ethical issues
- Challenge to healthcare financing systems

Source: Kenneth Kaitin

R&D moves from technology to market

R&D used to be "we have a molecule, a medicine, or a technology…looking for rich patients."

Now we start with patients – how can we help them?

~Chris Viehbacher, new CEO Sanofi-Aventis

Retail Clinics Growth

Source: Merchant Medicine

Wal-Mart Comes out of Rehab

- Wal-Mart projected 400 walk-in clinics by 2010…but instead went into reverse
- Of the 78 clinics in operation in 2008, all but 17 were closed by May 2009
- Wal-Mart reorganized in partnership with local hospitals and now has 33 clinics in operation, 26 with hospital affiliation

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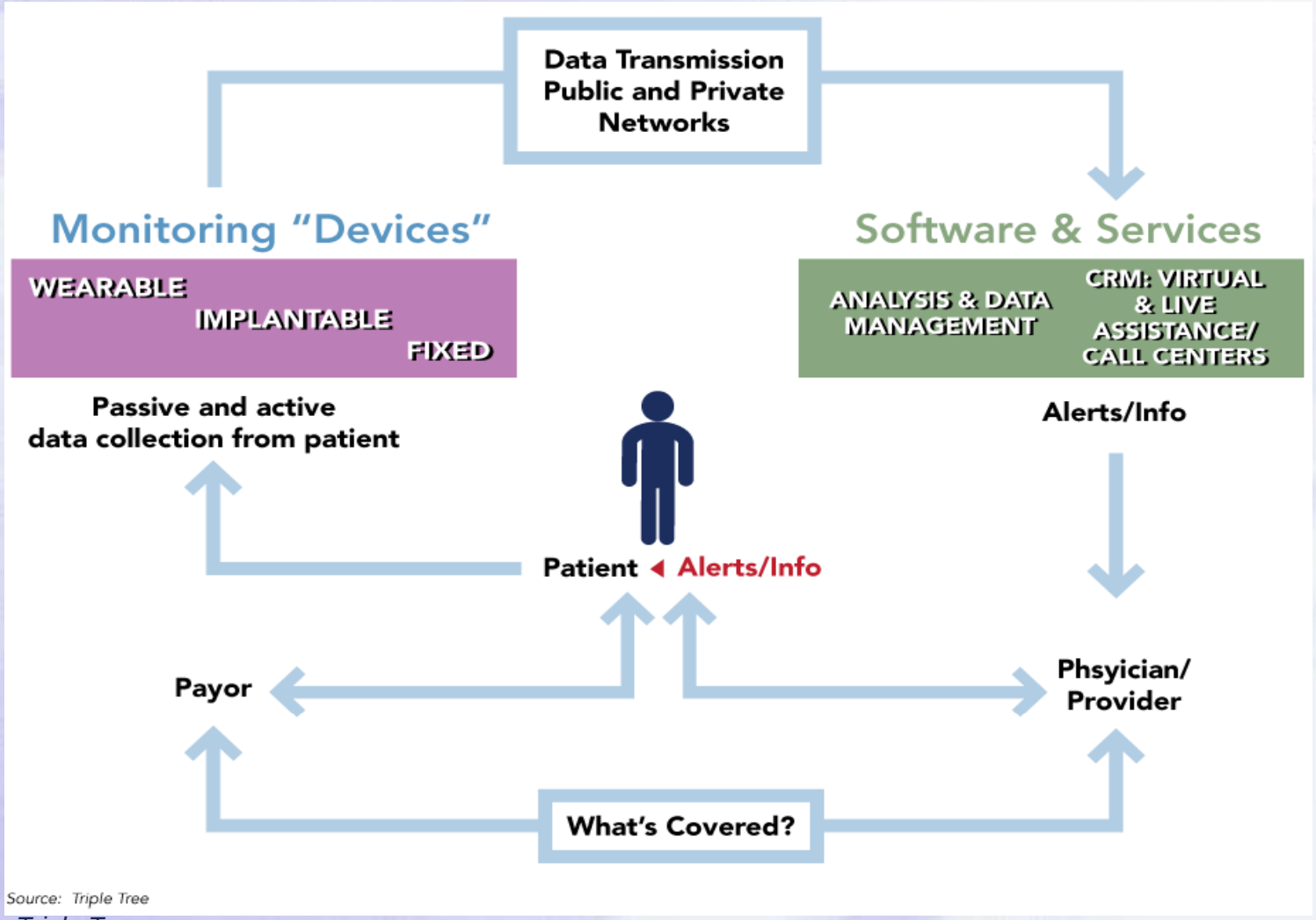
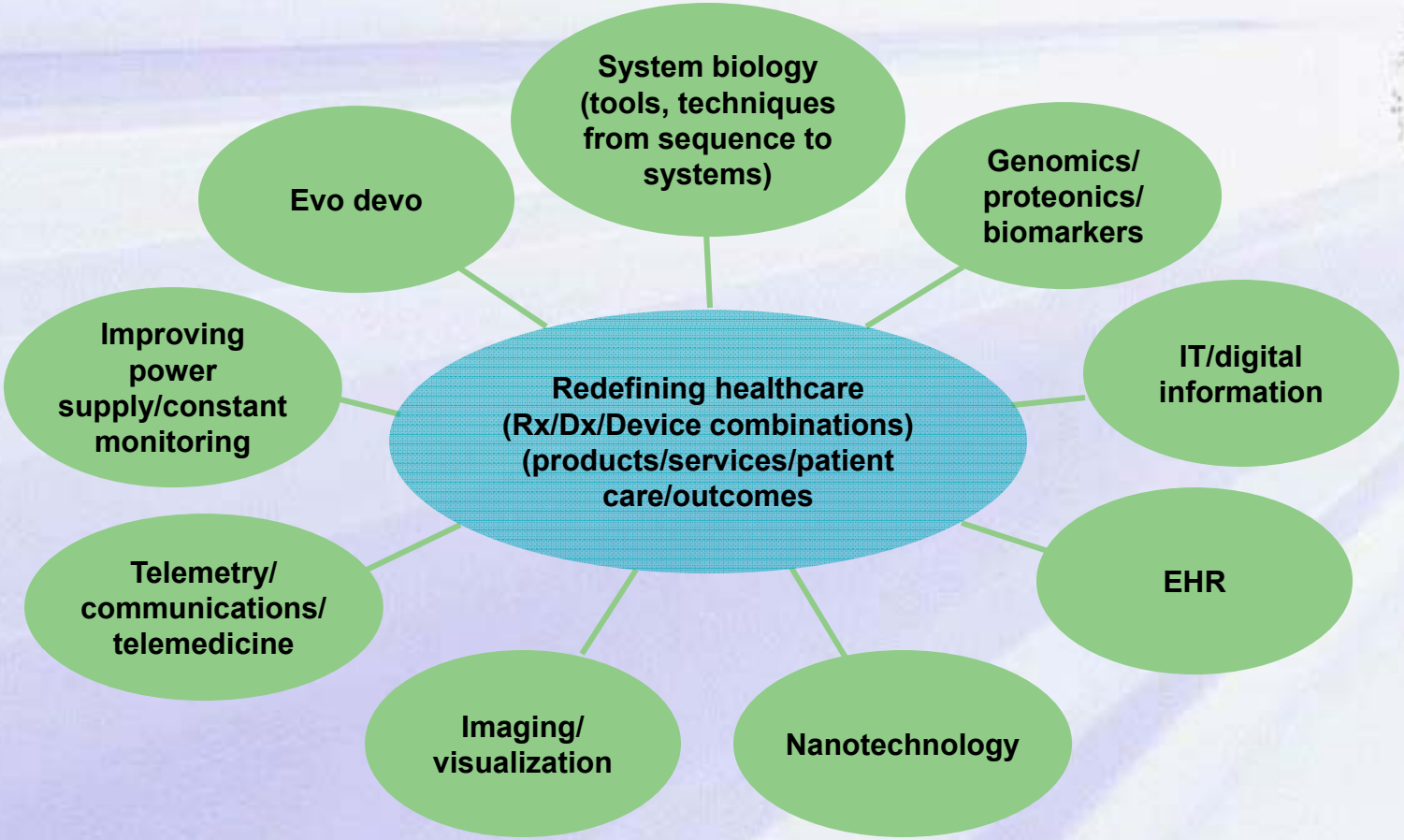
- Mayo Clinic looking for new model of care, opening 6 walk-in retail clinics, open early, on weekends, and closing late
- Geisinger Clinic opens 2 retail clinics in supermarkets

Ecosystems Based on Convergence



Source: Triple Tree

Confluence of Technology



Source: Burrill & Company

Evolution of Molecular Medicine and Information-Based Medicine: Foundation for Rational Care and Personalized Medicine

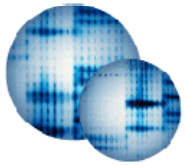
Rx 2009

Package insert

Drug

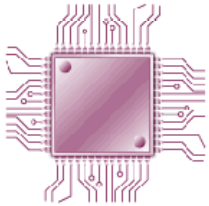
Medicine 2020

New competencies in molecular medicine and biomedical informatics



Molecular diagnostics

Genetic profiling



Real-time information for optimum decision-making

Drug

Disease management protocols, patient information

Source: George Poste

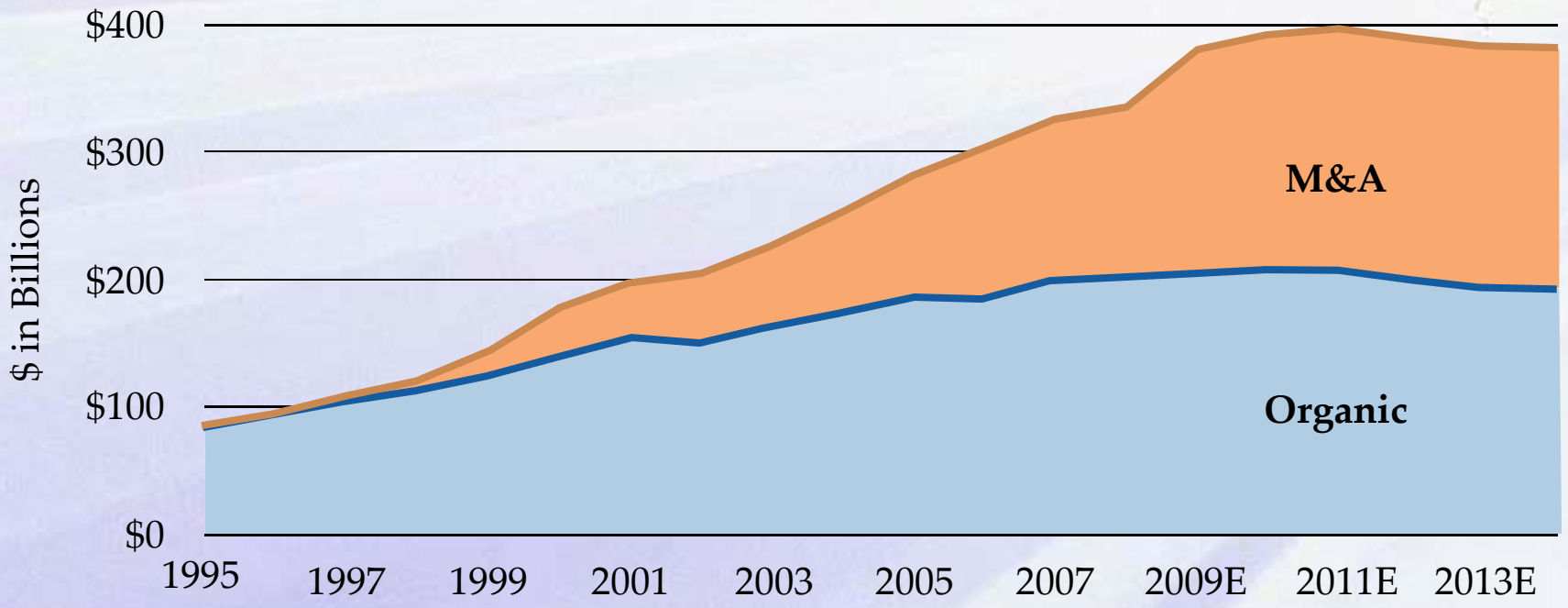
Re-Inventing the Biopharmaceutical Industry

- Changing the industry versus changing with the industry
- Escaping the myopia of current markets and investor horizons
- Organizational re-structuring and process re-engineering are insufficient for survival
- Creation of unimagined products, services and businesses
  - Integration of Dx, Rx and Ix

Where is the white space?
How do we adapt companies to a new and different competitive environment?

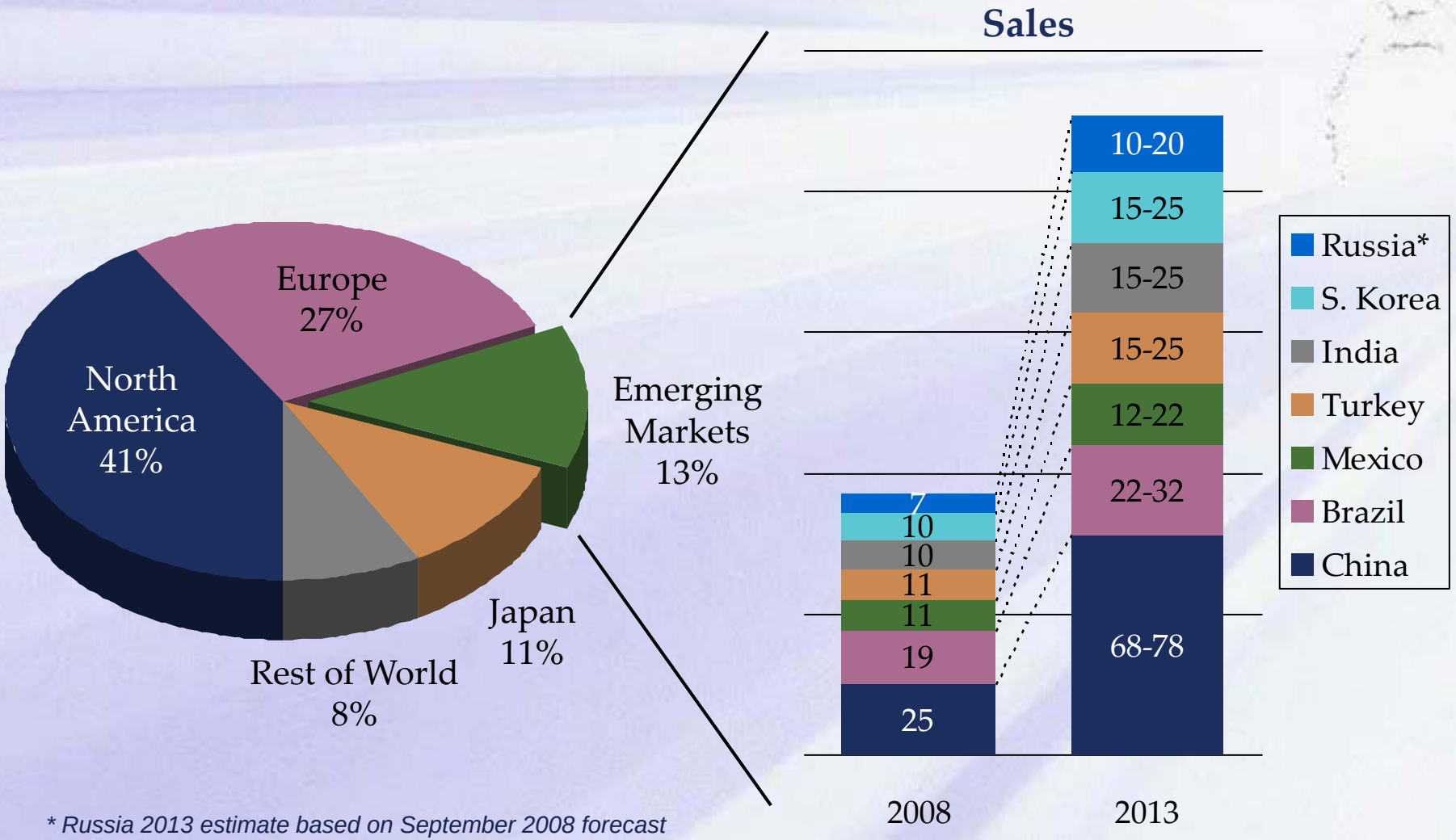
Source: George Poste / Burrill & Company

