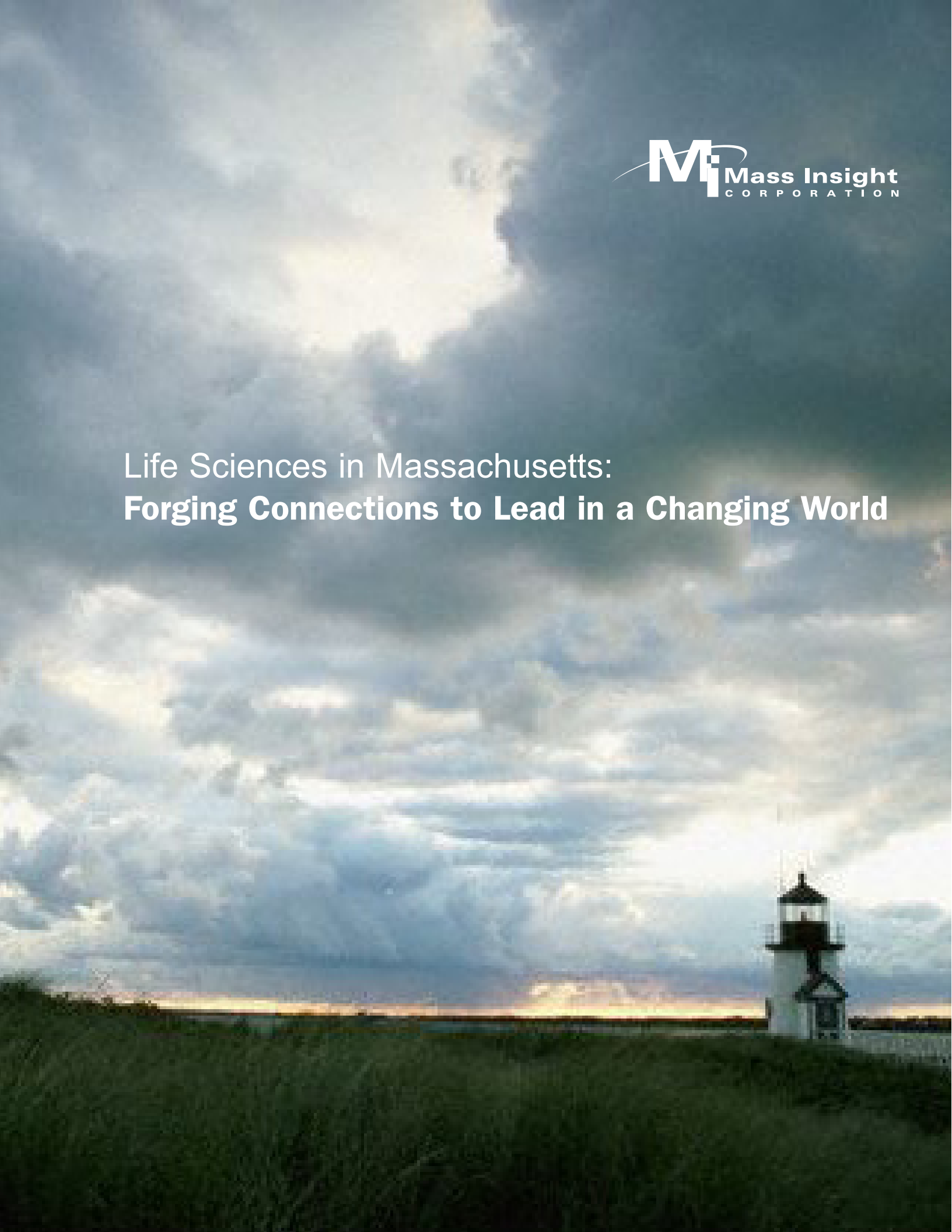
Mass Insight
CORPORATION
Life Sciences in Massachusetts:
Forging Connections to Lead in a Changing World

The development of the Mass Insight Life Sciences report was a community effort that brought together leaders in industry, academia and government. In addition to the generous contribution of McKinsey & Co. in assisting with the preparation of the report, Mass Insight would like to thank the following:

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Global Massachusetts 2015 is a two-year initiative organized by Mass Insight that brings together major business groups, industry, and higher education leaders to develop and advance a comprehensive economic agenda that will position Massachusetts to win the competition for talent – the key to securing the future prosperity for all our citizens. Others in the series include Financial Services and IT/Tech/Defense. Together these three sectors comprise the traditional business innovation core of the Massachusetts economy.

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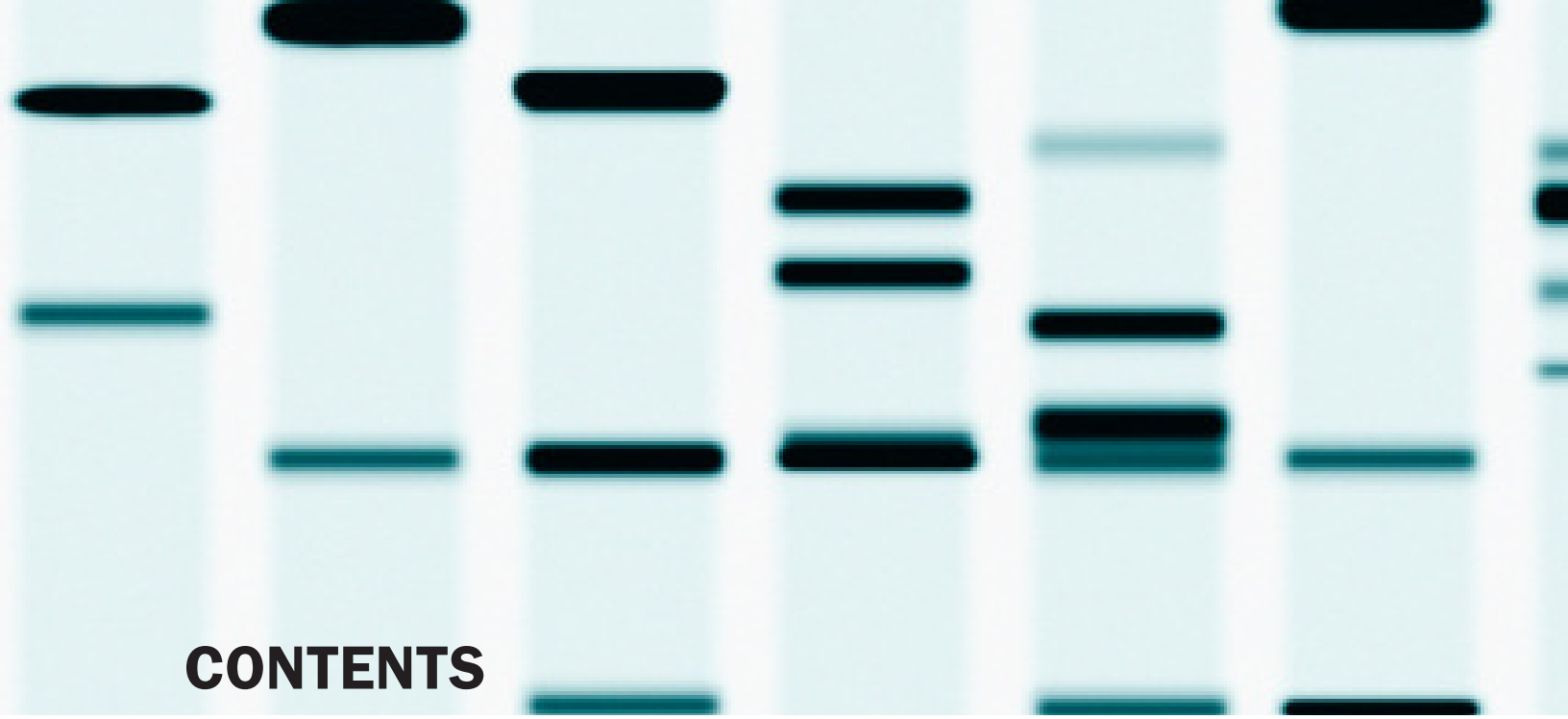

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EXECUTIVE SUMMARY

Maintaining leadership in a changing world

Thanks to its unique cluster of leading companies, universities, medical centers, capital, talent, and government agencies and officials, Massachusetts is among the world's premier centers for the life sciences industry. The Commonwealth sets the pace in a wide range of endeavors, from biotechnology and next generation pharmaceuticals to devices, diagnostics, tools and equipment.

Given its natural advantages, Massachusetts is in a good position to benefit from dramatic growth in the industry in the next decade and from the changes that will result from new technologies over the longer term. But the state will miss several of these opportunities if it fails to adapt to dramatic changes now taking place.

We see five major forces shaping the industry today that will have an impact on the viability of a life sciences cluster in Massachusetts: globalization and the increasing power of competing clusters; economies of scale and scope driving industry consolidation; pressures to reduce the costs of healthcare; the emergence of personalized medicine; and the convergence of technologies and disciplines.

MA is competing with new and fast growing innovation clusters around the world. New life sciences clusters in the U.S., Europe and Asia are attracting talent, capital and the interest of large pharmaceutical firms. As healthcare companies look to consolidate operations and pursue acquisitions to broaden their product portfolios, many are reluctant to consider the Commonwealth, given the relatively high costs of doing business here.

As payors become more cost-conscious, they will continue to put pressure on prices, especially for pharmaceuticals, medical devices, and diagnostics. This trend disproportionately affects producers of high-cost therapies, which is a large segment of the Massachusetts industry. Any increase in price pressures adds to economic challenges producers face as a result of dramatically increasing development costs. On the other hand, there are forces at work that would improve Massachusetts' position of relative advantage.

Personalized medicine offers the promise of more effective targeted therapies and it is hailed by many as the future paradigm of healthcare. Massachusetts' research strengths position it well to benefit from the new approaches to development and application that personalized medicine promises. Yet although Massachusetts enjoys a disproportionate lead, the state will need to make a more deliberate effort to harness its strengths to continue to retain that lead. Likewise, Massachusetts is well positioned to lead the convergence of engineering, information technology and life sciences, and the convergence of drugs, devices, and diagnostics. In both cases, however, decision-makers must promote cross-disciplinary and cross-institutional collaboration.

A vision for life sciences in Massachusetts

To build on its success and continue growing its economy and employment base, we propose that Massachusetts adopt three aspirations for its life sciences sector over the coming decade: become the global hub for life sciences talent; achieve global leadership in generating financial capital and intellectual property in the life sciences; and become even better at attracting new life science companies while nurturing those already here, so that a core of companies scale up and maintain their headquarters in the state.

These aspirations represent a strategic choice to build on existing strengths in research and development. We recommend this choice because we see enormous value in innovation in the life sciences and we believe the state is uniquely positioned to meet emerging global challenges in the field.

Success through collective action

To compete with the likes of Silicon Valley, San Diego, and North Carolina, as well as offshore clusters in Switzerland, India and China, Massachusetts will need to choose a destination, set a clear course and harness all of its collective resources. Government, industry, academia and capital will need to work together better to leverage their respective contributions. And given that their resources are limited, and that each constituency has its own priorities, they will have to focus on a narrow set of initiatives.

Collective action has the greatest impact when there is some kind of "market failure," where the private motivations of individual constituents leave valuable opportunities unexploited. This kind of failure can occur for a variety of reasons, most commonly because no single constituent will make an investment without assurances that other constituents are going to make investments as well.

We see symptoms of such market failure in the Massachusetts life sciences cluster, including barriers to collaboration within the state, underexploited collaborations with other life science hubs and lack of investment in human capital. Under the broad themes of enhancing collaboration and human capital, we propose a multi-tiered approach to increase the Commonwealth's competitiveness in the life science sector. The primary goal for Massachusetts is to leverage its assets as a knowledge hub. It can achieve this goal by increasing coordination and developing its talent base.

Leverage Massachusetts as a Knowledge Hub

Massachusetts should leverage its knowledge base by supporting collaborations within the life sciences sector and across industry clusters. We propose two concrete initiatives to foster collaboration and increase global competitiveness:

- Promote "translational medicine" as a mechanism for academic-industry collaboration: Create a translational medicine center (TMC) to overcome cultural inertia against collaboration across academia and industry and enhance the state's position in translational research. The TMC would evaluate proposals for collaborative research undertaken by Massachusetts institutions and local research operations, whether they are mounted by Massachusetts companies, such as Genzyme, Biogen Idec or Boston Scientific, or by out-of-state or foreign entities with operations in Massachusetts, such as Novartis, BMS, Pfizer or Merck.
- Network with other clusters to take global leadership in innovation and knowledge development: Work together to build connections with existing and emerging life science clusters, such as those in New Jersey and the European Union, as well as emerging clusters, particularly in India and China, consistent with the themes of talent development, healthcare policy and delivery, and local industry development.

Pool Resources and Enable Coordination

- Unify the IRB to increase clinical trial activity: Develop a unified, multi-medical-center institutional review board (IRB) to streamline clinical trials and make Massachusetts a more attractive location for research.
- Coordinate tissue banking to accelerate research: Expand, enhance and coordinate existing tissue banking activities to make Massachusetts the world's primary pre-clinical research center. Coordinating the activities of area hospitals would create a large virtual tissue bank with standardized permissions, cataloging, storage and retrieval. Researchers could then search across multiple institutions simultaneously, place a single order covering samples from multiple institutions, and be confident that every sample will be of high quality and uniformly prepared. Such a bank would provide researchers with access to a broader sample pool and speed research.

Develop a Broad and Deep Talent Base

- Broaden the talent pool to help the cluster expand beyond research and discovery: Close the mid-level talent gap with targeted investments in community and state colleges and the UMass system, involving industry in curriculum design and awareness-building.
- Nurture the next generation to ensure that there is future talent pool: Develop Pre-K-12 outreach programs to improve the long-term, in-state talent pipeline, leveraging scalable learning platforms and industry input for awareness-building.

We recognize that several hurdles stand in the way. Key constituents may question why these initiatives should be pursued or point to other priorities. We have highlighted specific ways to address these concerns and make these initiatives "actionable". This report describes our research and presents our recommendations for improving collaboration (both within the core LS cluster and with related clusters, e.g. IT and materials science), building human capital, recruiting and retaining life sciences companies, and enhancing infrastructure. We include data from our interviews with leaders in the life sciences sector (executives who lead the companies that make up the cluster, leaders of the academic institutions and a broad range of thought leaders), economic research, industry feasibility studies, and competitive research. We have identified big, exciting opportunities within the Commonwealth's grasp—opportunities not only to thrive financially but to provide the world with lifesaving products and innovations and inspire and attract the brightest of minds. These are worthy goals indeed, and they should inspire us all to work together. We take great encouragement from the initiatives that emerged as this report was being completed, including especially the Governor's 2007 Life Sciences Initiative. We hope that this report will add to the momentum gathered behind grasping opportunities in the sector.

2. STRATEGIC OPTIONS FOR MASSACHUSETTS

2.1. MASSACHUSETTS STARTS FROM A POSITION OF REAL STRENGTH IN LIFE SCIENCES

Massachusetts has a vibrant life sciences (LS) sector that spans devices, diagnostics, tools and equipment, and biotech. The cluster around the Boston-Cambridge area has grown over the last 25 years into one of the most significant innovation centers in the world, producing around 8 percent of the global drug pipeline.

