The California Healthcare Institute

The California Healthcare Institute is a non-profit public policy research organization for California’s biomedical R&D industry. CHI represents more than 250 leading medical device, biotechnology, diagnostics and pharmaceutical companies and public and private academic biomedical research organizations. CHI’s mission is to advance responsible public policies that foster medical innovation and promote scientific discovery.

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PricewaterhouseCoopers Pharmaceutical and Life Sciences Industry Group

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Cover image: Many branches by J.A. Traeney. This image was designed for the California Biomedical Industry 2010 Report and represents the many branches of the biomedical industry and the people in California and around the world who benefit from its research and innovation. The cells and their placement suggest that anyone at any time in their lives can be touched by a disease and helped by the global advances in healthcare that this important industry provides.

NIH Grants

Data

Data for this analysis come from the National Institutes of Health Office of Extramural Research, available at http://grants.nih.gov/grants/oer.htm. The 2008 data do not include research and development contracts due to the unavailability of that data at the time of publication of this report. Prior year’s data may also not include research and development contracts to ensure comparability across years. The data include all awards to California from NIH, some of which do not necessarily fund basic biomedical research. For example, some grants were used for training programs and projects that are designed to support the research training of scientists for careers in the biomedical and behavioral sciences, as well as to help professional schools to establish, expand, or improve programs of continuing professional education. Other grants were used to fund health policy or behavioral science research. Despite these caveats, overall the NIH grant funding demonstrates the federal commitment to health science research in California. The 2008 data reflected in this report were collected in the fall of 2009. Data for prior years are from the California Biomedical Industry 2009 Report in order to ensure comparability between reports.

The data come in two forms:

2. NIH SBIR and STTR grants: http://grants.nih.gov/grants/Funding/award_data.htm

Product Development

IMS Research Methodology

IMS experts reviewed the IMS Company Profiles database to focus on companies headquartered in or with significant presence in California, and then linked that information to the IMS R&D Focus database to look at products in development.

R&D Focus covers aspects of global pharmaceutical and biotechnology product development, from discovery-stage research to availability on the market. Products including small molecules, monoclonal antibodies, proteins, gene therapies, vaccines and immunotherapies, as well as fixed combination products, biosimilars, in vivo imaging agents/diagnostics are included in the scope of the database. Also covered are compounds in specialized delivery systems, targets for use in drug discovery and research collaborations/discovery programs. Drug design technologies and drug delivery systems are included if they are available for partnering.

The main source of information for R&D Focus are company press releases, company interviews and Web sites, scientific conferences (e.g., ASCO, AACR), academic institutes and universities (including technology transfer offices) and company meetings/R&D days.
What happens in California affects the world. Our fantastic biomedical industry proves this, as our discoveries and advancements speed across the globe, spreading revolutionary treatments, cutting-edge medical devices and groundbreaking research to millions of people. Countless lives are changed and saved thanks to the work that goes on right here in our Golden State.

Of those many lives that are changed, we can’t forget all the Californians who have gainful employment because of our great biomedical industry. This community of thinkers and doers is an engine that powers our economy, generating revenues that will certainly help us emerge from the economic challenges of our times.

My gratitude goes to you and to everyone who plays a role in the success of our biomedical industry, from academic and professional organizations to the individuals in the lab coats and suit coats who are turning the gears of innovation. We have a tremendous legacy to uphold, and I applaud all those who are leading the way and ensuring that California remains a place of learning and invention.

Please accept my gratitude for your actions to improve public health and quality of life in our state and world, along with my best wishes for your continued success.

Sincerely,

Arnold Schwarzenegger
Letter to Our Stakeholders

This report presents a picture of California’s biomedical industry at the beginning of 2010. In these turbulent times, in many respects it is a positive image. Life sciences companies and academic research institutions now directly account for some 274,000 jobs throughout the state. These are high-wage jobs, paying an average of $75,000 annually. Factoring in the multiplier effect—the additional workers who provide services and support for every person working directly for a biomedical firm—the industry represents more than 750,000 jobs. Among high-tech sectors, only the broad field of information technology products and services is larger.

Beyond its pivotal role in the state’s economy, our biomedical industry is a major contributor to global health. From HIV/AIDS to cancer, heart disease and diabetes, California has been the source of breakthrough treatments, extending and enhancing the quality of patients’ lives. And the next chapter of advanced medicine, based on discoveries in genomics, stem cell research, wireless technology and other areas of leading-edge science, is already emerging from our laboratories. California has the talent, intellectual capital and extensive infrastructure to maintain global leadership in life sciences for many years to come.

The trouble is, there’s another side to the balance sheet. Our biomedical industry’s formidable assets and future value are offset by daunting liabilities and serious risks. Of these, the most immediate stem directly from the Great Recession. The meltdown of the worldwide credit markets in 2008 had a disproportionate impact on California. Real estate deflation was catastrophic. Construction and financial services, two of the state’s largest industries, were devastated.

If the biomedical industry was not directly hit by the crash, it could not escape the after-shocks. Stock prices of public companies fell sharply, making it impossible for firms to raise capital through secondary offerings. Development-stage firms with products in clinical trials had to have ample cash reserves to complete their studies or risk being acquired at substantial discounts, if they could remain solvent at all. Even the most successful large pharmaceutical and medical device manufacturers trimmed expenses and limited their strategic investments in smaller firms.

Academic institutions, too, faced unprecedented financial challenges. With a sharp drop in tax receipts and the state swamped by a structural deficit exceeding $20 billion, the University of California, California State University and California Community College systems have all been saddled with deep budget cuts. They have responded by raising tuition and fees, cutting services and class offerings, increasing class sizes while reducing enrollment, and furloughing or laying off staff. Capital improvement projects have been postponed, and hiring freezes are in place.

While many economists suggest that the national economy technically has moved out of recession and is on its way to recovery, California lags behind. In December 2009, the state’s unemployment rate was 12.5 percent, 20 percent above the national average. Until employers step up hiring, California tax receipts continue to drop, foreshadowing more cuts in the next budget cycle. Federal stimulus dollars will run out by the end of 2010, putting extra pressure on the 2011 state budget. Meanwhile, state lawmakers find themselves constrained by ballot initiatives—beginning with Proposition 13, passed in 1978, which narrowly restricts local property taxes—and by needing a two-thirds supermajority to pass a budget or raise taxes.
Recognizing that California’s tax system—overly reliant on high-income earners and corporations—makes the state vulnerable to boom-bust cycles, in 2009 Governor Schwarzenegger and the legislature appointed a Commission on the 21st Century Economy to make recommendations for change. After statewide hearings, the commission’s majority report suggested reducing the marginal tax rate for individuals, eliminating the corporate tax and state portion of sales tax, and replacing these with a so-called “business net-receipts tax.” This would be, in effect, a state value-added tax, applied to services as well as products. Unsurprisingly, the legislature was divided over the commission’s findings, putting off tax reform until 2010 or beyond.

Meanwhile, for all the uncertainty in California’s business environment, national healthcare reform has brought new clouds of unpredictability to the life sciences. The reforms envisioned by Congress have the potential to change the market for drugs, devices and diagnostics in important ways. Government-sponsored comparative effectiveness research, for example, could improve clinical medicine by producing better evidence of which tests and treatments offer the best outcomes. But it could also pose a new set of hurdles for innovative technologies, slowing their time to market and increasing their cost. In the same vein, biosimilars legislation may help reduce the cost of biologics, but raises questions about patient safety and adequate protection of innovators’ intellectual property to encourage future biotech investment. Certainly new taxes and fees on medical technologies, designed to offset some of the cost of expanding access, will weigh on manufacturers’ research and development budgets, though nobody knows the ultimate costs.

More than ever, the sustainability of California’s biomedical industry is influenced by decisions made in Sacramento and Washington. While state and federal legislators cannot control the larger economy, they do set key rules and conditions for the playing field. At the state level, these include:

1. **Higher Education**—The University of California, California State University and community colleges are the foundation for the state’s life sciences workforce and much of the industry’s intellectual property. Without adequate funding they will decline, reducing the California biomedical industry’s competitive edge.

2. **Tax Policy**—Addressing the state’s fiscal crisis and budget imbalance will require major changes to tax policy. These changes will have a long-term impact on companies’ decisions about whether to grow in California, or elsewhere.

3. **Environmental Regulation**—If California leads the United States in clean-tech innovation, it also tends to pass environmental legislation with little thought about the practical consequences.

In 2009 healthcare reform was the biomedical industry’s main concern; in 2010 the focus will shift to the implementation of policy within key federal agencies. Among the most important:

1. **Federal Research Funding**—National Institutes of Health funding benefited from the stimulus package, but pressure to reduce the federal deficit is likely to make recent gains difficult to sustain.

2. **Medicare**—Enormous increases in the federal deficit will bring renewed efforts to contain increases in Medicare spending, with medical technology in the spotlight.

3. **Food and Drug Administration**—The device industry faces legislation to remove FDA preemption while the biotech industry braces for the impact of biosimilars. More important, perhaps, will be the agency’s approach to balancing risks and benefits, and whether its leaders can encourage improved efficiency and responsiveness.

4. **Intellectual Property**—Patent reform legislation stalled in congress, but life sciences companies are likely to see renewed efforts to rewrite patent laws in ways that would weaken intellectual property protections.

Each of these areas is of real importance to the biomedical industry’s future. And each is complicated, both with respect to substance and to partisan politics. If there is any one lesson to be drawn from the past year, it’s that government is prepared to intervene in the market and that industry will suffer if it does not work energetically with legislators to shape policy choices.

David L. Gollaher, Ph.D.  
President and Chief Executive Officer  
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National Life Sciences Partner  
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The biomedical industry produces technological innovation that advances human health. Drugs, medical devices and diagnostics have long played a significant role in the California economy. But the industry entered a new era in 1986 with the founding of the first biotechnology firm, Genentech. Since then the growth of the biotechnology, biologics and biopharmaceutical sectors has been nothing less than astonishing, and much of it has taken place in the Golden State.

California’s preeminence in the life sciences is rooted in the state’s colleges, universities and basic research institutions. They have been the source of thousands of inventions—from synthetic heart valves to genetic engineering to embryonic stems cells—that have inspired entrepreneurs to create new companies throughout the state. And the pace of scientific discovery is accelerating. The mapping of the human genome, advancements in nanoscience, discoveries in stem cell research, the harnessing of bioinformatics, and the advent of cross-functional, multi-disciplined translational research—these are just some of the areas that make 21st-century biomedicine so promising.

Still, realizing the full promise of today’s scientific revolution is enormously complicated, expensive and competitive. Every industrial nation appreciates the value of the life sciences, both in terms of economic development and improved public health. And most are investing to emulate what California has achieved. In 2010, however, California maintains a global advantage. The state has a unique combination of intellectual property, cutting-edge equipment, materials and techniques, world-class research centers, and a highly specialized, well-paid workforce, all infused with an entrepreneurial culture, that may bring many more years of leadership in biomedical discovery and innovation.

Over the past two decades, California has built an unsurpassed biomedical infrastructure. The state is home to world-renowned universities and research institutions that continue to attract the finest minds in medicine, engineering, mathematics and science. These institutions continue to secure the largest share of NIH grants and other government funding. California boasts three of the nine major biomedical clusters in the world, in part because it has created an environment that is conducive to cutting-edge technologies and the emergence of revolutionary new industries.
California is the clear leader in embryonic stem cell research, in nanotechnology, in biologics, and in bioinformatics. These fields are changing and growing at breakneck speed owing to the great intellectual capital at work in California. The immediate payoff in constraining their work might shift funds to cover shortfalls elsewhere. The unacceptable consequence would be to waste the visionary investments that built the world's most accomplished biomedical community in the first place.

Using the latest, most comprehensive data available, this report presents a snapshot of the biomedical industry in 2008, just past its peak. It illustrates all that the biomedical industry offers California and all the state has already invested in the technologies, people, facilities and promise that the industry encompasses.

It is still too soon to measure the full impact of the recent recession, but it remains abundantly clear that the biomedical industry can be a significant player in advancing the state’s economy and securing its future. To harness that potential, California must look again to the promises and possibilities beyond the immediate horizon.

Industry Sectors

The California biomedical industry spans the full range of technologies and entities whose ultimate goal is the improvement of public health, human therapies and the quality of life for patients around the world.

**Basic research** adds to the body of scientific knowledge. California’s universities and public and private research centers provide the training ground for scientists, engineers and technical specialists. They also continue to fuel the state’s legacy of innovation with breakthroughs in basic research, the transfer of technology and formation of spin-off companies.

**Biopharmaceutical companies** include enterprises whose biologics or bioengineered products are produced by altering or replicating proteins (including antibodies) or nucleic acids (DNA, RNA or antisense oligonucleotides) for therapeutic or diagnostic purposes. The category is rounded out by companies developing small-molecule drugs manufactured from chemical compounds.

**Diagnostics** are technologies that help physicians diagnose and better characterize and treat their patients’ conditions. Older examples include pregnancy tests, cholesterol screenings, blood tests and more. Today’s cutting-edge technologies—such as polymerase chain reaction (PCR) assays, mass spectrometry and microarrays—are driving new treatments and research as well as the field of personalized medicine.

**Medical devices** encompass all mechanical tools for improving or diagnosing human health and mobility. “Medtech” includes implants, such as artificial hips, heart valves or dental implants, that are surgically placed to perform a function that the body cannot perform or adequately perform for itself. The category also includes instruments, such as scalpels, lasers, drills and monitors, used by medical professionals in their work.

**Laboratory services** are those service providers that test patient or research samples with precisely calibrated and strictly regulated equipment and procedures to ensure accurate results.

**Wholesale trade companies** manage the import, export and exchange of pharmaceuticals, medical devices, diagnostics and research reagents and other supplies in the global market.
California enters 2010 with its highest unemployment rate in postwar history, 12.5 percent, and economists and political leaders worry that payrolls will not bounce back to 2008 levels for years to come.

Jobs are the main driver of any economy. So concerns about employment are pervasive within California’s biomedical companies and academic research institutions, which are already suffering from pressure on the capital markets, the state budget, government grants and philanthropy. California researchers, innovators and entrepreneurs who work for startup companies or depend on government grants traditionally describe their funding in “months remaining.” This metric is becoming more common even among the state’s largest, best-financed entities as well. With consolidation, layoffs and downsizing among global pharmaceutical firms, the job market is being flooded with highly talented, trained and experienced scientists, engineers and clinicians. It remains unclear how deep the cuts in biomedical employment in California have gone—or what the full impact of employment dislocation through 2009 will turn out to be.

If there is good news in this unfolding story, it is that the biomedical industry possesses the key characteristics correlated with resilient job markets. Recent research by author and urban studies theorist Richard Florida shows that markets with higher numbers of science and engineering, legal and management jobs tend to be most resilient. Likewise, communities with higher percentages of adults with bachelor’s and advanced degrees also fare better in economic downturns.

To measure resilience of job markets, the researcher in November 2009 compared the ratio of unemployed workers to job openings in the 50 largest U.S. metropolitan areas. San Jose, with two unemployed workers for every job opening, and San Francisco, the world’s largest biomedical cluster, with a ratio of 3:1, ranked behind only Washington, D.C. and Baltimore in the survey. (Boston, another top biomedical cluster, also had a 3:1 ratio.)

As the following data show, in 2008 the biomedical industry included a workforce and salary base as vital to the state’s economy and continued leadership role in scientific, engineering and medical excellence as it was to the health and well being of patients the world over.

**Jobs**

In 2008, the biomedical industry employed nearly 274,000 Californians (Figure 1). The industry was not only a pillar in the overall state economy but a significant player in local communities throughout the state as well. The largest concentration of industry-related jobs was in the San Francisco Bay Area. Companies and academia there employed more than 53,000 people. Los Angeles County companies and institutes employed more than 44,000 people, while Orange County recorded over 30,000 biomedical industry jobs. San Diego County rounded out the top four clusters with more than 23,000 industry positions.

**Figure 1: Total Biomedical Employment by Cluster (2008)**

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Employment</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacramento</td>
<td>2,907</td>
<td>1.1%</td>
</tr>
<tr>
<td>Bay Area</td>
<td>53,399</td>
<td>19.5%</td>
</tr>
<tr>
<td>Ventura/Santa Barbara</td>
<td>9,998</td>
<td>3.7%</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>44,093</td>
<td>16.1%</td>
</tr>
<tr>
<td>Orange County</td>
<td>30,270</td>
<td>11.1%</td>
</tr>
<tr>
<td>San Diego</td>
<td>23,479</td>
<td>8.6%</td>
</tr>
<tr>
<td>Riverside/San Bernardino</td>
<td>7,959</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

Examined by sector, the overall biomedical employment in the state included approximately 112,000 people in the medical devices, instruments and diagnostics sectors. That number represented about 41 percent of the overall total jobs. Biopharmaceutical companies employed the next largest segment with more than 81,000 jobs or about 30 percent of the total. The state’s academic research centers employed more than 43,000 people in life sciences positions for approximately 16 percent of the total. Wholesale trade accounted for nearly 32,000 personnel or about 12 percent of the state’s biomedical employees. The remaining 5,400 employees or 2 percent worked in the laboratory services sector.

In the big picture, the industry’s full contribution to employment reaches well beyond workers whose salaries are paid directly by biomedical organizations. It is estimated that approximately 783,000 Californians are employed either part- or full-time because of the life sciences industry. This figure includes those who are employed directly, those hired by companies in the biomedical industry’s supply chain, and those whose jobs rely on spending by biomedical or supply chain employees. Construction, financial and legal professionals—indeed all the jobs associated with providing goods and services to life sciences employees—weigh into the multiplier effect. Combined, biomedical industry-related jobs make up 3.8 percent of the state’s total employment numbers.

Wages

In 2008, California biomedical industry employees earned a total of $20.5 billion. The average annual wage for the industry across the state in 2008 was nearly $75,000, as it was in 2007.

Naturally, the averages continued to vary among the industry’s sectors (Figure 3). Biopharmaceutical companies paid the industry’s highest average annual wages at nearly $109,000 in 2008, a figure that was virtually unchanged from 2007. Wholesale trade came in second with average annual wages of about $80,000, down nearly 6 percent from 2007 levels. Academic research, laboratory services and medical device organizations paid salaries in the mid-$50,000 range in 2008. The more equitable numbers across the sectors as compared to 2007 were due to increases in academic research and laboratory services compensation and a slight decrease among “medtech” jobs.

Adding together the indirect and collateral impact of the biomedical industry on the state, total wages for 2008 were estimated to be $59 billion. Moreover, the value added—the additional value created through employee compensation, proprietors’ income, income to capital owners from property and indirect business taxes—totaled $86 billion.
Trends

In 2008, California’s biomedical industry continued to add jobs (Figure 4) for cumulative growth between 2004 and 2008 totaling approximately 24,000 jobs.

Figure 4: California Biomedical Employment by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>249,591</td>
</tr>
<tr>
<td>2005</td>
<td>255,808</td>
</tr>
<tr>
<td>2006</td>
<td>267,001</td>
</tr>
<tr>
<td>2007</td>
<td>270,791</td>
</tr>
<tr>
<td>2008</td>
<td>273,559</td>
</tr>
</tbody>
</table>


Over the same time period, every biomedical segment except for laboratory services increased its overall employment levels (Figure 5). Growth rates varied among the biomedical industry sectors, however. Biopharmaceutical employment expanded at an average annual rate of 3.14 percent, while laboratory services grew at the slower pace of 0.99 percent.

Figure 5: Biomedical Employment by Year

At the end of the first quarter of 2009, the California biomedical industry had shed more than 2,500 jobs as compared to the same period the year before (Figure 6). Employees of companies or institutions within regional biomedical clusters fared better than those in outlying areas. Given that jobs within all but the Riverside-San Bernardino cluster increased by 2,724, operations in less-concentrated communities lost 5,251 jobs altogether.

In Richard Florida’s study, Los Angeles and San Diego had ratios of six unemployed people for every job opening, and Riverside, which ranked poorest among the California regions, had a 9:1 ratio. Higher ratios are evident in communities with greater shares of blue collar or unskilled jobs. While Los Angeles and San Diego are biomedical hubs, perhaps their diversity among a broader reach of professions and a range of income levels make them more vulnerable to economic downturns.

Figure 6: Change in Total Biomedical Employment (March 2008 to March 2009)

<table>
<thead>
<tr>
<th>Region</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>-2,527</td>
</tr>
<tr>
<td>Bay Area</td>
<td>539</td>
</tr>
<tr>
<td>Los Angeles County</td>
<td>908</td>
</tr>
<tr>
<td>Orange County</td>
<td>334</td>
</tr>
<tr>
<td>Riverside &amp; San Bernardino Counties</td>
<td>-141</td>
</tr>
<tr>
<td>Sacramento County</td>
<td>254</td>
</tr>
<tr>
<td>San Diego County</td>
<td>578</td>
</tr>
<tr>
<td>Ventura &amp; Santa Barbara Counties</td>
<td>111</td>
</tr>
</tbody>
</table>

Certain sectors within the life sciences also were more secure than others (Figure 7). Medical devices, instruments and diagnostics as well as wholesale trade lost nearly 3,000 jobs between March 2008 and March 2009. Because firms in these sectors are more sensitive to market conditions than are academic researchers or biopharmaceutical research and development (R&D) companies, they may have responded more quickly to the economic downturn. It is expected that full-year numbers for 2009 will enable a more informed comparison of job security across biomedical sectors.

**Figure 7: Change in California Biomedical Employment by Sector (March 2008 to March 2009)**

<table>
<thead>
<tr>
<th>Biomedical Sector</th>
<th>Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic Research</td>
<td>173</td>
</tr>
<tr>
<td>Biopharmaceuticals</td>
<td>252</td>
</tr>
<tr>
<td>Laboratory Services</td>
<td>4</td>
</tr>
<tr>
<td>Medical Devices, Instruments &amp; Diagnostics</td>
<td>-2,216</td>
</tr>
<tr>
<td>Wholesale Trade</td>
<td>-739</td>
</tr>
</tbody>
</table>


The biomedical industry is just one of the high-tech sectors for which California is known, yet among high-tech employers it is second in numbers of employees only to computer and Internet-related services and computer and peripheral manufacturing (Figure 8). In 2008 the information technology sectors (including computer and Internet-related services and computer and peripheral manufacturing industries) employed an estimated 435,000 people as compared to the biomedical industry’s 274,000. The next largest employer was the motion picture industry with 163,000 employees.

**Figure 8: California Biomedical vs. Other High-Tech Employment (2008)**

<table>
<thead>
<tr>
<th>Sector</th>
<th>Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Computer and Internet-Related Services</td>
<td>275,615</td>
</tr>
<tr>
<td>Biomedical</td>
<td>273,559</td>
</tr>
<tr>
<td>Motion Pictures</td>
<td>163,392</td>
</tr>
<tr>
<td>Computers and Peripheral Manufacturing</td>
<td>159,306</td>
</tr>
<tr>
<td>Telecommunications</td>
<td>117,539</td>
</tr>
<tr>
<td>Aerospace Manufacturing</td>
<td>73,135</td>
</tr>
</tbody>
</table>


All of the state’s high-tech industries downsized between the first quarter of 2008 and the first quarter of 2009. The job losses in that time period showed the biomedical industry to be the most resilient (Figure 9). The motion picture industry lost nearly 8 percent of its total jobs. Telecommunications employment decreased by more than 5 percent, and the information technology sectors cut 4.5 percent of their jobs. California’s biomedical industry was less than 1 percent smaller at the end of the first quarter of 2009 than it had been a year prior. Again, R&D organizations may be slower than commodity or service firms to cut staff, so more data will be needed to fully gauge the economy’s impacts on life sciences employment.

**Figure 9: Change in California Biomedical vs. Other High-Tech Employment (March 2008 to March 2009)**

<table>
<thead>
<tr>
<th>Sector</th>
<th>Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerospace Manufacturing</td>
<td>-733</td>
</tr>
<tr>
<td>Biomedical</td>
<td>-2,527</td>
</tr>
<tr>
<td>Computer Programming</td>
<td>-11,286</td>
</tr>
<tr>
<td>Computers and Peripheral Manufacturing</td>
<td>-8,417</td>
</tr>
<tr>
<td>Motion Pictures</td>
<td>-12,480</td>
</tr>
<tr>
<td>Telecommunications</td>
<td>-6,107</td>
</tr>
</tbody>
</table>

Among respondents to the most recent California Healthcare Institute (CHI) and PricewaterhouseCoopers (PwC) California Biomedical Industry Survey, most (64 percent) had expanded or sustained their workforce over the previous year. Yet 36 percent had reduced their overall staffing in California. Figure 10 shows that R&D staff was more likely to have been increased, with general and administrative (G&A) staff experiencing the deepest cuts.

**Figure 10: CHI-PwC Survey: Have the following activities expanded, held steady or reduced for your company's operations inside California in the past year?**

<table>
<thead>
<tr>
<th>Overall Workforce</th>
<th>Expand</th>
<th>Hold steady</th>
<th>Reduce</th>
</tr>
</thead>
<tbody>
<tr>
<td>36%</td>
<td>28%</td>
<td>36%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Research and Development</th>
<th>Expand</th>
<th>Hold steady</th>
<th>Reduce</th>
</tr>
</thead>
<tbody>
<tr>
<td>46%</td>
<td>43%</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Manufacturing</th>
<th>Expand</th>
<th>Hold steady</th>
<th>Reduce</th>
</tr>
</thead>
<tbody>
<tr>
<td>28%</td>
<td>61%</td>
<td>11%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>General and Administrative</th>
<th>Expand</th>
<th>Hold steady</th>
<th>Reduce</th>
</tr>
</thead>
<tbody>
<tr>
<td>28%</td>
<td>54%</td>
<td>18%</td>
<td></td>
</tr>
</tbody>
</table>

Almost half of the companies that reduced operations within California in the past year cited the overall business climate and cost of doing business as the cause for cutbacks. Among the respondents, 13 percent had infrastructure established somewhere else that enabled them to reduce their California operations.

**Figure 11: CHI-PwC Survey: If your company's R&D, manufacturing, general and administrative or overall workforces inside California have been reduced in the past year, select the choices (all that apply) that describe why.**

- Overall business climate/cost of doing business: 45%
- Lack of tax incentives/unfavorable tax environment: 4%
- Infrastructure established elsewhere: 4%
- Cash incentives from other regions: 4%
- Qualified workforce elsewhere: 4%
- Willingness to tailor packages to individual company needs elsewhere: 4%
- Cost of living elsewhere: 13%
- Other: 13%

The companies responding to the CHI-PwC Survey that also maintain operations in locations (states or countries) outside of California showed more robust growth out-of-state. That is, most (63 percent) had added out-of-state manufacturing jobs, nearly half (46 percent) had increased their R&D staff, and 31 percent increased their G&A staff outside of California.
Figure 12: CHI-PwC Survey: Have the following activities expanded, held steady or reduced for your company’s operations outside California in the past year?

Looking forward, the respondents to this year’s CHI-PwC Survey remained confident in their ability to sustain and grow their California-based operations (Figure 13) over the next two years. Across the categories, G&A employees were the most at-risk of downsizing, with 19 percent of respondents expecting reductions in that category by the end of 2011.

Figure 13: CHI-PwC Survey: Do you expect the following activities to expand, hold steady or reduce for your company’s operations inside California in the next two years?
As evidence of the erosion of California’s biomedical manufacturing sector, 66 percent of the survey respondents expected to increase their out-of-state manufacturing workforces in the next two years. At the same time, California’s reputation for being the R&D location of choice may also be under pressure. More than half (58 percent) of respondents anticipate adding out-of-state R&D personnel in the coming two years.

Figure 14: CHI-PwC Survey: Do you expect the following activities to expand, hold steady or reduce for your company’s operations outside California in the next two years?

For the most part, the infrastructure that has supported the California biomedical industry remains in place. The people, laboratories and companies that comprise the sector remain committed to one mission: discovering and developing innovative solutions to prevent, treat and manage debilitating human disease and conditions. The state’s biomedical industry remains a vital link to jobs, innovation and a healthy economy. It also is a key instrument in ensuring California’s continuing leadership role in scientific, engineering and medical excellence.
Industry-Supported Programs to Improve STEM Education and Diversity

A number of organizations throughout the United States are working together to excite young people about science, technology, engineering and mathematics (STEM) education opportunities—and the careers for which that training could prepare them. Recognizing that future growth, success and products depend on quality STEM education today, California’s biomedical companies are committed to supporting and developing learning opportunities for the Golden State’s students.

A sampling of STEM programs includes:

Biogen Idec Community Lab

Located within the company’s research campus, the Biogen Idec Community Lab is designed to help transform today’s young students into the discoverers of tomorrow. The Community Lab, open to local middle and high school students and teachers, operates teaching laboratories at Biogen Idec’s headquarters in Cambridge, Mass., and at its research and corporate campus in San Diego. All programs are offered at no cost to participants.

Genentech Foundation

The Genentech Foundation funds schools, universities and nonprofit organizations that share its commitment to furthering health science education to help develop the next generation of scientists. Its current health science education focal areas include pre- and post-doctoral research fellowships at U.S. universities, undergraduate research programs at U.S. universities, and K-12 California-based science education programs.

New Science Teacher Academy (Supported by the Amgen Foundation)

The National Science Teachers Association (NSTA) and the Amgen Foundation co-founded the New Science Teacher Academy to provide new teachers with a meaningful professional development experience and extra support. Each year, 150 Academy Fellows are selected to receive extensive online mentoring from more-experienced teachers in their discipline, in addition to a wide variety of online resources. The Fellows also participate in live Web seminars with nationally acclaimed experts in discussions about specific teaching issues. The program also pays for the Fellows’ attendance at the NSTA National Conference.

The Amgen Foundation committed $3 million over three years to support 500 science teachers in 50 states. The Amgen Foundation has worked closely with NSTA to engage other corporations and funders; last year, Agilent Technologies, Astellas Pharma US, and Bayer all came on board to support additional Academy Fellows.

California’s STEM programs:

- Alliance/Merck Ciencia Hispanic Scholars Program
- Amgen American Society of Hematology Annual High School Symposium
- Amgen Award for Science Teaching Excellence
- Amgen Bruce Wallace Biotechnology Laboratory Program
- Amgen Scholars
- Bay Area Biotechnology Education Consortium
- Bayer’s Making Science Make Sense
- Biogen Idec Community Lab
- Biological Sciences Curriculum Study
- Biotech Partners
- California Academy of Math & Science
- California State University, East Bay MESA Center
- Cedars-Sinai Youth Employment and Development Program
- Chabot Space & Science Center
- Citizen Schools
- Discovery Science Center
- Edwards Lifesciences Fund
- Elementary Institute of Science
- Eugene and Ruth Roberts Summer Student Academy
- Genentech Foundation
- Genentech Scholars
- Girls Incorporated Operation SMART
- High Tech High
- Human BioMolecular Research Institute
- Inner World Discovery
- Johnson & Johnson RxeSEARCH
- Life Sciences Summer Institute
- Medtronic Community Link
- Mentor LA
- Merck Index Women in Chemistry Scholarships
- National Society of Black Engineers (NSBE) Saturday Science, Technology, Engineering, Math and Robotics Program
- New Science Teacher Academy (NSTA) (Supported by Amgen)
- Pfizer Education Initiative
- Pfizer Solutions in Green Chemistry
- Preuss School
- Project SEED
- San Francisco Education Fund
- San Mateo Biotechnology Career Pathway
- Science Buddies
- Science Matters
- Skyline College Biomanufacturing Training Partnership
- Teach For America Amgen Fellows Program
- The Salk Institute High School Summer Enrichment Program
- The Scripps Research Institute High School Student Research Education Program
- United Negro College Fund/Merck Science Initiative
Investment

The business model for life sciences companies has generally worked as follows. Entrepreneurs with an invention, in many instances stemming from an academic research discovery, obtained first-round financing from private investors (friends and family, wealthy individuals and others) to set up companies. As the need for capital increased, many sought venture capital (VC) investment. VC firms raised their money from limited partners, typically entities like university endowments or pension funds. In return for their investments, VCs received equity stakes in startup companies. In order to capture a return on their invested capital, VCs needed a so-called “liquidity event,” that is, a way to convert their ownership stake into cash. The classic liquidity event has been an initial public offering (IPO), when a company offered its shares to the public stock market. More recently, instead of going public, many early-stage companies have been acquired by larger firms, a different way of providing liquidity to investors.

