Super Cluster

Ideas, perspectives and updates from the Massachusetts life sciences industry

NEHI
New England Healthcare Institute

MASSACHUSETTS TECHNOLOGY COLLABORATIVE

PRICEWATERHOUSECOOPERS

About PricewaterhouseCoopers Boston

With over 2,500 employees, PricewaterhouseCoopers is the largest professional services firm in New England. We serve as the trusted advisor to hundreds of public and private companies and organizations, large and small, in New England. We have particular strength in the life and health sciences industries. Committed to the transformation of healthcare through innovation, collaboration and thought leadership, PricewaterhouseCoopers Health Industries Group is the nexus of industry and technical expertise across all health-related industries, including providers and payers, health sciences, biotech/medical devices, pharmaceutical and employer practices.

About the Massachusetts Technology Collaborative

The Massachusetts Technology Collaborative is the state's development agency for renewable energy and the innovation economy. It works to stimulate economic activity in communities throughout the Commonwealth by bringing together leaders from industry, academia, and government to advance technology-based solutions that lead to economic growth and a cleaner environment in Massachusetts. www.mtpc.org

About the New England Healthcare Institute

The New England Healthcare Institute (NEHI) is a not-for-profit collaborative dedicated to transforming health care for the benefit of patients and their families. Through research, education and policy change, NEHI finds and promotes innovative ways to improve health care quality and lower health care costs. Working in partnership with members from all across the health care system, NEHI brings an objective, collaborative and fresh voice to health policy. www.nehi.net

Introduction by Governor Patrick

April 2007

Dear fellow citizens of Massachusetts,

Massachusetts is home to some of the world's best medical and research facilities and has a wealth of brilliant, dedicated researchers, technicians and practitioners. For decades, this Commonwealth has been a national leader in the life sciences and continues to provide fertile ground for your industry. Today, we lead the nation in per capita NIH funding, biomedical venture capital investment, and life science PhDs, and feature world-class colleges and universities all across the state.

Combine these advantages with a tradition of innovation and entrepreneurial spirit that dates back centuries and we have everything you need to spark innovation and growth.

The Massachusetts Life Sciences Collaborative brings together leaders from hospitals, universities, large and small businesses, venture capital firms and others to develop comprehensive strategies for robust expansion of the life sciences in Massachusetts.

I am happy to welcome this rapidly growing, cutting edge industry. You bring to Massachusetts not only economic opportunity, but also the chance to help millions of people around the globe. I know from my own experiences with loved ones who have suffered with Alzheimer's disease and diabetes just how important it is that you succeed.

I look forward to an active working relationship with all of you. I commend the achievements of our life sciences community, and look forward to building upon them now and in the future. I invite you and your colleagues to join the most important and impressive life sciences cluster in the world.

Sincerely,

Governor Deval Patrick

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Executive summary

A super cluster, defined as a large grouping of gravitationally associated clusters of galaxies, is among the largest structures of the cosmos. Likewise, the Massachusetts super cluster is comprised of several industry and academic sectors which touch and enhance the life sciences—and is one of the largest such groupings in the world. The Massachusetts life sciences super cluster includes the activities of the state's world-class universities, teaching hospitals and research institutions, biotechnology, medical device and pharmaceutical companies, as well as the many software, venture capital, plastics and IT companies that contribute to the growth and vitality of the life sciences. Through the years it has provided a sustainable, growing economic foundation for the Commonwealth. Because of the groundbreaking work that has emanated from the super cluster, Massachusetts is recognized globally for discovering treatments and cures for the infectious and chronic diseases that afflict society.

At a time when the state's traditional manufacturing industry is receding, the life sciences industry has continued to grow:

- Nearly one in six residents is employed by this cluster, and the jobs pay high wages. Two thirds of organizations with R&D activities and six in ten with manufacturing activities surveyed by PricewaterhouseCoopers said they plan to expand operations in the next two years.
- The organizations that make up the cluster have been especially productive at attracting public and private capital to the state. Massachusetts leads the nation in government research funding on a per-capita basis. The Boston metropolitan area alone is the nation's top recipient of NIH funding and one of the biggest centers of venture capital in the world. Venture financing of Massachusetts' life sciences companies was up 43% over the previous year to $1.1 billion in 2006.
- The number of life science patents per capita awarded to Massachusetts institutions between 2001 and 2005 was more than triple the U.S. average.
- The top 25 publicly traded life science companies in Massachusetts nearly doubled their annual sales revenues between 2002 and 2006.[1] In 2006 alone, these companies generated more than $23 billion in annual sales.

Massachusetts' cluster of research organizations, entrepreneurial leadership, highly educated talent, and strong public and private funding bring a competitive advantage that many states would envy. Yet, research for this report indicates key challenges ahead:

- Top scientists and universities are the biggest draw that companies cite for moving to Massachusetts. However, survey respondents indicated that gaps in K–12 education produce a local workforce inadequately prepared to work in the life sciences sector.
- NIH funding represents one of the largest sources of funding to the Commonwealth's life sciences cluster with approximately $2B annually, yet growth of the federal NIH budget has stalled.
- The region's economic prosperity from life sciences may be making the region unaffordable and unworkable. Housing prices are driving talent out of the market, and transportation is in gridlock. Of those surveyed, 59% said transportation is a major problem, and 83% said it was hard just to get to work.

These challenges highlight opportunities for improvement to ensure Massachusetts retains its leadership position in the life sciences. Collaborative efforts should focus on:

- Developing a strategic plan to improve math and science curriculum required to fill the demand for high quality workers in the life sciences industry.
- Solving the most pressing issues affecting the retention of workers, including high housing costs and long commuting times.
- Providing consistent, predictable, and efficient tax, regulatory, licensing and permitting policies to nurture company growth.
- Strategically responding to growing competition through innovative measures, such as a bond referendum to fund life sciences resources.

This report is both a celebration of the success and potential of the Massachusetts life sciences super cluster as well as a warning against complacency. It contains articles by and interviews with some of the super cluster's biggest stars, including a Nobel Prize winner, top pharmaceutical, biotechnology and medical device CEOs, and experts from academia, medicine, venture capital and state government. It describes the current state of the life sciences super cluster, the outlook for the future, and critical areas of improvement so it can realize its true benefit to society.

[1] The list includes the top 25 life science companies identified by the Boston Globe as of 2/1/2007. The list ranks the top 25 by market capitalization and excludes companies such as Philips Medical Systems and Tyco Healthcare, which are part of larger conglomerates.

Introduction by PricewaterhouseCoopers

Since its founding, Massachusetts has been one of the most influential states in America and on the leading edge of innovation, which initially transformed the Commonwealth from an agricultural to a manufacturing, then to a knowledge-based economy. Massachusetts is now leading the transformational change taking place in our healthcare system. New directions in medicine and ways of diagnosing, preventing, treating and curing diseases are being discovered and developed here, giving birth to an industry that is now the heart of the Massachusetts economy and the future of medicine.

Whether by design or destiny, the four major pillars of the Massachusetts economy—academia, healthcare, technology and financial services—have come together to create the foundation for a life sciences super cluster. The sixth smallest state in the nation, Massachusetts has the world's largest concentration of life sciences firms, researchers and academic medical centers. Per capita, our life sciences sector receives more patents and more funding from the NIH and venture capitalists and has more PhDs and Nobel Prize winners than anywhere in the country. It is an optimal combination of skills, talent, resources and facilities that has been more than 200 years in the making and cannot be replicated elsewhere overnight.

But Massachusetts is not alone in recognizing the value of the life sciences as an economic engine of growth. Other states and foreign countries are aggressively and creatively seeking to attract life sciences firms and build their own centers of excellence. As noted in this report, this competition is one of many threats facing the Commonwealth's life sciences industry. Massachusetts' life sciences industry, academic and government leaders must work collaboratively to build on the industry's strengths, invest in its future and strengthen the collaborative ties that make up the super cluster.

PwC is committed to the economic vitality of Massachusetts, the growth of its life sciences sector, the future of medicine and sustainability of our nation's healthcare system. As one of the leading advisors to Massachusetts' health industries across the entire spectrum of healthcare—biotech firms, pharmaceutical companies, academic medical centers, providers, payers, employers and policymakers—we have a distinctive, broad view of industry challenges and opportunities. That, combined with our work on such important initiatives as the Translational Genomics Research Institute, the California Institute for Regenerative Medicine and the Institute for Systems Medicine, means a unique ability to offer research-driven insights and integrated solutions that support the needs of the state and the life sciences sector.

The Massachusetts Super Cluster report is the culmination of four months of work that draws on the vast knowledge that exists throughout PricewaterhouseCoopers' Health Industries Group. Working with the New England Healthcare Institute and Massachusetts Technology Collaborative, we conducted in-depth dialogues with more than 25 of Massachusetts' leading health industries leaders and surveyed more than 100 executives across the spectrum of the health industries that make up the life sciences super cluster. In addition, many leaders have provided their perspectives on the state of and the challenges facing the life sciences and healthcare sectors. The result is a snapshot of the Massachusetts life sciences super cluster as it exists today. More importantly, we hope that it provides impetus and insight to ensure that Massachusetts maintains its global leadership in the life sciences economy in the future.

Sincerely,

James M. Connolly
Partner, Health Industries
PricewaterhouseCoopers LLP

Gerald J. McDougall
Partner, Health Industries
PricewaterhouseCoopers LLP

Introduction by NEHI and MTC

Massachusetts is home to some of the country's oldest and best universities, teaching hospitals and research institutions, as well as some of the newest and most innovative biotechnology, pharmaceutical and medical device companies. As a small state, we are fortunate to have such a remarkable blend of the old and the new—a combination of time-honored learning and vital entrepreneurship that brings passion, energy, and dedication to the institutions and companies that make up our life sciences industry. From the cores of Boston and Cambridge to the more recently established clusters of universities and innovative companies in the north, south, central, and western parts of the state, Massachusetts has created a "super cluster" of knowledge and innovation that is world class.

The Massachusetts Technology Collaborative (MTC)—a non-partisan, economic development agency—and the New England Healthcare Institute (NEHI)—an innovative health policy organization—have been working with leaders throughout government, industry, academia and leading non-profits to build on the strengths of the life sciences in the Commonwealth. Our two groups are devoted to advancing innovation by forming dynamic collaborations among these groups—all of us sharing the ultimate goal of saving lives, improving health and curing disease for the world at large.

Massachusetts is known for its rich history of innovation and leadership on the most pressing socio-economic challenges of the past four centuries. As the global economy becomes smaller, flatter and more competitive, providing national leadership in the life sciences is yet another opportunity for the state to shine. With NEHI's and MTC's collective ability to forge educated and impassioned partnerships, and with new leadership in the Governor's office, Massachusetts is well positioned to increase its stature as a global leader in the life sciences.

To this end, we have formed an exceptional coalition known as the Massachusetts Life Sciences Collaborative, comprised of leaders from every sector of the Commonwealth's life sciences arena. This Collaborative will create lasting partnerships and bridge gaps across industry, academia, and government to strengthen and grow our life sciences efforts across the state. Our shared goal is to maximize our resources in ways that produce new economic vitality and improve our quality of life through new discoveries, medical advances and treatments. From stem cell research to personalized medicine to unlocking the mysteries of genomics, we are committed to blazing new trails.

In addition to the resources that Massachusetts rightfully showcases, we have some hurdles to clear. They range from improving access to capital for early stage technology companies to addressing the state's astronomically high cost of living to strengthening early childhood math and science education so that we have young people prepared for our workforce in the future.

Working together, we believe that the power of our historical education and health care traditions will enable us to surmount these challenges and strengthen our global leadership in the life sciences.

Sincerely,

Mitchell Adams
Executive Director
Massachusetts Technology Collaborative

Wendy Everett, ScD
President
New England Healthcare Institute

Massachusetts Life Sciences Collaborative

The Massachusetts Life Sciences Collaborative (LSC) is a unique, cross-sector coalition of life sciences leaders in academia, industry and government. This partnership is committed to enhancing the Commonwealth's preeminent position in the research, development, and commercialization of products that address critical needs in health care and treatment of disease, and in doing so, expand economic opportunities for the citizens of the state.

The LSC's mission is to sustain productive dialogue among stakeholders and to reach consensus with government policy-makers on a comprehensive strategy to expand the life sciences cluster in Massachusetts. The Collaborative uniquely leverages the assets of our world-class universities; teaching hospitals and research institutions; biotechnology, medical device, and pharmaceutical companies; as well as the many software, venture capital, plastics, and IT companies that contribute to the growth and vitality of the life sciences. The objectives of the Collaborative are to integrate the disparate elements of the cluster, identify the obstacles to full economic and competitive potential, and create a path and direction that will focus the cluster on achieving its strongest position in the worldwide competition for talent and industry. The effort will be supported by an administrative, financial, and staff structure that can ensure sustainability and results.

The importance and need for this initiative has been broadly acknowledged, and is underscored by the strong financial support provided by a variety of stakeholders. The LSC is taking a role in supporting key life sciences priorities for Massachusetts including the following:

- Increasing funding for innovation
- Preparing a skilled life sciences workforce
- Improving and enhancing clinical trials in Massachusetts
- Improving connectivity among life sciences stakeholders
- Improving the life sciences business environment
- Capturing increased share of downstream manufacturing
- Addressing the availability and cost of housing
- Increasing NIH and FDA funding

Massachusetts Life Sciences Collaborative Organizing Committee

Chair: Steven Hyman, Provost, Harvard University

Mitchell Adams, Executive Director, Massachusetts Technology Collaborative

Burt Adelman, Executive Vice President, Biogen/IDEC

Christopher Anderson, President, Massachusetts High Technology Council

Joseph Aoun, President, Northeastern University

Robert Anderson, Division Counsel, Abbott Laboratories

Jamshed Bharucha, Provost, Tufts University

Edward Benz, President, Dana-Farber Cancer Institute

Paul Bleicher, Chairman and Founder, Phase Forward Inc.

Abbie Celniker, Head of Program Office, Novartis Institutes for BioMedical Research

Aram Chobanian, Dean Emeritus and former President, Boston University

Charles Cooney, Faculty Director, Deshpande Center for Technological Innovation, MIT

Franklin Douglas, Executive Director, Center for Biomedical Innovation, MIT

John Erwin, Executive Director, Conference of Boston Teaching Hospitals

Walter Ettinger, President, UMass Memorial Medical Center

Wendy Everett, President, New England Healthcare Institute

Gayle Farris, President of Forest City Science & Technology Group

David Fleming, Group Senior Vice President, Genzyme

Jonathan Fleming, Managing Partner, Oxford Bioscience Partners

Ansbert Gadicke, Founding General Partner, MPM Capital

Gary Gottlieb, President, Brigham and Women's Hospital

Michael Green, Professor, UMass Worcester

Robert Green, COO, Lyme Properties

C. Jeffrey Grogan, Partner, Monitor Group

Paul Grogan, President, The Boston Foundation

Paul Guzzi, President, Greater Boston Chamber of Commerce

Robert Healy, City Manager, City of Cambridge

Hal Jenson, Chief Academic Officer, Baystate Health

George Langford, Dean of the College of Natural Sciences and Mathematics, UMass Amherst

Patrick Larkin, Director, John Adams Innovation Institute

Paul Levy, President and CEO, Beth Israel Deaconess Medical Center

Lisa Lopez, Executive Vice President & General Counsel, Haemonetics Corporation

Mark Maloney, Chairman, Boston World Partnerships

James Mandell, President and CEO, Children's Hospital Boston

Richard Packer, President and CEO, ZOLL Medical Corporation

Joyce Plotkin, President, Massachusetts Technology Leadership Council

Kevin O'Sullivan, President and CEO, Massachusetts Biomedical Initiatives

Mark Robinson, President, Massachusetts Biotechnology Council

Peter Slavin, Chief Executive Officer, Massachusetts General Hospital

Thomas Sommer, President, Massachusetts Medical Device Industry Council

Marilyn Swartz-Lloyd, President and CEO, MASCO

Lex Van der Ploeg, Vice President of Basic Research and Site Head, Merck Research Labs

Elaine Ullian, President and CEO Boston Medical Center

Jack Wilson, President, University of Massachusetts

Perspective

Living the life sciences in Massachusetts

By Susan Hockfield and Henri Termeer

Susan Hockfield, PhD
President
MIT

Henri Termeer
CEO and President
Genzyme Corporation

Massachusetts has a well-earned reputation as a place where innovation and entrepreneurship thrive, where our greatest natural resource is the brainpower and ingenuity of our citizens, and where premier institutions of research and learning continuously feed our life sciences industries with new discoveries and top talent.

Yet, while Massachusetts is home to an enviable group of public and private institutions, life sciences-based businesses and trade associations that support the growth of individual sectors of the life sciences cluster, it has done little to systematically address the needs of the life sciences community as a whole.

To reach the region's full economic and competitive potential and to ensure our continued preeminence in the life sciences, leaders in government and the life sciences cluster must work together to transcend traditional boundaries and address the very practical needs that all members share. These challenges include such overarching priorities as improving our transportation and information technology infrastructures, educating a more skilled workforce, securing adequate NIH research funding to support advances in basic research, fostering private financial support for early stage companies, and creating a more responsive review and permitting system at all levels of government.

To be sure, there have been many successful joint research efforts between institutions and industry. Just as the Broad Institute, the MIT Center for Biomedical Innovation, the University of Massachusetts—Lowell Biomanufacturing Center, the New England Healthcare Institute and other institutions are providing leadership in fostering collaboration across traditional boundaries, so must the rest of the life sciences cluster.

The future of the life sciences cluster will depend on how well Massachusetts leaders build on these successes and create an environment for consistent and continuous collaboration between and among our institutions of research and learning and industry. Competitors in the United States and abroad are doing just that in an effort to win the global competition for talent and industry.

Even the especially difficult challenges of affordable housing and workforce development become surmountable if addressed with a spirit of collaboration and partnership. These two issues demand immediate attention to stem the flow of our graduates and younger workers out of the state and to assure a steady stream of scientific and technical talent into it.

We commend initiatives like the Massachusetts Life Sciences Collaborative, whose mission is to create a cross-sector collaboration that can both sustain dialogue among life sciences leaders in academia, industry and government and also develop a comprehensive, integrated strategy to grow the Massachusetts life sciences cluster and sustain our position as the world leader in life sciences research and development.

The message of Governor Deval Patrick during his recent campaign was "together we can." We believe that working together we can assure the vitality and sustainability of the life sciences community in Massachusetts.

About the Massachusetts life sciences super cluster

The Massachusetts economy is highly dependent on its thriving life sciences industry, from research to discovery to commercialization to the manufacture of life-saving products. The country and the world are highly dependent on the medical breakthroughs and products that have resulted from across the state. Massachusetts is a leader in the life sciences on many measures, and its history as a preeminent center of both education and innovation cannot be replicated overnight.

Being complacent with its past success is not an option, however. Competition from other states and other countries compels the industry and the government to work to ensure Massachusetts' future success in the life sciences. This report provides several "Opportunities for Action," which provide insight on ways to ensure that Massachusetts remains a leader in the life sciences in the face of challenges on the horizon. This report begins with a brief history of how Massachusetts became a leader in the life sciences. The remainder highlights the current state of the Commonwealth's life sciences industry and the outlook for its future. The report focuses on the inputs to the industry—a steady stream of public and private funding and an educated workforce—and its outputs: research, development and manufacture of innovative biomedical products.

This report draws on economic research and the 2007 PricewaterhouseCoopers Massachusetts Life Sciences Cluster Survey. The economic analysis provides trends related to employment, wages, and public funding. The survey provides insight on future opportunities and threats from over 100 executives in all sectors of the life sciences in Massachusetts.[2] Woven into the report are the perspectives of key leaders in life sciences in Massachusetts, who focus on the groundbreaking work being performed in the Commonwealth and its global implications.

Emergence of the Massachusetts life sciences super cluster

Massachusetts owes its success in the life sciences to its ability, dating back to the seventeenth century, to innovate. In economics terms, the Bay State has developed a competitive advantage over the centuries in the life sciences. This competitive advantage is the result of clustering, first made prominent by Michael Porter of the Harvard Business School, in which inter-related organizations collaborate, share infrastructure, and form synergies in a geographically concentrated area. Clustering brings enormous benefits to the organizations and communities involved, from access to innovation to ease of collaboration. Clusters attract the best and brightest workers, who are drawn to the many opportunities for career advancement.

Because it is one of the largest life sciences clusters in the world, and given its importance to the Massachusetts economy, this report refers to the Massachusetts life sciences industry as a super cluster. In astronomy, a super cluster is a large grouping of smaller galaxy groups and clusters, and are among the largest structures of the cosmos, an apt analogy for the Commonwealth's life sciences industry. The Massachusetts life sciences super cluster includes the activities of our universities, teaching hospitals and research institutions, our biotechnology, medical device, pharmaceutical, and diagnostic and instrumentation companies as well as the many software, venture capital, trade councils and associations, and other specialized business services companies that contribute to the growth and vitality of the life sciences.[3]

The core of the cluster is the Boston–Cambridge area, which houses some of the country's most prestigious institutions of higher education, including universities, medical schools, and graduate programs. As the cluster has grown over the years, this core has since spread across much of Massachusetts, with an additional "anchor" in Worcester, as well as life sciences companies developing operations in cities such as Framingham, Natick, New Bedford, Fall River, and Devens.

[2] See the Methodology section at end of this report for more information on the survey and methology for the economic analysis.

[3] Porter, Michael. *Massachusetts' Competitive Position in Life Sciences: Where Do We Stand?* September 12, 2003. Information in this section also draws from The National Governors Association. *A Governor's Guide to Cluster-Based Economic Development*. 2002.

Figure 1. Progression of the life sciences super cluster in Massachusetts

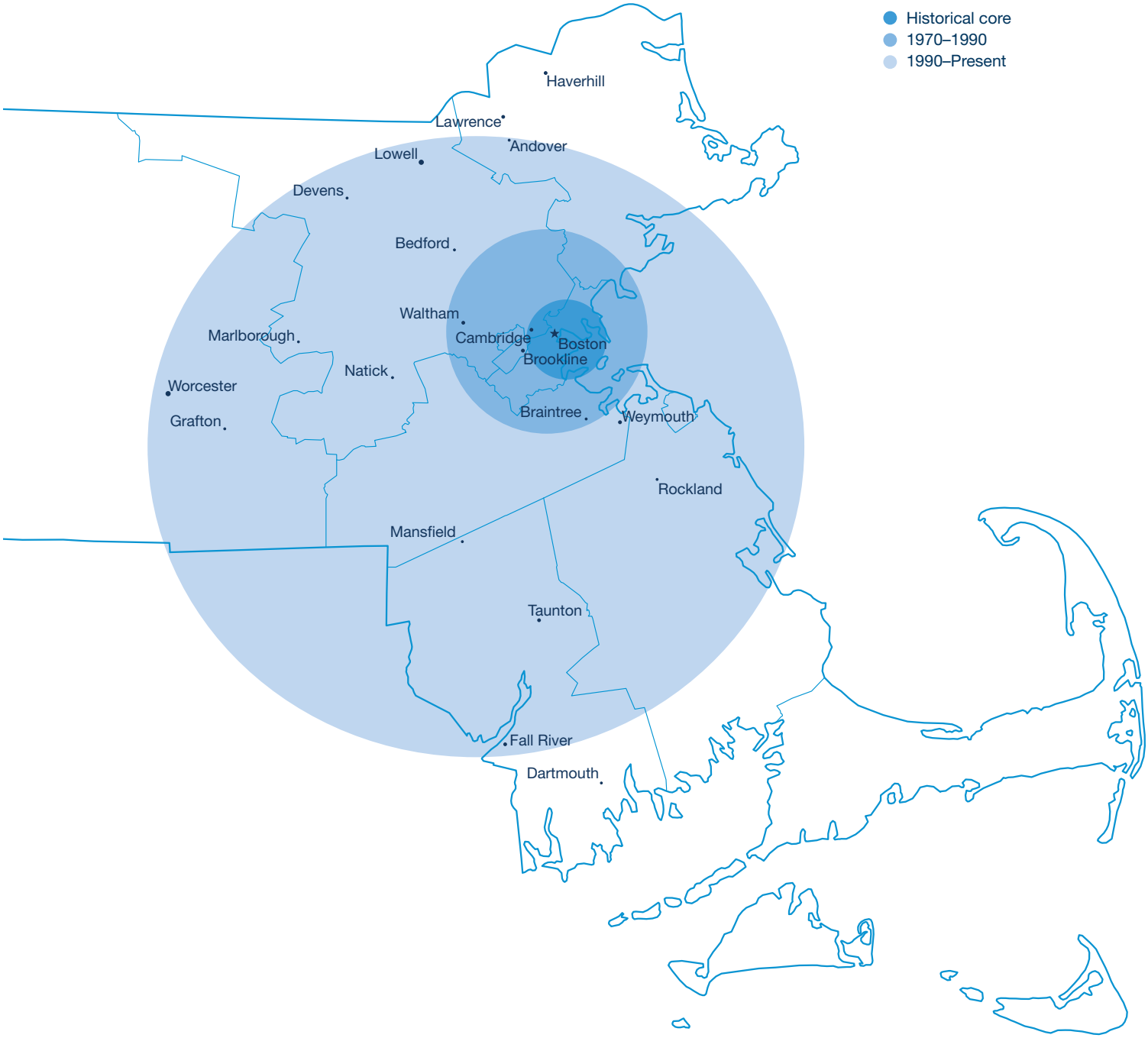


Table 1. Life sciences-related organizations in the Longwood Medical Area

Hospitals and health centers
Brigham and Women's Hospital
Beth Israel Deaconess Medical Center
Dana-Farber Cancer Center
Children's Hospital Boston
Joslin Diabetes Center
Massachusetts Mental Health Center
Schools
Harvard University Medical School
Harvard University School of Public Health
Harvard School of Dental Medicine
Massachusetts College of Pharmacy and Health Sciences
Simmons School for Health Sciences
Commercial organizations
Merck Research Laboratories
CBR Institute for Biomedical Research, Inc.