Big Pharma Sales Growth



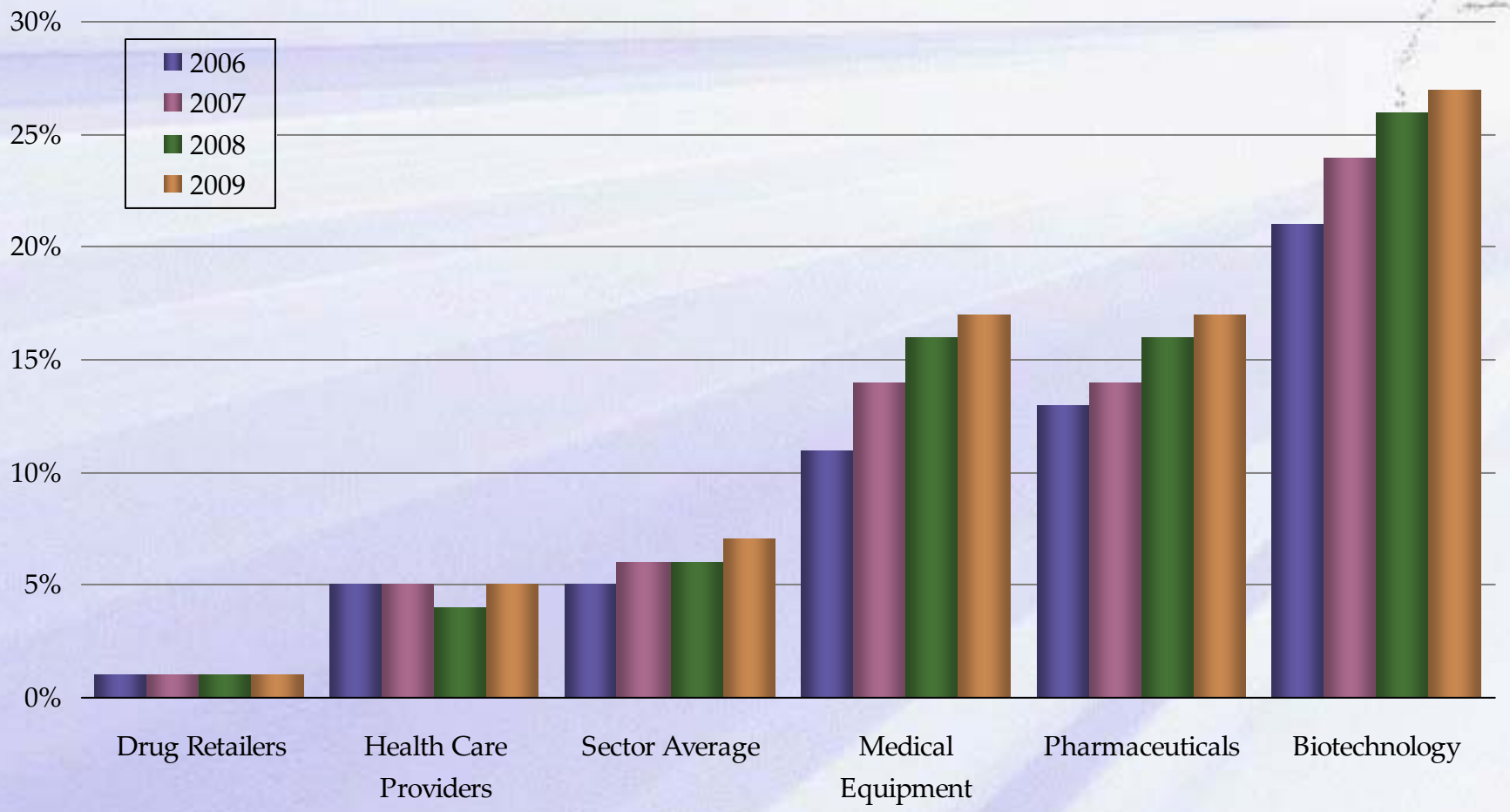
Source: Datamonitor

Global Pharmaceutical Market Forecast



** Russia 2013 estimate based on September 2008 forecast*
Source: IMS Health, Market Prognosis

U.S. Health Care Industry Profit Margins



** Calculated by dividing calendar year net income by revenue for the companies in the S&P 500 Health Care Index*
Source: Bloomberg

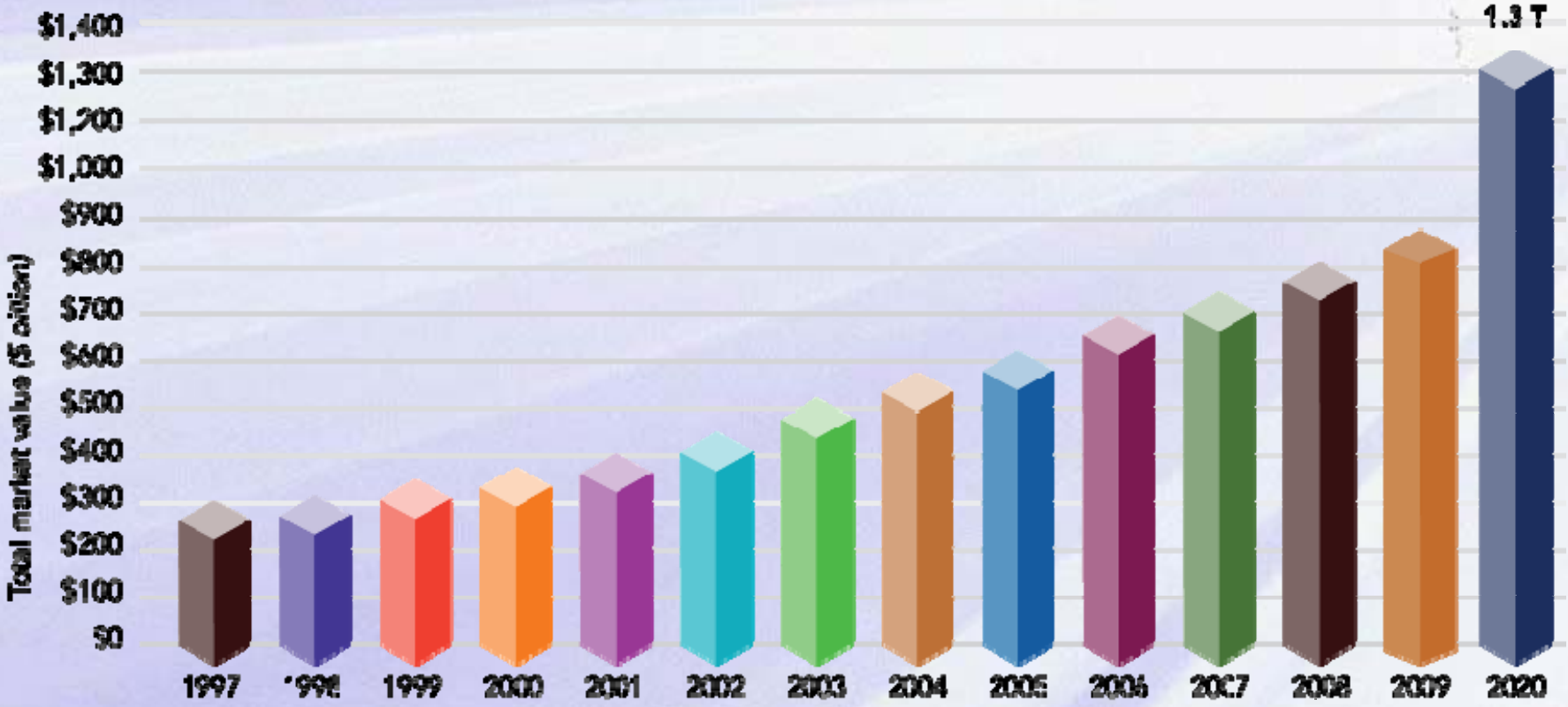
Global Pharmaceutical Sales in 2008

Audited Market 2008	Sales		% Growth (const US$)	
	US$bn	%Mkt Shr	2008	2003-2008 CAGR
Worldwide	**$773.1**	**100%**	**4.8**	**6.6**
North America	311.8	40.3	1.4	5.7
Europe	247.5	32.0	5.8	6.4
Asia/Africa/Australia	90.8	11.7	15.3	13.7
Japan	76.6	9.9	2.1	2.7
Latin America	46.5	6.0	12.6	12.7

Note: All forecasts are from IMS Market Prognosis International 2009-2013 which provide a view of the audited and unaudited market, using audited sales and adjusting for unaudited sales. The forecast are based on the March 2009 Market Prognosis release.

Source: IMS Health, March 2009

Worldwide Global Pharmaceutical Sales

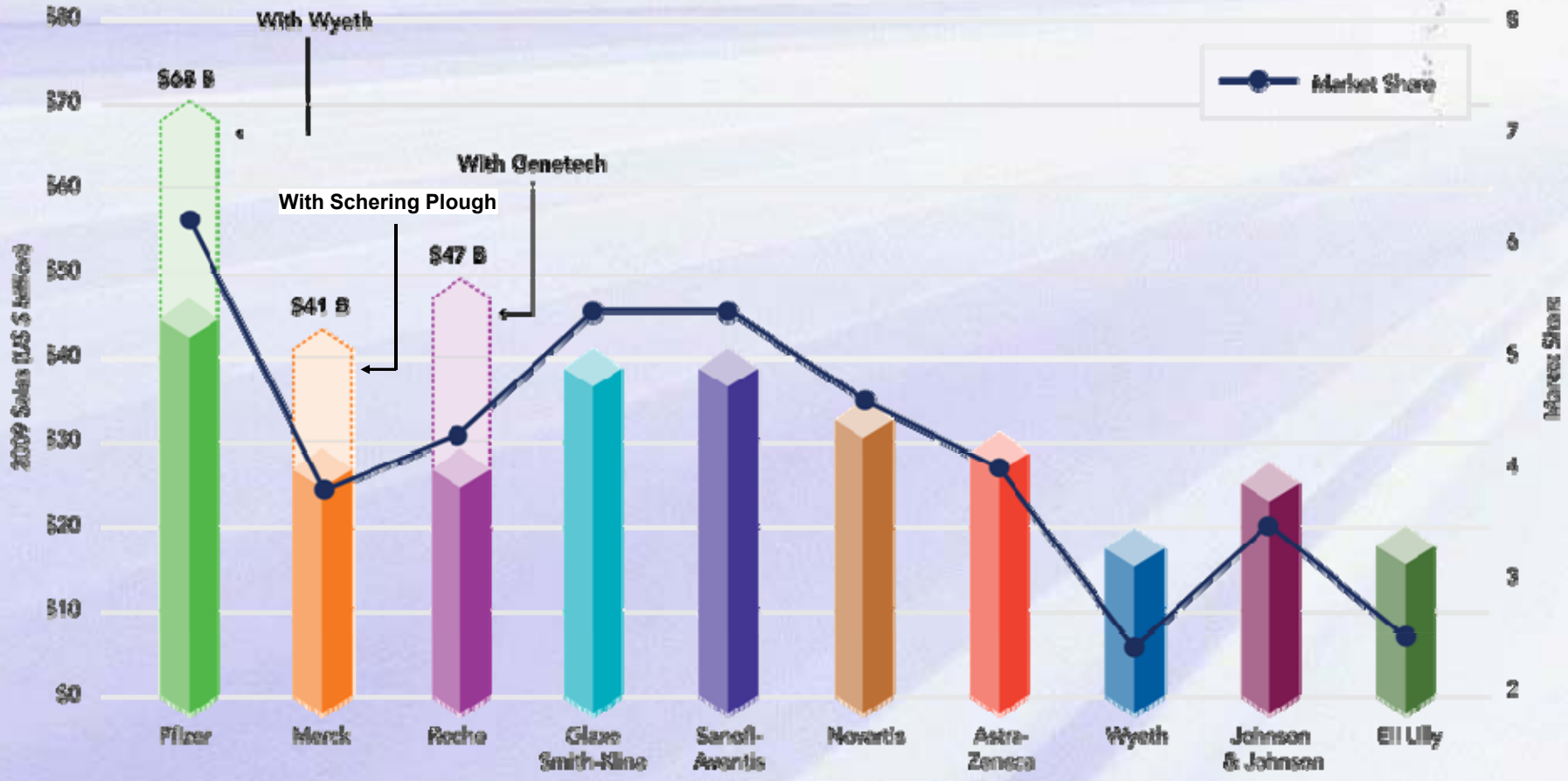


Source: IMS Health

Significant Mergers and Acquisitions (2009)

Pharma/Pharma	*Pfizer/Wyeth $ 68 billion*	*Merck/ Schering Plough $ 41.1 billion*	*Abbott/Solvay $ 6.6 billion*	
Pharma/Specialty	*GlaxoSmithKline/ Stiefel Laboratories $ 3.6 billion*	*Warner Chilcoot/ P&G Pharmaceuticals $ 3.1 billion*	*Dainippon Sumitomo Pharma/Sepracor $ 2.6 billion*	
Pharma/Biotech	*Roche/Genentech $ 46.8 billion*	*Bristol-Myers Squibb/ Medarex $ 2.4 billion*	*J&J/Elan Stake $ 1.4 billion*	*J&J/Cougar Biotechnology $ 1 billion*
	Lundbeck/Ovation Pharmaceuticals $ 900 million	*Endo Pharmaceuticals/ Indevus Pharma $ 637 million*	*Novartis/Corthera $ 620 million*	
Biotech/Biotech	*Gilead/CV Therapeutics $ 1.4 billion*	*Onyx Pharmaceuticals/ Proteolix $ 851 million*	*Celgene/Gloucester Pharmaceuticals $ 640 million*	*Vertex/ViroChem $ 377 million*
Diagnostics	*Beckman Coulter/ Olympus $ 800 million*	*Thermo Fisher Scientific/B.R.A.H.M.S $ 470 million*	*Inverness/Concateno $ 201 million*	*Inverness/ACON Labs $ 200 million*
Medtech	*Abbott/Advanced Medical Optics $ 1.4 billion*	*Danaher/MDS $ 1.1 billion*	*Johnson & Johnson/ Acclarent $ 785 million*	*Medtronic/Core Valve $ 700 million*

Market Share/Pharmaceutical Industry 2009



Significant Partnerings (2009)

Pharma/Biotech	**Roche/PTC Therapeutics** ***$ 1.9 billion***	**AstraZeneca/ Nektar Therapeutics** ***$ 1.5 billion***	**AstraZeneca/Targacept** ***$ 1.2 billion***
	BMS/ZymoGenetics ***$ 1.1 billion***	**Novartis/Incyte** ***$ 1.1 billion***	**Takeda/Amylin** ***$ 1.1 billion***
	BMS/Alder ***$ 1 billion***	**Sanofi-aventis/Exelixis** ***$ 1 billion***	**GSK/Concert** ***$ 1 billion***
	GSK/Chroma Therapeutics ***$ 1 billion***	**Wyeth/Santaris Pharma** ***$ 847 million***	**Sanofi-aventis/Regeneron** ***$ 800 million***
Biotech/Biotech	**Amgen/Cytokinetics** ***$ 650 million***	**Onyx/S*BIO** ***$ 550 million***	**Biogen Idec/Acorda** ***$ 510 million***
	Celgene/GlobeImmune ***$ 500 million***	**Cephalon/ImmuPharma** ***$ 500 million***	**CominatoRx/Clinical Data** ***$ 252 million***

“Pharmadapting”

- Mega-mergers for growth in major markets
- Acquiring biotechs aggressively for pipeline and access to innovation (including tools)
- Expansion of investment in emerging economies
  - Especially BRIC
- Acquiring/building products/services in lower risk, healthcare services

"Pharmadapting" (continued)

- Teva (global generics leader) → therapeutics
- Life Technologies/(Invitrogen/AB1) → diagnostics
- Sanofi-Aventis → Animal health; generics in emerging markets
- Novartis → Eye care (Alcon) – consumer products
- Roche → Genentech for pipeline enhancements
- Merck/Schering Plough → for scale
- Pfizer/Wyeth → biologics (including stem cells) and vaccines
- Pfizer/Strides Arcolab → generics in India
- Pfizer/Protalix Biotherapeutics → rare diseases
- GlaxoSmithKline → Dr. Reddy's (generics)
- Merck KGaA/Millipore → bioequipment/supply/services

…and everyone wants to look like J&J with a diverse business model

Virtual Pharma: New Organizational Models for Leverage of Open-Source Services

- PharmaCommons: integration of rapidly expanding open-source data sets
  - Discovery, toxicology, clinical trials
- Network of web-based turn-key contract services
- China/India/other low cost (R&D, clinical development and manufacturing) sites will dominate
- New role of Big Pharma as integrator to generate value across the entire disease episode spectrum
  - Wellness to terminal care

Source: George Poste/Burrill & Company

Generics –Why is it Booming?

- Major blockbusters coming off patent
- Scale/globalization is key
- Emerging markets growing
- Fewer NCE approvals
- Little growth in primary care markets

Major Pharma Patent Expirations

2009		2010		2011		2012	
Product	Sales ($MM)	Product	Sales ($MM)	Product	Sales ($MM)	Product	Sales ($MM)
Prevacid	3,514	Aricept	1,810	Lipitor	7,493	Singulair	3,327
Topamax	2,302	Cozaar/Hyzaar	1,454	Plavix	4,483	Enbrel	3,274
Lamictal	2,099	Protonix	1,132	Advair	4,321	Diovan	2,848
Valtrex	1,777	Taxotere	1,078	Seroquel	3,772	Lexapro	2,617
Flomax	1,485	Arimidex	729	Actos	2,957	Lovenox	2,539
Imitrex	1,312	Gemzar	722	Zyprexa	2,670	Viagra	1,046
Adderall	1,309	Xalatan	544	Levaquin	1,779	Geodon	989
Keppra	1,247	NovoSeven	497	Avapro	843	Detrol	905
CellCept	968	Combivir	407	Caduet	485	Provigil	867
AmbienCR	899	Mirapex	402	Femara	447	Zometa	796
Suboxone	468	CoregCR	311	Xeloda	420	Avandia	676
All Others	2,335	All Others	3,260	All Others	2,366	All Others	4,584
Totals	$19,715	Totals	$12,346	Totals	$32,036	Totals	$24,468

Source: Kenneth Kaitin

Biologics Prompt an Exclusivity Debate

Drug	Companies	Uses	Approved	Key Patent Expirations	U.S. Sales
Epogen/Procrit	Amgen/Johnson & Johnson	Anemia	1989	2012-2015	$3.8B
Enbrel	Amgen, Wyeth	Rheumatoid arthritis, psoriasis, others	1998	2012	$3.4B
Neupogen/ Neulasta	Amgen	Prevent infections during chemotherapy	1991/2002	2013/2015	$3.4B
Avastin	Genentech	Cancer	2004	2017/2019	$2.7B
Rituxan	Genentech, Biogen Idec	Cancer, rheumatoid arthritis	1997	2014/2016	$2.6B
Avonex	Biogen Idec	Multiple sclerosis	1996	2012	$1.3B

Source: company reports, Deutsche Bank

World Market for Health and Wellness is Expanding

- China and India have large populations, growing wealth and middle class and increased demand for high quality healthcare
  - Additional growth markets: South Korea, Middle East, Latin America, South Africa, Russia, Eastern Europe
- Burden of disease is changing in developed and developing countries: chronic diseases (cardiovascular, diabetes, cancer, CNS et al.) on the rise everywhere
- Aging populations around the world
- National healthcare and private payor/employer models are converging and all facing issues of affordability, quality and equal access
  - Consumers becoming an important factor in the healthcare equation

2020 – Globalization / Changing the environment too

- Markets - demand increases in Asia & developing world
- R&D migrates to Asia
- Regulations – International agencies collaborate
- Information – healthcare payors share data on performance (clinical & financial)
- Diseases know no boundaries
- Every company is global from day one!