The cluster framework

The life sciences sector relies on the co-location of many interdependent entities, including the core industry segments (biotech, devices, diagnostics, tools & equipment, and integrated pharmaceutical companies); universities and academic medical centers that supply talent and many innovative ideas; providers of capital, business services and health care; consumers; and the state and federal government, who drive reimbursement and shape the regulatory landscape covering LS and business activity more broadly. All of these constituents will need to work together to enhance the LS cluster in Massachusetts.

Our research revealed significant opportunities for the cluster over the coming decade—and real challenges. Efforts to further strengthen Massachusetts' LS sector should be focused on the major opportunities, and should also be informed by the challenges.

2.2. MAJOR FORCES SHAPING THE LS INDUSTRY

We see five major forces shaping the LS industry over the coming years, which present opportunities and risks for the state. Potential challenges include increased consolidation within the industry and increasing pricing pressure from payors. Increased globalization will present opportunities and threats. Developments in personalized medicine, and more generally the convergence of technologies and disciplines, present significant opportunities for the LS sector, and MA is well positioned to benefit disproportionately from them.

While we are optimistic about the future for the LS sector in Massachusetts, we see genuine threats to its position that it can and should address now. It can also act now to maximize its share of gains in the sector by enhancing and fully exploiting its natural strengths.

The Massachusetts cluster

The Massachusetts life sciences cluster owes its success to the quality, breadth and concentration of academic centers in and around Boston. The Boston and Cambridge area has no fewer than seven of the world's top 100 LS institutions within a few minutes of each other, including research universities and advanced medical centers (AMCs). The San Francisco Bay area, Massachusetts' only U.S. rival in biotechnology innovation, has three, separated by about an hour travel time. Minnesota, its major competitor in devices innovation, has none. These institutions cultivate and attract human capital and financial investments from government and venture capitalists, which drive innovation in the cluster.

2.2.1. Globalization

Massachusetts will face a greatly expanded range of competitors for talent and capital. For example, the state will be confronted by the emergence of new clusters in Singapore, China, and India, all significant sources of innovation and talent, and fast-growing healthcare markets. These countries will attract more investment from big pharma R&D and from venture capital, and become stronger competitors for top-level talent. China is on track to produce 11,000 life science Ph.D.s annually by 2015, an output that dwarfs the 400 we expect from Massachusetts, even though it is fewer in per-capita terms. We can expect these numbers to grow in quantity and quality and to be clustered in key regions, which will become powerful competitors.

The emergence of additional R&D hubs has implications for Massachusetts. A significant fraction of Massachusetts' current Ph.D. base comes from abroad, including many from these emerging hubs. Approximately 36 percent of graduate students at MIT and Harvard Graduate School of Arts and Sciences are international, including approximately 8 percent from India and China[1]. Competition from domestic institutions may constrain Massachusetts' access to talent from those countries, in the short term through reduced retention of top-end graduates, and over the longer term through reduced admissions as domestic institutions abroad become more attractive.

Several major LS companies, including Novartis and Astra-Zeneca, have already established R&D facilities in China. Several of the executives we interviewed forecast a more important role for China and India in their company's R&D program in coming years. The head of a major pharmaceutical company R&D facility, for example, went so far as to say that in his opinion most R&D work globally would be carried out in China and India within 10 to 15 years. If he is right, Massachusetts would find it difficult to maintain its current share of high-end talent and R&D investments—with obvious consequences for growth.

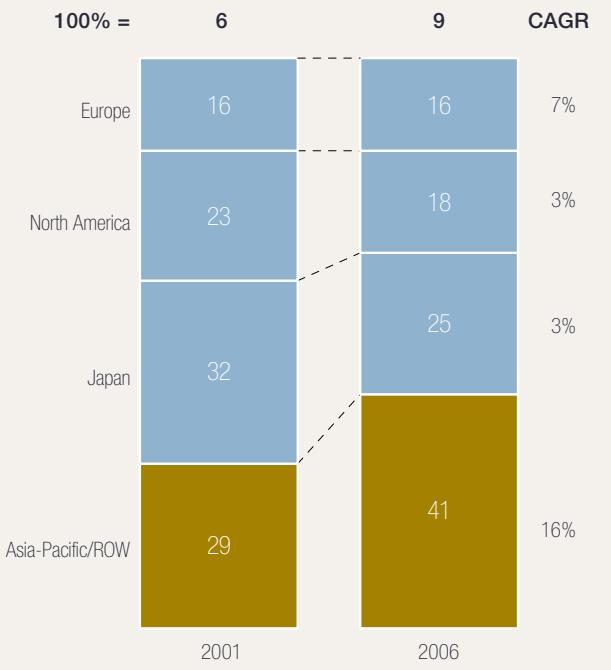
Emerging economies have already started to compete for manufacturing activities. Small-molecule manufacturing has substantially shifted to low-cost locations such as India, as well as to locations, such as Ireland and Singapore, that offer substantial tax incentives. Because biologics manufacturing is much more complex, requiring a more expert workforce and more advanced technology, cost considerations are not yet driving location decisions. We see signs, however, that this is changing as technological capabilities spread outside North America, Japan, and Europe. Recent years have seen numerous facilities open in East Asia, including Singapore and China, and Eastern Europe (particularly in the Czech Republic and Slovakia).

I can get everything I need here in China. If I stay, I will know more people here and have better connections. If I go abroad, I'll lose all of that. If you want to build a long-term career back in China, it's not always clear that going to the U.S. is in your best interests

- Tsinghua science student Wang Yong

1 Harvard International Office; MIT International Students Office

EXHIBIT 1: Evolution of semiconductor capacity distribution
Wafer Starts Per Month (8" Equivalent WSPM)
Million units



Source: World Fab Watch

Major pharmaceutical companies are increasingly prepared to site manufacturing in such lower-cost regions. The semiconductor industry shows how rapidly companies will respond to changes in technological leadership (see Exhibit 1). Semiconductor manufacturing remained concentrated in relatively high-cost locations for much of its history, but when the technology matured and penetrated emerging economies, there was a ground-shift in the distribution of semiconductor manufacturing in just five years.

Despite these changes, Massachusetts has and will retain a competitive position as the site of pilot plants, thanks to synergies in co-location of discovery and process development staff. The state should work to reduce regulatory and infrastructural barriers to firms' trial manufacturing. The recently approved BMC initiative should significantly help retention, as would further streamlining site approval procedures (see section 4.2.4 *Recruit & retain LS companies*). In the longer term, Massachusetts will need to address availability of water rights in areas close to the existing hubs, as current allocations will not support radical increases in manufacturing.

Growth in emerging economies presents opportunities, of course, because it can mean bigger markets for products made in Massachusetts. The pharmaceutical market in China, for example, is expected to grow from about $14 BN in 2007 to $19 BN by 2010. Demand in emerging nations will be constrained, however, by the relatively small segment of the population that can afford modern medical care, particularly the relatively expensive therapeutics most Massachusetts companies produce. Over the longer term, as China's standard of living converges with that of the West, its billion-plus people will constitute a key market for LS companies. American firms will benefit by establishing connections to Chinese firms and institutions early, fostering privileged status as partner of choice for institutions and companies. The same holds true for India, Singapore (already a significant market), and other emerging LS nodes.

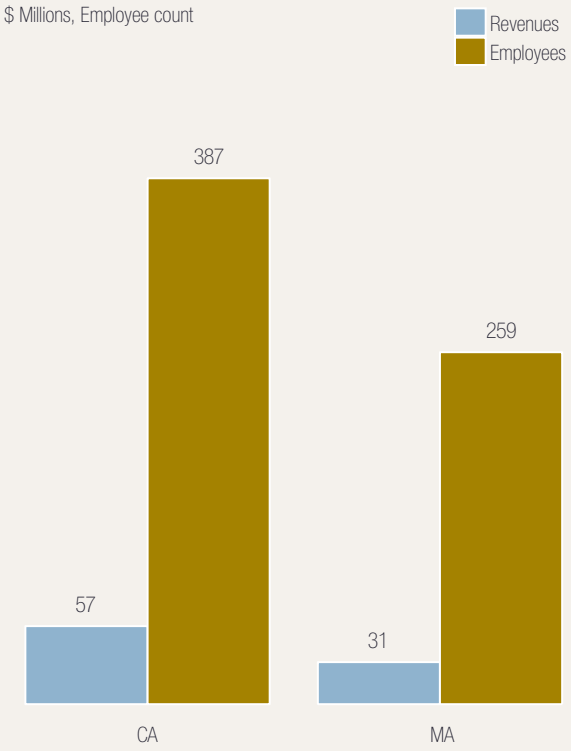
Similarly, it is critical that Massachusetts develop and maintain strong connections to the research and talent centers that will emerge in Singapore, China, India and elsewhere over the coming decades. To a large extent, this will be a result, rather than a cause, of continued success as a research center. If Massachusetts gets the fundamentals right and remains the research powerhouse it is today, it will remain relevant to emerging hubs and maintain access to talent flows from those and other source locations. Yet collective action across stakeholder sectors—academia, government, providers and industry—could help forge stronger and more valuable connections to other hubs. We recommend that these sectors explicitly consider the scope for such collaborative activities, now and as competitive dynamics evolve.

2.2.2. Industry consolidation

Massachusetts' thriving biotechnology sector is heavily concentrated in the research stage of the value chain. That reflects both the ultimate driver

EXHIBIT 2

Total Revenues and In-State Employees
(Per NCE In Pipeline Owned By In-State Entity)



Source: Compustat

of the cluster's success, which is the presence of a wealth of research talent in universities and academic medical centers (AMCs), and the relative youth of the cluster. Boston's status as a biotechnology hub is a recent phenomenon—as is the biotechnology industry itself. If the establishments of Biogen (1979) and Genzyme (1981) represent the birth of the biotech cluster, it is less than 30 years old.

The Bay Area cluster is somewhat older—Genentech was founded in 1976, and the region produced the world's first biological engineering company, Cetus Corp., in 1971. The region's more broadly pharmaceutical startup history dates back at least as far as Syntex, in 1964. Thanks in part to its age, the Bay Area cluster has penetrated further into later stages of the value-chain than has Massachusetts, with a number of fully-integrated biopharmaceutical companies. This has led to a different economic activity profile: the Bay Area cluster has markedly higher employment and revenues for each new chemical entity (NCE) in its companies' pipelines. (see Exhibit 2)

Many stakeholders are hopeful that Massachusetts will emulate its counterpart on the West Coast and develop its own cluster of fully-integrated companies. One might think that it is simply a matter of time—as one CEO put it, "Massachusetts is San Francisco 10 years ago." But a changing industry structure may mean that the transition San Francisco made is no longer a viable option for Massachusetts. The last 10 years have seen significantly increased industry consolidation. In part, this is a result of the same forces that are playing out in other industries, as markets react to new potential for economies of scale and scope in an increasingly global economy. Section 2.2.1, *Globalization,* noted the industry's increasingly urgent search for lower-cost manufacturing locations, and there is every reason to believe it will accelerate and broaden as new locations for manufacturing, R&D, and ultimately commercial operations gain competitive advantage. Other trends contribute to consolidation, as large pharmaceutical and device companies, facing capital market pressures over their narrow pipelines, consolidate their way to growth. Pharmacos have increasingly been acquiring biotech companies for access to their innovations.

Companies acquired by non-Massachusetts entities are not realistic candidates for developing commercial stage activity in the state. It is true that, in addition to intellectual property, purchasers of biotech companies acquire talent, and since human capital is not very mobile, acquirers might want to maintain existing operations in Massachusetts. Few larger acquirers will locate late-stage activity in Massachusetts, however, for several reasons: few acquisitions have built up much late-stage human capital; few acquirers have commercial talent in Massachusetts; and they find relatively limited synergies in physical co-location of R&D and commercial functions. In any case, pharmacos would find it difficult to move commercial operations to the Bay State. As one executive told us, "half our staff would leave if we moved to Massachusetts,"

and given the thin local commercial talent pool, they would be difficult to replace.

Hence, if the rate of acquisition by large pharmaceutical companies significantly increases, that can be expected to slow the pace of organic development of commercial activity within the state. In an extreme version of this scenario, Massachusetts might be left only with early- to mid-stage companies, whose capital providers do not aspire to organic growth but to sale to a large integrated pharmaceutical company.

2.2.3. Increased price pressures

Although LS therapeutic innovation continues to offer enormous value, there is a risk that pricing pressures may erode that value over the coming decade. As the cost of R&D rises, too, we could see significantly reduced investments in research.

Both private and public payors are becoming increasingly cost-conscious, demanding provable cost-effectiveness from innovative therapies. The costs of pharmaceuticals and devices are rising faster than other components of healthcare expenses, focusing payor attention on the industry.

The shift of costs to consumers exacerbates this trend. Payors are increasingly shifting costs and utilization decisions to end-consumers through health savings accounts (HSAs) and other methods. These consumers have incentives and the power to shop for cheaper drugs or cut utilization, and experience has shown that their behavior is affected accordingly; a recent McKinsey survey showed that 58 percent of those with HSAs have asked their physicians about cheaper drugs, compared to only 32 percent of those without. We expect consumers to have increasing responsibility for costs in future years, which will add to the downward pressure on drug prices.

This trend disproportionately affects producers of high-cost therapies, which is where Massachusetts' sector is focused, especially in the realm of biotech and integrated devices. Average prices for biotech products are much higher than for small molecule therapies—often several times as expensive by volume. While biotech products tend to be aimed at relatively price-insensitive market segments, such as cancer patients, and have been sheltered from this trend thus far, revenues may fall in the future. The likely emergence of a significant market in biosimilars—essentially biologic generics—will only add to these pressures. One payor we interviewed said that he expected drug costs overall to fall by 25 to 50 percent, and that drugs and devices could continue to command price premiums only if they demonstrated their value through improved outcomes.

At the same time, drug development costs continue to skyrocket. From 1987 to 2005, the cost of developing a single new drug has risen from $231 MM to $802 MM. In an environment of diminished absolute returns on research investments, venture capital and big pharma may become more reluctant to make those investments, slowing Massachusetts' growth.

The sector's ability to innovate efficiently will continue to come under pressure, as development costs continue to rise. As we shall discuss in the next section, personalized medicine promises to contribute substantially to a solution, but not before significant work is done.

Although it would be unwise to ignore the risk of diminished investment, we are cautiously optimistic about the ongoing value of innovation. While the industry will face increasing pressure to demonstrate value, therapeutics costs represent only 12 percent of overall healthcare spend. Further, advances in therapeutic and diagnostic science, including most notably personalized medicine, promise to deliver substantial and demonstrable outcome and efficiency improvements (see section 2.2.4 *Personalized medicine*). We believe that payors will continue to reward these improvements.

2.2.4. Personalized medicine

Commercialization of technologies associated with personalized medicine will create major growth opportunities, and major challenges, for Massachusetts. Advances in genomics, proteomics,

Pharmacogenomics prove Herceptin's value

Herceptin shows the benefits of pharmacogenomics to clinical practice and drug development. After Genentech completed Phase III trials for the drug in 1997, overall results suggested that it was not effective. But when they were analyzed through a genomic lens—dividing the trial population into those whose cancers were positive and negative for human epidermal growth factor receptor 2 (HER2)—it emerged that the drug was effective in HER2-positive patients. The FDA granted fast-track designation for the drug and approved a diagnostic test for identifying HER2-positive patients. Patients in the responsive group are now readily identified and treated with Herceptin.

and metabolomics have raised the prospect of medical care tailored to an individual's genetic makeup and its expression in that person's phenotype. This new paradigm of personalized medicine (often also referred to as "pharmacogenomics") offers several benefits.

