



# IMPACT 2020

Advancing Massachusetts Leadership  
in the Life Sciences For Patients

HEALTH ADVANCES



Full Report  
April 2014

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We drive innovation by creating a forum for the biotechnology community to come together, educating the public and policymakers, influencing public policy and advancing the economic interests of individual companies, as well as the sector as a whole.

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## HEALTH ADVANCES

Health Advances is a healthcare strategy consulting firm based in Weston, Massachusetts. With over 95 professional staff, a team of eight partners, and offices in San Francisco, Washington DC, and Zurich, the company advises life sciences companies, including biotech, pharmaceutical, medical device, diagnostic, and information technology companies, as well as organizations that invest in, service, and collaborate with those companies on product commercialization, corporate strategy, and transactions.

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## Foreword

Impact 2020 is the culmination of nearly nine months of meetings, discussions, interviews, online and in-person focus-sessions with a diverse set of life sciences stakeholders about the future of the industry. What these conversations brought to light is that although the current headlines are rosy—the NASDAQ Biotech Index was up 60% at the end of 2013 and 37 biotech IPOs occurred last year<sup>1</sup>—there is a very real reason for concern about the cluster's future. With ongoing national conversation about healthcare costs and a shrinking pool of seed and early-stage funding options, the Massachusetts life sciences cluster is at a crossroads.

This document is a call for action. Over the next five years, we will see a transformation in healthcare, the outcome of which no one can fully predict. If life sciences industry leaders do not take a leadership role in crafting a balanced approach to assessing value, the rules will be dictated to them.

MassBio will continue to serve as the greatest advocate for the Massachusetts life sciences cluster and for all the life-altering therapeutic and diagnostic solutions that its academic research centers, teaching hospitals, and companies provide for patients. MassBio embraces and accepts the recommendations of this report as a mandate to advocate for change, to convene industry leaders, and to offer relevant programs that prepare our constituency to respond to the rapidly changing environment.

Bending the healthcare cost curve, constraints on government R&D spending, and consolidation of healthcare decision-making are global trends and the opportunity to influence these trends is not always local. But the cluster has a lot at stake and the decision on whether to take up the challenge will have global implications. Other life sciences clusters are looking to Massachusetts for leadership. Only in Massachusetts, where there is an aggregation of leadership across all sectors, is rational change possible.

Therefore, the messages contained in this report are not limited to the leaders of the pharmaceutical and biotech industry, but extend to leaders of government, universities, hospitals, payers, service providers, investors, and other organizations involved in healthcare. If all agree that the life sciences cluster in Massachusetts is special, if new products emerging from local universities, hospitals, and companies are valuable, if consumers and patients deserve a better outcome, then all stakeholders must be engaged and ready to act with a sense of urgency. The implications of decisions today, the clinical trials that start or don't start, the companies that are founded or not founded, will not be evident for 10 to 20 years.

Healthcare is all about patients, and value will ultimately be measured in patient outcomes. Massachusetts is in a strong position, but with success comes responsibility. MassBio and its Board of Directors are prepared to engage, provide leadership, champion innovation, and ultimately help deliver meaningful new solutions for patients.



## Chairman's Note – The Unintended Consequences

An attractive public market creates more options for building viable life sciences companies, and, after years without a real public market for biotech stocks, it is exciting to see the rebound of the last year. Venture investors are more willing to take on risk knowing there are multiple options for an exit. Carrying products deeper into clinical development before licensing the product or selling the company is possible. As an industry we benefit from more strategic options with multiple models for success. Ultimately, more products will be developed and delivered into the hands of patients, and more companies can mature into fully-integrated operations employing hundreds of people.

As explored in the 2020 Report, Massachusetts has long served as a model for healthcare innovation and healthcare reform for the rest of the U.S. MassBio supports evidence-based healthcare reform. In implementation, it is critical to establish value-based decision making; otherwise we will likely see short-sighted decisions based only around cost control versus value creation. Part of MassBio's role is to ensure that the healthcare reform implementation process prizes proven innovation, and ultimately that patients will benefit.

Based on recent events, Organogenesis (our company), can serve as a case study in this regard, as we have just gone through the opposite experience. Founded from technology developed at MIT, we were the first company to successfully commercialize and mass-produce an FDA-approved product containing living human (skin) cells.