Biomedical companies are capital intensive. (The principal reason for this is the expense of extensive clinical testing required by the U.S. Food and Drug Administration.) At the extreme are biotech firms, which may need to raise $1 billion over a dozen years to bring a novel product to market. But even smaller medical device startups may require $50 million in investment. As the global capital markets deteriorated in 2008, VCs, private equity investors and hedge funds retrenched, with less money available for new companies and available funds being channeled to later-stage ventures. Meanwhile, in order to stay afloat, biomedical companies brought in cash from licensing future rights to their inventions to larger, profitable drug and device manufacturers. The U.S. biomedical industry did benefit from research and development (R&D) stimulus grants managed by the National Institutes of Health (NIH), the American Recovery and Reinvestment Act (ARRA) and other programs for an estimated total of $21.5 billion.

Because biomedical investing is inherently risky—only a small percentage of products ever recoup their investment—the industry’s financing has always been precarious. In a recession it becomes more tenuous yet. As of the third quarter of 2009, an estimated 334 biotechnology companies with an aggregated market cap of $352.1 billion were publicly traded on major U.S. markets. Of those, 135 had less than one year of cash remaining, and 42 percent had less than six months of funding left.

The new data presented here include 2008, three quarters of which took place at the peak of the biomedical industry’s growth and development. The weaknesses revealed in 2008’s performance metrics foreshadowed the downturn wrought in 2009. So did Burrill & Company’s finding that as of the third quarter of 2009, more than 100 U.S. biomedical companies had announced corporate restructurings during the year. Those actions included reducing staff and shelving projects.

Venture Capital

Venture capital drives many of the country’s innovative new companies. All told, venture capital investments in the United States totaled $28.1 billion in 2008 and $17.7 billion in 2009. In both years, half of the national total was put to work by California companies. Venture capital fueling the state’s industries in 2008 totaled more than $14 billion through over 1,600 deals involving more than 1,300 companies. In 2009, nearly $9 billion was put to work via more than 1,100 deals and over 900 companies.

Figure 15: Venture Capital Investment in California Companies by Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Companies</th>
<th>Deals</th>
<th>Investment ($MM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>1,126</td>
<td>1,380</td>
<td>7,448</td>
</tr>
<tr>
<td>1999</td>
<td>1,737</td>
<td>2,197</td>
<td>21,834</td>
</tr>
<tr>
<td>2000</td>
<td>2,361</td>
<td>2,935</td>
<td>41,255</td>
</tr>
<tr>
<td>2001</td>
<td>1,295</td>
<td>1,527</td>
<td>15,883</td>
</tr>
<tr>
<td>2002</td>
<td>930</td>
<td>1,075</td>
<td>9,085</td>
</tr>
<tr>
<td>2003</td>
<td>939</td>
<td>1,140</td>
<td>8,289</td>
</tr>
<tr>
<td>2004</td>
<td>1,051</td>
<td>1,241</td>
<td>9,984</td>
</tr>
<tr>
<td>2005</td>
<td>1,131</td>
<td>1,322</td>
<td>10,888</td>
</tr>
<tr>
<td>2006</td>
<td>1,294</td>
<td>1,564</td>
<td>12,757</td>
</tr>
<tr>
<td>2007</td>
<td>1,367</td>
<td>1,663</td>
<td>14,605</td>
</tr>
<tr>
<td>2008</td>
<td>1,340</td>
<td>1,626</td>
<td>13,999</td>
</tr>
<tr>
<td>2009</td>
<td>958</td>
<td>1,137</td>
<td>8,858</td>
</tr>
</tbody>
</table>

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTreeTM Report based on data from Thomson Reuters.
The largest beneficiaries in the state were the biotechnology, medical devices and equipment, semiconductor, media and entertainment, and telecommunications industries (Figure 16). Yet the biomedical industry, which combines biotechnology and medical devices and equipment, secured the bulk of the investment dollars (Figure 17) at approximately $3.5 billion in 2008 and $2.6 billion in 2009.

Figure 16: Percent of Total U.S. Venture Capital to California Firms and, by Percentage, to Biotechnology and Medical Device Companies

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Venture Capital Investments ($MM)</td>
<td>$27,992</td>
<td>$17,680</td>
</tr>
<tr>
<td>Percentage of VC in California</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Percentage of CA VC in Biotechnology</td>
<td>13%</td>
<td>16%</td>
</tr>
<tr>
<td>Percentage of CA VC in Med Devices</td>
<td>11%</td>
<td>13%</td>
</tr>
</tbody>
</table>

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report based on data from Thomson Reuters.

For the country, VC investment in life sciences companies totaled $7.8 billion in 2008 and $6.0 billion in 2009. As in the past, in 2008 and 2009 California companies also attracted the largest share of U.S. life sciences venture capital (Figure 18).

Figure 17: Top Five Industries in California by VC Investment

<table>
<thead>
<tr>
<th>Industry</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotech/Medical Devices</td>
<td>$3,481,915,900</td>
<td>$2,597,945,600</td>
</tr>
<tr>
<td>Software</td>
<td>$2,635,232,800</td>
<td>$1,665,063,100</td>
</tr>
<tr>
<td>Industrial / Energy</td>
<td>$2,319,824,000</td>
<td>$1,213,303,800</td>
</tr>
<tr>
<td>Media and Entertainment</td>
<td>$1,046,410,500</td>
<td>$709,992,200</td>
</tr>
<tr>
<td>Semiconductors</td>
<td>$1,168,699,000</td>
<td>$645,477,100</td>
</tr>
</tbody>
</table>

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report based on data from Thomson Reuters.

Figure 18: Venture Capital Investment in Life Sciences by State ($MM)

<table>
<thead>
<tr>
<th>State</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA</td>
<td>$4.5</td>
<td>$4.0</td>
<td>$4.0</td>
</tr>
<tr>
<td>MA</td>
<td>$3.0</td>
<td>$2.5</td>
<td>$2.5</td>
</tr>
<tr>
<td>NJ</td>
<td>$1.5</td>
<td>$1.0</td>
<td>$1.0</td>
</tr>
<tr>
<td>CO</td>
<td>$0.5</td>
<td>$0.5</td>
<td>$0.5</td>
</tr>
<tr>
<td>WA</td>
<td>$0.5</td>
<td>$0.5</td>
<td>$0.5</td>
</tr>
<tr>
<td>NC</td>
<td>$0.5</td>
<td>$0.5</td>
<td>$0.5</td>
</tr>
<tr>
<td>PA</td>
<td>$0.5</td>
<td>$0.5</td>
<td>$0.5</td>
</tr>
<tr>
<td>MN</td>
<td>$0.5</td>
<td>$0.5</td>
<td>$0.5</td>
</tr>
<tr>
<td>MD</td>
<td>$0.5</td>
<td>$0.5</td>
<td>$0.5</td>
</tr>
<tr>
<td>CT</td>
<td>$0.5</td>
<td>$0.5</td>
<td>$0.5</td>
</tr>
</tbody>
</table>

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report based on data from Thomson Reuters.
Figure 19 shows how California’s share of life sciences VC investments were allocated between biotechnology and medical device companies over the past three years.

**Figure 19: California Life Sciences Venture Capital Investment by Sector, 2007 to 2009 ($MM)**

Focusing on U.S. investment in biotechnology companies shows that support remained strong in the early quarters of 2008, with the dampening effect of that year’s global credit crisis apparent by year end (Figure 20). The total U.S. venture capital investment in biotechnology of $4.3 billion in 2008 marked an 18 percent decline from the prior year’s total—and the historical peak—of $5.3 billion. The full effects of the damage became apparent in 2009 with the year-end total of $3.5 billion in biotechnology VC investment down nearly another 19 percent from the 2008 level.

**Figure 20: U.S. Biotech Venture Capital Over Past 10 Years**

<table>
<thead>
<tr>
<th>Year</th>
<th>Investments ($MM)</th>
<th>Number of Deals</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>$1,503</td>
<td>279</td>
</tr>
<tr>
<td>1999</td>
<td>$2,031</td>
<td>270</td>
</tr>
<tr>
<td>2000</td>
<td>$3,987</td>
<td>353</td>
</tr>
<tr>
<td>2001</td>
<td>$3,359</td>
<td>339</td>
</tr>
<tr>
<td>2002</td>
<td>$3,212</td>
<td>315</td>
</tr>
<tr>
<td>2003</td>
<td>$3,602</td>
<td>348</td>
</tr>
<tr>
<td>2004</td>
<td>$4,233</td>
<td>390</td>
</tr>
<tr>
<td>2005</td>
<td>$4,047</td>
<td>398</td>
</tr>
<tr>
<td>2006</td>
<td>$4,611</td>
<td>471</td>
</tr>
<tr>
<td>2007</td>
<td>$5,287</td>
<td>494</td>
</tr>
<tr>
<td>2008</td>
<td>$4,351</td>
<td>501</td>
</tr>
<tr>
<td>2009</td>
<td>$3,543</td>
<td>406</td>
</tr>
</tbody>
</table>

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report based on data from Thomson Reuters.
A closer look at the allocation of VC investments in correlation with companies' stages of development (Figure 21) also is revealing. Historically, venture capitalists have funded R&D firms from startup through development and commercialization—whether for therapeutic use for patients or as assets for larger pharmaceutical or device companies. With increasing risks, costs and competition, however, venture capitalists have become most interested in funding companies that are close to launching a new therapy or device or entering into a licensing or merger transaction.

**Figure 21: Venture Capital by Stage**

**U.S. Biotechnology**

<table>
<thead>
<tr>
<th>Year</th>
<th>Start-up/Seed stage</th>
<th>Early stage</th>
<th>Expansion stage</th>
<th>Later stage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Investment ($MM)</td>
<td>Number</td>
<td>Investment ($MM)</td>
<td>Number</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Investment ($MM)</td>
<td>Number</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Investment ($MM)</td>
<td>Number</td>
</tr>
<tr>
<td>2008</td>
<td>$535</td>
<td>118</td>
<td>$1,185</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$1,287</td>
<td>119</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>$1,364</td>
<td>124</td>
</tr>
<tr>
<td>2009†</td>
<td>$656</td>
<td>94</td>
<td>$1,386</td>
<td>138</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$529</td>
<td>61</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>$976</td>
<td>113</td>
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<td></td>
<td>$1,191</td>
<td>212</td>
<td>$2,571</td>
<td>278</td>
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<td></td>
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<td></td>
<td>$1,796</td>
<td>180</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>$2,336</td>
<td>237</td>
</tr>
</tbody>
</table>

**U.S. Medical Devices**

<table>
<thead>
<tr>
<th>Year</th>
<th>Start-up/Seed stage</th>
<th>Early stage</th>
<th>Expansion stage</th>
<th>Later stage</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Investment ($MM)</td>
<td>Number</td>
<td>Investment ($MM)</td>
<td>Number</td>
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<td>Number</td>
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<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Investment ($MM)</td>
<td>Number</td>
</tr>
<tr>
<td>2008</td>
<td>$285</td>
<td>63</td>
<td>$662</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$929</td>
<td>96</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>$1,532</td>
<td>120</td>
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<tr>
<td>2009†</td>
<td>$424</td>
<td>63</td>
<td>$807</td>
<td>99</td>
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<td></td>
<td></td>
<td></td>
<td>$372</td>
<td>58</td>
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<td>$898</td>
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</tr>
<tr>
<td></td>
<td>$710</td>
<td>126</td>
<td>$1,469</td>
<td>203</td>
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<td></td>
<td></td>
<td></td>
<td>$1,301</td>
<td>154</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>$2,431</td>
<td>209</td>
</tr>
</tbody>
</table>

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report based on data from Thomson Reuters.
† Note: Includes data through 3rd quarter of 2009.

**Revenues**

California’s life sciences companies continued to expand through 2008 (most recent data available). Total revenues from the state’s biomedical sectors of $75.9 billion marked a nearly 2 percent increase over the $74.5 billion generated in 2007. Most of the revenues were attributed to product sales by such California-headquartered biopharmaceutical powerhouses as Genentech, Amgen, Gilead Sciences and Allergan, as well as medical technology leaders Edwards Lifesciences, Gen-Probe and Illumina. When one surveys the industry statewide, however, it’s clear that it remains immature, with the vast majority of companies still developing their first products, months and years away from product revenues and profitability.

**Market Capitalization**

At the beginning of 2009, the U.S. biotechnology industry’s total market capitalization was $404 billion. With the Roche Group’s acquisition of Genentech, Inc. (valued at $100 billion), the industry’s market cap dipped below $300 billion in May. At the start of 2010, however, the number had recovered to $350 billion—up 16 percent from the low point.

**The Current Reality**

Today’s investors—venture capitalists, companies seeking strategic acquisitions or licenses, funds and individuals—are dealing with numerous unknowns. Although the recession may be diminishing in technical terms, confidence will be slow in returning until economists see a positive trend in employment, stability in the housing markets, and increased productivity and sales. Those who would invest in the biomedical industry are waiting to see what shape healthcare reform takes and how its cost-control measures change the risk-reward ratios for potential new therapies. Would-be entrepreneurs are pragmatically gauging the best time and means to found their companies and, in some cases, deciding that this is not the time.

Despite the promise of breakthrough new drugs, devices and diagnostics for unmet medical challenges, the current economy is struggling to sustain demand even for services and commodities that have long been deemed necessities.

**Thoughts on the Future**

Respondents to the CHI-PwC Survey anticipate that the next two years will find them in a holding pattern at best, navigating risks and events that have not been part of the biomedical industry experience. For instance, 78 percent expect expanded M&A activity along with accelerated consolidation of the industry. More than half expect bankruptcies, which were virtually unheard of in the industry before 2008, to increase. Only 4 percent expect a reduction in bankruptcies.

On the positive side, nearly half predict increased revenues and 44 percent expect revenues to remain steady. Nearly a quarter of the respondents foresee an expansion in R&D investment and in access to capital, and 40 percent believe there will be an increase in industry IPOs.
Figure 22: CHI-PwC Survey: Do you think the following activities for the biomedical industry in California will increase, stay the same, or decrease in the next two years?

<table>
<thead>
<tr>
<th>Activity</th>
<th>Increase</th>
<th>Stay the same</th>
<th>Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mergers and Acquisitions</td>
<td>78%</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>IPOs</td>
<td>40%</td>
<td>44%</td>
<td>16%</td>
</tr>
<tr>
<td>Bankruptcies</td>
<td>52%</td>
<td>44%</td>
<td>4%</td>
</tr>
<tr>
<td>Industry Revenues</td>
<td>48%</td>
<td>44%</td>
<td>8%</td>
</tr>
<tr>
<td>Access to Capital</td>
<td>24%</td>
<td>60%</td>
<td>16%</td>
</tr>
<tr>
<td>Excess Debt</td>
<td>27%</td>
<td>65%</td>
<td>8%</td>
</tr>
<tr>
<td>R&amp;D Investment</td>
<td>23%</td>
<td>54%</td>
<td>23%</td>
</tr>
</tbody>
</table>

State Priorities

Other states, as well as countries around the world, are assertively pursuing biomedical companies. The current economic environment may tip the scales in favor of relocating if continuing to do business in California is deemed too expensive or difficult. Participating business leaders in this year's CHI-PwC Survey cited corporate taxation (72 percent as “extremely important”) as the most important issue in keeping companies in California (Figure 23). Tax incentives for innovation came in at 69 percent “extremely important,” with workforce preparedness ranked extremely important by 62 percent of respondents.

Figure 23: CHI-PwC Survey: Rate the influence of each of the following issues on the industry’s ability to keep biomedical research, innovation and investment in California.

<table>
<thead>
<tr>
<th>Issue</th>
<th>Extremely Important</th>
<th>Somewhat Important</th>
<th>Not at all Important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corporate Taxation</td>
<td>72%</td>
<td>24%</td>
<td>4%</td>
</tr>
<tr>
<td>Tax Incentives for Innovation</td>
<td>69%</td>
<td>28%</td>
<td>3%</td>
</tr>
<tr>
<td>Workforce Preparedness</td>
<td>62%</td>
<td>35%</td>
<td>3%</td>
</tr>
<tr>
<td>State Environmental Regulations</td>
<td>38%</td>
<td>59%</td>
<td>3%</td>
</tr>
</tbody>
</table>
In the area of tax incentives for innovation, the respondents to the CHI-PwC Survey cited R&D tax credits as the most important with allowances for net operating losses ranked second and single sales factor rounding out the responses (Figure 24).

**Figure 24: CHI-PwC Survey: Rate the influence of each of the tax incentives for innovation on the industry’s ability to keep biomedical research, innovation and investment in California.**

![Tax Incentives](image)

Among California environmental regulations of concern to biomedical companies, chemical bans and manufacturing restrictions were rated as most important (tied at 62 percent). Both of those issues and product stewardship had combined “somewhat important” and “extremely important” scores of 97 percent. Only 3 percent of life science company respondents felt that environmental regulations “were not important at all” in keeping research, innovation and investment in California.

**Figure 25: CHI-PwC Survey: Rate the influence of each of the state environmental regulations on the industry's ability to keep biomedical research, innovation and investment in California.**

![Environmental Regulations](image)

**Federal Policies**

As for federal policies that impact their businesses, survey respondents ranked the regulatory process as the most important (89 percent) with patent reform second (86 percent). Figure 26 depicts the participants’ responses.
Drilling down into respondents’ thoughts on federal tax and finance issues, the CHI-PwC Survey showed that R&D tax credits were of the most interest, followed by the federal manufacturing excise tax. Repatriation, which ranked third among the key issues, was rated at least as “somewhat important” by 100 percent of the respondents.
The final question in the CHI-PwC Survey sought participants’ perceptions about threats to the future of the biomedical industry’s growth over the next five years (Figure 28). Most—88 percent—pointed to price controls and government intervention, a response to the ongoing debate and progress in Washington regarding healthcare reform. At the same time, 84 percent felt that a risk-averse FDA, which would make drug, device and diagnostics approvals more difficult to secure, would set the industry back. While none of the other topics gleaned as many “extremely important” ratings, only foreign competition and product liability were seen as “not important at all” by more than 8 percent of the participants.

Figure 28: CHI-PwC Survey: Rate how you perceive the greatest threats to the industry’s growth in the next five years.
Since the inception of the biotechnology industry in the mid-1970s, startup companies have looked to venture capitalists to help them move innovations through human trials and into medical practice. This endeavor requires a lot of assistance: the drug development process can take more than 12 years and $1.2 billion. This is the cost for the approximately 10 percent of drug candidates that are successfully commercialized. Nearly 90 percent will fail in development.

Working with emerging companies, venture capitalists often provide five to eight years of equity to startups whose stock essentially is valueless. The goal for both the investor and the company is to advance the potential product through Phase I and Phase II clinical trials and use positive results to complete an initial public offering (IPO) or to engage in a merger and acquisition transaction to regain their investment and advance therapies to the patients who need them.

The firms that have successfully negotiated this pathway have been well rewarded for their work. They are also only a very select group (Figure 29).

The current economic climate is threatening the formation, funding and forward progress of small biomedical companies—and the therapies, cures and technologies of the future.

With the stock market crash of 2008, institutional investors rebalanced their risk in part by reducing their venture capital investments. Even venture capital firms specializing in biotechnology are using their reserves to fund their prior investments rather than seeking out new startups.

Although three specialty pharmaceutical companies completed IPOs in the summer and fall of 2009, the IPO window has been essentially shuttered.

As the economy recovers, venture capitalists and other investors will return to biotechnology in proportion to their assessment of the overall lifecycle risks and the lifecycle duration of potential products. They also will calculate the potential value of their investment at their exit. That means that California’s biomedical industry entrepreneurs need to use this time to verify the validity of their ideas, shore up their business plans and lay the groundwork for bringing their dreams to fruition—and trust that investors continue to see the value of biomedical breakthroughs.

**Figure 29: Biotechnology Companies by Stage of Development**

- US companies started (since 1980): 1,800
- Public: 237
- Generating revenue today: 178
- Made more than spent: 6
  - Amgen
  - Biogen Idec
  - Genentech
  - Genzyme
  - Gilead Sciences
  - Medimmune

Of the more than 1,800 U.S. biotechnology companies founded since 1980, fewer than 200 are generating revenues on product sales today. Of those, only six have earned more than they spent in development. Amgen, Genentech and Gilead Sciences are the California-headquartered companies in that group.

Note: The content for this page was derived from the presentation Amgen made to the California Assembly and Senate Select Committees on Biotechnology Informational Hearing on June 18, 2009.
Entrepreneurs with breakthrough technologies should use their passion and resources to drive their discoveries—not to reinvent the wheel.

That is the premise behind the San Jose BioCenter, a science and technology incubator co-sponsored by the San Jose Redevelopment Agency and the San Jose State University Research Foundation. The BioCenter is a 40,000-square-foot, state-of-the-art research facility that houses 40 life sciences and cleantech companies. Its mission is to provide emerging science and technology companies with a “big company advantage” through a new generation of specialized facilities, capital equipment, full laboratory and operational services, along with commercialization support, contacts and expertise. With that infrastructure in place, the BioCenter helps emerging companies with compelling promise to apply their time and capital towards advancing their discoveries and accelerating their path to market.

Opened in 2004, the BioCenter has already guided an impressive list of emerging companies to independence, whether as standalone entities or partners, acquisitions or subsidiaries of larger firms. In fact, the BioCenter reports that its clients have raised more than $800 million in growth capital and have fostered more than 600 jobs, all of which has helped bolster the local economy.

Establishing the BioCenter required significant commitment and funding from its founding partners. The San Jose State University Research Foundation and the San Jose Redevelopment Agency invested approximately $10 million in facilities and equipment at the BioCenter. Prescience International, a firm that specializes in starting and managing centers of excellence, oversees operations of the incubator facility and provides world-class lab operations and commercialization services. The public-private partnership works closely with the portfolio companies to provide access to the resources, networks and experience they need to commercialize their technologies.

Also believing in the strength of synergies among its affiliate and resident companies, the BioCenter is home to complementary enterprises in drug development, diagnostics, device, nanotech, clean technology, energy, material science, bioinformatics and biophotonics. It further balances its portfolio with companies at various stages of development and affiliate members from around the globe.

To help ensure that client companies become significant, long-term market leaders, the BioCenter selects firms that meet a number of key criteria. Successful candidates must have credible teams in business, science and technology. Each must be working in an area of significant medical or market need, and their products must represent a qualified and profitable market opportunity. They must be pursuing a compelling discovery or technology for which they own or are securing intellectual property rights. And they must demonstrate financial solvency.

Executive Director Melinda Richter noted that even though the BioCenter stands out among its peers in regard to its specialized facilities, capital equipment and laboratory and business services, it operates on a model that could and should be replicated elsewhere. “Our novel yet efficient common-sense model changes the probability of success of innovation; it makes the process faster, less expensive, less risky, and more likely to succeed,” she said. “This model allows for more innovations in the pipeline and for companies to prove out their technology faster and to bet on the things that win.”
Both comparative effectiveness research and changes to reimbursement and incentives have the potential to positively impact our nation’s healthcare system, encourage the sort of innovation that is well-grounded in California, and accelerate the advancement of new approaches to diagnosis and treatment of a broad range of patient conditions. But they also can stop innovation in its tracks if they create an environment in which private capital is no longer attracted because the potential returns are low or come with greater levels of risk.

Much energy and spirited debate throughout 2009 has centered on our healthcare system, with its marvelous strengths and glaring weaknesses. In the end, national healthcare reform may lead to significant changes in the way our biomedical ecosystem operates. This is of particular interest in California, given its leadership in biomedical innovation. Healthcare reform elements that impede the flow of innovation would harm Californians, as well as patients around the world who stand to benefit from the research, clinical development, manufacturing and commercialization of diagnostics, pharmacotherapeutics and devices.

Essential to California’s biomedical ecosystem is the flow of investment capital to scientific research areas that show the most promise and that investors believe would yield a profitable return. While federal and state governments provide funding for basic discovery research, private capital is vital to take science from the laboratory to the clinic.

Over the next five years, due to a number of dynamics that are playing out globally, the biopharmaceutical industry faces particular stress in funding innovation investments. For starters, companies are facing the loss of patent protection for many of their leading drugs, which currently generate sales of more than $135 billion. As these drugs succumb to generic competition, the commercial impact is unlikely to be offset by new products. The result is expected to be historically low levels of industry growth in the United States and around the world. The fragile state of economic recovery also is dampening the demand for—and funding of—innovative biopharmaceuticals. Meanwhile, the costs and complexity of developing new products are rising substantially relative to their potential commercial value. Attrition rates for new drug candidates remain very high, especially for the most innovative approaches, leading to an increase in the total investment required to yield just one successful product. Regulatory requirements also are on the increase, resulting in more expensive clinical trials and evidence development before new drugs can be made available to patients. Ongoing risk management activities and programs once a product is launched also add to the cost and complexity.
In the near term, healthcare reform—the details of which remain undecided at the time of this writing—may have little impact on funding for the investment in the flow of innovative products. However, the direct and indirect impact longer term may be more significant.

In particular, two areas likely to be a part of legislated change in 2010—comparative effectiveness research, and changes in drug and diagnostic reimbursement and incentives—require special attention to ensure that they advance medicine and patient access while maintaining the flow of capital to sustain investment in innovation.

Comparative effectiveness research: The systematic evaluation of alternative approaches to treatment can bring enormous benefits to patients, as it informs physicians’ understanding of what to do for specific patients. In fact, the ability to identify what works best is entirely consistent with the science-based objectives of genomic technologies that are being developed in California to enable a better genomic-based understanding of disease, its diagnosis and treatment.

However, the experiences of many countries that have adopted national health technology assessment in one form or another during the past two decades—notably Australia, Canada, England, Sweden, France and Germany—provide some useful lessons for the United States. One hopes that we can avoid the tension that exists elsewhere among stakeholders when it comes to the usefulness and application of comparative effectiveness research.

These lessons include ensuring that comparative effectiveness research is conducted at the appropriate patient-segment level, rather than a “one-size-fits-all” approach. This would represent the antithesis of the personalized medicine approach so many companies are pursuing.

The definition of “patient segment” is complex, based not only on the presence or absence of specific genetic markers, but also on the extent of disease progression, presence of co-morbidities, etc. And this definition may need to change over time based on advances in scientific and clinical understanding.

In addition, comparative effectiveness research needs to be designed carefully to ensure that what is being compared is meaningful and advances clinical understanding. For example, the isolated comparison of one diagnostic test versus another without considering the full downstream effects to the healthcare system may be technically correct but hardly a useful comparison. Similarly, the comparison of one therapeutic to another needs to be performed in the context of the full course of interventions for a patient.

Finally, comparative effectiveness gets used in many different ways—from setting broad treatment protocols for all patients, to serving as the basis for rationing of healthcare, and restricting access based on cost-effectiveness. And there is enormous risk from research being designed for one purpose and used for another. Because we are operating in a very dynamic scientific area, the continuous use of retrospective analysis is needed, along with prospective studies to ensure that findings and conclusions are updated and current based on the best available information.

The movement toward comparative effectiveness research can be positive—and indeed essential to the full embrace of personalized medicines—but the challenges in designing and implementing studies are substantial, dynamic and interrelated.

Drug and diagnostic reimbursement and incentives: The promise of healthcare reform is that over time it will enable us to move toward a more rational system than we currently have—one that rewards efficient use of our provider system, more accurate diagnosis and quicker resolution of a patient’s disorder. An essential element involves a balanced approach to reimbursement that accepts higher costs in some parts of the healthcare budget if they can be more than offset by lower costs in other areas. For example, potentially higher spending on better and speedier diagnosis can lead to lower overall spending on treatment. Our reformed system for reimbursement must fully embrace the prospect that patients can be pre-identified through diagnostics to determine which therapeutic will likely be most effective, and at what dosage. And, to encourage their further development and adoption, we need a reimbursement approach that recognizes the value of this linkage between diagnostics and therapeutics brings to the entire healthcare system.

Managing healthcare costs in silos of expenditures—with separate budgets for diagnostic tests, drugs, physician services, hospital stays, surgical interventions and rehabilitation services—does not lead to optimal healthcare system management and inevitably drives higher overall costs. Managing healthcare expenses—and rewarding those parts of the system that can help lower costs while maintaining or improving patient care and outcomes—is an essential part of successful reform. Absent these changes to reimbursement and incentives, the current distortions, inefficiencies and growing healthcare funding deficits will surely increase. The incentives to encourage investment in innovation that can lead to improved outcomes at a lower cost—and consequently the advances that healthcare reform should be encouraging—will be missing.
Global sales of all biotechnology and pharmaceutical products reached $719 billion in 2008, reflecting growth of 5.4 percent over the prior year. Of this total, biologic products contributed about $120 billion. Biologics can include products such as vaccines, blood and blood components, gene therapy, tissues, monoclonal antibodies and recombinant therapeutic proteins created by genetic engineering.

Michael Kleinrock, IMS

Michael Kleinrock is director, Thought Leadership at IMS, responsible for leading a team of analysts covering U.S. and global issues and trends in the pharmaceutical market. He joined IMS in 1999 and served in a variety of roles supporting key pharmaceutical clients as well as developing products and services. Since joining IMS’ thought leadership team in 2006, he has taken on increasing responsibility for U.S. market analytics, oncology, R&D pipeline analysis and market forecasts. Named to his current role in November 2009, he was previously senior manager, Thought Leadership. Kleinrock received a master’s degree in journalism from the University of London, Goldsmiths College in 1996. He also earned a bachelor of arts degree in history and politics from the University of Essex, Colchester, England, in 1994.

California remains an important source of the scientific innovation that creates the commercial value of these products and the benefits they bring to patients around the world. In fact, at the end of August 2009 there were some 869 products in the California biopharmaceutical pipeline, including those in pre-clinical and clinical development through registration. The pipeline includes products that California companies originated or invested in to address a broad range of diseases. The California biopharmaceutical pipeline represents about 15 percent of the total worldwide biopharmaceutical pipeline of 5,850 products.

### Figure 30: Top Diseases Foci in California’s Product Pipeline

<table>
<thead>
<tr>
<th>Disease Focus</th>
<th>Number in CA Pipeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncologics</td>
<td>272</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>117</td>
</tr>
<tr>
<td>Immune System and Inflammation</td>
<td>110</td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>109</td>
</tr>
<tr>
<td>Cardiovascular and Blood Diseases</td>
<td>70</td>
</tr>
<tr>
<td>Diabetes and Metabolics</td>
<td>66</td>
</tr>
</tbody>
</table>

Source: IMS Health R&D Focus, July 2009

### Figure 31: Number of Biopharmaceuticals in California Product Pipeline

Source: IMS Health R&D Focus, July 2009
While successes and setbacks in scientific research are normal, there were some significant developments last year that are worth noting. Since January 1, 2008, six new products with connections to California were approved and launched in the United States:

- **Promacta** (eltrombopag), launched by San Diego-based Ligand Pharmaceuticals, is a medication that has been developed for conditions that lead to thrombocytopenia (abnormally low platelet counts).
- Thousand Oaks-based Amgen’s **Nplate** (romiplostim) is a fusion protein analog of thrombopoietin, a hormone that regulates platelet production.
- Bausch & Lomb’s **Besivance** eye drops (besifloxacin ophthalmic suspension) was approved in May 2009 for the treatment of bacterial conjunctivitis. Besivance is the first antibacterial in the fluoroquinolone class to be specifically developed for use in the eye.
- In October 2009, Allos’ **Folotyn** (pralatrexate) was launched in the United States as the first and only treatment for relapsed or refractory (resistant to treatment) peripheral T-cell lymphoma, which is a diverse group of aggressive blood cancers that has a poor prognosis. It received accelerated approval from the U.S. Food and Drug Administration for this indication in September 2009. It is also being developed for other oncologic therapies.
- **Pristiq** (desvenlafaxine) from Pfizer (formerly Wyeth) was approved by the FDA in March 2008 for the treatment of major depressive disorder (MDD) in adults and launched in the United States in April 2008. The drug is also in development for the treatment of vasomotor symptoms (such as hot flashes) associated with menopause.
- **Lexiscan** (regadenoson) is being developed by Foster City-based Gilead Sciences (through its 2009 acquisition of CV Therapeutics) and Astellas in the United States as a drug to simulate cardiac stress in patients too weak or infirm to perform an exercise-based test for heart disease.