Medical Tourism on the Rise

- Market for medical tourism in 2008 about $60B, expected to grow to over $100B by 2010
- Originally cosmetic/elective procedures, now: CABG, heart valve replacement, orthopedic including hip/knee replacement, cancer, transplant, etc.
- 750,000 Americans traveled overseas for surgery in 2008, expected to be 6 million by 2010
- Cost including travel 2-3x lower than in US
- Patient financing programs becoming available, some insurers providing incentives
- Magazines, associations, conferences

Price Shopping for Procedures

	Hip Replacement	Heart Valve Replacement	Hysterectomy
United States 	$43,000	$160,000	$20,000
India 	$5,000 to $7,100	$9,000	$2,300 to $6,000
Thailand 	$12,000	$10,000	$4,500

Source: San Francisco Chronicle Magazine, January 4, 2009

Medical Tourism Growth Drivers

- **Costa Rica**
  - One in five visitors is a medical tourist
- **India**
  - Government investing $3.6 Billion in medical tourism infrastructure.
  - McKinsey estimates Indian medical tourism at $2.3B by 2012.
- **Korea**
  - Big focus: "New growth empire"
- **Mexico**
  - StarMedica hospital groups built 7 hospitals in last 5 years;
  - AmeriMed opening 10 new hospitals by 2012;
  - Grupo Angeles (largest private hospital group in Mexico) spending $700 million to build 15 hospitals in the next 3 years
- **Singapore**
  - More internationally accredited facilities than any other country.
- **Thailand**
  - One Bangkok hospital (Bumrungrad) served over 500,000 health travelers last year.

Source: Health Travel Guides

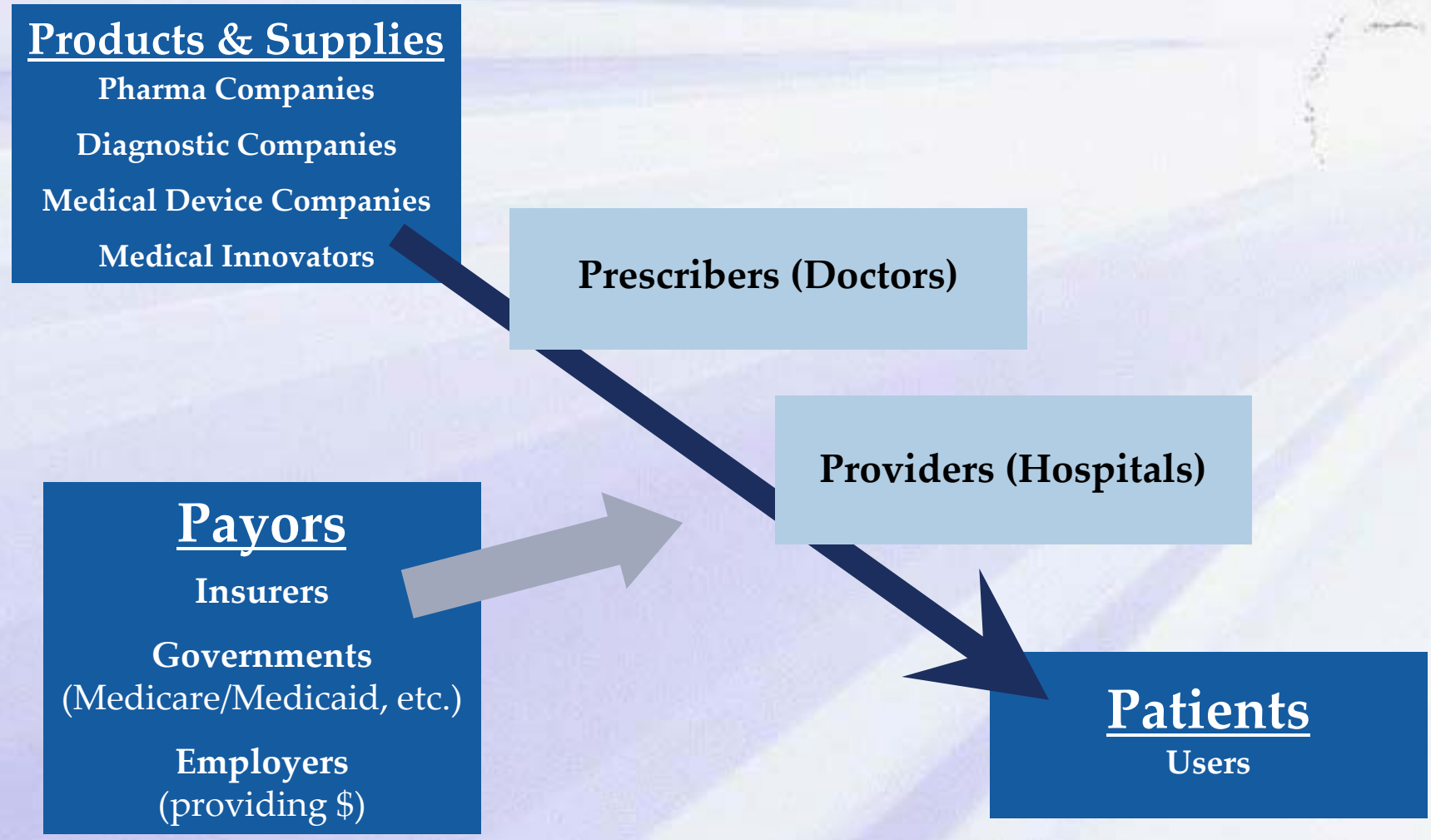
Major Government Initiatives in Biotechnology

- Australia/New Zealand
- Canada
- China
- Eastern Europe/Russia
- EU: Germany, Italy, Scandinavia, Spain, Switzerland, UK
- India
- Israel
- Japan
- Korea
- Latin America (esp. Brazil/Chile/Argentina)
- Malaysia
- Singapore
- GCC: UAE (Abu Dhabi/Dubai), Qatar, Bahrain, Kuwait, and Oman

Regulatory News –FDA Developments (2009)

- FDA approves first therapeutic protein produced in genetically engineered goals
- Margaret "Peggy" Hamburg appointed as Head of FDA
- Genzyme shuts down its US plant after virus developed in one of bioreactors
- FDA delays start of Geron's first human stem cell therapy study
- FDA approves 4 HINI vaccines (Sanofi-Aventis, CSI, MedImmune and Novartis). In November, fifth approved (ID Biomedical, Quebec)
- Senate panel votes to bar pharmaceutical companies from paying generic drug makers to delay bringing their cheaper drugs to market

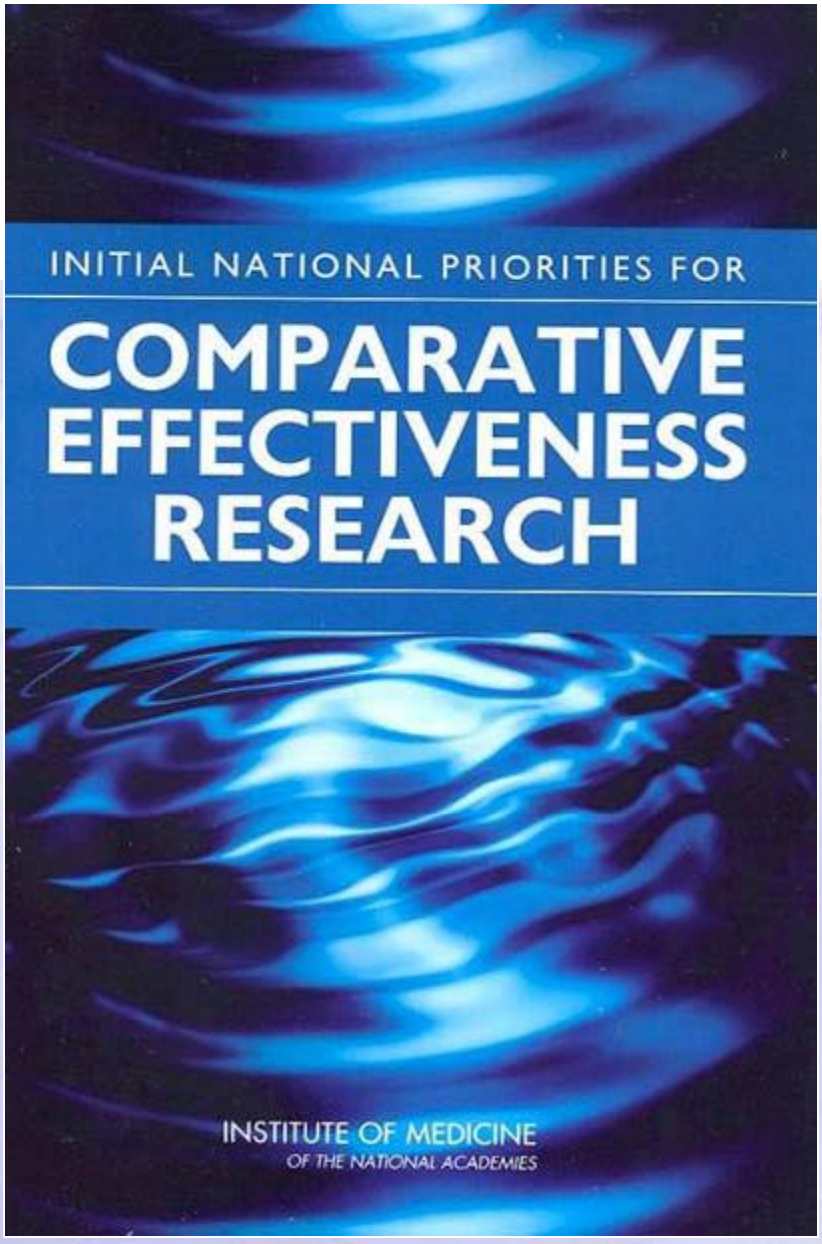
… and who is the payor?



Patient Access to Selected Biologics Restricted or Denied by NICE

Drug	Indication	Company	Patient Access
Tysabri (natalizumab)	MS	Biogen-Idec/Elan	Restricted
Humira (adalimumab)	Psoriatic arthritis	Abbott	Restricted
Rituxan/MabThera (rituximab)	RA	Genentech/Biogen-Idec	Restricted
Fludara (fludarabine)	CLL	Bayer	Denied
Gemzar (gemcitabine)	Breast cancer	Lilly	Restricted
Avastin (bevacizumab)	Colorectal cancer	Genentech	Denied
Erbitux (cetuximab)	Colorectal cancer	ImClone Systems	Denied

Source: BioCentury, 2008



Source: George Poste

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

MAY 7, 2009

Does Comparative-Effectiveness Research Threaten Personalized Medicine?

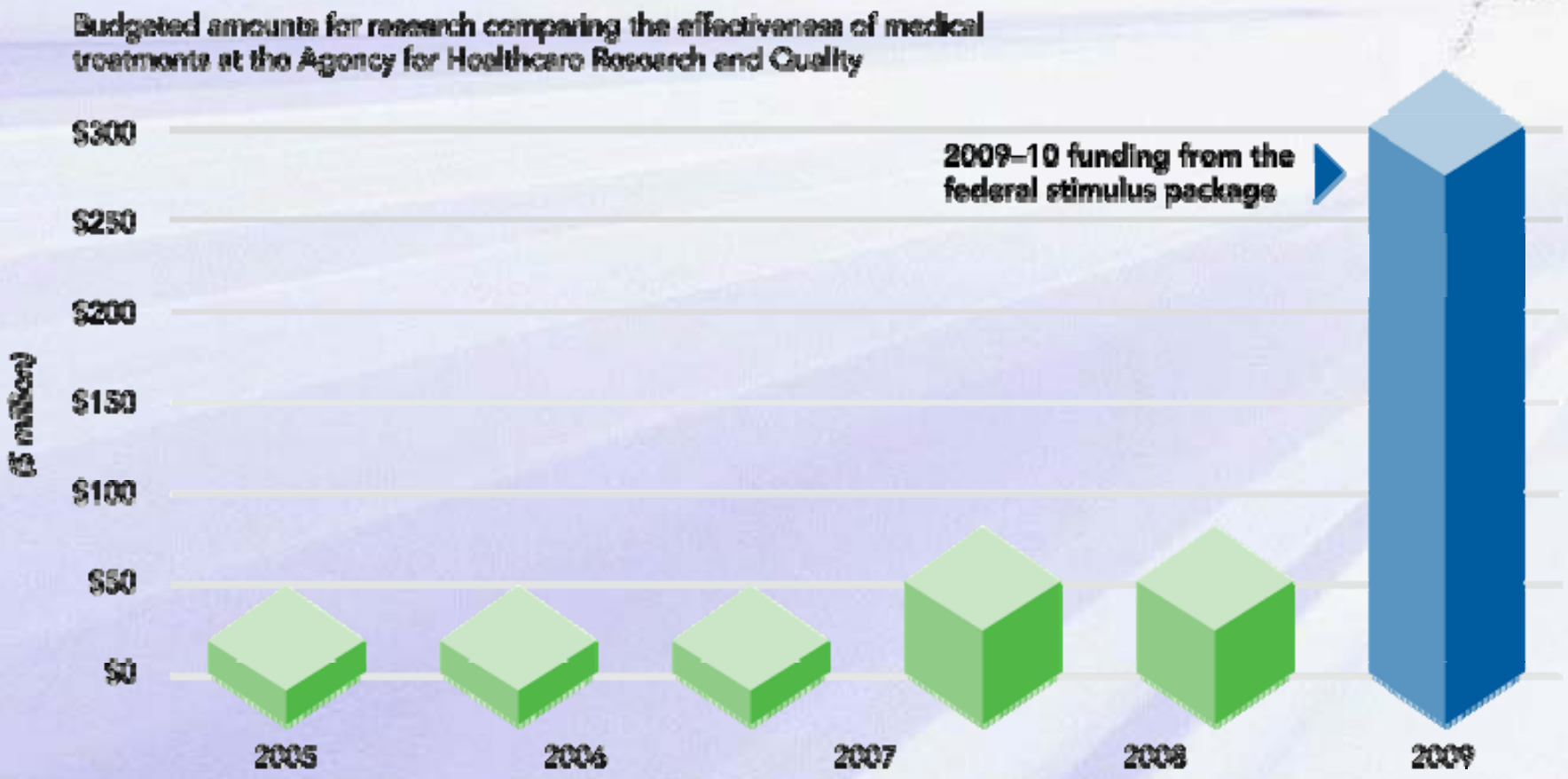
Alan M. Garber, M.D., Ph.D., and Sean R. Tunis, M.D.

The American Reinvestment and Recovery Act gives comparative-effectiveness research (CER) a large boost in funding over the next 2 years. Despite a consensus that better information about the relative effectiveness of different medical interventions is needed to improve the quality and value of care, some view CER with skepticism. Recently, the Partnership to Improve Patient Care, a coalition of 36 industry, patient-advocacy, and clinician organizations, raised concerns that CER will not take adequate account of individual patient differences and may impede the development and adoption of improvements in medical care and "stymie progress in personalized medicine."[1]

The controversy stems in part from a perceived contradiction between the concepts of CER and personalized medicine. In CER, groups of patients are analyzed to compare the effectiveness of alternative medical strategies, with the intent of informing clinical decisions and policies affecting health care. The very name "personalized medicine" suggests an approach to care that is based on individuals rather than groups. The term has been used to describe the consideration of characteristics such as age, coexisting conditions, preferences, and beliefs in crafting an individual management strategy; the use of advanced individual genomic information in choosing an expensive biologic agent; and the development of therapies biologically tailored to patient needs, such as customized monoclonal antibodies and vaccines. But far from impeding personalized medicine, CER offers a way to hasten the discovery of the best approaches to personalization, providing more and better information with which to craft a management strategy for each individual patient.