Personalized medicine offers the prospect of a shift from symptoms-based medicine to genetics-based medicine. Today, diagnosis and treatment are based largely on the detection of disease symptoms. Richer understanding of the genotypic contribution to many disease states promises to reveal genetic markers that can predict disease development, enabling better preventive treatment. These genetic markers are increasingly identifiable through the use of diagnostic testing. For example, identifying people at risk of developing Type 2 diabetes can guide preventive medication, such as metformin or statins, and behavior changes, such as diet and exercise.

Increased understanding of the genetics of drug metabolism could optimize therapies for effectiveness and safety, based on an individual's response profile. Patients vary widely in the way they metabolize and respond to drugs, but much drug and dosage selection today is the result of trial and error, which can be difficult or even dangerous for the patient and expensive for the payor. The ability to optimize therapy according to a response profile based on genetic, protein, or metabolite "biomarkers" predictive of response would considerably enhance therapeutic safety, effectiveness, and efficiency. Recent advances in diagnostic technology, including gene sequencing, have enabled these biomarker diagnostic tests to be commercialized and available to treating physicians.

Finally, the same biomarker information promises to significantly enhance the drug development process. Identifying likely responders before a clinical trial, and excluding likely non-responders and those for whom the drug many not be safe, offer a significant improvement in the development process.

How quickly will personalized medicine deliver real impact? Optimists see major change within the next 5 to 10 years, while pessimists point to the range of obstacles that remain (see sidebar on next page) in suggesting that full impact is decades away. Experts do agree, however, that personalized medicine will be a major driver of value creation across the LS landscape in coming decades. Benefits will accrue to manufacturers of drugs, devices and instruments, and diagnostics; service providers, such as medical centers and laboratories; and patients.

Massachusetts is particularly well positioned to play a leading role in this evolution. The state enjoys a strong position across the range of sectors that will generate value in personalized medicine: drugs, devices, instruments, and diagnostics. A number of Massachusetts companies and institutions are engaged in research and product development that will help realize the promise of personalized medicine, with work on pharmacogenomics and associated diagnostics. We cannot attempt a complete survey of the wealth of commercial activity, but a few examples are in order. Genzyme's research focus since its inception has been on the genetic basis of a number of diseases, and it is developing companion diagnostics for a range of therapeutics, including through its subsidiaries Genzyme Diagnostics and Genzyme Genetics. Millennium Pharmaceuticals, to name one more example, is working on biomarkers to predict Velcade response in multiple myeloma patients.

Massachusetts also hosts a number of players with important programs in platforms for molecular diagnostics that will be crucial for personalized medicine. For example, Philips Medical Systems has an active program in molecular imaging through next-generation positron emission tomography and single photon emission computed platforms. Cytyc's ThinPrep Pap test and companion Imaging System, used for breast cancer diagnosis, now offers promise for applications in ovarian, colon, bladder, prostate, and lung cancer. Since the ThinPap system has broad applications and could provide multiple in-vitro diagnostics on a single sample, it is positioned for a leading role in personalized medicine.

Massachusetts has great strength in relevant basic research, given its many leading research institutions. For example, the Broad Institute is one of the world's leading centers in research into genomics, informatics, and proteomics. The HMS-Partners Center for Genomics and Genetics, active in basic research, is also providing genomically informed clinical services and developing enabling clinician education as part of its MD and nurse training programs. More generally, Massachusetts' unparalleled concentration of top-ranked academic medical centers (AMCs) constitutes an enormous asset in efforts to use genomics to span the gap from bench to bedside, through the wealth of data they can collectively make available to pre-clinical development activity.

Massachusetts therefore has real strengths in areas that will generate major value over the coming decades. Harnessing those strengths effectively will require a deliberate effort to boost collaboration—an area where our research reveals that Massachusetts is not consistently strong. Accordingly, this study recommends an effort to leverage the state's assets through an expanded and enriched tissue banking program, creating a unified "virtual bank" of tissue samples and associated clinical data that researchers can use with confidence, thanks to uniform procedures for tissue collection, storage, and data maintenance.

Hurdles for personalized medicine

Personalized medicine must overcome challenges in science, economics, talent and education, and legal/regulatory frameworks.

Scientific hurdles include the failure thus far of genomics, proteomics and metabolomics to live up to early expectations. In particular, there are deep challenges in informatics—the use of computational and statistical techniques to understand gene structure and expression.

Economic issues include uncertainty about business models for personalized medicine. Pharmacos are concerned about their position in a post-blockbuster world, since personalized medicine could reduce markets to relatively small subsets of responsive patients, and about the vertical shift of value distribution, as biotechs, diagnostics, and AMCs garner more value. Payors will need to grapple with the economics of high upfront costs for diagnostics whose benefits—prevention and more effective therapy for existing conditions—may accrue over many years, well beyond the likely coverage period.

Talent and education will become issues as providers need new skill sets, particularly deeper grounding in genetics and clinical pharmacology. Patients will need to be educated about the changing nature of care and how they are protected from genetic discrimination.

Legal frameworks will need to change as governments rethink privacy and anti-discrimination laws to address patient concerns. Government oversight agencies, such as FDA, will process a much larger volume of applications—each covering a smaller subset of patients, and including more post-launch data collection for safety biomarkers. FDA will need new processes for more complex approval decisions, such as drug/device combinations.

Over the longer term, there remain serious obstacles to the full development of truly personalized medicine. We believe that many can be addressed by collective action. Accordingly, we recommend that a body with broad oversight over the LS cluster, perhaps the newly-formed Life Sciences Collaborative, for example, take on the mandate to maintain an active cross-sectoral dialogue with the aim of identifying potential areas for collective action, and coordinating champions for concrete initiatives that emerge.

2.2.5. Increased value in cross-sectoral collaboration

We believe the value of collaboration in LS research and product development will rise. Basic discovery is increasingly occurring on the margins of disciplines. We see convergence in previously distinct sectors, such as devices and drugs, and the growth of industrial biotech. The near to medium term should also see significant value created through the application of information technology to life sciences and healthcare, across the value chain—in research, development, diagnosis, and treatment.

One important area of value creation is the convergence of information technology and LS R&D. The role of informatics in pharmacogenomics is one obvious example, where convergence is helping shift research from opportunistic trial-and-error discovery to the engineering perspective of systems biology[2]. This trend will demand deeper integration of information technology and biological disciplines. Achieving systems-level perspectives is likely to involve cross-disciplinary research teams including mathematicians, geneticists, computer scientists, engineers, physicists, and cell and chemical biologists working together.

Moving from research to development, advances in the software that analyzes and predicts genetic interactions and gene expression will likely be a major source of value creation, as may database software to facilitate pre-clinical development drawing on massive tissue sample banks. Over the longer term, "in-silico" testing may replace some animal testing in pre-clinical work, as computer models of response pathways become capable of providing reliable information about drug safety and effectiveness in real time.

Information technology also promises to deliver changes to the provision of care. Electronic medical records (EMR) represent a huge potential value-creation opportunity; analysts estimate that a shift to EMR would generate $81 BN[3] in annual savings, and enable entirely new platforms for healthcare delivery. Sensors capable of detecting biochemical levels will enable telemedicine—remote monitoring of a patient's condition, with real-time updates provided over wireless connections, and automatic real-time adjustments to drug dose through implanted drug-delivery mechanisms, such as for insulin release in diabetics.

The flow is not one-way: insights from biology also promise to transform information technology. Some advances are in the enabling nanotechnology, as researchers explore the use of biology to develop new chips. For example, MIT's Angela Belcher (Scientific American's Researcher of the Year for 2006) has genetically engineered a virus that forms a transistor component by coating itself in a semiconductor sheath and bridging two electrodes. Other researchers are working on using the structure of DNA to perform computing tasks—offering both cost savings and immediate reactivity to biophysical or biochemical conditions.

Convergence of drugs, diagnostics and devices will be a feature of future value-creation in LS. Perhaps the highest-profile existing example is the drug-eluting stent, Taxus, introduced by Boston Scientific. This technology is an instance of a more general trend toward complex drug-delivery systems, innovating by combining pharmaceuticals and devices. Instruments will play an important role in diagnostics for personalized medicine as it matures.

2 Systems biology consists in understanding complex biological systems in terms of the interactions among its constituent parts – much like an engineer understands a complex mechanical or electrical system.

3 From *Health Affairs*, based on healthcare safety and outcome improvements

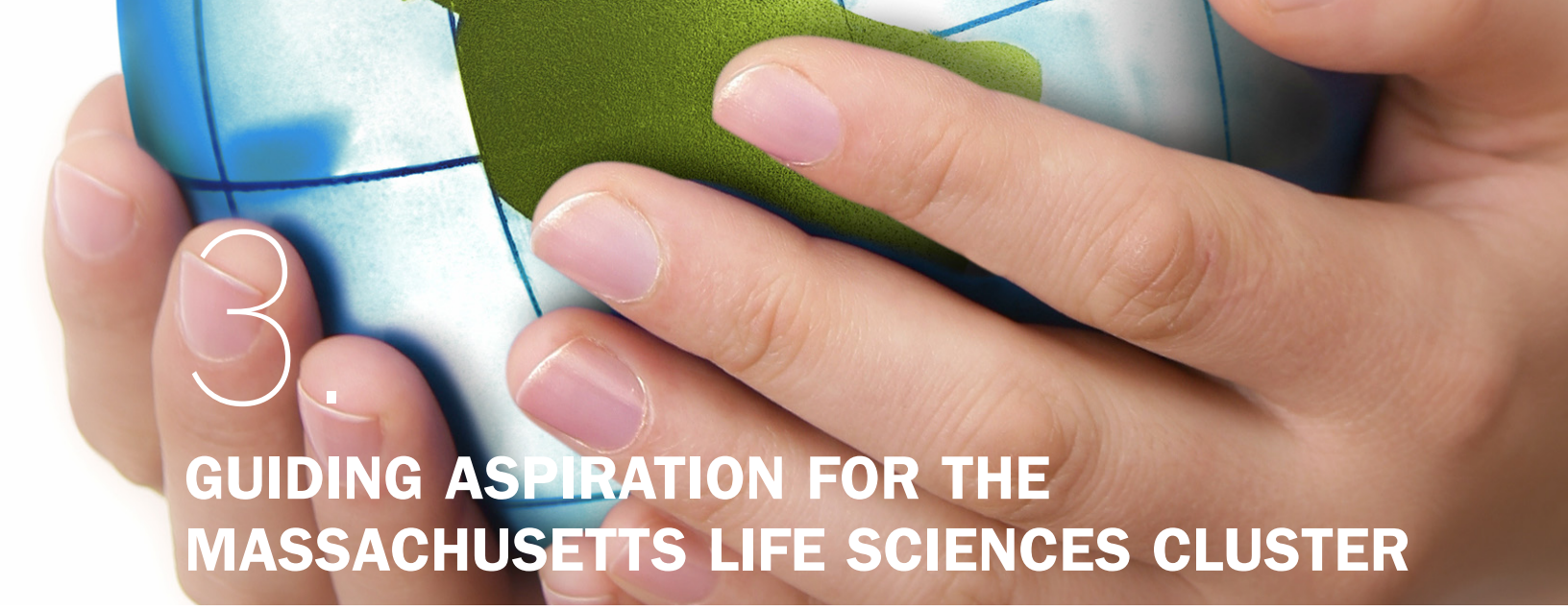
Another high-profile area of convergence between engineering and LS is the rapidly growing field of industrial biotech: the use of molecular biology to generate new industrial materials and processes. One of the best-known applications is biofuels, where genetic manipulation offers prospects for clean energy from plants and algae. We anticipate opportunities for a wide range of bio-based materials, including bioplastics, which are renewable and can be engineered for desirable mechanical properties or biodegradability. Finally, we see exciting potential for engineered biological catalysts—which is, after all, what proteins are—to play roles in industrial processes in the chemical, food and feed, paper and pulp, and textile industries.

The Massachusetts LS cluster is in an excellent position to pursue developments like these if the key stakeholders can work together better. Given its combined stature in engineering, chemistry, physics and biology, the state has the potential to be a leader in this rapidly growing sector. As the recent award of a $500 MM BP biofuels research grant to a consortium led by UC Berkeley shows, however, it faces strong competition; MIT had also competed for the grant. Early investments, such as the BP investment in California, will play a role in the talent location decisions that will shape future dominance. It is therefore important for Massachusetts to build collaboration to ensure it can take its share of the pie.

Stakeholders should consider the scope for concrete mechanisms to more fully exploit and publicize Massachusetts' strengths in these emerging areas of research, in particular through enhanced cross-disciplinary and cross-institutional collaboration.

Massachusetts faces increasingly strong and well-coordinated competition

MIT's unsuccessful bid for a half-billion-dollar research grant from BP underlines the strength and motivation of Massachusetts' competition. In June 2006, BP invited bids from leading institutions to establish a biofuels research institute. The bid from UC Berkeley, in partnership with Lawrence Berkeley National Laboratory and the University of Illinois at Urbana-Champaign, leveraged an already-planned investment from the state of $30 MM for a bio-energy program. Gov. Schwarzenegger promised an additional $40 MM of state funding if BP chose UC. BP awarded the fund to the Berkeley consortium in January 2007. Observers credited the Governor's intervention as a significant factor in the decision.



3. GUIDING ASPIRATION FOR THE MASSACHUSETTS LIFE SCIENCES CLUSTER

3.1. OUR ASPIRATION FOR MASSACHUSETTS

We propose the following aspirations for the Massachusetts life sciences cluster in 2015:

1. Become the global hub for the flow of talent
2. Achieve global leadership in generating LS intellectual property and market capitalization
3. Become the U.S. headquarters site of choice for the next generation of LS companies by nurturing the growth of a critical mass of local companies into full-fledged commercial entities and attracting new ones.

3.1.1. Become the global hub for the flow of talent, ideas and capital

As we argued in section 2.2.1, *Globalization*, the coming decades will see a major expansion of the foci of LS research and development. Massachusetts cannot realistically expect to increase, or perhaps even maintain, its share of world value creation over the long term. Yet it can aspire to remain a central node in the network of increasingly geographically distributed LS activity. Its geographic accessibility and discovery pre-eminence position it well for this outcome. Apart from its unparalleled academic resources, Massachusetts has the best potential to simultaneously link into major clusters in New Jersey and Europe and thereby provide access to job opportunities in the entire LS value chain – from discovery to commercialization.

3.1.2. Achieve global leadership in generating intellectual property and attracting new capital

Already one of the world's leading centers of LS activity, Massachusetts will need to leverage its resources better to move to the front of the pack while new entrants gain ground and existing centers continue to challenge the state. Given the rapid advances of several emerging hubs, such as North Carolina, Israel and Singapore, Massachusetts will face more competition in the coming years. At the same time, established hubs like New Jersey, California and Basel, Switzerland, will continue to be major forces in the sector. Therefore, Massachusetts must leverage its institutional assets to continue to be a world leader in intellectual property generation. It must also increase the push for commercialization to ensure the local sector is able to extract value from this innovation. In this way, the state will not only continue to be a Mecca for talent and research, but will be able to create value and improve health outcomes in ways other centers cannot.