The seeds of the Massachusetts life sciences cluster were sown with the founding of Harvard University in 1640 and the Massachusetts Institute of Technology (MIT) in 1865. On each side of the Charles River sit two of the key centers of the cluster: Kendall Square in Cambridge and Longwood Medical Area (LMA) in Boston/Brookline.

The two centers are less than three miles apart, and they house institutions that lay claim to some of the oldest, as well as some of the most recent scientific discoveries in the fields of medicine. One, LMA, represents the cutting edge of medicine; the other, Kendall Square, represents the laboratories and discoveries of biotechnology and pharmaceuticals.

LMA—a one-third square mile section of Boston—grew up around Harvard Medical School, which purchased 26 acres of nearby property in 1906 and built a quadrangle of five buildings on Longwood Avenue. Harvard sold some of the remaining property to other hospitals, to ensure that Harvard students could benefit from collaboration, and this section of the cluster was born. Today, LMA is home to more than a dozen life sciences organizations, several of which are rated among the top five in the U.S. in their respective fields.

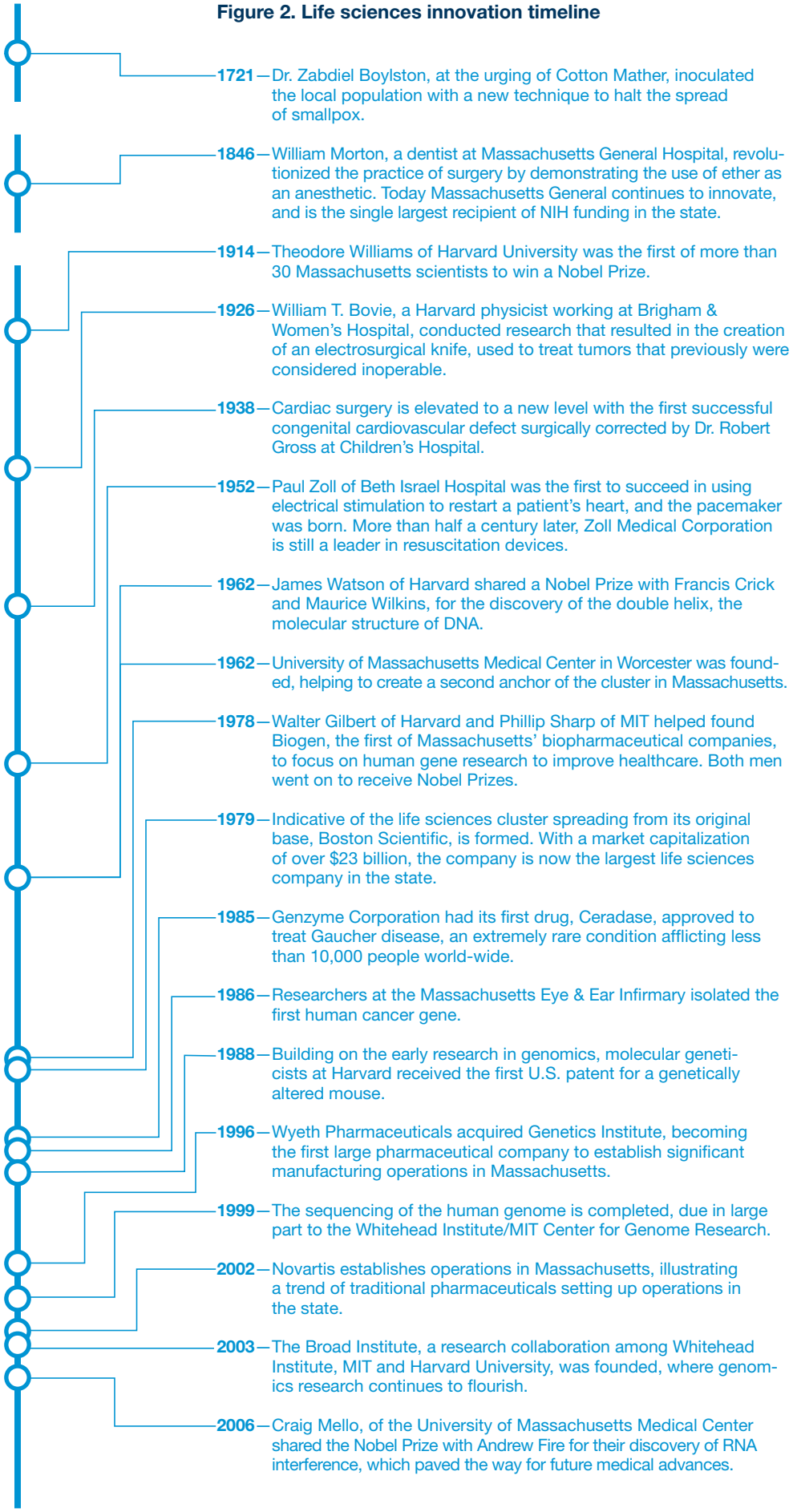
Kendall's Square's birth as a life sciences hub in Massachusetts began in 1915, when MIT moved its campus to the area. After molecular biology breakthroughs in the 1940s and 1950s, MIT converted a factory into Technology Square in the 1960s. The following decades saw top research organizations, as well as top biotechnology firms plant roots in the area. Large pharmaceutical companies, such as Novartis, were also drawn to the area for the research capabilities and opportunities for collaborations. Today, there are over 150 life sciences companies in this area.[4]

The Boston–Cambridge area boasts the nation's highest density of world-renowned medical research facilities. As science and medicine has grown and evolved, so has the life sciences cluster continued to evolve and grow. While the original core of Boston–Cambridge remains strong, more recent mini clusters have been created north, west, and south of Boston. Dating back to the early eighteenth century with stories of innovation, the timeline[5] (to the right) provides a summary of some of the important discoveries and milestones of the cluster, and how the cluster has spread from Boston–Cambridge to across Massachusetts.

[4] Massachusetts Institute of Technology Entrepreneurship Center. *Building an Entrepreneurial Ecosystem: The Example of the Kendall Square Biotech Cluster*. 2007

[5] This timeline draws from information from www.bostoninnovation.org/bostoninnovation/healthcare.htm; Conference of Boston Teaching Hospitals, *Driving Greater Boston and New England: The Impact of Greater Boston's Teaching Hospitals, 2007*; company websites.

Figure 2. Life sciences innovation timeline



1721—Dr. Zabdiel Boylston, at the urging of Cotton Mather, inoculated the local population with a new technique to halt the spread of smallpox.

1846—William Morton, a dentist at Massachusetts General Hospital, revolutionized the practice of surgery by demonstrating the use of ether as an anesthetic. Today Massachusetts General continues to innovate, and is the single largest recipient of NIH funding in the state.

1914—Theodore Williams of Harvard University was the first of more than 30 Massachusetts scientists to win a Nobel Prize.

1926—William T. Bovie, a Harvard physicist working at Brigham & Women's Hospital, conducted research that resulted in the creation of an electrosurgical knife, used to treat tumors that previously were considered inoperable.

1938—Cardiac surgery is elevated to a new level with the first successful congenital cardiovascular defect surgically corrected by Dr. Robert Gross at Children's Hospital.

1952—Paul Zoll of Beth Israel Hospital was the first to succeed in using electrical stimulation to restart a patient's heart, and the pacemaker was born. More than half a century later, Zoll Medical Corporation is still a leader in resuscitation devices.

1962—James Watson of Harvard shared a Nobel Prize with Francis Crick and Maurice Wilkins, for the discovery of the double helix, the molecular structure of DNA.

1962—University of Massachusetts Medical Center in Worcester was founded, helping to create a second anchor of the cluster in Massachusetts.

1978—Walter Gilbert of Harvard and Phillip Sharp of MIT helped found Biogen, the first of Massachusetts' biopharmaceutical companies, to focus on human gene research to improve healthcare. Both men went on to receive Nobel Prizes.

1979—Indicative of the life sciences cluster spreading from its original base, Boston Scientific, is formed. With a market capitalization of over $23 billion, the company is now the largest life sciences company in the state.

1985—Genzyme Corporation had its first drug, Ceradase, approved to treat Gaucher disease, an extremely rare condition afflicting less than 10,000 people world-wide.

1986—Researchers at the Massachusetts Eye & Ear Infirmary isolated the first human cancer gene.

1988—Building on the early research in genomics, molecular geneticists at Harvard received the first U.S. patent for a genetically altered mouse.

1996—Wyeth Pharmaceuticals acquired Genetics Institute, becoming the first large pharmaceutical company to establish significant manufacturing operations in Massachusetts.

1999—The sequencing of the human genome is completed, due in large part to the Whitehead Institute/MIT Center for Genome Research.

2002—Novartis establishes operations in Massachusetts, illustrating a trend of traditional pharmaceuticals setting up operations in the state.

2003—The Broad Institute, a research collaboration among Whitehead Institute, MIT and Harvard University, was founded, where genomics research continues to flourish.

2006—Craig Mello, of the University of Massachusetts Medical Center shared the Nobel Prize with Andrew Fire for their discovery of RNA interference, which paved the way for future medical advances.

Today's Massachusetts life sciences super cluster

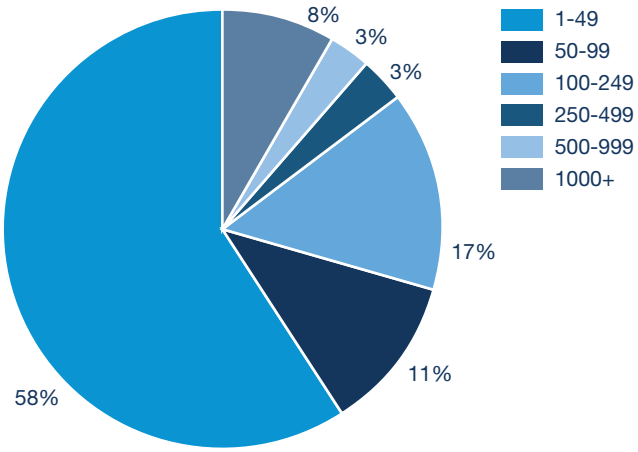
Today, Massachusetts continues its tradition of innovation in genomics and other areas of the life sciences. In addition to the academic and medical research facilities that drive life sciences R&D in the state, Massachusetts is home to approximately 600 biotechnology companies, more than 475 medical device and equipment manufacturers and more than 75 pharmaceutical companies.[6] According to respondents of the PwC Life Sciences Survey, four out of five indicated that their corporate headquarters are in Massachusetts, and six in 10 have operations solely in the Commonwealth.

The life sciences cluster has and continues to seize the opportunity to transform basic research into innovative technologies at a significant rate, a testament to the vibrancy of its interaction. Not surprising for a state that has historically been a hotbed for young, innovative companies, 58% of survey respondents have fewer than 50 employees. While the original Boston–Cambridge cluster remains strong, many of these new companies are located throughout eastern and central Massachusetts.

The growth in the cluster in recent years has been robust. The top 25 publicly traded life sciences companies in Massachusetts nearly doubled their annual revenues between 2002 and 2006.[7] In 2006 alone, these companies generated more than $23 billion in net revenues. In addition, the number of life science patents per capita awarded to Massachusetts institutions between 2001 and 2005 was more than triple the U.S. average and far exceeded the number of patents per capita awarded to California, New Jersey, Maryland and Pennsylvania—states that are top competitors in the life sciences arena.

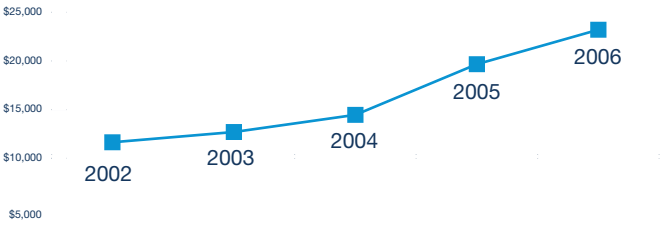
The Massachusetts life sciences cluster is continuing to gain strength. While the Commonwealth has long been home to life sciences start-ups, today large, established pharmaceutical companies are joining the cluster as well. Wyeth, Schering-Plough, Merck, Pfizer, Abbott Laboratories, Amgen, Astra-Zeneca, and Novartis all have substantial R&D or manufacturing facilities in the state. In addition, Bristol–Myers Squibb will add 550 manufacturing jobs through its opening of a new facility on a former military base.

Figure 3. How many employees (full and part-time) does your company have in Massachusetts?



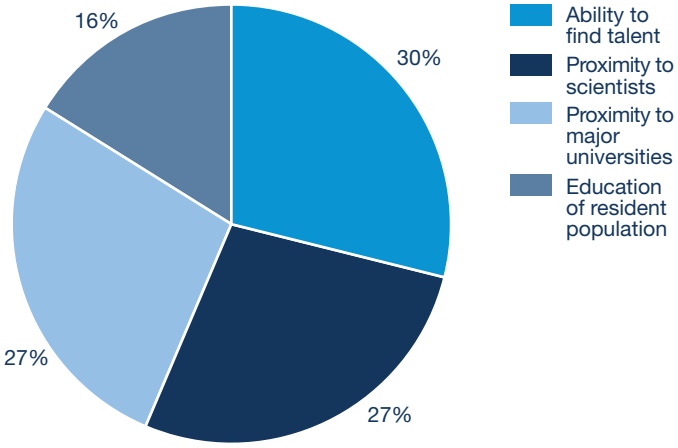
Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

Figure 4. Sum of net revenue of top 25 public life sciences companies in Massachusetts ($ millions)



Source: Boston Globe Top 25 Life Sciences

Figure 5. Top factors influencing company's decision to establish or expand your operations in Massachusetts



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

[6] Bureau of Labor Statistics Quarterly Census of Employment and Wages.

[7] The list includes the top 25 Life science companies identified by the *Boston Globe* as of 2/1/2007. The list ranks the top 25 by market capitalization and excludes companies such as Philips Medical and Tyco Healthcare, which are part of larger conglomerates.

Perspective

MicroCHIPS' solutions offer hope for patients with chronic conditions

By John T. Santini

John T. Santini, Jr., PhD
President & CEO
MicroCHIPS

Last year, the world's nations converged to formally acknowledge a disease that quietly kills millions of people each year. The United Nations made history in December 2006 when, for the first time, it passed a resolution recognizing a non-infectious disease—diabetes—as a global epidemic.

MicroCHIPS, a Massachusetts medical research and development company, is developing solutions that help clinicians—and patients themselves—manage serious diseases and improve quality of life. The company is pioneering the next generation of implantable drug delivery and biosensing devices that will increase therapeutic control, reduce painful interventions, and help maintain and improve health for millions of diabetes sufferers.

Diabetes, a primary focus of MicroCHIPS, will potentially afflict 380 million people worldwide within 20 years, with 300 million of them in developing countries. If this prediction by the International Diabetes Foundation is correct, the number reflects a staggering 1,000% increase since 1997.

Many diabetics must perform painful finger-stick blood-glucose measurements several times daily to manage the disease. While newer, short-term sensors allow for continuous blood-glucose measurements, patients still must manipulate numerous devices to manage their blood-sugar levels. To help alleviate this painful inconvenience, MicroCHIPS is conducting research on long-term glucose sensing using unique implant protection technologies. This technology will preserve a series of short-term sensors to provide long-term sensing capabilities—reducing the need for cumbersome and painful blood tests and helping patients better control the disease.

Osteoporosis, also an important focus for MicroCHIPS' research and development efforts, is another grave global concern that leads to the deaths of an extraordinary number of people worldwide. MicroCHIPS' advances in this area offer equal promise as in diabetes. The company is developing technology to overcome a key hurdle to patient acceptance of the bone-building drug, parathyroid hormone—painful daily injections that last for 18 months. MicroCHIPS' subcutaneously implanted drug-release device will deliver a potent daily dose of parathyroid hormone, ensuring that patients adhere to the therapy for the required course of treatment by eliminating the frequent, painful injections.

Initially started at MIT under the direction of Professor Robert Langer, a world-renowned medical inventor, MicroCHIPS has advanced the technologies required to create medical solutions that can dramatically affect the care of patients with chronic and debilitating conditions. MicroCHIPS' patented technologies are vital to the development of the next generation of implanted devices and include the development of tiny reservoirs to house sensors or potent drugs as well as microelectromechanical systems and techniques for sealing, protecting and precisely controlling components of implanted devices. MicroCHIPS also has demonstrated experience in the development of stable, highly concentrated formulations of proteins and peptides—making them suitable for delivery from an implanted device.

To highlight these key technological breakthroughs, MicroCHIPS recently conducted a breakthrough preclinical study demonstrating the successful in vivo operation of an "active" therapeutic implant. The study, published in *Nature Biotechnology*, demonstrated for the first time that it is possible, using an implanted microchip device and wireless technology, to actively control the release of drugs in the body over a period of several months.

MicroCHIPS' technology promises great impact in the biopharmaceutical area of protein and peptide drug development. Treatment with these innovative new drugs is extremely difficult with conventional methods (pills, patches, drug pumps and sprays); however, MicroCHIPS' unique formulation and delivery techniques will enable successful therapies with the most potent new drugs. Recognizing the global nature of diseases and patient populations, MicroCHIPS' is seeking to apply these advances to managing and improving the health of patients worldwide.

Interview

Robert S. Langer, ScD

From Bench to Bedside: The story of a drug from Bob Langer's lab to commercialization

- **1979**—MIT Professor Robert Langer launches program to create new polymers for medical use
- **1982**—Graduate students Howie Rosen (later president of ALZA) and Robert Lindhardt (now an RPI professor) synthesize polymers at MIT
- **1983**—MIT postdoc Kam Leong (now a professor at Duke) develops methods to make polymers degrade
- **1984**—Collaboration to use polymers to treat brain cancer starts with Dr. Henry Brem (now chief of neurosurgery at Johns Hopkins)
- **1985**—Nova Pharmaceuticals licenses polymers, begins funding research towards brain cancer research
- **1986**—MIT graduate student Cato Laurencin (now UVA's chief of orthopedic surgery) shows these polymers are safe in animals
- **1987**—Phase I/II clinical trials start at Johns Hopkins, Duke, University of Alabama, Northwestern, and UCLA
- **1990**—Phase III trials start at 27 medical centers
- **1992**—Guilford Pharmaceuticals acquires Gliadel program
- **1995**—Treatment IND approved for Gliadel for recurrent glioblastoma
- **1996**—NDA filed
- **1996**—FDA board recommends approval for recurrent glioblastoma
- **1996**—September—FDA approves Gliadel for recurrent glioblastoma
- **1999**—Clinical trials start for primary glioblastoma
- **2003**—FDA approves Gliadel for primary glioblastoma

On his background

My getting on the science track really dates back to being a little boy. My dad and my grandfather played math games with me. I had a Gilbert chemistry set and I liked playing with chemicals and mixing solutions together so that I could change colors. I enjoyed the magic.

On his first breakthrough

One of the people in my lab mentioned to me that there was this guy Judah Folkman, and that he sometimes takes unusual people—I'm not sure he meant that as a compliment. So I wrote him and he offered me a position. That was great; we in fact isolated the first angiogenesis inhibitor—that's what I did for my post doctoral work. It was great for me because I got to see a whole bunch of areas of medicine and to think of different ways I could apply chemical engineering to address those problems.

Later on, when I got a faculty position, that's what I began doing. I'd develop patents, but after a while I would become dissatisfied with that, too. It's nice to publish papers, but I wanted to make more of an impact. I could see that companies, particularly small companies, would live or die by our invention. So I got involved in helping get some of them off the ground.

Today, I've been involved in many companies, many right around here, and they've been wonderful. I mean those companies have transformed Massachusetts and transformed the world, and they've made products that save and improve peoples lives. It's something I believe in. It's created tons of jobs, too.

On collaboration

So many of the things that go on today involve both engineering and biology. Drug delivery is a terrific example of that. People are creating new drugs but some of those drugs, particularly some of the newer ones like DNA or siRNA, run into huge delivery problems. The new cell-based therapies that we and others are trying to work on, have wonderful biology that goes on but, its also important to have a good engine to create products.

There's all kinds of collaboration. Our lab is unique in that in a lot of ways. We probably have people from 10 or 15 different disciplines right in my own lab. That's very unusual. I look for excellent people no matter what they do. Probably in any one year we get 3,000 to 5,000 applications from people who want to come to the lab. Our lab has close to 100 people, but in any one year we take in maybe six or seven people.

Bob Langer runs the largest biomedical engineering lab in the world at the Massachusetts Institute of Technology, where he is a professor of biochemical engineering. At age 58, Langer holds nearly 560 patents, more than 100 of which have been licensed or sublicensed, and his research has led to the creation of more than a dozen biotech firms and more than 35 products on the market or in testing.

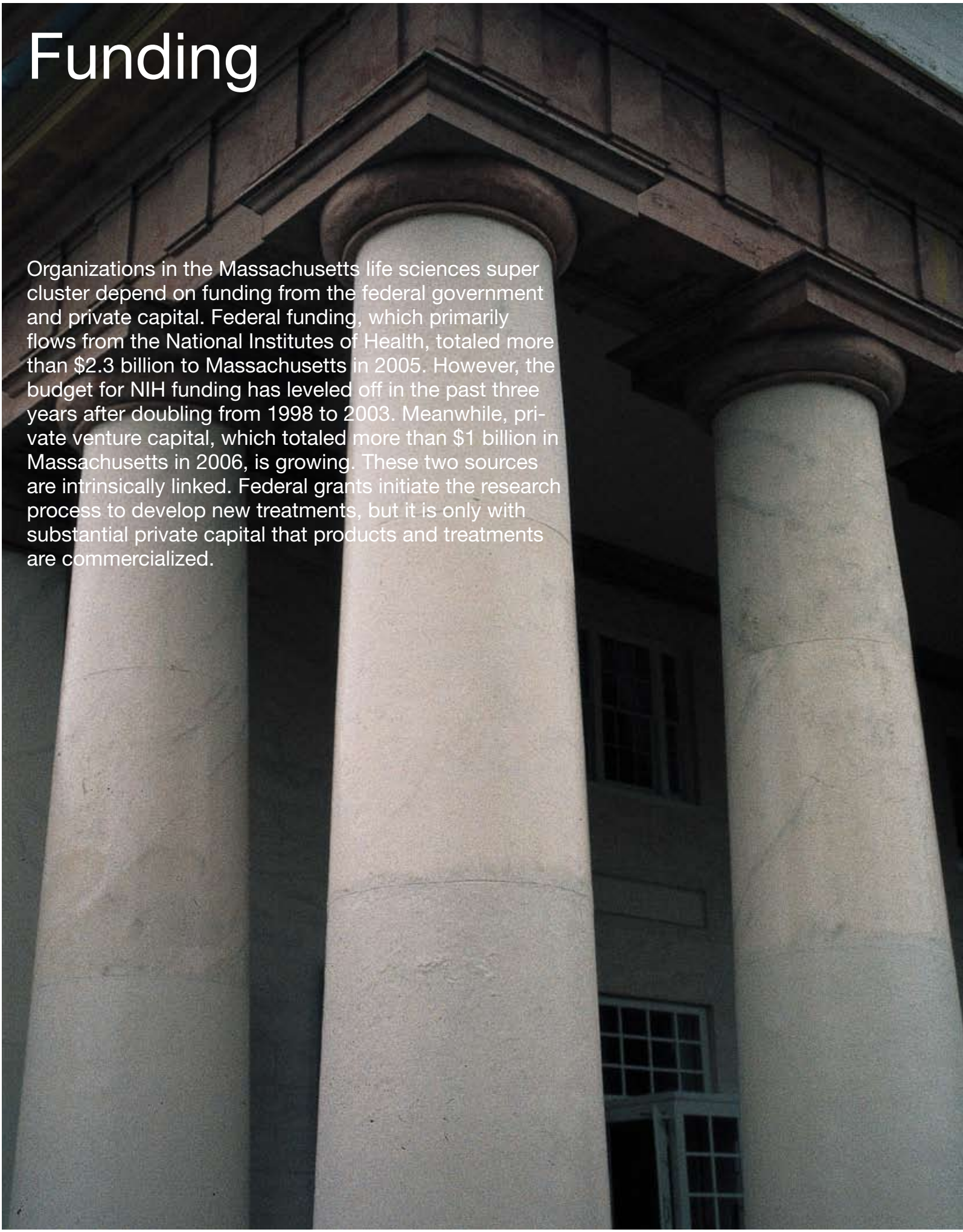
On the future

We're very interested in strategies to someday create new tissues and organs. There are a lot of things that drugs can treat although a lot they can't. You can't treat someone who's paralyzed with a drug. If somebody's heart's gone you can't treat that. With diabetes you can treat them but it's hardly a cure. There are lots of situations where if we could create new tissues or organs, we could do a lot of good.