Perhaps the most prominent examples of modern personalized medicine are genomic tests designed to guide treatment choices (see table). Some are widely recognized as useful, such as testing for human epidermal growth factor receptor type 2 (HER2, also referred to as HER2/neu) to select patients with breast cancer who will benefit from trastuzumab and of testing for the *KRAS* mutation to determine who is likely to benefit from therapies inhibiting the epidermal growth factor receptor. Genomic medicine, however, has had little impact to date in most areas of care — a fact that some critics blame on payers, claiming that they impose

Comparative Effectiveness is real…



Source: WSJ, April 14, 2009

Out-sourcing / Off-shoring

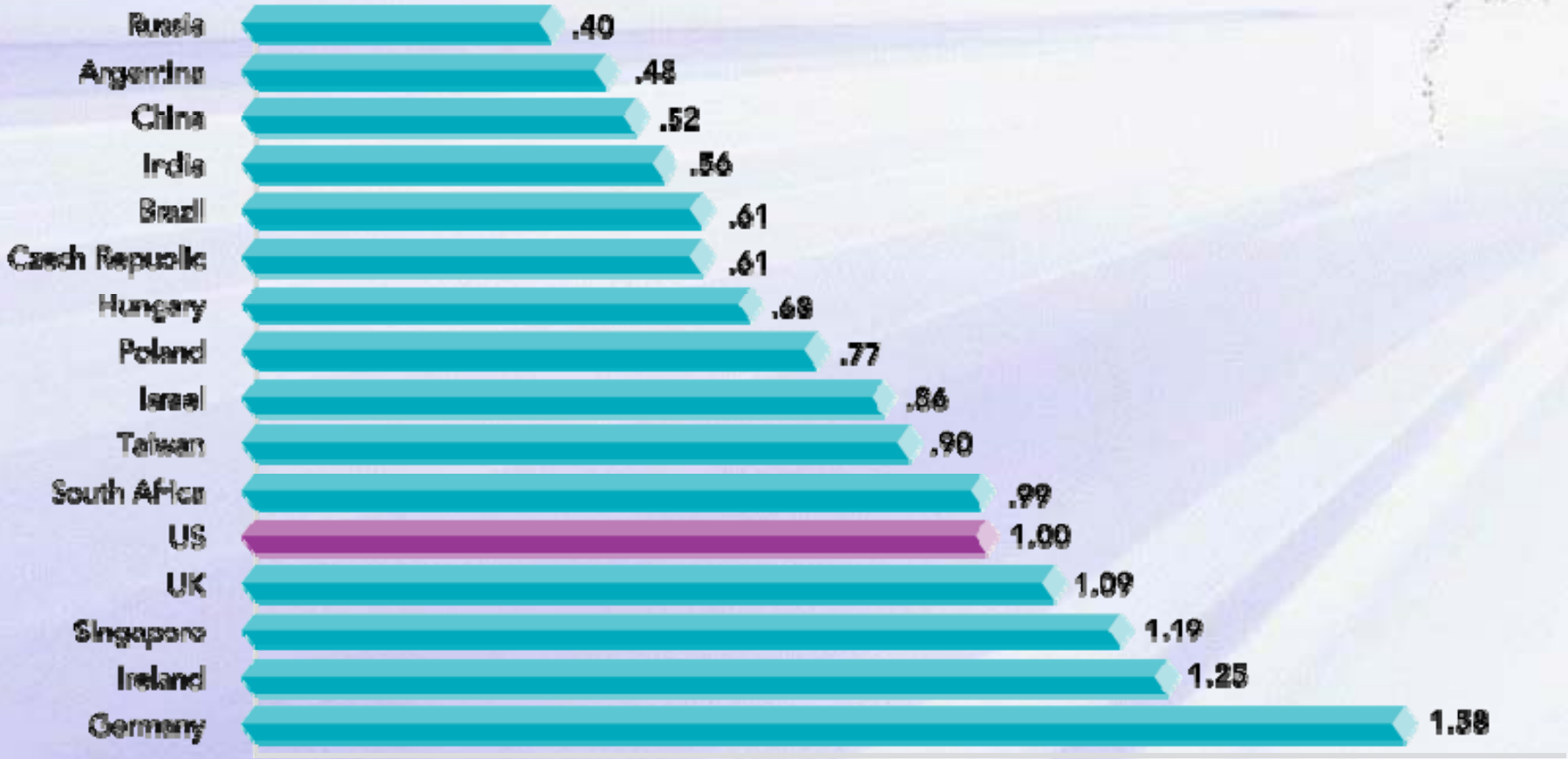
- Out-sourcing
  - Subcontracting to a third-party company
- Off-shoring
  - Relocating business processes from one country to another

Is it happening?

YES!

(Key example: Eli Lilly – Chorus model)

Overall Indexed Clinical Trial Costs



Source: SalaryExpert.com; WDI Database; Economist Intelligence Unit; CBRE Global Markets Rent 2005; A.T. Kearney analysis, Aug 2005; Clinical Trial Offshoring

Healthcare – It's changed/changing…

- Technology
- Markets
- Regulatory
- Reimbursement/payment
- Delivery
- Patients

BioGreentech

- Enhanced productivity of plants with minimal impact on the environment
- Modification of plants and other organisms to enhance value as sources food, feed, fiber and feedstocks
- Conversion of biomass into feedstocks for renewable fuels and products
- Fermentation and chemistries for the production of chemicals, materials from biomass derived feedstocks
- Carbon sequestration

FOOD *vs* FUEL

Not as simple as it sounds

The Press had a Field Day

Use of Land for Food and Fuel will be a long term issue

Complex factors influence food prices

- Historic low-cost food policies based on crop subsidies
- Commodity & Food prices linked to oil prices
- Disruptive pace of change
- Limited arable land, Shortage of water
- Hedge funds speculating in the Commodity Markets
- Demand from China and India and global economic growth
- Climate change leading to more extreme weather patterns
- Wide spread restrictions on export of food grains
- Historically underfunded research in agriculture and food
- **And reallocation to biofuels**

- Recent CBO report finds that only 10 – 15% of increased food price was due to corn ethanol production during 2007 - 8

Conditions Changed in Late 2008

Corn Futures

Soybean Futures

Ethanol

Sugar

Canola

… and Have Largely Remained Depressed

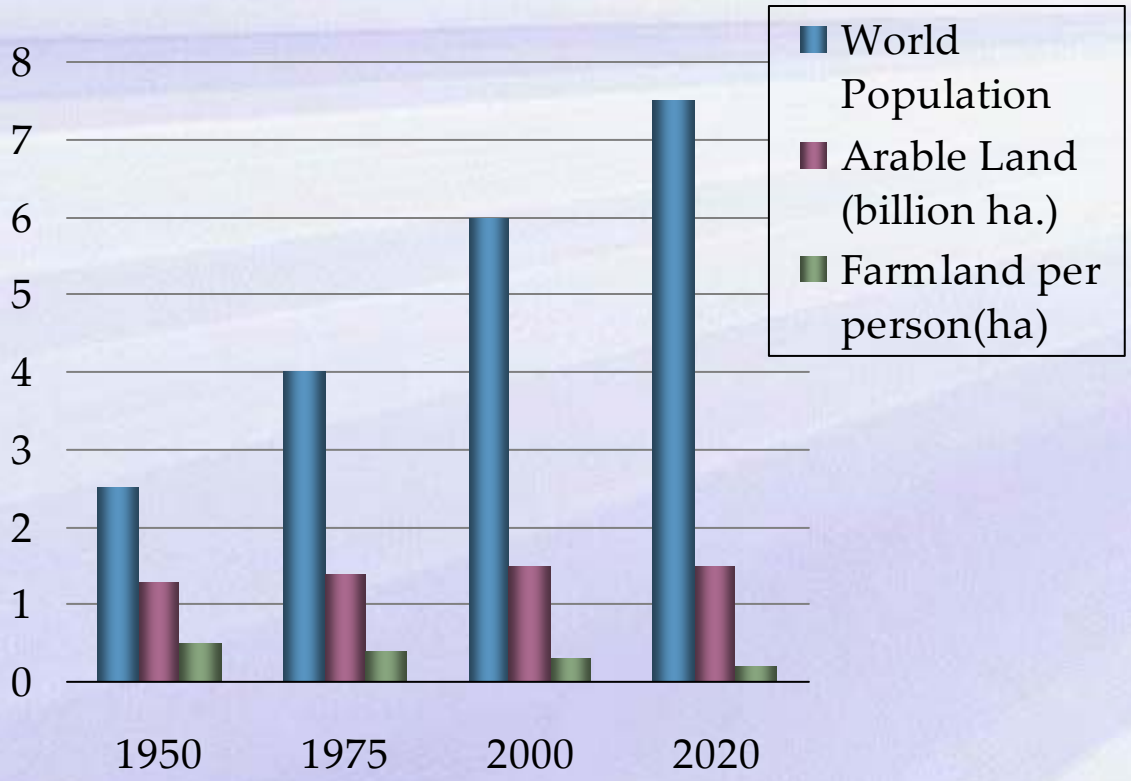
Corn Futures

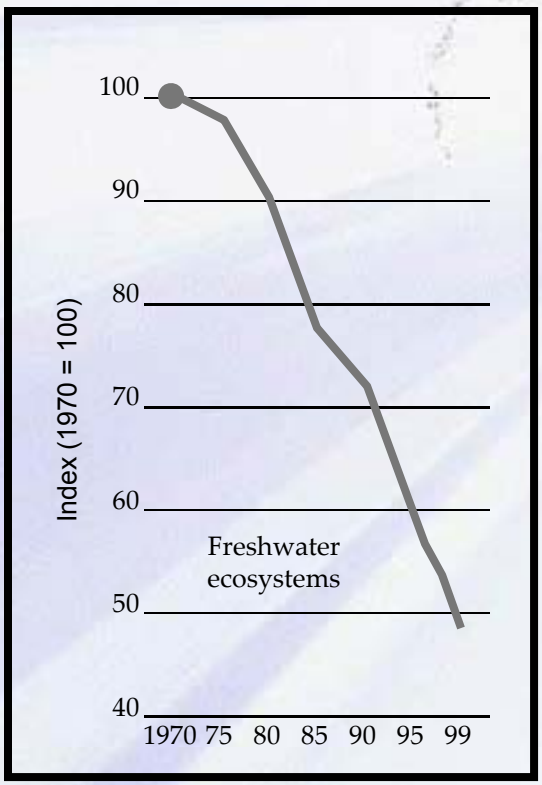
Soybean Futures

Ethanol

Canola

The Demands for Agriculture Stay the Same





More food on less land with half the water

Source: United Nations, 1999

The future of Ag inputs is at the intersection of breeding and trait technologies

Biotech

Agrobacterium

Gene Gun

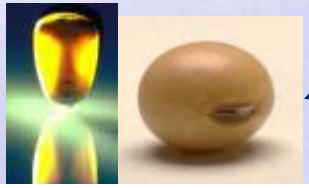
Breeding

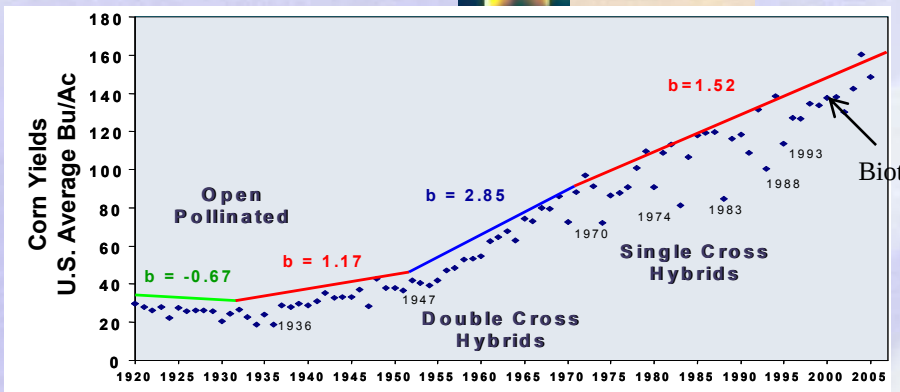
- ↑ productivity (complex)
- ↑ reliability
- ↑ quality
- Integration of native and biotech traits

Seed is the carrier of genetic information

Traits

- Pest protection
- Stress alleviation
- Superior nutrient use
- Enhanced nutrient density
- Elevated safety
- Processor friendly





Chemistry

- Pest control
- Nutrition
- Growth regulators

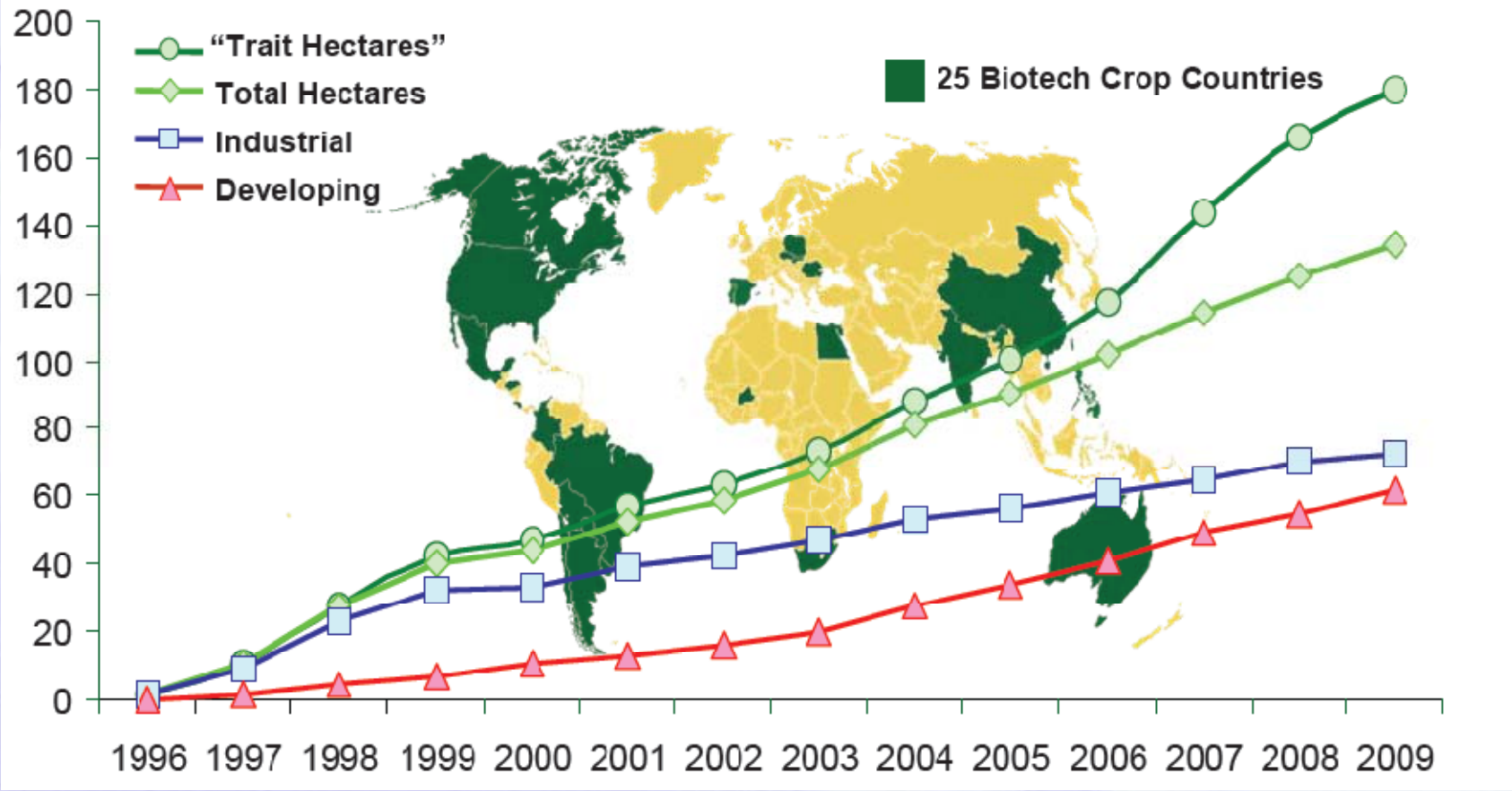
Nearly 150 M Acres Not in Corn Cultivation !

Near to Market Traits

- Increased yield
- Drought tolerance and water use efficiency
- Nutrient use efficiency
- Increased spectrum of pest and disease resistance
- Gene stacking technologies that will reduce cost and time to market of complex trait combinations

Global Area of Biotech Crops

Million Hectares (1996 to 2009)

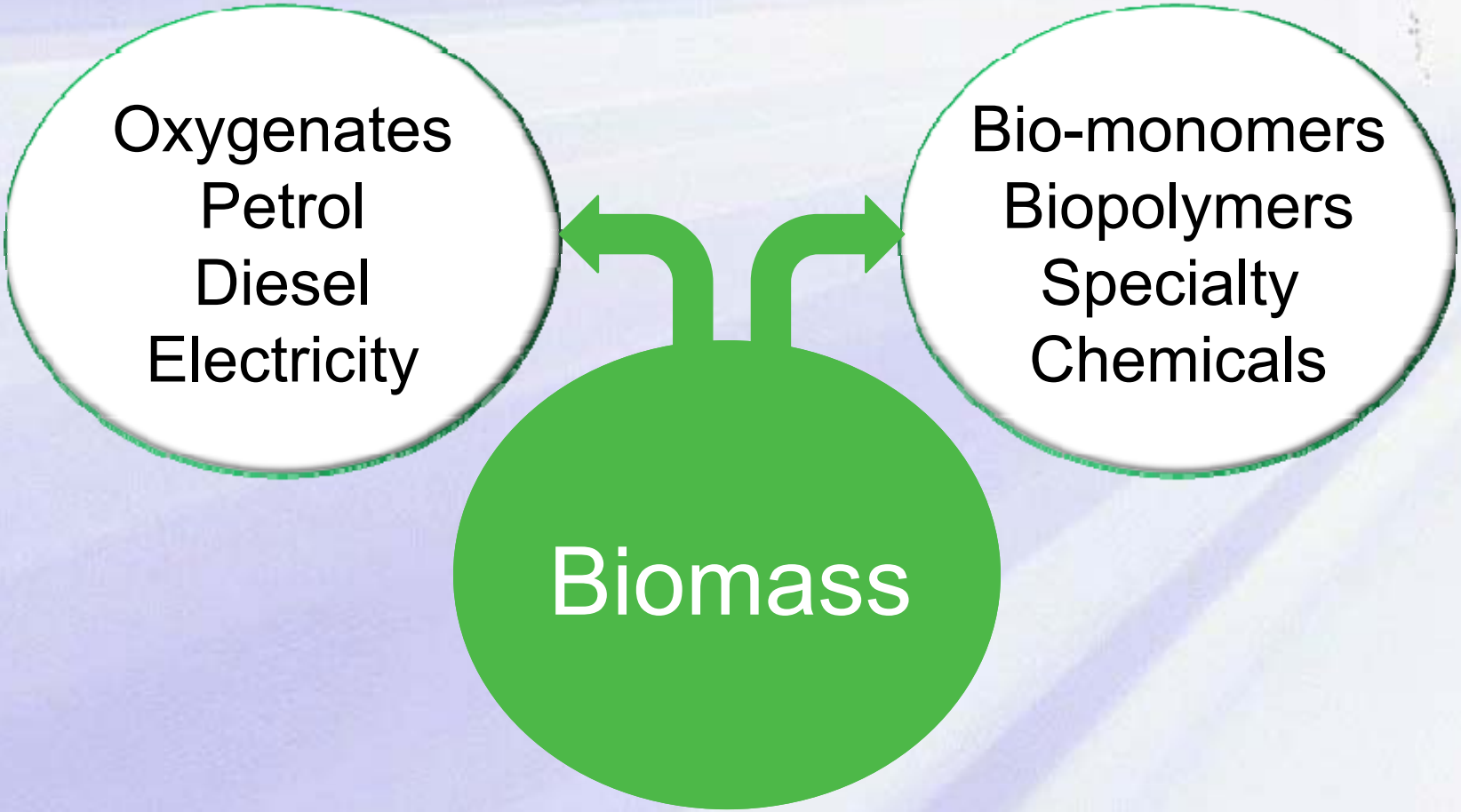


A record 14 million farmers, in 25 countries, planted 134 million hectares (330 million acres) in 2009, a sustained increase of 7% or 9 million hectares (22 million acres) over 2008.

