

Biotechnology Industry: Role of Syntex Syva Alumni in Its Success

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Topics to be Covered

- ❖ Overview of Biotech Industry
- ❖ Role of Syntex Syva Alumni in Success of Bay Area Cluster

Life Sciences Umbrella

◆ Technology impacting discovery and development of products for:

- Enabling technology (genomics, combinatorial chemistry)
- Human healthcare (therapeutics, diagnostics, drug delivery, cell and gene therapy...even moving toward some devices and drug/device combinations)
- Agriculture (food, feed, fibers, transgenics)
- Environment (bioremediation)
- Industrial processes and efficiency
- Energy
- Supply (reagents, biologicals)

Source: BIO, **Guide to Biotechnology**

Therapeutic Proteins versus Small Molecule Drugs

- ❖ Large complicated molecules (100-1,000 times larger)
- ❖ Heterogeneity (based on natural biologic diversity)
- ❖ Produced by genetically modified living cells (usually mammalian and bacteria)
- ❖ Complex mode of action mediated by large surface area (may achieve more specificity)

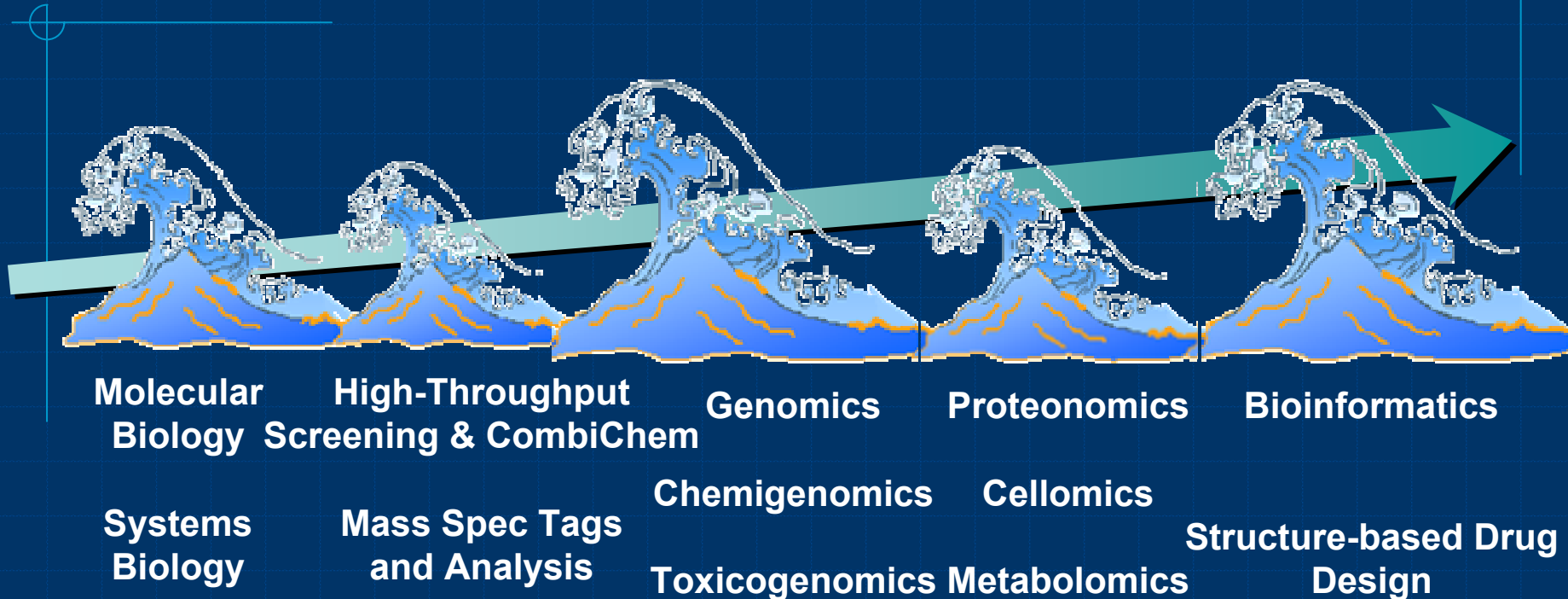
Therapeutic Proteins versus Small Molecule Drugs (cont.)

- ❖ Complicated production and purification (difficult CMC)
- ❖ Relatively unstable (more sensitive to temperature and storage conditions)
- ❖ Require injection for most part (lose their activity in digestive system)