Another big one is what I call the drug delivery system. That's very broad, everything from implants to smart delivery systems to new kinds of patches that deliver complex drugs to new kinds of aerosols to even new ways of delivering some of these newer drugs you hear about, like siRNA or DNA.

I'd also like to see more things that we have been doing to keep going into the clinic and to keep helping people. Over the years we've had a real track record of moving things from the laboratory to the clinic. In fact, these companies have been instrumental in doing that. The more we can do that the better. I'd like to see us save and help as many people as possible.

Funding



Organizations in the Massachusetts life sciences super cluster depend on funding from the federal government and private capital. Federal funding, which primarily flows from the National Institutes of Health, totaled more than $2.3 billion to Massachusetts in 2005. However, the budget for NIH funding has leveled off in the past three years after doubling from 1998 to 2003. Meanwhile, private venture capital, which totaled more than $1 billion in Massachusetts in 2006, is growing. These two sources are intrinsically linked. Federal grants initiate the research process to develop new treatments, but it is only with substantial private capital that products and treatments are commercialized.

Public funding

Public funding for Massachusetts' academic research centers is vital to the health of the cluster. This funding pays for research and development that is leveraged by budding entrepreneurs who launch new ventures.

NIH grants to Massachusetts

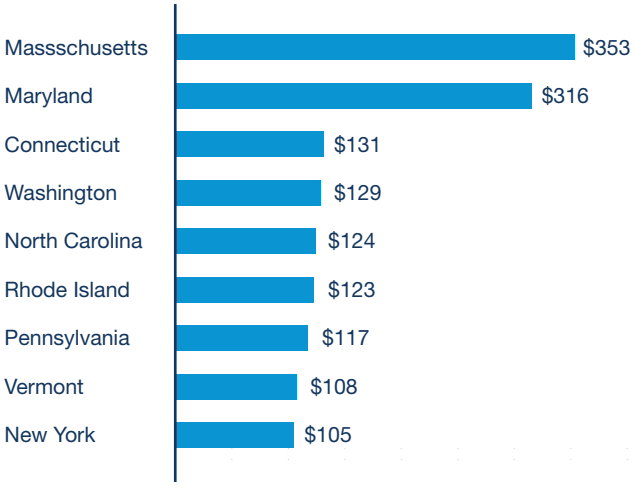
Both established institutions and start-up life sciences companies benefit from the enormous amount of funding from the National Institutes of Health (NIH) that flows into the state. The NIH, comprising 27 separate Institutes and Centers, is the federal focal point for medical research in the United States. In 2005 alone, the NIH awarded Massachusetts $2.27 billion in funding—almost 10% of the U.S. total. Of the 5,193 grants and contracts awarded the state, almost 90% were used for research projects, and the remaining funding went to activities such as fellowships, training, and construction. (See Table 2.)

Although California leads in terms of the absolute dollar amount of NIH funding received in 2005, Massachusetts led the nation in per capita funding with $353 per capita. Furthermore, despite its small geographic size, Massachusetts was second in absolute NIH dollars received. (See Figure 6.)

Sources of NIH funding

Massachusetts received the largest total amount of grants from the National Institute of Allergy and Infectious Diseases. Table 3 lists the amounts Massachusetts received from each Institute, and the percentage share that these funds contributed to the NIH funds received in Massachusetts. While only 4% of the state's total funding came from the National Human Genome Research Institute (NHGRI), this represents almost one-quarter of all funding provided by NHGRI—not surprising, given the state's pioneering work in this area.

Figure 6. 2005 NIH funding per capita



Source: National Institutes of Health, Office of Extramural Research

Table 2. Top ten NIH grantee states—fiscal year 2005

Rank (total funding)	State	Amount of funding received ($ millions)
1	California	$3,301
2	Massachusetts	$2,273
3	New York	$2,021
4	Maryland	$1,764
5	Pennsylvania	$1,452
6	Texas	$1,150
7	North Carolina	$1,078
8	Washington	$813
9	Illinois	$734
10	Ohio	$717

Source: National Institutes of Health, Office of Extramural Research

Table 3. Massachusetts' share of NIH funding by funding institute, 2005

Institute	MA amount ($millions)	% MA share
National Institute of Allergy and Infectious Diseases	$371	16%
National Cancer Institute	$311	15%
National Heart, Lung, and Blood Institute	$278	12%
National Institute of General Medical Sciences	$188	8%
National Institute of Diabetes and Digestive and Kidney Disorders	$181	8%
National Institute of Neurological Disorders and Stroke	$133	6%
National Human Genome Research Institute	$94	4%
National Institute on Aging	$91	4%
National Institute of Mental Health	$88	4%
All Other Institutes	$538	23%
Total—All Institutes	$2,273	100%

Source: National Institutes of Health, Office of Extramural Research

Top grantee institutions in Massachusetts

Massachusetts' NIH funding is distributed among a variety of institutions, from medical, undergraduate and graduate programs to hospitals and specialist research organizations. For fiscal year 2005, Massachusetts General Hospital received about 13% of the dollars, the largest amount of any institution in the state. Table 4 below provides the top fifteen grantee institutions in Massachusetts for 2005.

Table 4. Fifteen largest NIH grantee institutions in Massachusetts, fiscal year 2005

Rank	Organization	Dollars awarded ($ millions)
1	Massachusetts General Hospital	$287
2	Brigham and Women's Hospital	$253
3	Massachusetts Institute Of Technology	$172
4	Harvard University Medical School	$169
5	Boston University Medical Campus	$123
6	Beth Israel Deaconess Medical Center	$123
7	Dana-Farber Cancer Institute	$117
8	University of Massachusetts Medical School	$115
9	Children's Hospital Boston	$103
10	Harvard University (School of Public Health)	$102
11	Tufts University Boston	$75
12	Harvard University	$51
13	New England Medical Center Hospitals	$50
14	Boston Medical Center	$39
15	Whitehead Institute For Biomedical Research	$35

Source: National Institutes of Health, Office of Extramural Research

Recent trends

Competition for NIH funding is fierce. While organizations in the state received $383 million more in NIH funding in 2005 compared to 2001, this funding was a slightly smaller percent of all NIH funding, representing aggressive efforts by other states interested in the economic development produced by life sciences research.

An even bigger concern is a flattening of the national NIH budget for biomedical research in recent years. The impact of this slowdown in federal funding is being felt across the U.S., but the consequences for the Commonwealth are greater than for other states due to its reliance on the life sciences cluster to fuel the economy's growth. If the decline in NIH funding continues, it could have a tremendous impact on the Massachusetts economy. Federal grants to teaching hospitals in Boston alone total $1.4 billion annually. These grants help fuel the biomedical innovation engine that is essential to the health of the Commonwealth's life sciences cluster. Medical institutions in the Boston area employ more than 150,000 workers and add more than $24 billion to the state's economy each year.[8] Clearly, the stakes are high.

Respondents to the PwC survey were divided over whether they believed the state will maintain or increase its share of NIH funding over the next five years. Industry leaders and Massachusetts policymakers must work together to persuade the federal government to make funding of biomedical research a top priority, and to ensure that Massachusetts continues to receive a substantial share of NIH grants.

Opportunity for action: increase NIH funding

NIH funds have enabled Massachusetts' preeminent academic health centers to achieve successful breakthroughs in the treatment of many of our nation's most persistent diseases. They have also fuelled innovations in drugs and medical devices that have led to the creation of many of the businesses that now constitute our life sciences cluster. However, after doubling between 1998 and 2003, the total amount of NIH funding has been either stagnant or falling in the past few years. This diminution of NIH funding poses a threat to the system of innovation that drives both critical medical research and also life sciences growth in the Commonwealth. A public-private coalition led by the Governor and the state's Congressional delegation could mobilize advocacy for increased NIH funding to speed the progress of scientific innovation.

[8] Christopher Rowland, "Funding Slowdown Worries Hospitals," *Boston Globe*, March 6, 2007

Collaboration with academia and industry

Thirty-nine percent of those participating in the PwC 2007 Massachusetts Life Sciences Cluster Survey credited a Massachusetts academic or research institution for playing a central role in the creation or growth of their companies.

Often, new ventures must rely on collaboration with academic researchers for a variety of reasons, including:

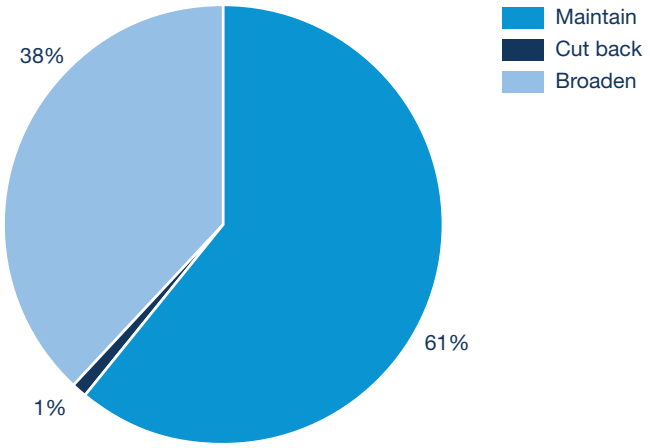
- creating intellectual property;
- generating proof of concept data;
- co-authoring proposals for funding requests; and
- collaborating on early stage clinical trials.

As a result, start-ups regularly forge research agreements with Massachusetts universities. Two out of five PwC survey respondents said their companies have at least one clinical research or sponsored research agreement with a public or private academic institution in the state. Those respondents who already have research agreements with academic partners overwhelmingly indicated that they will either maintain or expand their agreements over the next two years.

Almost two fifths of PwC survey respondents said that they have intellectual property that was developed at academic institutions in Massachusetts. Of these respondents, 61% expect to maintain patent license agreements with their academic partners over the next two years, and more than one-third expect to broaden those agreements.

Survey respondents also indicated that they expected to see additional collaboration between universities and life sciences companies in Massachusetts. A majority indicated that they plan to establish research agreements with academic institutions in the next two years.

Figure 7. Companies planning to broaden, cut back or maintain patent license agreements with academic partners over the next two years



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

Perspective

Bioresearch collaboration: Merck and Harvard University

By Steven Hyman and Lex Van der Ploeg

Steven Hyman, MD
Provost
Harvard University

Lex Van der Ploeg, PhD
Site Head
Merck Research Laboratories Boston

Collaboration between academia and industry is a critical element of the growth of the life sciences. These partnerships allow creativity, innovation, and resources not possible without both important pieces of the development cycle working together. The collaborations between Harvard University and Merck Research Laboratories Boston are an example of such success.

Harvard and Merck have worked collaboratively on several efforts which help bring fundamental research forward as a potential new therapy. By combining the licensing rights and the expertise behind the original findings, and partnering with a leading company, research can be advanced into clinical development and application much faster than would otherwise be possible. For example, in 2006 Harvard and Merck put into place a multimillion-dollar license agreement to develop potential therapies for macular degeneration, an eye disease that affects older people and can lead to blindness. The agreement provides Merck with licenses to specific molecules that could ultimately slow the production of toxic byproducts that form in the eye and that have been implicated in some forms of age-related macular degeneration and Stargardt disease, a juvenile form of blindness.

Another example of collaboration which serves the needs of both academia and research is a $1 million gift from Merck Research Laboratories to Harvard University's Department of Molecular and Cellular Biology (MCB) to create three new opportunities for research, fellowships, and summer school genomics education. The gift funds will allow MCB to launch the Merck Pilot Research Program, the Merck Scholars Program, and the Merck Core Educational Support Program. This precedent demonstrates the mutual benefit of collaboration between private industry and academic research, and will encourage other corporate allies to consider this enlightened approach. The interdisciplinary research enabled by this gift ultimately translates into benefits for patients, in ways that we are unable to imagine today.

This is just the beginning of a focused and developing relationship where we build for strong future alliances aimed at drug discovery and development alliances. These partnerships allow fundamental research at major research universities to have a more immediate impact on therapeutic approaches, and this new dynamic requires both world class science and strong partnerships between technology transfer organizations, academic scientists and industry. It is through such collaboration that research will continue to flourish in this region.

SBIR and STTR NIH grants

The substantial NIH funding that Massachusetts organizations receive provides a solid foundation for biomedical research. The life sciences cluster also benefits from two grant programs, administered by the Office of Technology of the U.S. Small Business Administration (SBA). The programs are designed to facilitate the commercialization of novel technology and intellectual property licensed from universities to small high technology firms employing less than 500 people.

The Small Business Innovation Research (SBIR) program requires federal departments and agencies with annual extramural research and development budgets exceeding $100 million to reserve at least 2.5% for awards to small U.S. high technology firms. The Small Business Technology Transfer Research program (STTR) requires federal departments and agencies with annual extramural research budgets exceeding $1 billion to set aside 0.3% for small U.S. high tech firms. These awards, which are smaller than SBIR grants, fund R&D projects in which small businesses and non-profit research institutions collaborate.

These two programs represent the strongest indicator of how university-derived intellectual property is being transformed into future life changing commercial products. SBIR/STTR funding helps companies bring research to market faster through:

- Setting defined milestones required to initiate further funding;
- Forcing small firms to focus on commercial products not just basic science; and
- Putting the companies' development strategies through a peer reviewed process that lends credence to the technology development process.

As shown in Table 5, Massachusetts received over $84 million in funding through SBIR and STTR programs in 2005. Only California received a higher level of funding in absolute dollars. However, as Table 6 shows, on a per capita basis Massachusetts received $13.10 in funding—the highest of any state, and more than triple the figure for California. While SBIR and STTR grants represent only a small fraction of the total NIH funding Massachusetts receives annually, these funds provide an essential boost to biotechnology start-up companies in the state.

Such a differential is a clear indicator of a competitive strength of the cluster. In the future this advantage may be curtailed as there have been attempts at the federal level to restrict ownership of SBIR/STTR-funded companies by venture capitalists. This is counter productive to the commercialization of life-saving products that on average can take hundreds of millions of dollars to bring to market.

Table 5. NIH SBIR and STTR grants to Massachusetts, fiscal year 2005

Grant category	Number of grants	Total amount
SBIR		
Phase 1	114	$21,494,643
Phase 2	110	$53,281,572
Total	224	$74,776,215
STTR		
Phase 1	20	$3,882,197
Phase 2	10	$5,637,129
Total	30	$9,519,326
Total SBIR and STTR	254	$84,295,541

Source: NIH Office of Extramural Research

Table 6. Per capita NIH SBIR and STTR grants, select states, 2005

State	SBIR and STTR funding	Per capita funding
Massachusetts	$84,295,541	$13.10
California	$121,701,208	$3.40
North Carolina	$22,611,990	$2.60
New York	$34,470,500	$1.80
New Jersey	$15,118,188	$1.70

Source: NIH Office of Extramural Research

Perspective

A commitment to academic research

By Peter Slavin

Peter Slavin, MD
President
Massachusetts General Hospital

Research is a dynamic enterprise, a vibrant part of the mission of an academic medical center. Massachusetts General Hospital is proud of its broad-based research program, the largest of any hospital in the nation, which have evolved throughout our 196-year history. We are proud of the extraordinary work and important knowledge that have emerged from our laboratories, inpatient units and outpatient programs. Staying on the frontlines of research takes a willingness to restructure and organize programs in innovative ways that lead to higher levels of success.

At the MGH, one visible symbol of such innovative thinking is the Richard B. Simches Research Center. Opened in 2005, the 267,000-square-foot facility is home to centers that have been organized thematically rather than by traditional clinical discipline, encouraging greater collaboration and interaction among researchers. The Center for Regenerative Medicine and Technology explores stem cells and tissue engineering to repair damaged tissues and organs. The Center for Computational and Integrative Biology applies discoveries from biomedical research and bioinfomatics to develop drug therapies. The Center for Human Genetics Research explores the building blocks of life to study the causes and effects of disease. And the Center for Systems Biology and Physiologic Genomics analyzes the way the body's complex systems work together.

This interdisciplinary philosophy at the MGH, however, didn't begin with the Simches Building. The Wellman Center for Photomedicine, established more than 30 years ago, has pioneered light-based technologies used in many disciplines for diagnostic and therapeutic purposes. And the MGH Cancer Center has long embraced the idea of cross-fertilization and collaboration, recognizing that cancer reaches into every specialty.

Collaboration between and among disciplines makes perfect sense as we address the complex biomedical challenges of the 21st century. Burgeoning knowledge at the molecular level is enabling us to decipher basic processes of life. Promising scientific fields such as genomics, stem cells and bioinfomatics have relevance to virtually every biomedical discipline. Mindful of the complexity of disease, we also collaborate with engineers, physicists, computer scientists and mathematicians.

The demands of research can exact a tremendous toll on investigators, especially those beginning their careers. Women scientists of childbearing age are hit particularly hard. Like all researchers, they feel pressure to devote the extraordinary time required to build a research portfolio that will enable them to advance academically and win vital grant funding. Family demands, however, often conflict with career, with the head-on collision coming in the 30s.

To support women researchers at this difficult time, the MGH offers the Claflin Distinguished Scholar Awards, which provide funding to women scientists who are responsible for the care of young children. The two-year awards provide $50,000 a year in scientific support, enabling women to achieve a better balance between career and motherhood. Of the 40 women who have earned Claflin Awards, 36 have stayed at the MGH, and 22 have earned promotions at Harvard Medical School. Claflin scholars have brought in funding totaling more than 20 times the MGH's investment in the program.

Claflin scholars embody the kind of exceptional investigator at the MGH, which is teeming with brilliant, motivated people who have collectively shaped an environment that fosters scientific inquiry, from basic to translational to clinical research. It is these talented scientists who have enabled the MGH to remain a leader in biomedical research. And it is they who have helped Massachusetts become a national leader in the life sciences. The MGH remains committed to ensuring that this region strengthens its leadership position in biomedical research for years to come.

Perspective

Through collaboration Joslin fights the diabetes epidemic

By Ranch C. Kimball

Ranch C. Kimball
President and CEO
Joslin Diabetes Center, Inc.

One of the strongest outcomes of Joslin Diabetes Center's mission of research, care, and education is the ability to successfully partner with other institutions, organizations and companies. With the largest diabetes patient database in the world, a $44 million research budget, and a strong team of researchers in one building, collaboration becomes almost effortless. A hallmark of this collaborative environment is Joslin's solid relationship with industry, with 55 active industry-sponsored research projects at Joslin, including 15 industry-sponsored clinical trials. While we have been among the most successful organizations in obtaining NIH funding, we have established significant relationships with industry and look forward to more of these types of partnerships.

Being in the center of the Massachusetts life sciences cluster, researchers from around the world come to Joslin to perform interdisciplinary research in diabetes and metabolic diseases. As with other Boston-area institutions, the research done here draws worldwide talent, whose work in turn has a worldwide impact. Massachusetts is leading the fight against diabetes. Diabetes, especially type 2, is growing rapidly both in the U.S. and abroad. What is particularly noteworthy is that of the 21 million Americans with diabetes, one third do not even know they have it. In addition, approximately 150 million people around the world have the disease, and in the world's two most populous countries, China and India, the growth rate of diabetes exceeds even that of the United States.

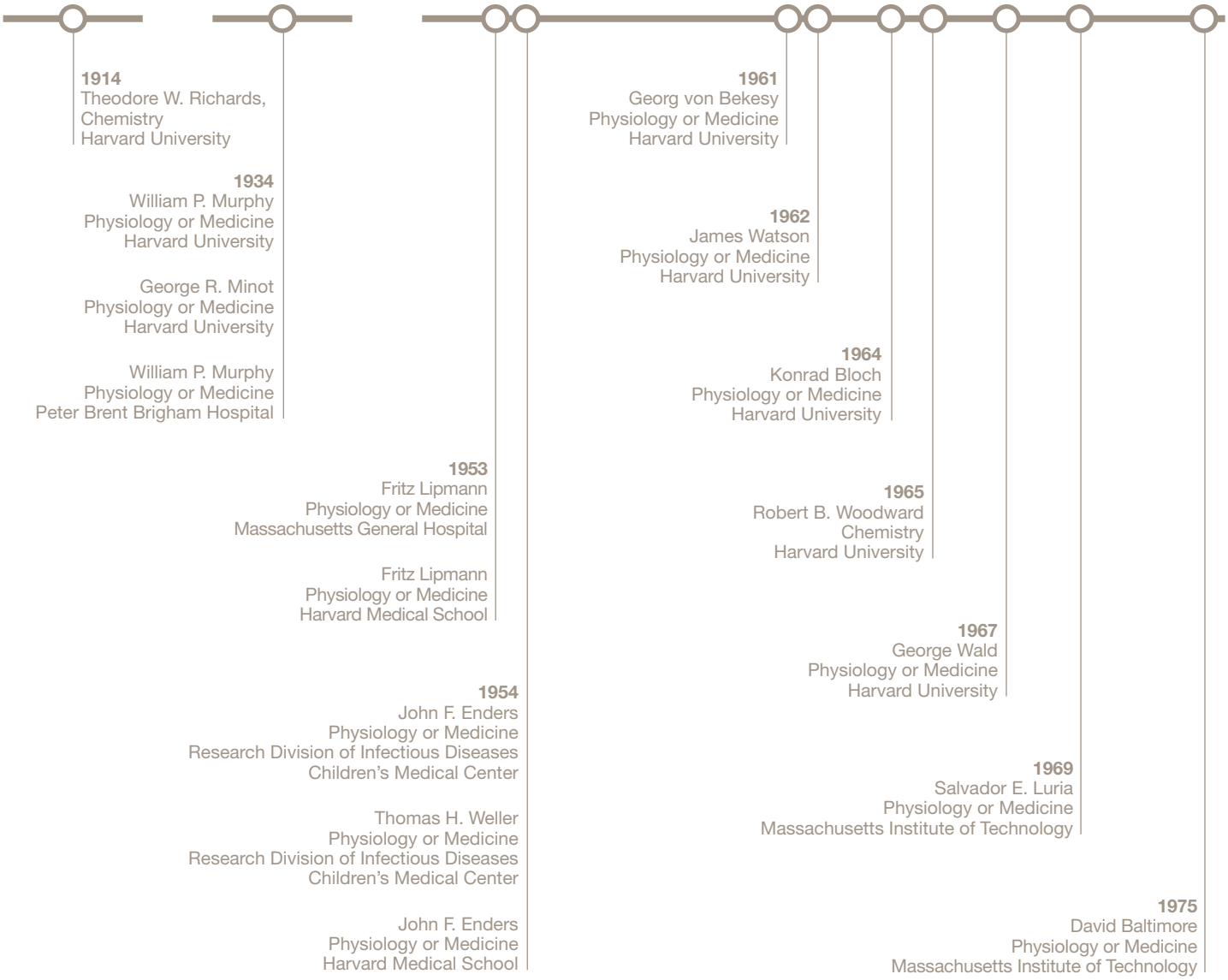
Although the rate of diabetes is growing, our level of understanding of the diabetes mechanisms at the cellular level, at the system biology level, and at the immune level are so far ahead of where they were even five years ago that very rapid research innovations are finding their way into treatment. If left untreated, a person with diabetes is at significant risk of losing an eye, kidney or foot. A key aspect of our work, which results from our focus on complete patient care, is early detection and treatment of the complications of the disease. The research conducted at Joslin, which is the foundation for nearly all other diabetes research in the world, has also led to a reduction in the rate of blindness from diabetic retinopathy from 75 percent to less than two percent. Joslin investigators were the first to discover that kidney disease in people with type 1 diabetes is frequently reversible in its earliest stages.