3.1.3. Become the U.S. HQ site of choice

Massachusetts has a strong history of local research spawning new companies. Less impressive is the state's record in helping to turn those startups into thriving, larger businesses. Despite success stories in several sectors, including LS, the vast majority of LS companies in Massachusetts remain small or are acquired by out-of-state players. The challenge is thus not only to create a continued

and growing stream of new ventures, but to nurture these companies to grow to significant scale. As the LS sector shifts from its big pharma roots, this will be increasingly important. It is an opportunity for Massachusetts to lead the birth and growth of the next generation of LS companies.

Massachusetts' accessibility to other major hubs (as noted earlier, it is within easy reach of New Jersey, Europe and California, and its time zone facilitates collaboration with those centers), its strong connections to other hubs (for example, through its hosting of big pharma R&D centers), and its depth of research and managerial talent, position it well for a headquartering role. Some venture capital interviewees reported making a shift to Boston a condition of investment for precisely these reasons. If those strengths are supplemented by a deeper commercial talent pool—which the organic development of integrated pharmacos would provide—Massachusetts could become an even more attractive site for foreign pharmacos looking for headquarters for U.S. operations.

3.2. ASPIRATION REFLECTS A HIGH-LEVEL STRATEGIC CHOICE

The Massachusetts cluster overall has a substantial bias toward early stages of the value chain, which is consistent with its research emphasis and strengths. While the devices, tools and equipment sub-sectors are dominated by a handful of large, integrated companies, the biotech sub-sector, growing much faster than others, contains about 1300 small startup companies, whose value creation is dominated by R&D activities.

Given that starting point, Massachusetts faces a high-level strategic choice between focusing on its existing strengths in R&D and seeking to increase or accelerate its diversification into a cluster that is more balanced across the value chain, with more manufacturing and commercial activities, including marketing and sales, reimbursement, regulatory, and so on.

Past reports (e.g., Mass 2010, prepared by MBC in 2002) have stressed the benefits of a more diversified sector. This is not difficult to understand. While there is substantial economic *value* associated with Massachusetts' research-focused cluster, later stages of the value chain involve significantly more economic *activity*, as measured in terms of revenues and jobs. As indicated in section 2.2.2, *Industry consolidation*, more balanced clusters like that in the San Francisco Bay Area have markedly higher employment and revenues per NCE than does Massachusetts. The state government has a clear fiscal interest in activity, since it drives corporate and personal income taxes. In addition, the Commonwealth has a natural concern for the quantity and quality of jobs located in Massachusetts.

On the other hand, the Commonwealth should not ignore the economic value associated with research, not to mention the broader benefits of the R&D sector, which attracts and retains highly talented people for high-quality, environmentally clean and socially beneficial jobs.

In addition, in choosing to boost the sector at the state level, stakeholders should consider where and how collective action can add value to the activity that is already occurring in Massachusetts. A more balanced cluster, with more late-stage activity, has undeniable appeal, but collective efforts might not help achieve that outcome.

We believe that collective actions to boost the cluster should focus initially on its existing strengths in research and development. While Massachusetts may nurture a number of fully integrated firms over the long term, we think initiatives directed at enhancing its research strength will be most impactful, for the following reasons:

1. Despite payor pressures, we believe innovation will continue to create enormous value. As we noted in section 2.2.3, *Increased price pressures*, the cost of therapeutics will remain a relatively small proportion of overall healthcare spend. If anticipated advances in therapeutic and diagnostic science deliver substantial and demonstrable outcome and efficiency improvements, we believe payors will continue to fund them.

2. Massachusetts' strengths position it well for future innovation, especially in emerging growth segments such as personalized medicine. We saw in section 2.2.4, *Personalized medicine,* that Massachusetts has the foundation to play a leading role in value creation in this area, as well as in value creation arising from convergence across sectors and industries. More generally, Massachusetts enjoys a strong position in basic biological and commercial life science research by virtue of its intellectual capital and access to financial resources. It cannot take those advantages for granted for the longer term. In the face of significantly increased international competition for talent and capital, it must invest in its foundations to maintain its edge.

3. We believe that significant market failures in the R&D segment may respond to collective action. Research and development requires considerable integration of knowledge among individuals—and it requires patient investors. The networks that support collaborative activity are ad-hoc and thin because investigators' time and resources are limited, and because of institutional, geographic, or cultural boundaries. The resulting lack of information and barriers to collaboration mean that collaborative opportunities are often not captured. Meanwhile, venture capital flows suggest that the investor community has become considerably more risk-conscious over the last decade or so (see Exhibit 4 on p. 24). This could be a correction for an earlier "irrational exuberance" in venture capital, rather than an over-correction and hence a sign that the market for risk capital is failing to deliver resources to innovation efficiently. We suspect, though, that the truth probably lies somewhere between: the venture capital market was over-exuberant in the late 1990s, and is overly cautious now. Collective action might help correct for any such market failure.

4. We do not see evidence of similar market failures lying behind Massachusetts' low penetration into later stages of the value chain, with the exception of our anomalously low share of development activity (the target of one of our recommended initiatives). The following paragraphs present our reasons for this view.

We believe that Massachusetts has opportunities to significantly expand its share of clinical development, currently estimated at 2 percent of total U.S. activity (MBC 2010). This is a surprisingly small share, given that Massachusetts has 12.5 percent of the U.S. pipeline, or 8 percent of the global pipeline, and some of the most prestigious clinical centers—ideal hosts of trials, from a developer's perspective. Drug developers have good reasons to shift at least part of their clinical trial activity offshore, where they find larger patient volumes, lower costs, and a broader range of genotypes. Significant activity in the U.S. will continue, however, particularly over the medium term, and particularly for earlier-stage trials. Given its proximity to the discovery center for such a large fraction of the pipeline, and its excellent credentials for execution, Massachusetts should aspire to a much larger share of that activity. One of our recommended initiatives is aimed at realizing that goal.

As we argued in section 2.2.1, *Globalization*, Massachusetts should aspire to attract pilot manufacturing facilities, and should leverage its strengths (including the recent BMC initiative) to do so. We do not believe it has a long-term competitive advantage as a location for bulk manufacturing, however. That activity will increasingly be outsourced and off-shored to lower-cost locations such as Eastern Europe and East and South Asia.

In contrast, we think Massachusetts has real prospects of hosting more commercial functions, especially if and when its local mid-size companies develop into integrated firms on the scale of Genzyme, or even to the scale of its West Coast rivals, such as Amgen and Genentech. If enough local companies mature to create "critical mass" and a strong pool of experienced commercial talent, that would also make Massachusetts an attractive site for U.S. headquarters of future international LS companies.

Our interviews made it clear that the state has a long way to go in this regard: for maturing local companies in the process of developing commercial functions, attracting the requisite talent is clearly a problem. We do not see how collective action could accelerate that maturation process, however, and we do not see any sign of market failure. As we noted in section 4.2.2, *Enhance human capital position*, the market seems to function reasonably well, in that the supply of talent is responding to emerging opportunities.

4.

SETTING PRIORITIES FOR INITIATIVES

4.1. OUR BASIC BELIEFS ABOUT INITIATIVES

We believe collective action can remove barriers to the efficient allocation of resources by markets. Existing institutions, including the National Institutes of Health, big pharma, and the venture capital community, allocate capital to research programs and potential product innovations. We think collective action should work with these mechanisms, not against them.

More broadly, we believe competition among institutions, firms, ideas and products will promote high-value innovation, and will best position the cluster for growth over the long term. Accordingly, the state should not protect players in the LS sector from external or internal competition. Instead, initiatives should improve the state's ability to leverage its available resources to help the life sciences industry compete.

Since the resources for collective action are limited, and since impactful initiatives will typically require significant investments of financial and human resources, efforts must be keenly focused. Among the many efforts that we believe might benefit the cluster, we have narrowed our focus to a handful of concrete initiatives anchored to a common theme. In this way, we hope to maximize our chances of attracting the resources required for successful implementation.

We have sought to avoid duplicating existing efforts, especially where they do not require large-scale collaboration across stakeholder sectors in academia, industry and government. Previous reports and stakeholder discussions have highlighted many issues requiring attention, including changes to R&D and other tax credits, smoother permitting procedures, improved government outreach to industry, and transport infrastructure improvements including the Inner Ring. We endorse these efforts. While there is clearly progress to be made, these issues are already on the agenda, and we see little added value in our adding to the existing commentary on them.

To summarize our guiding principles to prioritize initiatives, we believe that collective initiatives should:

i. Remove barriers to open competition among ideas, technologies, products, firms, and academic institutions

ii. Encourage those long-term investments the market is otherwise likely to significantly under-invest in, such as human capital and infrastructure

iii. Be carefully focused, preferably anchored to a theme that will motivate engagement over the long term.

Legislative agenda for taxes and permitting

The Massachusetts Biotech Council (MBC) has drafted amendments to the corporate tax code, fixing some technical issues around R&D tax credits (the definition of R&D activities and eligible expenses, and what sorts of corporate entities qualify—corporations, LLCs, joint ventures, etc.). The bill enhances startups' access to those and other credits by establishing a secondary market in them; alternatively, they could be made refundable. Last year's House Bill 5207 (an Act Relative to Streamlining and Expediting the Permitting Process in the Commonwealth) has made substantial progress in addressing longstanding concerns about the timeliness of permitting in the state. The Romney administration also established the Office of Business Development to enhance company recruitment and retention.

There is a lot more work to be done against these initiatives. For example, given the opt-in structure of Bill 5207, it is imperative to expand the number of communities that bind themselves to the streamlined procedures. Since these efforts already have clear owners, however, and since progress is being made, we do not focus on them in this report.

In addition, the prioritized initiatives should not:

i. Second-guess market choices or make overly prescriptive bets on narrow technologies or research programs

ii. Insulate firms, ideas, or institutions from external competition

iii. Focus narrowly on Massachusetts' share of any LS pie, rather than on overall value to the state. Collaboration with other clusters may add more value to those clusters than to Massachusetts but still result in an improved bottom line for the state. Initiatives to cement partnerships with emerging clusters, such as China, India, or Singapore may fall into this category.

4.2. CHALLENGES TO ACHIEVING THIS VISION FOR MASSACHUSETTS

4.2.1. Increase collaboration

In our discussions, many Massachusetts thought leaders shared concerns about inconsistent local collaboration. Time and again, interviewees referred to "the Massachusetts culture" as an impediment. Many said bluntly that cross-institutional collaboration is something "Massachusetts doesn't do". This plays out in a range of arenas: patchy performance at technology transfer, limited collaboration between LS and business programs, limited collaboration between the region's medical centers—even those nominally part of the same parent institution—and a perception that the region's business leaders do not work together on key issues.

Within and across the state's institutions, collaborative research and education programs lag those of other states. Both up-and-coming and established states like North Carolina, Georgia, California and New Jersey have been working hard on cross-disciplinary and cross-institutional programs to take advantage of the best available resources. They have also been using these efforts as a way to draw talent and capital because grants, such as those from the National Institutes of Health, increasingly favor collaborative projects.

When Massachusetts institutions have collaborated, such as on the Harvard-MIT Division of Health Sciences and Technology (HST), or when the Harvard medical centers worked together for National Cancer Institute funding, the results have been positive. The key is to increase the volume and scope of collaboration to make sure Massachusetts is leveraging its unrivaled institutional resources.

Deriving maximum value from innovation requires institutions to connect with the business world. Yet technology transfer and commercialization have not been consistently strong in the state. With some exceptions, there is a cultural bias against "commercial" research. Institutional incentives frequently mean that time spent on licensing a discovery rather than focusing on journal publication could put a professor's career in jeopardy. This is in

stark contrast with the culture and practices in other states and institutions; many of our interviewees cited Stanford as a model. Professors there not only work on commercializing their research but often spend part of their time in companies. Professors who move their labs to Genentech, or work part of the time in a startup, are not uncommon at Stanford, and the school is not alone.

In the new geography of science, it is those who are good at sharing, rather than protecting knowledge, who will flourish.

- James Wilsdon, Head of Science & Innovation, Demos (From China: Next Science Superpower?, Demos)

We see opportunities for significantly enhanced collaboration with other major clusters, both current and emerging. Given the local presence of players from California, New Jersey, the UK, Switzerland and elsewhere, Massachusetts is well positioned for deeper relationships with existing hubs. These relationships should include government, institutions and industry in Massachusetts and abroad to ensure the state's relevance to other key players.

The next generation of LS centers, such as North Carolina and perhaps Arizona, or Eastern Europe, the Middle East and Asia, will present a new kind of external collaboration mandate. To date, Massachusetts has benefited from informal or disjointed efforts at collaboration and connection to emerging centers, such as one-off fellowship programs and the individual activities of select Massachusetts companies in an emerging country. What has been lacking is a coordinated effort that pools players from each sector to have a more powerful message.

4.2.2. Enhance human capital position: the talent challenge

The LS sector relies on a pool of workers who are relatively immobile geographically and who earn mid-level wages. Examples in core life sciences include research lab technicians and technologists, pharmacologists and pharmacology technicians, clinical trials technicians, medical equipment technicians, and bioprocess technicians. Mid-level workers in converging fields will also be in demand: for example, there is a growing need for technicians with the generalist scientific training that prepares them for cross-disciplinary applications, and for bioinformatics technicians, and diagnostic lab technologists. Skilled people to fill these roles are in short supply across the country. As a large and highly geographically concentrated cluster, Massachusetts faces a special challenge in maintaining a sufficient supply of suitably qualified labor. This is exacerbated by the high cost of living in the state's life science cluster zones, and by historically low levels of investment in public education, particularly at post-secondary levels.

Mid-level talent: a scarce resource

Medical and laboratory technologists and technicians prepare, monitor, and analyze experiments and diagnostic tests. Technologists perform relatively complex tasks – making cultures, analyzing samples for chemical content, and determining concentrations of compounds. Technicians perform less complex procedures, preparing specimens and operating automated analyzers, for example, or performing manual tests under technologist supervision. The usual requirement for an entry-level position as a laboratory technologist is a bachelor's degree with a major in one of the life sciences, and some have master's degrees. Laboratory technicians generally have an associate degree.

We have tech positions we can't fill. You can do a global search for lead scientists, but you need lab tech talent in-state.

- Hospital CEO

While Massachusetts has enviable access to elite, innovative talent through its first-rate research universities and teaching hospitals, it has not nurtured its public universities to the extent of some of its rivals, such as California and North Carolina. Community colleges perform well below the national average in three-year graduation rates, and although the UMass system has clear pockets of strength, such as Craig Mello's Nobel-prize winning work on RNA interference (RNAi), it does not compare favorably overall with some of the better-funded public institutions in other states.

Things have gotten dramatically worse over the last 18 months: technician salaries are growing two to three times as fast as those of our other employees.

- Biotech CEO

As a result, Massachusetts employers consistently identify a shortage of mid-level talent as an obstacle to growth. Virtually all the companies and institutions we interviewed have difficulty filling positions. This shortage is reflected in relatively high salary increases for these positions in recent years.