There are additional products in several important areas, such as central nervous system and infectious disease, which have been approved but have yet to launch. These include:

- **Fanapt** (iloperidone), which was licensed by Vanda Pharmaceuticals in the United States from Sanofi-Aventis (also known as Fanapt, Fanapt, and previously as Zomaril) is an atypical antipsychotic for the treatment of schizophrenia.
- Forest’s **Savella** (milnacipran) is a psychoactive drug that functions as a serotonin-norepinephrine reuptake inhibitor (SNRI). It is used for the treatment of clinical depression as an antidepressant and for chronic pain, especially fibromyalgia.
- Another is **Vibativ** (telavancin) by Theravance, a synthetic derivative of vancomycin, which is a glycopeptide antibiotic indicated for life-threatening staphylococcal infections resistant to other antibiotics (also called MRSA, the so-called super-bugs).

At the same time, three products had delays or were discontinued, reflecting the typical challenges facing innovative companies in the biopharmaceutical market today:

- One of the oncologic products highlighted in the 2009 CHI/PwC California Biomedical Industry Report was **Prolia** (denosumab), a fully human monoclonal antibody for the treatment of osteoporosis, treatment-induced bone loss, bone metastases, rheumatoid arthritis, multiple myeloma and giant cell tumor of bone. The FDA has delayed its approval decision seeking more information from Amgen. It is unclear how long it will take for Amgen to meet the requests, but according to public statements the company plans to respond to the requests soon. Analysts on Wall Street believe that the approval will come at the beginning of 2010.
Victoza (liraglutide) is one of a new class of type 2 diabetes therapies called GLP-1 (a naturally occurring hormone that controls appetite and insulin levels in non-diabetics). The drug, which is being developed by Novo Nordisk and is licensed from the California company Scios, experienced a split FDA panel review; once daily dosing, cardiovascular safety and weight management were clear advantages, but concern over cancer risk remains unresolved.

Two other products were discontinued by their California developers. In March 2009, San Diego-based Cadence Pharmaceuticals announced it has discontinued development of Omigard (omiganan) after it failed to meet its primary trial objective of prevention of central venous catheter-related bloodstream infections. In January 2009, Menlo Park-based Cogentus Pharmaceuticals filed for bankruptcy protection and as a result terminated the development of CGT 2168, a once-daily tablet formulation of a fixed combination of clopidogrel and omeprazole, as thrombosis therapy that minimizes the side effects of gastrointestinal bleeding and ulcers.

**Key Therapy Areas**

The top six disease focal areas comprised 86 percent of the California pipeline, with oncology research and development remaining on top with 272 products. What follows is an outline of products under development in California within some of the most important therapeutic areas.

![Figure 32: Number of Biopharmaceuticals in California Product Pipeline by Disease Foci](image-url)
Cancer is the second-leading cause of death in California after heart disease, causing more than 50,000 deaths each year, according to the American Cancer Society.

Amgen, Genentech and Exelixis (all headquartered in California) have numerous pipeline products in oncology. Amgen is developing motesanib, currently in Phase III evaluation; it targets the receptor activation that results in the overexpression, mutation, and autocrine production of growth factors, which are a common factor in a variety of cancers. Genentech, based in South San Francisco, is currently developing R 7347, an anti-neuropilin-1 (NRP-1) antibody for the treatment of solid tumors; it is currently in Phase I development. Exelixis, based in South San Francisco, is developing foretinib, an orally administered multi-kinase inhibitor for the treatment of stomach, kidney and head and neck cancers, currently in Phase II trials. Bristol-Myers Squibb (which acquired Medarex of California) is developing ipilimumab, a fully human monoclonal antibody for the treatment of previously untreated metastatic melanoma patients, a group of patients with few treatment options and poor outlook. It has received fast track status for both a combination use and a monotherapy. It has also been awarded Orphan Drug status for the treatment of high-risk stage II, stage III and stage IV melanoma.

Source: IMS

Diana Lindsay: Deploying the Oldest and Latest Therapies to Fight Lung Cancer

Diana Lindsay met her husband, Kelly, a California native, when both were attending Stanford University. Diana graduated with degrees in music and in dance education, taught at Cabrillo College in Palo Alto and was head of the children’s dance program at Stanford from 1981 to 1989. The couple founded Lindsay Communications, a marketing consulting and communications company, in 1989. They have two children and three grandchildren and live on Whidbey Island, Wash.

The scary “to do” on Diana Lindsay’s calendar in April 2006 was surgery to alleviate a chronic sinus infection and cough that had not responded to three rounds of antibiotics.

When Diana reported to her GP for pre-op, “She told me that she wasn’t buying a sinus infection for the cough.” An X-ray, MRI and three days later, Diana learned she had Stage IV lung cancer, with cancerous cells in both lungs; the mediastinum, or the section of the chest cavity that holds the lungs; and her brain. She was 54 years old and had never smoked.

Diana said that based on statistics, her GP would have given her three months to live. Her ear, nose and throat specialist estimated four months, and her oncologist suggested a year “because he said I looked strong.” None of them appreciated just how strong.

With the diagnosis, Diana studied everything she could about her cancer and its therapies. “I looked into the oldest forms of care, in Eastern modalities,” she said, “as well as the latest breakthroughs in Western medicine.” She and her husband, Kelly, taught themselves meditation, visualization, touch therapy, acupuncture and massage. Simultaneously, Diana’s oncologist prescribed a targeted therapy.

“My treatment regimen ran backwards,” Diana said. “We started out with palliative treatment and the thought that there was no possibility of a cure and worked toward curative procedures.” In addition to her targeted therapy, which Diana is still taking, she underwent a CyberKnife® procedure for her brain lesions. The non-surgical robotic radiosurgery system reduces or eliminates certain lesions and tumors with fewer complications than open surgery. (The CyberKnife systems are developed and manufactured by Accuray Inc. of Sunnyvale.)

Doctors removed a section of Diana’s lung in May 2009 and found no sign of cancer. A CT scan in December 2009 also was clear. In the years following Diana’s prognosis of only months to live, she has welcomed two additional grandchildren into the world and is instigating research into the curative powers of the human mind.
Kimberly Hicks: A Story of Courage

While most of her classmates were thinking about homecoming rallies, SATs and first loves, Kimberly Hicks was focused on surviving. At age 15, Kimberly was diagnosed with Ewing’s Sarcoma, a rare form of bone cancer. Over the next two years, she had to undergo a biopsy, an experimental limb-salvage procedure whereby her diseased knee and tibia were replaced with titanium prosthetics, 17 week-long rounds of chemotherapy with all its debilitating side-effects, including nausea and hair loss. She had to learn to walk with a new prosthetic leg, a feat that took more than a year to accomplish. Along with the physical strains she endured, Kim was faced with the emotional consequences of a cancer diagnosis. Despite these challenges, she returned to school and graduated with her classmates—on time.

After high school, Kimberly packed her bags and entered the University of California, Davis. She lived her freshman year like any college student, and had begun putting her cancer experience behind her. However, during Kimberly’s sophomore year, it was discovered that the bone cancer had metastasized to her lungs. She again endured the same physical and emotional challenges as before, only this time she didn’t lose her knee and tibia; she lost one lobe of her left lung. But she remained focused on surviving—and living her life. She continued to take a full course load, while working a part-time job and undergoing treatment. She had once again beaten the odds and finally felt like she was back on track.

Then at age 22, shortly before graduation, Kimberly once again heard those dreaded words, “You have cancer.” This time her doctors told her to plan for the short term, tie up loose ends, and to say her good-byes. Kim snapped at her doctor, “You don’t know me very well, do you?” She prepared herself for another battle and, after months of treatment and the removal of a kidney, she survived. Through all of this, she beat the odds, continued her studies, graduated from UC Davis on time with a bachelor of science degree in human development and psychology. She even went on to work for the American Cancer Society, before taking a job with the Leukemia & Lymphoma Society. Today, Kimberly has been cancer-free for more than six years and is currently applying to medical schools. Her ultimate dream? Becoming a pediatric oncologist.

Vermillion Ovarian Cancer Tests

Vermillion, based in Fremont, is developing three ovarian cancer blood tests. These tests are designed to improve the ability to distinguish between benign and malignant tumors, to diagnose early stages of the disease and to better predict prognosis and recurrence. Vermillion’s ovarian tumor triage test (OVA1) is the most advanced test among the company’s ovarian diagnostic programs; it utilizes a panel of biomarkers to help identify patients with cancer. This test, called OVA1, was recently cleared by the U.S. Food and Drug Administration and will be available to physicians and patients starting in 2010.
### Figure 33: Expected Incidence, Mortality, and Prevalence of Common Cancers in California, 2009

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>New Cases</th>
<th>New Deaths</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MALE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>17,890</td>
<td>3,060</td>
<td>205,500</td>
</tr>
<tr>
<td>Lung</td>
<td>8,760</td>
<td>7,075</td>
<td>18,200</td>
</tr>
<tr>
<td>Colon &amp; Rectum</td>
<td>7,250</td>
<td>2,620</td>
<td>54,700</td>
</tr>
<tr>
<td>Leukemia &amp; Lymphoma</td>
<td>5,950</td>
<td>2,490</td>
<td>42,600</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>4,585</td>
<td>975</td>
<td>38,700</td>
</tr>
<tr>
<td><strong>All Cancers Combined</strong></td>
<td>69,225</td>
<td>27,725</td>
<td>512,500</td>
</tr>
</tbody>
</table>

| **FEMALE**           |           |            |            |
| Breast               | 22,115    | 4,170      | 272,800    |
| Lung                 | 8,075     | 6,260      | 20,200     |
| Colon & Rectum       | 7,000     | 2,520      | 57,400     |
| Uterus & Cervix      | 5,435     | 1,115      | 37,500     |
| Leukemia & Lymphoma  | 4,730     | 1,975      | 37,500     |
| **All Cancers Combined** | 71,59 | 26,735     | 656,000    |

**Gen-Probe, Inc.: PROGENSA® PCA3 Assay**

For men over the age of 50, prostate cancer is the second deadliest cancer after lung cancer. This cancer originates in the prostate and can metastasize to the surrounding areas including the lower spine, pelvic bones or lymph nodes. However, not all prostate cancers are lethal. In some cases the cancer can grow very slowly over many years and never produce any symptoms and even stay confined in the prostate. About 20 to 40 percent of the prostate cancer cases diagnosed today are labeled as "indolent," meaning they are unlikely to progress and lead to other complications.

The only way to diagnose prostate cancer is a prostate biopsy. The biopsy is an invasive procedure that can lead to infection, discomfort and bleeding. To determine if a patient needs to undergo a prostate biopsy, two tests are usually conducted: a digital rectal examination, which analyses the size, shape and texture of the prostate, and a blood test, which analyses the levels of prostate specific antigen (PSA). Elevated levels of PSA in the blood may indicate the presence of prostate cancer. However, the PSA protein is produced by both cancerous and non-cancerous cells. This can lead to unnecessary biopsies and misdiagnosis—and anxiety for a patient who may not have prostate cancer to begin with.

Gen-Probe Inc., a global leader in the development, manufacture and marketing of rapid, accurate and cost-effective nucleic acid tests, has developed the first-ever assay that screens for Prostate Cancer gene 3 (PCA3) from only a urine sample. PCA3 is highly specific to prostate cancer and is not produced by other conditions in the prostate. Gen-Probe’s revolutionary gene-based test, called PROGENSA PCA3, screens the amount of PCA3 in the sample and produces a score, which indicates the likelihood that a patient’s biopsy will be positive. The PROGENSA PCA3 assay is currently used in Europe, and clinical trials are underway that may lead to approval by the U.S. Food and Drug Administration.

**MammaPrint**

Laura van’t Veer, Ph.D., led the bench-to-bedside development of the MammaPrint®, the first and only breast cancer recurrence test cleared by the FDA. Van’t Veer co-founded Agendia, a molecular cancer diagnostics firm based in Huntington Beach and Amsterdam. Now, in collaboration with researchers and physicians at the University of California, San Francisco, she sees new opportunities to develop additional clinical applications to benefit breast cancer patients, based on new knowledge of genetic abnormalities and molecular markers in cancer. The MammaPrint test is a new generation of genetic testing; it detects patterns of gene activity in samples prepared from breast tumors. It can be used to indicate the likelihood of breast cancer returning in patients who underwent surgery. Research has shown the test to be more accurate in gauging breast cancer prognosis than previously established measures.

**California Cancer Statistics**

- Cancer incidence rates in California declined by 8 percent from 1988 to 2005.
- Over the same period, cancer mortality rates declined by 17 percent. Mortality rates declined for all four major racial/ethnic groups in the state.
- Cancer incidence in California is about the same or somewhat lower than elsewhere in the U.S. for most types of cancer.
- Despite these improvements, nearly one in two Californians born today will develop cancer at some time in their lives, and it is likely that one in five will die of the disease.

Source: California Cancer Registry, California Department of Public Health, as cited in California Cancer Facts & Figures, 2009 (American Cancer Society)
Disorders of the central nervous system include debilitating diseases that affect patients of all ages. The category includes Alzheimer’s disease and multiple sclerosis (MS), depression and neuropathic pain.

In 2008, 13 percent of the California pipeline, a total of 117 products, targeted central nervous system diseases. Medivation, along with Pfizer, are in Phase III studies of dimebolin, an oral antihistamine that also has potential as a neuroprotectant, for the treatment of Alzheimer’s disease and Huntington’s disease. According to studies, the compound appears to interrupt a cell process associated with neurodegenerative diseases. The FDA has granted dimebolin Orphan Drug designation for the treatment of Huntington’s disease. In 2010, Medivation expects to apply for U.S. and European marketing approval for the treatment of mild to moderate Alzheimer’s disease. Raptor Pharmaceuticals of Novato (formerly TorreyPines Therapeutics of La Jolla) is in Phase II development of tezampanel, in-licensed from Eli Lilly & Co., as a potential treatment for migraine and pain. Irvine-based Cortex Pharmaceuticals is developing CX 1739, for the treatment of sleep apnea and attention deficit hyperactivity disorder. CX 1739 is an ampakine compound, which is a new class of compounds known to enhance attention span and alertness and facilitate learning and memory. Phase I trials have been conducted in the United States.

Source: IMS
Joan Bissell: Escaping Relentless Pain

In June 2006, Joan Bissell was diagnosed with advanced degenerative disc disease of the neck. It was a diagnosis that explained her intractable pain. In September 2004, Joan started to experience severe neural pain that affected her neck, shoulders, arms, hands, and fingers. The pain was so intense that it interfered significantly in her personal, professional, and social life. As Joan recalled, “My life was dominated by efforts to control the pain.”

By May 2006, the pain reached a nearly unmanageable level. In fact, Joan was no longer able to work on a computer due to the pain of raising her arms. She struggled to control the pain: “My only hope of surviving the pain and getting through the day was to cover my neck, shoulders, arms, and back with topical pain relief products and therapeutic patches,” Joan said.

When she was diagnosed with degenerative disc disease in June 2006, Joan was referred to an orthopedic surgeon who specialized in neck disorders and then to a pain specialist. She was treated with a series of steroid injections and then trigger-point injections at particularly painful locations. This provided short-term, limited relief but did not address the severity and constancy of the pain.

In September 2006, Joan’s husband, a medical marketing executive, told her that he had read about the Boston Scientific Precision Spinal Cord Stimulator and that it sounded as though it could reduce her pain significantly.

Spinal cord stimulation (SCS) has been on the market since the 1970s, and approximately 200,000 U.S. patients have been implanted with the technology to date. SCS works by blocking the pain signal before it gets to the brain. An implanted generator sends low-power electrical impulses to specific nerve fibers along the spinal cord through thin wires called leads. These impulses cause a soothing, tingling sensation, called paresthesia, that is sent to the brain instead of the pain sensation. It differs from other primary types of pain treatment in that it directly blocks the pain signal. It does not require major surgery and, unlike prescription pain medications, it does not have debilitating side effects of habit-forming drugs.

In October 2006, a trial of the Boston Scientific Precision Spinal Cord Stimulator was undertaken with dramatic results. “During the two days of my temporary implant, I experienced a freedom from pain that was continuous,” Joan remembered. Following a successful test-drive of the therapy, a permanent implant was performed on October 27, 2006 that changed her life. “Since that day, I have been almost totally pain-free after years of relentless, excruciating pain,” Joan said. “There have been dramatic changes in every aspect of my life. I am again a cheerful, exuberant, and fulfilled wife, mother, and professional.”

Device advancements:

Boston Scientific’s EGL Scan™
(Electronically Generated Lead Scan)
Technology electronically senses and displays the relative position of two implanted leads, without fluoroscopy or X-ray, in seconds. While EGL Scan is not a replacement for fluoroscopy or X-ray, the information it provides may help clinicians program spinal cord stimulator (SCS) systems more efficiently. The information that EGL Scan provides is particularly relevant because lead migration is commonly reported in SCS.
Arthritis is a term used to describe more than 100 different conditions that affect joints as well as other parts of the body. One of the most prevalent chronic health problems, it’s a leading cause of disability in California and across the country.

California’s pipeline for immunological and inflammatory disease was the only category to show an increase for the year, with 110 products, up from 92 last year, with the most additions being in Phase I. Genentech and Biogen Idec are in Phase III development of ocrelizumab for the treatment of rheumatoid arthritis, lupus nephritis, and multiple sclerosis. Pfizer, through its R&D location at Rinat in South San Francisco, is in Phase III development of tanezumab for the treatment of chronic pain associated with osteoarthritis of the knee or hip. Rigel Pharmaceuticals of San Francisco is in development of fostamatinib, a drug for rheumatoid arthritis. Irvine-based Allergan has reached Phase II development for AGN 203818, which is being developed as a potential treatment for pain associated with fibromyalgia syndrome, which is characterized by chronic, joint and soft-tissue pain, and also allodynia, a heightened and painful response to pressure. Ligand Pharmaceuticals is developing CR 665 for the treatment of postoperative pain.

Immunological and Inflammatory Disease

Arthritis in California:

- 5.3 million California adults have doctor-diagnosed arthritis
- 16 percent of men in California have arthritis
- 25 percent of women in California have arthritis
- 42 percent of California adults with arthritis have activity limitation due to arthritis or joint symptoms
- 29 percent of California adults 45 to 65 years old have arthritis
- 50 percent of California adults over 65 years old have arthritis

Source: U.S. Centers for Disease Control, 2007 data
Infectious Disease

From HIV/AIDS to Hepatitis B and Hepatitis C, infectious diseases remain an important focus for California.

California’s infectious disease pipeline contains 109 products. Gilead Sciences leads this area and it continues to focus on HIV with the development of elvitegravir. Elvitegravir acts as an integrase inhibitor, a class of antiretroviral drug designed to block the action of a viral enzyme that inserts the viral genome into the DNA of the host cell. Gilead is also in Phase I development of GS 9191, a topical ointment formulation of a nucleotide prodrug for the treatment of genital warts caused by human papillomavirus infection. Additionally, Roche and InterMune, based in Brisbane, have signed a collaboration agreement to develop and commercialize products from InterMune’s protease inhibitors program for the treatment of hepatitis C virus infections, including ITMN 191, an oral protease inhibitor for the treatment of hepatitis C virus (HCV) infection, which is currently in Phase II development.

Source: IMS

HIV/AIDS in California
- 67,505 Californians were living with AIDS as of April 2009, according to the California Department of Public Health
- Of the HIV cases reported in California in April 2009, 85.5 percent were male and 13.5 percent were female
- Of the AIDS cases reported in California in April 2009, 87.9 percent were male and 11.3 percent were female

Hepatitis B Disparities in California
Hepatitis B is a liver disease caused by the hepatitis B virus (HBV). The virus is spread through direct contact with the blood, serum, or sexual fluids of an infected person. HBV is most commonly spread through unprotected sexual intercourse; from mother to child at the time of delivery; by contaminated drug injecting equipment; or through needle stick injuries. Chronic viral hepatitis B is a leading cause of cirrhosis, end-stage liver disease, and liver cancer.

There are approximately 280,000 chronic hepatitis B infections in California.
- Chronic HBV infection rates: Asian/Pacific Islanders (API), 7%; African-Americans, 0.5%; and Caucasians and Latinos, 0.1%.
- As many as 1 out of 10 API Americans are chronically infected with HBV (ranging from 5-15% based on country of origin), compared with 0.1% of Caucasian Americans.

Hepatitis C Disparities in California
Hepatitis C is a liver disease caused by the hepatitis C virus (HCV). Hepatitis C is primarily spread by blood to blood contact, including contaminated drug injecting equipment or blood transfusions before 1992, but about 15 percent of cases are related to sexual transmission. Chronic viral hepatitis C is a leading cause of cirrhosis, end-stage liver disease, and liver cancer, and hepatitis C-related liver disease is now the leading cause of hospitalizations and death in persons with HIV.

- 600,000 persons in California have been exposed to HCV, and 450,000 are chronically infected.
- Between 4,500 and 22,000 Californians may die from hepatitis C without treatment.
- Prevalence of hepatitis C: African Americans, 3.2%; Latinos, 2.1%; and Caucasians, 1.5%

Source: CalHEP (California Hepatitis Alliance), March 2008 Factsheet.
Diagnostic advancements:

**FDA Grants Emergency Use Authorization for Gen-Probe Influenza Test**

In October 2009, the U.S. Food and Drug Administration (FDA) granted an Emergency Use Authorization for Prodesse's ProFlu-ST™ assay. The molecular test can be used in CLIA high complexity laboratories to diagnose, from a single sample, 2009 H1N1 influenza virus infection and differentiate it from seasonal influenza A/H1 virus and seasonal influenza A/H3 virus in people who were previously diagnosed with influenza A. Because these three influenza A subtypes currently have different susceptibilities to antiviral drugs, identifying the specific strain can help clinicians treat patients appropriately. Prodesse is a wholly owned subsidiary of Gen-Probe, a global leader in molecular diagnostics.

**BD Probetec Neisseria Gonorrhoeae (GC) QX Amplified DNA Assay**

In March 2009, BD received FDA clearance for the BD ProbeTec™ Chlamydia trachomatis (CT) Qx Amplified DNA Assay and BD ProbeTec™ Neisseria gonorrhoeae (GC) Qx Amplified DNA Assay on the next-generation BD Viper™ System with XTR™ Technology. The BD Viper System with XTR Technology enables laboratories to process a higher volume of tests automatically from swabs or urine samples, with significantly less labor and more reliable test results. This improvement in process efficiency may lead to a higher number of accurate diagnoses and more appropriate patient care for the two most common sexually transmitted infections—chlamydia and gonorrhea. If left untreated, these infections in women can lead to pelvic inflammatory disease, infertility, ectopic pregnancy and chronic pelvic pain. The fully automated system processes up to 736 patient samples in a single work shift. It offers the least hands-on time for setup, sample extraction, workflow and maintenance.

**Cepheid Xpert C. Difficile Test**

Sunnyvale-based Cepheid’s Xpert C. difficile test is the first on-demand molecular diagnostic test for *Clostridium difficile* infection (CDI). It can detect the bacterium caused by CDI in 45 minutes. This is the first rapid turnaround test with a high degree of accuracy offered for CDI. *Clostridium difficile* is a spore-form bacterium that is hard to detect but spreads quickly. With this test physicians are able to detect and treat patients in the same day versus prior therapies, which took longer. The Xpert C. difficile test received FDA clearance in July 2009.
Heart disease is the leading cause of death in California and the nation. Cardiovascular disease (CVD), including heart disease, heart failure, and stroke, accounted for more than 73,000 deaths, or almost one-third of all deaths in the state in 2004.

The fifth largest focus of the California pipeline is cardiovascular disease, with approximately 70 programs in the pipeline. Despite the relatively small number of research projects, several in this area are expected to serve large patient populations and generate significant sales. Gilead Sciences is in Phase III development of darusentan, a high blood pressure medication for patients where other therapies, including the multiple drug regimens commonly used by physicians today, have failed to control their disease. Portola Pharmaceuticals, based in South San Francisco, has licensed elinogrel, a Phase II thrombosis (blood clot) treatment, to Novartis in an agreement granting exclusive worldwide development and commercialization rights. Elinogrel is an ADP receptor antagonist for the prevention and treatment of blood clots (thrombosis) in patients with severe heart conditions or undergoing a procedure to widen blocked blood vessels (angioplasty), and for the secondary prevention of heart attacks (myocardial infarction) and stroke. San Diego-based Metabasis Therapeutics, which has agreed to be taken over by Ligand Pharmaceuticals, is in Phase I development of MB 07811 for the treatment of high cholesterol (hyperlipidemia).

Cindy Block: Seeing Humanity in Medical Technology

Cindy Block teaches science at Crawford High School in San Diego. She established a biotechnology program at the high school, a mission she felt compelled to pursue given her daughter’s experiences with medical technology. The mother of two, Cindy and her husband, Assemblymember Marty Block of the 78th District, recently celebrated their fifth wedding anniversary. They live in the San Diego neighborhood of Del Cerro.

Nothing went as expected when Cindy Block checked into the hospital in April 1988 to deliver her second child. First, the baby was a girl; Cindy believed she was carrying a son. Second, although her daughter’s heartbeat sounded strong in the womb, she turned blue as soon as the umbilical cord was cut.

“They rushed her by ambulance to Children’s Hospital leaving me behind, and she had her first open-heart surgery within two hours of being born,” Block said. The prognosis was poor, and the girl’s father quickly named her April for her birth month so that she would not die “baby girl.”

April underwent six more open-heart surgeries before her doctors implanted a pacemaker. The device allowed April to live and function as a mostly healthy little girl, yet her doctors wondered if she would live past 30.

April, now 21, received her second pacemaker about seven years ago from Medtronic, Inc. Medtronic’s pacemakers have three components: first, the pacemaker, which is a small metal case containing electronic circuitry and a battery; second, a pacing lead, or insulated wire, that carries an electrical impulse from the pacemaker to the heart when needed; and third, the programmer that enables clinicians to monitor the pacemaker and adjust it if necessary.

The pacemaker’s features are not as impressive to Block as its benefits. “When April received her new pacemaker, her new cardiologist and the Medtronic specialist conferred, and they told me that there is no reason why she can’t have children”—a possibility discouraged up until then. In fact, they said that if April has children, she should be as confident as any mother of seeing them grow up. That is a strong statement given that April’s implant paces her heart 93 percent of the time.

April married in February 2009, and she and her husband live in South Carolina. Block looks forward to someday having her first grandchild. “It gives me so much hope,” Block said, “not just to have grandchildren and not just for April but for another generation after her.”
Jack Eade: Driving Forward

Jack Eade loves the fast muscle cars of the 1960s and 1970s. He and his wife, Susan, count among their leisure activities traveling to hot rod car shows and vintage car races. After a heart attack in 1994 and three angioplasty procedures over the next seven years, Jack’s heart was being monitored regularly. His cardiologist knew he had a heart murmur and that one day Jack would need an aortic valve replacement.

As pressure increased within Jack’s heart, valve surgery became necessary. Jack and Susan, an ICU/CCU nurse, researched his options and determined that a tissue valve was the best choice to avoid long-term medication and its associated complications. Thanks to a dedicated healthcare team and a Carpentier-Edwards PERIMOUNT Magna aortic valve, Jack hasn’t had to slow down since his valve replacement in March 2004.

Richard J. Shemin, M.D., chief of cardiothoracic surgery at the UCLA Medical Center, is a cardiac surgeon who performs this type of procedure. He said, “Durability, performance and quality-of-life benefits are all important features for patients receiving tissue valves, and the PERIMOUNT Magna’s optimal hemodynamics, flow characteristics and advanced tissue treatment all meet these needs.”

California Statistics

- During 2007 in California, there were 82,943 deaths attributed to cardiovascular disease (CVD).
- This equates with approximately 225 CVD-related deaths each day. Data indicate racial/ethnic disparities in death rates, with African Americans having a 50 percent higher death rate than the next highest-risk racial group (white).
- California hospitalizations (discharges) attributed to CVD in 2007 tally to 1,745,162, equating to more than 4,700 hospitalizations per day statewide.
- On average, patients with a CVD diagnosis were hospitalized for 6.8 days—3 days longer than the average length of stay for all other hospitalizations.
- The average cost per CVD hospitalization was $66,435 (note that hospital-based physician fees are excluded).
- Similar to the pattern in California CVD-related death figures, African Americans had a CVD-related hospitalization rate that was approximately 70 percent higher than white Californians.

Source: American Heart Association.
Device advancements:

**Medtronic® Attain Ability™ Model 4196 Lead—P080006 by Medtronic, Inc.**

The Medtronic® Attain Ability™ Model 4196 Lead (Model 4196) is a surgically implanted insulated wire that is designed to be used as part of a biventricular pacemaker system. The device is used to help treat heart failure patients. In some heart failure patients, the right and left sides of the heart may not contract together at the same time. The Model 4196 lead, as part of a biventricular system, sends electrical impulses to the heart to promote simultaneous contraction of both ventricles. Its thin design, which incorporates materials developed by NASA Langley Research Center, helps physicians treat hard-to-reach areas of the heart. According to a press release from Medtronic, a clinical study involving 190 patients at 25 centers around the country showed that physicians were able to successfully place the device in the heart 96.4 percent of the time. Medtronic’s Attain Ability™ Model 4196 Lead received FDA approval on April 7, 2009.

**Corventis, Inc. AVIVO Mobile Patient Management System**

Corventis, Inc. a San Jose-based developer of wireless cardiovascular solutions, created the AVIVO Mobile Patient Management System. This patient-friendly wearable device is intended to continuously record, store and transmit the cardiac health of a patient. With advanced computational algorithms, global wireless capabilities and a comprehensive Web-based infrastructure, clinicians now have a way to closely monitor their patients and help identify potential health risks from anywhere in the globe. This system is a major step in wireless technology and has improved our ability to detect, prevent and treat cardiovascular conditions. The AVIVO system was approved by the FDA on Feb. 3, 2009 and is now commercially available to clinicians.

**Edwards Lifesciences’ Carpentier-Edwards Physio II™ Annuloplasty Ring, Model 5200**

The Carpentier-Edwards Physio II™ Annuloplasty Ring, Model 5200, by Irvine-based Edwards Lifesciences, is intended for the correction of diseased mitral heart valves. This device represents the next generation of the most widely used Carpentier-Edwards Physio ring, and has unique features such as it can be matched to the shape of the patient’s diseased mitral valve and it is easier to implant. This new device provides surgeons with the flexibility to treat patients suffering from a number of mitral valve diseases with a high-quality valve repair. The Carpentier-Edwards Physio II ring received FDA clearance in January 2009.

Diagnostic advancements:

**CardioDx Genomic Test for Coronary Artery Disease**

CardioDx, based in Palo Alto, in August 2009 completed a multicenter validation study for Corus CAD, the first and only gene expression test to quantify the likelihood of obstructive coronary artery disease (CAD) in patients with stable chest pain. This major milestone in genomic testing for coronary artery disease will provide unique genomic information about an individual’s disease processes at the molecular and cellular levels. This test will help physicians obtain a more complete picture of their patient’s disease and can better individualize patient care.

**XDx Allomap®**

XDx, based in Brisbane, uses modern genomics and bioinformatics technology to develop molecular diagnostic assays based on gene expression patterns in blood cells. Allomap® is a blood test intended to aid in the identification of heart transplant recipients with stable allograft function who have a low probability of moderate/severe acute cellular rejection (ACR) at the time of testing in conjunction with standard clinical assessment. The AlloMap test is a 20-gene real-time quantitative polymerase chain reaction (qRT-PCR) assay. AlloMap testing applies a proprietary mathematical algorithm that combines the gene expression values from genes associated with cardiac allograft rejection to generate an objective, actionable score. Results are reported as an AlloMap score—an integer ranging from 0 to 40. This testing is currently adopted by more than half of the transplant centers in the United States.