As the largest diabetes center in the world, Joslin Diabetes Center has been at the forefront of diabetes research, care, and education since its founding more than a century ago by a single physician, Elliott P. Joslin, M.D. Joslin's pioneering research covers both type 1 and type 2 diabetes and their many complications. For example, the research of C. Ronald Kahn, M.D., has literally defined the field of insulin signaling transduction and mechanisms of altered signaling in disease. This heroic effort is one of the most cited pieces of diabetes research in history. Joslin scientists have pioneered novel therapeutic targets for treatments of diabetes by increasing insulin sensitivity, islet survival, immune recognition and decreasing inflammation. Many of these targets are the intense focus of investigations by pharmaceutical and biotech companies. Further, Joslin investigators have collaborated with pharmaceutical scientists to design and develop pharmaceuticals to treat complications of diabetes which are in phase 2 and 3 clinical trials.

The importance of this work cannot be stressed enough; the work being done and the continuing medical education for physicians and allied health professionals emanating from Joslin is helping to cope with this looming potential healthcare disaster. Despite mounting challenges, such as a lack of full reimbursement for patient care, the research, care, and education that is built upon a foundation of collaboration will allow Joslin to accelerate the fight against the epidemic of our time.

Translating research dollars into results

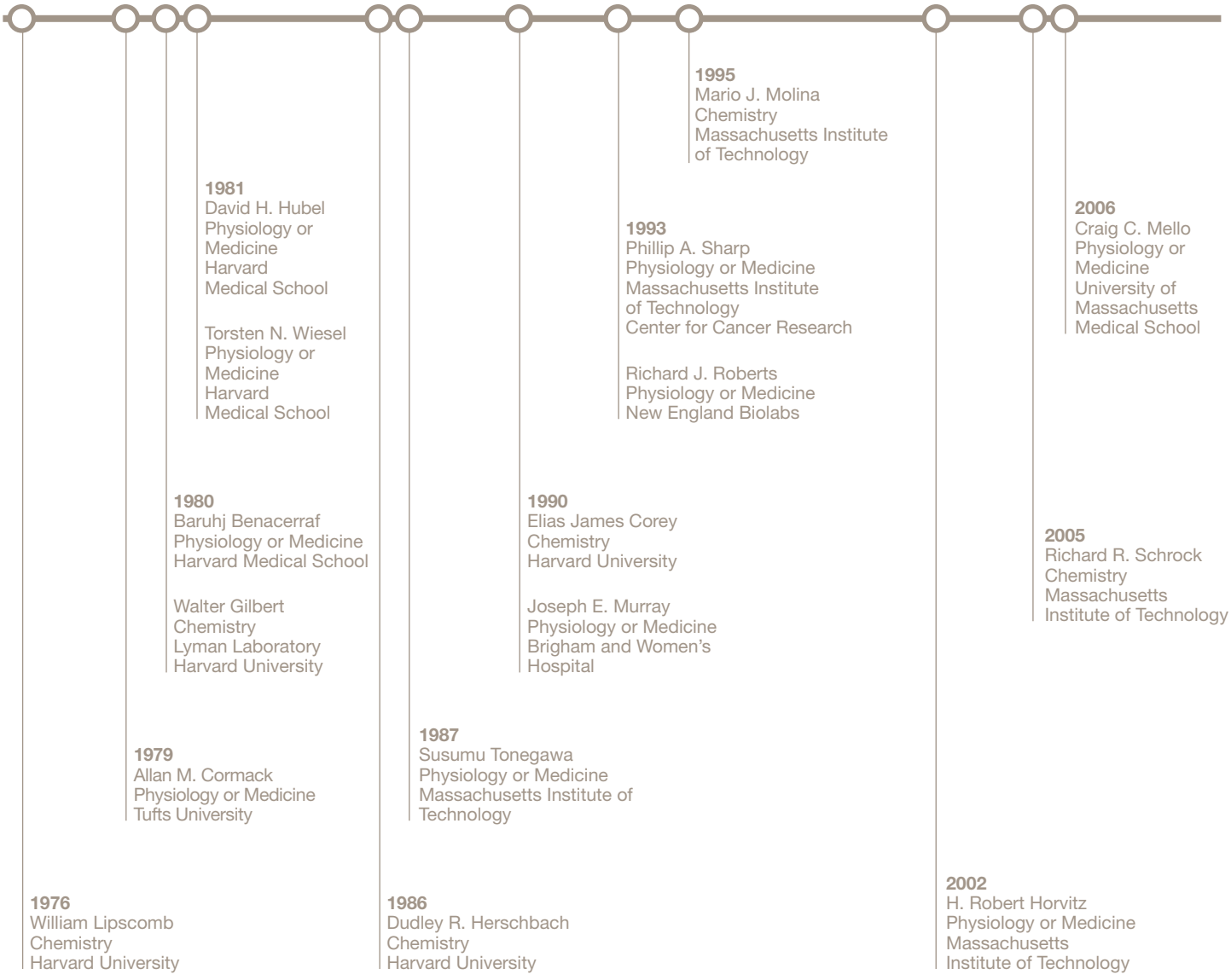
Figure 8. Massachusetts Nobel laureates



The public funding of life sciences research in Massachusetts has resulted in numerous biomedical breakthroughs over the past three decades. Numerous Massachusetts scientists have received Nobel Prizes for their seminal discoveries, which have saved countless lives and opened up new possibilities for understanding and treating disease.

This history of scientific excellence is a key reason why Massachusetts receives more NIH funding per capita than any other state. As the timeline below illustrates, the biomedical researchers of the future will be standing on the shoulders of these giants.

Massachusetts' history of scientific excellence continued in 2006, with Craig Mello of the University of Massachusetts Medical School sharing a Nobel Prize for his groundbreaking research on RNA interference, or gene silencing. Mello's research provided the foundation for future development of gene therapies as a replacement for traditional pharmaceuticals.



Interview

Craig C. Mello, PhD

2006 Nobel Laureate

On his interest in science

My dad was a paleontologist for the Smithsonian. I had every kid's dream come true: To go into the museum and see the dinosaur bones behind the scene. I thought it was cool. I think most kids start out with that kind of curiosity about the world.

In high school, what captured my imagination was learning that the human insulin gene had been cloned, and that the human gene—when placed into the bacterial cell—could allow the bacterium to make the human protein. I still think it's amazing.

I think science is wonderful. But to me the most powerful kind of science is the kind that can change the world—not only learn about the world but do something that can change the future of mankind. That became a goal for me in my own scientific career.

On the impact of his discovery

It's amazing how important molecular biology has been, for example, in type 1 diabetes. The cloning of insulin was the first step in making a therapeutic supply of insulin. My six-year-old daughter, Vicky, has this disease, and she is using this insulin to stay alive every day. This is the beauty of science: making life and death differences in people's lives. When you have a child who is chronically dependent on a medicine from molecular biology, you really begin to appreciate the important work that the pharmaceutical industry does.

RNAi is a lot like that kind of therapeutic. It will help treat a disease, but it might need to be applied constantly. It's exciting to think that there are diseases, like neurodegenerative disease, that we did not know how to treat and that might be addressed with RNAi. It's very encouraging that RNAi results are promising in animal studies.

How the Nobel Prize has changed his life

It has given me an opportunity to have a voice and get the message out that today we have tremendous opportunities in biomedical science. We can accomplish in one day the equivalent of a week's work when I started in 1982. But it hasn't sunk in with decision-makers in Washington that progress has a cost, and the investment would bring huge cost benefits down the road.

Look, we have something really valuable here that could allow us to make a lot of headway in medical science in the next 10 years. We may develop new drugs. We may cure neurodegenerative diseases. We may make lots of progress on infectious diseases. We're maybe going to figure out how to prevent obesity and diabetes.

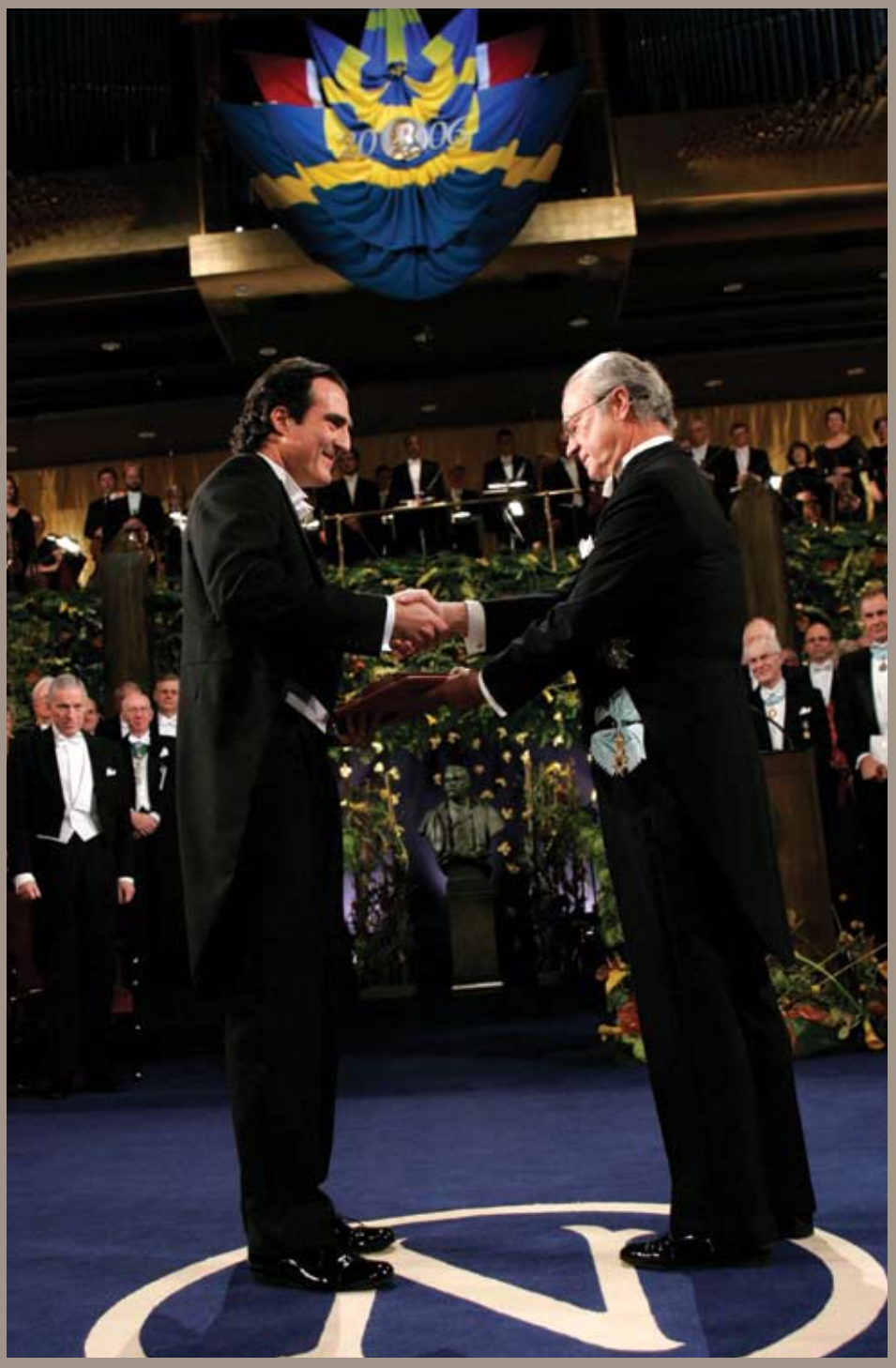
It's all at our fingertips. But we have to aim to steadily increase the expenditures we've been making so we can reap the awards. I hope I can energize the politicians in Washington and around the world to spend a little more money on research. It's an investment that's going to have really great returns. It's already benefiting mankind.

Note: Material from previously published interviews was used in this article.

Craig Mello was checking his diabetic daughter's blood sugar late on the night of October 2 last year when the telephone rang. Mello was told that he had just won the Nobel Prize in Physiology or Medicine. A professor and researcher at the University of Massachusetts Medical School in Worcester, Mello shared the prize with Andrew Fire of Stanford University Medical School for their groundbreaking discovery of a biological effect called RNA interference (RNAi) or gene silencing.

On the University of Massachusetts Medical School

We can accomplish more at UMass because it is not burdened by an existing and complicated structure like some places are. We can create something here without having to invade other people's turf. We have all the ingredients to make a difference for citizens of Massachusetts and the world. As a colleague here at UMass, I think my voice is heard and listened to a lot more than if I were another small cog in a big wheel. I feel like I can help plan and grow this institution.



Private financing

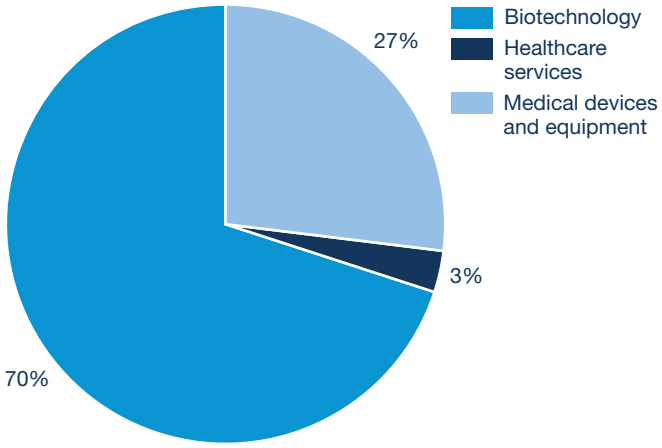
Venture capital investment in the Massachusetts' life sciences industry

Translating the results of biomedical research into new products requires extensive development and testing which, in turn, requires substantial capital. The capital must come from investors who understand the underlying science, the commercial potential of the science and the risks associated with successful commercialization.

Venture capitalists fill this critical need. In addition, they bring a wealth of business and industry expertise to the boards of these early-stage life sciences companies. In 2006, according to *PricewaterhouseCoopers' New England Health Industries MoneyTree Report*,[9] venture capitalists provided $1.1 billion in funding to Massachusetts life sciences and health industries companies, a 43% increase over the previous year. The number of deals completed rose by nearly 30%, to 108. Almost two-thirds of the deals ($755 million) were in the biotechnology sector with companies targeting cancer, autoimmune disease and diabetes continuing to draw substantial venture investment. The remainder went to medical devices and equipment companies ($292 million) and healthcare services companies ($37.5 million). Perhaps most telling is the fact that 42% of all venture capital invested in New England in 2006 went to life sciences companies, surpassing the amount invested in software and information technology. The 42% is the highest share in the 12 years of the PricewaterhouseCoopers MoneyTree Report and up dramatically from an 11% share in 2000.

Massachusetts-based venture capital firms in many cases finance local entrepreneurial companies. Since 2005, MPM Capital, Polaris Ventures, Clarus Ventures, Atlas Ventures, Oxford Bioscience Partners and SV Life Sciences collectively raised nearly $3 billion and they started to put this money to work in life sciences companies in 2006. The increase in venture capital funding in 2006 was also the result of venture capitalists pouring additional money into portfolio companies they have been backing, preparing them for initial public offerings (IPOs) or acquisition by a pharmaceutical or major medical device company. Mergers and acquisitions have been the preferred exit strategy for venture capitalists in the life sciences sector as it is typically is the quickest route to liquidity and often offers higher valuations than IPOs. With $80 to $100 billion in blockbuster brand-name pharmaceutical products coming off patent by 2010, cash-rich pharmaceutical companies need new products from Massachusetts life sciences companies to fill the gap. This has led to a growing trend of pharmaceutical company acquisitions of biotechnology companies.

Figure 9. Percent of $1.1 billion invested in Massachusetts health industries, by sector 2006



Source: PricewaterhouseCoopers and the National Venture Capital Association. *Venture Capital Investment in Health Industries Full-Year 2006 Report, the MoneyTree Report*

[9] This section draws from information from *Venture Capital Investment in Health Industries Report: New England Health Industries Full-Year 2006 Results, the MoneyTree Report from PricewaterhouseCoopers and the National Venture Capital Association based on data provided by Thomson Financial*, 2007.

Among the 108 venture capital deals in the Massachusetts life sciences industry in 2006, several were noteworthy due to the substantial size of the investments. The top six investments accounted for $289 million in funding, distributed among five biotechnology companies and one medical device company:

- Microbia, Inc., of Cambridge, which develops drugs to treat gastrointestinal disorders—received $75 million in financing;
- Insulet Corp., of Bedford, which develops disposable insulin delivery systems for the treatment of diabetes—received $50 million in financing;
- Concert Pharmaceuticals Inc., of Lexington, which develops small-molecule drugs for unmet medical needs—received $48.5 million in financing;
- Synta Pharmaceuticals Corp., of Lexington, which develops small molecule drugs for cancer and chronic inflammatory diseases—received $40 million in financing;
- Artisan Pharma Inc., of Framingham, which develops a treatment for a condition often found in sepsis patients—received $39 million in financing; and
- ToleRx, Inc. of Cambridge, which develops therapies that induce or remove immunological tolerance—received $35 million in financing.

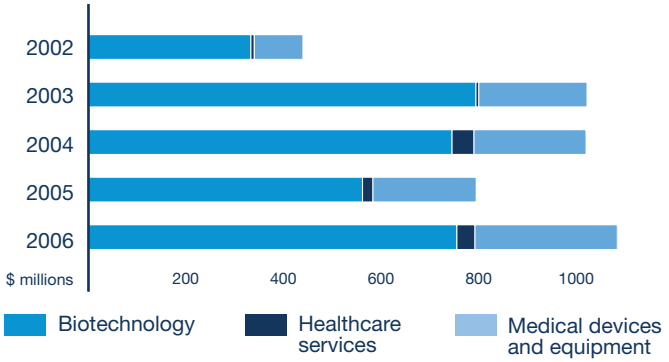
Continuing a positive trend

Massachusetts ranks second behind California in terms of total venture capital financing of life sciences companies and number of deals. But Massachusetts' 43% growth in venture investments in 2006 far surpassed the 10% growth rate for California. Overall, between 2002 and 2006 venture capital investments in the Massachusetts life sciences cluster more than doubled. (See Figure 10.)

Opportunity for action: venture financing

The so-called "Valley of Death" in the financing of innovative ventures and technologies often stunts the development of potentially breakthrough products. This valley refers to the pivotal stage prior to a company determining if they have a safe, commercially viable product. Most affected by this "valley" are companies preparing to transition innovative research from an academic setting to an early stage company. These companies typically have exciting science but lack key "proof of principle" data that would mitigate investment risk. To foster the life sciences innovation economy, Massachusetts policy makers and the life sciences cluster stakeholders should explore collaborative opportunities to improve access to capital for companies in the transition stage between research and creation of products. They should also work to explore creative uses of state and federal funds to assist companies in this transition period.

Figure 10. Massachusetts health industries investment by sector, 2002–2006



Source: PricewaterhouseCoopers and the National Venture Capital Association. *Venture Capital Investment in Health Industries Full-Year 2006 Report, the MoneyTree Report*

Perspective

Venture capital and biotechnology in Massachusetts

By Jonathan Fleming

Jonathan Fleming
Managing Director
Oxford Biosciences

The tradition of venture capital is as old as New England. We think of venture capital as a group of investors forming a syndicate to invest in projects that are quite risky but very lucrative if they succeed. Groups of individuals or financial institutions acting like venture capitalists supported whaling ventures and clipper ship trading ventures to China. Often vessels were lost at sea, but when "your ship came in," the profits could be huge. Later investors and entrepreneurs helped start the textile, shoe, minicomputer, software and internet industries in the region. While the tradition of start-up capital investment goes back to the China Trade, it was also critical in the formation of Boston's cluster of biotechnology companies over the past 25 years.

Biotechnology, like whaling, is not a game for the faint of heart. To begin with, it takes a large commitment of capital. The management team is critical—the wrong captain of the ship and you are likely to lose everything. Specialized technology and skills are required. Finally, biotechnology ventures, like shipping and trading ventures 250 years ago, take lots of time to mature. Without access to the pools of patient risk capital that existed here in the Boston area, biotechnology would not have gotten off to the early start it did, and it would not have developed to the size and sophistication it has achieved today.

In the early days of the modern biotechnology industry, the amounts of capital required to start the company were not as large as now. However, no one knew how quickly and successfully a new biotechnology company could develop a product. Entrepreneurs and their investors were venturing into uncharted waters. In the last twenty years, the amount of capital needed to start and develop a biotechnology venture has increased rapidly because the industry has matured and now measures success by actually getting new products approved. Today, any company trying to develop a therapeutic drug can expect to spend tens or hundreds of millions of dollars prior to actual approval or sale of the product. The odds on any one product working are still quite low, so a portfolio approach is the only rational way to finance the industry.

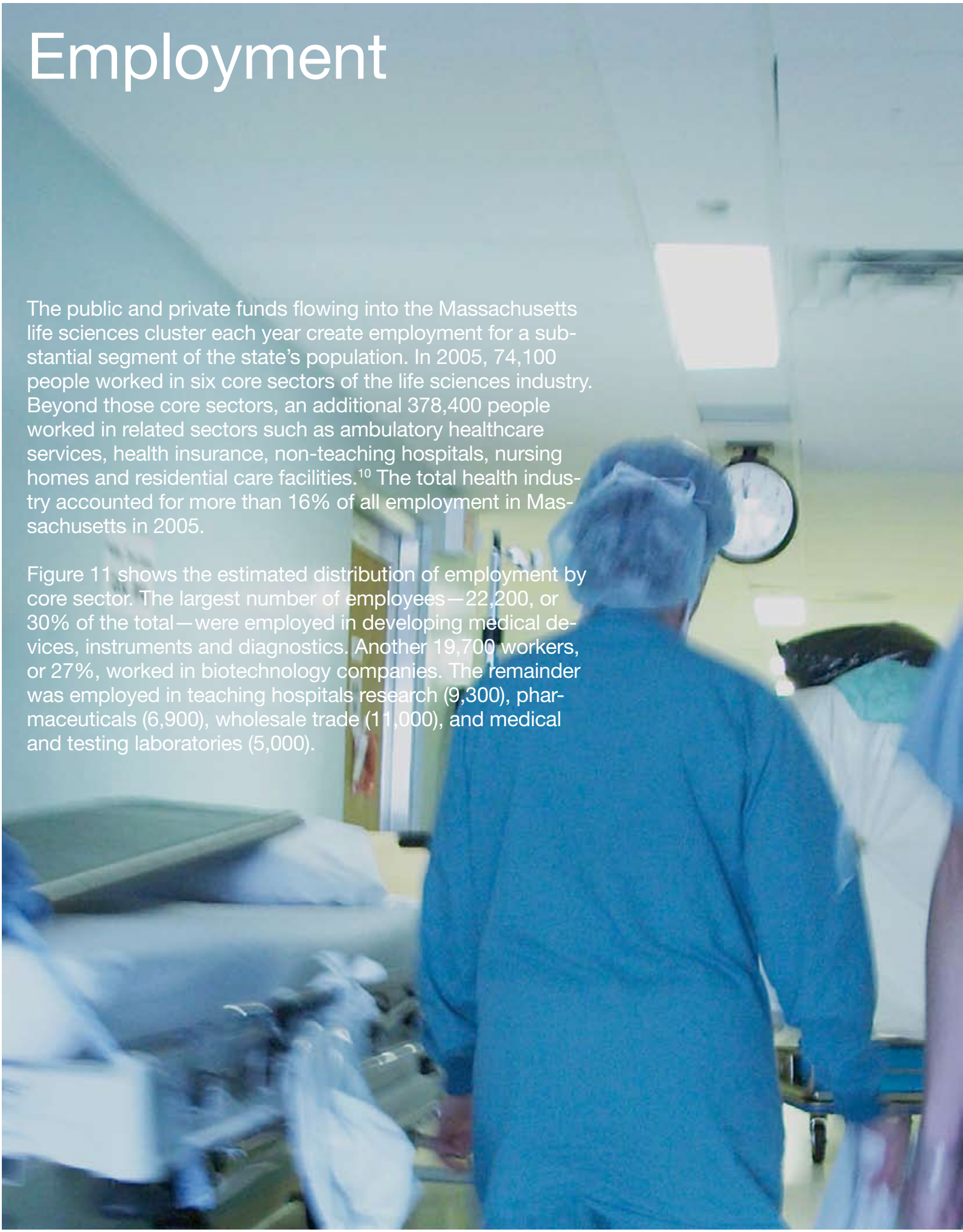
Money is not the only reason the region developed so rapidly and successfully. The "brain capital," concentrated in the Boston area, is world class. This capital resides in universities, medical schools and research institutes, as well as in the management teams and pools of highly educated workers of the biotechnology and pharmaceutical companies already up and running. Success in biotechnology requires highly specialized skills to go from scientific insight or breakthrough to a product taken by thousands of patients. Very little of this expertise is employed within the individual biotech company. Instead, they are contracting daily with providers of specialized skills and technologies to perform the tasks necessary to move a product through pre-clinical testing and clinical testing prior to approval. What ties the brain capital and the risk capital together is the venture capital firm.