The Centers for Medicare & Medicaid (CMS) recently “bundled” proven, FDA-approved products (like ours) for wound healing, alongside FDA-cleared products and supplies used as wound coverings. The unintended result of this decision is that healthcare providers are now financially incentivized to use products with little to no evidence of effectiveness on patients who are at serious risk of amputation. As a result of these misguided efforts, innovation and patient access to important health modalities are being stifled.

Impact 2020 sends a clear message. Value is important, but what is even more important is the process by which we assess and measure value, and institute cost containment. For with every decision that is made, there are unintended consequences that we cannot fully anticipate. Investors, whether it is a venture fund, a mutual fund, or the federal government, need some measure of predictability. Otherwise, the risk in an otherwise already risky business is untenable. As this report documents, investors are already pulling back and the Massachusetts life sciences cluster is highly vulnerable.

Who loses if U.S. healthcare reform is not well-implemented? Ultimately it is the patient, who loses access to proven medicine and care.

While the burden is largely on life sciences companies to demonstrate value, we must have a productive discussion among leaders of all sectors—government, scientists, product companies, payers, healthcare providers, and patients—regarding the metrics, data, and analytic processes that will drive reimbursement decision-making. For instance, is it better to save money during an episode of care in treating a patient with a chronic condition? Or is it ultimately better practice to utilize breakthrough technologies up front, in order to improve the patient's overall health and to avoid complications created by the disease? The consequences of these decisions will affect not only a few patients with one condition, but the entire life sciences industry and patients for generations to come.

On behalf of the Board of MassBio, I would like to thank the Impact 2020 team and all the contributors for raising our awareness of these critical questions and issues. For my fellow industry executives and Massachusetts business leaders, it is now our challenge to listen, to engage and to lead.



Geoff MacKay  
Chairman of the Board, MassBio  
President & CEO, Organogenesis Inc.





## Chairman Elect's Note – Nurturing our Entrepreneurs

Over the past decade I have had the good fortune to lead three biopharmaceutical companies through their formative years as CEO; Acceleron, BIND and most recently Civitas. The opportunity to improve patients' lives provides a unifying sense of urgency and clarity of purpose within each company as well as across the broader life sciences community. For me personally, the Massachusetts life sciences cluster made the improbable act of starting a successful company not only possible but repeatable.

While Massachusetts provides the world's most fertile ground for biotech startups, Impact 2020 highlights some troubling funding trends. NIH funding is declining in real dollars. Venture funding has dropped by two-thirds. Seed funding is particularly challenging to access. We are fortunate to have venture funds in Massachusetts that continue to cultivate bold new ideas and fund fascinating companies, but the universe has shrunk to where even seasoned entrepreneurs are finding it increasingly difficult to secure the necessary funding.

This comes at a time when many innovations in life sciences are arguably reaching a breakthrough point. Companies like Epizyme (epigenetics), bluebird bio (gene therapy), Foundation Medicine (actionable genomic information platform), BIND (nanoengineering and cellular targeting) and Alnylam (RNAi) are now translating concepts into products that enable entirely new approaches to disease management. In the not too distant past these technologies were largely viewed as futuristic visions. With an unprecedented wealth of advances on the horizon, will worthy ideas be able to secure funding to fulfill their promise to patients or, alternatively, remain unrealized visions?

We all have something at stake in the future of life sciences startup vitality in Massachusetts. Impact 2020 raises important questions for our industry leaders about starting companies.

A decade ago, working at Millennium provided me and many of my colleagues the entrepreneurial education and broad network that made my leap to a startup possible, just as Genetics Institute, Genzyme, and Biogen Idec did for others. The resulting diaspora spawned generations of new companies that continue to grow the workforce, expand specialized service industries and maintain a highly mobile talent pool. For example, with Civitas' Parkinson's disease therapy entering the final stages of development, I stepped down as CEO in January and hired a successor uniquely experienced in commercializing products, the priority being to ensure our important therapy becomes a successful product. This critical process of matching the right talent to the needs of an evolving company is just one of the many dynamics uniquely facilitated by our cluster's ecosystem. With the growing headwinds from the macro-environment, this historic model may not be self-sustaining without a coordinated effort.