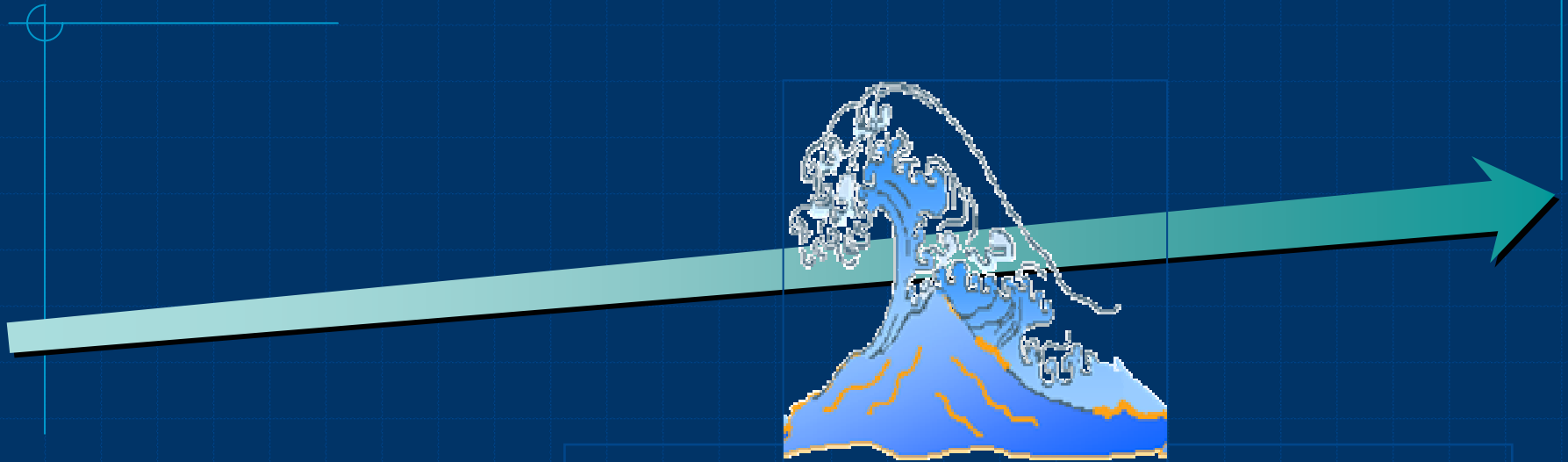
Biotech/Biopharma/Platform/Diagnostic Company Characteristics

- ◆ A discovery research company
- ◆ New company grows alongside product development
- ◆ Often founded by scientist/engineer entrepreneur
- ◆ May be one product or one technology company
- ◆ May out-license first product or Japanese territory rights to get early funding; may sell the company
- ◆ Depends on angel investors, VCs, development contracts and out-licensing for funding in early years

Biotech Innovation Waves



Biotech Innovation Continues



**Pharmacogenomics
or Personalized Medicine**

Business model yet to unfold

Possible Paths to Success?

- ◆ Big Biotech using their current model of high priced biologics for small patient populations? e.g., Herceptin
- ◆ Specialty tool and discovery companies enabling personalized medicine?, e.g., Surromed
- ◆ Big Pharma companies developing Dx and Rx capabilities under one umbrella? e.g., J&J
- ◆ Specialty Pharma marketing Rx and Dx to specialists? e.g., Prometheus Labs

Might Syntex-Syva organization have played a key role in achieving this shift in medical development successfully?

U.S. Biotech At a Glance

(\$ in Billions)

	Public Companies			Industry Total	
	2003	2002	+/-%	2003	2002
Financial					
Product Sales	\$25.9	\$20.8	25.0%	\$28.4	\$23.2
Revenues	35.9	28.7	25.0	39.2	32.0
R&D Expense	13.6	16.3	-16.9	17.9	20.6
Net Loss	3.2	9.7	-66.5	5.4	11.9
Market Capitalization	\$298.7	\$188.7	58.3%	NA	NA
# of Companies	314	324	-3.1	1,473	1,472
Employees	146,100	128,200	14.0	198,300	179,900

Source: Ernst & Young, **Resurgence: The Americas Report 2004**, p. 26.

Data shown largely for December 31, 2003 and December 31, 2002 are estimates based on January-September quarterly filings and annual financial performance data for some companies. 2002 R&D expense and net loss were significantly impacted by significant write-offs for acquired in-process R&D due to Amgen's acquisition of Immunex and Medimmune's acquisition of Aviron. 2002 data have been restated for comparability with 2003 estimates.

Bay Area vs New England Regional Biotech Industry-- 2003

Public Companies

	Bay Area	New England
Revenues	\$10.3 billion	\$6.4 billion
R & D expenses	\$4.1 billion	\$2.6 billion
Net loss	\$.7 billion	\$1.3 billion
Market capitalization*	\$95.9 billion	\$43.0 billion
Number of companies	59	51
Employees (2002)	31,844	24,447
Total assets	\$25.8 billion	\$23.4 billion

Source: Ernst & Young, *Resurgence: The Americas Report 2004*, p. 43.

Ernst & Young and company financial statement data. New England: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island

* Market capitalization data is as of 12.31.03.

Numbers may appear inconsistent because of rounding.

Non-Drug Biotech Sectors

- ◆ Instrumentation--\$23 billion in 2002*
- ◆ In Vitro Diagnostic Market Sales-\$20.3** in 2000 and worldwide market in 2003--\$26.0 billion***
- ◆ Surgical Biomaterials Revenues--\$1.1 billion in 2000****
- ◆ Worldwide Sales of Other Biomaterials
 - Heart valves--\$683 million
 - Growth factors and synovial fluid substitutes (est. 10 years in future)--\$8 to \$31 billion*****

Sources: *Strategic Directions International; **Estimated sales by Merrill Lynch found in Burrill & Co.'s **Biotech 2001** p. 66; ***Boston Biomedical Consultants; ****Estimated by Stephens Inc in **Biotech 2001**, p. 132; *******Biotech 2001**, pp. 134 and 138.