The Boston area boasts a large and sophisticated venture capital industry that provides access to the best people and practices needed to succeed in an industry where the odds are long. There is frequent contact between the venture capital firm and the worlds of science and medicine; investment bankers call weekly to find out which companies they can IPO or sell to a strategic buyer. The office of the VC firm thus serves as a convenient place for all of them to get together. What makes it work especially well in the Boston area is that the university professors and doctors, managers, and venture capitalists all tend to live in the same general area and have frequent contact, whether at work, at school or in the community. This happy combination of proximity coupled with the right people using the best practices backed by venture capitalists means that more companies will get started on the right track in New England.

The result is that since Biogen, Collaborative Research and Immunogen began operations more than 25 years ago, the local biotechnology industry has grown into hundreds of companies, as well as hundreds of service and product providers that make up the contract research and research tool sectors. More than a dozen pharmaceutical firms have opened research centers in the last twenty years trying to capture some of the innovation magic that exists here.

The magic is the people and their history and culture. Brain capital and venture capital have combined in New England for 300 years. By putting capital behind daring entrepreneurs with visions of great things based on breakthroughs in genetics and molecular and cell biology, venture capitalists have created a successful economy focused on the betterment of patient health.

Employment



The public and private funds flowing into the Massachusetts life sciences cluster each year create employment for a substantial segment of the state's population. In 2005, 74,100 people worked in six core sectors of the life sciences industry. Beyond those core sectors, an additional 378,400 people worked in related sectors such as ambulatory healthcare services, health insurance, non-teaching hospitals, nursing homes and residential care facilities.[10] The total health industry accounted for more than 16% of all employment in Massachusetts in 2005.

Figure 11 shows the estimated distribution of employment by core sector. The largest number of employees—22,200, or 30% of the total—were employed in developing medical devices, instruments and diagnostics. Another 19,700 workers, or 27%, worked in biotechnology companies. The remainder was employed in teaching hospitals research (9,300), pharmaceuticals (6,900), wholesale trade (11,000), and medical and testing laboratories (5,000).

Growth in industry employment

Employment in the life sciences cluster in Massachusetts has been on a growth trajectory, even as jobs in many other sectors have left the state. Between 2001 and 2005, employment across all industries in Massachusetts declined by 3.6%, and the manufacturing sector saw a substantial 21.5% decline. Over that same period, employment in the life sciences cluster grew by 3.5% overall. (See Table 8.) This growth can be expected to continue as a strong majority of survey respondents indicated that they expect their workforce to increase in the near future.

While the level of employment growth in the life sciences cluster is high relative to other industries in the state, it is lower than the U.S. average. Between 2001 and 2005, the life sciences industry grew by 5.9% nationwide, making it one of the fastest growing industries in the country. Massachusetts' growth rate also was significantly lower than that of North Carolina, which has been aggressively marketing itself as a future life sciences hub, an effort that has been highly successful, especially in biotechnology.

Sector growth

Within the cluster, some sectors have experienced greater growth than others. (See Table 9.) Biotechnology was the strongest sector, with 20.9% growth between 2001 and 2005. During that period, biotechnology companies contributed 3,400 new, high-wage jobs to the Massachusetts economy. The 20.9% growth rate in biotechnology reinforces the robustness of the cluster concept. With an array of leading educational institutions concentrated in the Boston–Cambridge area, biotech companies are naturally drawn to the area, where they take root and grow, further strengthening the cluster.

However, not all core sectors of life sciences fared as well as biotechnology. The pharmaceutical sector experienced a 4.2% decline in jobs. A majority of this decline came from the loss of positions focused on the preparation of finished pharmaceuticals. In addition, the medical devices and equipment sector declined by 12.9%, with a majority of the lost positions coming from manufacturers of surgical and medical instruments, such as clamps, catheters and syringes. Therefore, both pharmaceuticals and medical devices experienced losses in areas where products have become "commoditized." Producers prefer to locate operations of these commoditized products in areas with lower labor costs.

Table 7. Life sciences industry employment by select states 2001 and 2005

State	2001	2005	Change	% change
California	247,400	260,700	10,900	5.4%
Massachusetts	71,600	74,100	3,300	3.5%
New Jersey	113,400	108,300	-5,100	-4.5%
New York	120,500	122,800	2,300	2.0%
North Carolina	50,500	59,500	9,000	17.7%
United States	1,739,200	1,842,400	103,200	5.9%

Source: BLS, Quarterly Census of Employment and Wages, and PricewaterhouseCoopers analysis.

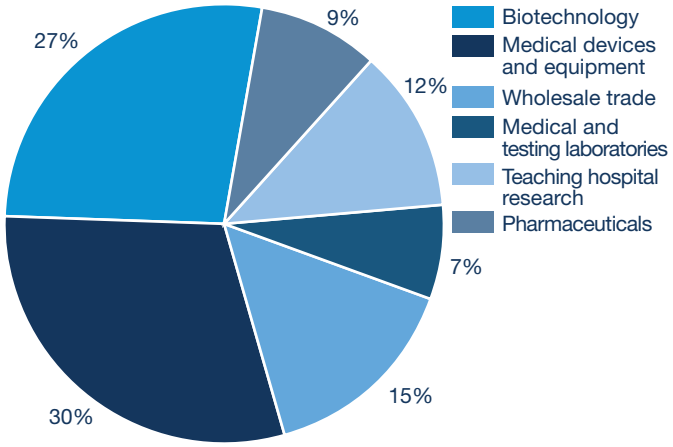
Table 8. Massachusetts life sciences industry employment compared to other select Massachusetts sectors, 2001 and 2005

Industry	2001	2005	Change	% change
All Industries	2,861,800	2,758,300	-103,500	-3.6%
Manufacturing	389,200	305,500	-83,700	-21.5%
Wholesale Trade	141,100	132,700	-8,400	-5.9%
Healthcare Industry†	371,400	400,400	29,000	7.8%
Life Sciences Industry	71,600	74,100	3,300	3.5%

Source: BLS, Quarterly Census of Employment and Wages, and PricewaterhouseCoopers analysis. Numbers may not sum due to rounding.

† Analysis includes hospitals, ambulatory healthcare services, nursing homes, and health insurance carriers. Ambulatory healthcare services excludes NAICS 621511 medical laboratories and 621512 diagnostic imaging centers, with are included in the life sciences industry.

Figure 11. Distribution of employment in the Massachusetts life sciences industry



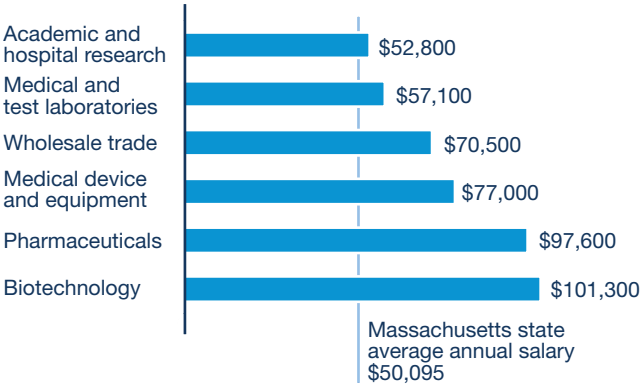
Source: Bureau of Labor Statistics Quarterly Census of Employment and Wages and PricewaterhousCoopers analysis

[10] For a list of industries that comprise the healthcare industry, please see Sources and methodology.

Industry wages

As measured by average wages, the quality of jobs in Massachusetts' life sciences cluster is impressive. In 2005, the estimated average annual wage of employees in the cluster was $81,900. There was substantial variation in pay among sectors, as illustrated in Figure 12. However, even the lowest average annual wage ($52,800), for employees in hospital research, exceeded the average annual salary in the state ($50,095). And the highest-paid workers, those employed by biotechnology companies, earned an average of $101,300—double the state average. In addition, individually and as a whole, life sciences industry sectors on average pay higher annual wages than do healthcare sectors. (See Table 10.)

Figure 12. Average life sciences wages by sector, 2005



Source: Bureau of Labor Statistics Quarterly Census of Employment and Wages, and PricewaterhouseCoopers analysis.

Table 9. Life sciences industry employment in Massachusetts by core sector, 2001 to 2005

Sector	2001	2002	2003	2004	2005	Percent Change 2001-2005
Biotechnology	16,300	17,300	17,100	18,800	19,700	20.9%
Medical and testing laboratories	4,300	4,500	4,800	4,900	5,000	16.6%
Teaching Hospitals Research	8,200	8,700	9,000	9,100	9,300	13.4%
Wholesale Trade	10,100	10,300	11,500	11,400	11,000	8.9%
Pharmaceuticals	7,200	7,700	8,100	6,200	6,900	-4.2%
Medical Device and Equipment	25,500	25,400	23,400	22,500	22,200	-12.9%
Total	71,600	73,900	73,900	72,900	74,100	3.5%

Source: Bureau of Labor Statistics Quarterly Census of Employment and Wages, and PricewaterhouseCoopers analysis. Numbers may not sum due to rounding.

Table 10. Healthcare industry wages

Sector	Wage
Health insurance carriers	$49,500
Ambulatory healthcare services	$52,200
Hospitals	$51,000
Nursing homes and residential care facilities	$29,000
Overall weighted average† healthcare industry wage	$46,000
Overall weighted average life sciences industry wage	$79,800

† These figures are weighted by employment.

Source: Bureau of Labor Statistics Quarterly Census of Employment and Wages, and PricewaterhouseCoopers analysis.

An educated workforce[11]

The workers who fill the variety of jobs in the Massachusetts life sciences cluster are a diverse group, with a wide range of requisite skills represented. This diversity is a source of strength, as it enables local firms to fulfill almost all of their hiring needs from within the state, minimizing the time required to find qualified workers outside of the state and the cost to relocate them.

The Massachusetts labor force is the product of a strong educational system. The state ranks high on many measures of academic achievement, including the percentage of residents with some college education. As of 2003, Massachusetts led the nation in the percentage of working-age residents with a Bachelor's degree or higher. The state's focus on educational achievement has resulted in the development of some of world's leading medical research institutions.

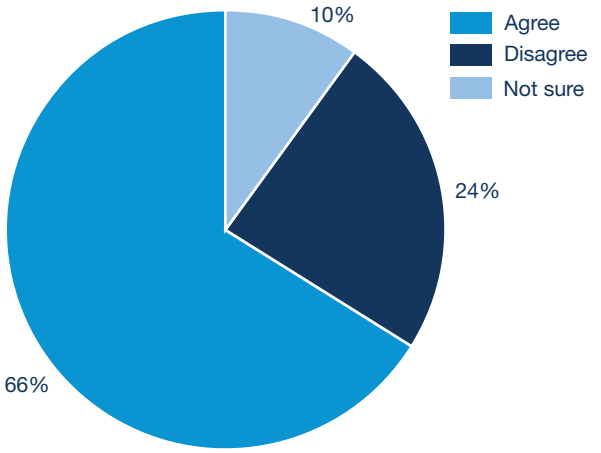
Massachusetts' educational system has thus far produced a steady stream of workers to support the life sciences cluster. However, to maintain its differentiation and competitive advantage, the state must use public resources to strengthen the state's life science workforce. Some shortages have been identified, including shortages of technicians and workers with manufacturing expertise. In addition, almost a quarter of respondents to the 2007 PwC Massachusetts Life Sciences Survey indicated that they do not believe the workforce is adequately prepared for work in the life sciences industry. In particular, they suggest that the key areas for improvement are in K-12 education as well as post high school training.

Opportunity for action: educating our future workforce

Massachusetts educators should focus on math and science curriculums that will hone the types of skills most needed for the future in the life sciences (e.g., the increasing use of automation in the life sciences) and understand its impact on the types of skills workers will need in the future. Doing so will help to ensure that the state's academic institutions continue to provide education that is relevant to the needs of the cluster.

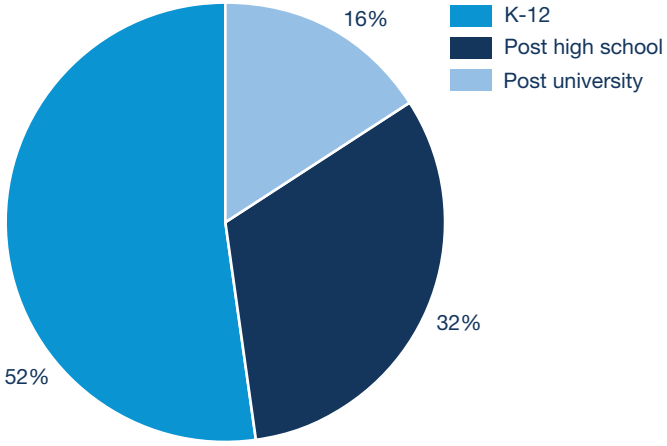
Massachusetts could improve its educational programs in animal studies. The life sciences industry has a need for workers with training and experience in veterinary technology and laboratory animal medicine and related skills. This presents an opportunity for vocational high schools, colleges and state agencies to adopt or strengthen their programs in animal husbandry and research, to ensure that Massachusetts is preparing sufficient numbers of workers to fill these important roles.

Figure 13. The workforce in Massachusetts is adequately prepared for work in the life sciences



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

Figure 14. If disagree: In which areas are improvements needed



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

[11] Portions of this section draws information from Andrew Sum, *Mass Economy: The Labor Supply and Our Future*, The Massachusetts Institute for a New Commonwealth, December 2006.

Perspective

Ensuring talent for bio-pharma's future in Massachusetts

By Jack Wilson and Michael D. Webb

Jack Wilson, PhD
President,
University of Massachusetts

Michael D. Webb
CEO,
Ascent Therapeutics

Talent is key to the success of the bio-pharma industry

Access to highly-skilled talent has been key to the emergence of Massachusetts as a global leader in the bio-pharma industry sector. According to data compiled by the UMass Donahue Institute, Massachusetts had over 48,000 bio-pharma employees, ranking us 7th in the U.S. in terms of employment in 2004. The state attracts more NIH funds and venture capital funds per worker, and it has the highest wages per worker of any state in the nation. By any measure, Massachusetts is a real success story in terms of developing a highly productive workforce for the bio-pharma industry.

The Commonwealth's higher education enterprise will be challenged to meet the growing and changing workforce needs of this industry

However, it appears that the demand for new talent in this sector in Massachusetts is now growing faster than the pipeline that produces it.

Bio-pharmaceutical employment in the state grew by 44% from 1998 to 2004. Major new firms are moving into the state, in both R&D and manufacturing, and existing firms are growing. Many are now reporting workforce challenges, both in terms of the numbers and skill sets of workers.

In light of the state's stagnant population growth, restrictions on immigration and difficulties attracting out-of-state talent to move here, it will be more important than ever for the state to develop its home-grown workforce to meet the needs of this sector.

At the same time, we in academia must also respond to a variety of national studies that have highlighted the need for new teaching approaches and curriculum in the life sciences. For example, the National Academy of Sciences in its "Biotech 2010" report called on higher education to move toward more interdisciplinary and quantitative courses to respond to such innovations as recombinant DNA, genomics and proteomics, and digital technology.

A new higher education/industry/government partnership is needed to help meet future industry needs

Given the above pressures, the state's higher education institutions—particularly UMass, the state and community colleges—must do all we can to address bio-pharma's workforce needs.

Much good work is already underway. UMass Lowell, Worcester Polytechnic Institute, Middlesex and Mount Wachusett community colleges and others worked together to help recruit Bristol–Meyers Squibb to Massachusetts. With support from the Howard Hughes Medical Institute, UMass Amherst is reforming its undergraduate curriculum so as to better integrate the teaching of biology with the physical and quantitative sciences. UMass Lowell, Boston, Dartmouth and Worcester are collaborating on an interdisciplinary graduate program in biotechnology and biomedical engineering.

Even more innovative and collaborative efforts of this sort will be needed in the future in order to develop a seamless system of workforce development that effectively links K-12, the community colleges, four-year colleges and universities in the state.

As we've done in other sectors such as information technology, we at the University of Massachusetts are fully committed to working with the Commonwealth, the Massachusetts Biotechnology Council and bio-pharma industry, and others in higher education to meet the future talent needs of this key sector of our economy. Let the collaboration begin.

Note: Figures in this perspective refer to the bio-pharma industry, defined as the biotechnology and pharmaceutical industries. The body of this report refers to the broader life sciences industry, which accounts for the discrepancy in the data.

Perspective

The burgeoning growth of the biomedical industry: the central Massachusetts region perspective

By Kevin O'Sullivan and Ted Lapres

Kevin O'Sullivan
President and CEO
Massachusetts Biomedical Initiatives

Ted Lapres
President and CEO
Nypro Inc.

The Worcester area is an emerging economic development engine within the life sciences industry in Massachusetts due to its renowned academic resources, strong research capacities, and quality medical and healthcare innovation and support. These strengths are the solid foundation as the region builds upon promoting its medical and healthcare growth. The most recent life sciences cluster development in Worcester county—medical devices and biotechnology—are creating increased employment and an expanded tax base for Massachusetts.

Biotechnology and medical devices are an outgrowth of a life sciences industry that is described as one of the Central Massachusetts area's most highly visible new economic assets. In partnership with UMass Medical School, UMass Memorial Medical Center, Tufts School of Veterinary Medicine, St. Vincent Hospital, the Fallon Clinic, Fallon Community Health Plan, Mass College of Pharmacy and Health Sciences, Worcester Polytechnic Institute, Massachusetts Biomedical Initiatives and others, this field has helped elevate the area's profile as a very attractive place for life sciences related business and professional growth. The newly proposed Gateway Park, a development partnership between WPI, its Bioengineering Institute and the Worcester Business Development Corporation, is an exciting private/public partnership focusing on the development of innovative medical device technology.

Another public-private partnership, the Massachusetts Biotechnology Research/Alexandria Technology Park is a shining example of this industrial trend. The Park, which is now home to approximately 20 companies with 1,700 jobs filling one million square feet, currently generates close to $3 million in tax revenue. Additionally, commercial partnerships led by Nypro, a worldwide medical device leader, and Abbott Bioresearch, a major biotechnology company, are prime examples of the successful production of jobs and tax base that continues to grow throughout our region.

A strong and highly successful life sciences corridor is growing in the Commonwealth between Central Massachusetts and Cambridge/ Boston. The commuter rail and the Route 146/Mass Turnpike interchange offer access to affordable housing and good school systems. Building upon this base with more frequent commuter rail service and other public transportation enhancements will help not only Central Massachusetts but the life sciences super cluster as a whole. This revitalization of Central Massachusetts rebuilds the "golden triangle of commerce" that has historically facilitated the movement of people and goods between Worcester, Boston and Providence, RI.

The Worcester area is an integral part of the Commonwealth's emphasis on a statewide strategy to compete within the life sciences in a global economy. The Central Massachusetts Legislative Caucus has been a major contributing factor supporting this effort. With such focus the medical device and biotechnology industry in Central Massachusetts has grown to over 100 companies with 7,500 employees generating yearly revenue of approximately $1 billion. The challenge of both of these industries will be to continue to focus on creating products, operating efficiently, and improving the care for patients locally and globally.

Retaining skilled workers[12]

Another workforce challenge Massachusetts faces is the high cost of living and doing business in the state—particularly in the Boston metropolitan area, the hub of the cluster. Massachusetts already is experiencing a net out-migration of residents, and the cost of living is cited frequently as a reason why people choose to take jobs elsewhere. The exodus is greatest among those aged 20 to 54, who are in the prime of their working lives. The net loss of residents is occurring across all educational backgrounds, but out-migration is particularly strong among workers without a college education.

It is not just the high cost of living but a scarcity of jobs that is driving less educated workers to move out of the state. While Massachusetts excels at providing jobs for those with Master's degrees or PhDs, there is a shortage of manufacturing and other positions for residents who lack those credentials. In 2005, more than 80% of Massachusetts residents with a Master's degree or higher held jobs in the state, while only two-thirds of high school graduates and just two in five residents without high school diplomas were employed.

Furthermore, it appears that more college graduates are moving to Massachusetts to attend graduate school than to join the state's workforce, and that college graduates are leaving the state in search of jobs in lower-cost regions. In fact educating and training doctoral level life science researchers could be viewed as one of the Commonwealth's greatest exports. Fourteen Massachusetts universities granted 609 PhDs in biology, chemistry, and chemical engineering in 2005 according to the National Science Foundation. On a per capita basis this is significantly more than any other state in the nation. If this pattern continues, it could have a significant impact on Massachusetts' ability to maintain a thriving life sciences industry.

Already, many lower-cost regions of the country are investing in building life sciences capabilities, and luring employees with the promise of lower housing costs and a higher quality of life. More than 40 states have targeted biosciences as an engine of economic growth. Those efforts are beginning to pay off in states such as North Carolina, which experienced a 17.7% increase in life sciences jobs between 2001 and 2005.

Table 11. Life sciences PhDs granted per 100,000 people

	Biology	Chemistry	Chemical engineering
Massachusetts	6.51	2.05	0.90
Maryland	3.88	0.45	0.30
New York	3.13	0.72	0.28
North Carolina	3.10	0.92	0.16
Pennsylvania	2.22	0.89	0.48
California	2.05	0.81	0.28

Source: NSF Science and Engineering Doctorate Awards: 2005 Report

Opportunity for action: retaining skilled workers

Despite Massachusetts' historical preeminence in the life sciences, complacency is not an option if the Commonwealth is to retain its leadership position into the future. Government officials are actively collaborating with corporations in an effort to attract more businesses to the state. In addition, despite the higher costs of living and working in Massachusetts, several executives have commented that once companies put down roots in the Commonwealth, they tend to stay. These actions provide the environment and the opportunities for workers in our state; however, they do not address the root causes of the out-migration of residents. The underlying factors, e.g., high cost of living and tax policy, directly impact the working age population's decision to remain or leave the state. Because both companies in the life sciences cluster and the Massachusetts economy as a whole depend on this group to deliver economic growth, addressing these issues is a top priority and should be systematically addressed.

[12] Portions of this section draws information from Andrew Sum, *Mass Economy: The Labor Supply and Our Future*, The Massachusetts Institute for a New Commonwealth, December 2006.

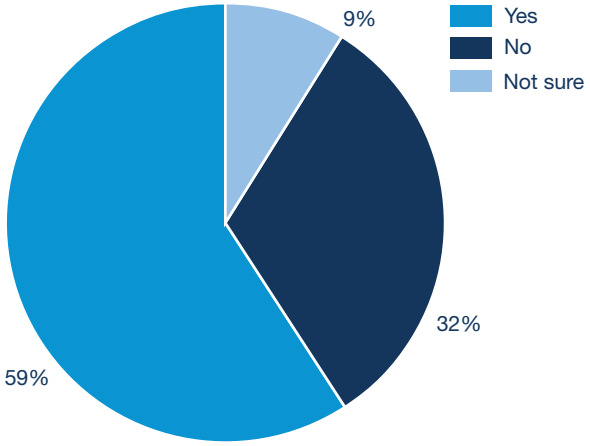
Workforce issue: transportation

Transportation difficulties have been a problem in the Bay State for years and could be hampering the Commonwealth's growth, including that of the life sciences industry. A strong majority of survey respondents cite transportation as a significant issue in Massachusetts. For those that believe it is an issue, the primary problem cited is the commute to work, not surprising given that Massachusetts drivers ranks sixth in the nation in terms of average commuting time.[13]

Opportunity for action: improving transportation

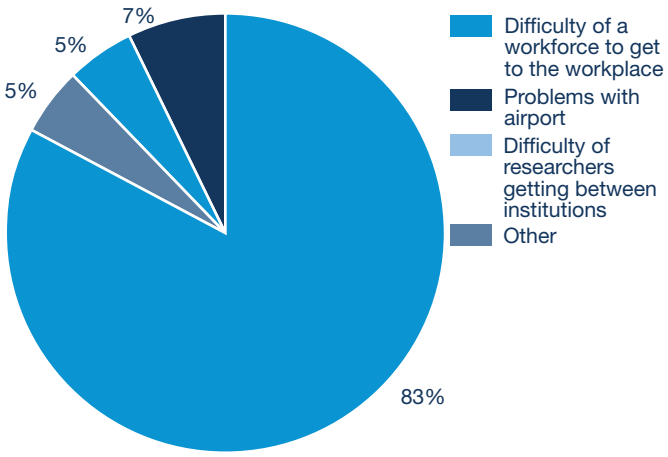
Development of the full potential for life sciences growth and expansion in the Commonwealth demands connectivity in the form of the very best transportation infrastructure. This may include more frequent rail connections between Boston and Worcester and improved rapid transit between MIT, Harvard Square, Allston, Boston University, Longwood Medical Area, the Boston Medical Center and the University of Massachusetts. The needs of the life sciences cluster must be a prominent consideration in the planning of and decision making for transportation policy.