**Vermillion Peripheral Arterial Disease Test**

Fremont-based Vermillion is developing a blood test for peripheral arterial disease (PAD). The PAD test is designed to identify among people at risk (the elderly over 70 years old, diabetes patients over 50 years old, and smokers over 50 years old) for PAD who should be further evaluated because of an increased PAD test score.
Diabetes and Other Metabolic Disorders

In California, 8.3 percent of adults were diagnosed with diabetes in 2008, and the percentage continues to rise, according to the Centers for Disease Control. Medicines for diabetes and other metabolic disorders make up about 8 percent of California’s biopharmaceutical pipeline, and companies such as Amylin Pharmaceuticals of San Diego and Amgen have multiple products in this therapy area. Amylin is developing davalcintide, a second-generation amylin analogue, for the potential treatment of obesity; the agent, which is administered subcutaneously, may also have potential as a therapy for metabolic disorders including diabetes and is currently in Phase II development. Amgen is in Phase II development of AMG 222, one of the newer class of type-II diabetes drugs, DPP-IV inhibitors, which include marketed products Januvia, Galvus and a number of other pipeline products. These compounds lower blood glucose levels, increase insulin secretion and control appetite by decreasing stomach emptying. Metabolex and Ortho-McNeil are developing the oral compound arhalofenate as a potential therapy for type 2 diabetes.

Source: IMS

For Kella Smith, July 25, 1983 was a fateful day that changed her life forever. She was only six years old when she was diagnosed with type 1 diabetes. For 17 years, she managed her disease with insulin injections—before meals and bedtime. That’s more than 24,820 injections! The shots hurt and they didn’t give Kella the glucose control she needed to stay healthy. Waking up with high glucose levels every day became exhausting and she simply wanted to live a more normal life.

Kella’s life changed dramatically nine years ago when she began using a Medtronic insulin pump. She immediately experienced freedom and flexibility. She could eat what she wanted—when she wanted—and could deliver insulin by touching a few buttons on her insulin pump. As Kella’s glucose control improved, she felt better and healthier. But it wasn’t until she added continuous glucose monitoring that she was able get the control she wanted.

Today, Kella is 33 and enjoys playing co-ed softball, walking her dog, and traveling whenever she can, which was nearly impossible while on shots. In fact, Kella traveled to India on her own because of her confidence in her insulin pump. A highlight of her trip was seeing the Taj Mahal.

By viewing her glucose trends in real-time, she can make proactive management decisions before her glucose becomes harmful. Kella feels this cutting-edge technology helps her live her life to the fullest and that it’s the next best thing to a cure for diabetes.

TYPE 1 DIABETES (in the past known as Insulin Dependent Diabetes, or Juvenile Diabetes), describes a type of diabetes where there is an absolute lack of insulin. The Beta cells (in the pancreas) normally responsible for making and secreting insulin die because the body’s immune system has attacked them. Therefore no cells are available to make the insulin. In this case, the body will die without getting supplemental insulin in the immediate or near-immediate future. The incidence of type 1 diabetes has probably been underestimated in the past, and may represent 10 percent or more of people with diabetes. The only treatment at this time is insulin shots.

In TYPE 2 DIABETES (in the past, known as Non-Insulin Dependent Diabetes or Adult Onset Diabetes), beta cells are present, and therefore insulin is present. However, the amount of insulin available is less than the individual requires (i.e., there is a relative lack of insulin). Furthermore, the insulin itself, in someone with type 2 diabetes, doesn’t work as well as it should when it gets to the cell, a state called Insulin Resistance. About 90 percent of diabetics fall into this category. Treatment may include proper diet, activity/exercise, and pills, but sometimes insulin is necessary.

Source: Diabetes Home
Pharmaceutical advancements:

**Arena Pharmaceuticals’ Lorcaserin Hydrochloride for Obesity**

Arena Pharmaceuticals’ lorcaserin hydrochloride is the company’s most advanced obesity drug candidate. According to Arena, lorcaserin is a novel single agent that represents the first in a new class of selective serotonin 2C receptor agonists. The serotonin 2C receptor is expressed in the brain, including the hypothalamus, an area involved in the control of appetite and metabolism. Stimulation of this receptor is strongly associated with feeding behavior and satiety. Currently, the drug is in a Phase III clinical trial program for weight management. The trial consists of three individual trials called BLOOM (behavioral modification and lorcaserin for overweight and obesity management), BLOSSOM (behavioral modification and lorcaserin second study for obesity management) and BLOOM-DM (behavioral modification and lorcaserin for overweight and obesity management in diabetes mellitus), which focus on obesity and diabetes management. So far more than 7,800 patients have enrolled in the study.

**Obesity in California:**

- 23 percent of Californians are obese
- Another 37.1 percent of Californians are considered overweight
- African-American Californians have a 51 percent higher prevalence of obesity compared to whites
- Hispanics have a 21 percent higher prevalence of obesity compared to whites
- 46.4 percent of adults in California with diabetes are obese
- 32.9 percent of adult Californians considered obese are between the ages of 55 and 64

Source: U.S. Centers for Disease Control, 2008 statistics

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**Figure 34: Percentage of California Adults with Diagnosed Diabetes, 1994—2008**

Source: Centers for Disease Control and Prevention
One day in the early 1990s, Mike Honda was listening to KGO AM 810 Newstalk Radio in the Bay Area when the subject matter jumped from interesting to life changing. “Dr. Dean Edell was talking about sleep disorders,” Honda said. And the symptoms he described—snoring, halted breathing and waking up gasping—described Honda exactly.

“I had just started in my job for the Santa Clara County Board of Supervisors, for which I needed a physical,” Honda said. “I asked, as part of that, to go to Stanford for a sleep study.” The exam was supposed to last two nights, with Honda attached to electrodes to determine the quality and depth of his sleep state.

“My case was so pronounced,” Honda said, “that the technician barged in after four hours.” For the remainder of the evaluation, Honda slept with a continuous positive airway pressure (CPAP) machine, developed by ResMed. The San Diego-based company develops, manufactures and markets products for a range of sleep-disordered breathing and other respiratory conditions. “After just four hours [on the CPAP], I woke up so rested and my mind was so clear,” he said. “The difference was profound.” For the first three days, he felt like a completely different person.

Honda has sleep apnea, a condition in which people stop breathing during sleep—sometimes hundreds of times during the night, and often for a minute or longer. With each episode, the brain rouses the person from sleep to resume breathing. The condition is quite common and affects more than 12 million Americans. Sleep apnea is linked to high blood pressure and other cardiovascular disease, memory problems, weight gain, impotency and headaches—as well as diminished motor skills caused by sleep deprivation. Left untreated, the disorder can be life-threatening.

Honda’s sleep apnea was a lifelong problem that made it difficult for him to retain information or to concentrate. He habitually dozed off at traffic lights. “CPAP has changed my life,” he said.

CPAP is the most widely recommended treatment for moderate to severe obstructive sleep apnea. CPAP entails wearing a mask that provides moderately pressurized air to prevent the airway from collapsing during sleep.

Other treatment options include making behavioral changes such as sleeping on one’s side or stomach, losing weight, and avoiding alcohol and other depressants. In addition to surgical options to create a more open airway, some sleep apnea patients try oral appliances to realign the jaw or tongue to keep the airway open.

Honda’s experience with sleep apnea has changed his perspective on healthcare. “I would not have known to seek help if I hadn’t heard the radio program,” he said. Without insurance, he may not have had access to the evaluation or the medical device that now gives him a good night’s sleep.

Since 2001, Mike Honda has represented the 15th Congressional District of California in the U.S. House of Representatives. He is in his sixth year as Chair of the Congressional Asian Pacific American Caucus and also serves on the Appropriations Committee, with postings on several of that body’s subcommittees. Although born in California, Honda spent his early childhood with his family in an internment camp for Japanese Americans in Colorado during World War II. In addition to serving in the Peace Corps for two years in El Salvador, Honda earned bachelor’s degrees in biological sciences and Spanish, and a master’s degree in education from San José State University. As an educator, Honda was a science teacher, served as a principal at two public schools, and conducted educational research at Stanford University. His political career has included stints on San Jose’s Planning Commission, the San José Unified School Board, and the Santa Clara County Board of Supervisors. Honda also served in the California State Assembly from 1996 to 2000 before being elected to Congress. He is widowed with two grown children and three grandsons.
Honda sits on the congressional committee funding the National Institutes of Health (NIH) and National Science Foundation (NSF) and serves as Chairman of the Congressional Asian Pacific American Caucus (CAPAC). In both roles, he has been a strong advocate of healthcare equity. On the appropriations committee he has consistently advocated for increased funding for Title VII diversity training programs and written report language aimed at increasing awareness about health equity issues. As Chairman of CAPAC, he has focused on health equity issues that particularly affect the Asian-Americans and Pacific Islanders (AAPI).

“Our [healthcare] system simply is not serving everyone equally,” Honda wrote in a February 2009 editorial. “Providing quality and affordable healthcare is a step in the right direction, but accessing those services remains especially difficult for ethnically diverse AAPI.”

On November 7, 2009, the House of Representatives passed historic healthcare legislation, the Affordable Health Care for America Act, HR 3692. Honda, in response to the bill, said, “HR 3692 will cover 96 percent of Americans and guarantee stability, lower costs, higher quality, and a greater choice of plans for all Americans, and I am encouraged by the inclusion of legislative language addressing racial and ethnic health disparities.”

Among the obstacles to healthcare equity, Honda said, are daunting cultural and language barriers and a lack of sufficiently disaggregated data. The AAPI population is diverse, with 76 percent of the Hmong community, 70 percent of Cambodian, 68 percent of Laotian and 61 percent of Vietnamese identified as having limited English proficiency (LEP). Studies show that the difficulty that LEP individuals have in communicating with healthcare providers who speak only English significantly negatively impacts the quality and quantity of the care they receive.

“They face complicated diagnoses and prescription directions,” he said. Misunderstandings can “result in poorer health outcomes and even death.”

The diversity of the AAPI community also prevents the health challenges of the communities from being adequately understood and addressed. For example, AAPIs have a higher prevalence of chronic Hepatitis B infection and, as a result, a greater incidence of liver cancer, but there are comparatively few federal resources devoted to prevention, education, and management activities. Likewise, there is anecdotal evidence indicating that the prevalence of diabetes in the AAPI community is increasing, and yet the Centers for Disease Control and Prevention (CDC) only gathers data on diabetes in the categories of “black, white, or Hispanic/non-white,” Honda notes.

To address the specific healthcare equity issue presented by the challenge of chronic viral hepatitis B infection, Honda introduced the National Hepatitis B Act, which sought to develop a comprehensive prevention, education, research and management program. An estimated 2 million people in the United States are infected with Hepatitis B, but only 200,000 have been diagnosed. Asian Americans account for half of chronic Hepatitis B infections and half of the resulting deaths. The legislation (HR 4550) was introduced in 2005 but not acted upon. On October 30, 2009, he introduced HR 3974, the Viral Hepatitis and Liver Cancer Control and Prevention Act of 2009. The legislation, supported by a strong bi-partisan coalition of 11 original co-sponsors, calls for the government “to establish, promote, and support a comprehensive prevention, education, research, and medical management referral program for viral hepatitis infection that will lead to a marked reduction in the disease burden associated with chronic viral hepatitis and liver cancer.”

During the 109th Congress (2005—2006) Honda was also the lead sponsor of the Health Equality and Accountability Act, designed “to assist healthcare professionals in providing appropriate cultural and language services, increasing federal reimbursement for these services, and creating a clearinghouse for culturally and linguistically appropriate ‘best-practices.’”

Honda said that each congressional session for the past 10 years has seen the Health Equity and Accountability Act introduced by a member of the Hispanic, Black or AAPI caucuses. He said that it serves as a platform for equity provisions to healthcare reform discussions in Washington. “We want to make sure that health plans incorporate standards for cultural and linguistic outreach and address affordability issues,” he said.
Edward Abrahams, Ph.D., is executive director of the Personalized Medicine Coalition (PMC). Representing a broad spectrum of academic, industrial, patient, provider and payer communities, PMC seeks to advance the understanding and adoption of personalized medicine concepts and products for the benefit of patients. It has grown from its original 18 founding members in November 2004 to more than 160 today.

Mike Silver, Ph.D., is the founder and principal consultant of Synaptix Communications, focused on providing strategic communications to life science companies and organizations seeking to catalyze transformation in research and development or healthcare delivery. As a science writer and industry analyst, Silver draws from more than 25 years of experience in biomedical and market research. Silver holds a bachelor of arts degree from Columbia University, and a Ph.D. in biochemistry and molecular biology from Harvard University.

Personalized medicine is an extension of traditional approaches to understanding and treating disease. Physicians have always used observable evidence to make a diagnosis or prescribe a treatment tailored to each individual. In personalized medicine, the tools provided to the physician are more precise, probing not just the visually obvious, such as a tumor on a mammogram, but the molecular makeup of each patient. A profile of a patient’s genetic variation can guide the selection of drugs or treatment protocols that minimize harmful side effects and ensure a more successful outcome. It can also indicate susceptibility to certain diseases before they become manifest, enabling the physician and patient to set out a plan for monitoring and prevention.

The ability to profile the structure, sequence, and expression levels of genes, proteins, and metabolites is redefining how we classify diseases and select treatments, allowing physicians to go beyond the one-size-fits-all model of medicine to make the most effective clinical decisions for each patient.
It is an approach that is well suited to the medical challenges of the 21st century. Although we have prevailed over many of the diseases that have plagued humanity throughout the ages, what remain are diseases of greater complexity: diabetes, cancer, heart disease, and Alzheimer’s disease. They are not caused by a single gene or a single event but by a combination of genetic and environmental factors, and they tend to be chronic, placing a heavy burden on the healthcare system. Personalized medicine provides the tools needed to better manage chronic diseases and treat them more effectively.

**Real-World Applications**

We can now point to real-world applications of almost every aspect of personalized medicine’s promise: Genetic profiles can better discern different subgroups of breast cancer, guiding physicians to select the best treatment protocol or, in some cases, forego the expense and risks of chemotherapy altogether; tests detecting variation in the way individuals metabolize the blood-thinning drug warfarin can help predetermine the right dose for a patient, navigating the narrow therapeutic passage between reducing risk of clots, and triggering internal bleeding.

A test for mutations in the genetic coding for an enzyme can help physicians select the most effective drug for a colon cancer patient, avoiding a costly and protracted trial-and-error approach that can leave the patient suffering needlessly from adverse effects or losing precious time in battling the disease. As evidence of the benefits continues to grow, an infrastructure of laws, policy, education, and clinical practice is building around personalized medicine:

- Medical institutions across the country have announced their commitment to putting personalized medicine into practice through dedicated centers or statewide initiatives.
- Personalized medicine approaches are becoming best practice in hospitals, in order to ensure that patients with serious conditions such as cancer are given optimum therapy from the start.
- The regulatory system is integrating genetic testing into the labels of pharmaceutical products, ensuring that a drug is administered in a way that minimizes the risk of adverse effects and improves the chances of effective treatment.
- Nearly every major pharmaceutical development project is incorporating information on genetic variation and its effects on the safety and effectiveness of the candidate drug.
- Personalized medicine applications have extended beyond cancer to improve treatments in cardiovascular disease, infectious diseases, psychiatric disorders, and transplantation medicine.
- Several of the nation’s leading medical schools are launching genomics-based medical education programs to train the next generation of care providers.
- The American Association of Health Plans has advocated policy encouraging genetic testing and preventive care, while several large private insurers have begun paying for genetic tests identifying presymptomatic high-risk populations.
- The U.S. Department of Health and Human Services (HHS), the President’s Council of Advisors in Science and Technology (PCAST), and the Personalized Medicine Coalition (PMC) have defined wide-ranging policy recommendations for personalized medicine; a genetic privacy law has been passed, and other legislation supporting personalized medicine has been introduced in the U.S. Senate and House of Representatives.

**Clinical Applications**

Ultimately, the success of personalized medicine will rise or fall on its ability to demonstrate value to the healthcare system, to the industries that develop its products, and to patients. The promise of personalized medicine, for which tangible evidence already exists, includes the ability to:

- Shift emphasis in medicine from reaction to prevention
- Enable the selection of optimal therapy and reduce trial-and-error prescribing
- Make the use of drugs safer by avoiding adverse drug reactions
- Increase patient compliance with treatment
- Reduce the time and cost of clinical trials
- Revive drugs that are failing in clinical trials or were withdrawn from the market
- Reduce the overall cost of healthcare

**Shift Emphasis in Medicine from Reaction to Prevention**

Personalized medicine introduces the ability to use molecular markers that signal the risk of disease or its presence before clinical signs and symptoms appear. This information underlies a healthcare strategy focused on prevention and early intervention, rather than a reaction to advanced stages of disease. Such a strategy can delay disease onset or minimize symptom severity. One example is a test used to look for BRCA1 and BRCA2 genetic mutations indicating a hereditary propensity for breast and ovarian cancer. Women with BRCA1 or BRCA2 genetic risk factors have a 36 to 85 percent lifetime chance of developing breast cancer, compared with a 13 percent chance among the general female population. For ovarian cancer, women with certain BRCA1 or BRCA2 gene mutations have a 16 to 60 percent chance of disease,
compared with a 1.7 percent chance among the general population. The BRCA1 and BRCA2 genetic test can guide preventive measures, such as increased frequency of mammography, prophylactic surgery, and chemoprevention.

Select Optimal Therapy
On average, a drug on the market works for only half of the people who take it. The consequences for quality and cost of care are significant, leaving patients to switch from one drug to another until they find an effective therapy. Studies have linked differences in response to the differences in genes that code for the drug-metabolizing enzymes, drug transporters, or drug targets. The use of genetic and other forms of molecular screening allows the physician to select an optimal therapy the first time and avoid the frustrating and costly practice of trial-and-error prescriptions.

Make Drugs Safer
According to a review of several studies, about 5.3 percent of hospital admissions are associated with adverse drug reactions (ADRs). Many ADRs are the result of variations in genes coding for the cytochrome P450 (CYP450) family of enzymes and other metabolizing enzymes. These variants may cause a drug to be metabolized more quickly or slowly than in the general population.

As a result, some individuals may have trouble eliminating a drug from their bodies, leading in essence to an overdose as it accumulates, while others eliminate the drug before it has a chance to work. The consequences of not considering variation in these genes when dosing can range from futility to unpleasant or even fatal side effects.

Increase Patient Adherence to Treatment
Patient non-compliance leads to adverse health effects and increased costs. When personalized therapies prove more effective or present fewer side effects, patients are more likely to comply with their treatment regimens. The greatest impact could be for the treatment of diseases such as asthma and diabetes, in which non-compliance commonly exacerbates the condition. At least one study supports this point. Inherited forms of hypercholesterolemia (high cholesterol) can increase the risk of myocardial infarction before the age of 40 more than 50-fold in men and 125-fold in women. Conventional monitoring of cholesterol levels can catch the condition early, but genetic testing offers additional benefits. In addition to detecting the condition before there are observable signs of disease, knowledge of a genetic predisposition for hypercholesterolemia provides patients with a powerful incentive to make lifestyle changes and to treat their condition seriously. Patients with a genetic diagnosis have shown more than 86 percent adherence to their treatment program after two years compared to 38 percent prior to testing.

Reduce Time, Cost, and Failure Rate of Clinical Trials
Developing a new drug is a costly and lengthy process. Theoretically, the use of pharmacogenomic data, or information about how patients’ genes affect their drug responses, could reduce the time and cost of drug development in addition to reducing the rate of drug failures by allowing researchers to focus on subsets of patient populations. Using genetic tests, researchers could preselect patients for studies, using those most likely to respond or least likely to suffer side effects. Enriching the clinical trial pool, as this approach is called, could reduce the size, time, and expense of clinical trials.

Reduce the Cost of Healthcare
The cost of healthcare in the United States is on an unsustainable upward curve. Incorporating personalized medicine into the healthcare system can help resolve many embedded inefficiencies, such as trial-and-error dosing, hospitalization of patients who have severe reactions to a drug, late diagnoses, and reactive treatment.

Authors of a recent study exploring potential healthcare cost savings from using genetic testing estimated that the use of a genetic test to properly dose the blood thinner warfarin could prevent 17,000 strokes and 85,000 serious bleeding events each year, and avoid as many as 43,000 visits to the emergency room. If the 2 million people that start taking warfarin each year were to be tested at a cost of $125 to $500 per patient, the overall cost savings to the healthcare system would be $1.1 billion annually. Similarly, researchers showed in a 2006 article published in Cancer that adjusting dosage of the colon cancer drug irinotecan based on UGT1A1 testing results in about $1,000 in savings per patient tested by reducing adverse events.
“Smile” is among the most frequently proffered advice for children, beauty pageant contestants, teachers, sales representatives, and, well, human beings in general. A smile connotes confidence and warmth, and the act of smiling can make a person feel more gracious. A smile can spark a friendship or diffuse a tense encounter. Smiles bridge language and cultural gaps and bond people together.

California’s Dental Devices Sector: Something to Smile About

Studies also suggest that healthy smiles may be key to longer lives. Epidemiologic researchers have shown a correlation between periodontal disease and atherosclerosis, or the build-up of plaque in the arterial blood vessels. The cause-and-effect relationship between the two diseases is not yet clear, but perhaps good oral care saves more than teeth—it may save lives.

Repairing or replacing teeth is a worthwhile objective on its own. Take away the main function of teeth—biting and chewing—and the individual’s nutrition and digestion suffer. Poor nutrition can lead to constipation, weight loss, arthritis and rheumatism as well as heart disease, Parkinson’s disease and certain types of cancer. Studies have shown that people with few or no remaining teeth have much higher rates of atherosclerotic vascular disease, heart failure, ischemic heart disease and joint disease. From a purely social perspective, teeth support the lips and cheeks, keeping faces attractive. They also are critical for the proper pronunciation of words and sounds.

Brushing and flossing remain the best tools individuals have for preventing tooth and gum disease. For the full range of supplies and products they need to further their patients’ oral health, dentists and orthodontists turn to California dental companies. Dental professionals also have come to rely on the state’s entrepreneurs for the latest innovations and cutting-edge educational opportunities.

Innovations for Those Pearly Whites

Dental Implants

In 1952, Professor Per-Ingvar Brånemark of Sweden was conducting bone-grafting research, when he accidentally discovered that living bone tissue would grow around and attach to titanium—an observation that contradicted all scientific theory at the time. Brånemark went on to demonstrate that under carefully controlled conditions, titanium could be structurally integrated into living bone with a very high degree of predictability, and without long-term soft tissue inflammation or rejection. Brånemark’s technology was used for dental implants in Sweden starting in 1968 and, in the mid-1980s, began gaining awareness in the United States.

In contrast, Medtronic’s INFUSE® Bone Graft uses a bone morphogenetic protein (rhBMP-2) that stimulates the patient’s own stem cells to grow or regenerate their own new bone in indicated applications (i.e., ridge augmentations). INFUSE Bone Graft was originally approved for use in spine surgery and treatment of severe tibia (shin bone) fractures. In oral use, the innovation has been shown to have very similar rates of effectiveness to autogenous bone graft. The clinical studies also showed that the bone generated by INFUSE Bone Graft is normal, mature, 100%-percent viable bone with no residual graft material, as evidenced by core samples taken at the time of dental implant placement.

California companies are key players in all three steps as evidenced by the recent introduction of a breakthrough technology by Medtronic, Inc., which has California operations in Northridge, Santa Ana, Irvine and Carlsbad. The standard of care in building the jawbone—the first step in dental implants—has been to harvest bone cells from the patient’s own chin or other non-essential bones and graft them to the bone that needs to be built back up. This approach, called autogenous bone graft, avoids the risk of cell rejection. It does, however, require an additional surgical site with the associated potential for post-operative pain and complications.
The second step in the implant procedure is to place the titanium anchor that serves as the “root” of the new tooth. One of the largest developers and manufacturers of titanium implants is Zimmer Dental Inc. of Carlsbad. The company’s offerings include implants to replace a single missing tooth or multiple teeth, or to serve as moorings for partial dentures or bridges. Zimmer Dental also has a comprehensive line of regenerative offerings for soft tissue and bone grafting procedures as well as restorative products.

Zimmer Dental began as a materials and surface technology company. A critical component of dental implants is the surface treatment that stimulates adjacent bone tissue growth and bone-to-implant bonding. The company has invested nearly two decades of continuing clinical research into the development of its proprietary hydroxylapatite (HA) particles and HA coating process.

In addition to Zimmer, which is a subsidiary of Zimmer Holdings in Warsaw, Ind., leaders in the dental implant sector include Nobel BioCare and Straumann AG, both headquartered in Switzerland, and BIOMET 3i, of Palm Beach Gardens, Fla.

Once the bone has firmly attached to the anchor, the patient is ready for the final step in the dental implant process. A titanium post is set into the anchor and fitted with a crown designed and manufactured to match the patient’s other teeth. The crowns are custom-ordered from dental labs such as California’s largest: Glidewell Dental Laboratories in Newport Beach.

The full dental implant process typically averages four to nine months, yet can take from three to 18 months to complete depending on the complexity of the case. In contrast to dentures and bridgework, implants look, feel, and perform like natural teeth and are proven to last for many years.

Invisible Orthodontics

Just as Zimmer Dental and other implant companies are replacing dentures and bridges with more realistic prostheses, Align Technology, Inc. is providing an alternative to the silver bridgework of traditional orthodontic “braces” for straighter smiles.

Align, headquartered in Santa Clara, pioneered the invisible-orthodontics market with the introduction of its Invisalign®. Invisalign is a patented proprietary system that uses 3D modeling software and leading-edge manufacturing technology to design and fabricate “aligners” to straighten teeth in stages as determined by the treating doctor. The aligners are made of clear, medical-grade plastic, are removable, and each set is worn for two weeks. Align reports that Invisalign is effective for treating a wide variety of orthodontic issues and, on average, patients require one full year of treatment and approximately 24 sets of aligners.

Founded in 1997, Align has grown into a global medical-device company with about 1,300 employees and more than 160 patents worldwide. The homegrown California company has manufactured more than 44 million unique Invisalign aligners, each a class 2 medical device, and started more than 1 million patients in treatment.

Challenges of Serving the Dental Devices Sector

In addition to the product development, competitive and regulatory challenges that every medical device company faces, dentistry inventors and entrepreneurs must manage other aspects unique to their sector. Among these are reimbursement issues. More than 100 million Americans lack dental coverage. Many employer-sponsored healthcare plans do not include dental insurance, and those that do typically offer only limited benefits. For example, most dental policies pay for preventive care like twice-a-year checkups, but cover only a
fraction of higher-cost procedures like root canals. Individual private insurance is costly, and Medicaid and Medicare offer only limited safety nets.

Dental care costs are rising faster than inflation, even as the economy has diminished individuals’ ability to pay for out-of-pocket procedures. Whether the deterrent is cost, fear or indifference, people are putting off a visit to the dentist. A March 2009 Gallup poll found that 35 percent of Americans had not visited a dentist in the previous 12 months.

The combined realities of dental insurance and the current economy are being felt by dental device companies. That statement is especially true for companies that sell orthodontics primarily for cosmetic benefits, and for developers and manufacturers of dental implants, which are far preferable to dentures or bridges and priced accordingly.

A second challenge—in good times and lean—is that the dentistry industry is highly fragmented. As of 2006, there were nearly 150,000 dentists in private practice in the United States. Of these, nearly 63 percent worked alone, while approximately 21 percent worked with one other dentist. Only slightly more than 14 percent worked in a practice with three or more dentists.

Reaching out to these professionals with traditional products and supplies is an exercise. (California companies in that category include Sybron Dental Specialties, Inc., an Orange-based subsidiary of Danaher Corporation and a manufacturer of dental, dental implant and infection prevention products. Another is 3M Unitek, which is based in Monrovia and provides instruments and supplies to orthodontists.)

The third difference between serving dentists and physicians is that dentists advance directly from dental school to practice. With no residencies, they are not as likely to have the hands-on experience of learning advanced techniques from mentors or peers in a real-world setting before starting their practices.

Rising to the Challenges

For companies on the leading edge of the dental devices sector, the current economic downturn provides a space in which to continue to build the foundations of their businesses—to expand their product lines, to quantify and promote the long-term benefits and cost-efficiencies of their offerings, and to build confidence, value and community within their customers’ practices.

Both Zimmer and Align are reaching dental specialists through company institutes. These programs, which provide hours of continuing education to dentists, orthodontists, oral surgeons and others, are designed to ensure proper use of the companies’ innovative products as well as positive experiences for patients.

Zimmer’s opportunity is to build the reputation of and consumer demand for implant technologies one successful procedure at a time. The Zimmer Institute, which opened in 2006, offers four levels of training options, some of which are carried out in the company’s on-site, state-of-the-art simulation lab. The classroom features 26 work stations, each equipped with a computer screen that enables students to follow the instructor’s demonstrations while “operating” on their own patients. Each patient is a mannequin with interchangeable mouths to replicate actual, patented patient cases—mouths that are constructed of a material that feels like actual tissues. The simulated patient’s eyes also flash if the student makes a mistake. Through the repetitive, hands-on learning experience, students perform all of the steps of preparing and placing the implants.

“Our classes end at 7 p.m.,” said Harold C. Flynn, Jr., president of Zimmer Dental, “and at 7:30 we’ll still be chasing students out. They can’t get enough.” The enthusiasm of participating clinicians bodes well for Zimmer, for implants and for patients. The Zimmer Institute has locations in Carlsbad and Winterthur, Switzerland, and is set to open an East Coast facility in Parsippany, N.J., in early 2010.

Align also provides ongoing education for dentists and orthodontists in order to expand the sources patients have for accessing the company’s invisible braces. AlignTech Institute, the company’s professional education Web site, provides continuing education in Invisalign techniques and ways to grow one’s practice. The company also hosts more than 100 live education events each year, and provides exclusive education events at more than 60 universities worldwide. Since its inception, Align has trained more than 56,700 doctors.

“With most dentists and orthodontists working in private practice offices,” said Thomas M. Prescott, president and chief executive officer of Align, “they tend to learn [about new technologies] through corporate events, university reunions and industry conferences. To that end, we do hundreds of training events per year, and we’re creating a community as well as providing continuing education.”

Both Flynn and Prescott compared their niche markets to Lasik eye surgery to correct near- and far-sightedness or astigmatisms. Innovative dental devices and the industry-changing ophthalmic surgery are areas driven by consumer demand. Both are more expensive in the short term than traditional options, yet provide longer-term cost savings and quality-of-life benefits. Both are being impacted by the current economy and consumers’ reluctance or inability to pay the added out-of-pocket expenses of elective procedures.

“We are still very early in the adoption process,” Prescott said of Align’s technology and products. He added that the dental devices sector is where Lasik was 20 years ago: laying the foundations now for a future worth smiling about.
Healthcare-associated infection (HAI) is a large and growing challenge in several regards. Caused by antibiotic-resistant bacteria, the infections are becoming more prevalent and more deadly, impacting increasing numbers of patients and their healthcare providers every year. Among the leading causes of death in the United States, HAIs affect nearly 2 million patients annually and, in 2008, accounted for more than 100,000 deaths. A patient with an HAI is about seven times more likely to die than an uninfected patient, and about one in 20 Americans will contract an HAI during a hospital stay in their lifetime.

In addition to the substantial human suffering exacted by HAIs, their financial burden is staggering. Each year such infections cause an estimated $28 billion to $33 billion in excess healthcare costs as a result of longer hospital stays and increased treatment expenses. And the threat of HAIs in healthcare facilities—including hospitals, acute care centers, outpatient surgical practices and nursing homes—undermines patient confidence and the effectiveness of the healthcare system.

By necessity, healthcare providers are stepping up to combat HAIs. To meet the demand, California biomedical companies are developing the tools they need.

**MRSA: Prevention is the Best Medicine**

With methicillin-resistant *Staphylococcus aureus* (MRSA) (see sidebar on next page), the best defense for hospitals and other healthcare facilities is to keep patients who are colonized or infected with the bacteria from coming into unprotected contact with clinicians, other patients and medical equipment.

Determining which patients are carriers of MRSA at admission enables the facility to better contain and eradicate the bacteria. In 2005, BD (Becton, Dickinson and Co.), which has operations in San Diego, introduced rapid molecular testing for MRSA. In 2008, Sunnyvale-based Cepheid launched a similar test.