Threats to Growth

- ◆ Conflict between healthcare viewed as “inalienable right” and ROI basis of new product development
- ◆ Failure to value drugs’ major role in improving health, enhancing quality of life and replacing more expensive medical procedures and hospitalizations equals negative view of increasing drug costs
- ◆ Specter of controlled drug pricing to avoid increasing share of national budget devoted to drugs
- ◆ “Don’t mess with Mother Nature” thinking, etc.
 - Stem cell research
 - Genetic food modification

Bioscience Industry Drivers

- ◆ Big Pharma's needs for new drugs
- ◆ Improving safety in bioscience products
- ◆ Meeting new market needs with solutions
- ◆ Ability to personalize Rx
- ◆ Need to cut costs and speed up R&D
- ◆ Ongoing pressure to find funding and increase valuation
- ◆ Maintenance, expansion and protection of IP
- ◆ Search for successful business model or face acquisition

New Challenges

- ◆ Avoid the negative shadow of Big Pharma
- ◆ Maintain viable business model
- ◆ Handle changing funding paradigm
 - VCs don't invest in early stage companies
 - Develop sufficient funding without removing incentive for later VC funding

Syntex Corporation: The First Biotech Company Was Born

- ◆ Started in Palo Alto in 1964
- ◆ Had combination of innovation and entrepreneurial talent
- ◆ Financed by investors
- ◆ Practiced new business model vs. that of traditional pharma
- ◆ Had close relationship with academia, especially Stanford

Bay Area Biotech Cluster Built on Syntex Example

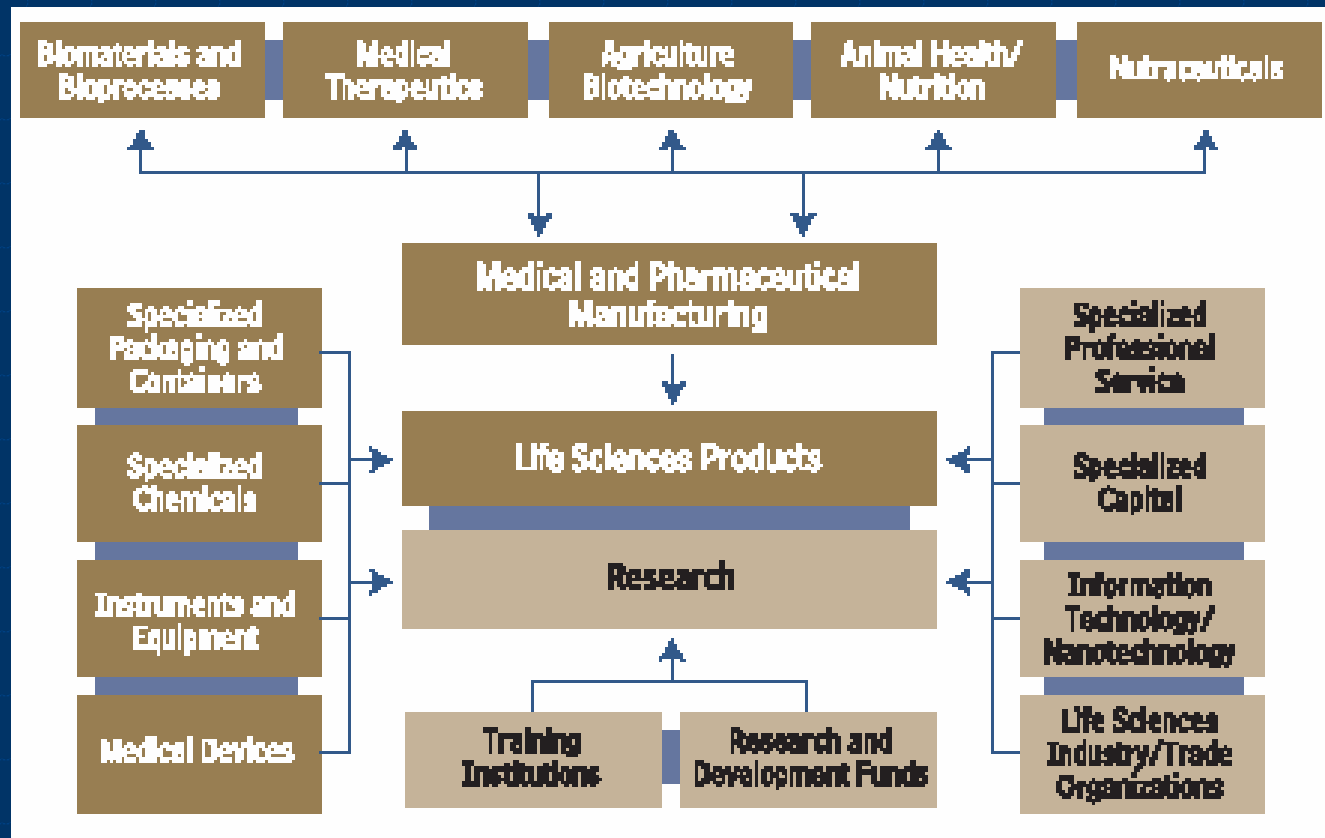
- ◆ Cetus (merged with Chiron) founded in Berkeley in 1971
- ◆ Collaboration of two Stanford geneticists and two UCSF professors led to process to construct DNA molecule that was to start recombinant DNA technology
- ◆ Genentech founded in 1976 by chemist and VC