Figure 15. Is tranportation a significant issue in Massachusetts



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

Figure 16. What is the main transportation issue your organization faces



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

[13] MassInc. *Commonwealth Agenda* 2006.

Perspective

Developing a climate for life sciences

By Daniel O'Connell and Steve Rusckowski

Daniel O'Connell
Massachusetts Secretary of
Housing and Economic Development

Steve Rusckowski
CEO
Philips Medical Systems

Massachusetts is a global leader in medicine and health care technology, and its stake in those industries has been raised significantly by an explosion in life sciences. Much of the human genome was mapped here, much of the biotechnology industry was invented here, much of the medical device industry has grown here, and an important segment of the global pharmaceutical industry has moved here. In addition, many world-renowned universities, medical research centers and teaching hospitals are located within the state. The Milken Institute, in its 2004 Technology and Science Index, ranked Massachusetts first in the nation for its ability to leverage economic development through the wealth of technology and science assets here. The Massachusetts life sciences industry comprises over 500 companies and represents over 50,000 jobs. This "cluster" is unique to our area and is among the most important drivers of job growth in the Commonwealth.

However, with global leadership comes global competition. Cities and countries around the world, as well as cities and states across the nation, have forged close partnerships with government leaders, industry and research institutions in order to capture growth in the life science industries. Regions that foster an attractive business climate with an outstanding workforce and research facilities will win the race for life sciences jobs.

Massachusetts must respond in order to keep its edge. We are forming a smart, new partnership that aims to sustain our historic leadership in scientific research and create a pro-business environment in which life sciences firms can grow their research, development, marketing and production segments in the Commonwealth.

To create an environment that truly fosters and sustains company growth, we need to tackle some of the biggest challenges to businesses head-on.

We know that life sciences firms must move quickly and efficiently to build facilities when they pass major milestones in the development of new drugs and devices. While Massachusetts has made real progress in streamlining its permitting and other regulations, we now must do more so that growing a business here is not an exercise in navigating red tape. Governor Deval Patrick has directed state government to operate at the speed of business and implement regulatory reforms that will protect the public and the environment while giving industry the predictability and the responsiveness it needs to make critical investment decisions. In addition, Massachusetts has assembled a "Business Resource Team" to serve as a single point of contact for businesses seeking to locate or expand within Massachusetts. The BRT plays a pivotal role in coordinating the activities of industry, academia, and government, so that growing a business here is as streamlined and simplified as possible.

We must also address a number of other problems, including the high cost of housing, the stagnation of federal funding for biomedical research, and the shortage of skilled workers—all of which threaten our ability to sustain our current healthcare and research activities.

The housing crisis is the single most onerous burden to the state's economic growth and retention of talent, including growth in the life science industries. The state needs to invest and partner with businesses in creating workforce housing and foster the construction of new housing, particularly in and around greater Boston, where the cost of living has become prohibitive even for many skilled life sciences workers. We are working to create initiatives that will make new resources available to young lab technicians, residents, nurses, and other entry-level employees who struggle with housing costs. We are taking a "smart growth" approach at developing residential areas by taking into account quality of life aspects such as museums and parks important to this community, as well as transportation infrastructure needs to allow life scientists and others in this industry to get to and from the key areas of research. We also need to continue to invest in science, math, technology and engineering at all educational levels to offset the growing shortage of skilled workers within the life science industries. All of these initiatives will help us ensure that Massachusetts continues to be a place where people with ideas and initiative want to be.

Perspective

Massachusetts' medical device industry focuses on the global market

By Tom Sommer

Tom Sommer
President
Massachusetts Medical Device Industry Council

Massachusetts is quickly emerging as a dominant U.S. player in the medical device industry, boasting the second highest per capita concentration of medical device companies, industry employees and a host of additional indicators. According to U.S. Department of Commerce data, Massachusetts ranks within the top five medical device states in value of shipments, employment, payroll and value-added by both per capita and absolute size. While the state's medical device industry has long enjoyed robust product distribution and sales within the U.S., developers and manufacturers now realize that their greatest growth opportunities lie outside North America.

In the past decade, growth of Massachusetts' medical device exports internationally has been explosive. Driven by increasing foreign demand for U.S.-made devices that feature Massachusetts industry trademarks—advanced technology and high value-added production standards—medical device exports to foreign countries grew 42% between 1992 and 1997, then surged an additional 69% in just the next two years. An index of Massachusetts merchandise exports shows growth of medical device exports at 78% between 1998 and 2003, compared to growth in total exports of 18% in the same timeframe. That combustive growth greatly exceeded the national average growth of medical device exports over the same period.

Massachusetts exports nearly 40%, or approximately $2.4 billion, of its medical device products internationally, based on 2005 figures, representing the state's top internationally exported commodity. This strongly indicates that medical device companies are increasingly learning they must take a global sales and marketing approach to remain competitive. Europe and the Pacific Rim are two areas where the Massachusetts medical device industry is heavily entrenched and experiencing strong growth. These markets have high demand for medical equipment that is more than durable; they insist upon the most innovative products that deliver the newest approaches for improved healthcare delivery.

The number of established and emerging companies headquartered or operating in the state is growing rapidly. Along with the industry behemoths, a vibrant, early-stage medical device community, focusing primarily on niche products and applications, thrives in the state. Currently, nearly half of the highly innovative medical device companies operating in Massachusetts have 25 or fewer employees with $5 million or less in annual sales. Fuelling the growth of these small firms is the recent escalation of venture capital investment.

According to data from the PricewaterhouseCoopers and National Venture Capital Association Money Tree Report, the medical device industry in the New England region, of which Massachusetts is the primary constituent, consistently ranks second after Silicon Valley for successfully securing VC investment for early-stage companies, which often drive the most pioneering technologies and novel approaches to healthcare delivery.

Small and emerging companies are especially important to the long-term growth and vitality of the medical technology sector in Massachusetts. They draw on capabilities of the region to develop and manufacture the most innovative healthcare products. For example, the state is home to one of the nation's largest plastic injection molding sectors, which has efficiently and creatively served the medical device industry. Additionally, contract manufacturers that specialize in electronic components and in the various materials used in medical device production are abundantly available. This combination of resources and entrepreneurial spirit fuels the cycle of innovation essential to the continued growth and expansion in the life sciences cluster.

Massachusetts' medical device industry has also established its reputation as developers and manufacturers of a wide array of the most advanced instruments and devices:

- 40% develop and manufacture surgical instruments or surgical appliances;
- 30% develop and manufacture electromedical equipment;
- Medical imaging is also an important, thriving segment; and
- Numerous companies are increasingly developing innovative products as device and therapeutics converge.

As Massachusetts' medical device industry sets its sights on the future, companies look forward to continued growth, powered by mounting worldwide demand for superior health services and the state's comparative advantage in the development of advanced technologies. In realizing that their greatest potential growth lies beyond U.S. borders, companies can now focus their sales and marketing efforts on developing the boundless opportunities of those key global markets.

Interview

Richard J. Meelia

On a local boy from Melrose ending up as CEO of a $10 billion company

It was serendipitous. I graduated from Boston College Management School with a master in business administration, and American Hospital Supply was one of the companies that was coming through; and that is how it happened. I looked at the company and looked at the industry and realized that health care was only going to continue to grow. So that's how I ended up in health care.

On being headquartered in Massachusetts

The base business of Covidien was the Kendall Co., which started in Walpole in 1903. It had been headquarted in either Boston or Mansfield over the last 20 years. So we started in Massachusetts and we stayed here. We do some manufacturing in the western part of the state, but Mansfield really is headquarters. We stayed here because there is an excellent talent pool, proximity to some of the esteemed Boston hospitals, and we collaborate with people like Partners Health Care on different projects throughout our divisions. So there are a lot of good reasons other than the weather and the winter to be here.

On bringing jobs to Massachusetts

We more than doubled our R&D spending in the last 5 years and we will continue to increase this investment after we separate from Tyco. The R&D expansion over the next several years will be primarily directed at our largest business which is medical devices; this is 60% of our sales. We have R&D activities located at all of our global business sites including Mansfield, St. Louis and Boulder, Colorado. So as we increase R&D spending, we will focus on the faster growing and more profitable technologies and business segments. With Massachusetts and the strong educational resources and the number of areas which support our business needs, we will be looking to add significant R&D resources here in the Mansfield area as well.

Two-thirds of our employees are in our manufacturing locations and as we expand and look to locate our manufacturing facilities, we will look at locations where we can be cost competitive and where we've got a solid technological base and most importantly a pool of talented potential employees. So while business incentives such as investment tax credits are considered a very positive thing, they are usually secondary in the overall decision making process when we look to locate a plant. Other incentives available in the state such as R&D credits or hiring credits are certainly welcome; that said our business outside the U.S. is growing much faster than inside the U.S. and as such we'll also be adding jobs to support that international growth as well.

On the Massachusetts workforce

We are looking forward to being a stand-alone healthcare company with a pressing need to attract top talent. Through this process we are bringing about 300 additional positions, mostly public company related positions and tax, treasury, audit and financial positions. We look at the availability of a well-educated workforce in which we can source the more routine administrative and technical positions and in addition we expect strong governmental support through incentives and tax credits, infrastructure investments and local support.

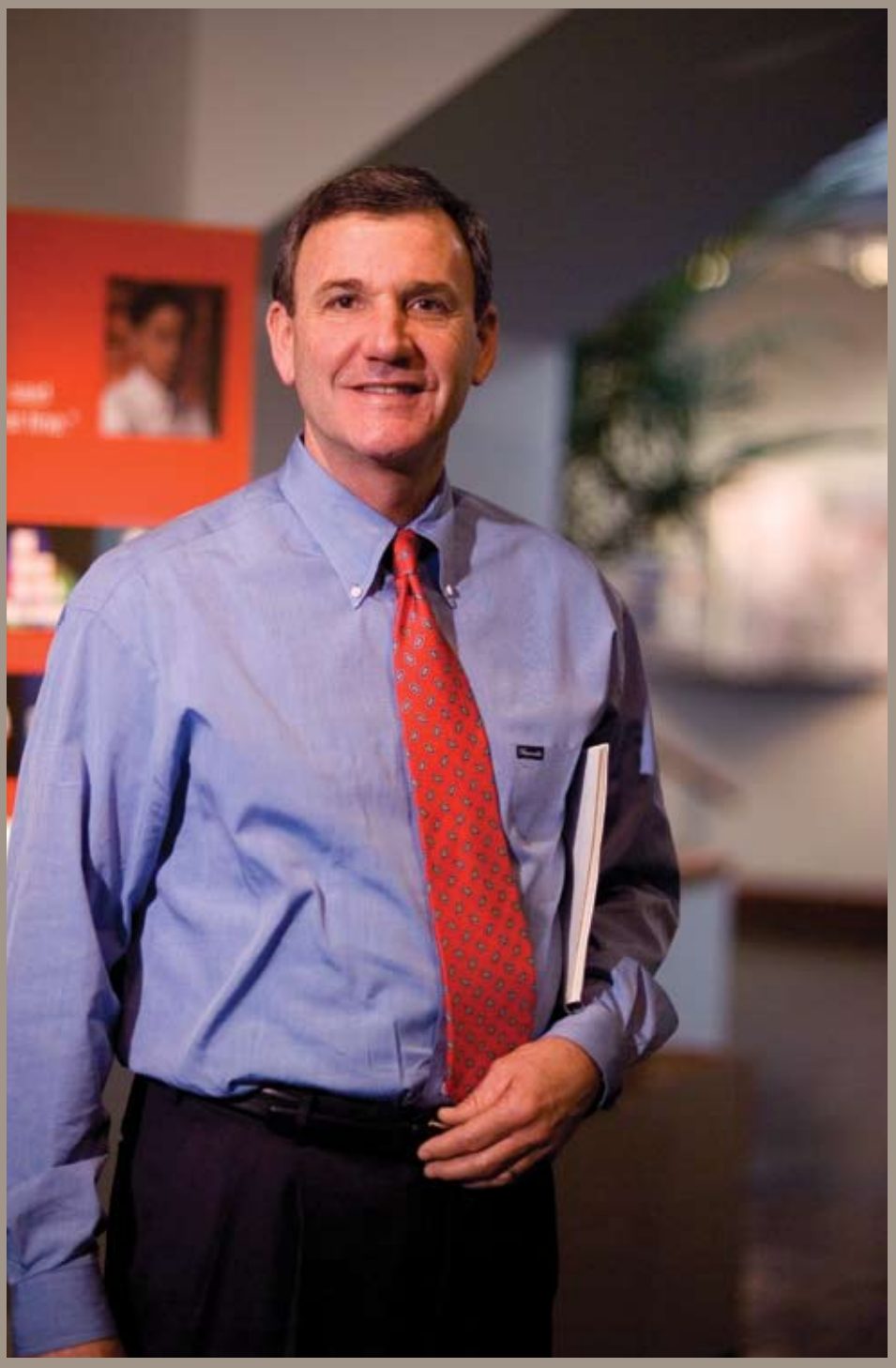
The medical device or life sciences industry is growing very significantly, so there are more people like us looking for that shrinking group of talented employees. It takes longer to fill these positions than it used to.

Rich Meelia is the 57-year-old CEO of Tyco Healthcare, which will become Covidien Ltd. when it spins off from Tyco in Spring 2007. Covidien will be a $10 billion medical-supplies maker with 43,000 employees worldwide, some 2,000 of them in Massachusetts. The new company will be headquartered in Mansfield, Massachusetts.

On the future

We are looking to significantly expand our whole business development and licensing activities as we separate from Tyco. This expansion will enable us to accelerate our internal organic growth and give us access to ideas and technologies faster than we could develop them internally. We will be increasing our collaboration with leading universities to broaden our presence and develop stronger bonds. This should increase our visibility and really accelerate the expansion of our business as we move more towards innovation and understanding customer needs and bringing technology to meet those needs.

We see this as a unique opportunity to take a $10 billion dollar company public and to create a whole knew identity, focus more on growth and innovation and customers, less on just acquiring and integrating like we did for a number of years at Tyco. Everyone gets blessed with certain opportunities along the path, and suddenly we are here with a company with 43,00 employees on the brink of something really exciting. How it gets managed will have a great impact on how these employees do, so we take this as a huge responsibility as well as an exciting opportunity.



Product development

An astounding eight percent of the entire world's pipeline of new drugs comes from companies headquartered in the Massachusetts life sciences super cluster.[14] This success is due to the Commonwealth's strong research and development capabilities, aided by the presence of a highly skilled workforce. Many of the cluster's academic medical institutions collaborate with industry to create life saving products from diabetes to cancer. Even Massachusetts' perceived weakness in this area, i.e., conducting clinical trials, is stronger than is generally thought. At the same time, mounting challenges, such as soaring R&D costs, competitive pressures, a complex regulatory environment, and a difficult public climate are confronting the cluster's ability to bring new drugs to market.

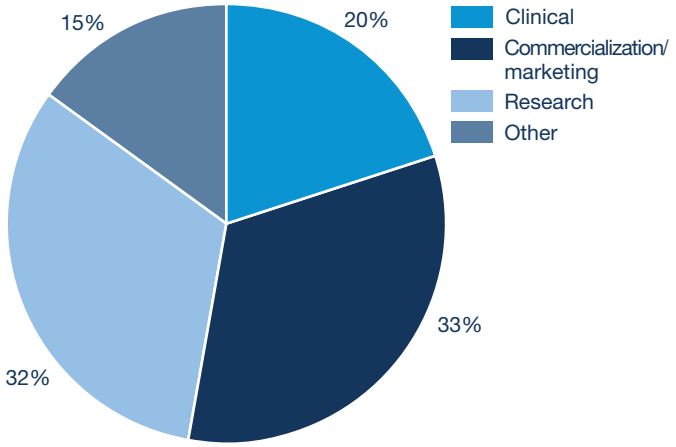
Research and development in Massachusetts

Research and development, the hallmark of the Massachusetts' life sciences, remains strong. Results of the 2007 PricewaterhouseCoopers Massachusetts Life Sciences Cluster Survey illustrate a maturation of the life sciences industry in Massachusetts, as more companies are commercializing products. In addition, the significant number of companies in the research stage suggests that the Commonwealth has a strong foundation for future products. Ninety-nine percent of survey respondents doing R&D in Massachusetts reported that they plan to maintain or increase their R&D activities in the Commonwealth over the next two years. The biggest reason cited for expanding those activities is the availability of a skilled workforce.

While the vast majority of companies surveyed do not have R&D activities outside of Massachusetts, of the few that do, a majority have expanded in the past year, to other states as well as to Europe and Asia, mainly to access lower cost skilled labor but also due to more favorable regulatory environments and business tax perks. States included California, Maryland, Pennsylvania, and New Jersey, as well as states not considered life sciences hubs, such as Connecticut, Missouri, New Hampshire, Ohio, Texas and Vermont. Globalization of R&D activities represents an ever present threat to Massachusetts' historic competitive advantage that must be taken seriously.

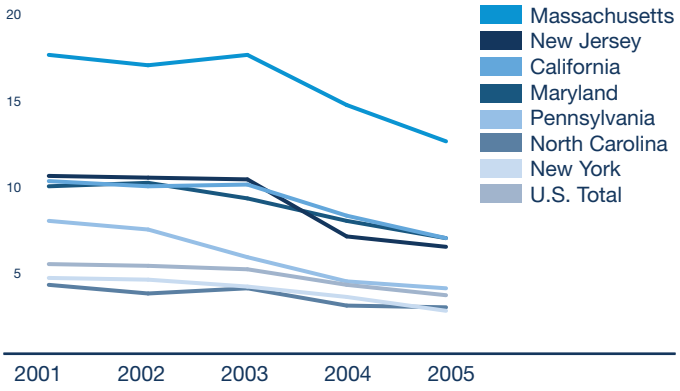
Massachusetts receives the highest per capita number of life sciences patents of any state. However, over the past six years there has been a nationwide decline in life sciences patents issued. While it is appreciated that each patent offers a unique scope of protection if the downturn in the number of patents issued continues, it could have a disproportionate effect on the Commonwealth's economy, which is becoming increasingly dependent upon the life sciences cluster for growth.

Figure 17. How would you describe your company's primary stage of development



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

Figure 18. Life sciences patents issued per 100,000 people



Source: Patent and Trademark Office

[14] MassBiotech 2010: Achieving Leadership in the Life-Sciences Economy. 2002.

Perspective

Innovation at a crossroad: challenges and opportunities for the research-based pharma and biotech industry

By Kenneth I Kaitin

Kenneth I Kaitin, PhD
Director, Tufts Center for the Study of Drug Development

Unprecedented challenges confront biopharmaceutical companies in their quest to bring innovative new medicines to market. Rapidly growing R&D costs, increasing competitive pressures, an uncertain regulatory environment, and a highly volatile public and political climate represent significant threats to the research-based industry.

Let's look at each of these threats more closely. R&D spending on new drugs in the United States continues to spiral upward, exceeding $40 billion in 2006. At the same time, the number of new molecular and biological entities approved by the Food and Drug Administration has declined. Based on newly published data by the Tufts Center for the Study of Drug Development (Tufts CSDD), the average capitalized cost to bring one new biopharmaceutical product to market, including the cost of failures, is $1.24 billion, in 2005 dollars. These costs reflect the difficulty of developing products for ever more chronic and complex indications, for example neurologic and immunologic diseases, the rapid growth in the size of clinical studies, the difficulty recruiting and retaining subjects for these studies, and late stage failures in the drug development process. Current Tufts CSDD data reveal that the average time to bring a biopharmaceutical product to market from the start of clinical testing is eight years, and the likelihood of success is 30%, compared with 7.5 years and 21.5% for traditional pharmaceutical products.

Drug developers must also deal with increasing competition in the marketplace. The current worldwide focus on containing healthcare costs and restrictive price control policies in many industrialized countries, combined with dwindling market exclusivity periods on new therapeutic products and the expiration of patent terms for a number of major blockbuster drugs, have led to a reassessment of R&D strategies in many pharmaceutical companies. These new strategies emphasize value, both economic and therapeutic, in the search for new medicines.

Regulatory hurdles create additional obstacles for drug developers, as well, especially in the current climate, where the highly publicized withdrawals from the market of several high-profile drugs for safety reasons have created a risk-averse climate for drug approval at the FDA. As Congress debates reauthorization of the Prescription Drug User Fee Act (PDUFA), due to expire in September 30, 2007, a host of salient issues are on the table, including the following: enforcement and review of post-marketing research commitments by the industry; the structure and funding of drug safety review and other safety-related activities at the FDA; required pre-market risk management plans and comparative efficacy trials; financial support for the Critical Path Initiative; and establishing a regulatory pathway for the approval of biogenerics.

Finally, increasing public and political hostility toward the research-based industry, fueled by restiveness over drug industry pricing, profitability, and marketing practices, poses a very real threat to developers. Public enmity has a direct bearing on federal funding of initiatives in support of biopharmaceutical R&D and increases congressional pressure on the FDA to impose restrictive regulatory policies on the industry.

Despite these threats, I believe there is cause for optimism for the future success of the research-based industry. First, there has been a sizeable increase in the number of phase I clinical studies initiated. A 2006 study by Tufts CSDD reported that for the top 10 firms, the number of new drugs entering clinical testing jumped 52% in 2003-05.

Second, we are witnessing the emergence of the small/mid-tier industry sector as a potent force on the pharmaceutical landscape. For example, since 2000, the percentage of FDA approved new drugs that were developed and brought to market by small/mid sized pharmaceutical and biotechnology companies skyrocketed from 33% in 2001 to 71% in 2004. The maturing capabilities of this sector have attracted significant investment by big pharma firms, looking for new drug leads and licensing opportunities. Boston and other regions of the country with high numbers of small pharma and biotechnology companies have been major beneficiaries of this interest by large pharma companies.

Third is the renewed focus on the Critical Path Initiative (CPI) and other programs for identifying new research and discovery tools for improving the likelihood of success of drugs entering the drug development pipeline. The creation of the Biomarkers Consortium in October 2006 is a significant milestone in this endeavor. The Biomarkers Consortium, which brings together the complementary

perspectives of the National Institutes of Health, the FDA, the Center for Medicare and Medicaid Services, the trade associations PhRMA and BIO, industry, academia, and patient groups, represents the kind of public/private partnership envisioned by the CPI.

Finally, across the pharmaceutical and biotechnology industry spectrum, companies are reexamining old and inefficient models of R&D and embracing new approaches to enhance productivity and performance. In particular, companies are increasing their utilization of global outsourcing, expanding their use of information technologies in clinical trial protocols and patient recruitment, and speeding the adoption of enhanced clinical study designs, including adaptive clinical trials. Most importantly, many companies are reassessing their focus on R&D strategies that emphasized broad disease areas with large potential for sales, or blockbuster drug development strategies, with those that address smaller patient populations, specialized care, and unmet medical needs.

We are in a period of dynamic change in the research-based pharmaceutical and biotechnology industry. There is a dramatic shift in power from the large pharmaceutical companies to the small/mid-tier firms, an emerging sector that has been credited with being more nimble, more focused on innovation, and less risk averse than their large pharma counterparts. Likewise, there is a shift in the geographic focus of the life sciences industry. In view of the rich diversity of reputable teaching hospitals, the high number and caliber of academic research scientists, and the extraordinary concentration of small and highly innovative pharmaceutical and biotechnology companies, I would not be surprised to see Boston and the Northeast region become the life sciences hub of the United States within the next decade.

Figure 19. Biopharmaceutical development

Drug research and development is a complicated and expensive process. On average, it takes 10 to 15 years and costs over $1 billion to advance a potential new medicine from a research concept to a treatment approved by the FDA. Potential products being moved through the development process are said to be in the product pipeline. The phases of drug development are:

Research is the first stage of bringing a new medicine to market. It involves systematically identifying a process or protein causing a problem in the body and then identifying and engineering a compound to correct the problem.