If we want to see more companies started, we need to find ways to provide more support to counteract escalating startup hurdles. As cited in Impact 2020, MassBio has been able to reduce the hurdles for tenacious and talented entrepreneurs through initiatives like the education programs, networking Forums, Purchasing Consortium, and MassCONNECT. This is a start; a focused effort can make a difference.

Twenty-five years from now I am hopeful that we will be able to look back on this period of time and say that our concern was over blown. The best ideas did indeed receive funding. Investors were able to craft a business model that made financial sense. Intrepid entrepreneurs did find a way to start new companies. More virtual, capital-efficient business models evolved and reversed the current investment trends. Given the stakes, we cannot leave this to chance.

As the next Chairman of the Board for MassBio, I look forward to working with my fellow Board members, my industry colleagues and the MassBio staff to internalize these challenges and translate them into actionable initiatives. We are aware of the looming existential threats and will leverage every resource available to preserve entrepreneurial vibrancy and ensure innovation continues to thrive and improve the lives of patients.



Glenn Batchelder  
Vice Chairman of the Board, MassBio  
Founder and Board Member, Civitas Therapeutics



## President and CEO's Note – A Bold Vision

Impact 2020 challenges us all to recognize the global trends facing healthcare and the impact these changes could have on our local life sciences ecosystem. Massachusetts is the best place in the world to start and grow a life sciences company and our goal at MassBio is to provide the support necessary for industry to continue to thrive. The project team behind this report has worked diligently to capture the voices of diverse stakeholders, and we hear the message loud and clear: focus on value, company formation and sustainability, the opportunity in information technology, and ultimately, the patients. These themes and the associated recommendations will guide MassBio's programs for the next several years.

Today, more than ever in our history, we represent a very broad and diverse constituency: biopharma companies of all sizes, contract research and manufacturing organizations, academic institutions and medical centers, suppliers, vendors and disease foundations. Impact 2020 addresses each level of the value chain, from academic research to marketed products, and we strive to do the same.

As this report shows, Massachusetts' strength depends on its vibrant startup and early-stage research activities, but funding for those activities—the fuel for industry growth here—is getting more difficult to come by. We must explore new and innovative funding models, and we at MassBio are poised to connect our companies with the diverse range of sources of capital that do exist.

Toward this end, we strongly endorse the re-authorization of the Life Sciences Initiative (LSI) and support for the Massachusetts Life Sciences Center. As we heard in the course of this work, we cannot underestimate the value of the positive message that is sent to the industry by the state's support of the LSI. Massachusetts' success in research and development is the model for many other clusters around the world, but for larger companies with commercial and manufacturing operations, the argument to locate in Massachusetts is more tenuous. The state needs to provide incentives and attain a critical mass of biomanufacturing and commercial talent so recruiting here is easier than elsewhere. Our education foundation, the Massachusetts Biotechnology Education Foundation (MassBioEd) can support the state by playing a pivotal role in connecting companies with secondary and higher education institutions to identify and implement best practices in workforce training. Commercial and manufacturing organizations do not need to be in Cambridge, as evidenced by Shire, Organogenesis, Cubist, EMD and others. The broader state stands to benefit.

I am particularly excited by the opportunity presented by the report to establish Massachusetts as a leader in life sciences information technology. We stand ready to work with leaders in the information technology industry to explore potential collaborations, to exchange insight on applying IT solutions to complex life sciences problems, and to build a skilled workforce to support data collection, analysis, and application in product development.

We in industry understand why we do what we do: it is all about the patients. While the next five years will be characterized by disruption in healthcare, with battles over new delivery models, reimbursement paradigms, and funding approaches, we must not lose sight of the patients counting on us to find new treatments and cures. We must take time to celebrate the impact that products like Apligraf, Tecfidera, Kalydeco, Kynamro, and others have had on patients' lives. At this report's recommendation, MassBio will take on a very personal challenge to collect, curate, and share patient stories, not just within industry, but with the public. Patients around the world are alive and enjoying a better quality of life today because of our vibrant life sciences cluster, and as an industry we need to let people know that.

I would like to thank the Board of Directors, Steering Committee, Advisory Board and everyone who contributed to the planning process, along with the teams from Health Advances and the MassBio staff for preparing a thorough and thoughtful strategy.