Definition of Industry Cluster

“An industry cluster ...is a geographically proximate group of interconnected companies and associated institutions in a particular field, linked by customer, supplier, or other relationships.” -- Michael Porter, Harvard University Professor and Monitor Group co-founder.

Source: **California Life Sciences Action Plan: Taking Action for Tomorrow**, Bay Area Bioscience Center et al., p. 18.

Life Science Cluster Definition



Source: California Life Sciences Action Plan: Taking Action for Tomorrow, Bay Area Bioscience Center et al., p. 19.



Role of Syntex Syva Alumni

- ◆ Provided innovation and entrepreneurial talent to develop early biotech ventures in the 1980s and first half of 1990s as Syntex Syva employees left to found or staff these new companies

Dispersal of Syntex Syva Alumni Slow in Early Years of Industry



Source: Spring Dandelions - 2004-06-19, PDPhoto.org



Source: Fluffy, 2003-06-01, PDPhoto.org

Role of Syntex Syva Alumni

- ◆ Provided innovation and entrepreneurial talent to develop early biotech ventures in the 1980s as Syntex Syva employees left to found or staff these new companies
- ◆ Starting with layoffs in November of 1992 through final takeover by Roche and Behring—highly educated, skilled, experienced, innovative and organizationally savvy individuals provided the large, dynamic workforce needed to support the rapid expansion of the Bay Area Biotech Cluster, especially, after renewed funding in 1995

Major Dispersion after 1993



These rugged and beautiful wildflowers--not hothouse roses of traditional pharma--provided the needed staffing for the dynamic new companies.

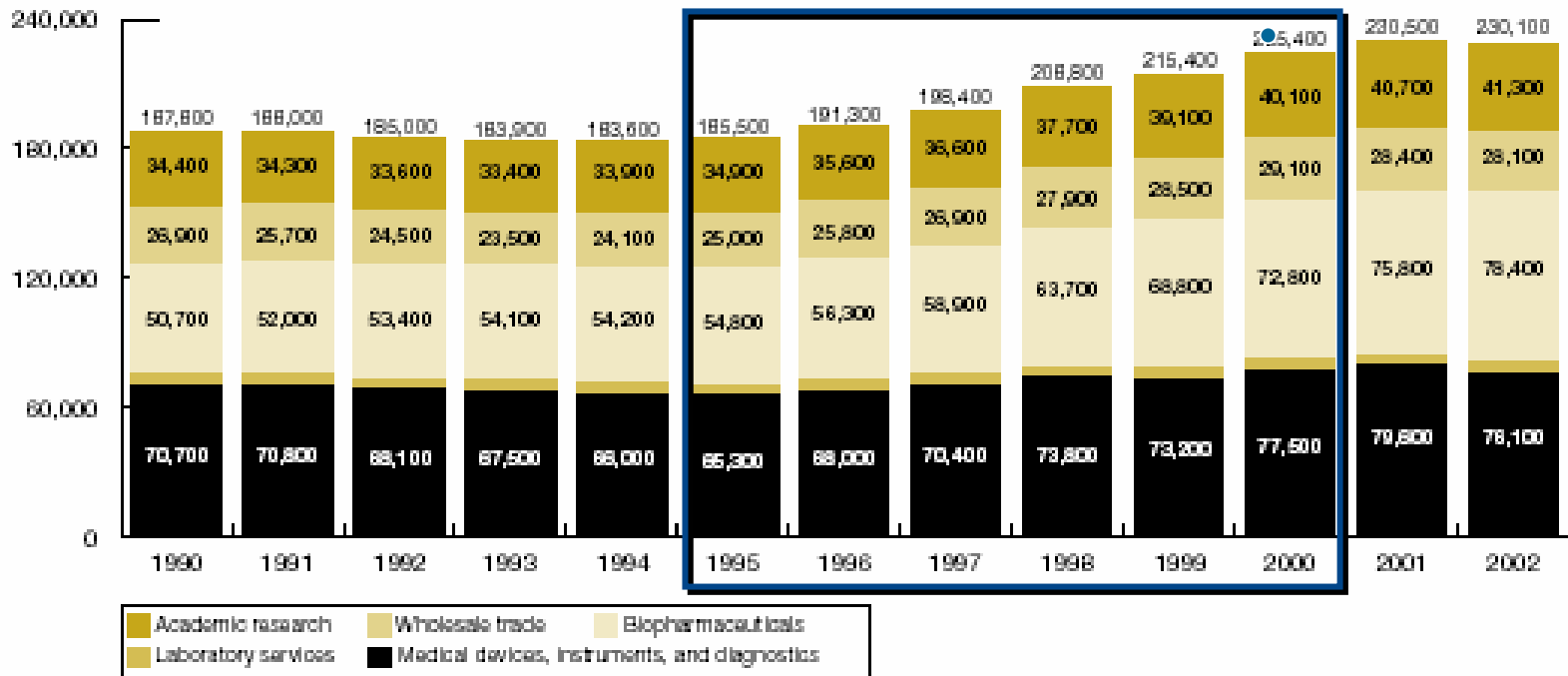
Source: Flower 2003-04-26 , PD Photo.org