Many employers in Massachusetts also expressed difficulty in attracting commercial talent. This largely reflects the stage of development of the Massachusetts cluster as a whole. Employers and talent agencies alike agreed that it was difficult for a small commercial cluster to attract talent—after all, if a location offers few potential opportunities, the risk of moving there is much higher. While Massachusetts now contains an appreciable number of companies that need commercial talent, it still has much thinner demand than more established clusters, such as New Jersey, which raises the bar to attract workers to the state.

Nevertheless, observers note that as the number of commercial opportunities in Massachusetts has increased, the talent pool has grown, too. Over the medium to long term, therefore, the supply of commercial talent seems to respond to demand signals in the market.

That does not obviate the need for collective action. One clear opportunity is in enhanced collaboration between management and scientific academics. Massachusetts has, in Harvard and MIT, two of the top business schools in the world situated in one of the world's foremost centers of LS innovation and startup activity. Despite that juxtaposition, there is surprisingly little formal integration of management and technical classes in the state's major academic institutions.

Consider two examples:

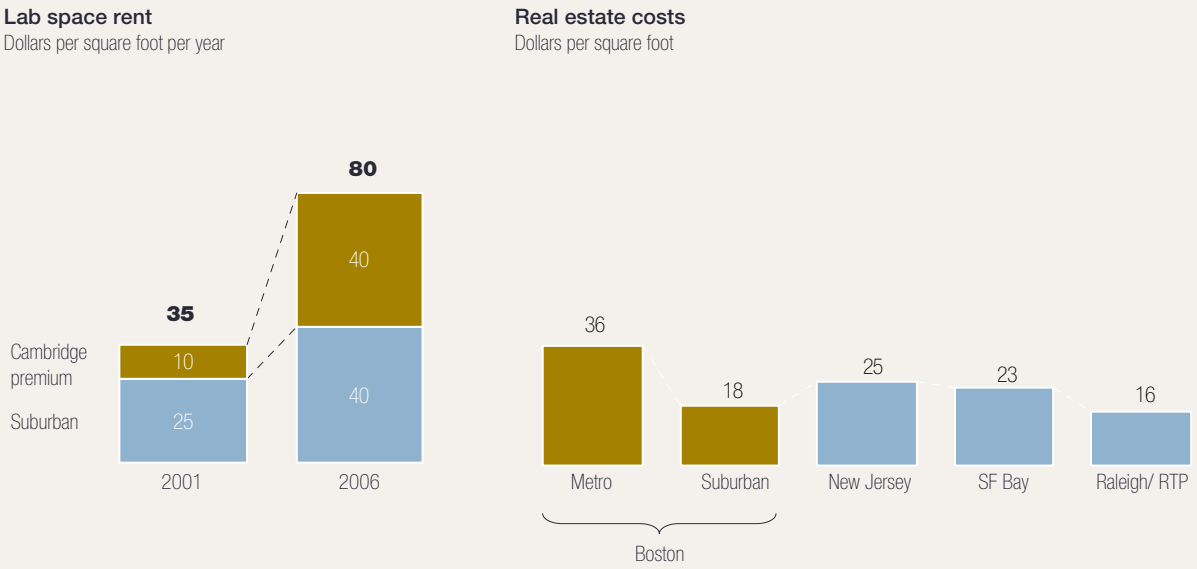
The Biomedical Enterprise Program (BEP) of the Harvard-MIT Division of Health Sciences and Technology offers its students interdisciplinary cross-fertilization to produce more technically-informed managers and more commercially-informed scientists – which cannot help but boost the scale and quality of LS commercialization activity in Massachusetts. Yet it is at small scale, for the size of the Massachusetts cluster, with 7-10 students annually.

Harvard Business School offers five LS-oriented second-year electives, but they are standalone, rather than packaged into a coherent program that provides a "company-ready" grounding in the field. Harvard also offers a dual MD/MBA program, with seven students enrolled in the joint-degree program in addition to the 12 to 18 MDs who enroll in HBS per year. These numbers are relatively low, given a base of nearly 1,000 students per class at HBS and 350 at MIT/Sloan.

By contrast, the San Diego and Los Angeles clusters can draw on the graduates of the Keck Graduate Institute of Applied Life Sciences whose masters and Ph.D. programs provide in-depth training in the nexus of LS science and business, including focus tracks for specialization in a particular component of the value chain, such as a track in Clinical and Regulatory Affairs.

EXHIBIT 3

Cost of lab and office space is becoming an entry barrier for MA startups



Source: CB Richard Ellis, 2006; Cummings Real Estate Life Science Team

4.2.3. Strengthen the startup environment

Many of our interviewees stressed the challenges faced by startup companies in Massachusetts. Along with more established businesses, they face high costs for talent and lab space, which is more expensive in Cambridge than in any other cluster. While costs for both talent and space are lower to the South and West of the Cambridge/Boston cluster, our interviewees stressed that ready access to principal investigators was crucial to a company's first years, so that moving to Worcester or Fall River, for example, is not a viable option for most startups.

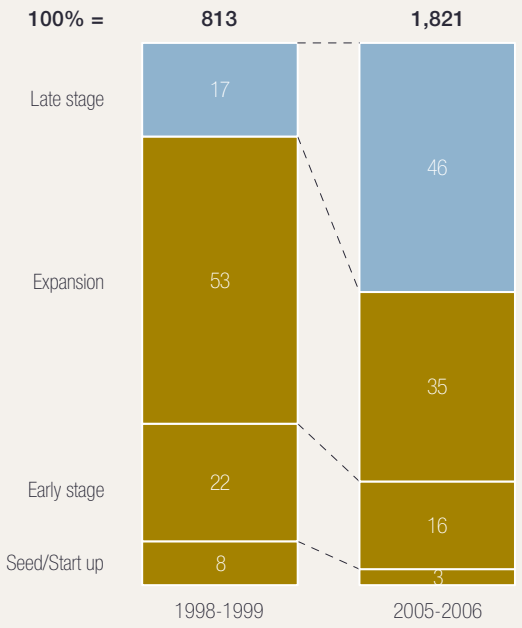
Added to those systemic issues in Massachusetts are a collection of challenges specific to the startup business model. Venture capital has become significantly less willing to fund high-risk early-stage projects in recent years, with a significant shift to late-stage investments over the last decade or so. In addition, while Massachusetts has a superficially generous R&D tax credit of 10 percent, it suffers from a relatively short lifespan of five years, compared to 10 years under the Federal tax code. This means that it is effectively unavailable for early-stage companies that do not expect to make a profit until around their tenth year of operation, when their first drug reaches the market. In addition, Massachusetts presents several technical problems with the way it defines R&D activities and eligible expenses, and what sorts of corporate entities qualify.

Several competitor states, New Jersey in particular, have addressed these issues by making relevant tax credits (specifically the net operating loss credit) transferable, thus establishing a secondary market through which startups can monetize their credits. Massachusetts should consider a similar move, or perhaps simply make the relevant tax credits refundable (which would enable companies to directly monetize their credits without the time and expense of going through brokers).

EXHIBIT 4

VC LS Funding Patterns in MA

Percent, $ MM



Source: PWC Moneytree

The Massachusetts Biotech Council has designed bills to achieve these changes, and they are now before the legislature. Accordingly, while we believe these initiatives would have positive impact, we do not focus on them in this report, which seeks to identify near-term opportunities that are without champions today.

4.2.4. Recruit & retain LS companies

Interviews with LS companies demonstrated a consistent theme of their being courted by other states while Massachusetts remained relatively quiet. Referring to state and local officials in Massachusetts, several executives said, "They don't hurt us, but they're not helping us either." From issues with permitting and site selection, to transportation, tax policy, and payroll and real estate costs, it can be costly and difficult to do business in the state. That can make it hard to justify moving to Massachusetts or even expanding within the state.

Several other states, such as Arizona, have hired staff to recruit new companies or institutions to the state and work with existing players to ensure they get the help and attention they need. These staffers serve as a single point of contact with the city or state government.

Massachusetts has had success in the past, such as the recent Bristol-Myers Squibb manufacturing plant decision for the former Fort Devens site. Massachusetts also created the Business Resource Team to serve existing companies in the state. This is a good foundation, and the BMS example shows that the state can be competitive. Massachusetts must be more proactive, however, and invest the time, analysis and creativity to help those already here thrive, while taking advantage of and creating opportunities to attract new investment. Given efforts already underway, we did not focus our recommendations here.

4.2.5. Enhance infrastructure

Massachusetts has long been known for its commuting challenges. While the Central Artery enhancements have helped ease congestion around Boston, commuting in the state is still problematic. This is exacerbated by high housing costs: people either pay premium housing prices to live near the Boston-Cambridge LS cluster, or they pay in commute times to live where housing is more affordable. Even commuting within the core cluster, such as from the Longwood Medical Area to Kendall Square or MGH, can take up to an hour with traffic, with no direct public transportation option. This diminishes the value of the one of the cluster's key assets—its concentration of institutions.

For someone considering relocation, this is a strong negative. It came up in interviews with companies and recruiters as a consistent challenge. It can't always be overcome, even with hefty relocation packages.

Some companies are addressing the problem by locating facilities to the West, North and South of Boston, in places like Framingham, Worcester and Fall River. This usually precludes them from

accessing talent in the Cambridge and Boston area, but opens them up to talent living elsewhere, such as people with families who moved out of the city to take advantage of more affordable housing. Other companies, such as Genzyme, provide corporate shuttle services to connect various offices and aid in commuting.

Further work is needed on public transportation to better connect the state, ease commuting, and aid collaboration within the Cambridge/Boston cluster and across the state. For example, a direct rail connection between Kendall and Longwood would aid collaboration within the cluster, by facilitating richer interactions between researchers in biotechs, universities, and AMCs. Improved commuter rail access, scheduling and reliability would shorten the commute from areas of affordable housing, while allowing companies to spread to areas outside the Boston-Cambridge core. Similar solutions exist in other states, like the New Jersey Transit system and the Bay Area's BART.

Again, transport infrastructure issues are already being addressed via the inner ring initiative, and improvements beyond the inner ring have already begun. Because this work is on the agenda, and because its benefits are relatively diffuse (affecting many industries other than LS), we do not focus on it in this report.

4.3. FOCUS ON ENHANCED COLLABORATION AND HUMAN CAPITAL

In light of our beliefs about which sorts of initiatives are likely to be effective, we suggest a focus on enhanced collaboration and human capital. We have three broad reasons for this view.

First, enhanced collaboration is a source of significant value creation. As we argued in section 2.2.5, *Increased value in cross-sectoral collaboration*, new sources of value in LS will increasingly depend on collaboration across disciplines, institutions, and sectors (e.g. across clinical and discovery, devices and therapeutics).

Second, we believe that market forces do not always effectively promote collaboration or the building of human capital. Section 4.2.1, *Increase collaboration,* contains the argument regarding collaboration. As for human capital, we have several reasons to think the market will under-invest. Payoffs are diffuse (there are positive externalities) and payoff horizons are too long for corporate investment criteria. Students typically lack information about the long-term consequences of the education decisions they make, and they do not always make rational choices even when armed with good information.

Third, initiatives to boost collaboration and human capital development are timely, given the efforts already underway. A wealth of other initiatives in tax, permitting, and transport infrastructure are already on the agenda, under the auspices of MBC, MHTC, and groups with broader mandates such as ABC. We have sought to avoid replicating that work, instead identifying other initiatives that are not on the agenda but offer near-term benefits.

Under the broad themes of enhancing collaboration and human capital, we propose a multi-tiered approach to increase Massachusetts' competitiveness in the life science sector. The primary goal for Massachusetts is to leverage its assets as a knowledge hub. Massachusetts can support the primary goal through developing supporting infrastructure through pooling resources and better coordination and developing and maintaining its talent base.

Leverage Massachusetts as a Knowledge-Hub

- Create a state translational medicine center to overcome cultural inertia against collaboration and to enhance Massachusetts' position in translational research
- Collectively build connections with existing and emerging LS clusters, such as New Jersey, the EU, Israel, India and China, under the themes of talent development, healthcare policy and delivery, and local industry development.

Pooling Resources and Better Coordination

- Develop a unified, multi-AMC IRB to make Massachusetts the most attractive location for clinical trials
- Expand and enhance existing tissue banking activities to make Massachusetts the world's primary pre-clinical center.

Develop Broad and Deep Talent Pools

- Close the mid-level talent gap through targeted investments in community and state colleges and the UMass system, involving industry in curriculum design and awareness-building
- Develop Pre-K–12 outreach programs to ensure a long-term, in-state talent pipeline, leveraging scalable learning platforms and industry input.

The next section spells out a detailed action plan, including, for each initiative: the case for action; a detailed description of what actions are required; potential challenges and an assessment of feasibility; and which stakeholders are the natural owners of the initiative and are therefore in the best position to drive action. Where we could, we have used high-level models and key parameters to make economic estimates of costs and benefits. Although we present them as directionally accurate comparisons rather than precise forecasts, we think they make a compelling case for action.

5. PRESCRIPTION FOR ACTION

5.1. INITIATIVE 1: CREATE A TRANSLATIONAL MEDICINE CENTER

Traditionally, basic research, development of drugs and devices, and clinical medicine have been largely insulated from each other. Increased understanding of disease pathways, and the growing availability of biomarkers for disease states and response profiles, have helped drive stronger connections. Information from clinical research is being applied to early development, and therapeutics are receiving earlier testing and evaluation. In the realm of life sciences discovery and development, "translational medicine" typically refers to the "translation" of basic research into effective therapies for real patients, creating a "bench to bedside" link.

As we saw in section 2.2.4, *Personalized medicine*, Massachusetts is well placed for leadership in translational medicine. A translational medicine center (TMC) would help realize that potential by providing institutions and industry with grants for collaborative research in the area of translational medicine. This could help the state overcome cultural inertia against collaboration. We recommend a sum of about $50 MM, initially funded by state or philanthropists, to provide direct incentives for collaboration, with a 1:1 institutional and 2:1 corporate match. Institutions and industry would cooperate on research.

A "research clearing house" could help researchers in industry and academia identify opportunities for collaboration. The clearing house would be a repository for information about industry research interests, and academic research activity. It would thus help investigators identify potential commercial partners for further developing their research, and help companies identify potential academic partners. Our research suggests that many on both the academic and industry sides of the fence lack this information, which significantly limits collaborative activity.

If I had an idea, I probably wouldn't know whom to call – and I'm pretty well plugged-in. These connections are made by word of mouth, and lots of people just don't know whom to talk to.

- University investigator and start-up founder

It would be great if someone could create a clearinghouse for this kind of information. To know which company is looking for what…that would greatly impact the amount and quality of collaboration.

- Pharmaceutical company R&D manager

The Massachusetts-based company Innocentive offers one possible model for a clearing-house. Innocentive advertises industry research needs and matches those needs with investigators able to fulfill them. Social networking sites provide other examples of the kind of mechanism we have in mind. As these examples suggest, the clearing-house represents a concrete opportunity for cross-sectoral collaboration between the LS and IT clusters in MA.

5.1.1. Gap analysis

Boston boasts more leading life science research institutions per square mile than anywhere else in the world. It is also home to many commercial research operations. Collaboration between these two camps has been sub-optimal, however. Bringing them together could unlock greater innovation.