The companies’ polymerase chain reaction (PCR) assays amplify genes and detect the gene target through the use of specialized reagents and temperature cycling. Cepheid’s tests can be run on demand for individual patients with an in-laboratory turnaround time of about an hour, and BD’s tests are run in batches with an in-laboratory turnaround time of less than two hours. That contrasts to traditional culture-based tests that require between one to three days of laboratory time to produce results.

Active surveillance testing with real-time PCR assays enables hospitals to quickly assign incoming patients to the appropriate protocols, and better protect all of their patients and their staff. To prove the effectiveness of MRSA control efforts, several hospitals or hospital systems have conducted highly controlled studies in recent years. Among them was a project led by researchers at Evanston Northwestern Healthcare (ENH) in Evanston, Ill. Starting in August 2005, ENH implemented an “all-admissions” active surveillance testing program to detect MRSA carriers at the organization’s three hospitals. (This was no small effort: ENH hospitals admit 40,000 patients annually. Patients who tested positive were isolated, treated with nasal ointments and antiseptic baths, issued patient-dedicated equipment, and cared for by staff who wore gloves and gowns when tending the patients. In addition, the patients’ rooms were subject to a more stringent cleaning checklist.

Study authors reported that through the program, ENH reduced MRSA infection rates by 70 percent in less than two years. The reductions were significant in every category measured, such as surgical site, bloodstream, urinary tract and respiratory infections.

The study’s economic model projected that the average cost of an HAI was $25,000 and that reducing infections by 50 percent would prevent 75 incidents and save nearly $1.9 million. Even accounting for the added
The Main Culprits

Several types of bacteria have grown resistant to antibiotics, yet the two most prominent types implicated in HAIs are methicillin*-resistant Staphylococcus aureus (MRSA) and Clostridium difficile (C. diff).

MRSA

MRSA comprises about 40 percent of all Staphylococcus aureus, a common type of bacteria that lives on the skin and in the nose of many healthy people without effect. This state is known as “colonization,” yet even people with large numbers of MRSA bacteria typically show no symptoms or signs of being at risk. Dangerous infections can occur, however, when the bacteria enter the body through wounds or via surgical instruments. MRSA infections occur most frequently among people in hospitals and healthcare facilities (such as nursing homes and dialysis centers) who have weakened immune systems.

An estimated 126,000 Americans are hospitalized with MRSA each year, a number that has more than tripled since 2000 and increased nearly 10-fold since 1995. An estimated 40 percent to 60 percent of hospital MRSA infections are resistant to first-line antibiotics, and the percentage is increasing.

C. diff

People with C. diff infection have millions of microscopic C. diff spores in their feces—spores that can survive for months on dry surfaces. These spores are spread by ingestion, usually when people inadvertently touch their mouth or other mucous membranes after coming in contact with a contaminated surface. Healthcare workers can spread the bacteria to patients or contaminate surfaces through hand contact.

More than nine out of 10 hospital infections with C. diff occur in people who have received antibiotic treatment. Such regimens kill many different types of pathogens, including the “good” bacteria in the gut that keep C. diff at bay. The resulting overgrowth of the C. diff bacteria produces toxins that can lead to diarrhea, which is often severe; intestinal inflammation known as colitis; sepsis; and, increasingly, death.

C. diff sickens about 500,000 Americans annually. Early in this decade, C. diff became four times more lethal, with death rates increasing from 5.7 per million Americans in 1999 to 23.7 per million in 2004. The increases are attributed to the NAP1 C. diff strain, which emerged in about 2000. More resistant to fluoroquinolone antibiotics than other C. diff strains, NAP1 also makes 16 times more toxin A and 23 times more toxin B. By mid-2008, the NAP1 strain had been reported in 37 U.S. states and the District of Columbia.

* Methicillin is an antibiotic used to treat bacterial infections. Most strains of MRSA are treatable with a “last line of defense” antibiotic called vancomycin, but it appears that MRSA is developing a resistance to that antibiotic as well.
For example, stool culture for *C. diff* has long been the most sensitive test available, but it is labor-intensive, takes three to seven days, and does not differentiate between toxigenic and non-toxigenic *C. diff* strains and therefore, needs to be followed by a toxin detection assay. Cytotoxicity assays, with sensitivity ranging from 70 percent to 95 percent, are expensive, require extensive operator input, and take three to seven days to complete. Because enzyme immunoassays (EIAs) are inexpensive and rapid—usually taking less than four hours—they have become the default test for *C. diff* at most institutions. Yet EIAs have such poor sensitivity that clinicians often treat for *C. diff* regardless of the lab outcomes, resulting in the over-treatment and unnecessary isolation of many patients.

A rapid, reliable PCR assay changes the picture entirely. Real-time PCR can reduce the number of false positives by half and can nearly eliminate false negatives. A rate of false negatives close to zero introduces, for the first time in *C. difficile* infection management, a scientific basis for appropriately diagnosing and treating patients, and instituting infection control measures. Given PCR’s outstanding sensitivity and specificity, hospitals may also reduce the frequency of re-testing, thus saving both time and money.

Both BD and Cepheid introduced their *C. diff* rapid tests in 2009. Not only are the molecular diagnostics faster and more sensitive than previous testing technologies, they promise usefulness despite the bacterium’s ongoing evolution. The tests work by detecting targeted nucleic acid sequences, which remain constant across strains of *C. difficile*.

In the fight against both MRSA and *C. diff*, healthcare facilities can apply real-time PCR tests toward reducing infections in patients and those around them; better, more effective treatment of infections; higher physician confidence; and more prudent use of antibiotics. In the interest of controlling healthcare costs, the tests ensure that medications and isolation measures are used only where they are needed and that HAIs are avoided or minimized, decreasing treatment regimens in these serious infections.

**The Future: More Fronts in this War**

Treating HAIs with better or more effective antibiotics benefits today’s patients, yet it also ensures that infection-causing bacteria will continue to evolve. To learn more about—and to keep pace with—that process, Cepheid founded its Healthcare-Associated Infection Consortium. The company hired Fred Tenover, Ph.D., previously the director of the Office of Antimicrobial Resistance for the Centers for Disease Control and Prevention (CDC), to head it up. The consortium is a cooperative effort between the company and a number of academic medical centers all over the world to share strains of HAI pathogens. The thousands of strains collected thus far are being compared and studied for ongoing changes in their genetic construction, drug resistance and virulence.

Not only does the project enlarge the scientific body of knowledge on the pathogens and how they evolve, it informs Cepheid’s ongoing product development efforts.

Molecular diagnostics promise to be an equally effective tool in fighting other diseases and conditions, too. For instance, Cepheid is finalizing an on-demand molecular diagnostic that will detect and differentiate between the H1 seasonal flu, H1N1 swine flu and H3 seasonal flu viruses.

“The three influenza strains are poised to converge this winter,” said David H. Persing, M.D., Ph.D., Cepheid’s chief medical and technology officer. “And they respond differently to antiviral medications, which promises mass confusion” at healthcare facilities. Persing noted that Cepheid’s test will provide accuracy and speed at the point of treatment, helping clinicians and patients know how to best manage each specific case.

In other development efforts, BD and Cepheid are advancing different tests for drug-resistant tuberculosis. Between them, the companies also are marketing tests for enteroviral meningitis, Group B Streptococcus, *Candida albicans*, *Enterococcus* species, *Escherichia coli* (*E. coli*), *Bacillus anthracis* (the bacterium that cause Anthrax) and *Mycobacterium* species. Future applications include tests that enable physicians to identify patients who would best benefit from pharmaceuticals aimed at narrow indications and for determining exact subsets of various cancers.

“There is no shortage of projects,” Persing said. “Let’s put it that way.”
The advice about finding “safety in numbers” was not originally directed at patient groups, yet it applies just the same. Those who are diagnosed with a disease will have the most treatment options and the best prognosis if their condition is a common one. Americans with rare diseases—those with fewer than 200,000 patients—face far more difficulties than those whose conditions are well characterized.

As Henry J. Fuchs, M.D., senior vice president and chief medical officer for BioMarin Pharmaceutical Inc. in Novato, said, “The population is small. But the development costs are about the same as for a blockbuster drug.” (Blockbuster drugs are those with annual sales exceeding $1 billion.)

Financing aside, the biggest obstacle to finding cures for rare diseases is a function of their scarcity. Because so few people are affected, it is hard to determine what causes these conditions in the first place. It is difficult to gather enough patients to ensure statistical validity in clinical trials. And with a limited group of potential trial candidates, the trial designers are under tremendous pressure to get it right the first time.

As formidable as the challenges to treatments for rare diseases may appear, California innovators are stepping up to make therapies available.

Translational Research Catalysts

In his fifth year, Paul and Debra Miller’s son was diagnosed with Duchenne muscular dystrophy (DMD), a rare degenerative disorder that typically leaves its patients wheelchair-bound by their 10th birthdays, paralyzed by 18 and dead by 20. Both of the Miller’s had strong business backgrounds and founded CureDuchenne, a Corona Del Mar non-profit that helps biotech companies fund promising research. The organization has helped three biotechnology companies move promising compounds into Phase II trials. CureDuchenne also donated $200,000 to the University of California, Los Angeles in November 2009 for a new Center for Duchenne Muscular Dystrophy at the university.

The Millers’ son is now 12 years old and, through aggressive steroid and other treatments, is doing well.

Beth Anne Baber, Ph.D., is another parent making a difference. She is a cancer researcher, as is her husband. So when they were told that their then 15-month-old son, Conor, had stage 3, high-risk neuroblastoma, “We knew that the survival rate for him was probably less than 40 percent,” Baber said. Before long, Baber was committed to accelerating the use of personalized medicine in pediatric cancer.

Through the Nicholas Conor Institute for Pediatric Cancer Research, Baber and her founding partner, Martin Latterich, Ph.D., are working to lower research and development (R&D) costs and to speed the availability of diagnostics and therapeutics specifically for pediatric cancer. The institute’s strategy is to target emerging technologies and actively translate them to the clinic while reducing R&D costs for the industry partner. The San Diego-based institute has ongoing collaborations with AltheaDx in San Diego, CollabRx, Inc. of Palo Alto and Prognosys Biosciences, Inc. in La Jolla.

In 2009, Conor marked his three-year anniversary of ending chemotherapy and remains staged as “NED” for no evidence of disease. He continues to have MRIs every three months to ensure that any recurrence is detected as early as possible.

Virtual Communities

Nicole Boice, a marketing professional and founder of the Children’s Rare Disease Network, was touched by rare diseases when her friend Kelly’s son was born with what eventually was diagnosed as Joubert Syndrome. “I experienced first-hand Kelly’s and [her husband] Darryl’s feelings of helplessness, isolation, stress, frustration and anger.” She also was surprised to find that while each rare disease has a small patient population, there are approximately 7,000 identified rare diseases that affect more than 30 million Americans. At least 150 organizations are devoted to better understanding and treating rare disorders.

Using her marketing, branding, communications and social networking skills, Boice established The Children’s...
Rare Disease Network, an online community for all patients and caregivers who are trying to become more educated and better manage rare diseases. Based in Dana Point, the network serves as a clearinghouse for information on legislation pertaining to rare diseases, resources for specific disease research and information, and a referral site to enable parents and other caregivers to access the resources they need from a single portal.

Policy Change Agents

Emil Kakkis, M.D., Ph.D., has more than 18 years of experience in developing novel treatments for rare genetic disorders. At Harbor-UCLA, Kakkis developed an enzyme replacement therapy for the rare disorder mucopolysaccharidosis I (MPS I). He joined BioMarin in 1998 to finish developing that drug, Aldurazyme® (laronidase), an achievement realized through a 50-50 joint venture with Genzyme Corp.

In 2009, Kakkis was moved to focus his energies on improving the approval process for rare disease therapies. He founded the Kakkis EveryLife Foundation and launched the CureTheProcess™ campaign. The campaign "strives to inspire science-driven public policy that will increase the predictability of the regulatory process for rare disease treatments."

Kakkis is advocating three key changes in the regulatory process. The first is to establish a new review office within the Office of New Drugs at the FDA staffed with experts in genetic and biochemical diseases. The second is to create new standards for evaluating the benefit of drugs for rare diseases in clinical trials.

Instead of measuring clinical outcomes, which are difficult if not impossible to demonstrate in small patient groups with complex conditions, Kakkis said, clinical trials for rare diseases could measure changes in scientifically qualified biomarkers. And, third, the CureTheProcess campaign calls for a creative effort to design new paradigms for clinical study designs and analyses that are better able to detect individual benefit in a broad array of patients.

In July 2009, Senator Sam Brownback (R-Kan.) and Senator Sherrod Brown (D-Ohio) sponsored an amendment to the 2010 FDA appropriation bill that shows progress in the CureTheProcess effort. The amendment directs the FDA to assemble a team to evaluate various aspects of the regulatory process for rare and neglected diseases. Kakkis anticipates that spotlighting weaknesses in the current system will open opportunities for improvements in the future.

BioMarin was founded in 1997 specifically to discover and develop therapies for rare and neglected diseases and thus far has commercialized three such new drugs. The company’s approximately 700 employees continue to be committed to that mission, and through both its internal discovery efforts and licensing agreements, BioMarin maintains a solid product pipeline.

Working exclusively in rare diseases is a business model that advances science along with patient care, BioMarin’s Fuchs noted. “Developing drugs for a rare disease can be helpful in understanding more common diseases,” he said. Fuchs was part of the team at Genentech, Inc. that developed Herceptin® (Trastuzumab) for the subset of breast cancer patients whose tumors are marked by the presence of the HER2 gene. “Through Herceptin, we learned a great deal about monoclonal antibodies in cancer,” Fuchs said, noting this knowledge is being used in new product development across the biomedical industry.

Industry

Amgen, one of California’s pioneering, largest and most successful biotechnology companies, has succeeded by “following the science where it leads,” sometimes into rare diseases. In 2008, Amgen introduced a new drug for use in adult patients with chronic immune thrombocytopenic purpura (ITP). Patients with ITP have low platelet counts, live with the possibility of dangerous excessive bleeding from even a minor injury, and have few long-term treatment options. Amgen’s drug, Nplate® (romiplostim), has been approved for treating the condition in the United States, Europe, Russia and Australia.

Patients and caregivers who are dealing with specific rare diseases may lack the safety of huge numbers. Yet the people who care about them are compensating with commitment and passion. They are revealing the underlying biology of rare disorders. They are rewriting the rules for advancing discoveries to patients. And they are drawing together the unprecedented potentials of gene therapy, personalized medicine, cooperative financing and public health policy to ensure that even the smallest subset of patients can be assured of safe and effective treatments.
Manufacturing a Therapy for a Rare Disease

Approximately 100 U.S. cases of infant botulism are reported each year, with 30 to 40 occurring in California, the state with the highest birthrate. The condition affects all racial and ethnic groups from all populated areas and strikes infants between three weeks and six months old. It is caused by the unintentional ingestion of spores of the bacterium *Clostridium botulinum*, which can be found in soils and dust worldwide and also in honey. (The spores in honey are dangerous for infants but not adults.)

The bacteria produce botulinum toxin—the most poisonous substance known—in the digestive track. This toxin is absorbed and spreads throughout the body, leading to muscle weakness and difficulty breathing. Most infants fully recover, although if not diagnosed quickly they may require time in the intensive care unit on ventilators.

Stephen Arnon, M.D., chief of the Infant Botulism Treatment and Prevention Program, and his team at the California Department of Public Health (CDPH) developed a therapy for the condition as a public service orphan drug. BabyBIG®, Botulism Immune Globulin Intravenous (Human) (BIG-IV), human-derived botulism antitoxin antibodies, is indicated for infant botulism types A and B.

Development took 15 years, but resulted in U.S. Food and Drug Administration (FDA) licensure in 2003. Since then, the CDPH has been mandated by federal and state law to produce and distribute BabyBIG nationwide.

BabyBIG is made by harvesting toxin-neutralizing antibodies from plasma. When the original manufacturer discontinued its plasma fractionating activities, CDPH approached Baxter International, Inc. to manufacture the therapy. In January 2009, Baxter’s Los Angeles facility was licensed by the FDA to produce the BabyBIG drug substance, and the first lots completed manufacture in June that same year. To help defray the cost of the manufacturing transfer and production of this product, many Baxter staff volunteered their time under Baxter’s global service initiative.

BabyBIG is an orphan drug, and CDPH is the only source in the world of this effective therapy for infant botulism. Although the patient numbers are small, this product reduces healthcare costs associated with infant botulism by more than $100,000 per patient by shortening hospital stay by almost one month per patient. Since introduction of BabyBIG into clinical practice, its use in the United States to treat infant botulism patients has resulted in more than 45 years of avoided hospital stay and $70 million in avoided hospital costs.
In the global battle to contain and manage the HIV/AIDS epidemic, monitoring patients’ immune systems is essential. The key measure of immune system health in HIV/AIDS patients is their CD4 cell level. CD4 is a cell surface marker found on a class of infection- and disease-fighting white blood cells and, the fewer CD4 cells in a patient’s blood, the more at risk he or she may be for infections.

The measurement of CD4 counts enables clinicians to determine when to initiate antiretroviral treatment. The treatment reduces susceptibility to opportunistic and potentially lethal infections and is also useful in evaluating the effectiveness of and adherence to therapy.

To expand the developing world's access to advanced CD4 cell-counting technology, BD entered into a special pricing agreement with the Clinton Foundation in 2004. Through the partnership, more than 3,900 flow cytometry systems have been placed in countries where the technology is needed most.

BD recognized that placing clinical and laboratory products is only one step toward improving a community’s capacity to provide healthcare, so the company set out to make a greater impact. It started by strengthening the laboratories that would use its medical devices, instrument systems and reagents to help patients in need.

Laboratory Strengthening Initiatives
Laboratories in developing countries often lack resources and qualified health workers, even as they are faced with high burdens of disease. BD implemented its lab strengthening program to help address those challenges. The program includes two distinct initiatives that draw upon the company’s core technical competency.

The first initiative, Good Laboratory Practices (GLP) Workshops, provides hands-on training to laboratory workers. The workshops help lab workers implement standard operating procedures for immune system monitoring of HIV/AIDS patients, including accurate measurement of their CD4 counts. The workshops are taught by BD trainers, usually from the country or local region, and include training-of-trainers. In collaboration with health ministries, universities, non-governmental organizations and international agencies, BD has conducted nearly 520 GLP workshops in 59 developing countries and provided hands-on training for more than 4,700 laboratory workers.

The second initiative, BD Volunteer Service Trips, sends teams of BD associates to remote health facilities in Africa for two or three weeks each year to help address healthcare problems in local clinics. These personnel help build local health capacity through training, construction, and laboratory strengthening.
The experience and knowledge that BD gained from its GLP Workshops and the Volunteer Service Trips made the company an attractive partner for the U.S. Office of the Global AIDS Coordinator. As a result, BD and the President’s Emergency Plan for AIDS Relief (PEPFAR) are now collaborating on three programs to bring BD’s efforts to scale in countries across Africa.

President’s Emergency Plan for AIDS Relief (PEPFAR) Partnerships

Improving Laboratory Operations

The first initiative between BD and PEPFAR was launched in October 2007 with the goal of strengthening the quality of laboratories in sub-Saharan Africa through training and improved diagnostic capabilities. The first of its kind, the public-private program is valued at $18 million over five years, with $9 million donated by BD in cash and in-kind services. By enabling expanded counseling and testing efforts, the BD-PEPFAR initiative is ensuring that more Africans will know their HIV/AIDS status, benefit from appropriate prevention counseling, and receive referrals for anti-retroviral medicine.

Scientists and lab technicians participating in the training programs serve a total of eight sub-Saharan nations representing an overall population of 336 million people. The countries’ national HIV/AIDS rates range from 2.1 percent to 23.9 percent, while national TB prevalence rates range from 426 to 692 infections per 100,000 people. (In comparison, approximately 1.1 million people or 0.3 percent of the U.S. population were living with HIV in 2006, and TB prevalence was estimated at 3.6 per 100,000 in 1999–2000.)

Wellness Centers

In October 2008, BD, PEPFAR and the International Council of Nurses (ICN) announced a three-year, public-private partnership valued at $1.25 million to establish a new Wellness Center for Healthcare Workers in Kampala, Uganda. The goals of this collaboration are to strengthen the healthcare system and address health worker shortages.

Uganda has just 29,000 healthcare professionals to serve a population of 30 million people. Doctors, nurses and other skilled healthcare workers in sub-Saharan Africa are particularly vulnerable to the impact of HIV/AIDS, TB and malaria. Although at risk for developing illness, stress and depression through their jobs, they may find it difficult to access the same services they routinely provide for others.

The Wellness Center, which is to be managed by the Uganda National Association of Nurses and Midwives, will offer confidential voluntary counseling and testing, treatment for HIV and TB, post-exposure prophylaxis and prevention of mother-to-child transmission services for healthcare workers and their families. In addition, health workers can learn about stress management and occupational safety, take up training opportunities, and find other resources for continuous professional development.

Blood Collection Safety

In August 2009, BD and PEPFAR announced a third joint initiative—a program to help protect health workers and patients in African countries by improving blood collection safety. The project will train hospital and clinical personnel in blood-drawing procedures and specimen-handling processes that are critical to the proper management of HIV/AIDS patients. The initiative will also work to help prevent needlestick injuries and control exposure to the virus among healthcare workers by providing post-exposure prophylaxis.

Success through Public-Private Partnerships

Through the initiatives and collaborations described above, BD has seen firsthand the empowering effect of private companies working with local governments, health ministries, and healthcare providing organizations.

As more and more focus is brought to the weakened state of healthcare systems in the developing world—and to the realization that funding alone cannot solve this problem—collaborations between global health organizations in the private and public sector will become recognized as the best method for achieving sustainable change. BD is committed to deploying its people, products and knowledge in ongoing collaboration with global health partners with one goal in mind: sustainable improvements in healthcare worldwide.
Special Section: Los Angeles and Ventura Counties
The Diversity Cluster

Los Angeles Basin Highlights*

- Total estimated biomedical employment: 52,684
- Total estimated biomedical wages: $3.9 billion
- Average biomedical wage: $74,709
- Percentage of total California biomedical workforce: 19.3%
- Statewide ranking: Second

*Includes both Los Angeles and Ventura Counties

One of the distinguishing features of the life sciences industry is its tendency to cluster in certain geographic regions. California’s oldest cluster is the greater San Francisco Bay Area. But since the late 1980s other regions have emerged, each with its own combination of basic research, venture capital and professional services infrastructure.

All enjoy basic essential support systems. These include the presence of leading research universities that encourage technology transfer and the companies that advance breakthrough technologies for patient care and in turn create jobs. Thriving clusters have a history of successfully introducing therapies, diagnostics, medical devices and research instruments and techniques to improve public health. Each is nurtured by the availability of venture capital for startup and established companies as well as the support of local, state and federal government agencies. As a cluster blossoms, so does its abundance of skilled workers, its growing commitment to workforce development, and the expertise of ancillary service providers.

Given California’s legacy of innovation and exploration, it is little wonder that of the nine U.S. areas considered major biomedical clusters, three—San Francisco, San Diego and Los Angeles—are in California.

**Figure 35: Major U.S. Biomedical Clusters (in Alphabetical Order)**

- Cambridge/Boston
- Los Angeles
- New York/New Jersey/Connecticut
- Philadelphia
- Raleigh/Durham
- San Diego
- San Francisco
- Seattle
- Washington DC/Baltimore


Whereas the Bay Area and San Diego have longstanding international reputations as life sciences hot spots, the research centers, companies and organizations in Los Angeles and Ventura counties have been quietly building the region into a biomedical powerhouse. In fact, when measured by numbers of employees, the LA Basin ranks second among California’s clusters.

**Figure 36: 2008 Biomedical Employment by Cluster**

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Employment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bay Area †</td>
<td>53,399</td>
</tr>
<tr>
<td>Los Angeles County</td>
<td>44,093</td>
</tr>
<tr>
<td>Orange County</td>
<td>30,270</td>
</tr>
<tr>
<td>San Diego County</td>
<td>23,479</td>
</tr>
<tr>
<td>Ventura &amp; Santa Barbara</td>
<td>9,998</td>
</tr>
<tr>
<td>Riverside &amp; San Bernardino Counties</td>
<td>7,959</td>
</tr>
<tr>
<td>Sacramento County</td>
<td>2,907</td>
</tr>
</tbody>
</table>

† Includes Alameda, Contra Costa, Marin, Napa, San Francisco, and San Mateo, Santa Clara, Solano, and Sonoma Counties.

Like its people and neighborhoods, the Los Angeles biomedical industry is diverse. It encompasses six major universities and research institutes, each with world class programs in a wide range of disciplines. In addition to training tomorrow’s leading medical, research and business leaders, the institutions’ technology transfer offices are putting potential breakthrough ideas on a fast track. Out-licensing new inventions promises to accelerate the availability of important therapies to improve public health and to generate licensing fees and royalties to fund institutions’ ongoing research and training missions.

The region is home to more than 300 companies focused on new therapies, devices, diagnostics, and research tools—as well as such supporting technologies as bioinformatics and genetic sequencing. They are advancing therapies and breakthrough discoveries across the full range of human health conditions and identifying new targets and techniques for preventing, diagnosing and treating disease.

While these educational and commercial enterprises employ highly trained individuals, they are also actively developing tomorrow’s workforce. By sponsoring programs in K-12 education, community college and university classrooms, the biomedical industry is ensuring that students become acquainted with the possibilities of engineering, science, math and medical careers.

People not directly employed by the biomedical industry help make the Los Angeles area fertile ground for the cluster. Among these are thought leaders, policy makers and patient advocates. They include champions of new research directions such as regenerative medicine (stem cell research), gene therapy, nanotechnology and preventative care. Included in their ranks are those who see public policy as a tool for preventing costly and debilitating chronic conditions such as obesity, diabetes and cardiovascular disease. They include investors willing to provide capital to enable emerging and early-stage companies to move innovative ideas through proof-of-concept, safety and efficacy testing and manufacturing. Their financial support ensures that products that might improve quality of life reach the patients who need them.

At the same time,Los Angeles is also a rigorous proving ground for new therapies and healthcare policies. As pointed out by the University of Southern California, whose medical facilities serve the city’s center, the Los Angeles metropolitan area is home to one of every 21 Americans and is more populous than 46 states. The population in the heart of the city includes nearly 6 million people; 85 percent are non-white, 30 percent are under 18 years of age, one in five residents (one in three children) lives below the poverty level, and 57 percent of adults did not complete high school. More than 90 languages are spoken here. As in other large cities, the disease burden is high. Cardiovascular disease, cancer, violence, trauma, communicable disease, pollution-related disease, substance abuse, and obesity/diabetes are leading causes of morbidity and mortality.

The following pages highlight a few of the institutions, firms and individuals that are rising to the challenges and opportunities present here. These entities are making the greater Los Angeles area one of the nation’s most productive biomedical clusters.

Abraxis BioScience is a Los Angeles-based, fully integrated biotechnology company that offers the world’s first and only protein-based nanoparticle chemotherapeutic compound.

Scientists at Abraxis developed the proprietary tumor targeting system known as the nab™. The technology is a blood-based delivery system that wraps an active drug in the human protein albumin, said Abraxis’ founder and chairman, Patrick Soon-Shiong, M.D. In contrast to solvent-based chemotherapy agents, nab-based drugs can be administered to patients at higher doses over shorter time periods (i.e., 30 minutes versus three hours) to deliver higher concentrations of drug directly to the tumor site.

The first product to incorporate the nab technology, ABRAXANE®, was launched in 2005 for the treatment of metastatic breast cancer. Metastatic means the cancer has spread to other organs of the body, and Soon-Shiong said that a protein called Sparc (secreted protein acidic and rich in cysteine) makes that migration possible. Long implicated by researchers in the spread of colon cancer to the liver, Sparc may be key to the spread of melanoma, breast cancer and some brain tumors.

Among its characteristics, “Sparc seeks out albumin and sucks it into itself,” Soon-Shiong said, which may make ABRAXANE and other nab-based therapies a viable weapon in the battle against some of the most aggressive and lethal forms of cancer.

ABRAXANE is indicated for the treatment of breast cancer after the failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. It also is being tested for expanded applications in metastatic breast cancer as well as for the treatment of non-small cell lung, malignant melanoma, pancreatic and gastric cancers.

In addition to investigating and developing new compounds for lung, head and neck, ovarian and prostate cancers, Abraxis is combining its biologically interactive delivery system with other water-insoluble drugs for the potential use across a broad range of tumors. For instance, a number of the pipeline products in development are natural products or derivatives of natural products that benefit from Abraxis nab technology. A key feature of natural products is their enormous structural and chemical diversity. This diversity makes natural products a fertile resource for finding novel compounds that interact with new targets for drug discovery.

Soon-Shiong said that the company’s success has been driven by its high-caliber scientific, regulatory, clinical, manufacturing and sales staffs. The discovery team, in particular, draws on the Los Angeles, Orange County and San Diego universities for proteomics and genomics specialists, biologists, computer scientists, mathematicians, physicists and engineers, among others. “They literally all work together in one facility,” Soon-Shiong said, and inspire one another with ideas that span disciplines.

**Headquarters:**
Los Angeles

**Established:**
November 2007 as a spin-out from American Pharmaceutical Partners

**Employees:**
Approximately 1,000

**Product:**
ABRAXANE® (nab-paclitaxel) for the treatment of metastatic breast cancer

**2008 Revenues:**
$258 million
Agensys may have been in the right place at the right time not only to survive but thrive in the current economic environment.

As Paul Kanan, Agensys’ executive vice president, finance and operations, explains, the privately held company raised $41 million in June 2007. The proceeds were earmarked for continued development of the firm’s pipeline of therapeutic fully human monoclonal antibodies (MAbs) to treat solid tumor cancers.

Then Astellas, the Japanese pharmaceutical company, became interested in bolstering its antibody research in cancer. Given Agensys’ team, pipeline and strong intellectual property position—the target portfolio and related products are protected by 119 issued patents, 33 allowed patents and more than 300 applications—Astellas felt the company would be a perfect match. For its part, Agensys realized it needed the resources and expertise of a large pharmaceutical company in order to complete the pivotal clinical trials, scale up manufacturing and undertake the marketing of its promising compounds.

“We had a contract signed by Thanksgiving, and the deal closed in mid-December” of 2007, Kanan said. The transaction was valued at $387 million in cash plus $150 million in possible milestones going forward.

Since then Astellas has proven to be “a tremendous company to work with,” Kanan said. He added that the new parent company sustained Agensys’ original management team, which operates as it always has except that its board of directors is now a committee consisting of Agensys and Astellas senior executives. The arrangement has enabled Agensys’ scientists to focus on the research and development tasks for which they are trained.

The company’s science is complex. Its MAbs are designed to specifically bind to a target molecule expressed on the surface of solid tumor cells destroy the cancerous cell, leaving healthy and untargeted tissue alone. Agensys has three “naked” MAbs—compounds delivering only the antibody—in clinical trials. The firm’s AGS-1C4D4 is directed to prostate stem cell antigen (PSCA), a novel target for prostate, pancreatic, and bladder cancers. That compound is in a Phase II trial for pancreatic cancer. The compound AGS-16M18 is directed to a novel target for kidney and liver cancers, while AGS-8M4 is directed to a novel target for ovarian cancer. The latter compounds are in Phase I trials.

Agensys, in conjunction with Seattle Genetics, also is developing antibody-drug conjugate (ADC) therapeutic antibodies. These compounds both seize on targeted cells and deliver a drug (i.e., a chemotherapy agent) to the tumor. The collaboration is advancing its first ADC directed to AGS-5, a novel target in multiple epithelial tumors.

With three drug candidates in clinical trials, Agensys’ R&D team is fully engaged. With its diverse portfolio of proprietary, clinically relevant cancer targets encompassing 14 types of solid tumors, much work remains to be done.

Headquarters: Santa Monica

Established: 1997 as UroGenesys; changed its name to Agensys in 2001

Acquired: By Astellas in December 2007

Employees: Approximately 130

Pipeline: Agensys is advancing a pipeline of naked and antibody-drug conjugated (ADC) therapeutic antibodies directed at a variety of cancer indications.
Amgen, a biotechnology pioneer since 1980, discovers, develops, manufactures and delivers human therapeutics.