Employee Exodus from Syntex Syva in California

- ◆ Syntex Corporation employees worldwide (including Syva) totaled 11,200 in November 1992 (subsequent Palo Alto layoffs in thousands prior to buyout)
- ◆ 2,960 at Syntex in Palo Alto in Oct. 1994 at time of Roche takeover dropped to under 1,000
- ◆ 1,000 at Syva dropped to 750 after Behring layoffs heightened in summer of 1995

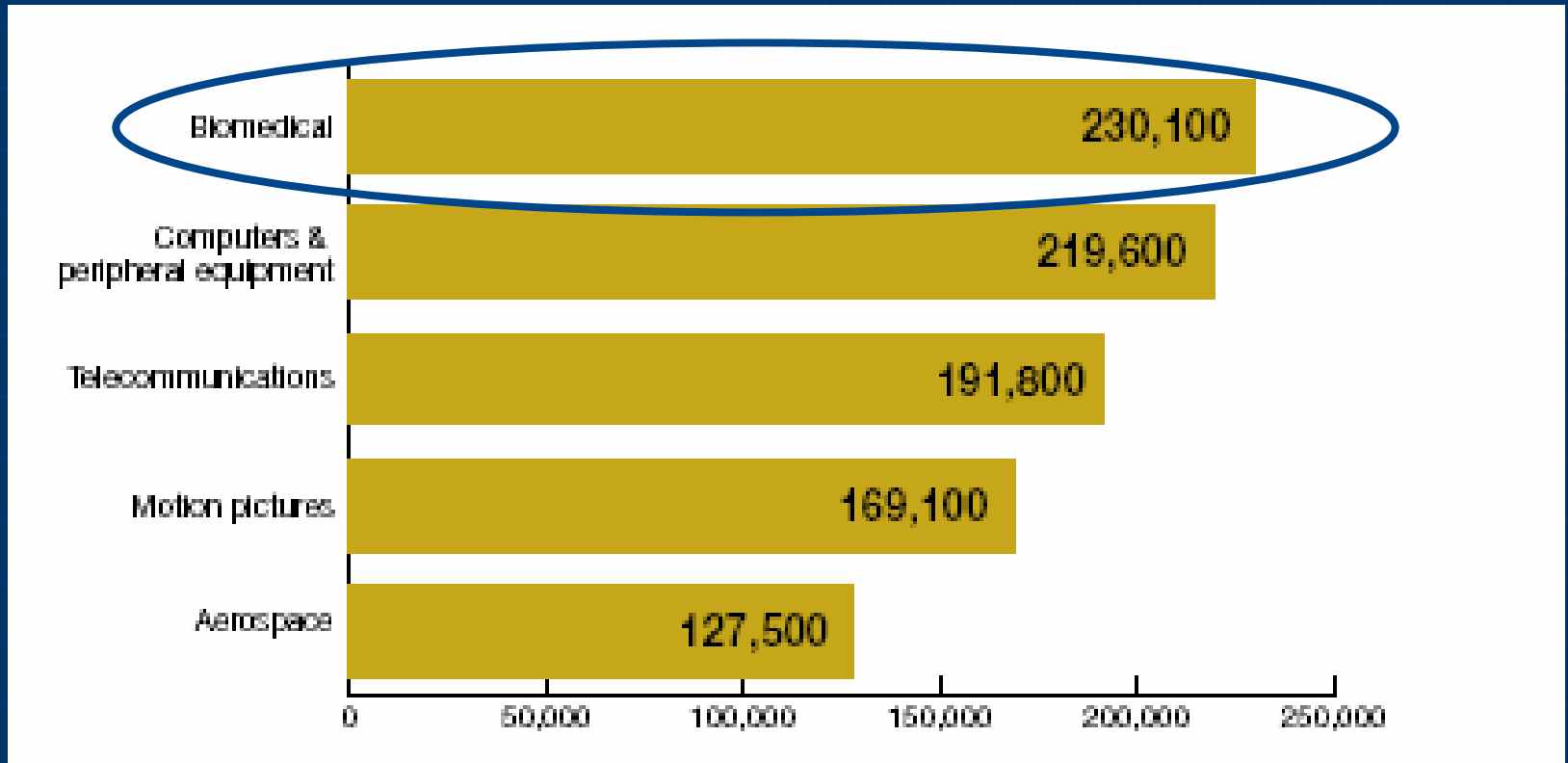
Source: Former Syntex Syva staff, Syntex press releases and **Synopsis**.