Getting people together who are interested in collaboration, and willing to jump over hurdles to work across disciplines, institutions, academy/industry, is the key.

- Director, collaborative research program

Historically, institutional research in Massachusetts and beyond has not been guided by commercial opportunities, but a new wave of collaboration is spreading across competitor states and countries. As they seize the opportunity by providing their institutions and industry with incentives for collaboration, they threaten Massachusetts' relevance.

Part of the state's insularity is cultural, and part is structural. New England is known for the independence of its institutions, local governments and people. Structurally, institutional incentives are not aligned with commercial gains. Furthermore, Massachusetts institutions receive more NIH funding—nearly $3 BN per year—than those of any other state but California, and they have massive endowments, which have blunted their incentives to work with commercial organizations.

Massachusetts has some of the key companies, research institutions and talent to further develop translational medicine, Its AMCs provide a unique resource for its biotech, tools and equipment companies to get early clinical input into the development process. Its strength in the key capabilities for personalized medicine offers a potentially leading position in leveraging understanding of disease pathways, associated biomarkers and diagnostic innovations into targeted clinical interventions.

A mechanism for funding collaborative projects between the academic and commercial sectors could help spark more innovation in the state. In addition, collective action could help drive vital capability-building. Translational medicine will require enhanced skill-sets and experimental resources. A translational medicine center could usefully fund education in immunology and pharmacology, for example, through translational science scholarships. It could also help small companies access expensive enabling resources. Non-human primates, for example, can be important experimental models for accelerating pre-clinical work without compromising safety. Maintaining a pool of experimental subjects is prohibitively expensive for individual small companies, and might be a valuable contribution by a translational medicine center. Facilitating access to platforms for enhanced in-vivo testing capabilities may be another investment area worth the center's attention. The tissue bank, we also propose, is another example of a valuable pre-clinical resource that individual companies cannot provide for themselves.

Proposed initiative

Massachusetts should follow other states, such as California, in offering grants contingent on collaboration between institutions and commercial R&D operations. Such a grant system would build upon the mechanisms already in place to foster collaboration, such as the John Adams Innovation Institute, by providing added scale commensurate with the volume of activity in Massachusetts.

Specifically, the state should help establish a Translational Medicine Center by providing $50 MM in initial seed funding, or helping organize philanthropy to build the initial funding. The center would secure ongoing funding through grants from NIH and other sources, donations from sources like Howard Hughes Medical Institute (HHMI), venture capitalists or other philanthropists, and the state.

California's collaborative grants

The UC Discovery Grant program provides up to $250,000 annually to faculty for up to four years for research conducted with a California company, which must match 1:1. Two of the seven program areas, biotech and LS IT, are in LS.

California State University's Program for Education and Research in Biotechnology (CSUPERB) offers similar grants up to $30,000.

The TMC would evaluate proposals for collaborative research projects undertaken by Massachusetts institutions and local research operations, be they those of Massachusetts companies, such as Genzyme, Biogen Idec, Boston Scientific, or of out-of-state or foreign companies that have operations in Massachusetts, such as Novartis, BMS, Pfizer or Merck.

Each project seeking funding would need to be focused on translational medicine, and include funding contributions from the institution (at 1:1 matching) and the industry partner (at 2:1), as well as staff participation from each. In this way, the $50 MM initial fund could be leveraged into a $200 MM research investment[1].

There are many benefits from this research activity to each actor, including job creation, talent attraction, tax revenue, license revenue, and profits from commercial product sales.

New research creates jobs, even projects that do not succeed in developing a new test or a new drug. For the state, this generates personal income tax revenue from researcher salaries that will help recoup investments in the fund. Between direct and indirect employment creation by this initiative, the state can expect to recoup $10 MM for every $50 MM it puts in[2].

Research that yields a marketable drug produces additional financial gains for the state, the institutions and the companies involved. The state benefits by $120 MM in corporate tax revenue over the life of a drug. Overall, this yields a total return of 2.6x for the state. Institutions would earn roughly $175 MM through licensing agreements on a jointly-developed drug, providing them with a 3.5x return on their investment. Finally, the company marketing the drug would earn over $225 MM, or a 4.5x return on its investment, even after paying royalties to its institutional partner[3]. This sort of research activity and funding can also help attract new talent to institutions and companies.

1 Because companies are engaging and investing in this type of research already, we assume that half of their contribution is truly incremental, thus making the total new investment $150 MM per year. Assuming $8 MM per research project, 19 projects could be funded by the center. Given typical R&D success rates, we estimate that two drugs would come from this work.

2 Annual LS salary of $83 K; employment multiplier of 2.64 based on Bureau of Labor Statistics data, with 50% of new jobs being incremental and paying $26 K per year; 85 employees per successful project; 16 employees for 5 years for failed projects; 5.3% state personal income tax

3 48% margins for 10 years of patent protection per NDA (ex R&D); $413 MM development cost over 5 years per NDA from Phase I on; 20% institutional licensing fee on annual profits; 9.5% corporate tax rate; 12% corporate and 9% institutional discount rates

We believe the investments required for the associated clearing-house are quite modest. We estimate establishment costs would be approximately $100,000, and there would be ongoing management costs of approximately $100,000 per year.

Potential complication

Barriers include cultural norms and a history of strong not-for-profit funding. Initial funding requirements could pose a challenge, particularly in light of the history of budgetary constraints at the state level. Having said that, the Governor's recent commitment to life sciences is encouraging. And, given the strong returns to all contributors, this is a program worth government investment as it will pay for itself in the long term.

Feasibility

Once funding is established, the key to feasibility would be overcoming cultural norms barriers to collaboration. In each institution and company, some researchers are already open to collaboration; engaging them will be a key factor in success. Once champions for the initiative are identified and engaged, their success stories can demonstrate the value of collaborative research in the field of translational medicine.

It is a real eye-opener for the academics to find that we can teach them things that matter to them. For example, we recently mentored an MIT grad student because they realized we could help on the informatics…. Even at MIT, we had a PI ask our scientists, "You guys publish?"

- Biotech SVP

Because the program is working against established cultural norms, it will be important for those establishing the center to think about the details of how the program works, including eligibility requirements, mechanisms for publicizing the program and attracting applications, approval processes, project ownership structures, confidentiality and publication guidance.

Owners

While the government may provide seed money, the center would be an independent body.

5.2. INITIATIVE 2: CONNECTIONS TO OTHER LS CENTERS

Industry, institutions and government must coordinate to develop strong connections to existing and emerging life science hubs throughout the nation and the world.

Modern medicine serves a billion people. In 25 years, we'll add three billion more to that via new markets. You simply have to be in those markets.

- Biotech CEO

5.2.1. Gap analysis

While Massachusetts holds a leadership position in life sciences today, other states and countries are emerging as leaders in their own right. Singapore, China and India, for example, are investing heavily

Biopolis enhances Singapore's LS profile

Biopolis demonstrates Singapore's commitment to life sciences research. Constructed between 2003 and 2006 for $350 MM, its seven buildings on 18.5 hectares (46 acres) will eventually house 1500 scientists in a mix of laboratories and incubators. Tenants include government agencies, five publicly-funded research institutes, startups, and research labs of pharmaceutical and biotechnological companies. Major foreign tenants include Novartis, Abbott, Becton-Dickenson, Eli Lilly, GSK, Siemens, and Johns Hopkins. Biopolis is helping to build Singapore's LS profile. Several of our interviewees mentioned it. A venture capitalist, for example, called Singapore "now state of the art."

in their LS sectors. Key investments include capital projects (see sidebar on Singapore's Biopolis), education initiatives to produce the right talent, such as China's LS Ph.D. production increasing 28 percent per year, and infrastructural and procedural improvements, such as India's push in clinical trials and manufacturing.

The growth of these centers is both a threat and opportunity for Massachusetts: they will increase competition for money and talent while offering the promise of larger markets.

Their growth could help increase LS value overall. For example, they could help bring personalized medicine to fruition. Establishing mutually beneficial connections early, through partnerships, joint ventures and shared talent pools, will increase Massachusetts' prospects of sharing in this growth.

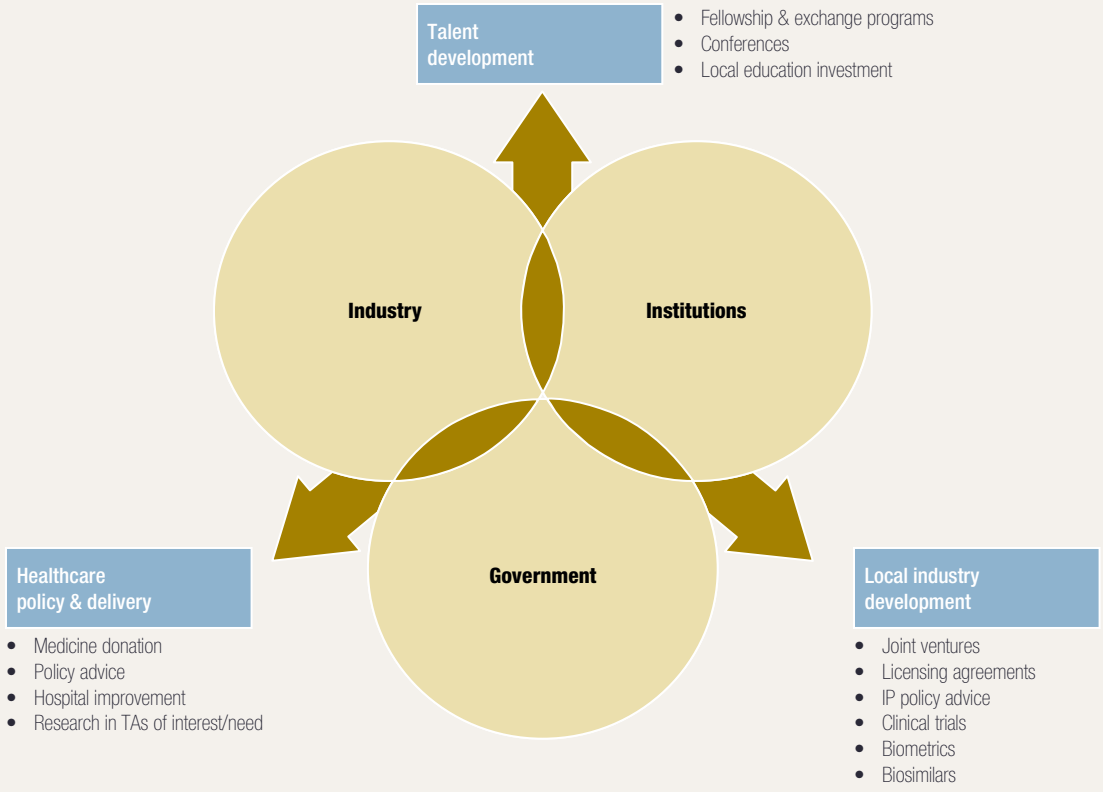
As these foreign centers grow, more top talent will pursue education and research outside Massachusetts. Given that the state's institutions and talent are the foundation of the local sector's strength, the state must work to preserve them. Establishing key connections with emerging research institutions will help.

5.2.2. Proposed initiative

Massachusetts can become the partner of choice with enhanced access to established and emerging centers of LS activity by building meaningful connections between and across government, institutions and industry. Implementation could begin by assembling a consortium of experts from these three sets of players to identify areas where they can add value:

EXHIBIT 5

Collaborative Mechanisms for Building Connections



- **Pooling resources to achieve economies of scale**
  Work together in outreach and connection to gain critical mass and clout, and thus have greater impact
- **Enhanced coordination**
  Coordinate to deliver consistent messages more powerfully
- **Correcting misalignment of key actors and benefactors**
  Those receiving the benefits may not be the right ones to make the connection. For example, government could negotiate a drug supply agreement that benefits local biopharma companies. Collaboration helps ensure the highest total benefits.

Activities should focus on three major themes:

- Talent development:
  - — Fellowship & exchange programs
  - — Conferences
  - — Local education investment
- Healthcare policy and delivery:
  - — Policy advice
  - — Hospital improvement
  - — Medicine donation
  - — Research in treatment areas of greatest interest or need
- Local industry development:
  - — Joint ventures
  - — Licensing agreements
  - — IP policy advice
  - — Clinical trials
  - — Biometrics
  - — Biosimilars

Potential complications

Successful, coordinated outreach requires that actors in the state collaborate, despite their different agendas. Massachusetts culture is not historically as collaborative as it needs to be.

Feasibility

Informal outreach has already begun with such activities as institutional fellowships and exchange programs, corporate donations and marketing activities and a wide range of conferences. This activity should be maintained and coordinated across all of the key actors.

To provide coordination, champions must be identified to organize and push the process. The champions can organize a leadership group to coordinate efforts, and strategize about how the state can best approach other centers of LS activity.

Benefits of a unified IRB

A unified, multi-academic medical center (AMC) institutional review board would help make Massachusetts a better location for clinical trials because it would do the following:

- Replace the existing approvals patchwork with one authority over all clinical trials in area AMCs
- Streamlined approval criteria and processes with more frequent IRB meetings
- Include representatives from area AMCs
- Allow a multi-institutional indemnity fund to offset risks.

Owners

Unlike the other initiatives, there is no explicit owner for this work. We anticipate that industry and academia would pursue the outreach for their natural respective purposes and continue to coordinate with each other. The public sector, through its convening power, can play a role in facilitating such coordination.

BRANY's approach can guide Massachusetts medical centers

SITE IDENTIFICATION

- Identify potential trial sites for a trial
- Assess site demographics, history and staff expertise
- Provide BRANY investigators
- Single IRB, budget and contract for sponsors and contract research organizations (CROs)

CENTRAL IRB SERVICES

- Personalized attention for sponsors and investigators
- Assigned project managers
- Compliance Audits conducted by certified staff
- Weekly meetings
- Next business day notification of IRB decisions

Central Institutional Biosafety Committee (IBC)

- Central biosafety committee for gene transfer protocol review one week after IRB approval
- Committee composed of local IBC chairs & biosafety officers
- Expedites gene transfer trial initiation

MONITORING

- Supply monitoring for CROs, sponsors and investigator sponsors
- Supply medical monitoring by expert researchers
- Supplement trial staff; decrease travel time and cost

5.3. INITIATIVE 3: UNIFIED INSTITUTIONAL REVIEW BOARDS

Drugs, diagnostics, devices and other life science innovations are tested for efficacy and safety in clinical trials. Researchers use trials to learn more about how to improve and save lives, and trials can help a hospital earn income to fund other research and patient care.

An institutional review board (IRB) must review a trial before it can begin, but since each Massachusetts hospital operates its own IRB, drug and device companies cannot access all of the state's top medical centers at once.

By unifying the IRBs of Massachusetts hospitals, companies looking to conduct trials would have easy access to an unrivaled cluster of medical centers and patients. The state's share of clinical trial activity would increase accordingly, improving area hospital finances and providing local researchers with access to cutting-edge medicine. Increased trial activity would also give Massachusetts patients access to more innovative treatments.

5.3.1. Gap analysis

Clinical trials account for $10-20 BN in revenue for hospitals around the world. While Massachusetts contributes 8.1 percent of drugs in the world's pipeline, and 12.5 percent of the U.S. pipeline, it has only a 2 percent share of U.S. clinical trial activity. Given the state's strength in development, its unrivaled cluster of top AMCs close to top drug researchers, and its diverse population, Massachusetts should win a larger piece of the pie.