In 1983, Amgen research scientist Fu-Kuen Lin was the first to isolate the gene for erythropoietin, a hormone that controls red blood cell production. Subsequently, the company determined how to produce human erythropoietin in a form and quantity that made its therapeutic use possible. Those discoveries led to the development of Epoetin Alfa, which in 1989 would reach patients as EPOGEN®. EPOGEN® was Amgen’s first marketed product—and the biotechnology industry’s first blockbuster medicine.

Today Amgen has more than 50 molecules in the pipeline from late discovery research through Phase III, including programs in bone, cardiovascular disease, inflammation, metabolic disorders, nephrology, neuroscience, oncology and hematology and 24 novel development programs. Amgen has nearly 30 active studies underway and more than 45,000 patients enrolled in Amgen clinical trials in more than 50 countries around the world.

Amgen Oncology: pathways to progress

Amgen takes a comprehensive approach to addressing cancer by exploiting numerous biologic pathways and multiple scientific modalities. Amgen’s cancer therapeutic research targets both tumor cells and the supporting normal cells that the cancer recruits for its own purposes (the “tumor stroma”). Amgen’s approaches include developing products that target proliferating cells, inhibit cancer cell nutrient supply, and interdict survival signals.

New pathways in bone biology

Amgen, in collaboration with UCB, a biopharmaceutical company headquartered in Brussels, Belgium, is developing a monoclonal antibody that targets the protein sclerostin. Sclerostin acts as a brake to control bone formation, mass and strength. Blocking the protein could provide a potential treatment for various bone-related conditions, such as osteoporosis.

Separately, scientists in Amgen’s genomic drug discovery program and at Immunex (which Amgen acquired in 2002) identified osteoprotegerin (OPG) and the RANK Ligand signaling pathway, which is responsible for the body’s natural and necessary process of breaking down old bone. Yet the resulting bone loss and destruction is problematic in conditions, such as osteoporosis and rheumatoid arthritis.

Amgen discovered that when the RANK Ligand binds to its receptor, it triggers all stages of osteoclast (the protein responsible for bone destruction) formation, function and survival. Amgen is conducting late-stage clinical trials of a novel antibody that targets RANK Ligand as a means of managing bone loss.

Novel approaches to inflammation

Amgen is studying new ways to target the chronic inflammatory disease of the respiratory system in asthma and other respiratory conditions.

The company also has programs in multiple sclerosis, chronic obstructive pulmonary disease, lupus, osteoarthritis, idiopathic pulmonary fibrosis, inflammatory bowel disease, psoriasis, and rheumatoid arthritis.

Since its inception nearly 30 years ago, Amgen has introduced therapeutics that have helped people around the world in their fight against cancer, kidney disease, rheumatoid arthritis and other serious illnesses. So far, more than 17 million patients globally have been treated with Amgen products.
Baxter International, Inc.
BioScience Division

Founded in 1931, Baxter may be the grandfather of all of Los Angeles biomedical entities. The company has played a significant role in elevating biotechnology in California, with more than 50 years of history in developing and producing innovative therapies in the state.

For instance, in 1941 Baxter introduced the first system for separating plasma from whole blood and storing it for later use. In 1952, Baxter acquired Hyland Laboratories, the first company in the United States to market human plasma commercially, and in 1953 built a facility in Los Angeles to begin producing immune therapies, albumin, and a variety of blood bank, coagulation, and biochemical test products.

In 1966, Baxter discovered and produced the first commercially available plasma-derived factor VIII concentrate to treat hemophilia A. Hemophilia A is the hereditary disorder marked by the blood’s inability to clot because of a missing protein known as factor VIII. About one in 10,000 people are born with hemophilia A each year, and approximately 18,000 people living in the United States have the condition. These individuals can experience uncontrolled bleeding and debilitating joint pain.

By making treatment easier and more convenient than whole blood transfusions, Baxter’s innovation has given patients with hemophilia greater health and independence. It also has contributed to a doubling of the life expectancy for hemophilia patients.

Further progress has been made in this area with the development of recombinant FVIII therapies, which have now become a therapy of choice for people with hemophilia. In 1992, Baxter introduced the first recombinant FVIII therapy, processed in its recombinant technology facility in Thousand Oaks. This paved the way for the company’s latest generation therapy, which launched in 2003. Additional production capabilities for this therapy will be added in the Thousand Oaks facility in 2010.

Other Baxter therapies produced in California include plasma-derived immune replacement therapies for people with primary immune deficiency, hereditary lung disorders and “orphan drugs” for rare, blood-based disorders.
Boston Scientific Neuromodulation was founded with the goal of using current-steering technology originally developed for cochlear implants to treat chronic pain.

The company met that goal when it introduced the first rechargeable implantable pulse generator (IPG). The small electronic device typically is inserted into the patient’s lower back. It features wires, called “leads,” that run from the IPG up through the spinal column. By supplying precise pulses of electrical current to specific electrodes at predetermined sites along the spinal cord, the IPG masks pain signals to the brain and allows patients to control chronic neuropathic pain.

Patients, who can test the device before it is implanted to ensure that the therapy will work for them, receive a remote control that enables them to pinpoint coverage to different areas of their body. Boston Scientific Neuromodulation’s IPG is the only such product to fractionalize current and provide smoother, more complete pain coverage to patients. After being implanted with the device, many patients are able to eliminate—or dramatically reduce—their use of pain medications and avoid the side effects. The device promises patients with chronic pain a path toward living more physically active and comfortable lives.

In addition to refining future generations of the Precision Plus IPG for spinal cord stimulation, Boston Scientific Neuromodulation is developing IPGs for use in occipital (eye) nerve stimulation to alleviate chronic migraines. The company also is pursuing a “deep brain” stimulation (DBS) platform for treatment of Parkinson’s disease and essential tremor. This device uses electrical signals to trigger electrodes implanted deep into the brain. Instead of masking pain, DBS electrodes may be able to alter electrical signals in the brain to reduce tremors. The DBS approach may also have applications in epilepsy, depression and obesity.
CytRx Corp.

CytRx is a biopharmaceutical research and development company that found early success in developing RNA interference technology, for use in treating a variety of diseases.

In 2007, the company’s chief executive officer, Steve Kriegsman, decided to spin that successful platform technology out as a separate publicly traded company—RXi Pharmaceuticals (Nasdaq: RXII). To enhance its small molecule pipeline, CytRx in 2008 acquired Innovive Pharmaceuticals and its drug candidates for cancer.

The strategy was designed to provide CytRx with the potential for near-, medium-, and long-term revenue generation. The near-term promise from the acquired Innovive pipeline is tamibarotene, a synthetic retinoid compound that is in a pivotal Phase II study in the United States, Canada and Europe for the treatment of acute promyelocytic leukemia (APL). APL is diagnosed in about 1,500 new patients in the United States annually, and nearly 200,000 Americans are estimated to be living with the disease.

The current standard of care is treatment with all-trans retinoic acid (ATRA), a derivative of Vitamin A, and arsenic trioxide. There is no marketed treatment for patients with relapsed or refractory APL following standard of care. Tamibarotene, however, is covered by a Special Protocol Assessment (SPA) with the FDA that is enabling a Phase II clinical trial to evaluate the efficacy and safety of tamibarotene in those patients. The trial is ongoing and currently includes seven clinical sites in the United States.

CytRx’s mid- and long-term opportunities include developing INNO-206 and bafetinib. INNO-206 will move into two Phase II trials for advanced gastric cancer and sarcomas. Bafetinib is a drug targeting leukemias that completed a Phase I trial and is ready for Phase II. The company’s other clinical projects include its molecular chaperone regulators, arimoclomol and iroxanadine, for a number of potential indications including ALS, stroke and vascular diseases. CytRx maintains a 36 percent equity interest in RXi Pharmaceuticals, which provides a source for potential non-dilutive financing to help CytRx advance its development candidates.

Headquarters:
Los Angeles

Established:
1985

IPO:
1986

Employees:
18

Product Pipeline:
Tamibarotene for Acute Promyelocytic Leukemia (Phase II)
Arimoclomol for ALS, stroke recovery (Phase II)
INNO-206 for solid tumors (Phase I)
Iroxanadine for diabetic complications (Phase I)
Bafetinib, a third-line Chronic Myeloid Leukemia treatment (Phase II)
Medtronic, Inc. is a global leader in medical technology with a broad reach into many of the world’s most debilitating human conditions. Among the Minneapolis-based corporation’s California operations is Medtronic Diabetes in Northridge.

The company’s diabetes business is the world leader in insulin pump therapy and continuous glucose monitoring. Medtronic’s first insulin pump was introduced in 1983, and through advancements in the technology and the products, the MiniMed Paradigm Pump is the most prescribed pump today. The pump is a key component in Medtronic’s full diabetes management system. The system, which also includes continuous glucose monitors, wireless transmitters and therapy management software, helps patients and their physicians and other specialists refine their treatment and lifestyle for smoother blood sugar maintenance.

Comprised of approximately 2,000 people, Medtronic Diabetes’s Northridge staff includes the full management team as well as marketing, research and development, light manufacturing, and customer support professionals. This latter group provides patient information materials and events to help those with diabetes better understand and manage their disease. Customer support also includes a 24/7 helpline that patients, caregivers or physicians can call with questions about their insulin pumps or related issues.

Medtronic Diabetes acquired MiniMed, Inc. in 2001 and kept the diabetes division in Northridge to sustain its staff and operations. The organization is served well by the region, according to Rob Clark, senior director of state government affairs for Medtronic. He said that the local workforce is made up of “exceptional, high-quality people,” including the company’s world-class customer service operations team which must fully understand the technology and have the “people skills” to walk patients through the products’ operations and features.

Through 25 years of developing medical technologies to help people better manage their diabetes, the Medtronic team in Northridge has made significant advancements toward its ultimate vision: to create a virtual pancreas. That is, Medtronic Diabetes intends to use its integrated systems to make glucose sensing and insulin delivery automatic—just as a healthy pancreas does in individuals without diabetes.

Headquarters:
Minneapolis, Minn.

California operations:
Northridge as well as Carlsbad, Goleta, Irvine, Santa Ana, Santa Rosa and Sunnyvale

Established:
1949

Employees:
Approximately 38,000 worldwide, including 2,000 in Northridge

Products:
Full diabetes management systems that include monitors, insulin pumps, transmitters and therapy management software

Product Revenues for FY2009:
$1.1 billion
In 1945, the University of California Board of Regents voted to establish a medical school at UCLA. The first class entered UCLA’s School of Medicine in 1951. The school was renamed in 2002 for David Geffen, who established a $200 million unrestricted endowment for the school.

Today, the biomedical research conducted at UCLA’s school of medicine and its other life sciences departments spans the basic sciences from biological chemistry to human genetics, molecular medicine to neurobiology and physiology. UCLA also is home to a number of institutes and centers, all of which are conducting research aimed at expanding scientific knowledge and improving the practice of medicine.

Among the school’s higher profile research programs are:

- **The Brain Mapping Center** is collecting images of brains from thousands of individuals to comprise a Brain Atlas that will be used to help neuroscientists around the world with research and clinical breakthroughs.

- **The Jules Stein Eye Institute** is pursuing research in basic vision science in areas such as biophysics, genetics, and neurobiology to pursue breakthroughs in treating glaucoma, corneal and retinal disease.

- **The Semel Institute for Neuroscience and Human Behavior** is an interdisciplinary research and education institute devoted to the understanding of complex human behavior, including genetic, biological, behavioral and socio-cultural underpinnings of normal behavior, and the causes and consequences of neuropsychiatric disorders. Research is being conducted in areas ranging from autism to Alzheimer’s disease.

- **The Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research** provides close and ongoing collaboration across UCLA’s scientific, medical and academic disciplines. The initial focus of the Broad Center at UCLA includes stem cell growth and differentiation; genomic reprogramming; hESC cell gene expression; muscle (skeletal and cardiac), bone, and cartilage; cancer stem cells; neural stem cells; hematopoietic and immune systems; HIV/AIDS; and metabolic disorders.

- **The Jonsson Comprehensive Cancer Center** is one of the largest comprehensive cancer centers in the nation. It has established an international reputation in developing new cancer therapies, providing the best in experimental and traditional treatments and training the next generation of medical researchers. Numerous successful targeted therapies were developed based on the basic sciences done in UCLA laboratories and later clinical research with UCLA patients. A few of the well-known therapies include Herceptin, a targeted breast cancer drug and the first approved that attacks cancer at its genetic roots; Gleevic, a once-a-day pill that targets a common form of adult leukemia; Tarceva, a targeted lung cancer drug; and Avastin, a targeted drug for colorectal, lung and breast cancer.

With the research and training ongoing within its schools, UCLA is ranked as the seventh-largest employer in Los Angeles. Economic activity associated with UCLA generates more than $1.2 billion annually in local, state and federal taxes. The UCLA Health System and the David Geffen School of Medicine have more than 14,000 full-time employees.

The university also has been a potent technology transfer engine. The UCLA Office of Intellectual Property, which collects data for the entire UCLA campus, reports that the school has registered 1,388 inventions. There are 415 active patents, 530 active foreign patents and 220 active license agreements.
City of Hope is a leading independent biomedical research, treatment and education center for cancer, diabetes and other life-threatening diseases. Since its founding nearly a century ago in 1913, the institution has pursued its mission of advancing medical research, developing cures and novel therapies, and providing future scientists with practical laboratory skills in the biological sciences.

City of Hope is designated as a Comprehensive Cancer Center, the highest honor bestowed by the National Cancer Institute, which recognizes the impact and scope of resources that a center provides both within its own community and on a national scale. The institution’s research and treatment protocols advance care throughout the country.

City of Hope is a pioneer in the field of hematopoietic cell transplantation (HCT), also known as bone marrow transplantation, for the treatment of blood cancers such as leukemia and lymphoma. HCT is one aspect of City of Hope’s work in stem cell research and development. City of Hope’s clinicians and researchers continue the tradition through refining and expanding HCT to address other systemic conditions such as lupus and multiple sclerosis, as well as the treatment of HIV and AIDS-related cancers.

Clinical trials are currently underway of an HIV-targeted gene therapy developed by City of Hope researchers for the treatment of AIDS-related lymphoma. It may potentially cure both the cancer and AIDS. The therapy works on three levels—providing new HIV-resistant blood stem cells, preventing HIV infection of current immune cells, and restarting the immune system to attack and destroy HIV cells.

City of Hope is also a pioneer in genetics. Alongside the clinical cancer genetics program that identifies specific genes tied to the risk of developing certain cancers, the institution also has numerous programs that focus on developing targeted, personalized medicines tuned to individual genetic profiles. The multidisciplinary team approach to City of Hope’s research aids the translation of laboratory discoveries into novel therapeutics.

City of Hope’s infrastructure and collaborative environment facilitate pre-clinical testing of potential new therapeutics. One of the major pitfalls of drug development is the obstacle of validating the potential of new drugs through toxicity, dosing, and safety studies. City of Hope’s integrated approach pulls together basic science, pathology, pharmacology, on-site GMP manufacturing and clinical research on one campus that speeds the process of drug development.

The institution’s Office of Technology Licensing promotes the intellectual property and discoveries of the clinical and laboratory researchers. In addition to filing patents on technological inventions and scientific innovations, the group also manages licensing and development partnerships with biotech and pharmaceutical companies. City of Hope provides numerous opportunities to pursue development and testing of investigational products running the gamut from stem cells to nanotechnology, RNA interference and immunotherapeutics.

City of Hope’s mission is to find cures for serious diseases. Through research, treatment, education and collaboration, the institute advances the boundaries of medicine in pursuit of healing the patient. City of Hope has served the public interest for the past century and is strategically positioned to continue its legacy of medical advances well into its next century.
Established 1880, USC is a world-class research university. Located three miles from downtown Los Angeles, USC’s Health Sciences campus is a major center for basic and clinical biomedical research, especially in the fields of cancer, gene therapy, the neurosciences and transplantation biology. The 61-acre campus also is home to the region’s oldest medical and pharmacy schools, as well as to acclaimed programs in occupational and physical therapy.

In addition to Los Angeles County and USC Medical Center, which is one of the country’s largest teaching hospitals, the campus includes three state-of-the-art patient care facilities: the USC/Norris Comprehensive Cancer Center, USC University Hospital, and Doheny Eye Institute. USC faculty members staff these as well as many other hospitals in Southern California, including the nationally acclaimed Childrens Hospital Los Angeles (CHLA).

USC is focused on solving problems through interdisciplinary centers, institutes, and training programs. Working in this environment, clinical researchers at USC have already produced major advances in health. Some prominent examples include the first demonstration that lowering cholesterol regresses atherosclerosis; major contributions to reducing maternal-child HIV transmission and managing opportunistic infections in AIDS patients; and the first demonstration that type 2 diabetes is preventable.

In 2006, USC created the Los Angeles Basin Clinical and Translational Science Institute (CTSI) to elevate the university’s research strengths toward more interactive clinical and translational research for the health of urban populations. The CTSI combines the resources of USC, CHLA, three of urban of the leading clinical care systems in Los Angeles, and many community health organizations to promote scientific discoveries and their efficient application to address health problems of diverse populations living in urban environments. USC’s other current biomedical initiatives are described below.

Institute for Stem Cell and Regenerative Medicine

This premier science and research project pursues investigation into the biological mechanisms that control stem cell behavior.

USC/Norris Comprehensive Cancer Center

A research institute integrated with a state-of-the-art patient care facility, the USC/Norris Comprehensive Cancer Center is recognized for the excellence of its programs in epidemiology, therapeutic investigations and translational research.

Zilkha Neurogenetic Institute

At this center, USC faculty, fellows, and graduate students apply their expertise to characterize the genetic and molecular mechanisms underlying neurological and psychiatric disorders.

The Institute for Creative Technologies

A partnership of the U.S. Army and the education, entertainment and computer industries, the Institute for Creative Technologies is working to develop new media to improve the nation’s learning abilities and training programs.

Beyond working directly with researchers and healthcare providers in the community, USC has been a robust source of breakthrough ideas and the catalyst for the startup of new biomedical companies.
Cedars-Sinai Medical Center

Cedars-Sinai Medical Center was founded more than a century ago to meet the healthcare needs of a growing Los Angeles community. Today, Cedars-Sinai ranks as the largest private teaching hospital in the western United States. Research at Cedars-Sinai comprises more than 700 projects, and Cedars-Sinai ranks among the top non-university hospitals nationwide receiving research funding from the National Institutes of Health.

Cedars-Sinai offers a doctoral degree through its Biomedical Sciences and Translational Medicine Ph.D. Program. The program is designed to train a new generation of researchers in the science and culture of translating basic scientific discoveries into potential treatments, therapies, and cures for human disease. As such, the Ph.D.-granting program fills a major gap between the traditional training areas of biomedical research, typically led by Ph.D.s in basic science disciplines, and clinical research, currently carried out by physician-scientists (typically M.D.s). The first class for the new graduate program commenced in the fall of 2008. Each class is anticipated to have eight students, and 16 students currently are enrolled.

Translational research characterizes much of Cedars-Sinai’s ongoing operations, as illustrated by the following descriptions of the center’s highest profile programs.

Heart Institute
The Cedars-Sinai Heart Institute is a multidisciplinary entity comprising all aspects of heart-related research, clinical practice, education, and strategic planning within the Cedars-Sinai Medical Center.

Cancer Institute
Cedars-Sinai’s Samuel Oschin Comprehensive Cancer Institute provides multidisciplinary cancer care in one of the largest state-of-the-art clinical research and trials facilities of any private hospital in the nation.

Inflammatory Bowel and Immunobiology Research Institute
The Cedars-Sinai Inflammatory Bowel and Immunobiology Research Institute utilizes the most advanced concepts and techniques of laboratory, translational and clinical research to unravel the mechanisms leading to inflammation.

Transplant Center
The Cedars-Sinai Comprehensive Transplant Center integrates programmatic development, clinical care and scientific investigations that focus on the rejuvenation and restoration of failed solid organ function.

Gene Therapy
Cedars-Sinai’s Board of Governors Gene Therapeutics Research Institute is working to harness the power of the Human Genome Project to develop innovative gene therapy strategies with an eye toward clinical applications.

Regenerative Medicine Institute
The institute will be the hub for all stem cell and regeneration projects on campus.
The California Institute of Technology is an independent, privately supported university with undergraduate and graduate-level programs. Including its off-campus facilities, Caltech is one of the world’s major research institutions. It is also ranked among the most rigorous globally, an accomplishment achieved by matching a relatively small group of students with a relatively large faculty.

Caltech also equips its staff and student researchers with the most advanced equipment and technologies available—a benefit often made possible by the generosity of alumni and philanthropists. For instance, students pursuing degrees in biomedical arenas spend time in the Beckman Institute, which opened in 1990. Built with funds provided by the Arnold and Mabel Beckman Foundation and other private donors, the Beckman Institute enables scientists working there to invent new methods, materials, and instrumentation for fundamental research in biology and chemistry that will open the way for novel applications of scientific discoveries to human needs.

Similarly, Caltech in 2002 completed construction of the Broad Center for the Biological Sciences, which was realized in part through a $100 million campaign to support biological research.

Among its life sciences and biomedical programs, Caltech offers bachelors and/or advanced degrees in chemistry; chemical engineering; computation and neural systems; biology; biotechnology; bioengineering; biochemistry and molecular biophysics; and behavioral and social neuroscience. Beyond training students in the intricacies of their particular disciplines, Caltech emphasizes the synergies of multi-disciplinary research teams and projects, ensuring that breakthroughs in a particular area of science might find application in others.

Caltech also extends research opportunities—and “real world” experience—to all levels of its associates, starting with its undergraduates. In the Summer Undergraduate Research Fellowships (SURF) program, for example, undergraduate students work on individual research projects in a tutorial relationship with a mentor. Mentors typically are Caltech faculty but can be faculty or researchers at other universities. To apply, students write research proposals in collaboration with their mentors, and awards are made on the basis of reviewer recommendations and available funding. Following their 10-week summer project, “SURFers” submit a written report describing the project, methods, and results of their work.

Caltech, which is associated with 31 Nobel laureates, 49 recipients of the National Medal of Science, and 12 National Medal of Technology honorees, also has been the catalyst for the formation of numerous technology companies. In fact, Caltech has received more than 1,800 U.S. patents since 1980. Caltech receives more invention disclosures per faculty member than any other university in the nation. In the last 10 years, licensing efforts have resulted in 40 to 50 patent licenses per year, and its technology transfer office fosters start-up companies at a rate of about eight per year.
California State University Campuses: Partners in Biomedical Industry Growth in the Greater Los Angeles Region

Eight California State University (CSU) campuses are partners to the burgeoning biomedical industry in the greater Los Angeles region: CSU Los Angeles, Pomona, Fullerton, Northridge, Channel Islands, Long Beach, Dominguez Hills, and San Bernardino. They engage in joint initiatives coordinated through the CSU Program of Education and Research in Biotechnology (CSUPERB)—Los Angeles Basin (C-LAB). Five campuses have well-respected Professional Science Master’s (PSM) programs that involve partnerships with the biomedical industry.

**Cal State Fullerton**
- Location: Northern Orange County
- Established: 1959
- Associates: 850 full-time faculty; 37,000 students

**Cal State Los Angeles**
- Location: Central Los Angeles County
- Established: 1947
- Associates: 590 full-time faculty; 21,000 students

**Cal Poly Pomona**
- Location: Eastern Los Angeles County
- Established: 1966
- Associates: 600 full-time faculty; 21,000 students

**CSU Northridge**
- Location: Northern Los Angeles County
- Established: 1959
- Associates: 890 full-time faculty; 36,200 students

**Degree Program (PSM): Master of Biotechnology (MBt)**

The Program for Applied Biotechnology Studies is a three-campus, industry-oriented graduate program that includes concentrations in molecular biology, biochemistry, analytical chemistry, bioinformatics/biomathematics, regulatory affairs/clinical trials, bio-engineering, and bio-business, with additional areas under development. In addition, through funding from the California Institute for Regenerative Medicine (CIRM), the campuses prepare students to work in stem cell biology. Faculty research areas at Fullerton include antibiotic resistance, biochemistry of inflammation and progression of ovarian and other cancers, and neurodegenerative disorders and aging-related disease, including Alzheimer’s, Parkinson’s, Lou Gehrig’s disease, and cerebral stroke. Los Angeles has research in high-throughput screening for novel antibiotics and drug targets, analysis of cancer signaling, the molecular basis for cell progression in cancer, behavioral and neurochemical effects on neural regeneration, enhancement of the innate immune response, viral pathogenesis, and biological applications of microfluidics. Pomona has research in targeted delivery of drugs to treat diseases, resistance to antibacterial and chemotherapeutic agents, control of epileptic seizures and stroke, and anti-viral vaccines.

**CSU Channel Islands**
- Location: Southern Ventura County
- Established: 2001
- Associates: 90 full-time faculty; 3,800 students

**Degree Programs (PSM): Master of Science in Biotechnology and Bioinformatics, including Emphasis in Stem Cell Technology and Lab Management; Dual Degree: Master of Science in Biotechnology/MBA**

CSU Channel Islands’ Master of Science in Biotechnology and Bioinformatics, established in 2005, partners with more than 50 Ph.D. scientists from eleven biomedical firms and academic institutions in the Los Angeles region to offer high-quality research training to more than 120 students in its biotechnology education programs. Areas of research include stem cell technology, pharmaceutics, tissue engineering, diagnostics, high-throughput production mechanisms, instrumentation and imaging, biomaterials, and bio-energy. Amgen has been a primary partner and has donated scholarships to support the students enrolled in this program.
Greater Los Angeles Cluster: Nurturing the Biomedical Industry via Community Colleges

**What:** Los Angeles-Orange County Biotechnology Center

**Hosted by:** Pasadena City College

**Established:** 1998

**Connects:** 28 regional community colleges, eight California State University (CSU) schools in the Los Angeles Basin (C-LAB), regional four-year universities and local industry

“I see my role as capacity building,” said Wendie Johnston, Ph.D., Director of the Los Angeles-Orange County Biotechnology Center. Her key objective, she said, is to ensure ready connections among resources, missions and people.

The LA/OC Biotechnology Center is one of six statewide offices established in the mid-1990s by the California Community Colleges system to develop the biomedical industry workforce.* Through the Applied Biotechnologies Initiative, the biotech centers began developing new educational programs geared toward preparing California students to fill life science jobs.

Each center’s director works within his or her region to determine local workforce development needs. Johnston applies her energies and skills to building bridges among the various components of the Los Angeles basin biomedical industry cluster—from pre-college through economic development. Since the program’s inception in 1998, Johnston has seen firsthand that the region is fertile ground for the seeds her programs are planting.

*Another of the six biotechnology centers, the Central Coast Biotechnology Center, is located at Ventura College under the direction of Tricia Fausset. It also contributes to the workforce development in the LA/Ventura counties biomedical cluster.

**Pre-College Science**

Tomorrow’s scientists, engineers, physicians and researchers are middle and high school students today. The LA/OC Biotechnology Center is reaching out to them and their teachers by making compelling curriculum available to them.

One example is the Amgen-Bruce Wallace Biotechnology Lab Program. The course allows students to conduct protocols for recombinant DNA labs and PCR experiments. In addition to training teachers in the curriculum and the associated experiments, Pasadena City College also provides short-term loans of the necessary wet lab equipment.

“At Amgen deserves a gold star for this program,” Johnston said, adding that credit goes “both to corporate for the equipment and to the Amgen Foundation for the outreach.” She said that approximately 12,500 high school students from 80 Los Angeles and Orange County high schools have participated in the three-week program. More than a half dozen California high schools have parlayed or are in the process of parlaying the three-week program into a University of California-approved year-long biotech-biology course. The Amgen-Bruce Wallace Biotechnology Lab Program has been replicated in San Diego and the Bay Area through Amgen Foundation grants.

**Community Colleges**

The LA/OC Biotech Center region encompasses 28 regional colleges. All offer the basic math and science courses for a career in biosciences. A number offer certificate programs geared toward specific functions within biomedical companies (see sidebar). Other programs have been designed or are in development for launch once current budget constraints have been resolved.

Johnston notes that one advantage of offering workplace training at the community college level is that the courses are accessible to everyone—first-generation college students, talented high school students, individuals pursuing a new career, displaced workers and veterans.

“We have people of all ages,” Johnston said. She added that more than half of the students have earned their bachelor’s degrees and are seeking added training to secure employment or enter graduate or medical schools. Most of the skills courses are conducted in the evenings as a convenience to working adult students.

**Universities**

In addition to arming students with the math and science credits they need to transfer to four-year programs, the LA/OC Biotech Center also works to bridge the programs at community colleges with those in the region’s universities.

As a partner in the Southern California Summer Bioinformatics Institute at CSU Los Angeles, the LA/OC Biotech Center continues to assist in building career ladders to new and existing life sciences programs. The institute, which has just completed its seventh year of operation, is funded by a National Institutes of Health-National Science Foundation grant, for which Johnston is a co-principal investigator. More than 100 students have attended the 10-week institute and over 80 percent are working in computational biology or related scientific fields.

In other partnerships, universities provide internships and equipment donations for community college students. Among current internships are 10 one-year placements of Pasadena City College students at Caltech, the University of Southern California and Childrens Hospital Los Angeles. Johnston explained that the cooperative agreement is made possible by a California Institute for Regenerative Medicine (CIRM) Bridges to Stem Cell Research Award of $1.7 million in spring 2009 to Pamela Eversole-
Cire, Ph.D., director of the Biological Technology Program at Pasadena City College. In addition to the internships, the grant is being used to further develop Pasadena City College’s Stem Cell Culture program.

Industry

The LA/OC Biotech Center connects companies with academia in relationships that benefit both sides. Johnston said that she has helped identify and recruit members both for companies’ scientific advisory boards and for grant and development committees in academia. She has helped line up internships for students and garnered equipment donations from local private and educational labs for colleges and high schools.

Working with Oak Crest Institute of Science in Pasadena, Johnston and the LA/OC Biotech Center provide high school, community college and university students with real-world experience in biomedical science. The institute, founded in 1998 as a non-profit chemistry research and education center, has participated in Caltech’s Summer Undergraduate Research Fellowship (SURF) program for several years and has had a successful National Science Foundation Research Experiences for Undergraduates (REU) grant under which students from local community colleges held six- to 12-month fellowships—an invaluable experience, according to Johnston. The classroom education combined with hands-on experience gives students the training and confidence they need not only to secure a biomedical industry position but to launch an exciting, fulfilling career in research.

Economic Development

The final link in the interconnectedness that Johnston seeks through the LA/OC Biotech Center is the Pasadena Bioscience Collaborative (PBC), an “incubator” that provides space, equipment, interns and advice to startup “wet lab” companies. PBC is housed next door to Oak Crest in Pasadena. Its equipment, donated by industry to both PBC and Pasadena City College, promotes new company formation while providing additional specialized education and training for the biomedical workforce.

Bruce Blomstrom, president of the Pasadena Bioscience Collaborative, said that companies interested in participating in the incubator must have a proper business plan, the financial strength to pay rent, a demonstrated adherence to Good Laboratory Practices and a current liability insurance policy.

PBC may be the San Gabriel Valley’s best-kept secret for startups. “We provide access to the experts that early-stage companies may need,” Blomstrom said, “whether those are in biotech, nanotech, bioinformatics, grant writing, legal, marketing or business.” Since the incubator was opened in mid-2004, it has nurtured a number of companies with the goal of advancing the startups’ science and business acumen to the point of being able to secure outside funding. In 2008, the PBC expanded from 3,000 square feet to 6,700 square feet, and by the end of 2009 additional expansion will bring the area to more than 10,000 square feet.

Although local political support, the availability of facilities, and the founders’ personal preferences brought the incubator to Pasadena, Blomstrom joins Johnston in viewing their programs as serving the full LA Basin biomedical industry. They see the industry as an interdependent system that combines the strengths of academia, companies, investors and community services toward better medical knowledge and therapies—and better quality of life for patients everywhere.

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Larta Institute: Binding the Elements of Biomedical Success

Rohit K. Shukla

Rohit K. Shukla, Larta Institute’s chief executive officer, has worked in the high technology industry since 1983, first as an entrepreneur and founder of a database and communications solutions and devices company and, later, as the executive director of The Presidents’ Roundtable, a mentor group of CEOs from defense and aerospace companies throughout the United States. Prior to founding Larta in 1993, Shukla served as director of aerospace and high technology business at the Los Angeles Economic Development Corporation. Shukla holds a master’s degree in social and political sciences from Cambridge University and a master's degree in communications arts from Loyola Marymount University in Los Angeles.