California Biomedical Employment 1990-2002



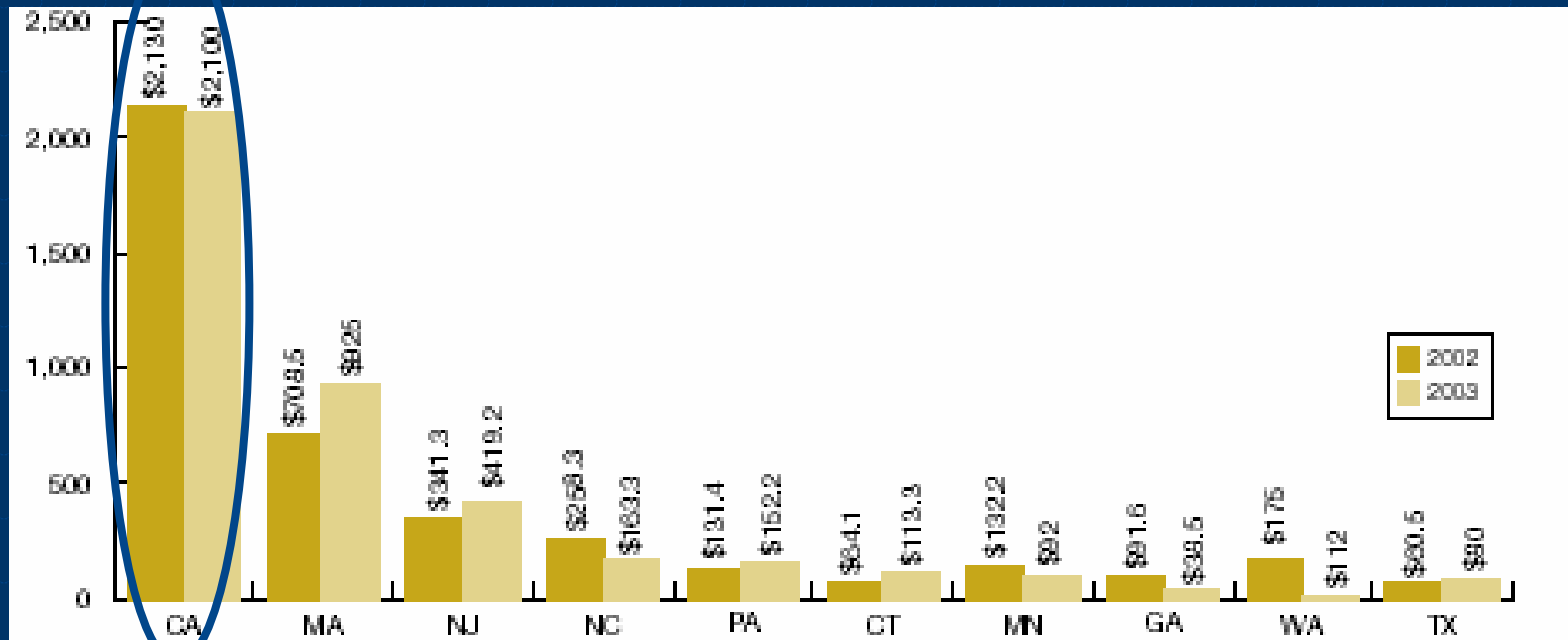
Source: California's Biomedical Industry 2004 Report, CHI and PWC, June, 2004, p. 9.