Source: Clive James, 2009

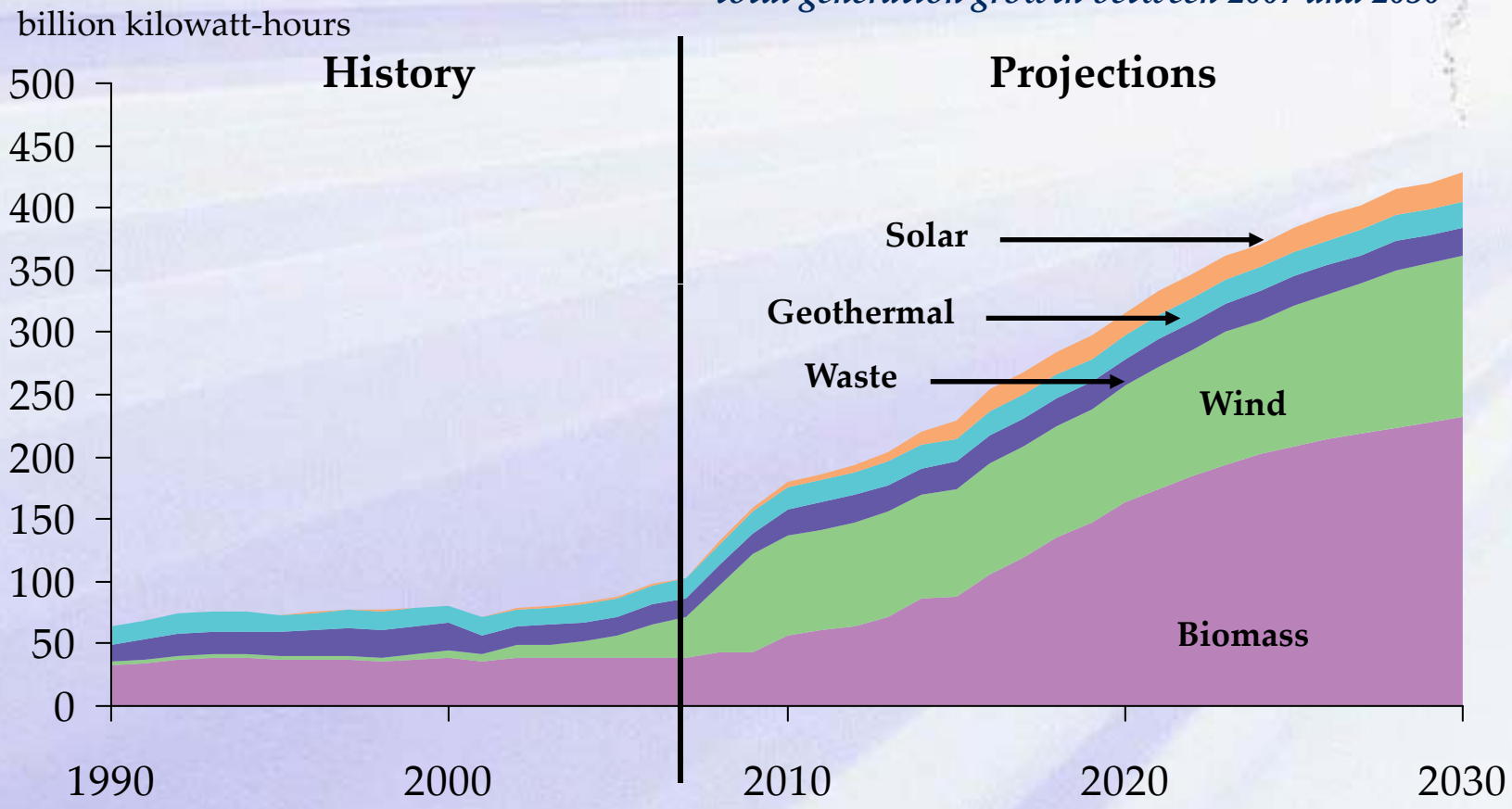
Industrial Biotech offers solutions for energy and material needs

The opportunity – multibillion dollars, rural economic growth



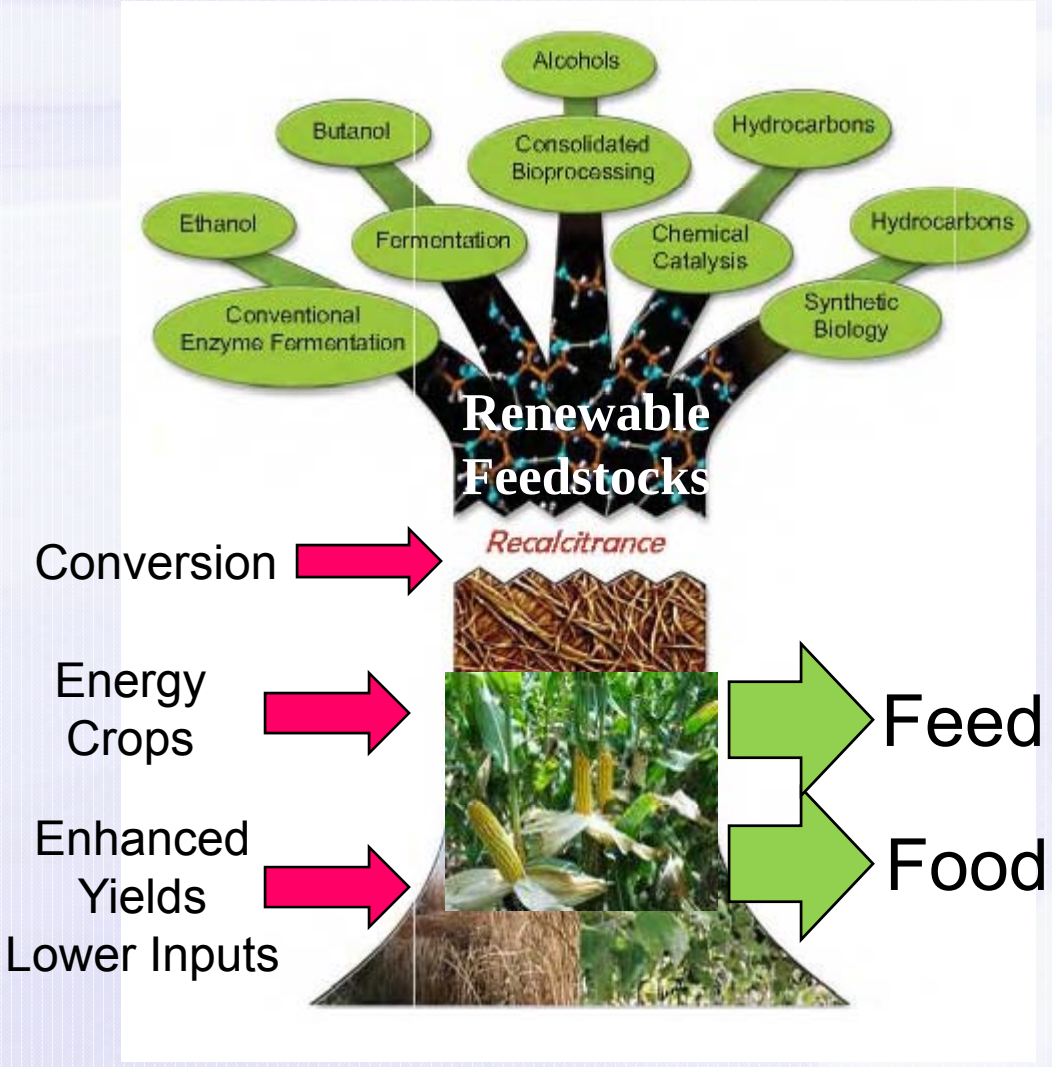
Future of Non-hydro Energy Generation is Biomass

Nonhydropower renewable power meets 33% of total generation growth between 2007 and 2030



EIA Annual Energy Outlook 2009 Reference Case Presentation -- December 17, 2008

The Biomass Feed Stock is Key



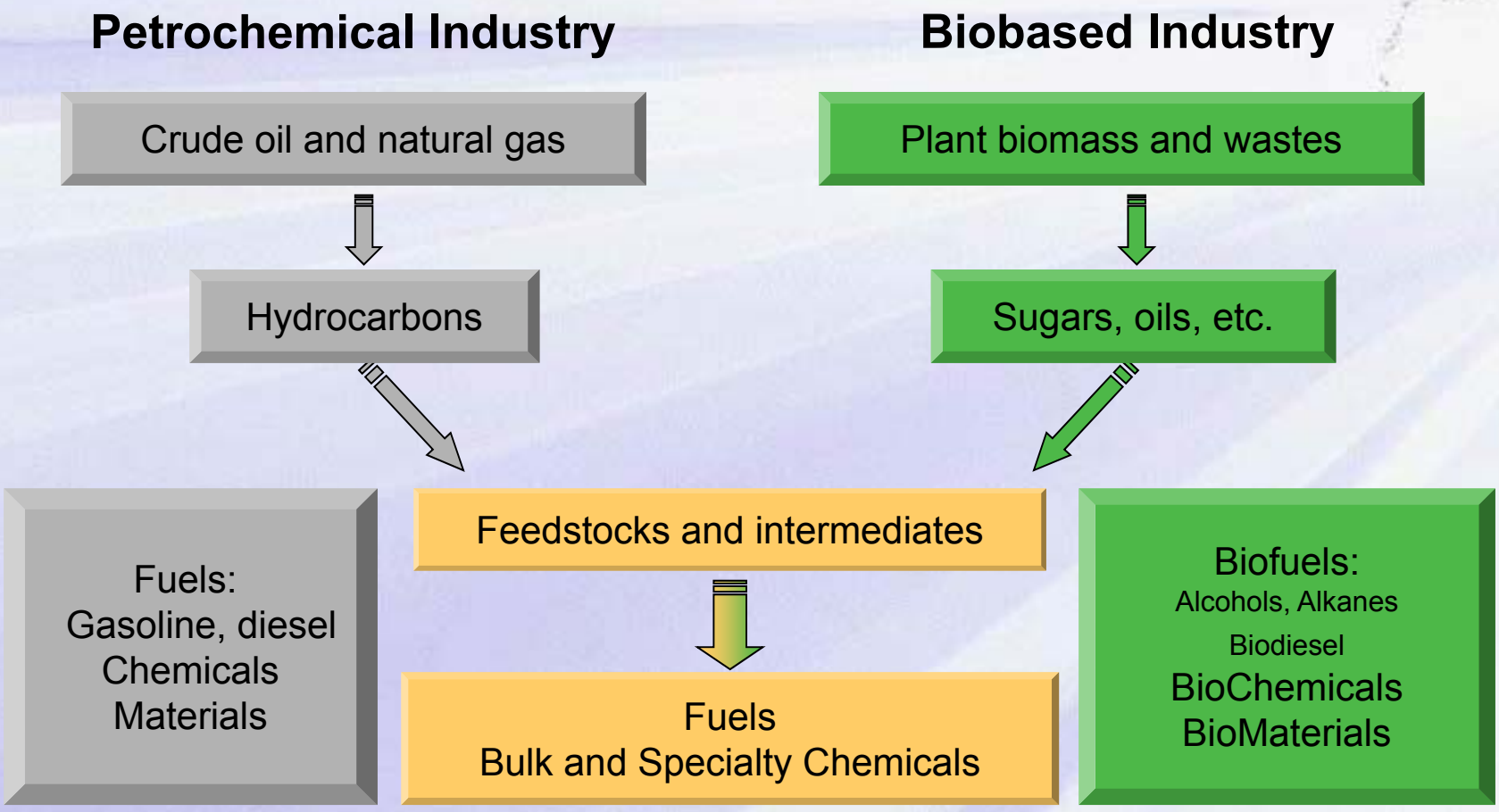
Investment Opportunities

- Increased productivity
- New Energy Crops
- Conversion technologies
- Fermentation Products
- Carbon sequestration
- Technology integration & adaption

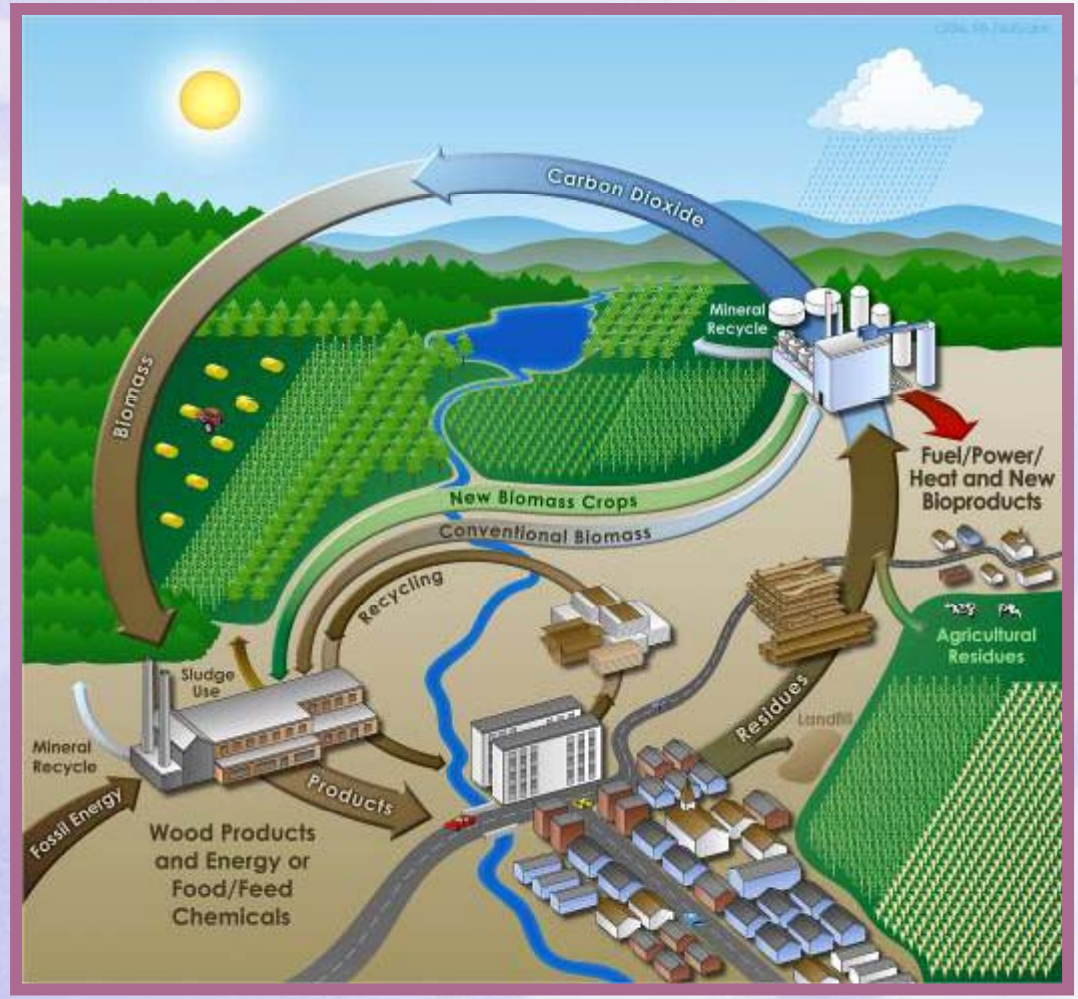
Obama and Government Leaders Worldwide Driving a Green Economy

- Increased research funding
- Incentives for use of renewables
- Subsidies
- Loan guarantees
- Conducive policies and regulations