Pre-clinical trials are the next stage, in which scientists conduct extensive testing of a molecule or compound in laboratory and animal studies to evaluate safety and biological activity in a targeted disease.

Clinical trials are those that test the molecule or compound in human volunteers. The first step is to file an Investigational New Drug Application (IND) with the FDA. With the Agency's approval, the investigational new drug enters clinical testing. The three stages are:

Phase I—Companies conduct studies on 20 to 100 healthy volunteers to determine the safe dosage range of a drug in the body as well as how it is absorbed, distributed, metabolized and excreted.

Phase II—Companies conduct studies on 100 to 500 volunteers who have the targeted disease to evaluate the drug's effectiveness in treating the disease. Only therapies that show promising results in Phase II trials advance to Phase III trials.

Phase III—Companies conduct studies on 1,000 to 5,000 volunteers who have the targeted disease to evaluate efficacy and long-term safety of the drug.

Filing or applying for FDA approval comes after, and only if, therapies show positive results in Phase III. Depending on the product type, companies file a Biologics License Application (BLA) or a New Drug Application (NDA).

FDA approval may come in months or years if the FDA agrees that the Phase III clinical data proves the safety and efficacy of the medicine. Drugs that survive into Phase III trials have only a 57% chance of making it through the FDA approval process and onto pharmacy shelves.

Clinical trials: weakness or strength?

Anecdotal evidence suggests that Massachusetts has a weakness in its ability to conduct large scale clinical trials, especially late stage phase II and III studies. This reputation may not be fully deserved, however. Although its rank for the number of clinical trials performed may not stand out as other aspects of the local industry does, it is, in fact, one of the top 10 states nationally. (See Table 12.) Furthermore, the city of Boston ranks third nationally for its number of clinical trials. (See Table 13.)

A primary barrier to Massachusetts' ability to gain even more clinical trials is one that is out of its control; namely, its relatively small population compared to its national and international competitors. As Table 12 illustrates, there is a strong correlation between population rank and the number of clinical trials being conducted in a state. Almost all of the states with more clinical trials have greater populations than Massachusetts. (Maryland, which ranks 19th in the country in population, and 7th in terms of clinical trials, is the one exception. However, potentially explaining this exception is that Bethesda, MD, is home to the NIH, which has significant amounts of research funding, and is responsible for over 450 clinical trials.)

When asked what percentage of clinical trials is completed in Massachusetts, survey respondents overwhelmingly indicated that they are completing 75–100% of their Phase I, II, and III trials outside Massachusetts. (See Figure 13.) Although Massachusetts has natural limitations to the number of clinical trials it performs, there is potential for increasing this number, especially in Phase I clinical trials where smaller cohorts of patients are required to generate relevant "safety" data.

In addition to its smaller population, there are other factors limiting Massachusetts companies' ability to conduct more clinical trials within the Commonwealth. For example, companies from all over the world compete with Massachusetts-based companies to conduct clinical trials with many of Massachusetts' highly regarded clinical practitioners. This global competition for the Commonwealth's clinical expertise leads to decreased access, limited enrollment capacity, and increased cost of performing clinical trials locally. Thus, local companies find it advantageous, with respect to time, cost, and access to applicable patients to perform trials outside the Commonwealth.

Table 12. Rank and number of clinical trials by state

Clinical trials national rank	Population rank†	Total active clinical trials	Percent of national total
1. California	1	2,077 I—367 II—915 III—795	6.1%
2. New York	3	1,830 I—318 II—793 III—719	5.3%
3. Texas	2	1,811 I—336 II—746 III—729	5.3%
4. Pennsylvania	6	1,515 I—229 II—621 III—665	4.4%
5. Florida	4	1,421 I—165 II—591 III—665	4.2%
6. Ohio	7	1,392 I—185 II—568 III—639	4.1%
7. Maryland	19	1,332 I—289 II—610 III—433	3.9%
8. Illinois	5	1,297 I—162 II—550 III—585	3.8%
9. Massachusetts	13	1,210 I—198 II—503 III—509	3.5%
10. North Carolina	10	1,202 I—136 II—478 III—588	3.5%

† U.S. Census Bureau 2006 population estimates.

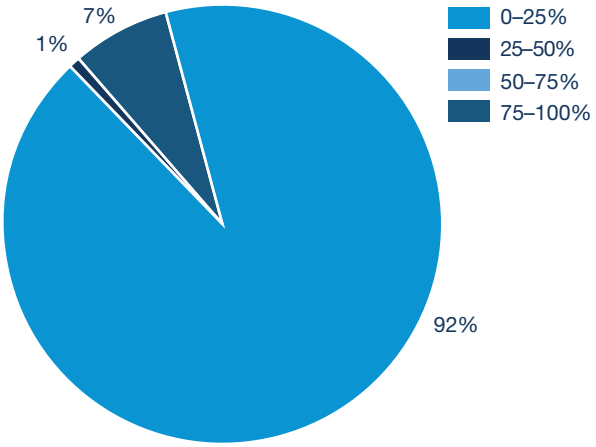
Source: http://clinicaltrials.gov

Table 13. Rank and number of clinical trials by city

Clinical trials national rank	Total active clinical trials	Percent of national total
1. Houston	1,106 I—237 II—476 III—393	3.2%
2. New York	1,098 I—206 II—460 III—432	3.2%
3. Boston	945 I—179 II—419 III—347	2.8%
4. Chicago	851 I—130 II—353 III—368	2.5%
5. Philadelphia	846 I—141 II—330 III—375	2.5%

Source: http://clinicaltrials.gov

Figure 20. What percentage of your company's phase I clinical trials are completed in Massachusetts



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

Opportunity for action: clinical trials

Clinical trials performed by Massachusetts' academic health centers and hospitals can continue to provide an invaluable service to the state's life sciences companies in securing prompt federal approvals for their products and in improving the quality of the healthcare system by expediting the introduction of potentially breakthrough drugs and therapies to the community. They can also provide a source of additional revenue to the institutions themselves. Further analysis of the total numbers of patients being enrolled into trials by Massachusetts based companies versus non-Massachusetts based companies compared with the national averages would also prove beneficial. The Commonwealth should undertake a thorough assessment of the strengths and weaknesses within the state's control to investigate means to increase clinical trials, especially among companies that already have operations in Massachusetts.

Perspective

Innovation, collaboration help Dana-Farber Cancer Institute quickly move discoveries from bench to bedside

By Barrett Rollins

Barrett Rollins, MD, PhD
Chief Scientific Officer
Dana Farber Cancer Institute

This year, U.S. physicians will diagnose 1.5 million new cancer cases. While the statistic is grave, Dana-Farber Cancer Institute (DFCI) is primed to challenge cancer's prognosis once and for all. By collaborating with industry leaders, DFCI continues to forge new links across the cancer community to spark the birth of novel ideas and approaches to long-standing challenges and opportunities.

DFCI's 60-year history includes important contributions that helped lead to the discovery, development, and targeted use of such groundbreaking drugs as Gleevec™ and Iressa. In that time, New England's leading cancer research and treatment facility has stayed true to its dual mission: to advance the understanding, diagnosis, treatment, cure and prevention of cancer and to provide expert, compassionate care for people with cancer. As the core institution in the Dana-Farber/Harvard Cancer Center, DFCI collaborates extensively with cancer researchers in the Center's seven member institutions and works closely with its partners to translate those research findings into clinical trials.

Because of the breadth of this work—member institutions perform as many as 500 clinical trials at any one time—the Institute collaborates with pharmaceutical and biotechnology industry constituents on over 70% of its trials. The industry increasingly turns to DFCI to conduct clinical trials and laboratory testing for some of its most promising new molecules. By working hand in hand with the industry, DFCI can unlock particular molecular treatment mechanisms and identify specific diseases for which a drug might prove to be an effective treatment.

While many Massachusetts pharmaceutical and biotechnology companies turn to out-of-state clinical research organizations (CROs) for outsourced drug testing, DFCI clinicians conduct the Institute's clinical research in-house. This hands-on approach allows DFCI to probe more deeply into the reasons a drug does or does not demonstrate an expected result, and DFCI scientists can then establish next steps to determine ways to improve the drug's efficacy.

DFCI also understands the need to partner closely with the industry at the earliest stages of drug development and testing. Over the years, DFCI has enjoyed mutually beneficial relationships with some of the industry's most prominent pharmaceutical companies—including Novartis, Pfizer and Merck, as well as many small, midsize and large biotechnology companies—to make greater strides in drug development and forward-thinking cancer treatment research. The Institute relies on this vast infrastructure of industry clinicians and testing facilities to help screen millions of compounds, perform toxicology and other necessary tests, and identify and develop the most advanced cancer treatments.

In addition to cancer treatment development, DFCI conducts cutting-edge research to understand the mechanisms that cause cancer and engages in population-based science to determine the most effective methods to disseminate treatments and prevent cancer. The Institute encourages its research teams to think beyond the boundaries of conventional cancer research to search for clues that might someday lead to additional innovative cancer-related discoveries. The Institute's current research into the seemingly unrelated areas of fat metabolism and diabetes and their possible effects on cancer cell growth reflects the Institute's dedication to this entrepreneurial spirit. Another example is the Institute's collaboration with the renowned Broad Institute of MIT and Harvard to more closely examine the genetics of cancer and the reasons people are susceptible to the disease.

Recognizing that the opportunity to conquer cancer is within reach, DFCI persists in its unrelenting search for answers through forward thinking, dedication to discovery and mutually beneficial industry alliances.

Perspective

Providing a forum for a revolutionary change in the biopharmaceutical industry

By Frank Douglas

Frank Douglas, MD, PhD
Executive Director
MIT Center for Biomedical Innovation

The biomedical industry is at an inflection point and needs a revolutionary and not evolutionary rethinking. New paradigms are needed both for the discussion, generation, and implementation of solutions to the principal issue facing the biopharmaceutical industry; that is, falling approvals of New Molecular Entities despite rising research and development expenditures. It is for this reason that the MIT Center for Biomedical Innovation (MIT CBI) has focused on two key approaches: the Safe Haven and Collaboration. We are convinced that by providing a safe haven in which members of industry, academia, government, payers and consumers can meet to collaborate, we will provide one of the key ingredients for transforming the way we innovate and make new therapies accessible.

There is hardly a presentation on biopharmaceutical R&D that does not include a graph that depicts the fall in approved New Molecular Entities since 1997 compared with the almost doubling of R&D global expenditures, every seven years. The reasons are due to a complex mixture of commercial, technological, regulatory and managerial forces.

Commercial forces involve the increase of the criteria of a blockbuster from yearly sales of $500 million to over $1 billion, thus leading to several clinical candidates being 'shelved' by large companies as they no longer meet the blockbuster criteria. Needless to say, the success of Lipitor has driven this redefinition of a "blockbuster." The reduction of the number of drugs in a particular class that is admitted onto the formularies or is reimbursed is the other side of this equation. Thus, drugs that will come to market third or later in a class and that are not differentiated from the leaders, with respect to efficacy and/or safety, are also less likely to be further developed.

The technological improvements, particularly with respect to automation, speed or throughput, simulation and improvement of level of detection, as well as those that have enabled molecular, genetic or structural determination of the basis or mechanism of disease, have contributed enormously to our ability to address the more challenging chronic diseases, such as Alzheimer and Osteoarthritis. On the other hand, it probably requires anywhere from ten to twelve years for the requisite integration of any technology to be able to observe an impact on ability to select and predict the best targets and molecules for discovery and development. One may therefore argue that the levels of New Molecular Entities Approvals that were achieved in 1996 and 1997 were probably due to the introduction of biotechnology and focus on mechanism based discovery in the 1980s. Thus one should expect a similar increase in New Molecular Entities Approved in 2010, when one controls for the other variables, namely commercial and managerial.

The regulatory landscape has also become more challenging as the FDA, for example, seeks to balance its role of ensuring the public safety while encouraging introduction of novel therapies to improve the well being of the society. This is a major challenge as the society demonstrates intolerance for side effects and the congress weighs in on issues of the issues of safety and cost. Finally, the pressures of financial performance continue to lead to mergers and acquisitions and the consequential restructuring and realignment of organizations.

MIT CBI focuses on the following areas as levers for transforming the industry: Safety, Redesigning R&D, Manufacturing and Distribution Systems and Finance and Risk Models. Several programs have been initiated in these areas and each program has the characteristic that it requires participation by at least two groups of the stakeholders and that they are pre-competitive. We have also been able to leverage and adopt techniques that have been used in other areas. This is perhaps best seen in our Post Marketing Surveillance project in which we have an active collaboration with the FDA and several biopharma and other companies. These projects have the additional feature that they have academic and industry members as co-leaders. We thus ensure that the problems are not only well identified, but that offered solutions are relevant. We continue to learn how best to develop this model of collaboration and have been delighted with the deep interest and commitment of all stakeholders in MIT CBI.

Interview

Mark C. Fishman, MD

On moving from academia to industry

I received an offer from Novartis to design a revolutionary approach to drug discovery that involved many elements, not the least of which was moving their headquarters to Cambridge. I was also motivated by my son who was ten at the time and said, “I really love your Zebra fish (what I used to work on), but don’t you think it would be more important to make a drug?”

On the reputation of pharmaceutical companies

The major impediment isn’t actually in the pharmaceutical companies, it is in the science. We simply do not know enough to predictably and reliably make drugs. So I think that the rap pharma has gotten around innovation is a little rough given the difficulty of making a medicine. People are also upset about the way drugs are advertised and the scope and scale of the companies. But I think that the fundamental frustration that the public has, which I share, is that there simply aren’t enough new medicines quickly enough to help patients and their families.

On the cost of drugs

The reason that you, me, everybody gets upset about pharmaceuticals is because we have to pay for them out of pocket at the drug store. It’s not simply the cost per se, but the fact that the impact is on the consumer directly. How we get out of that has a lot to do with legislation and policy and who picks up the tab. As long as it is the individual consumer, there is going to be a lot of concern.

On drug discovery

The biggest issue is whether it is viewed as a business or a scientific enterprise. From my vantage, the best way to discover drugs is to make sure that it is in every way a scientific enterprise focused by clinical need. So we needed to set up an environment where challenge was accepted and where there was a recognition that experiments do fail and that failure is that of the science and not the scientist, and there was a true sense of long-term vision with priorities set on healthcare that were not driven by any kind of annual artificial matrix.

On moving Novartis research to Cambridge

We came here for talent. There are few areas of the country like this, and the Boston/Cambridge area is notable for being able to get pretty much any kind of expertise and ambition that you would want in this field.

The only issue that persists is the problem of housing costs. But once you establish a community of scientists, it becomes by definition a place where other scientists want to come because there are opportunities and jobs and fluidity—people being able to stay in one area without moving even if they change jobs. There is a lot of fluidity here which as far as I can tell has not seen any other issues threaten it.

On the impact of life sciences

Our goal is to make medicines, but I also want to change the way we make and discover drugs. I see it as an opportunity to take the genome, which everyone has touted as important for health, and make it part of the process. It adds a new grammar for drug discovery; we have all of the words now in the genome but nobody knows how to make them into phrases, never mind make them into sentences or meaningful paragraphs. If we can figure that out, then we can more reliably link up the various components of the genome to make drug discovery more predictable. I want to make drugs today and change the way they are made tomorrow.

Mark Fishman is president of the Novartis Institutes for Biomedical Research in Cambridge. Prior to joining the company in 2002, Fishman was a professor at Harvard Medical School and chief of cardiology at Massachusetts General Hospital. Fishman, 56, is best known for his studies in developmental genetics.

On what drives him

What motivates me most is the health of people. I'm a physician and am really saddened when I see a patient and there is simply nothing we can do for them. I do go out and see patients—not as much as I would like—and I see people who are suffering and there's nothing we can offer. For a physician there's nothing more frustrating. You can offer them some solace, and you can hold their hand, and that's important, but it would be a lot better to look the parents in the eye and say I really think we can help your son or daughter.

Biomedical manufacturing

Over the past five years manufacturing operations have decreased in almost all industries across the Commonwealth. However, manufacturing in the life sciences cluster has quietly expanded and grown stronger. Almost half of respondents to the PwC 2007 Massachusetts Life Sciences Cluster Survey with manufacturing operations have these activities in the Commonwealth. Massachusetts is currently home to one of the largest biomanufacturing facilities in the U.S., and more leading device and biopharmaceutical companies have announced plans to establish or expand operations in the Commonwealth. Despite these strengthening fundamentals, Massachusetts continues to struggle with various factors, including the high costs of living and labor, permitting, and taxation, factors that play a crucial role in a company's decision to establish large scale biomedical manufacturing operations in the Commonwealth.

According to the survey, over half of companies with manufacturing operations in Massachusetts expanded their manufacturing capability in the past year, and 59% plan to expand further over the next two years. Companies point to Massachusetts' skilled workforce as a primary reason for manufacturing in the state. While the majority of companies with manufacturing activities in Massachusetts reported they plan to maintain or increase their manufacturing workforce inside the state, a quarter of respondents plan to reduce it, which is cause for concern.

Furthermore, none of the companies that reported having manufacturing outside of Massachusetts decreased that activity in the past year, and the vast majority intends to maintain or expand those activities outside of the state in the next two years. As with R&D, these companies are moving their manufacturing to Europe and Asia as well as to other U.S. states for the same primary reason: to access lower-cost skilled labor. The states cited include California, Michigan, North Carolina, Ohio, Pennsylvania, and Texas. The countries cited include China, Hungary, India, Ireland, Switzerland, and the UK.

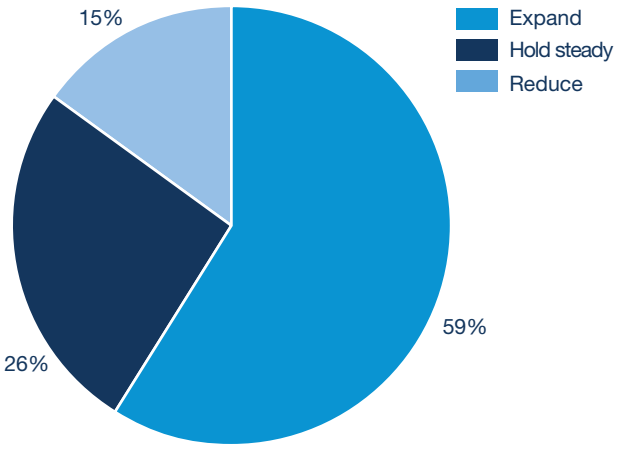
When asked to describe the top factors for establishing operations in Massachusetts, survey respondents cited the ability to find talent, proximity to scientists, and proximity to universities as the top three reasons. Rarely cited were the factors that would be consistent with attracting large-scale manufacturing operations. These factors include cost of labor, cost of living, permitting, and taxation, all factors that can be influenced by policy makers. That survey respondents did not consistently cite these factors as reasons to establish or expand operations in Massachusetts indicates that the state may not be realizing its full potential in the biomedical manufacturing sector.

Despite the hurdles, Massachusetts currently has a number of biopharmaceutical manufacturers, with addition life sciences companies moving their manufacturing operations into Massachusetts. For example, Bristol-Myers Squibb is moving some of its operations to the state, and is expected to provide 550 new manufacturing jobs. Existing biomedical manufacturers in Massachusetts include Abbott Laboratories, AVANT Immunotherapeutics, Boston Scientific, Genzyme, Haemonetics, Philips Medical Systems, Tyco Healthcare, Shire PLC, and Wyeth Pharmaceuticals. With the recent opening of the UMass Massachusetts BioManufacturing Center in Lowell and Millipore's new Bioprocess R&D Center focused on developing products to optimize biopharmaceutical manufacturing, new resources will be available in the near future to grow biomedical manufacturing in the life sciences cluster. These developments will continue the recent trend that companies are recognizing the importance of having access to the skilled workforce that the Commonwealth offers.

Opportunity for action: downstream manufacturing

Recent reports have shown a substantial potential for increasing employment in the life sciences through the capture and growth of downstream manufacturing in the Commonwealth. Consistent, predictable, and efficient tax, regulatory, licensing and permitting policies are essential to the creation of an environment that fosters and nurtures company growth. Whether the economic development strategy relies on attraction of companies from elsewhere or growth of indigenous companies, the certainty of the regulatory approval process for company decision-makers is critical for life sciences companies and institutions. Some advances have been made over the last few years in permitting, but more needs to be done in this and other tax and regulatory areas that affect life sciences. In addition, increased attention should be directed to infrastructure needs critical to bio-manufacturing, such as water and energy access.

Figure 21. If engaged in manufacturing activities in Massachusetts, do you expect this activity to expand, hold steady or reduce in the next two years



Source: PwC 2007 Massachusetts Life Sciences Cluster Survey

Perspective

Biomanufacturing in Massachusetts

By Carl W. Lawton

Carl W. Lawton, PhD
Director
Massachusetts BioManufacturing Center, UMass Lowell

The UMass Lowell Massachusetts BioManufacturing Center (MBMC) has a tripartite mission of education, applied research, and process development to facilitate the growth of biomanufacturing in the Commonwealth. At MBMC, we work with biopharmacuetical firms to help them transition from drug discovery to manufacturing. As an interdisciplinary center, MBMC assists biotechnology companies in developing procedures that lead to validated, cGMP-compliant manufacturing processes. Our partnerships focus on the application of sound biochemical and biological knowledge combined with state of the art engineering principles that allow our staff and students to solve complex real industrial challenges.

An expansion of the MBMC into a statewide center was recently funded by the Commonwealth of Massachusetts. This $25 million initiative provides funds for expanded process development and bioanalytical laboratories at Lowell, as well as for a large-scale engineering facility near UMass Dartmouth. The state support builds on the momentum of the MBMC at Lowell by expanding or developing five inter-related capabilities:

- Process development services;
- Large-scale engineering facilities;
- Applied research focused on critical biomanufacturing issues;
- Education for company leadership and technical staff; and
- Network of existing industry and academic expertise to disseminate best practices.

These capabilities allow us to assist with developing solutions to meet novel objectives as companies transition from research to commercial scale. Too often young biotechnology companies invest years investigating a therapeutic modality produced on research scale, without spending the appropriate amount of time considering complex principles required to manufacture on a commercial scale. As partners we can collaborate on process development work including strain and cell line expression development with both prokaryotic and eukaryotic expression systems. These efforts can also include media optimization, experimental design assistance, fermentation and cell culture development optimization. Partnerships can also be established to provide downstream processing optimization on a variety of scales using state of the art processes and equipment. MBMC practitioners also work with biomanufacturers to conduct customized training programs on location.

Our applied research focuses on helping companies improve the quality, cost and productivity of large-scale biomanufacturing production. Some of our applied research initiatives pursue both incremental and breakthrough advances related to these key performance metrics. Incremental advances include improved process control of bioreactors, increased expression levels, prolonged cell lifetimes and faster cell growth rates (cell cycle times) and disposable and new purification technologies. Breakthrough programs include perfusion reactors to convert batch processes to continuous ones, developing yeast as a replacement for mammalian cell cultures and using E. coli to create antibodies in soluble form.

The statewide initiative strengthens our partnerships with other academic institutions such as Worcester Polytechnic Institute and UMass Dartmouth and builds upon a network of people, education, facilities and services located throughout Massachusetts. From its governance structure to its operational design, the state-wide MBMC is a collaboration of industry, academia and government. In the future MBMC will be the catalyst for strengthening Massachusetts' role as the intellectual center of critical biomanufacturing technology. This focused role will help assure greater quality and consistency in biologics manufacturing for increased patient safety and profitability.

Perspective

Developing the life sciences

By Robert L. Culver

Robert L. Culver
President and CEO
MassDevelopment

The life sciences cluster in Massachusetts plays a critical role in driving the Massachusetts innovation economy. The Commonwealth's life sciences strength derives from its unique combination of intellectual and financial resources. The intellectual resources include some of the most prominent universities and academic medical centers in the world. The financial resources include one of the largest concentrations of venture capital in the world—Waltham, Massachusetts.

The benefits of this fortunate symbiosis have recently begun to spread beyond greater Boston thanks in part to MassDevelopment's Emerging Technology Fund (ETF), which provides financial assistance to technology-based manufacturing companies seeking to locate or expand their manufacturing operations in Massachusetts. Looking at some of the biotech companies that have benefited from this program reveals the program's statewide reach: Acusphere in Tewksbury, AVANT Immunotherapeutics in Fall River, BioVex in Woburn, Blue Sky Biotech in Worcester, Hyaluron in Burlington, Microtest in Agawam, and Spherics in Mansfield.