No cluster is better positioned to survive the turmoil and thrive over the next five years. We welcome the opportunity to work with our fellow leaders in Massachusetts on the next generation of treatments and cures.



Robert Coughlin  
President & CEO, MassBio



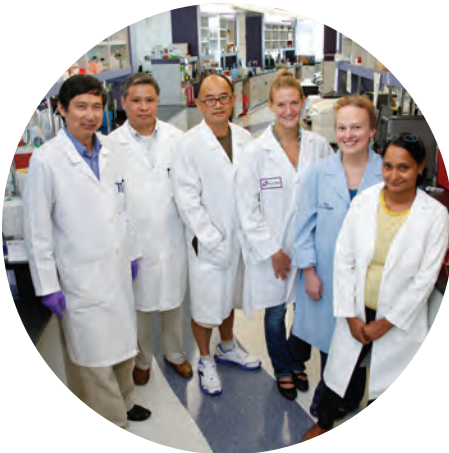
# Impact 2020 Executive Summary

## The Vision

**Advance Massachusetts' leadership in the life sciences industry, championing innovation in order to bring value to the global healthcare system and make meaningful impact on patient lives.**

Four **themes** dominated discussions during the Impact 2020 strategic assessment. Each one leads to a set of recommendations to ensure the industry's success into the future:

1. **Demonstrating Value** – There is a genuine concern across the industry that the intense focus on reducing healthcare spending will undermine the reward for innovation, elevate the risk for companies and investors, and stymie life sciences research and development.
2. **Supporting Company Formation and Sustainability** – Without focused, consistent support and attention, life sciences companies, particularly at the seed and Series A levels, will be at risk. Alternative sources of funds may not fill the gap, leading to fewer companies forming and surviving.



3. **Opportunities in Life Sciences Information Technology** – Massachusetts has an important opportunity to take the lead in developing information-based solutions that increase efficiency and mitigate risk at all levels of the biopharma value chain, from basic research to patient care.

4. **Articulating the Patient Focus** – The industry appears on the verge of major medical breakthroughs, yet concerns about company formation and reimbursement policies could prevent the benefits of those therapies from getting to patients.

## Massachusetts Life Sciences: A Potent Force, from Bench to Bedside

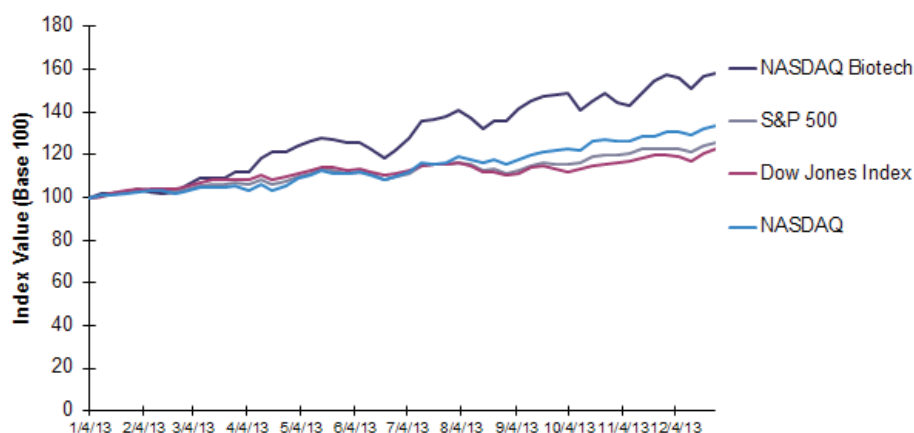
**“We need to continue to be aggressive; we cannot rest on our laurels.”**

**– Steven Knight, President and Managing Partner, Fidelity Biosciences**

At the time of this report's publication, Massachusetts is simultaneously driving and riding a renewed wave of interest in the life sciences industry. The NASDAQ Biotech Index was up 60% and 37 life sciences companies had IPOs by the end of 2013.<sup>2</sup> Fourteen IPOs were completed by Massachusetts companies in the last 12 months, raising over \$1.3 billion dollars<sup>3</sup>, which will directly translate into greater R&D investment and job growth. Massachusetts venture firms, many of whom survived the downturn in 2008, are reaping returns on a backlog of fascinating science.