A Bio-Refinery Industry is Emerging

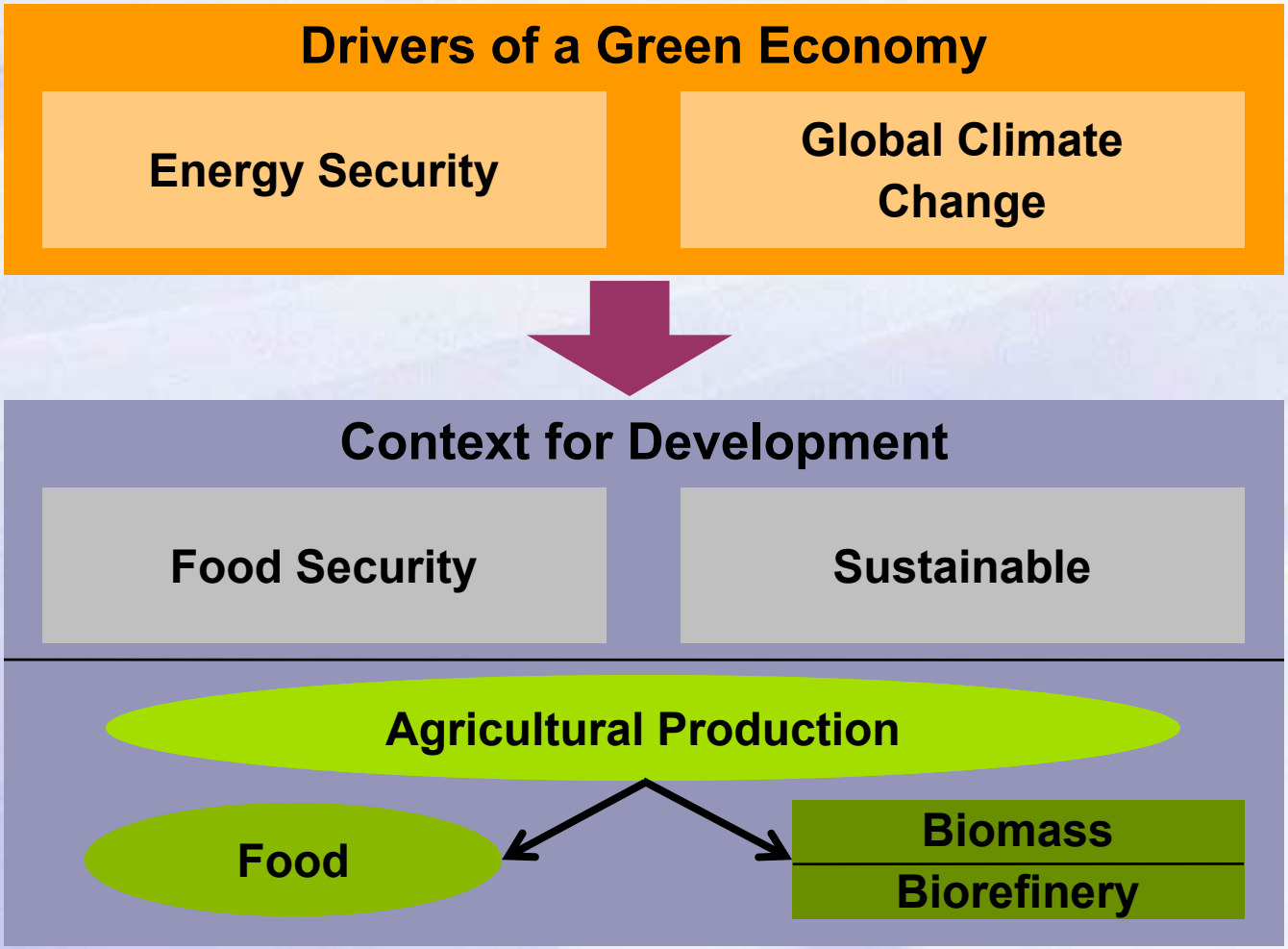


A Vision of the Future



http://genomicsgtl.energy.gov/biofuels/index.shtml

The Future Is Bright But Must Be Entered Carefully



Message

- Industrial biotechnology has huge potential, economically socially and environmentally, to contribute to a more sustainable world
- The industry is poised for growth
- Biofuels spurred interest in and growth of Industrial Biotech
- Biofuels got hijacked by political & environmental interests
- Urgent need to get back on track with a biofuels strategy and policy
- Obama administration very supportive

Building a business has risks: Biotech/Rx/Dx/Device Risks

- Technology
  - IP and FTO
  - Proof of concept
- Clinical/regulatory
  - Regulatory pathway (consider alternatives)
  - Non-US regulatory pathways
  - Focus on areas of unmet medical need
- Reimbursement/pricing
  - Understand payor and payor priorities (CMS, other governments, insurance companies, self pay, other)
- Financial
  - Construct capital efficient business models to achieve valuation step-ups
  - Tranche financing rounds to specific milestones and limit financial exposure
  - Syndicate investors
  - Creativity essential
- Execution
  - What will cause this to fail?
  - What is necessary to succeed?

"Bio-adaption" – The Secret for Success

- Creative financing for fuel to grow – increasingly from non-traditional sources (disease advocacy groups early, foreign markets late)
- Big biocompanies "selling" to global pharma
- Small companies focusing on more narrow market areas
- Increased risk sharing in partnering – big companies buying "options"
- VIDDOs- virtually integrated drug discovery development organizations
- Reducing FDA-centric risk, looking for pathways to market globally

Challenges Ahead

- Dueling forces/healthcare reform II, the real reform…
  - Increasing healthcare demand
  - Slowing growth of healthcare expenditure growth
- Innovation accelerating vs. market adoption
- Changing healthcare delivery venues
- Growth in emerging market exceeding growth in traditional markets (generics/brands vs. IP protected Rx/Dx)
- Comparative effectiveness – who will pay for studies?

Challenges Ahead (continued)

- Ethics (mistakes vs. fraud)
  - off label use
  - improper medicine changes
  - conflicts of interest
- De-linkage between users (patients), deliverers (doctors, hospitals, caregivers), and payors (government, insurance, managed care)
- Moving from a sickness to wellness system
- Pharma business changing…emergence of new business, new business models

My Predictions for 2010

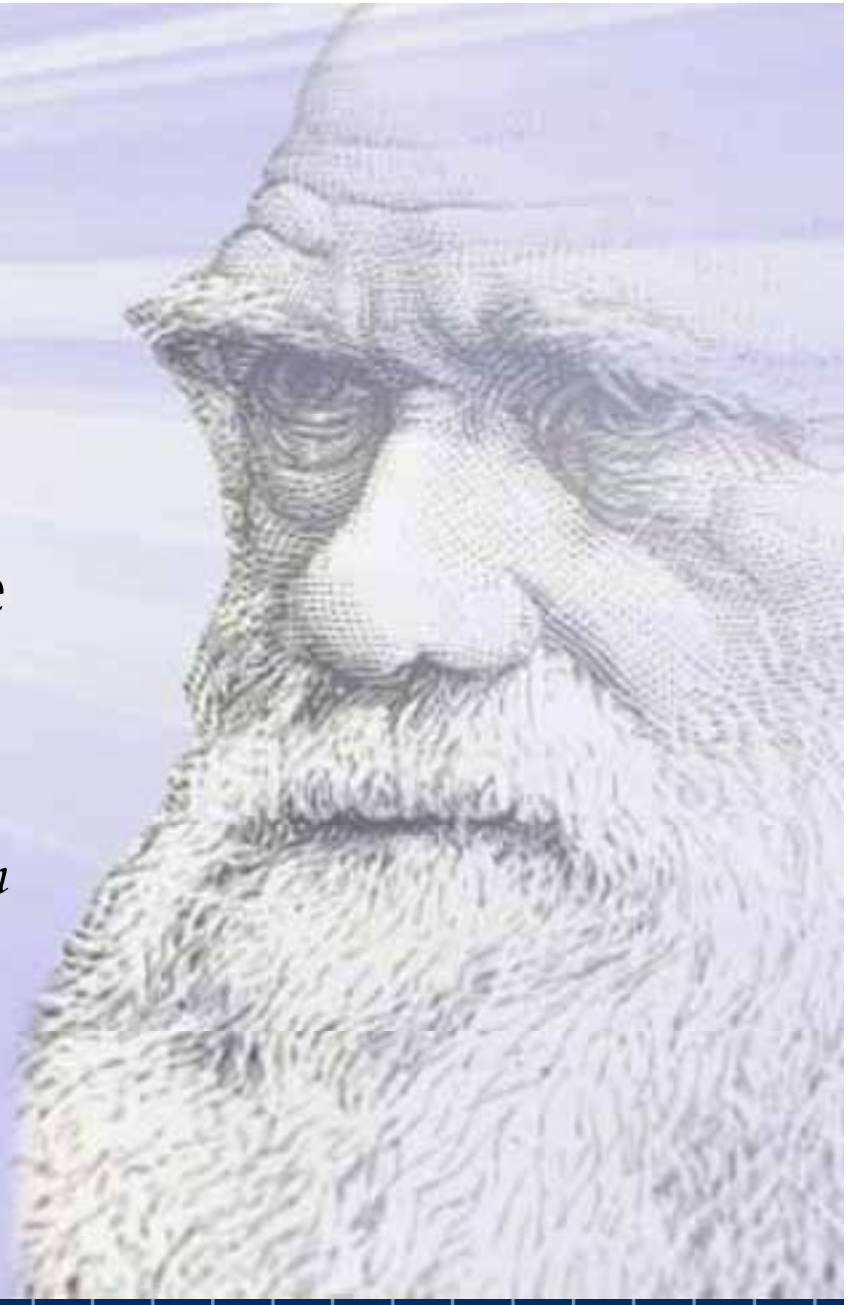
- Some elements of healthcare reform will pass – mixed impact on biotech industry
- Continued impressive developments in science/technology
  - More genomes sequenced, human genome $1,000
  - Regenerative medicines/stem cells – real progress
  - Personalized, predictive, preventative medicine progress
  - Antibodies vaccines will be big
- Regulatory world more complex, more international
  - Pharmacovigilence
  - Cost effectiveness
- Manufacturing/QC issues (Genzyme)
- Growth of generics/biosimilars

My Predictions for 2010… (continued)

- Dramatic changes in pricing/reimbursement on Rx side; Dx generating increased value
- Global markets increasingly important
  - China/India/Brazil (and all of Latin America), MENA
- Bio pharma consolidation continues evolution from vertically integrated to more virtually integrated; more distribution focused, (more like Johnson & Johnson, less like Merck!)
- Biogreentech is hot
- Funding world improving:
  - Capital available, but expensive and demand overwhelms supply of capital
  - Increased globalness: arbitrage value difference

"It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to change"

Charles Darwin



Adapt = Success

Biotech 2010 Life Sciences: Adapting For Success

It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to change

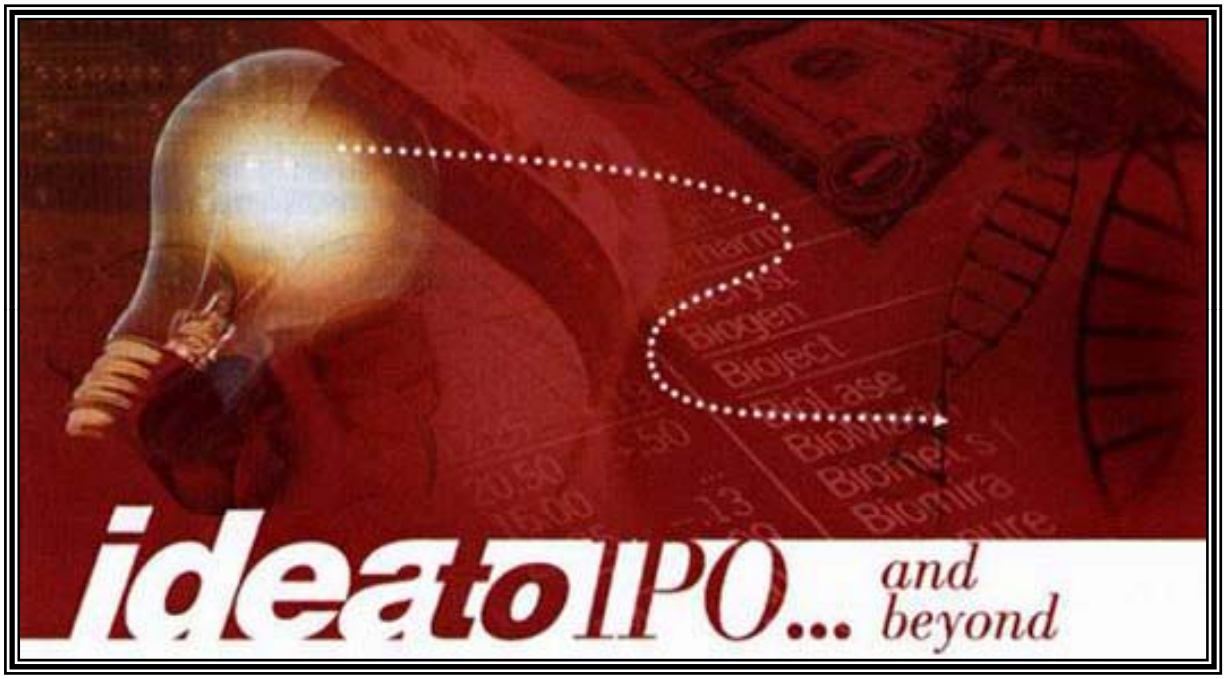
—Charles Darwin

University of Illinois at Urbana-Champaign

March 12, 2010

G. Steven Burrill

Chief Executive Officer
Burrill & Company


idea to IPO... and beyond

Entrepreneurial Experience

Bio – G. Steven Burrill

- Founder and CEO of Burrill & Company
- One of the original architects of the industry and one of its most avid and sustained developers
- Spent 28 years with Ernst & Young
- Received the 2008 BayBio Pantheon DiNA Lifetime Achievement Award for worldwide biotech leadership
- Awarded the 2008 Alan Cranston Living Legend Award by the Alliance for Aging Research
- 2008 University of Minnesota commencement speaker
- Recognized as the biotech investment visionary by prestigious Scientific American. magazine (The Scientific American 50, December 2002 issue honoring the top 50 science and technology leaders worldwide)
- Recognized for the unique contribution that insight, energy and leadership have made to the biotechnology industry at the 2002 American Liver Foundation "Salute to Excellence" award
- Awarded the 1995 Service Award by the Biotechnology Industry Organization (BIO) for outstanding leadership in the Biotech industry
- Board Chairman of Pharmasset (NASDAQ: VRUS), and BioImagene
- Board of Directors member of Catalyst Biosciences, DepoMed (NASDAQ: DEPO), Ikano Therapeutics, Proteogenix, Proventys, Targacept (NASDAQ:TRGT), and XDx
- Built and managed Ernst & Young's biotechnology/life sciences and high tech/manufacturing business to a $2.2 billion business (1/3 EY's revenues), 'retired' after 28 years (12/31/93), involved with formation of Genentech, Amgen, Chiron (Cetus), Alza and hundreds of other biotechs worldwide
- 43 years advising high tech/high growth entities
- Biotechnology industry luminary
- Author of annual report on industry (24 years)

My Career
Drivers and Highlights

The Ernst & Young Days

- 1966 Started at Arthur Young
  (Over forty years ago) as a "rookie" auditor
- 1976/1977 National Office – resident
- 1977 youngest partner in Arthur Young
- 1980's Arthur Young's High Tech "Guru"; National Chair - Manufacturing/High Tech Industry Group
- 1989 Merger, creating Ernst & Young (Mergers between Ernst & Whinney and Arthur Young)
- Chairman International High Tech/ Manufacturing Industry Group and managed $2.5 Billion in revenue at Ernst & Young (1/3 of Firms + 6 billion in revenue)
- December 31st 1993 Left E&Y (28 years) to be a "Professional Director" and start Burrill & Company

What made my Ernst & Young career successful?