In addition to administering the ETF, MassDevelopment works with its state-government and business-association partners to lure companies to Massachusetts. Last year, Bristol-Myers Squibb (BMS), a biopharmaceutical leader, announced that it would construct a $660 million plant that will employ 550 people in Devens, a planned community located 35 miles northwest of Boston. That a former military base shut down in 1996 could attract a company like BMS a decade later testifies to the fact that Massachusetts occupies a special place in the life sciences pantheon.

BMS came to Devens, Massachusetts instead of locales in other states for a number of interrelated reasons. Located close to Boston, Worcester—the third-largest city in New England and the home to more than a dozen colleges and universities—as well as New Hampshire, Devens represents a quick commute for talented workers from two of the most highly-educated states in the nation.

In addition to its geographical advantages, Devens has a number of unique attributes. The experienced Devens team features engineers, lawyers, real-estate professionals, and utility managers that can speed deal-making and construction. Alone among Massachusetts municipalities, Devens has a one-stop permitting process that takes 75 days or less. BMS received its permits in a record 49 days.

Devens had the land, the workforce, and the will to compete to win the BMS deal. The company will have a cutting-edge facility to develop compounds to ease organ transplants and to fight cancers; Massachusetts will get an employer that will bring good, high-paying jobs to the state.

As president and chief executive officer of MassDevelopment, I remain constantly cognizant of the fact that my agency has a double bottom line, namely, to stimulate business and to promote the public good. Like other industries, biomedicine is a bottom-line business, but it, too, has a double bottom line, one that all of us would do well to recall. As one of the strongest incubators for life sciences companies on the planet, Massachusetts recognizes the importance of both of these bottom lines and looks forward to welcoming the next generation of life sciences companies to our Commonwealth.

Perspective

Biopharmaceutical operations in the Bay State

By Marily Rhudy

Marily Rhudy
Senior Vice President, Public Affairs
Wyeth Pharmaceuticals

Wyeth Pharmaceuticals, a division of Wyeth, has a long history of pioneering developments in pharmaceuticals and biotechnology with leading products in a wide range of therapeutic areas. Through dedicated people, innovation, unique technologies and a promising pipeline, Wyeth is committed to improving patient lives.

An integral part of Wyeth's history is our partnership with the state of Massachusetts, which is home to Wyeth's clinical research, discovery and biopharmaceutical manufacturing operations for over 2,800 employees.

In Cambridge, Wyeth Research focuses on the discovery and development of new therapies targeting oncology, hemophilia, inflammation, and cardiovascular diseases. The Wyeth Biotech manufacturing campus in Andover is one of the largest biopharmaceutical operations in the U.S. and home to leading experts in the development and commercialization of medicines that improve human lives.

Wyeth looks forward to continuing our partnership with Massachusetts to support our innovation efforts. Moving forward, it is critical for state policymakers and business leaders to stay committed to the biotechnology industry and focus on policies that will enhance the state's competitiveness. Massachusetts is truly a leader in the global race to attract and retain biotech businesses and investment. As other states and countries recognize the importance of biomedical research and its ability to drive economic growth, Massachusetts must foster a business environment that allows innovation to thrive. While this includes creative economic development incentives, health policies that reward innovation and ensure patient access to new, groundbreaking treatments are equally important.

We live in a time of unprecedented opportunity—a new age of discovery. As our understanding of biotechnology's power and promise grows, we cannot afford to allow biomedical progress to stall. We must relentlessly pursue innovation as Americans have throughout our history. That's the opportunity here in Massachusetts—and the work of our generation is to make it happen.

Interview

Una Ryan, PhD

On her background

I'm in a highly risky business, probably with good training because I had a highly risky babyhood. I was born in an air raid shelter as the Japanese were walking down the Malay Peninsula towards Singapore. My parents' beautiful rubber planters estate was ransacked. I was two months old. When we got on the train to go to get onto the ship leaving for England, my mother turned around, and she couldn't see my father. It would be five years before we would see him again.

On running a biotech company

I had a very successful career in academia, but I got dissatisfied. I hadn't saved a life yet. What I wanted was to go from bench to bedside. The obvious place to do it was a small biotech company. I became the chief scientific officer of T-Cell Sciences here in Cambridge and later took over as CEO. Then it was really trial by fire: the company was running out of money, they had had this big lawsuit with the landlord, my predecessor had been let go by the board, so I was left holding the reigns—and it was wonderful. I settled all of that, and then I could build what I really wanted to build and that is what we have done at AVANT, build a vaccine company.

On drug safety

The U.S. has become absolutely paranoid about safety. Yes, they make some things that aren't completely safe and we'll never have drugs that don't have bad effects on somebody. But you and I are alive today because of vaccines. My grandmother had 10 children, to end up with five that survived birth. We don't think like that anymore; we think only about side effects.

On drugs and the developing world

Not enough biotech and pharma companies pay attention to the developing world. But it's critical that we do because unequal access to health care is a form of poverty that comes back as terrorism and lack of understanding. I see a huge social benefit in treating the world properly, because I grew up with a sort of missionary attitude about medicine. My English grandfather took smallpox vaccine over the Himalayas in the 1870's and 1880's.

On locating manufacturing in Fall River, Massachusetts

If you look at a map of the world and plot the cost of a fulltime worker, we would calculate $250,000 fully loaded per person here in Massachusetts. If you go to the UK and Northern Europe, it's about the same. It goes down a little below $200,000 in Eastern Europe, but when you get to India and China it's half, $100,000. So ultimately it will be very difficult to resist manufacturing overseas.

In Massachusetts, we were actually given good loans by the state to set up the manufacturing facility and it was a very good move for us for our first foray into manufacturing. Will I be able to grow and put manufacturing plants in the state again? There are huge arguments for manufacturing overseas as well as there are huge needs to manufacture here, and it is going to be very difficult to overcome just the cost of the workforce.

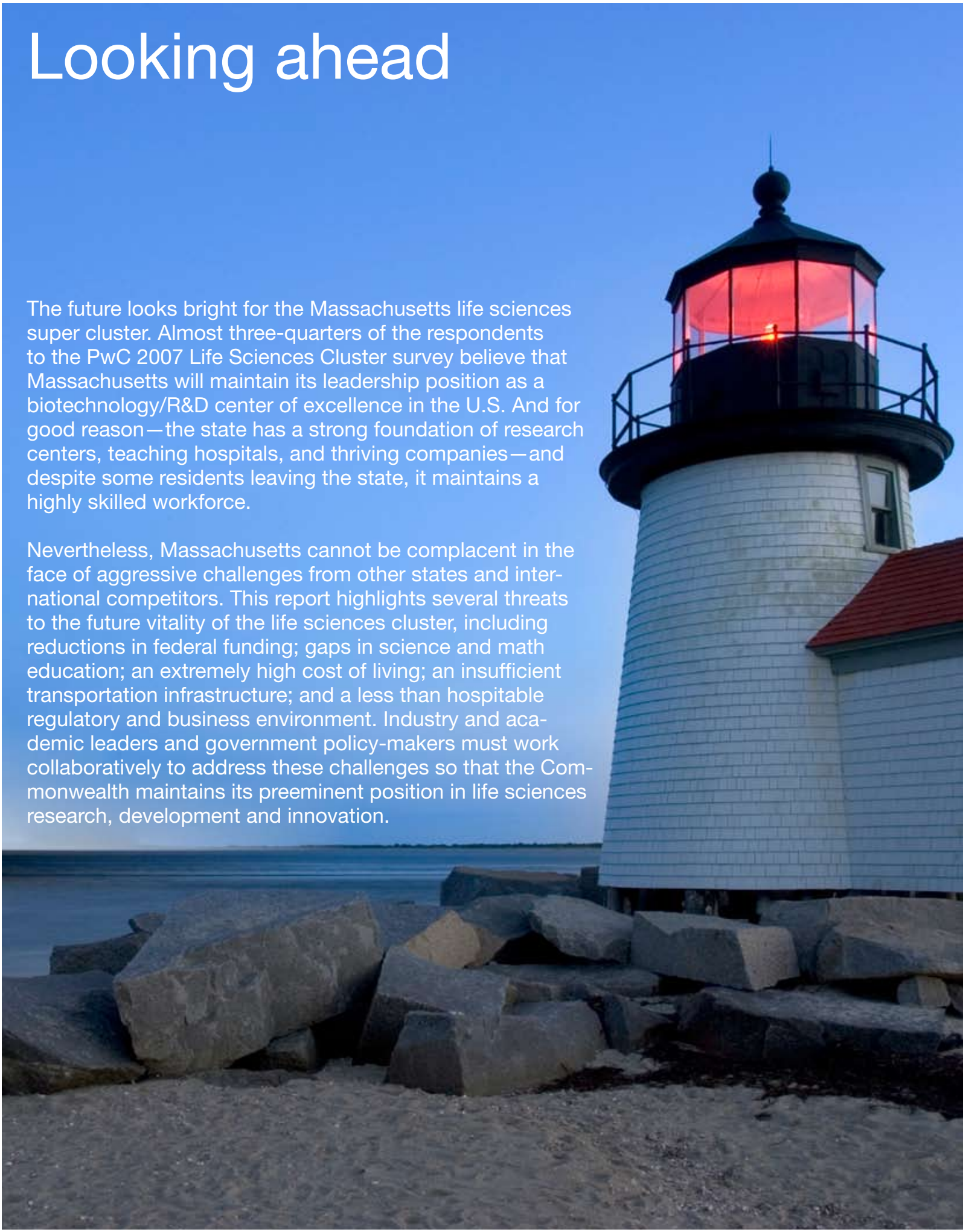
Una Ryan is the president and CEO of AVANT Immunotherapeutics, which is based in the Commonwealth and opened a manufacturing facility in Fall River in 2004. Ryan, who was trained in cellular and molecular biology, is the recipient of the Order of the British Empire for contributions to biotech.

On the future of biotech in Massachusetts

We are a wonderful state at starting biotech companies, but we need to nurture them through their difficult development years. But it is very difficult when you see the hatred of the pharma companies. Do people love biotech because we are young and not-profitable? Do they start hating us when we begin to make profits? I just find the attitudinal things difficult to understand. I think it's the money and the concept of big business that is unattractive to Americans.

Massachusetts is a global player because if you start up here you have a good chance of being successful. China and everyone is looking to Massachusetts for the model and competing with it. You can spend a minute enjoying that adulation and the second minute, you need to realize that they are competing and we need to stay at the forefront because it won't happen naturally. Envy is a real thing and people try to take it away from you, so we have to fight for it. I am a fighter.

Looking ahead



The future looks bright for the Massachusetts life sciences super cluster. Almost three-quarters of the respondents to the PwC 2007 Life Sciences Cluster survey believe that Massachusetts will maintain its leadership position as a biotechnology/R&D center of excellence in the U.S. And for good reason—the state has a strong foundation of research centers, teaching hospitals, and thriving companies—and despite some residents leaving the state, it maintains a highly skilled workforce.

Nevertheless, Massachusetts cannot be complacent in the face of aggressive challenges from other states and international competitors. This report highlights several threats to the future vitality of the life sciences cluster, including reductions in federal funding; gaps in science and math education; an extremely high cost of living; an insufficient transportation infrastructure; and a less than hospitable regulatory and business environment. Industry and academic leaders and government policy-makers must work collaboratively to address these challenges so that the Commonwealth maintains its preeminent position in life sciences research, development and innovation.

Massachusetts must confront these challenges with a decided strategic advantage given the depth and quality of its life sciences research establishment and the commitment of its many entrepreneurs and venture capitalists. However, if not seized in a timely and appropriate fashion, this advantage can become a lost opportunity. Many other states—including California, Connecticut, Ohio, Florida, Illinois, Maryland, Missouri, New Jersey, New York, Virginia, and Wisconsin—are now making substantial public investments in research, research facilities, science education, and funding for innovation and commercialization. These states are also providing accelerated paths for facility licensing and permitting. Massachusetts must also contend with the many international competitors who are challenging the Commonwealth for talent and industry. The life sciences community in Massachusetts must respond and must do so by joining with government officials to craft a prudent and integrated growth strategy of its own.

This report has cited issues that require attention from policy-makers and life sciences leaders to be part of any comprehensive strategy. These include early stage financing to assure that promising life sciences innovations are not lost because of a lack of capital; a K-16 education system that underscores science and math skills, so that graduates are prepared to fill the new jobs created by life sciences companies; growth in funding for basic research and facilities so that the Commonwealth continues to attract and retain the best scientific talent; investments in a transportation infrastructure that enables people to move efficiently between centers of science and medicine and enables product to move more swiftly to market; a fair and predictable regulatory and tax system at the state and local levels to nurture manufacturing; and a stronger working relationship between life sciences companies and academic health centers to, among other things, increase the number of clinical trials and joint research endeavors performed here.

Concerted action must be taken now to confront the challenges of affordable housing and the high cost of living. The troubling trend of the loss of younger workers and graduates and the concomitant loss of talent for our life sciences companies can be traced directly to the issue of high housing and other living costs. We cannot expect growth in the life sciences cluster—or any knowledge-based cluster for that matter—if the best and the brightest abandon the state for less costly locations.

Life sciences employment has a significant multiplier effect on the economy and creates a stable tax base. New life sciences jobs at higher incomes also serve to ameliorate some of the effects of the higher cost of living. Building from strength in R&D, the Commonwealth is well positioned to develop a more robust biomedical manufacturing and employment base while still financing targeted research initiatives. Balancing the need to expand employment in the manufacturing base will provide years worth of economic stimulus as targeted research initiatives migrate from bench to bedside. With global use of healthcare products destined to grow, this “new” manufacturing base will provide the “free cash flow” to finance future biomedical exploration. The Commonwealth must capitalize on this expectation of unprecedented international growth in life sciences to capture a substantial share of the resulting wealth and employment.

To achieve this life sciences-based economic expansion, the Commonwealth must draw on the lessons learned from other states and pursue its objectives in a collaborative way. Public/private agencies and public policy research organizations provide a foundation and rich resource for this collective response. The newly formed cross-cluster Massachusetts Life Sciences Collaborative provides a vehicle for thoughtful dialogue and effective action on critical issues between and among industry, academic and government partners. The newly legislated Life Science Center can serve as a fiduciary agency overseeing the investment of public funds in critical life sciences research and business initiatives. Eighty-five percent of participants in the PwC survey agreed that the state legislature should endorse a bond referendum to provide funding to the life sciences as a means to counter global and national competition.

Despite the significant challenges that Massachusetts faces in assuring future economic growth, the fact remains that no other place in the world can boast the concentration of academic and industrial excellence in life sciences. It is a gift that cannot be taken for granted or dissipated because of complacency and lack of investment. It affords the strongest possible platform for the future of the Massachusetts economy. In the past, the Commonwealth has successfully confronted economic and social challenges. It has succeeded because it has overcome parochial concerns and special interests and acted collaboratively for the common good. It will do so now and act in the spirit of a “Common” wealth to achieve its fullest potential in the life sciences.

Perspective

Biotechnology and the future

By Josh Boger

Josh Boger, PhD
President and CEO
Vertex Pharmaceuticals

The ground is shifting under the global life sciences industry, and New England is at the epicenter of the changes. Innovation of medicines, once the sole province of "Big Pharma," is increasingly centered in smaller and nimbler companies. "Biotech," from its origins in niche markets of recombinant protein drugs, has become the principal driver of innovation across the whole pharmaceutical industry, proteins and pills alike. This evolution has many upsides, starting with enhanced opportunities to make a difference for patients. But potential dangers come along with this innovator responsibility. The companies—and their home regions—that recognize and address the legislative, financial and relational challenges will be the ones left standing—and prospering—when the ground settles again.

Historically, Big Pharma unleashed its research powerhouses on drugs for the most prevalent diseases, always seeking the next blockbuster. But from large-scale illnesses to the rarer 'orphan' diseases, the discovery model is changing dramatically. Science is driving drug discovery toward diseases large and small. The mapping of the human genome was indeed an amazing interdisciplinary triumph of basic science, from physics to chemistry to biology. But the payoff from this basic research is just beginning, requiring a similar interdisciplinary approach in drug discovery and development. This cross-pollination and interdependency is the future of the industry, and by its own admission (the increasing frequency of in-licensing is proof), Big Pharma is struggling with the need to be nimble, versatile and new-science driven. Enter a huge part of the Massachusetts life-sciences industry: smaller companies that focus their energetic brainpower on specific diseases and on new mechanisms of action. We in Biotech are increasingly the drug-discovery supplier of choice for Big Pharma, and we are holding onto more and more of our discoveries, taking them to the patients ourselves. Along with this change in thinking about—and responsibility for—translating so much exciting basic research, come some considerable challenges.

We in Biotech are hypersensitive to the vagaries of governmental actions. We are not long-established giants with huge reservoirs of capital that could cushion the consequences of ill-considered public policy. We are not multi-product marketing powerhouses with armied sales forces. We do not have diverse cyclical interests in chemicals or consumer goods. Rather, we are small, focused, innovative companies in relatively delicate financial positions. So while it's tempting for policymakers responding to constituent frustrations with rising healthcare costs to take legislative swipes at Big Pharma, those jabs will inevitably hit even harder the companies now discovering the new drugs that are the best hope for good health for all of us. Using reimbursement or intellectual property weapons as short-term fixes for fiscal problems will simply destroy the companies increasingly responsible for innovation—and with them the future of innovative medicines.

Biotech lives in a delicate dependency to Wall Street: captives to the capital markets. The funding model for Big Pharma's research and in-licensing operations is pretty simple: cash and cash flow from operations. These companies are sitting on decades of profitable quarters. But for research-driven companies, most with many years of consistent losses, heavily dependent on the capital markets for operational capital, Wall Street needs to apply a different valuation standard, based not on today but on the promise of tomorrow. The payoff at the other end is not in doubt, but the risks are very high and the timelines are very long. When considering the long investment cycle for our most innovative companies, it will pay to concentrate on the value-delivery equation and not get distracted by the quarterly (or yearly) minutiae. This isn't fundamentally a trading industry; it's an investment industry. And the investment is in all of our future health.

Finally, the new order in drug discovery is changing how the biotech industry approaches its own suppliers and collaborators in innovation. Translational medicine, taking new discoveries from the academic laboratories to the patient, is increasingly a reality. To realize this potential, we need to support robust basic research in academia and build new models of how we interact. Without the financial resources of Big Pharma, we will need to forge more cooperation based on shared vision but with recognition of our different situations. Innovative biotech companies can become the agents for realization of the societal benefits that are drivers of society's support of the academic mission. We need each other more than ever. Along those lines, we are likely to see more motivated patient groups, like the Cystic Fibrosis Foundation, moving to drive this translational work directly, funding targeted drug discovery and development: patients investing directly in future treatment.

For the new innovators of Biotech, the 21st century world is an extremely interdependent place. Biotech requires viable Big Pharma, and vice versa. And we have never been more dependent on the health of the academic research enterprise. And vice versa. And we are more dependent than ever on the needs of patients and potential patients. And vice versa. We take all those responsibilities soberly. We in Biotech are privileged—and humbled—to stand for Innovation.

Methodology and sources

Survey

PricewaterhouseCoopers, with support from the New England Healthcare Institute, Massachusetts Technology Collaborative, Massachusetts Biotechnology Council, and Massachusetts Medical Device Industry Council, administered a survey for the 2007 Massachusetts Life Sciences Cluster report. PricewaterhouseCoopers provided a secure and confidential Web-enabled questionnaire. Participants' data was captured by the Website and loaded into a database, which was then downloaded for formatting and analysis by PwC staff. The survey, conducted in the winter of 2007, targeted 677 individuals from 580 life sciences organizations. The response rate to the survey was 15.5% of individuals from 92 organizations.

Respondents by sector:

- Biotechnology: 31%
- University research: 14%
- Medical device: 14%
- Pharmaceuticals: 16%
- Diagnostics: 10%
- Medical instrumentation: 1%
- Bioinformatics: 1%
- Other (including trade associations): 12%

A. Employment

The data used to estimate employment in the Massachusetts life sciences industry, as well as the broader healthcare industry, are from the Bureau of Labor Statistics Quarterly Census of Employment and Wages (QCEW), available at http://www.bls.gov/cew/home.htm. 2005 is the most recent year for which employment data is available for the entire year. Data from 2001 through 2005 are based on the North American Industry Classification System (NAICS), while data prior to 2001 is based on the Standard Industry Classification system (SIC). Data prior to 2001 and data from 2001 onward, therefore, are not comparable to one another. Note, data from the U.S. Census Bureau, which is published once every five years, was not used because the most recent year published was 2002. Instead, the Quarterly Census of Employment and Wages provided the amount of detail (6-digit NAICS) needed for this report's analysis.

The 2002 Economic Census was used to estimate the relevant life sciences percentages of two NAICS codes:

- 541710—Research and development in physical, engineering and life sciences
- 541380—Testing laboratories

The entirety of two aforementioned NAICS codes cannot be attributed to the life sciences industry and therefore their relevant life science portions had to be estimated. The Economic Census data was used to produce ratios for these two NAICS codes which were applied to the BLS data. With the exception of these two NAICS, one-hundred percent of the remaining NAICS codes were determined to be life sciences industry related.

Life science research at teaching hospitals is a core component to the life sciences industry in Massachusetts; however, it is not possible to determine the relevant life science percentage of the NAICS code which contains teaching hospitals. Therefore, an alternative data source was used to estimate employment in this sector: "Driving Greater Boston & New England: The Impact of Greater Boston's Teaching Hospitals," Conference of Boston Teaching Hospitals.

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

B. Clinical trials

Information on the clinical trials by state and by city is from http://clinicaltrials.gov. A U.S. search was conducted for each phase. This data represents current clinical trials, classified as either "Recruiting" or "Not yet recruiting."

C. Wages

Data used to estimate average wages in the Massachusetts life sciences industry are from the Bureau of Labor Statistics Quarterly Census of Employment and Wages. The average wage for a particular NAICS code is the total wages for that NAICS sector divided by the total employment in that sector. The wages for the different sectors of the life sciences industry are the weighted average (by employment) of the different NAICS codes that comprise them. Similarly, the life sciences average industry wage is the weighted average (by employment) of the wages for the different sectors that comprise the life sciences industry. The same methodology was used to estimate the average wage of the healthcare sector.

D. NIH funding

National Institutes of Health (NIH) funding data is made available by the NIH Office of Extramural Research, available at http://grants2.nih.gov/grants/award/awardtr.htm. Data is available by state, congressional district, NIH administering organization, and recipient institution on an annual basis. 2005 is the most recent year for which data is available and has been finalized. 2006 data is available from NIH; however, at the time the data was being put together for this report, the data was still in its preliminary stage.

E. Life sciences patent data

Information on life sciences patent data was obtained from the U.S. Patent and Trademark Office, Patenting by Geographic Region, breakout by Technology Class, www.uspto.gov/web/offices/ac/ido/oeip/taf/clsstc/regions.htm.

F. Life Sciences PhDs per 100,000 people

This information was obtained from the National Science Foundation's report on 2005 Doctorate Awards, www.nsf.gov/statistics.

Table 14. Life science NAICS codes

NAICS	Industry
Pharmaceuticals	
325411	Medicinals and botanicals
325412	Pharmaceutical preparations
325414	Biological products exc. Diagnostic
Biotechnology	
541710	R&D in the physical, engineering and life sciences†
Medical devices and equipment	
325413	In vitro and in vivo diagnostic substances
334510	Electromedical apparatus
334516	Analytical instruments
334517	X-ray apparatus and tubes
339111	Laboratory apparatus and furniture
339112	Surgical and medical instruments
339113	Surgical appliances and supplies
339114	Dental equipment and supplies manufacturing
339115	Ophthalmic goods manufacturing
339116	Dental laboratories
Wholesale trade	
424200	Druggists' goods and sundries
423450	Medical and hospital equipment
423460	Ophthalmic goods
Medical and testing laboratories	
541380	Testing laboratories†
621511	Medical laboratories
621512	Diagnostic imaging centers

† Indicates less than 100 percent of NAICS industry is attributable to the life sciences industry.

Note: life science related research employment at teaching hospitals is calculated using an alternative data source and methodology.

Table 15. Healthcare industry classification

NAICS	Industry
Health insurance carriers	
524114	Health insurance carriers
Ambulatory healthcare services†	
621	Ambulatory healthcare services
Hospitals	
622	Hospitals
Nursing homes and residential care facilities	
623	Nursing homes and residential care facilities

† Excluding NAICS 621511 medical laboratories and 621512 diagnostic imaging centers which are included in the life sciences industry.

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