Leading California Employer Jobs in High Technology Industries



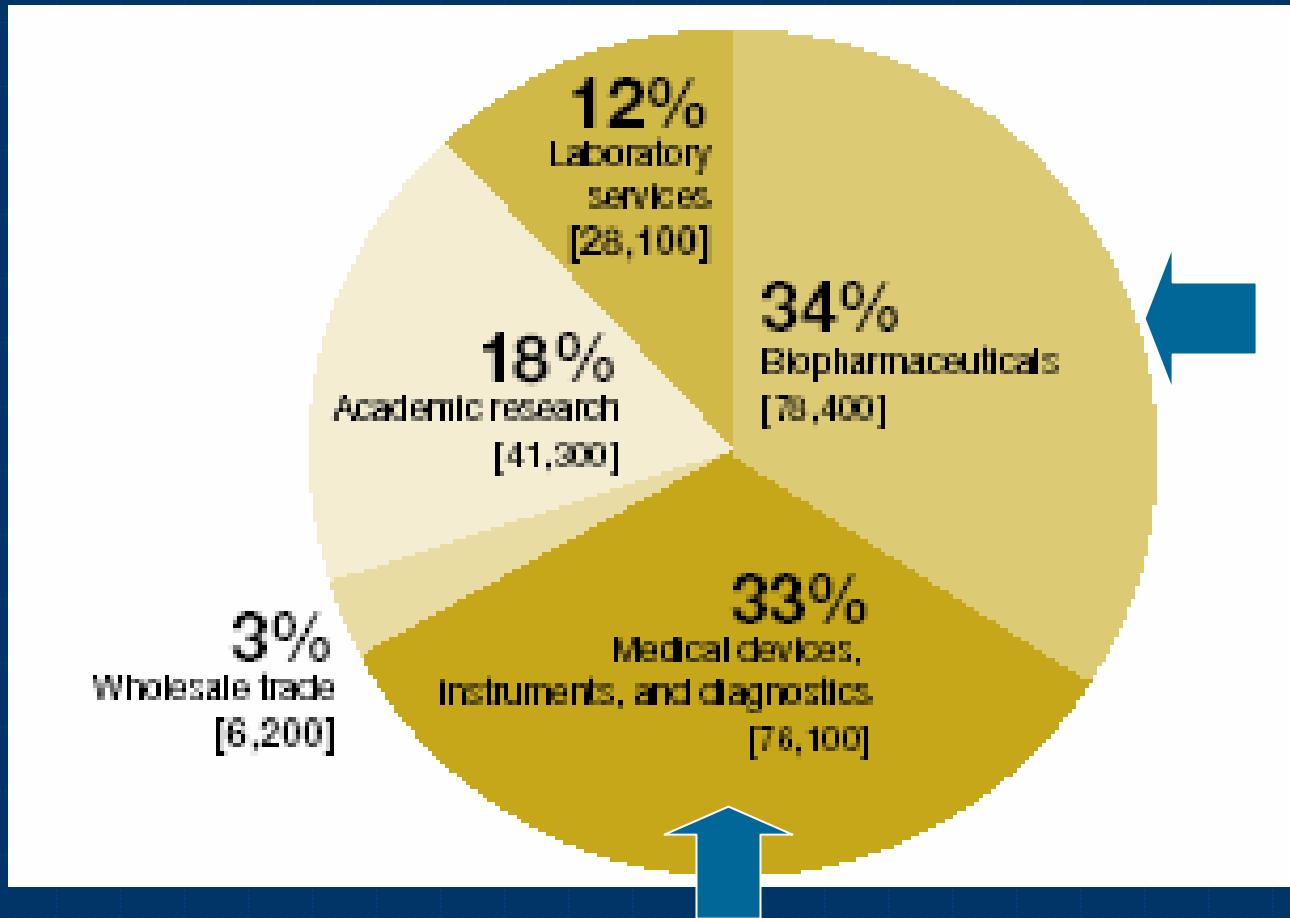
Source: Data from CA EDD, California Annual Average Industry Employment, 1983-2002, **California's Biomedical Industry 2004 Report**, CHI and PWC, June, 2004, p. 8.

Life Science Investments by State from 2002-2003



Source: PricewaterhouseCoopers/Thomson Venture Economics/National Venture Capital Association/MondayTree Survey, **California's Biomedical Industry 2004 Report**, CHI and PWC, June, 2004, p. 14.

California Distribution of 230,000 Biomedical Jobs



Source: CHI Methodology applied to CA employment charts, 2002, California's Biomedical Industry 2004 Report, CHI and PWC, June, 2004, 7.

Bay Area Cluster Rankings

Pharmaceuticals Manufacturing	Instruments Manufacturing	Medical Devices Manufacturing	Research
1. Philadelphia	1. Bay Area	1. Minneapolis-St. Paul	1. Bay Area
2. Los Angeles	2. Boston	2. Bay Area	2. Houston
3. Newark, NJ	3. Bridgeport	3. Los Angeles	3. Boston
4. Middlesex-Somerset-Hunderson	4. Los Angeles	4. Boston	4. Washington DC
5. Chicago	5. San Diego	5. Chicago	5. Los Angeles
6. Bay Area	6. Indianapolis	6. St. Louis	6. Cincinnati

Source: California Technology, Trade and Commerce Agency data, **California Life Sciences Action Plan: Taking Action for Tomorrow**, Bay Area Bioscience Center et al., p. 20

California Biomedical Clusters

Bay Area

- ◆ 85,600 employees
- ◆ 699 companies
- ◆ 31 academic research institutions
- ◆ Birthplace of biotechnology; home of Genentech and Chiron

San Diego

- ◆ 27,800 employees
- ◆ 502 companies
- ◆ 18 academic research institutions
- ◆ Home to major investments by global pharma companies

Source: California's Biomedical Industry 2004 Report, CHI and PWC, June, 2004, p. 6.

Syva Early Founding Entrepreneurs

- ◆ Gary Stroy – founded LifeScan (sold to J&J) and Abaxis
- ◆ Jerry Gin – cofounded Oculex, sold to Allergan
- ◆ Prithipal Singh founded Chemtrak
- ◆ Dave Rubenfein and Pyere Khanna cofounded Microgenics
- ◆ Ramesh Trivedi founded Robodoc
- ◆ Michael Allen cofounded Chemtrak and Metrika
- ◆ Eugene Tsi, Azeem Syed and Joel Ash cofounded DRI

Syva Late Founding Entrepreneurs

- ◆ Jan D'Alvise cofounded Metrika and with Nurith Kurn cofounded Nugen Technologies
- ◆ Tom Gutshall cofounded Cepheid
- ◆ Pyere Khanna founded DiscoverX