- Passion/ interest
- Industry knowledge vs. technical knowledge
- Hard work, tenacity
- Out-the-box thinking
- Do things differently
- Partnership
- Focus/ capacity to do right things
- Pricing model which worked

The Evolution of Burrill & Company

- Founded Burrill & Company on January 1st, 1994
- Burrill 1.0 (1994-1997) … (Burrill & Craves until 1996)
  - "Rent a Director" business model
  - Creation of M&A/ partnering business
  - Media - business inception (conferences/ publications)

The Evolution of Burrill & Company (continued)

- Burrill 2.0 (1998 – 2000)
  - Inception of Venture Capital Business through Investment of $300 Million from Strategic Investors *(Bayer/ Nestle/ IBM/ Mitsubishi/ Unilever/ Chiron/ Aventis etc)*
- Burrill 3.0 (2002 – 2005)
  - Raised 1st Institutional funded venture Fund ($211million) - BLSCF *(NC Retirement System/ Scottish Widows/ Northwestern Mutual Life, SamPension et al)*

The Evolution of Burrill & Company (continued)

- Burrill 4.0 (2006 – 2009)
  - Expansion of Venture Capital Business Internationally
    - Malaysia LSC Fund $150m
    - BLSCF III $223m
  - Converted Merchant Banking business into "broker dealer"
- Burrill 5.0 (2010→)
  - Expanding business to include
    - Private Equity business
    - Structured debts
    - Greater international reach/global arbitage (Europe, Middle East, Eastern Europe, Latin America, Korea/Pan Asia

Burrill & Company - Overview

- 100% focused on life sciences
- 50 full-time professionals with a combination of industry and financial backgrounds
- 35 world class advisors / 20 large corporate partners
- Venture Capital group has approximately $1 billion under management
- Relationships with other premier venture capitalists
- Close relationships with hundreds of life science and pharmaceutical companies
- World class conferences and events
  - The Burrill Consumer Digital Health Meeting
  - The India Life Sciences Partnering Meeting
  - The Pan Asia Life Sciences Partnering Meeting
  - The Burrill Latin America Life Science Conference
  - The Biotech Meeting at Laguna Niguel
  - The Indiana Life Sciences Forum
  - The Burrill Personalized Medicine Meeting
  - The Pacific Northwest Life Science Meeting
  - The Aging Meeting
- Media/Publishing
  - The 2010 Biotech Industry Book
  - The Burrill Report (monthly)
  - The Burrill Weekly Brief
  - The Journal of Life Sciences

Reasons for Burrill & Company's Success

- Industry knowledge and experience
- Information Insight
- Constant knowledge generation
- Burrill & Company is geographically located in the heart of the "Biotech Bay", the highest density biotechnology cluster in the world
- Willingness to take risks
- ½ Full vs. ½ Empty

What Makes VC's Successful

- Industry knowledge
- Robust "in-box"
- Idea generation
- "Where is the puck going to be"?
- Luck vs. opportunity
- Have (and work) the network
- Be different/ do different things
- Timing is critical

What Makes Merchant Banking Successful

- Industry knowledge
- Know what you can get done (project selection)
- Use network
- Success based fees
- Be creative
- Have (and work) the network

What Makes "Media" Successful (conferences/ publications)

- Industry knowledge
- Insight vs. information
- Use network
- Stay current
- Meet tomorrows needs, not yesterday's
- Be creative
- Have (and work) the network
- Timing is critical
- Uniqueness

What is unique about Life Sciences Companies

- Capital for a decade (or more) before self-financing
- Regulatory pathway before access to customer
- New products may increase cost to system (understanding reimbursement/payment mechanism)
- User (patient), doctor (prescriber), Provider (hospital, clinic), Payer (insurance company, managed care, government agencies [Medicare, Medicaid]) all de-linked
- Global from day one

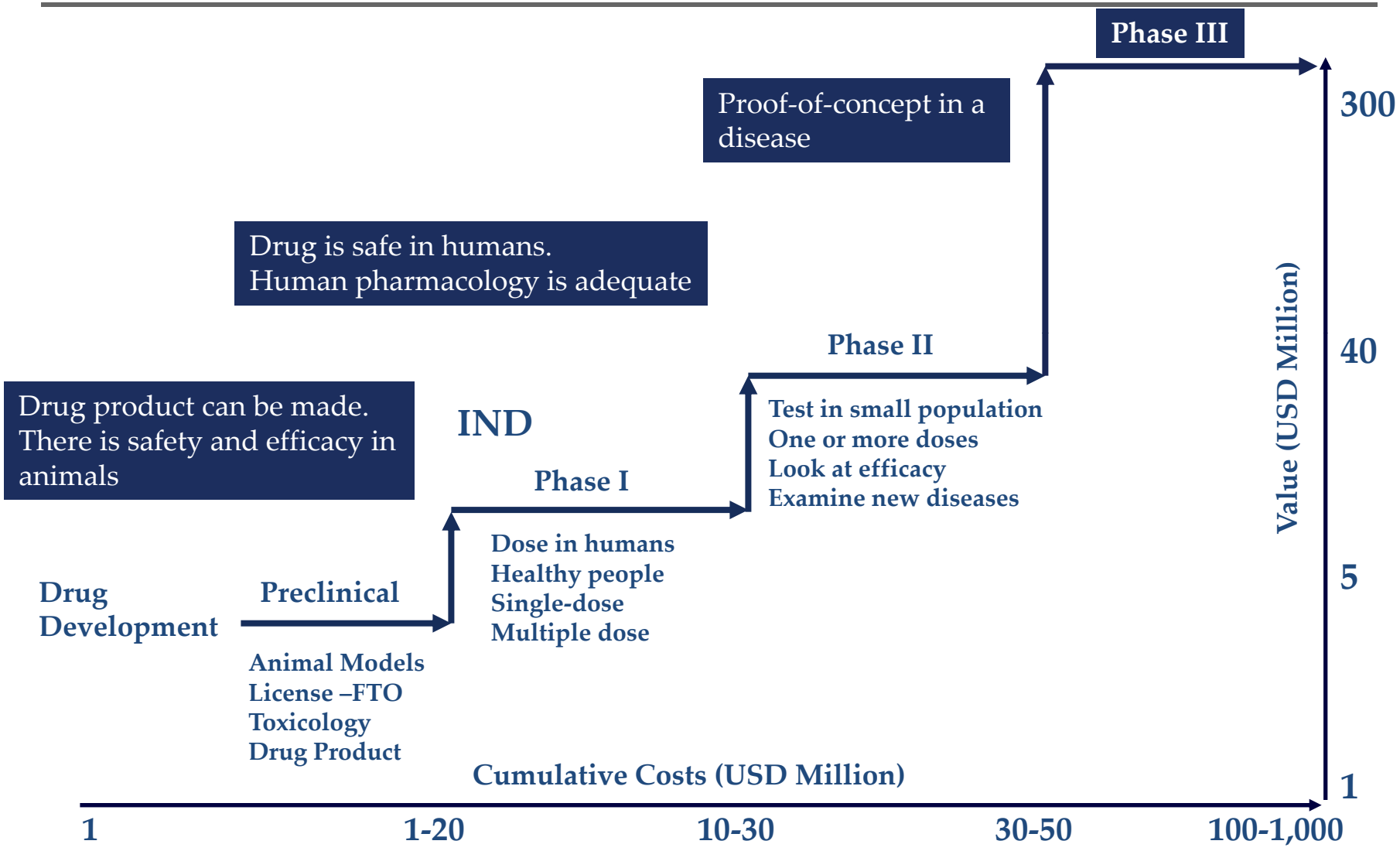
What is an Entrepreneur?

- Adult ADD under control.

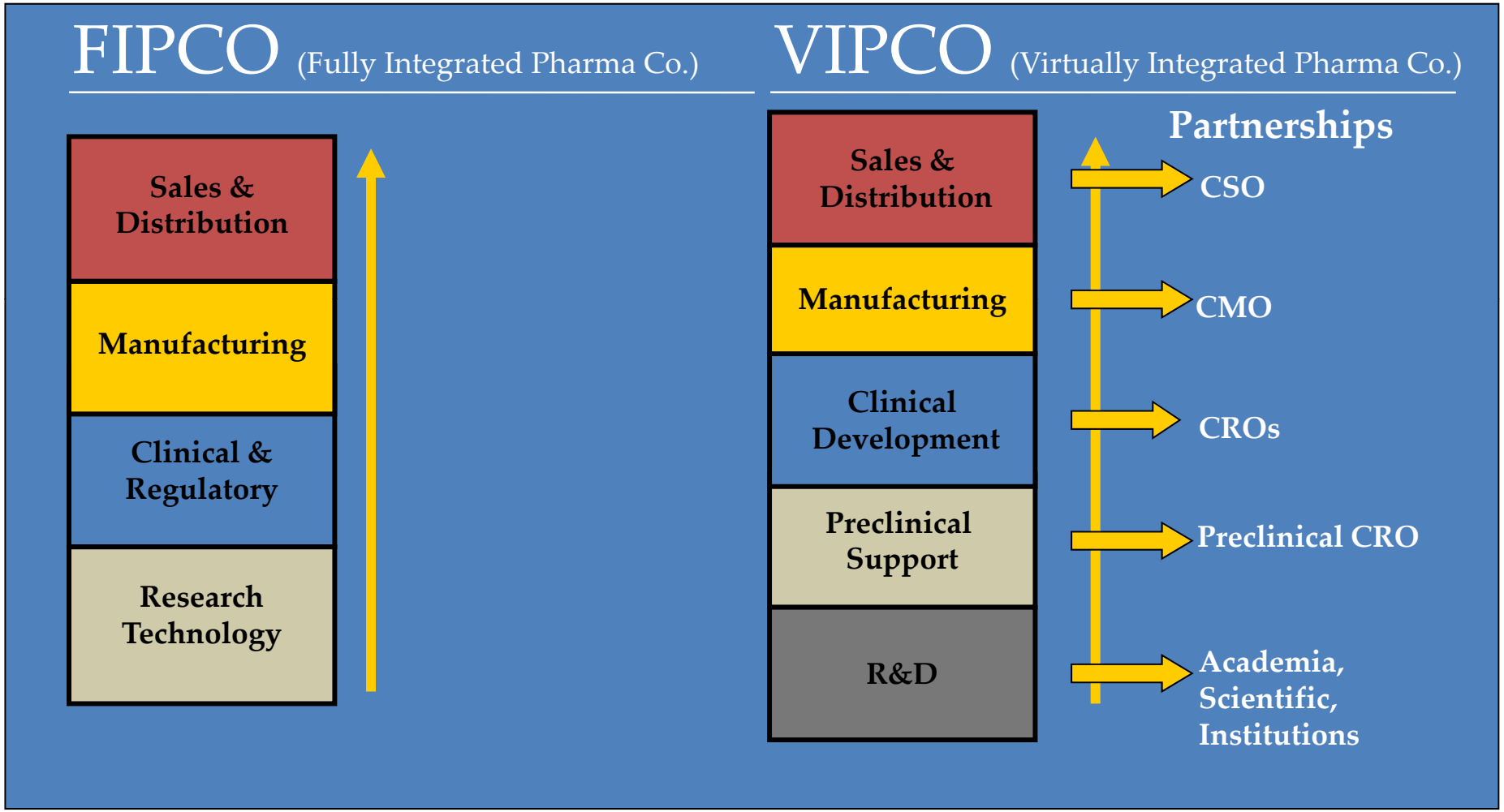
Entrepreneurship
"The pursuit of opportunity without regard to resources controlled."

~Howard Stevenson
Harvard Business School

Value Creation in Drug Development



Changing Business Models

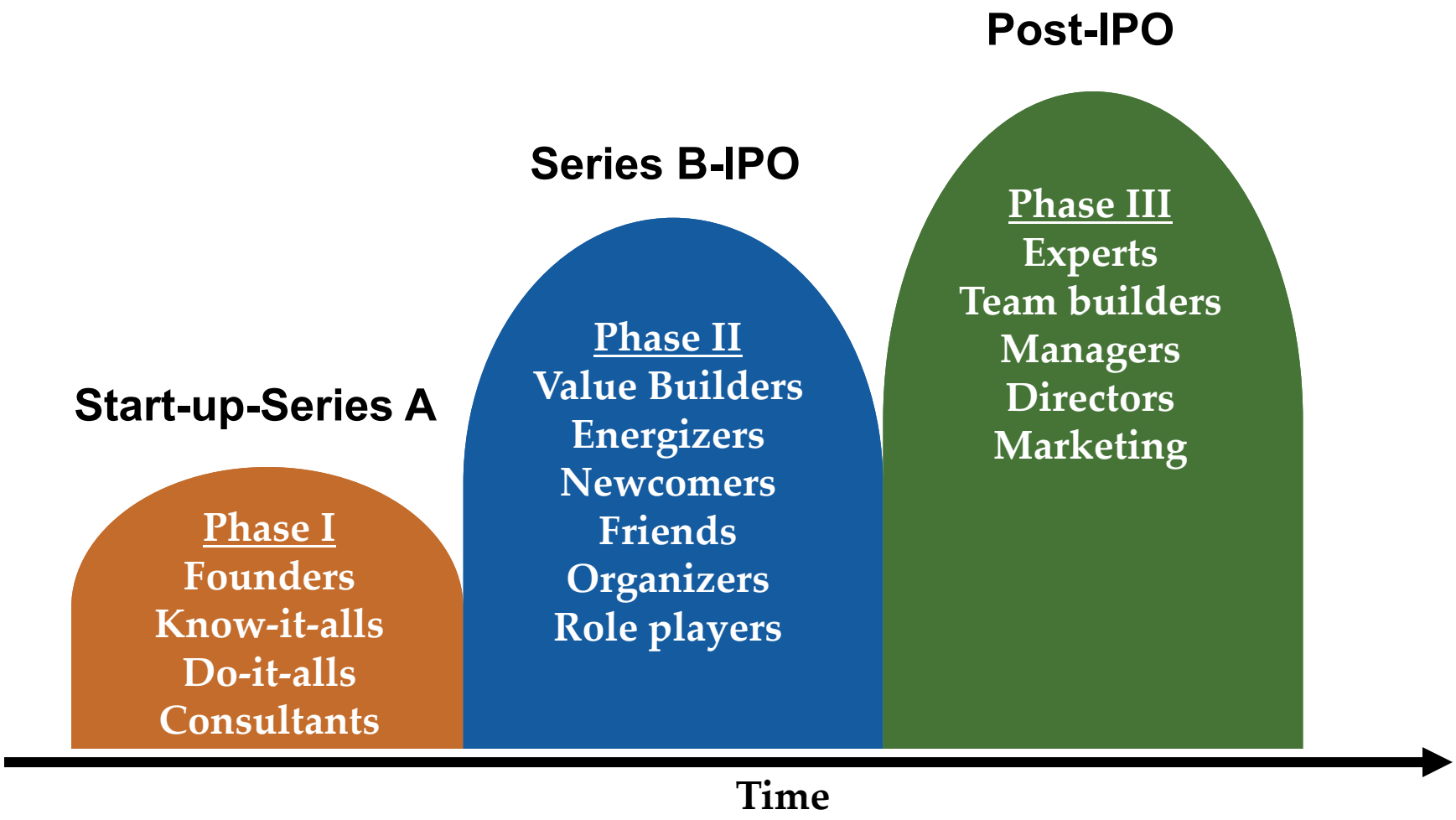


Virtual Pharma: New Organizational Models for Leverage of Open-Source Services

- PharmaCommons: integration of rapidly expanding open-source datasets
  - Discovery, toxicology, clinical trials
- Network of web-based turn-key contract services
- China/India/other low cost (R&D, clinical development and manufacturing) sites will dominate
- New role of BigPharma as integrator to generate value across the entire disease episode spectrum
  - Wellness to terminal care

Source: George Poste/Burrill & Company

Entrepreneurial Business Build



The First Hires

VC's Consultants Bankers Accountants Lawyers

- Recruit and hire like any permanent position.
- This is the first team.
- Look for key beliefs and behaviors not just "record".
- Watch the back door.
- Do the background check.
- They will have the biggest influence on the company.

Phase I Building

Start-up-Series A

- Founder(s)
  - Get coaching for expectations
  - Assess conflicts-of-interest
  - Complete disclosure
  - Establish working relationship
- Know-it-alls
  - Nobody knows it all
  - Every situation has uniqueness
- Do-it-alls
  - Find these people !!

Advice For Phase I Builders

- Establish who the key hires will be –EARLY.
- Broadcast key hires—to Board, to VC's, to Bankers, to Consultants etc.
- Be prepared to "give-up" equity for the key hires.
- When in doubt—Keep Looking !!!

Who are the "Right" People

Right People

- Ask insightful questions on science and near term goals.
- Career "risk" non- existent.
- Title unimportant
- Clear career goals that match company.
- Job description as "placeholder".
- Builds personal connections.

Wrong People

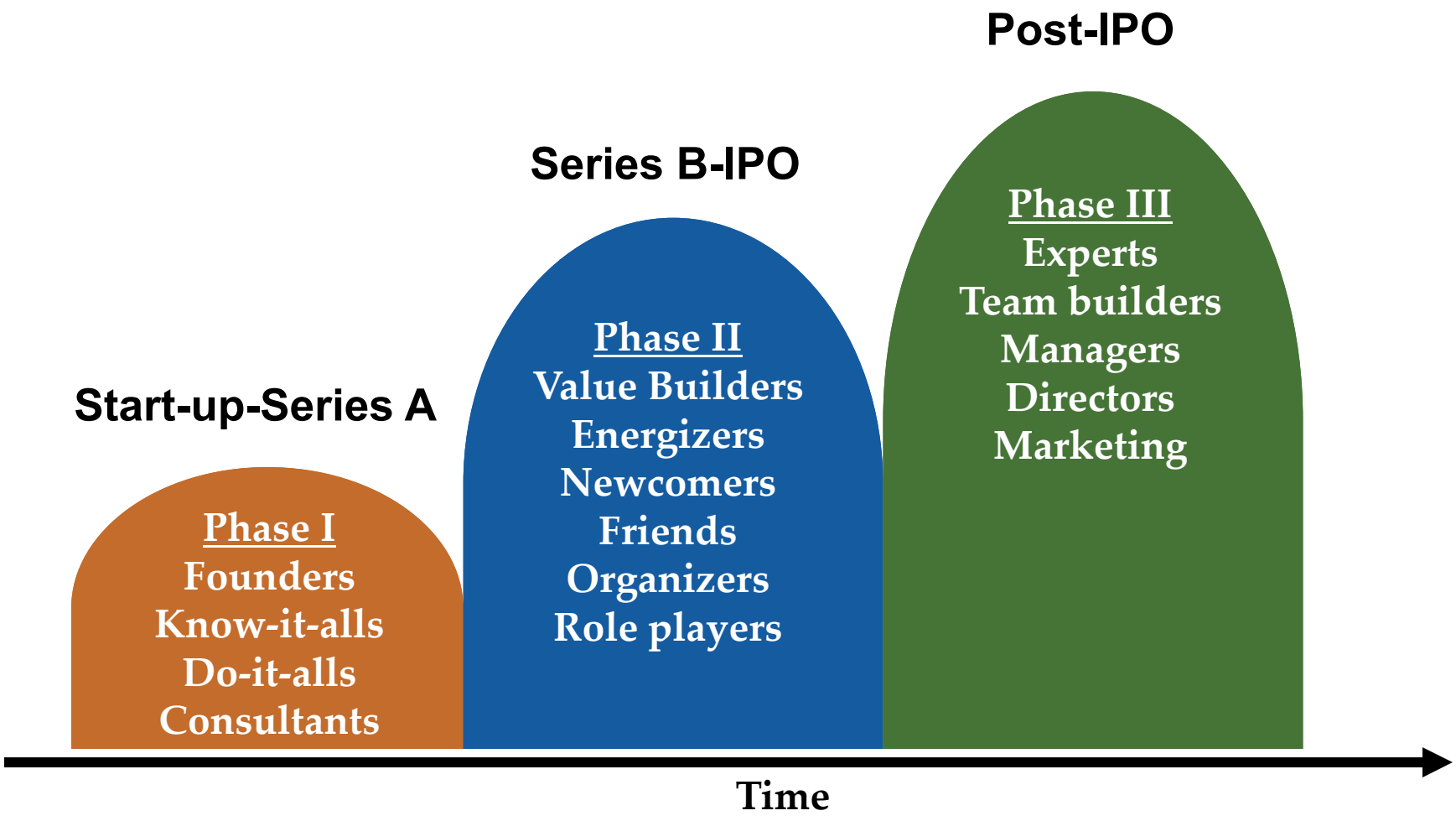
- Protracted discussions on dilution & capital structure.
- Focused on risk mitigation.
- Title is all important.
- Career goals are purely financial.
- Job description requires extensive redlines.
- Avoids personal connections.