The main reason Massachusetts has a low share of clinical trial activity, according to interviewees, is that

Clinical trials are among the costliest elements of developing drugs and medical devices. A successful trial includes three phases:

- Phase I: Researchers test an experimental drug or treatment in a group of 20 to 80 people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
- Phase II: Researchers give the drug or treatment to 100 to 300 people to see if it is effective and to further evaluate its safety.
- Phase III: Researchers give the drug or treatment to 1,000-3,000 people to confirm its effectiveness, monitor side effects, compare it to other treatments, and collect other information that will allow the drug or treatment to be used safely.

A hospital's IRB reviews the trial proposal for each phase and decides if the hospital will participate. In Massachusetts, each hospital has an independent IRB that does not coordinate with its counterparts in other institutions.

its clinical trial approval procedures are particularly difficult. According to interviews, Massachusetts IRBs typically take six months or more to approve a trial, whereas competitors approve trials in half or even a third as much time.

Delays in any stage of the development process can be extremely costly for drug makers. In fact, speeding up the IRB approval time by a mere two months at each trial phase could be worth nearly $150 MM over the lifetime of a drug[4]. Hence, researchers tend to avoid locations, including Massachusetts hospitals, where delays are perceived to be likely.

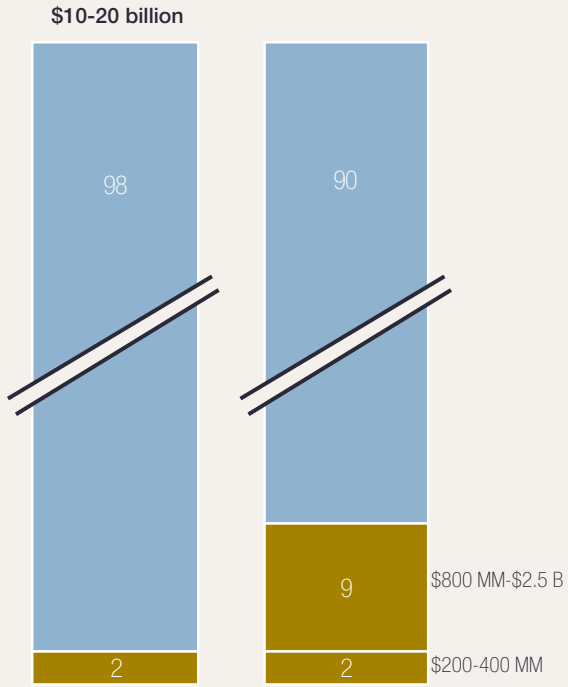
4 Assumes $800 MM annual sales; 2 month time saving per clinical trial phase, for 6 month earlier sales start

If Massachusetts' AMCs were to come together and create a streamlined, unified IRB, the trial activity in the state could balloon by two to 10 times, generating between $800 MM and $2.5 BN in additional revenue for area hospitals. Combining and restructuring the independent IRB activities of area hospitals would create a single point of entry into the world's leading cluster of AMCs, offering new incentives to conduct trials in Massachusetts.

5.3.2. Proposed initiative

To increase its share of clinical trial activity, Massachusetts must take two main steps:

EXHIBIT 6
Economic Impact of a Unified IRB



We wanted to do a trial at a Boston hospital. But by the time their IRB approved it, we had concluded the trial with other hospitals.

- SVP, Diagnostic company

1. Rationalize IRB decision-making criteria and procedures to generate a streamlined process that can be completed in less time

2. Develop a unified IRB to provide a single point of access to Massachusetts' cluster of top AMCs and diverse patient population.

A competitive analysis would show how other hospitals are able to approve trials faster. Interviews suggest two key drivers: increasing the frequency of IRB meetings and rationalizing the questions asked of investigators.

To unify the IRB activities of the area AMCs, a single IRB needs to be created and staffed by members of existing AMC IRBs. It should have approval authority for trials being proposed at any of the participating AMCs. In this way, it could uniquely facilitate multi-AMC research. It is imperative that the best practices identified through competitive analysis be applied to this new, unified IRB.

Potential complications

Some complications must be addressed for these steps to be successful. First, hospital IRBs take the time to ask the questions they do because they are concerned with patient safety and the value of the trial work. The competitive analysis must keep an eye on the safety outcomes and best practices of competing institutions.

Since a unified IRB would mean each hospital would surrender independent trial approval authority to another party, the unified IRB should include representatives from each participant hospital.

Even with representation, individual hospitals would no longer have direct control over trial liability exposure. For instance, the unified IRB may approve a trial in which a patient has an adverse reaction and sues the hospital where he or she was treated. That hospital might be held liable because of the decision of another party: the unified IRB. Participating hospitals should therefore establish an indemnity pool to purchase liability coverage over and above the insurance each hospital takes out for clinical trial activities. Providing an additional 50 percent coverage on top of what the hospitals purchase themselves would cost $8 MM per year[5]. Given that trial activity could exceed $2 BN per year in Massachusetts, this is a small sum and well worth the cost.

Feasibility

The key barrier to unifying the IRB process across area hospitals will be the issue of surrendering approval authority. This has been overcome elsewhere, such as in New York. The Biomedical Research Association of New York (BRANY) (see sidebar) unified the IRBs of several hospitals in New York and 36 other states and Canadian provinces, and also acts as an IRB-for-hire for other hospitals. As BRANY shows, with the proper structure, each hospital has sufficient input into the unified IRB's creation and representation on the unified board. The University of California also has a common review process in place, which allows multi-campus research to be conducted following approval from a single campus IRB (the arrangement covers research that is either subject to accelerated review or exempt). Other institutions, such as the multi-hospital Mayo Clinic, run single IRBs, proving that it can be done.

Owners

The key owners of the unified, streamlined IRB initiative are Massachusetts AMCs. They will need to work together to improve their IRB processes, and form a unified body with approval authority. Area hospitals especially have much to gain from this initiative.

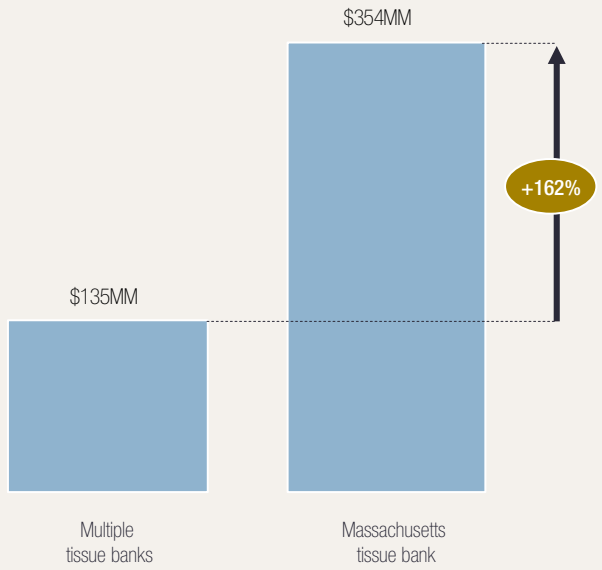
Those doing clinical research—pharmaceutical, biotech, device and diagnostic companies—should also help the AMCs create the new entity. One way industry can help is in performing the competitive assessment and identifying best practices. These companies have much to gain from improved access to Massachusetts' top AMCs.

5 Based on reserves required for premium necessary to cover new clinical trial activity (reserve requirement of 3:1 and premium of $0.55/$1,000 of revenue); adding 50% additional coverage above what hospitals would take out

We might spend three to four years in pre-clinical development, but if we had one place to get all of our samples, and they were consistent, we could easily take two to three years off of that time.

- Diagnostic Co SVP

EXHIBIT 7
Company Benefit
NPV of NDA PTOI



5.4. INITIATIVE 4: MULTI-AMC TISSUE BANK

We recommend that area hospitals create a large, virtual tissue bank. Working together, they would standardize tissue sample collection and permissions, cataloging, storage and retrieval.

This tissue bank would be a boon to researchers, who could search and order from multiple institutions simultaneously, confident that samples are of consistently high quality and uniformly prepared with longitudinal data for each sample. This would speed research by providing a broader and higher-quality sample pool. The tissue bank would be especially valuable in realizing gains in translational and personalized medicine.

5.4.1. Gap analysis

All hospitals engage in tissue banking in one form or another. Pathology departments regularly collect and maintain samples from patients, for example. But most institutions follow their own protocols for collecting and storing samples, and for obtaining permission for research use. The quality of patient history related to each sample also varies widely by institution, making research more difficult and time-consuming. It also significantly compromises the value of the samples themselves; if researchers cannot be confident about the clinical history of the patient, or about the exact methodology for collection and storage, their confidence in the integrity and scope of applicability of experimental results is reduced.

Unifying the banks of all of the state's top-flight AMCs would create an unrivaled resource for researchers, making Massachusetts the source of choice for pre-clinical samples. This would increase sample utilization and revenue. The AMCs would benefit by providing their own researchers with a superior sample bank.

The current state of tissue banking in Massachusetts, as in most areas, is therefore keeping area hospitals from realizing the full revenue potential of their banks, and impeding local AMC research activities.

Industry interviews revealed the great value of such a tissue bank, which could reduce development time by up to two to three years (see sidebar). This could translate to nearly $220 MM in additional value over the life of a drug, or a more than 160 percent increase[6]. Gains at this scale would make Massachusetts hospitals a focal point for LS companies as they develop their drugs, diagnostics, tools and devices.

6 Based on $800 MM in annual sales; $802 MM R&D cost; 2 year R&D time savings; 12% discount rate

Proposed initiative

The Harvard Medical School teaching hospitals, with funding assistance from the NIH, have created a centralized database of tissue samples. This facility, the Dana-Farber/Harvard Cancer Center Virtual Tissue Bank, focuses on providing tissue to speed research on cancer treatment. Researchers can search across all major HMS teaching hospitals to find relevant samples. The establishment funding provided for the digital cataloging of every sample, and a unified database and search system. What the funding did not do was standardize the procedures and practices around sample collection and storage, nor did it create a unified order or delivery method. Once researchers locate relevant samples, they must still approach the owners to gain access. The funding also did not extend to AMCs outside the Harvard network, such as the New England Medical Center or UMass Medical Center in Worcester.

Extrapolating from the work done at HMS AMCs to date (based on hospital size), it would cost an additional $2.9 MM to expand the HMS database to include other major hospitals in Massachusetts. The total project cost would be $4.5 MM to build and operate a multi-hospital virtual tissue bank[7].

While researchers would benefit from easier access to a broader sample bank, hospitals would benefit financially. First, they would increase tissue banking revenues as demand increases. They would also be able to charge more for each sample, since the service adds a great deal of value for researchers. With a 25-percent price premium over existing market rates for tissue samples, a 1.5-3x increase in demand would yield a 3-5x increase in profit for participating hospitals.

Participating institutions will also benefit to the extent that they license their research discoveries. Given that the lifetime value of these discoveries increases by 160 percent due to efficiencies gained from using the virtual tissue bank, as discussed above, license revenue to participating institutions would increase by the same amount. For instance, a $20 MM revenue stream would now be worth $53 MM.

Potential complications

Each hospital has its own methods of banking, and many have more than one set of procedures, given the autonomy of individual departments. This stands as a significant barrier to getting independent and competing institutions to adopt a set of standard operating procedures. While participation of some hospitals would be an improvement, the full value lies in universal participation.

A further complication lies in getting sample owners within the hospitals to comply. Pathologists and researchers tend to be protective of their samples, especially rare ones. Many sample owners balk at filling requests, especially when that is not their primary function.

Feasibility

The program needs to be structured and implemented to overcome these hurdles.

Sample owners could see value in participation if their departments collected part of the proceeds from sample sales. This could increase their budget for core activities, such as performing their own research. In addition to financial benefits, researchers would gain improved sample access themselves, thus enriching their own activities.

Hospital participation requires a similar solution. First, each hospital must be convinced that there is greater value in participating than in continuing stand-alone banking activities. Industry can help make this case by explaining that a virtual bank would significantly increase sample utilization, and thus drive up hospital tissue banking revenues. On top of sample demand growth, participating institutions could charge a premium above the market rate for tissue samples, given the added value to industry of using the virtual bank.

7 To develop a set of standards to control collection, cataloging, storage and delivery would take an estimated $1 MM. This money would fund an analysis of practices across area hospitals, and a view to best practices from outside institutions. It would then implement the set of best practices across all hospitals. Software that allows researchers to interface with the virtual tissue bank could be built off the existing HMS solution, at an estimated cost of $300 K. An additional $300 K would be required annually for systems upkeep and to fund a small management staff to coordinate and oversee the virtual bank.

Additionally, hospitals will want fair compensation and representation in virtual bank management. To this end, bank founders need to devise a management and compensation structure that fairly rewards those that contribute the most. Compensation could follow the same structure as discussed above for sample owners. To ensure fair representation, each participating hospital could designate a representative to the bank's oversight board, to which the bank management and coordination team would report.

Owners

As the owners and administrators of the current banks, the state's hospitals are the key actors in this initiative. The virtual bank design, and the standardized best practices and protocols, should be developed with industry participation to ensure that the resulting resource is optimal for researchers in both industry and institutions.

5.5. INITIATIVE 5: CLOSE MID-LEVEL TALENT GAP

We recommend that Massachusetts boost the supply of mid-level talent by improving community and state colleges and higher education, particularly the UMass system.

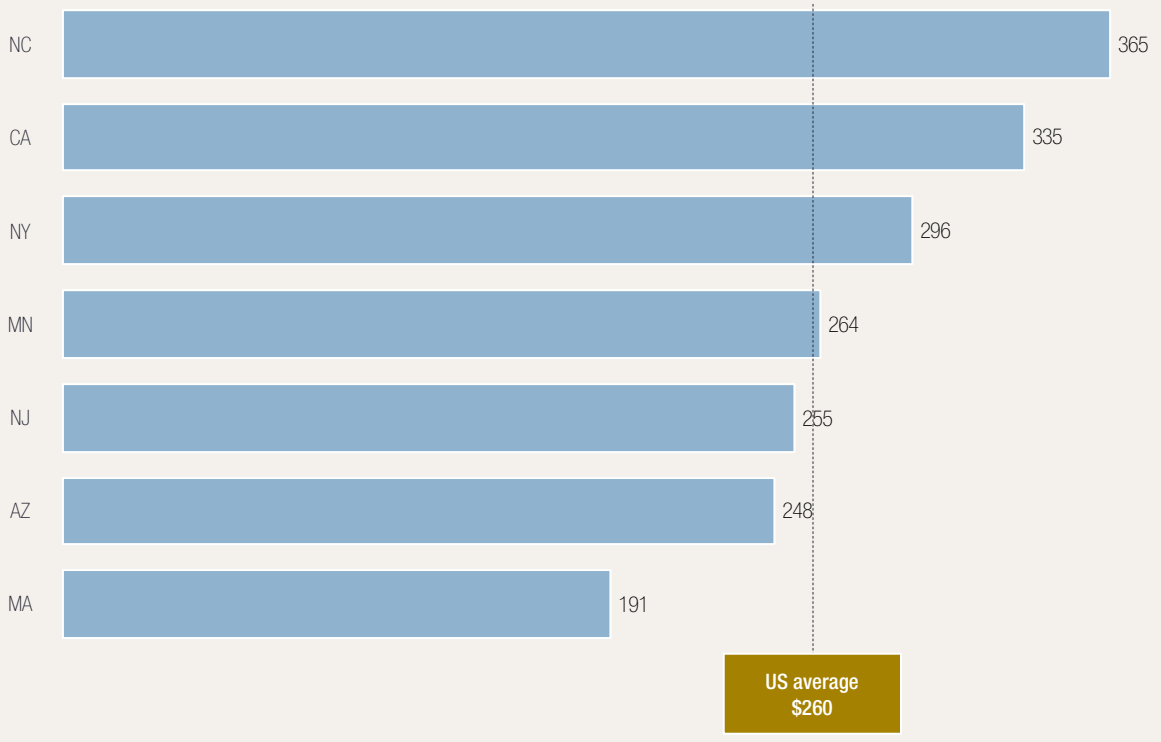
To develop best-practice programs, Massachusetts should look to other leading states, including California, Minnesota and New Jersey, and review the programs of states with aggressive LS aspirations and programs, such as Arizona, Georgia and North Carolina.