Carlos E. Gutierrez

Carlos E. Gutierrez is the Chief Strategy Officer at Larta Institute, overseeing all aspects of the organization’s strategic focus and business development efforts with clients, including U.S. federal agencies, universities, industry partners, and regional economies around the world. Prior to joining Larta, Gutierrez served on the management team of FirstLook.com, an Idealab company and venture-backed startup.

Larta Institute is a leading “innovation hub” and commercialization services firm based in Los Angeles and working globally to improve the transition of scientific and technological breakthroughs from the laboratory to the marketplace. The institute offers a range of services for states, government agencies, and regional partners in innovation policy and consultation, technology and commercial assessments, and hands-on commercialization programs with entrepreneurs under sponsored client programs.

Q. How did Larta Institute get started?

A. With the downsizing of California aerospace industry in the early 1990s, and the consequent job losses and loss of talent, we were convinced that there was a role for an organizational infrastructure to bring California’s diverse talents to bear on behalf of emerging entrepreneurs—to mentor them and to nurture their ideas with market-oriented practices. We helped to write legislation that received bipartisan support for a wide-ranging private-public partnership to build entrepreneurial companies in a challenging environment. The motivation was simple: the desire to corral bright innovations and to let no innovation go undiscovered.

As a key participant in CalTIP (California Technology Innovation Program), Larta Institute served as the State of California’s commercialization agent in the vast six-county Southern California geography (including Los Angeles, Orange, Ventura, Riverside, San Bernardino, and Santa Barbara counties). In that capacity, Larta identified and nurtured hundreds of early-stage life science and high technology companies that were recipients of state grants. In addition, Larta Institute offered a well-regarded entrepreneurial training platform, which came to be known as Larta University (and which the Wall Street Journal referred to as a “mini MBA for entrepreneurs”).

Keen to establish the primacy of California’s position at the center of innovation, the organization also established links with global locations interested in partnering with
entrepreneurs in California, including Finland (biotech and medical devices), Sweden (biotech and information technology) and many countries in Asia. The partially state-funded program ended in 2002. Since that time, we’ve expanded our core commercialization work to include national and international client partners.

Q. What does Larta Institute mean by the term “innovation hub”?
A. We saw the concept of the hub as a good visual image to describe our role and value proposition to entrepreneurs and entities that support innovation programs. In short, it means that Larta has a unique access and relationships to connect the various parts of the innovation ecosystem—capital providers, industry, government, professional services, academia, and private enterprise—for our client partners. It is driven by transactional need, to service specific innovations that we address through our various client engagements. All of our programs incorporate elements that engage entrepreneurs to the spokes of the hub. We surround ourselves with some of the best subject matter and domain experts in the world who coach and mentor companies in our programs, working through a system and a methodology we have honed over 15 years.

Among our activities, we have sought out and partnered with Fortune 1000 firms that are seeking disruptive technologies and solutions to some of their toughest customer challenges. We also convene a national commercialization training workshop in Los Angeles every year for National Institutes of Health (NIH) grantees, bringing entrepreneurs, industry professionals and advisors from around the country to the region, and invite local experts to participate as well. We also hold “feedback sessions” for the entrepreneurs in the program in Los Angeles every year, and seek to introduce them to potential partners in the region.

Q. What do you see as the key components of Larta’s successful technology transfer agreements?
A. Given the shifting landscapes, diverse motivations, and incentives that are in place for the various players, it would be somewhat foolhardy for us to pretend that we can structure technology transfer agreements. So, in fact, Larta itself does not structure such agreements. However, we have designed and launched initiatives to help support university technology transfer efforts to address some of the gaps and focus areas that prevent more robust technology transfer activity.

The important principle we have been exploring for many years (and to be frank, this is a difficult problem to solve) is fostering collaboration between technology transfer offices and to pool their intellectual property (IP). Such pooled IP would be focused on specific industry needs, where the sum of the parts is of greater benefit to industry buyers than the individual pieces of IP. After many years of such explorations, in partnership with the Kauffman Foundation and Southern California Edison, we have now established a program with Loma Linda University with support from the National Science Foundation focused on bringing stronger industry inputs and needs requirements to researchers, so they can better orient their work early on to meet real-world technical challenges and address market segments of keen interest to those same large companies.

Q. What attributes of the Los Angeles region have made it a significant biomedical cluster?
A. One of the best assets of the greater Southern California region is the array of intellectual assets spread throughout its large geography: a world-class collection of research institutes and universities like City of Hope; Cedars-Sinai; the University of California, Los Angeles; the University of Southern California; and the California Institute of Technology. We have been privileged to work with all of them, and with entrepreneurs, investors and industry in this extraordinary region.

The region is not accepted widely as a center of innovation, in part because it suffers from the tyranny of size. So-called “clusters” are said to flourish in relatively small geographical areas. However, we believe that given the wide distribution of technology, of ideas, of talent and of money in the global economy, the size of the greater Los Angeles region is actually a proxy for the way things are, and will be. In short, the biomedical and biotech attributes of the region should be seen as an embarrassment of riches, and given its outward-facing orientation, it will continue to be a hub of economically productive, profitable activity, even as the center of gravity moves to Asia.

Q. Is there anything you would like to share with California legislators and policymakers?
A. In order to maintain a commitment to higher standards of living, greater engagement with the world (via talent, money, brainpower and commerce), more stable revenues less dependent on the vagaries of capital gains, find the money, float a bond, stake your reputation as the center of gravity in the world of innovation. Most importantly, build a program that touches on maintaining a commitment to science, to both research and to commercialization, an integrated program of skills training, entrepreneurial development and incentives to attract, retain and grow our dynamic industry. It’s not just about jobs, it’s about high-value jobs.

“It’s not just about jobs, it’s about high-value jobs.”

Rohit K. Shukla
CEO, Larta Institute
Diabetes runs in California state Sen. Alex Padilla’s family (his mother has type 2 diabetes). Obesity and diabetes are key health concerns among all Americans, and are especially important to Padilla’s constituency—the strongly Latino communities of the San Fernando Valley.

“One in every three children born in 2000 will experience diabetes in their lifetime,” Padilla said. “For Latino and African American children, the number is closer to half.”

The numbers are alarming, but Padilla said that it took his mother’s experience with type 2 diabetes to bring the realities home. “All of a sudden,” he said, “all of the reports and studies coming across my desk made a lot more sense, and it just so happens that I’m in a career where I can influence policy.”

Padilla’s policy approach to helping his constituents and all Californians deal with key health issues—obesity and cancer as well as diabetes—focuses on pragmatic changes that empower people to better prevent, treat and manage disease.

For instance, while on the Los Angeles City Council, he urged the other members and city staff to wear pedometers. He has been a co-sponsor of public health events that encourage family activities such as walking, hiking, biking, skateboarding and running. In conjunction with the Mission Community Hospital’s Project ALTO, Padilla hosted a Diabetes Self-Management Education Series in his offices in the fall of 2009. The free eight-week program was presented in both English and Spanish and covered topics on preventing, treating and managing diabetes and its co-morbidities.

Padilla also chairs the California Task Force on Youth and Workplace Wellness. The task force issues yearly recommendations to combat obesity and promote healthy eating and exercise in California schools and workplaces.

As one of his early successes in the state legislature, Padilla introduced and gained passage of the menu labeling bill, which requires restaurant chains with 20 or more locations to provide customers with nutritional information for menu items. Required data includes the number of calories, grams of saturated fat, grams of carbohydrates and milligrams of sodium for all standard menu items.

The first phase took effect on July 1, 2009 and requires the information to be available in brochures at the point of purchase. The second phase, which begins January 1, 2011, will require that calorie information be printed directly on menus and indoor menu boards. More than

Alex Padilla

Alex Padilla has been a California State Senator representing the 20th District since 2006. In addition to serving on a number of full committees, he chairs the Select Committee on Obesity and Diabetes and the Select Committee on College and University Admissions and Outreach. Padilla previously served more than seven years on the Los Angeles City Council, where he was the first Latino and youngest person ever to be elected city council president. Padilla earned his degree in mechanical engineering from the Massachusetts Institute of Technology (MIT) and worked for Hughes Aircraft before entering public service. In his support of health advocacy organizations, he was Chair of the Los Angeles Leadership Council of the American Diabetes Association from 2006 to 2007 and now is Chair of the Honorary Board. He also was honored with a Latino Diabetes Association Legislator of the Year award in 2008. (See related article on page 79.)

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17,000 restaurant locations throughout California are covered by the bill, and Padilla said that many restaurant chains are leapfrogging from phase one to full implementation.

“Not a week goes by that I don’t hear from someone who tells me that at first they weren’t too sure about the bill, but they now find the nutritional information extremely helpful,” Padilla said. He noted that he uses the labeling to make healthier food choices and that the information can be surprising.

Giving consumers the information to make healthful choices is not only a service but, potentially, a cost-cutting measure. The California Department of Health Services estimates that obesity costs California at least $8.4 billion annually in medical care, workers’ compensation, and lost productivity. Nearly 16 million Californians are obese or overweight and many suffer from diseases such as diabetes, heart disease, and hypertension. One third of Californians aged nine to 11 are overweight or at risk of becoming overweight. They also are increasingly suffering from illnesses that normally occur in adulthood, including diseases such as type 2 diabetes and pre-hypertension.

Padilla said that continuing research and innovation in diabetes and obesity therapies is critical. He credited the biomedical industry with increasing the scientific knowledge around the conditions, their causes and potential treatments. Among California companies pursuing new knowledge and therapies are San Diego-based Amylin and Metabolex in Hayward. Medical device developers enabling patients to better manage their diabetes include Medtronic in Northridge, Abbott Diabetes Care in Alameda, and LifeScan, Inc., a Johnson & Johnson Company in Milpitas. Many of the Golden State’s university and independent research institutions also are pursuing breakthroughs in diabetes therapies. Among those in the LA/Ventura region are The Larry L. Hillblom Islet Research Center at University of California, Los Angeles, and the Leslie and Susan Gonda (Goldschmied) Diabetes and Genetic Research Center at the City of Hope.

“With all of the healthcare reform discussions, the biggest question is, ‘How do we afford it?’ ” Padilla said. “We have to recognize that the biggest increases in healthcare costs have been obesity-driven... We need to start highlighting the cost-effectiveness of prevention.” Toward that goal, Padilla is evaluating other incremental, real-world steps that policy makers might take to help individuals make more healthful choices. Citing a September 2009 research report linking soft drink consumption with obesity, he said he expects the findings to spur “soda tax” discussions.

Similarly, he is working on public health issues related to smoking. “In California,” he said, “retailers cannot sell liquor within 600 yards of schools. It’s not the same with cigarettes.” Cigarettes, he noted, are increasingly sold at video stores, donut shops and other venues where kids are likely to congregate. Further, Padilla feels the enforcement rules and penalties for tobacco sales violations are too lax to protect youngsters.

Long-term health and chronic disease are public policy issues, Padilla said, with profound policy challenges at all levels of government. With firsthand experience of the ramifications of chronic illness—both as a legislator and as a son—Padilla is committed to shaping policy and legislation to address those challenges.
Heberto M. Sanchez

Heberto M. Sanchez is the founder and former chief executive officer of the Latino Diabetes Association (LDA), a 501(c)3 nonprofit organization. Born in Los Angeles, he studied at California State University, Northridge, where he earned a bachelor’s degree in business administration—marketing and a master’s degree in public administration. In 2002, he received the Heritage of Excellence Honors from California State University, Northridge. In 2004, he was elected and served two terms as president of the Eastside Democratic Club, receiving Congressional recognition. He worked with California Rep. Joe Baca to introduce Congressional House Resolution 69 designating July 2009 as Latino Diabetes Awareness Month.

Randy Muñoz

Randy Muñoz is executive director of the Latino Diabetes Association. Raised in Boyle Heights in the Estrada Courts public housing projects, Muñoz hosts and produces his own community television talk show, “The People’s Channel,” on local, national, and international issues that affect primarily the Chicano/Mexicano/“Latino” community. He is also a community advisory board member of the David Geffen UCLA School of Medicine Caminemos Program, a member of the Montebello Chamber of Commerce, a committee member of the Los Angeles Department of Aging Hispanic Elderly Collaborative, and member of the City of Commerce I710 freeway extension Advisory Committee.
When his father died from complications of type 2 diabetes in December 2003, the loss catapulted Heberto Sanchez Jr. into patient advocacy. He started at “ground level” in both senses of the phrase: the younger Sanchez had never been involved in advocacy efforts before. He also was committed to fighting diabetes in his own stomping grounds, one friend and neighbor at a time.

He founded the Latino Diabetes Association (LDA) as a community-based nonprofit social service organization. He also recruited Randy Muñoz, whose mother, brother and niece have been diagnosed with the disease, as the organization’s executive director. Together, with their own time and money, the two men began working with community leaders, public health specialists and local volunteers to educate their neighbors about preventing diabetes in the first place—and managing the disease once they were diagnosed.

Their goal was ambitious. Among Latinos, diabetes is the sixth leading cause of death, and it is ranked fourth among Hispanic women and Hispanic elderly. An estimated 2 million, or 8.2 percent, of all Latinos age 20 and older have diabetes, with more than 10 percent of Mexican Americans in the same age group diagnosed with the disease.

Latinos, on average, are 1.5 times more likely to have diabetes than are non-Hispanic whites. They also are twice as likely as other populations to experience complications such as heart disease, high blood pressure, blindness, kidney disease, amputations and nerve damage. Yet they have less access to the means of preventing and managing the disease.

Muñoz said that the LDA focused initially on community outreach. “We go directly into these underserved communities where people contract these diseases to begin with,” he said. “We conduct diabetes prevention classes in local libraries, churches, senior citizen and community centers, public housing projects…wherever we can get people together. We canvass the neighborhoods ahead [of the classes]. We go door-to-door, work one-on-one with people.” He said such outreach is time consuming and expensive. “But we can invest the time and money now on community education, or we can pay later” for treatments and disease management, he said.

The classes in nutrition and exercise still comprise much of the LDA’s outreach efforts. With grants from National Association of Chain Drug Stores, Hispanic in Philanthropy Foundation, Acta Rite Aid, the Pharmaceutical Research and Manufacturers of America (PhRMA), Bayer HealthCare, and Kaiser (Bell Flower & West Los Angeles), the LDA has provided diabetes classes to hundreds of participants from Latino communities across Los Angeles. These classes provide residents with an opportunity to learn about diabetes and to empower them to make positive, healthy lifestyle changes in their communities.

Yet Muñoz notes there is so much more to do. “We must take a multi-pronged approach,” he said, to address systemic challenges in L.A.’s urban environment. Residents need to have better choices such as fresh produce in their grocery markets; sidewalk improvements, jogging paths, parks, and lighted walkways to make exercise safe; culturally relevant educational materials and other resources; conveniently located medical facilities; transportation, and access to such safety nets as discounted pharmaceuticals and coordinated social services.

“People need grassroots advocates who really want to help,” Muñoz said. “When you have diabetes, you don’t just have diabetes; you may also have high cholesterol, hypertension, heart problems, and other major health complications. You may also have domestic problems or other dysfunctional family and living problems. You might need a food bank or utility assistance.” He said the LDA is working to be a clearing house for those resources within its communities.

The organization, which now has a staff of five, is guided by a board of directors and an advisory board made up primarily of practitioners with expertise to provide information on the public health, economic, and social affects of diabetes. Under their guidance, the LDA has extended its reach to other underserved populations within Los Angeles County. These communities include other ethnicities, the elderly and low-income individuals. With all of its constituents, the LDA continues to reach out to one person, one neighbor, and one group at a time.

Type 2 diabetes

(Non-insulin-dependent diabetes mellitus) or adult-onset diabetes. Risk factors include obesity, race/ethnicity, family history of diabetes, prior history of gestational diabetes, impaired glucose tolerance, physical inactivity, and persons over 30 (although younger and younger persons, especially teens and “tweens,” are now contracting type 2 diabetes). Hispanic/Latino Americans, African Americans, American Indians, and some Asian Americans and Pacific Islanders are at particularly high risk for type 2 diabetes.
The early 21st century is an extraordinary time in the history of human life sciences. Thanks in part to the rapid evolution of information technologies—above all, the decreasing price and increasing power of microprocessors, and ubiquity of the Internet, which enables instant sharing of information—scientists are studying disease at the level of molecules. Never before have researchers possessed so much knowledge and such powerful tools to discover more. America and California are at the vanguard of the life sciences because they have made large and sustained investments in basic research.

Universities and independent research institutions’ bench-scale investigations reveal breakthrough findings that become the basis for licensing agreements with existing companies and the platforms for launching new ones. Companies contract with university researchers to conduct specific investigations and clinical trials. Academia and industry work hand-in-hand to provide internships, post-doctoral fellowships, continuing education and other training opportunities for scientists, engineers and business leaders in all stages of their careers.

While research institutions and commercial enterprises have always worked together closely, their continued success relies in good part on government grants and charitable support.

Grants from the National Institutes of Health

The National Institutes of Health (NIH) is a major source of grant monies to universities and other researchers and has been since the 1950s. Encompassing 27 institutes and centers, the NIH is focused on the full range of human health issues. Its specialties include oncology, cardiology, respiratory conditions, mental health, allergies, infectious diseases, aging and diabetes among others.

In recent years, the NIH has encouraged cross-functional research teams that bring together a wide range of scientific expertise to create interdisciplinary approaches to the problems of human disease. There is more and more interest in finding synergies in working across traditional boundaries of medicine, engineering, math and information technology to devise new means for preventing, diagnosing, treating and curing disease and other health-related conditions.

Beyond improving the understanding of human biology and the pathogenesis of disease, NIH grants have empowered young scientists, engineers, mathematicians and others to build successful careers in academia and in the private sector. NIH funding enables universities and research centers to inspire their students and postdoctoral fellows to advance basic research; to build and utilize capacity in their facilities; and to train faculty and staff to teach future generations.

Grants awarded by the NIH to California more than doubled between 1998 and 2004, the peak year thus far. Since then, however, funding has dropped back to an average of $3.2 billion annually (Figure 37).

No state has benefited more from NIH funding than California. Academic researchers here have consistently garnered larger shares of NIH funding than have investigators in other states. In 2008, California received NIH grants worth more than $3.15 billion. The Golden State’s share was approximately 40 percent more than that of Massachusetts, the next highest recipient (although measured against total population, Massachusetts garnered more NIH funding per capita than California).
Each of the 50 states receives some NIH funding every year. California has averaged approximately 15 percent of the total over the past decade, and was awarded 15.1 percent of the total in 2008.

As is typically the case, the bulk of the $3.1 billion that investigators in California received from the NIH was spent on research projects. The remaining monies—approximately $123 million or 4 percent of the total—funded fellowships as well as training and construction grants.

Training awards support workforce development in two ways. They can be used to provide research training for young scientists seeking careers in biomedical and behavioral sciences. They also help schools establish or enhance their continuing education programs for professionals already active in the workforce. Training grants and fellowships have long been a key component in the excellence of California’s biomedical institutions’ programs.

Since 1998, such funding has comprised an average of 3.6 percent of the overall NIH funding. At 3.7 percent, funding in 2008 remained steady as compared to 2007 and was slightly higher than the recent average. Similarly, training grants and fellowships have made up an average of 3.6 percent of the state’s total share of NIH funding over the past 11 years. In 2008, such grants comprised 3.7 percent of the total and were on par with the 2007 funding.
Nine of the top 15 California institutions receiving NIH grants in 2008 were universities—including seven of the 10 UC campuses. Stanford University was among the top five recipients. Four of the top 15 recipients are in or near San Diego, making the 53rd Congressional District the largest beneficiary of NIH funding in the state. The institutions there are UC San Diego, the Scripps Research Institute, the Burnham Institute for Medical Research and the Salk Institute for Biological Studies.

Source: National Institutes of Health, Office of Extramural Research.
Note: Data excludes Research and Development grants.
Small Business Administration Programs

Government funding to fuel the state’s biomedical industry also comes from the U.S. Small Business Administration’s (SBA) Office of Technology. The SBA’s two grant programs were implemented to increase the competitiveness of small, high-technology firms.

The first, the Small Business Innovation Research (SBIR) program, provides critical seed capital for biomedical entrepreneurs and occasionally provides initial funding for startup companies. Under the SBIR program, federal departments and agencies with annual extramural R&D budgets exceeding $100 million must reserve at least 2.5 percent of those budgets for awards to small U.S. high-tech firms. Since January 10, 2001, when the SBA Office of Hearings and Appeals ruled that any company with venture capital backing in excess of 51 percent was no longer eligible for a SBIR grant, many small biotechnology and medical device firms have been denied SBIR funding. CHI continues to support efforts to reverse this situation and restore broader eligibility to venture capital-backed life sciences firms.

Under the second program—Small Business Technology Transfer (STTR)—federal departments and agencies with annual extramural research budgets exceeding $1 billion must reserve 0.30 percent of such funds for awards to small U.S. high-tech firms. These awards are smaller than the SBIR grants and fund cooperative R&D projects involving small business and a nonprofit research institution.

In the past, SBIR and STTR dollars have been critical for the development of new biomedical products. The current economic climate makes this funding even more important. California companies have been successful in obtaining the highly competitive awards, taking the largest amount of the grants again in 2008.

California entities received SBIR and STTR awards totaling more than $114 million. That amount was 26.8 percent of the funds received by the top 10 recipients combined.

**Figure 43: Top 10 Recipients of NIH SBIR and STTR Funds in Fiscal Year 2008 (Millions of Dollars)**

<table>
<thead>
<tr>
<th>State</th>
<th>SBIR/STTR Funds</th>
</tr>
</thead>
<tbody>
<tr>
<td>California</td>
<td>$114.5</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>$83.6</td>
</tr>
<tr>
<td>New York</td>
<td>$36.6</td>
</tr>
<tr>
<td>Maryland</td>
<td>$34.9</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>$31.2</td>
</tr>
<tr>
<td>Texas</td>
<td>$28.9</td>
</tr>
<tr>
<td>North Carolina</td>
<td>$28.7</td>
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<tr>
<td>Washington</td>
<td>$24.1</td>
</tr>
<tr>
<td>Colorado</td>
<td>$23.6</td>
</tr>
<tr>
<td>Ohio</td>
<td>$20.9</td>
</tr>
</tbody>
</table>

Source: National Institutes of Health, Office of Extramural Research
Note: Data exclude Research and Development contracts.
John D. Stobo, M.D.

John D. Stobo, M.D., is senior vice president for health sciences and services for the University of California, responsible for system-wide coordination and communication among UC’s health sciences schools and medical centers (collectively referred to as UC Health). He is responsible for policy development for UC’s health system, and develops mechanisms for monitoring performance for the system’s 16 health sciences schools and 10 hospitals on seven campuses. He also oversees strategic planning and advocacy efforts as well as the development of system-wide initiatives for UC Health. Stobo has more than 40 years of leadership experience in the clinical and academic health science fields. He has served as president at the University of Texas Medical Branch (UTMB) and the William Osler Professor of Medicine and Physician-in-Chief of the Johns Hopkins Hospital. Stobo is a member of the Institute of Medicine, where he was also a member of the IOM Council. He is also a member of the board of directors of the American Hospital Association (AHA) Governing Council. Stobo received a mastership from the American College of Physicians for his distinguished contributions to internal medicine. He earned his bachelor’s degree from Dartmouth College in Hanover, N.H., and his M.D. from the State University of New York in Buffalo, N.Y.

Susan M. Baxter, Ph.D.

Susan M. Baxter, Ph.D., has served as executive director of the California State University Program for Education and Research in Biotechnology (CSUPERB) since March 2007. Baxter’s more than 20 years of research and management experience in business, nonprofit and academia includes serving as chief operating officer of the National Center for Genome Resources in Santa Fe, N.M. She also was executive director of computational sciences, Cengent Therapeutics; vice president of research and genome analysis, GeneFormatics; and research scientist for the New York State Department of Health and the Monsanto Agricultural Company. Baxter earned her bachelor’s degree in chemistry from the University of Virginia and earned her master’s and doctoral degrees in chemistry from Northwestern University. She was also a National Research Service Award supported postdoctoral fellow at the University of Oregon.

Stobo and Baxter are both members of the California Healthcare Institute’s board of directors.
A Blueprint for Educational Excellence

California, with its 1960 Master Plan for Higher Education, opened college to all residents and helped make the state an engine of economic growth and technological innovation. The plan coordinated the roles of the University of California (UC), California State University (CSU) and the community colleges, and promised every California student an affordable seat at an appropriate institution of higher education.

The Master Plan proved to be a visionary blueprint for establishing California as a driver of innovation and knowledge in traditional and emerging fields. Implementing the plan encouraged California’s children to pursue higher education, and it attracted some of the best minds from across the country and around the world to study here as well. For decades, other states and countries looked to California’s three-tiered system of higher education as a model for access, affordability and academic excellence.

At the end of fiscal year 2008-2009, the state had 110 community colleges, 23 CSU campuses, and the 10 UC campuses. UC reported approximately 220,000 students. CSU, the largest U.S. four-year university system, had 450,000 students, and the community colleges enrolled nearly 2.7 million students.

The growth has not been funded by the state alone. The colleges have implemented ambitious fundraising programs and revenue generating departments that have enabled them to prosper and to enhance services to their students, faculty, researchers and communities. UC’s annual budget is $19.2 billion, only about 16 percent of which comes from the state. Many university operations (i.e., auxiliary enterprises and hospitals) generate substantial profits for the institution.

Private giving adds greatly to what the university is able to accomplish.

California has seen a return on its investment. Millions of the state’s students stayed after graduating. They have paid taxes, built houses and families, made investments and established companies that have, in turn, drawn many more to work and contribute to the state. Economists have found that for every dollar the state invests in a CSU student, it receives $4.41 in return.

A Promise Neglected

Despite the tangible successes of the California Master Plan, state funding has not been sustained. The state’s per-student spending for education at UC has fallen nearly 40 percent since 1990—from $15,860 in 1990 to $9,560 today in current, inflation-adjusted dollars. Stated another way, the state’s funding for per-student education at UC has declined from 78 percent of the total cost of education in 1990 to 58 percent today.

As a group, California’s public universities and community colleges have half as much to spend today as they did in 1990 in real dollars. In the 1980s, 17 percent of the state budget went to higher education; today that number is 9 percent. Similarly, California’s K-12 education system has fallen from the top ranks 30 years ago to 47th in the nation in per-pupil spending now.

With the state already falling behind in its commitment to higher education, the economic downturn has battered the UC, CSU and community college systems. Facing a $24 billion budget deficit, the largest in state history, California is making drastic cuts to its education, healthcare and social services. That is a debilitating turn for the state’s educational institutions, which depend on the state for their largest single source of salary funding.

UC and CSU will receive 20 percent less state funding for fiscal years 2008-2009 and 2009-2010 than they did two years ago—for budget shortfalls of $813 million and $584 million, respectively. California’s community colleges will receive almost 6 percent less state funding than last year, even as its campuses struggle to accommodate a surge of military veterans and newly unemployed workers seeking training for new jobs.

To put the funding crisis in perspective, CSU’s $384 million in cuts is equivalent to the marginal cost funding provided by the state for instruction of about 95,000 students. Further, the $584 million figure does not represent the full picture. The February 2009 budget act included a $66.3 million permanent cut and imposed $40.5 million of new mandatory costs to CSU’s budget. The system also faces the loss of federal stimulus funds in the fiscal year 2010-2011.

The schools are responding as any fiscally responsible entity must: by increasing revenues and cutting expenses. In education those actions entail boosting fees, turning away students, expanding class sizes, eliminating programs, reducing class offerings, laying off staff, and putting professors and other employees on work furloughs.

The UC system first raised student fees by 9.3 percent for the 2009-2010 school year, bringing the average total for an undergraduate to $8,720, excluding housing. In November 2009, the UC Regents approved an additional 32 percent increase in student fees to be fully in place by the fall 2010 term, bring annual tuition and fees to $10,302. Some campuses intend to enroll significantly more out-of-state and international students, who pay a higher tuition. At the same time, UC is reducing freshman enrollment by 6 percent, and all 10 UC campuses are cutting programs, staff and faculty recruitment.
About 100,000 nonunion UC employees will have their pay cut this year through unpaid furlough days. The 12-month employee furlough program started on Sept. 1, 2009 and is based on a sliding scale—employees who earn more will experience the greatest number of furlough days. The furloughs will amount to pay reductions of between 4 and 10 percent, depending on the employee’s salary range.

CSU is reducing enrollment by 40,000 students over the next two years and closed spring 2010 admissions completely. Fees for in-state undergraduates will rise 32 percent to $4,827 a year; fees for full-time nonresident undergraduates will increase to $15,987 per academic year. Nearly all of CSU’s 47,000 employees have agreed to take furloughs two days per month, and more than 700 employees were laid off at one CSU campus alone. The campus, like others, is also closing its campus during winter and spring breaks. The community colleges are raising their fees by 30 percent, shrinking teaching staffs and reducing class schedules. The system also intends to enroll 250,000 fewer students this year than last.

Cuts in services across the systems include fewer discussion sections and seminars, reduced access to labs, a potential closure of libraries and research centers, and shortened library hours. Major support services and degree programs are being eliminated as well. For example, the California Poison Control Center, administered by UC San Francisco, will be discontinued, making California the only state in the nation without poison control services. The Irvine campus has halted admission to its doctoral program in education, and students on all campuses are having more difficulty getting the classes they need to graduate.

The University of California contributes to the state’s economic vitality and the quality of life through its educational opportunities, groundbreaking research and valuable cultural resources. With more than 225,000 students, 180,000 faculty and staff, 45,000 retirees and nearly 1.6 million living alumni, UC is transforming lives, inspiring innovation, empowering creativity and driving prosperity throughout the state, the nation and the world.

A California Economic Engine
- UC research has been critical to the development of many of California's leading industries—from biotechnology to information technology to telecommunications.
- Nearly 400,000 jobs in California depend on UC operations. That includes non-university jobs that university expenditures create.
- UC contributes more than $14 billion in California economic activity and more than $4 billion in state and local tax revenues each year.
- Driving the next wave of California’s economic growth, UC is taking a global role in developing new industries—from nanotechnology to digital media to green technology.
- More than 1,000 California biotech, high-tech and other innovative R&D-intensive companies put UC research to work every day.

Workforce Development
- With more than 1 million UC graduates, California has one of the best-trained workforces in the world. UC graduates more than 55,000 students a year.
- UC awards 7 percent of the nation’s Ph.D.s, more than competitors like Stanford, Harvard, Yale and other Ivy League universities.
- As a center for lifelong learning and continuing professional development, UC has the nation's largest continuing education program, with about 300,000 students each year enrolled in 17,000 extension courses around the state.

The California State University system is the largest university system in the world. It is a primary state resource for the technical workforce that staffs the biomedical industry and for undergraduates who go on to medical schools and doctoral programs. The CSU confers 44 percent of California’s life science and health professions bachelor’s degrees, approximately 50 percent of its bachelor’s degrees in engineering, and nearly 41 percent of the state’s healthcare and life sciences degree holders at the graduate level. CSU is committed to developing a professional biomedical sciences workforce by mobilizing CSU campus resources, advancing CSU faculty research, and developing innovating educational practices that respond to and anticipate the needs of the life science industry.

**CSU Highlights: Contributions to the State’s Economy**

- CSU’s direct economic impact on the state of California is enormous—$7.46 billion.
- The direct CSU economic contribution generates an impact of $13.6 billion in the state’s economy due to secondary effects.
- This impact sustains more than 207,000 jobs in California and generates more than $760 million each year in state and local annual taxes.
- More than half of all undergraduate degrees granted annually to Latino, African American and Native American students in California have been awarded by the CSU.
- The CSU graduates more than 82,000 professionals each year.
- More than 1.8 million CSU alumni are working in California and earning over $89 billion annually in income, of which $25.3 billion is attributable to their CSU degrees.
- When the additional impact of enhanced alumni earnings is taken into account, CSU’s total economic impact reaches $53 billion.
- For every dollar the state invests in a CSU student, it receives $4.41 in return.