Syntex Early Founding Entrepreneurs

- ◆ Alejandro Zaffaroni founded Alza, Affymax, Affymetrix, Symyx and Maxygen
- ◆ Dave Rammler founded Hana Biologics
- ◆ Brad Zaro cofounded Clinimetrix
- ◆ John C. Martin founded Gilead Sciences
- ◆ Brian Frenzel cofounded Centaur Pharmaceuticals, Genelabs and Vesta Medical
- ◆ Jack Zenger cofounded Zenger, Miller Associates
- ◆ Julie Tompkins founded MedSearch
- ◆ Susan Olsen founded WWMR

Syntex Late Founding Entrepreneurs

- ◆ Gordon Ringold and Alejandro Zaffaroni cofounded Affymax and Surromed
- ◆ Bernadette DeArmond founded Pacific Research (now ICON)
- ◆ John Farris founded Safebridge Consultants
- ◆ Hardy Chan, Bob Cook, Bob Ells and Jo Shen cofounded ScinoPharm
- ◆ James E. Brown cofounded Durect
- ◆ Jim Wilson founded Amira Medical
- ◆ Matthew Potter and Audrey Erbes cofounded Kowa Research Institute in U.S.
- ◆ Bob Weissberg founded Timely Data Research
- ◆ Fran Safier founded Search Alliance
- ◆ Pat Latterell founded Latterell Venture Partners
- ◆ Roberto Rosenkranz and Roger Whiting cofounded Roxro Pharma
- ◆ Y. Hashimoto founded Medibic
- ◆ Christine C. Kaspar founded The Edgewood Group

Serial CEOs, Presidents, CFOs and Board Members

- ◆ Richard Bastiani
- ◆ Mel Booth
- ◆ Rich Casey
- ◆ Alex Cross
- ◆ Liz Davila
- ◆ Paul Freiman
- ◆ Tom Gutshall
- ◆ Donald Hawthorne
- ◆ Pat Latterell
- ◆ Fred Kurland
- ◆ Bert Lee
- ◆ Joe Limber
- ◆ Art Mandell
- ◆ Douglas Norby
- ◆ Gary Petersmeyer
- ◆ Richard Powers
- ◆ Bob Roe
- ◆ Roberto Rosenkranz
- ◆ Hans P. Schmid
- ◆ Rivka Sherman-Gold
- ◆ William W. Sims
- ◆ Virgil Thompson
- ◆ Joe Vallner
- ◆ Jim Wilson
- ◆ Lee Wilson
- ◆ Alejandro Zaffaroni

Other Serial Key Management Team VPs

- ◆ Neil Ackerman
- ◆ Tony Allison
- ◆ Robert I. Blum
- ◆ Linc Bynum
- ◆ Tony Bourdakis
- ◆ Jack Cohen
- ◆ Nancy Cohen
- ◆ Ellen Cooper
- ◆ Ellen Curtis
- ◆ David Ellis
- ◆ Carolyn Feamster
- ◆ Carol C. Grundfest
- ◆ Norm Hallen
- ◆ Irwin Heyman
- ◆ Bonnie Horner
- ◆ Andrew G. Korey
- ◆ Tony Lima
- ◆ Jennifer Lorenzen
- ◆ Natalie McClure
- ◆ Chris McReynolds
- ◆ Larry McReynolds
- ◆ Jeff Miller
- ◆ Michael Miller
- ◆ Arlene Morris
- ◆ Cathy Murphy
- ◆ Florence Nixon
- ◆ Lee Rauch
- ◆ Clair Sater
- ◆ Jay Shepard
- ◆ William Spickler
- ◆ Marc Steuer
- ◆ Michael Venuti
- ◆ Roy Wu

Consultants--Bedrock of Biotech Industry

- ◆ Kenneth Altera
- ◆ William Buhles
- ◆ Joan Centofanti
- ◆ Mel Chaplin
- ◆ Robin Clark
- ◆ Betty Cohen
- ◆ Jack Cohen
- ◆ Audrey Erbes
- ◆ Kate Forrest
- ◆ Ronald Herman
- ◆ Bonnie Horner
- ◆ Jack Joseph
- ◆ Christine Kaspar
- ◆ Dan Liberthson
- ◆ Chris Mangan
- ◆ Sonia Martinez
- ◆ Barbara Paley
- ◆ Meggi Raeder
- ◆ Mimi Rodes
- ◆ Lynda Sanders
- ◆ Michael Shulman
- ◆ Cookie Straw
- ◆ Herwig von Morze
- ◆ Bonnie Wagner
- ◆ Marion Weinreb
- ◆ John Young

Special Thanks

- ◆ Tom Gutshall
- ◆ Cathy Murphy
- ◆ Mimi Rodes
- ◆ Larry Reynolds
- ◆ Earl Shelton
- ◆ Herwig von Morze
- ◆ Bonnie Wagner
- ◆ And many others who helped

My apologies to anyone overlooked. I'm sure there are many deserving alumni of Syntex Syva whose names I have failed to capture in this presentation. I have added several names from earlier research, subsequent to the actual presentation. My methodology included some basic criteria for inclusion that I used to query individuals and search database resources available to me.

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