## Public Biotech Index vs. Standard Indices 2013 Performance

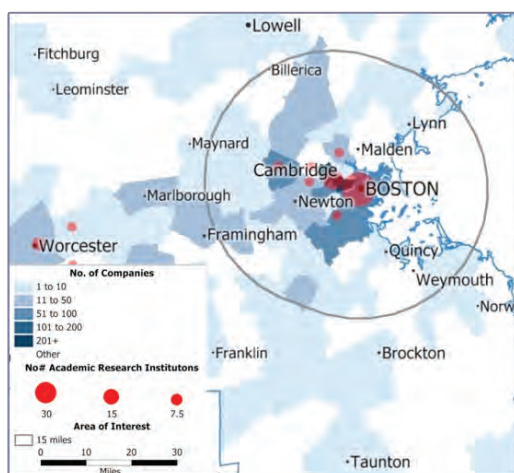


Source: NASDAQ, S&P 500, Dow Jones Index.

While Massachusetts is the second largest recipient of NIH grants<sup>4</sup> and therefore a leader in basic research, a quick review of 2013 IPOs demonstrates that Massachusetts also has a vibrant product development pipeline with potential advances in gene therapy (bluebird bio), genomics-based diagnostics (Foundation Medicine), orphan diseases (Agiros), epigenetics for cancer (Epizyme), RNAi therapeutics (Dicerna) and new antibiotics to address resistant bacterial strains (Enanta and Tetrphase). From basic research, to advanced product development, to transforming the lives of patients suffering from cystic fibrosis, multiple sclerosis, cancer, Gaucher's Disease, diabetic foot ulcers and many other conditions, Massachusetts is home to it all.

Massachusetts' strengths in the life sciences stems from a heritage of innovation and a rich density of leading organizations across sectors, from top NIH-funded hospitals, to world-ranked universities, to biotech pioneers, to large pharmaceutical companies, to highly respected investment firms. Leaders in other domestic and international clusters point to Massachusetts as a global model for innovation and highlight the unique advantage of a powerful, concentrated network with Kendall Square in Cambridge at its heart.

## The Concentration of the Massachusetts Life Sciences Cluster



*"The beauty of Massachusetts is that it has such a concentration in Kendall Square. This has created more of a culture of working together and being part of a club."*

*"I can walk 10 minutes and can talk with some of the best researchers in the world."*

*"When it comes to finding the necessary talent, it is all here."*

*"Even recruiting from outside the region is easier because if it does not work out with one company, recruits can find another position without moving their family."*

*"Not only do we have professional relationships, we run into each other on the soccer field on Saturday morning."*

*"VCs want to invest in the people they know."*

Source: Health Advances interviews and analysis.

# A Question of Value

**“Organizations can come together to solve problems that reduce cost, improve outcomes, and improve the quality of care.” – Paul Bleicher, CEO, Optum Labs**

Under the veneer of positive news, there are many concerns and questions regarding the sustainability of the cluster. Healthcare is going through a dramatic transformation and the outcome is unpredictable. A rapidly escalating national debate on controlling healthcare spending is already having a dramatic impact on life sciences in Massachusetts:

- NIH funding (in real dollars) is contracting and Massachusetts is particularly vulnerable. Only California receives more NIH dollars than Massachusetts. Academic institutions are feeling the pinch and are increasingly looking for supplemental sources of funding. With the average age of a first research project grant recipient now at 42 years of age,<sup>5</sup> research institutions must find other funds for talented new postdocs so they can generate data and publications and compete for grants.
- Teaching hospitals seeking a path to sustainability within the guidelines of the Affordable Care Act and operating as Accountable Care Organizations face difficult trade-offs. Declining revenues force difficult investment choices between preserving the quality of patient care, investing in outpatient care options, training doctors and other professionals, adopting new medical technology, and supporting research as they try to survive in an intensely competitive local healthcare marketplace.
- Some reports suggest that venture firms are investing in fewer life sciences companies, particularly at the seed and series A level.<sup>6</sup> There are still many strong funds in Massachusetts, but the hurdles are much higher even for a seasoned entrepreneur. Escalating competitive intensity should lead to stronger companies, but possibly at the cost of not funding companies with intriguing but less well-packaged ideas.
- Silicon Valley Bank, the National Venture Capital Association, Dr. Joshua Lerner from Harvard Business School and others have investigated trends in the level of venture funding and have concluded that funding is down significantly from its peak in 2007 and is not likely to return.
- Decisions made by the Centers for Medicare and Medicaid Services to dramatically cut reimbursement for entire classes of drugs and devices have sent a chilling message to companies and investors regarding their ability to count on a return on investment. Uncertainty and risk levels are higher for everyone.
- All life sciences companies with products face investment challenges. For companies like Cubist, AMAG, and Alnylam, the product value story is no longer just about efficacy and safety, but also about the cost and benefit to the healthcare system. Even emerging companies must learn “payer speak” and develop their strategies from the start on how they will secure market access.
- In the state legislature, discussions are underway regarding healthcare cost containment measures and drug reimbursement. The state has a mandate to look for avenues to reduce healthcare costs. However, any highly restrictive policies will have strong repercussions and potential unintended consequences for the local life sciences sector.



## Putting Patients First

**“Biotech and pharmaceutical companies need to show that they are there for the patients.” – Robert Beall, CEO, Cystic Fibrosis Foundation**



The benefit of life sciences innovation for patients cannot be overshadowed by the determination to rein in costs.

MassBio, the life sciences industry, and leaders in other healthcare sectors have an obligation to ensure that patients have access to new therapies, which means the value delivered by those new therapies are clearly understood and communicated. MassBio should communicate the unmet needs of patients and the opportunity to enhance patient care through life sciences innovation in its advocacy, public education, and programming efforts.

Value must be measured in terms of patient outcomes. All the critical stakeholders are here in Massachusetts and they have a huge incentive to get the value equation right. It

is tempting for product companies, payers, and providers to enter into zero-sum discussions around pricing. As Gary Gottlieb, CEO of Partners HealthCare, said, “When value is measured in terms of our patients and their outcomes, we are all on the same side of the table.” Susan Windham-Bannister, President & CEO of the Massachusetts Life Sciences Center, said “If all parts of the ecosystem work well together, then the ecosystem will be stronger.”

Life sciences industry leaders must be proactive participants in future discussions regarding the value of medical technology. Progress on the value discussion will require the collaboration of stakeholders in the life sciences and other healthcare sectors. They must define what is meant by value and how companies can best assess and demonstrate value for novel medical technologies. Massachusetts is widely seen by industry observers outside the state as the best place to make progress toward a productive debate on value-based goals, metrics, analytic tools, data requirements, and outcome assessment algorithms in healthcare.

Toward that end, there are **four key recommendations** for MassBio that will advance this effort:

1. **Convene a Value-Based Care Working Group** – Assemble a high-profile, cross-sector working group for quarterly or biannual meetings to engage in an ongoing dialogue regarding solutions for value-based care, reflecting the needs of all parties.
2. **Advocate for the Value of Innovation** – Work with national and state legislators and government officials to build awareness for how value is created by local companies, the importance of the life sciences sector overall, and how policy initiatives may hinder innovation. Communicate the value of innovation for patients to the public.
3. **Engage Payers and Providers** – Encourage engagement across various stakeholders. At the highest level, MassBio, its President and its Board should seek out opportunities to involve representatives from payers and providers in an ongoing discussion of the local opportunities, potentially through Board seats.
4. **Develop More Value Programming and Education** – Continually inform MassBio members regarding value initiatives and patient impact, and provide a curated resource center to educate companies on payers and providers, their interests and incentives.





# Ensuring a Vibrant Startup Environment

**“What I do find really disturbing is the longer term macro trend around the shrinking number of venture firms active in biotech – and the number of partners in those firms.” – Bruce Booth, Partner, Atlas Ventures**

Startups are the life blood that ensures the vibrancy of the cluster. Startup access to money and availability of small-footprint, flexible, affordable spaces are two critical issues that Massachusetts needs to address.