**Preparation of a Diverse Life Sciences Workforce**

- CSU has nearly 17,250 undergraduates and 1,150 graduate students in life science degree programs.
- Compared with all university systems in the nation, CSU has one of the largest groups of underrepresented students in its life sciences degree programs.
- More than half of its students in the life sciences are females, one-fifth are Hispanic, 3 percent are African-American, and more than 1 percent are American Indian or Pacific Islander.
- CSU offers industry-focused life sciences graduate degrees in bioengineering, bioinformatics, biostatistics, biotechnology, computational sciences, and medical product development management.
- Eleven CSU campuses are providing research training in stem cell technology designed to advance the field of regenerative medicine through support from the California Institute for Regenerative Medicine (CIRM).
- Like other CSU educational programs in the life sciences, these Bridges to Stem Cell Research projects provide hands-on training in both academic and industrial research settings.
- CSU Extended University programs offer certificates in fields critical to the state’s biomedical industry, including biotechnology, clinical laboratory sciences, medical technology, quality assurance, pharmaceutical engineering, health IT, and allied health.
Long-lasting Consequences

It will take the state a long time to recover from its current fiscal problems—and even to find the bottom. Not only is the current budget deficit the largest in California history, the cash flow imbalance is far from addressed. The state government spends approximately $10 billion more than it collects in tax revenue each year, and did so before the economic downturn. Three large tax increases from the February 2009 budget package are set to expire in 2011. They included increases in the personal income tax, which expire on January 1, 2011. Sales tax and vehicle license fee increases expire on July 1, 2011. Without those revenues, the state anticipates a $16 billion loss over three fiscal years, starting with 2010-2011.

The cuts aimed at bridging the immediate budget gaps, however, already are affecting students and staff and will quickly be reflected in the state’s record of innovation and discovery.

The damage done to the state’s research infrastructure today is real. Leading experts who have helped build such world-class research facilities as the California NanoSystems Institute at UCLA, the UC Davis Genome Center, and the specialized teaching, treating and research medical centers across California note that the buildings and the faculties are vital to the further advancements of science. Yet in the dynamic study of nanotechnology, regenerative medicine, pharmacogenomics, gene therapy and others, the body of scientific knowledge is growing at a tremendous pace. To postpone a project is to kill it; to withhold the funds necessary to further the research is to render the facility obsolete.

Back to the Drawing Board

Even as California’s higher education institutions are making the immediate cuts to close the current budget gaps, their thought leaders are reviewing long-term priorities and reexamining their missions. For example, the CSU Board of Trustees, in collaboration with Chancellor Charles Reed and the 23 CSU campuses, has adopted a new long-range strategic plan, Access to Excellence: A Strategic Plan for the California State University. UC President Mark Yudof and Regents’ Chair Russell Gould are co-chairing the UC Commission on the Future. The 20-person panel is to examine fundamental questions about the university’s operations.

California’s public universities and colleges clearly desire to extricate themselves from dependence on the state’s boom-and-bust budgeting cycles. Yet the key question before university administrators, political leaders and state taxpayers now—as it was in 1960—concerns the ranking of education, opportunity, cultural richness, inspiration and innovation on the public agenda. That is, should higher education be regarded as a public good, as envisioned in the Master Plan for Higher Education?

The alternative is to view learning, research, and workforce development as private endeavors to be paid for by students and their families, and augmented by private donors. This more exclusive approach not only diminishes the opportunity for today’s students, but it will impact the economic and societal returns in the generations to come.
Academic Research: The California NanoSystems Institute

What is Nanotechnology? A Quick Primer

Nanotechnology is microscopic. Literally. The term refers to the production or use of materials as small as 1 nanometer—one billionth of a meter—which is about 100,000 times thinner than a human hair.

At the same time, nanotechnology is huge. Microparticles potentially could revolutionize the fields of human health, information technology, energy and the environment.

Convinced of the promise of nanotechnology, the federal government in 2001 launched the National Nanotechnology Initiative, which has committed nearly $12 billion to date to further nanotechnology.

That money, plus billions more invested by the private sector, has generated a market that is growing with remarkable speed. More than 600 products incorporating some nanotechnology already are on the market. In 2007, the value of nanotech-enabled products worldwide totaled $147 billion. Valued at $254 billion at the end of 2009, nanotechnology products are expected to cross the $2.5 trillion mark by 2015.

As with previous innovations, California is at the crest of this wave of new technologies. One-tenth of the 1,218 companies, universities and other entities in the country that have jumped into the fast-growing field are in or around Silicon Valley. The Los Angeles, Long Beach and Riverside region is ranked sixth among the world’s nanotechnology leaders.

Among the notables of Southern California’s burgeoning nanorevolution is the California NanoSystems Institute (CNSI) at the University of California, Los Angeles. The CNSI was established in December 2000 through a State of California initiative to create four Institutes for Science and Innovation. The goal of each research center is to encourage university collaboration with industry and to enable the rapid commercialization of discoveries.

CNSI is comprised of faculty from UCLA and University of California, Santa Barbara (UCSB), a multi-disciplinary team of some of the world’s preeminent investigators in the life and physical sciences, engineering, and medicine. Work conducted at the CNSI targets four areas of nanosystems-related research: energy, environment, health-medicine, and information technology.

In addition to assembling a world-class faculty, the center in 2007 moved into a state-of-the-art nanosystems complex. Strategically located on UCLA’s Court of Science, the 188,000-square-foot structure houses wet and dry laboratories and three floors of core facilities with equipment including electron, atomic force, X-ray diffraction and specialized optical microscopes; high throughput robotics for molecular screening; and clean rooms for projects led by CNSI and other faculty.

In its biomedical applications, nanotechnology is rapidly advancing procedures, medicines and diagnostic tools, giving answers to doctors and researchers and hope to patients. For example, CNSI researchers have developed nanoscale biosensors. The technology, based on detection/cellular pressure-sensing techniques that differentiate between cancer and healthy cells, may lead to new methods for early cancer detection.

In another project, nanovalves and nanoimpellers are being synthesized at CNSI. Nanoimpellers are the first light-powered nanomachines that operate inside living cells. By storing anticancer drugs inside tiny pores and releasing them into cancer cells in response to light, nanoimpellers may open a new avenue for drug delivery.

Similarly, the use of mesoporous silica nanoparticles presents a drug delivery option that could solve the challenge of the poor water solubility of today’s most promising anticancer drugs and thereby increase their effectiveness.

Technology Transfer

The CNSI is working closely with companies and entrepreneurs in the greater Los Angeles area to accelerate the development of new discoveries that put nanotechnology to work for patients, the environment, and the betterment of society. The center’s biomedical industry partners include Abraxis Biosciences, which has been critical to the center’s development and early programs. Ongoing collaborations also are in place with Astellas and Medivation for the development of an investigational new drug for the treatment of prostate cancer. Fate Therapeutics, a stem cell therapeutics development company in La Jolla, is among the biomedical companies that already have licensed intellectual property rights from UCLA based on technology involving CNSI members. Fate’s July 2009 agreement covered small-molecule compositions and methods for inducing bone formation.
CNSI also opened its incubator space in March 2009. The facility features 2,000-square-feet of flexible lab space to house eight to 10 early-stage incubation projects. Entrepreneurs at the incubator have access to specialized equipment and technical expertise of essential core labs as well as to faculty and scientists from the schools of engineering, physical and life sciences, and medicine. These incubator startup companies also benefit from access to the expertise of the UCLA Anderson School of Management, the School of Law and the Office of Intellectual Property for guidance on all aspects of business development.

MediSens Wireless, a startup company that develops and manufactures personal body-monitoring systems for medical and health applications, is the most recent addition to the incubator, joining Matrix Sensors, Inc.—a startup company in the process of developing multichannel gas and biological sensor systems.

Educational Program

The goal of the CNSI education program is to nurture the future workforce of nanoscience and nanotechnology scientists and engineers. In its effort to maintain California’s position as a leader in nanotechnology research and development, CNSI is reaching out to students at all levels of the California education system.

Although not currently a degree-granting entity, the center is developing a graduate degree program for students interested in pursuing advanced studies in nanosystems research and technology. This program will be designed to include a number of multidisciplinary courses in nanosystems research.

A variety of fellowship and training program opportunities have been developed to encourage the region’s most promising young scientists and engineers. Participants engage in creative, cross-disciplinary research projects in bioengineering; chemistry and biochemistry; civil and environmental engineering; environmental energy; materials science; microbiology, immunology and molecular genetics; molecular cell and developmental biology; and physics and astronomy.

At the same time, CNSI recognizes that the next generation of nanoscience and nanotechnology graduate students are in middle and high school today. The CNSI has developed programs aimed at stimulating young people’s natural curiosity and creativity. One of these initiatives, in partnership with Center X at UCLA, is the CNSI High School Nanoscience Program, where graduate students and post-doctoral fellows develop nanoscience experiments that can be used to teach science standards. High school teachers from across the Los Angeles Unified School District travel to CNSI for Saturday workshops to learn how to conduct the experiments and get materials for use in their own classrooms.

Nano Safety Program

Nanotechnology is a new science that is poorly understood by the public and lawmakers alike. As with recombinant DNA and other breakthroughs, public acceptance of this new technology will depend on confidence in the safety of nanomaterials. The University of California Center for Environmental Implications of Nanotechnology (UC CEIN) was established in September 2008 with funding from the National Science Foundation and the U.S. Environmental Protection Agency to explore the impact of engineered nanomaterials on the environment. CEIN is creating libraries of standard reference materials that are being
used to implement safety testing under a range of biological conditions as well as a variety of different organisms and life forms in the environment. To keep abreast of the rapid pace of nanotechnology-based enterprises, the CEIN is developing high-throughput screening approaches and computerized learning technology to provide stratified risk ranking that can be adapted for use by the academic community, industry, the public and regulating agencies. By being able to predict which material properties are potentially hazardous, the UC CEIN will also be able to provide advice on the safe design of engineered nanomaterials from an environmental perspective. Another major goal of the UC CEIN is to train the next generation of nano-scale scientists, engineers, and regulators to anticipate and mitigate potential future environmental hazards associated with nanotechnology.

Critical Juncture

Nanotechnology, in addition to being miniscule and limitless, is vulnerable.

“CNSI has put superb facilities and a superb faculty in place,” said André Nel, M.D., Ph.D., chief of the Division of NanoMedicine at CNSI and director of the UC NanoToxicology Research Training Program. He added that California already is home to the largest numbers of nanoscientists in the world. “What’s not in place,” he said, “are the dollars to ensure integration of that potential into higher-level discovery programs.”

He noted that the CNSI is reaching critical mass in personnel, facilities and partnerships just as the economic downturn threatens the state’s return on investment—and its continued commitment to nanotechnology development. “The infusion of funding has dwindled at exactly the wrong time. If we delay implementation—with fierce competition in the states, Canada, Japan and China—we are potentially being put in a place where we could let California’s [nanotechnology] promise slip.”
The University of California, Davis (UC Davis) founded its Biotechnology Program in 1986. Currently, it is a Special Program of the Office of Research due to its interdisciplinary focus. The UC Davis campus is one of the few in the United States to house leading departments in each of the major areas where biotechnology has a significant impact: human and veterinary medicine, including therapeutics, diagnostics and pathology; agriculture covering plant, animal, and microbial science, entomology and sustainability; food science; bioprocess technology; and environmental science.

Judith A. Kjelstrom, Ph.D.

Judith A. Kjelstrom, Ph.D., is the director of the University of California, Davis Biotechnology Program, co-director of the Howard Hughes Medical Institute-Integrating Medicine into Basic Science Graduate Training Program and program manager of the Designated Emphasis in Biotechnology graduate program. She is also the director of the Advanced Degree Program (ADP) for corporate employees, as well as a lecturer in microbiology and molecular and cellular biology. Her interest in academic-industry/government partnerships led Kjelstrom to serve on the board of directors for the Sacramento Area Regional Technology Alliance (SARTA), as well as on the executive committee of the California Institute of Food and Agricultural Research (CIFAR), a program to enhance technology exchange between UC Davis and industry. She is a frequent partner with the Technology & Industry Alliance of the Office of Research and the UC Davis Graduate School of Management to develop entrepreneurship among the faculty and students. Kjelstrom earned a bachelor of science degree in biological sciences with a concentration in clinical laboratory technology from California State University, Sacramento, and her Ph.D. in microbiology from UC Davis.

More than 270 faculty members at UC Davis are engaged in biotechnology-related research, and they work in world-class facilities. Among these is the UC Davis Genome Center, which opened in 2004 and has core facilities in proteomics, metabolomics, bioinformatics, DNA expression and other specialized technologies. Its associated researchers have the tools they need to perform cutting-edge research. Other specialized facilities include the centers for: Functional Glycobiology; Comparative Medicine; Biophotonics; AIDS Research; Molecular, Cell and Developmental Biology; Neuroscience; and Cancer. UC Davis further offers specialized instrumentation or services to researchers through its Clinical and Translational Science Center, NMR Facility, Transgenic Animal Facility, Image Processing Facility, and Flow Cytometry Facility, among others.
The university’s biotechnology programs credit their growth and success, in part, to the cooperative efforts among departments, centers, schools and colleges. The university’s commitment to translational research programs—those that link academia, the clinic and industry in ways that immediately benefit both—have been key as well.

Judith A. Kjelstrom, Ph.D., the director of the UC Davis Biotechnology Program, and her team oversee three such programs. The first, called the Designated Emphasis in Biotechnology (DEB) graduate program (www.deb.ucdavis.edu), allows Ph.D. students from any of 28 UC Davis degree programs to receive and be credited for biotechnology training. The program is designed to provide well-coordinated, cross-disciplinary training to graduate students in critical areas of biomolecular technology research.

“We have close to 170 students in the program as well as over 100 faculty trainers,” Kjelstrom said. The DEB experience includes exposure to bioethics, business and legal aspects of biotechnology. She also assists the students in developing their professional skills and writing effective curriculum vitae. A significant advantage of the program is the three- to six-month internships in a life science company or government laboratory. “The internship gives our students a perspective of what research looks like in a different environment,” Kjelstrom said, noting that the assignments frequently segue into job offers.

The DEB is the formal training program for the National Institutes of Health (NIH) Training Grant in Biomolecular Technology (which is administered through the Biotechnology Program). UC Davis joins Stanford and UC Berkeley as one of only three California institutions to direct the grants, and its program has been extended through 2012. In addition to the five to six NIH fellowships, another four to five fellowships are funded by UC Davis and its industry partners each year. The DEB is also the formal training program for the National Science Foundation (NSF) CREATE-IGERT Graduate Training Grant. These trainees are focused on the use of transgenic plants in the production of vaccines, pharmaceuticals, and biofuels.

Many of the DEB graduate students are funded through the Howard Hughes Medical Institute’s Integrating Medicine into Basic Sciences Graduate Training Grant (recently renewed for another four years). These scholars receive a year of training in clinical translational medicine.

Another of the UC Davis biotechnology programs that more closely ties industry with the university is the Advanced Degree Program (ADP) for corporate employees. Kjelstrom explained that the program targets individuals who went directly to work after earning a bachelor’s or master’s degree and now want to expand their expertise and their potential for advancement by earning a Ph.D.

“We call it the ‘Do Overs Program,’” she said. To qualify, candidates must be accepted into a participating Ph.D. program, granted a 12- to 18-month leave of absence from their employer so they may complete their coursework; have a Ph.D.-level mentor designated at their company to oversee their thesis research project; and secure a donation from their company to the university.

Among UC Davis Biotechnology Program’s other activities connecting academia and industry are its popular Summer Technical Short Courses. The lecture/lab courses, which are conducted from 8 a.m. to 5 p.m. for four to five days, are attended by UC Davis graduate students, researchers and faculty along with professional researchers and teachers not otherwise connected to the university.

Topics offered in 2008 and 2009 included Flow Cytometry; Proteomics; Bioinformatics: Next-Generation DNA Sequencing; DNA microarrays, and Advanced PCR techniques. Besides providing the space and some of the equipment required for the courses, UC Davis brings in corporate sponsors. It also contracts faculty for the classroom and lab sessions from its core facilities, industry and other institutions. Enrollment is limited, and Kjelstrom said that the courses typically are sold out.

“It’s a way for researchers to stay abreast of the latest developments, techniques and technologies,” Kjelstrom said of the short courses, which UC Davis has offered since the early 1990s. She said the corporate sponsors help defray course costs such as reagents, chips, instrumentation and other necessary components for the laboratory portions of the courses. In addition to giving participants contacts for ongoing trouble-shooting once they have returned to their labs and workplaces, the courses “serve as a catalyst for bringing like-minded researchers together,” she said.

When she steps back and looks at all of the activities the Biotechnology Program is involved with, Kjelstrom is most proud of the many ways they bring researchers together. Cross-disciplinary partnerships are critical to its success.
California gained worldwide attention in 2004 when voters passed Proposition 71, the California Stem Cell Research and Cures Initiative, a $3 billion bond initiative to fund embryonic stem cell research. That proposition established the California Institute for Regenerative Medicine (CIRM), a new state agency devoted exclusively to distributing grant funding for stem cell research.

There is no question that California is ahead of most other countries in terms of the advancement of stem cell research,” said Fred H. Gage, Ph.D., a renowned stem cell researcher at the Salk Institute. He points to California’s “new jobs, new buildings and new researchers” as evidence that the new science is thriving in the state. He added, “In regard to cures for specific diseases, we are moving forward.”

Fred H. Gage, Ph.D.
Fred H. Gage, Ph.D., is a Professor and the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Diseases in the Laboratory of Genetics at the Salk Institute in La Jolla. He achieved national renown for his groundbreaking experiments demonstrating that neurons are constantly being born in the brain, forcing scientists to rethink some of their most basic ideas about how the brain works. His work may lead to methods of replacing brain tissue lost to stroke or Alzheimer’s disease and repairing spinal cords damaged by trauma.

Prior to joining the Salk Institute in 1995, Gage was Professor of Neuroscience at the University of California, San Diego, where he still holds an adjunct title. In addition to being the incoming president and a board member for the International Society of Stem Cell Research, Gage is a fellow of the American Association for the Advancement of Science, a member of the National Academy of Sciences and the Institute of Medicine, and past-president of the Society for Neuroscience. His honors include the prestigious 1993 Charles A. Dana Award for Pioneering Achievements in Health and Education, the 1997 Christopher Reeve Research Medal, the 1999 Max Planck Research Prize, the 2002 MetLife Award, and the Keio Prize in 2008. He earned his Ph.D. from Johns Hopkins University and his Bachelor of Science degree from University of Florida.

"Stem cells can give rise to every different cell type in the body," Gage said. They can be useful in both treating and understanding disease.

"There is no question that California is ahead of most other countries in terms of the advancement of stem cell research," said Fred H. Gage, Ph.D., a renowned stem cell researcher at the Salk Institute. He points to California’s “new jobs, new buildings and new researchers” as evidence that the new science is thriving in the state. He added, “In regard to cures for specific diseases, we are moving forward.”

Gage said that in order to understand the promise of stem cell research, one must consider the many ways the science is being used. Because embryonic stem cells are undifferentiated renewable source of cells, they can be useful in both treating and understanding disease.

"Stem cells can give rise to every different cell type in the body," Gage said. They can be used in three distinct ways to further biomedical research.

First, by studying how the cells develop and differentiate, researchers can better understand the complexities of early human development. At the same time, they may be able to determine the causes of early developmental disorders.
Second, stem cells may be used to replace damaged cells and to grow healthy ones. This approach is being studied in connection with diabetes, blood disorders, liver disease, spinal cord injuries and other applications. Gage added that every organ contains stem cells. “We would like to know more about how those cells interact in organs and employ them in organ repair,” he said.

Third, human embryonic stem cells can be used to model human diseases, particularly those with an understood genetic cause. Gage and his lab are using this approach to study amyotrophic lateral sclerosis (ALS), or Lou Gehrig’s disease, more closely. ALS is a neurodegenerative disease that attacks motor neurons controlling voluntary movement, leading to progressive paralysis and muscle atrophy. It is usually fatal and, although it was first classified as a disease more than 140 years ago, its causes are still poorly understood.

In earlier ALS research, positive results with drugs in transgenic mice, or those altered to show symptoms of ALS, could not be replicated in human patients with the disease. To better screen drug candidates, Gage’s team developed cell culture models that used both human neurons and astrocytes. Astrocytes are cells in the brain and spinal cord. Among their many functions, they are crucial for the survival and well-being of motor neurons, which control voluntary muscle movements. Defective astrocytes can lay waste to motor neurons and are the main suspects in ALS.

The team used its model to provide new insight into the toxic pathways that contribute to the demise of motor neurons in ALS, to open up new possibilities for drug-screening experiments using human ALS in vitro models, and to pinpoint potential clinical interventions using astrocyte-based cell therapies.

“There is an urgent need for new ALS models that have the potential to translate into clinical trials and that could, at a minimum, be used in conjunction with the murine [mouse] models to verify drugs and drug targets,” said Gage. His researchers are taking a similar approach in studying Parkinson’s disease.

A particularly exciting aspect of using stem cells to model diseases is that they can be generated from diseased cells. This contrasts to other in vivo and in vitro models, which may be created to mimic human symptoms of the disease. Generating diseased cells enables researchers to better understand variances within diseases and within individuals. One day, the technique may be a standard component of personalized medicine.

Stem cell research in California is being conducted with a goal of quickly moving findings from labs into clinics. In April 2009, CIRM approved $67.7 million to fund 15 grants focused on advancing basic research toward patients. In October 2009, the institute partnered with the Medical Research Council of the United Kingdom and the Cancer Stem Cell Consortium of Canada. The group awarded more than $250 million to 14 multidisciplinary teams of researchers in California, the U.K. and Canada to develop stem cell-based therapies for 11 diseases. The grant recipients in the highly competitive selection are targeting such under-treated diseases as leukemia, age-related macular degeneration, HIV/AIDS, sickle cell anemia, and type 1 diabetes. The four-year grants represent the first CIRM funding explicitly expected to result in a filing with the U.S. Food and Drug Administration to begin a clinical trial.

Emerging stem cell science also is being supported by breakthrough advances in other new technologies and disciplines. Genetic sequencing, high-throughput screening, nanoscience and other technologies are generating data and expertise that is accelerating the gathering of scientific knowledge and furthering California’s legacy of biomedical innovation.

Investigative cooperation extends beyond the state’s borders, too. CIRM is generating extra funds through partnerships with stem cell research and biomedical entities in other countries. Researchers from around the world are spending time in other stem cell centers. For instance, among Gage’s fellow investigators at the Salk Institute is Juan Carlos Izpisúa Belmonte, a visiting professor in the Gene Expression Laboratory who heads a stem cell research center in his native Spain. Data and findings are shared through peer-reviewed journals, numerous national and international conferences, professional organizations and other alliances as well.

Gage said that stem cell research continues to grow in its significance and in its discoveries. It is opening windows on diseases and doors to researchers, industry and patients. Yet, he said, the partnerships that may matter most to patients and their caregivers—as well as to California’s continuing dominance in stem cell research—are those between researchers and industry.

“What fuels the clinical trials is understanding how stem cells work, how they differentiate, what they do,” Gage said. Technology transfer enables those findings to be advanced through expensive clinical trials and made accessible to the patients who need them.
September 10, 1994 changed everything for Don Reed’s family. On that afternoon, Reed and his wife, Gloria, were watching their son, Roman, play football in the Chabot College Stadium in Hayward.

“It sounded like a board being broken,” the elder Reed said of the three-man collision that snapped Roman’s neck. “I’ll never forget it.”

“The doctors gave us no hope,” Reed said, that Roman would walk again, have a family, or even have much of a quality of life. The Reeds read everything they could find about spinal cord injury (SCI). By the time they realized how few available and experimental therapies were available, Don Reed was on a path to make a difference.

To help researchers discover a way to mend damaged spinal cords, Reed supported the fundraising efforts of the Reeve-Irvine Research Center that Christopher Reeve and Joan Irvine founded at the University of California, Irvine in 1996. Then he put a campaign in motion that resulted in the passage of California’s Roman Reed Spinal Cord Injury Research Act of 1999. Thus far, Roman’s Law has resulted in $12.5 million in California state funding and $50 million more in matching grants from outside sources.

The funds, which are allocated to the University of California, are managed through grants from the Reeve-Irvine Research Center. There, the Roman Reed Spinal Cord Injury Research Program enables faculty throughout the UC system and the state of California, to launch unique, creative research projects that may later qualify for federal and private funding. Scientists who receive the grants become part of the Roman Reed Research Consortium, which annually meets with other California SCI neural regeneration researchers to discuss ways to collaborate. The Roman Reed Core Laboratory at UCI further enables investigators who are new to the field to obtain training in SCI research techniques.

Reed has widened his advocacy work to support regenerative medicine efforts across all known techniques, disease categories, and state and international borders. Mostly, Reed said, he attends meetings and conferences, and writes hundreds of e-mails trying to bring advocates together. “We are the emotional muscle,” Reed said of patient advocacy groups. “We have to look at the needs of the biomedical industry and work together to make sure they have what they need to succeed.”

Don C. Reed

Don C. Reed is a patient advocate who has made it his life’s work to advance and protect all forms of stem cell research, particularly for its potential in treating spinal cord injuries (SCI). Currently vice president of public policy for the Americans for Cures Foundation, Reed is the chairman and a co-founder of Californians for Cures and also worked as a grassroots organizer for then-state Sen. Deborah Ortiz on stem cell research legislation from 2002 through 2003. He has been recognized with a number of honors, including the Willie Shoemaker Award for Advancing Spinal Cord Injury Awareness in 2005 and the Genetic Policy Institute’s Stem Cell Research Advocate of the Year in 2006. The author of numerous articles on SCI and stem cell research, he writes the blog Stem Cell Battles (stemcellbattles.com).
Conclusion

This report documents the extraordinary scope, diversity and scale of California’s biomedical industry. Its impact on the state’s economy, from wages to exports to tax revenues, is one of the few bright spots amidst the worst financial downturn since the Great Depression. And its contributions to human health are a source of hope for patients not just in California, but also around the world. Biotechnology was born in California, and medical technology thrives here more than anywhere else.

But the state’s problems, rooted in recession economics and partisan governance, are momentous. Left unsolved, they threaten to erode the fragile ecosystem of world-class research, quality public education, venture capital, entrepreneurial spirit and practical optimism that has enabled the life sciences to flourish.

California is renowned for its sense of possibility, of reinvention, of solving seemingly intractable problems (water, immigration, etc.) to pursue the new, new thing. From this perspective, the biomedical industry should be at the vanguard in writing the next chapter in the narrative of the California dream.
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Methodology

Employment

Data

The data used to estimate employment and wages in California’s biomedical industry are made available by the Bureau of Labor Statistics (BLS) Quarterly Census of Employment and Wages (QCEW), available at http://www.bls.gov/cew/. The 2008 data reflected in this report were collected in the fall of 2009. Data for prior years are from the California Biomedical Industry 2009 Report in order to ensure comparability between reports.

The QCEW is a near comprehensive census of employment and wage information at the national, state, and county levels for workers covered by state unemployment insurance laws and federal workers covered by the Unemployment Compensation for Federal Employees program. It does not include the self-employed, unpaid family workers, or private household employees. Jobs are counted regardless of full-time or part-time status. Individuals who hold more than one job may be counted more than once. In order to protect the confidentiality of firms’ information, the Bureau of Labor Statistics does not disclose data that would be easily identifiable to individual participating companies. Given the smaller number of establishments that can occur at the county level, county-level totals may not represent the full number of employment positions and wages for each industry. These positions would be included by the BLS in aggregated state level data.

For earlier reports, a review of employment data from company-specific Securities and Exchange Commission (SEC) filings was also used to estimate employment in the biomedical industry, specifically for the medical device, instruments, and diagnostics sector. The results of the review were carried forward in this year’s report. Company filings with the SEC can be obtained from the EDGAR database available at http://www.sec.gov/edgar/searchedgar/webusers.htm.

The sectors of the biomedical industry that are used in this analysis are comprised of several North American Industry Classification System (NAICS) codes that are assigned to sectors based on the description of the NAICS provided by the U.S. Census Bureau. Companies are assigned a single NAICS code by the Census Bureau, and therefore a company that manufactures both pharmaceuticals and medical devices would only be classified in one of these sectors depending on which is the primary production of the company.

Methodology

The most recent full year for which wage and employment data were available for the publication of this report was 2008. QCEW employment and wage data are broken down to the 6-digit NAICS code level. The relevant 6-digit NAICS code data are multiplied by the percent of the biomedical industry that is represented in the NAICS code, as derived by PwC from Census Bureau data. This methodology is identical to the process used in the California Biomedical Industry 2009 Report, so the results in both reports are directly comparable. Prior to the 2009 report, PwC estimated narrow industry categories based on broader industry statistics that were available in the most recent year. The new methodology provides a more accurate portrait of California’s biomedical industry but makes this report and the 2009 report incomparable to earlier publications.

Employment data from the QCEW were also used in conjunction with the IMPLAN economic model to quantify the direct and indirect impact of the biomedical industry. IMPLAN is a well known modeling system developed by the Minnesota IMPLAN Group for estimating economic impacts and is similar to the Regional Input-Output Modeling System developed by the U.S. Department of Commerce. The model is primarily based on government data sources. It can address a wide range of impact topics in a given region (county, state, or the country as a whole).

IMPLAN is built around an “input-output” table that relates the purchases that each industry has made from other industries to the value of the output of each industry. To meet the demand for goods and services from an industry, purchases are made in other industries according to the patterns recorded in the input-output table. These purchases in turn spark still more purchases by the industry’s suppliers, and so on. Meanwhile, employees and business owners make personal purchases out of the additional income that is generated by this process, sending more new demands rippling through the economy. Multipliers describe these iterations. The Type I multiplier measures the direct and indirect effects of a change in economic activity. It captures the inter-industry effects only (i.e., industries buying from local industries). The Type SAM (Social Accounting Matrix) multiplier captures the direct and indirect effects. In addition, it also reflects induced effects (i.e., changes in spending from households as income increases or decreases due to the changes in production).

Investment

Data

Data on venture capital investment nationally and by state were collected from The MoneyTree™ Report from PricewaterhouseCoopers and the National Venture Capital Association based on data provided by Thomson Reuters. The 2008 and 2009 data reflected in this report were collected in the fall of 2009. Data for prior years are from the California Biomedical Industry 2009 Report in order to ensure comparability between reports.
NIH Grants

Data

Data for this analysis come from the National Institutes of Health Office of Extramural Research, available at http://grants.nih.gov/grants/oer.htm. The 2008 data do not include research and development contracts due to the unavailability of that data at the time of publication of this report. Prior year’s data may also not include research and development contracts to ensure comparability across years. The data include all awards to California from NIH, some of which do not necessarily fund basic biomedical research. For example, some grants were used for training programs and projects that are designed to support the research training of scientists for careers in the biomedical and behavioral sciences, as well as to help professional schools to establish, expand, or improve programs of continuing professional education. Other grants were used to fund health policy or behavioral science research. Despite these caveats, overall the NIH grant funding demonstrates the federal commitment to health science research in California. The 2008 data reflected in this report were collected in the fall of 2009. Data for prior years are from the California Biomedical Industry 2009 Report in order to ensure comparability between reports.

The data come in two forms:

2. NIH SBIR and STTR grants: http://grants.nih.gov/grants/Funding/award_data.htm

Product Development

IMS Research Methodology

IMS experts reviewed the IMS Company Profiles database to focus on companies headquartered in or with significant presence in California, and then linked that information to the IMS R&D Focus database to look at products in development.

R&D Focus covers aspects of global pharmaceutical and biotechnology product development, from discovery stage research to availability on the market. Products including small molecules, monoclonal antibodies, proteins, gene therapies, vaccines and immunotherapies, as well as fixed combination products, biosimilars, in vivo imaging agents/diagnostics are included in the scope of the database. Also covered are compounds in specialized delivery systems, targets for use in drug discovery and research collaborations/discovery programs. Drug design technologies and drug delivery systems are included if they are available for partnering.

The main source of information for R&D Focus are company press releases, company interviews and Web sites, scientific conferences (e.g., ASCO, AACR), academic institutes and universities (including technology transfer offices) and company meetings/R&D days.