Phase II Building: Getting Scale

Series B-IPO

- Key risk: Hiring too quickly
- Milestone Pressure
- Make key hires a milestones
- Outsource other jobs but keep "hiring" a core competency.
- Budget for multiple interviews
- Look for personal dedication, sense of mission and desire to achieve as well as technical skill base.
- Look for business development skill
- "Everyone in business development".

Entrepreneurial Business Cycle

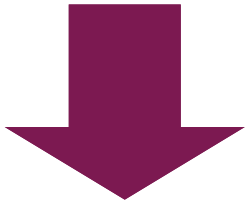


Market Analysis & Opportunity Assessment

Which market is more attractive?

A novel treatment for a lysosomal storage disorder that ***affects 30,000 worldwide***

A laboratory-based cholesterol level test marketed in the United States

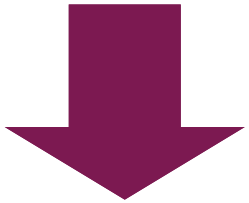


Which market is more attractive?

A novel treatment for a lysosomal storage disorder that ***affects 30,000 worldwide***

GENZ's Cerezyme for Gaucher's Type I
($850 million revenue in 2004)

A laboratory-based cholesterol level test marketed in the United States



~250 million tests per year
(with very small profits per test)

Market Analysis Primer

Key Points:

- Market analysis and describing how to address your target market (i.e. Marketing) sections are CRITICAL to your business plan
  - Identify your customer/end user (usually who is paying, not always)
  - Develop a value proposition (why?)
  - Segment your market thoughtfully (most profitable)
- Develop your marketing 'plan' based on the 4 P's
  - Product, Price, Place (distribution) and Promotion
- Avoid common mistakes and pitfalls

Why Market Analysis is Important?

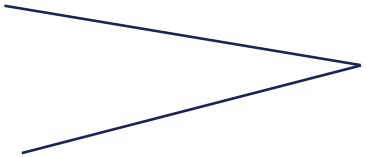
- VCs review 100's of business plans per year
- They seek ***good opportunities*** that are well thought out
- Investors can't 'see' your science or 'hear' your advisors – though important
- The ***opportunity*** is conveyed through the marketing plan
- 5X ROI rule of thumb for some VCs

Step 1: Who is your customer?

- Who will make ***the decision*** to buy?
- Not always clear (drug example):
  - ***Physicians prescription habits***
  - ***Insurance companies (formularies)***
  - ***Patients (consumer driven healthcare)***
  - ***The government (Medicare Drug Program)***
  - ***Big pharma (in-licensing programs)***
- Define your customer, think carefully about their ***true needs***
  - What do they ***want***? Physicians? Patients? Payors?

Step 1: Who is your customer?

- Examples of customer needs/wants:
  - Efficacy
  - Safety
  - Pharmaco-economic benefits
    - Lower cost/higher 'value'
    - Cheaper methods of production to contain costs
  - Clinical utility
  - Ease of use (patients, physicians, caregivers)
  - Pharmacokinetics/Pharmacodynamics
    - Highlight long half life if a desirable feature



Seem obvious but remember risk/reward, cost/benefit features across different customers

Step 2: Segment your market

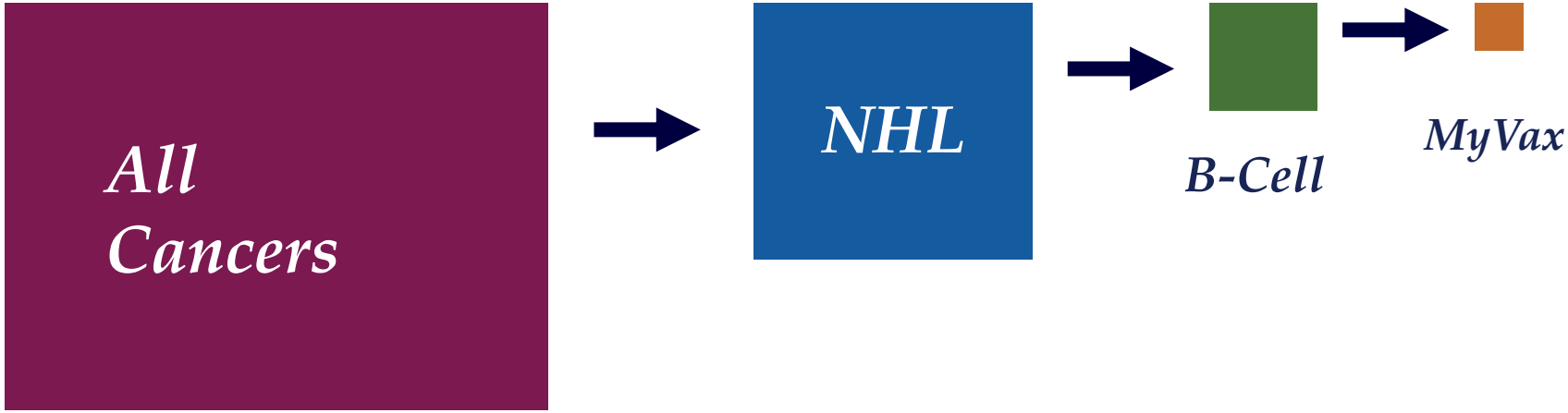
- Perform extensive research with various sources
  - ***Expensive Sources:*** *Datamonitor, IMS Health, Frost and Sullivan*
  - ***Less Expensive Sources:*** *Equity research reports (Cowen, etc)*
  - ***Free:*** *Google, your library, medical associations (AHA), white papers*
- Identify the key parameters of the market and its customers
- For diseases, use top-down and bottom-up estimations to triangulate
  - **Top-down:** Incidence and prevalence, diagnosed, eligible for reimbursement, treated with class of therapy, treated with "your drug or therapy"
  - **Bottom-up:** (# of plastic surgeons) x (# of patients with given disease) x (your proposed penetration rate)

Step 2: Segment your market

- IMS Health data: quintiles/deciles for physicians (tier 1, tier 2 - based on treatment volume)
- Hospitals: small, medium and large (number of beds)
- Laboratories: clinical reference, university (large and small) and research
- Think through how the value proposition fits/doesn't fit the various market segments
  - Product can address different markets differently
    - Ex: veterinary diagnostics v. human diagnostics

Step 2: Segment your market

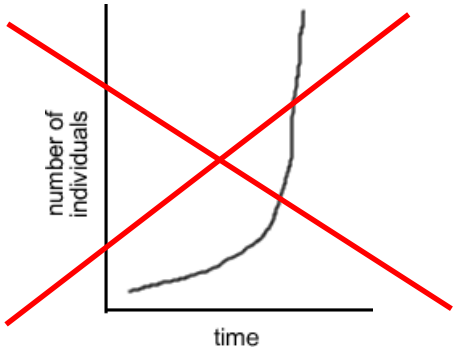
Genitope example



MyVax® Personalized Immunotherapy combines a protein derived from the patient's own tumor with an immunologic carrier protein and is administered with an immunologic adjuvant. The tumor-derived protein that is unique to each patient is the antibody expressed by the tumor cells. Each antibody has unique portions, collectively known as the idiotype, which can be recognized by the immune system. The antibody that is unique to a given patient's tumor is often referred to as the idiotype protein. Genitope's immunotherapy consists of the idiotype protein and a foreign carrier protein administered with an adjuvant to enhance the immune response. **MyVax® Personalized Immunotherapy is currently in a pivotal Phase 3 trial and additional Phase 2 trials for the treatment of B-cell non-Hodgkin's lymphoma and B-cell chronic lymphocytic leukemia.**

Step 3: Develop your 'plan'

- Make assumptions about the market segments
  - be realistic—avoid the 'hockey stick'
  - HOWEVER, make sure your plan is compelling
    - adoption and market penetration assumptions
      - look for comparable products in similar markets



- Develop pricing assumptions
  - should be based upon the value proposition
  - research competitors, justify pricing premium
- State all your assumptions clearly
  - build models to be able to adjust assumptions

Step 3: Develop your 'plan'

- Target market is affected by all 4 P's
  - **Product**: functionality, appearance, quality, packaging, brand, service/support
  - **Price**: list price, discounts, allowances, financing, leasing options
  - **Place:** channel members, channel motivation, market coverage, locations, logistics, service levels
  - **Promotion:** advertising, DTC, public relations, messages, media
- Various constraints affect the entire "Marketing Mix" not only financial

Avoid Common Mistakes/Pitfalls

- "There are no competing products"
  - Competition for the vacuum was a broom
  - Acknowledging the existing market shows grounding in reality
- "Our market is $12 billion per year"
  - The entire market, but not your segment (s)
- "40 million people have diabetes"
  - How many are actually being treated with your class of drug today?
- "Our test will sell for $500"
  - What do reimbursement trends suggest? $200?

Avoid Common Mistakes/Pitfalls

- "We will have Year 1 sales of $10 million"
  - Practically impossible, almost irrational
- "Physicians will use us because…"
  - What evidence suggests this?
  - Physician decision making process
- "We will sell 1,000 units/yr upon launch to labs because our equipment is better"
  - What is the sales cycle for the equipment you are replacing?

Market Analysis Primer

Key Points:

- The market analysis and marketing sections are CRITICAL to your business plan
- Identify your customer/end user, their needs
- Develop a value proposition for your product
- Segment your market thoughtfully, and in great detail
- Develop your marketing 'plan'
- Avoid common mistakes and pitfalls

Burrill Portfolio Company:
BioMimetic Pharmaceuticals

BioMimetic Initial Company Presentation

- Tennessee-based company
- Introduced to Burrill & Company by L.P. – Chiron Corporation
- Technology: PDGF formulated with a matrix carrier (biologic) for the restoration of bone and other tissues in periodontal and cranio/maxillofacial applications
- Lead product: rhPDGF-BB implanted into periodontal spaces during surgical procedures to enhance bone re-growth and proper healing
- Obtained composition of matter rights from Zymogenetics, supply agreement from Chiron, and exclusive rights to periodontal applications from Harvard University
- Initial focus on tissue engineering therapeutics

Why BioMimetic Was Attractive

- Regulatory Approval
  - Faster FDA approval for rhPDGF-BB as FDA already familiar with similar technology for different applications (Regranex for chronic foot ulcers in diabetic patients, J&J)
  - Data from human trials of BMPs showed faster and denser bone formation
- Market Size and Unaddressed Market
  - Worldwide annual market potential of $525M for treatment of periodontal disease and $279M for its diagnosis for a total of $804M
  - Orthopedic markets >$10B
  - No direct competition; recombinant growth factor product is currently marketed for the treatment of periodontal or CMF defects

Why BioMimetic Was Attractive

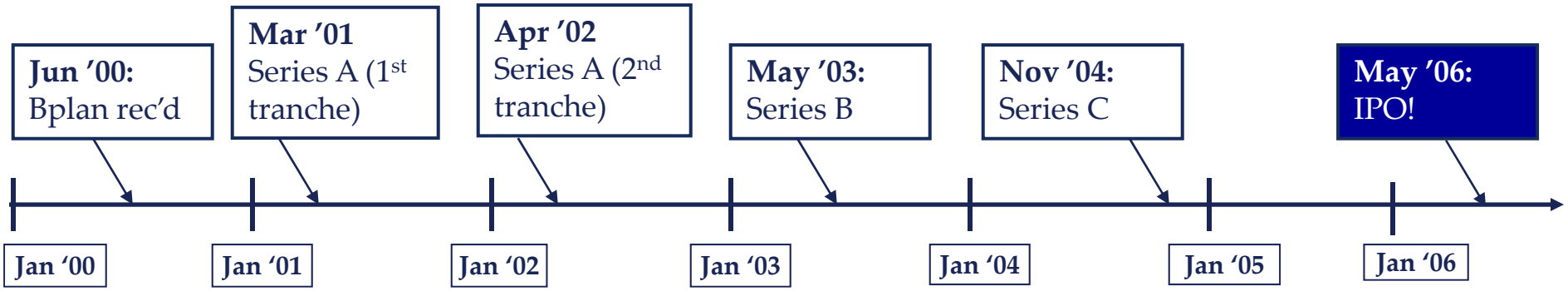
- Intellectual Property
  - 22 issued patents, 4 allowed patents (from Harvard and ZymoGenetics)
- Manufacturing
  - Already manufactured by Chiron
- Early staged company at an attractive valuation with short time to clinical trials and registration
- Founder
  - Dr. Samuel Lynch, Chairman and CEO.
  - Former VP at subsidiary of Sankyo Pharmaceuticals in same markets as Biomimetics where he managed P&L, FDA approvals, sales and marketing. Also has outstanding reputation as a academic clinician

BioMimetic Key Issues (pre-investment)

- No management team
- Did not have all licenses required from Zymogenetics, Chiron and Harvard
- Clinical trial conducted on small number of patients at an academic center in Brazil, and did not meet FDA requirements
- First trial performed with human allograft tissue
- European registration and commercialization
- Regulatory strategy for a drug vs biologic vs combined products

BioMimetic Timeline

- Burrill & Company invested a total of ~$9.3M in BioMimetic
  - Series A of $4M in two $2M tranches
  - Series B of $1.8M
  - Series C of $3.5M



BioMimetic IPO

Stock Price @ IPO (5/15/06)	$7.99
Stock Price (8/2/2010)	$12.21
52-week High	$15.81
52-week Low	$6.52
Market Cap. (3/5/10)	$263.9M
2008 Revenues:	$3.2M

Underwriters:

- Deutsche Bank (co-manager)
- Pacific Growth Equities (co-manager)
- AG Edwards
- First Albany

Burrill Laws

Burrill's First Law

"Stars lose…teams win."

Burrill's Second Law

"The acceptance of a product in the marketplace ultimately determines the company's success."

Burrill's Third Law

"The key to technology is the barrier to entry."

Burrill's Fourth Law

"Financing strategy dictates business strategy."

Burrill's Fifth Law

"Tactics are more important for success than strategy."

Lessons Learned in 40+ Years…

Lessons Learned in 40+ Years…

- It never really works out the way the business plan forecasts
  - Why?

Lessons Learned in 40+ Years…

- It never really works out the way the business plan forecasts
  - Why?
    - takes longer, costs more
    - roadblocks occur
    - clinical events (slower enrollment, bad outcome)
    - competition
    - power of the unknown

What do we know from winners

- Management: Back the best people!
- Market: Identify large market need and satisfy it
  (be aware of "snapshot mentality")
- Technology: Understand freedom to operate, needs to be real breakthrough innovation
- Execution: Essential
- Financial: Is there a well thought out road to success?

Start up CEO Attributes

- Vision – create or preserve it
- Understand pathway to success
- Be a great recruiter
- Motivate people, get buy-in
- Communicate goals/objectives
- Create/establish the right culture
- Manage Board
- Execute…Execute…Execute

Why do CEOs fail?

- Founder/CEO unwilling to transfer leadership when appropriate
- Tactical execution fails – this is an entrepreneurial environment, not a "corporate" or "academic" environment
- War with founders or investors

"Leadership is the art of accomplishing more than the science of management says is possible"

Colin Powell

Markets

- Technology changes markets
- Size big enough?
- Don't underestimate competition!
- Can a small company get to the customer?

Business Model

- Fail fast – "white hot risk"
- Complex products vs. simple products
- Get to POC with minimum capital
- Brave new world vs. better, faster, cheaper
- Understand cycles
  - FIPCOs (70s & 80s)
  - Tools (90s)
  - Specialty Pharma (2000)
  - Molecular Dx (2010 →)

Business Models (continued)

- Tools companies: "Picks & Shovels" (FBC)
  - Moderate capital
  - Revenue ramp is key
  - Margins critical
  - Issue: breadth – market risk
- Platform therapeutics: "The Gold" (BNW)
  - Very capital intensive
  - Must have corporate partners
  - Novel targets
  - Issue: financing risk, technology risk
- Specialty Pharma (FBC)
  - Niche markets
  - In licensing model
  - Clinical stage assets
  - Issue: clinical and market risk

Business Model (continued)

- Diagnostics (FBC/BNW)
  - Where's the drug?
  - Reimbursement
  - Can be capital intensive
  - Issue: technical and market risk
- Devices (FBC)
  - Moderate capital
  - All about clinical results
  - Issues: clinical risk and market risk

Lessons from "Losers"

- What can go wrong will go wrong
  - Technology is tough
  - IP:FTO
  - People issues
  - Time delays
  - Burn rates out of control
  - Clinical failures/delays
  - Reimbursement more challenging
  - Competition underestimates

Lessons Learned

- Stay focused
- Remove risks early
- Recruit the best teams, don't be afraid to change
- Business plans are a constant "work in process"
- Plan for surprises/problems
- Cash is king
- Board/VCs need to be knowledgeable, flexible, prepared, engaged

When the going gets tough, the tough get going –

Go for it...

Q&A


BURRILL & COMPANY
Life Sciences: Venture Capital, Private Equity, Merchant Banking, Media