Government should work with industry to recruit and develop talent and deliver courses to create an engaged work force with relevant skills.

EXHIBIT 8

Competitor State Investment in Public Higher Education

2005 Dollars Per Capita



5.5.1. Gap analysis

Companies and institutions need a steady stream of talented technologists and technicians to work under the researchers emerging from the state's masters, doctorate and post-doctorate programs.

This kind of talent cannot be imported economically. Companies can afford to provide substantial relocation packages to lead investigators who offer skills and knowledge that could lead to multi-million-dollar products. They can't afford a similar relocation package for someone now making $35K in North Carolina, who would need much more to afford a similar standard of living in the Cambridge area. Therefore, mid-level talent must be developed locally.

This has played out in several ways for area employers. Because finding mid-level talent is hard, companies often fill positions with over-qualified people. This drives turnover as employees move up or leave to look for better positions. Life science employers must pay more for mid-level staffers in Massachusetts than in the rest of the country. Overall, mid-level American salaries fell by 1.2 percent between 2000 and 2005, but in Massachusetts, salaries rose by 4 percent. Interviews show that the trend has gotten worse since 2005.

This challenge is fueled by several factors: lack of proper training programs; lack of student interest in LS careers, and poor graduation rates.

Colleges lack programs to prepare students for careers in the life sciences. Middlesex Community College has created a new program in biomanufacturing (see sidebar), but schools must do much more to supply mid-level talent beyond this one area of the LS sector.

This illustrates the second problem, which is a lack of student interest. In 2005, a mere 5.4 percent of bachelors' degrees awarded by the UMass system were in LS majors. This compares to 17 percent for the UC system in California.

Finally, while interest and enrollment are key, students need to complete their educations to fill the demands of the LS sector. The three-year completion rate of

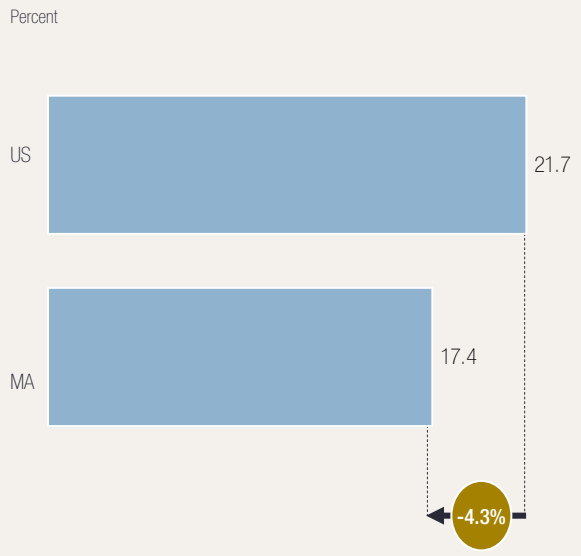
This project significantly reduced our recruitment costs and time. I was thrilled with the quality of the résumés I received.

Word is getting out that this training works. Our supervisors can really see the difference in the trainees.

The training was great for incumbent workers. They learned a tremendous amount about downstream and upstream processes that will help them be better in their own departments.

Massachusetts' community colleges is 20 percent below the national average. This shortfall reflects the paucity of full-time professors in the state's community colleges, and a lack of a support network or guidance for students as they face decisions about staying in school.

EXHIBIT 9
Community College 3-Year Completion Rates



This problem affects the non-profit world as well: area hospitals have trouble staffing technician jobs in their labs and in radiation and other departments.

5.5.2. Proposed initiative

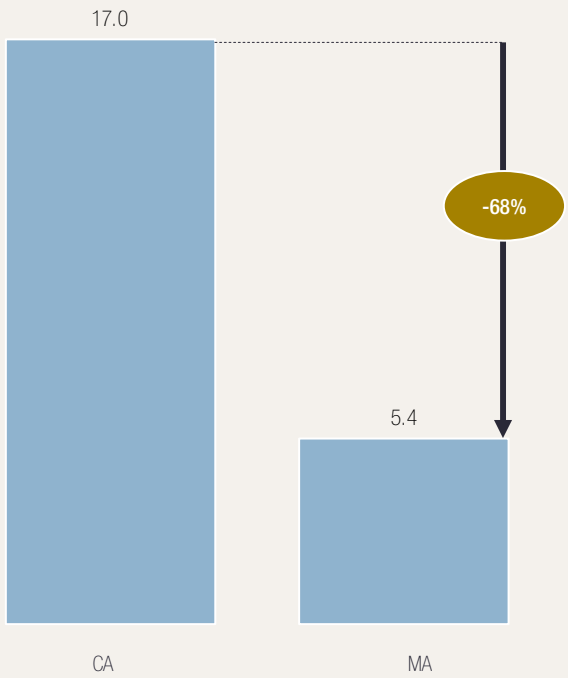
The state must perform a comprehensive competitive analysis to understand best practices for creating a robust mid-level talent pool. At the community and state college level, several approaches stand out:

- Develop LS-specific courses aimed at training and certifying technicians and technologists
- Ensure industry and academia collaborate on course and program design and delivery to ensure students graduate with relevant skills
- Ensure industry and academia collaborate on adult education and workforce training design and delivery to keep worker skills relevant

EXHIBIT 10

Public Undergraduate LS Degrees

Percent of total degrees conferred, 2005



- Take general steps, not LS-specific, to increase student graduation and completion rates, such as using more full-time professors or implementing a mentoring program with graduate students.

Undergraduate programs should focus on expanding existing LS courses while exposing students to LS employment opportunities. The industry and state can also take the following steps:

- Increase investment in UMass LS education to competitive levels (see Exhibit 10)
- Increase industry recruiting on campus to spark interest and enrollment by demonstrating a clear LS career path, using job fairs, posters, information sessions, and so on
- Offer internships to begin exposure to LS career tracks before graduation
- Recruit industry and institution leaders to speak at events and excite and educate students
- Institutionalize industry consultation on curriculum development to create and maintain relevant instruction that produces valuable employees, while defraying education costs by leveraging corporate resources.

Potential Complications

Lack of student interest presents a major barrier to producing mid-level employees. The technician program at Massachusetts community colleges was phased out as enrollment fell. Money is another issue. The state would need to spend more than an additional $400 MM on public higher education just to meet the national average[8], and nearly $660 MM more to match key competitors such as California, North Carolina, New Jersey and Minnesota.

Overcoming these hurdles requires stronger collaboration and cooperation between government, industry and academia.

8 Based on MA population and competitive per-capita spending levels

EXHIBIT 11

Proven approaches

States are succeeding with programs to improve education outcomes overall and for math and science in particular. w

Math & Science

- Math and science-focused programs are available at a local level
  - Russian School of Math
  - While scalable options can be brought in from outside
    - Singapore Math (OR)
    - US FIRST (NH)

General education

- Other programs in Massachusetts to improve pre K-12 educational outcomes
  - Stepping Stone
  - SquashBusters
  - Urban Scholars
  - Upward Bound

Feasibility

Other states have succeeded with collaboration between educators and industry to ensure sufficient resources, appealing jobs, and relevant curriculum.

In the high-technology sector, IBM's relationship with schools in California and North Carolina provides a good example of this kind of partnership. The company is a major employer of graduates from NC State and UC Berkeley, and worked with both schools to enhance the supply of consulting and support service employees by developing, funding and even teaching classes.

IBM attracted students by demonstrating a history of employment opportunities and a commitment to continuing it. The company even teamed up with competitors including HP, Oracle and Accenture to run collaborative curriculum design workshops to help others replicate its model.

Industry/university partnerships are nothing new. In the 1880s, California business leaders worked with UC Berkeley to develop a viticulture and enology program, which is now housed at UC Davis and considered one of the best programs of its kind in the world.

One of the ways this program maintains student interest is by engaging with industry to ensure relevance and to facilitate job entry. Close ties to Napa Valley and Sonoma Valley wineries are reflected in the program's active job database, which now lists nearly 100 positions open to students in the program, from internships to full-time appointments.

Owners

Academic institutions own these programs since they must secure funding and develop and run courses, but industry should be the driving force. Companies need skilled labor, and they must inform and inspire students about the opportunities. Companies may also be able to defray academic institution costs, for example by donating old equipment.

5.6. INITIATIVE 6: IMPROVE PRE-K–12 LS OUTREACH

To build its life sciences talent pipeline, Massachusetts must improve math and science outreach and performance in primary and secondary schools. The state should look nationwide for innovative solutions and new programs, such as Bio Bus, LS summer camp and internships. The state should also leverage new, scalable models of education to train teachers and supply improved curriculum and materials for students. Using resources such as MIT's OpenCourseWare and Singapore Math, Massachusetts can enhance curricula, bolster teacher knowledge and excite students about math and science.

5.6.1. Gap analysis

Primary and secondary (Pre-K–12) education builds the foundation of in-state talent. Massachusetts should invest in the community and state colleges and UMass and other universities, but for lasting impact, it must also improve students' prospects before they reach those institutions.

Massachusetts must address two challenges: the quality of education and students' interest in math and science. Education quality is a function of teacher skills and resources available. Interest arises from the quality of education, and cultivation throughout the elementary and secondary experience to show students the value of careers in science.

5.6.2. Proposed initiative

Massachusetts should work to improve math and science education and outreach. Other states have found innovative ways to foster general interest in math and science and build the abilities of students who show interest.

For example, several states have created traveling experiential programs called "Bio Bus" or "Mobile Lab." Arizona, Connecticut and Georgia have created exhibits that travel to every school in the state and stay for two to three days to engage students in interactive classes. Connecticut's BioBus, a program initially funded for five years at a cost of $3.6 MM, has been so successful that it has spawned related programs. Boston University has a similar program at select schools.

To maintain the interest of promising students, several states have started summer programs with a focus on the life sciences. Georgia, New York, Puerto Rico, Utah and others offer a variety of summer programs for high school students.

Massachusetts could offer a bio camp for under $1 MM by leveraging undergraduate LS majors as teaching staff, running the program as a day camp (thus saving on housing costs), and using idle lab and classroom facilities at local colleges and universities.

Another way to foster interest in life sciences is to offer an internship program to high school students. Several states have such programs, including California, New Hampshire, New Jersey and Pennsylvania. Programs range from assisting in hospitals and academic labs to commercial opportunities. New Jersey's program rotates students through biopharma companies, such as Johnson & Johnson and Merck.

Massachusetts could create an internship program relatively cheaply, as industry could bear the brunt of the cost. Only a small administrative staff is needed for program coordination. Internships could be unpaid, as well, to help control costs.

Potential complications

The state faces two key challenges: budgetary constraints and cultural biases.

Budgets are tight and show no signs of loosening. Paying for teacher training, new teachers, special programs and new equipment may seem impossible. One way around this is to leverage alternative resources such as corporate partnerships, as the

Massachussets Biotechnology Council has already done with its Bioteach program, which works to improve high school lab facilities and teacher skillsets in the state. Biogen Idec has carried out similar work in the Cambridge and Somerville school systems. Likewise, Mass Insight itself has recently received a $13M grant from Exxon-Mobil to improve AP math and science in Massachusetts' high schools.

Even when money can be found, cultural biases in Massachusetts may block such connections, since some people believe industry involvement changes basic education into vocational training. Designing a curriculum with industry assistance and support does not have to mean turning the program over to industry, however.

Feasibility

Two mechanisms can address financial constraints:

- Scalable programs can be rolled out widely without drastically raising costs. Models include Johns Hopkins CTY, a distance learning program for grades 4-12; MIT's OpenCourseWare, which provides online versions of every MIT course; and Singapore Math, a self-guided program based on Singaporean methods
- Non-traditional resources, such as corporate sponsors and classes developed and taught by industry leaders.

Scalable solutions, such as a Web-based curriculum, can impact a great number of students and teachers without the high costs of traditional solutions, such as buying new lab equipment and hiring a new science teacher at every school. They can also help ensure consistency and quality, and fill gaps in existing resources, educating students in areas where teachers may lack knowledge.

Non-traditional funding sources may also help fill gaps. As noted above, Bioteach and Biogen Idec's provision of laboratory and instructional resources saves the school systems money.

Owners

Ownership of this initiative should rest with school boards at the state and local levels. Industry and other institutions have important roles as partners in curriculum development and funding.

6. BUILDING MOMENTUM AND COMMITMENT

Our research leads us to believe that Massachusetts can make great leaps in the life sciences if it can take a few small steps in leadership, collaboration and fresh thinking. If a handful of champions will come forward, and interested parties will gather for discussion, major new opportunities lie within reach.

Key stakeholders should commit to regular progress reviews to maintain momentum and identify and address challenges as they arise. As new information becomes available, the group will undoubtedly adjust its priorities. Their decisions should be informed by a cluster-wide perspective, taking into account all of the state's options.

We believe Massachusetts needs an additional commitment to addressing longer-term challenges beyond the realm of the life sciences. An overhaul of Pre-K–12 education, for example, and new investments in transportation and communication infrastructure, would benefit all of the state's businesses and citizens.

Thus, this set of initiatives should be seen as a starting point for an ongoing process involving an evolving portfolio of initiatives.

Building and maintaining momentum to strengthen the life sciences cluster will require a concerted effort spanning the range of stakeholders. One of the themes that emerged consistently from our interviews was that Massachusetts lacks a strong collaborative culture. Some of our interviewees also believe that Massachusetts' success has hindered focused, sector-wide engagement because it has fostered a sense of complacency.

We hope that this report will help remove any complacency. Massachusetts has tremendous potential in the life sciences, but also faces genuine challenges. Taking success for granted could be disastrous in the face of new competition. As one of our interviewees said, "the days of a Massachusetts monopoly are over." Complacency aside, success will require greater coordination. Many of our interviewees pointed out that the cluster as a whole lacks a representative body, that no forum coordinates the diverse stakeholders who constitute the cluster.

The recently-established Life Sciences Collaborative (LSC) has the breadth of representation to fill that void; we hope that LSC, or some equally broadly representative body, can play the required role. Massachusetts has the assets to lead in LS innovation; stronger cross-sectoral collaboration will help it leverage those assets to maximum effect.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