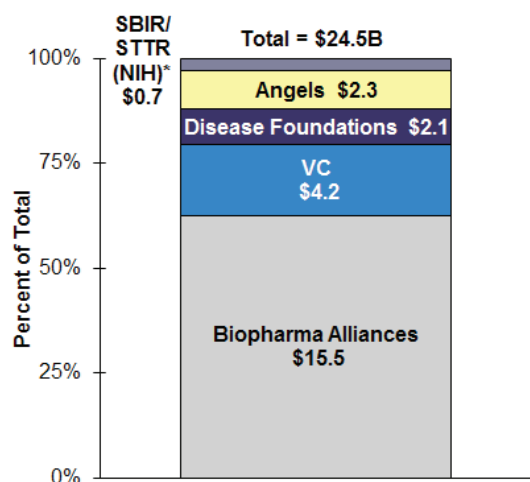
Obtaining a seed round or Series A round of funding is a critical milestone for a new technology as it progresses from the academic laboratory to the patient. There is evidence that there are fewer venture firms and fewer venture dollars available to invest in the life sciences, so the hurdle for new companies is rising. Below is one dataset from Silicon Valley Bank that illustrates a 50% decline in venture funds raised to invest in life sciences firms over the last five years.

**Recent Declines in Venture Capital Raised (\$M) for Life Sciences Investing**



Source: Silicon Valley Bank.

**Total Capital Invested in Biotech, U.S., 2012  
Venture Capital and Other Sources**



Source: NIH RePORT, NVCA, PWC, and Thomson Reuters - MoneyTree Report, Halo Report 2012, UNH Center for Venture Research.

In Massachusetts, the goal should be to optimize a fair playing field and then let science and markets determine what succeeds. Every company cannot receive all the funding it needs, but it is in the best interest of the cluster to help entrepreneurs, investors, and other stakeholders efficiently access novel science, capital, space, talent, and other resources to at least take the first steps toward company creation.

The venture capital model has changed and most believe few new funds will be formed in the future. Some funds have moved out of the life sciences completely and others have moved to later stage investments. Even the stronger, more experienced, committed life sciences funds are exploring new models, pursuing venture creation strategies and forming internal accelerators. Corporate venture firms now account for about 15-20 percent of life sciences venture capital deals and some of the larger pharmaceutical companies are experimenting with their own incubators and accelerators.<sup>7</sup>

Alternate funding channels like angels and angel groups, disease foundations, family foundations, wealthy individuals, and crowdfunding can account for as much capital as do venture funds. Today's early-stage entrepreneurs are increasingly exploring many or all of these funding channels to move their companies along. Entrepreneurs are determined to find funding to support their vision and technology platform. As one entrepreneur stated, "Venture has left us, now it is time for us to leave them." Their intrepid spirit bodes well for the future of the Massachusetts life sciences cluster.

Startup space is also a great concern for early-stage entrepreneurs. As larger, single tenant lab facilities have been built in Kendall Square, the availability of smaller spaces for emerging companies has tightened. Rents in Kendall Square have risen to \$50-\$60 per square foot.<sup>8</sup> Watertown, Waltham, Lexington, Worcester, Burlington, Woburn and other locations outside of Cambridge offer options for many companies, but for many early-stage companies, access to universities and the wealth of operational talent in Cambridge remains a strong preference.



Life sciences startups are the key to a vital local life sciences economy and Massachusetts should take steps to ensure entrepreneurs have a fair chance to succeed or fail. The Commonwealth of Massachusetts, local governments, established companies, and MassBio should **expand efforts** to provide assistance to early-stage companies through **several initiatives**:

1. **Expand MassCONNECT** – This program, sponsored by industry through MassBio, has proven to be a valuable vehicle for mentoring entrepreneurs. Beyond mentoring, MassCONNECT can become a central hub for accessing space, talent, and other external resources to support a capital efficient early-stage business model.
2. **Maximize Access to Existing Funding Options** – The “valley of death” from seed funding to Series B has expanded. MassBio can maximize access to existing funding options by collecting information on alternative sources and connecting entrepreneurs with a diverse range of investors.
3. **Convene Startup CEOs in Small Group Forums** – Each funding source has its own learning curve. Startup CEOs are eager to learn from each other, to determine which models might work best for their businesses, and to quickly adopt best practices for pursuing funds, convincing decision-makers, and managing investors. Sharing information and best practices on alternate financing could be achieved through more startup CEO group forums.
4. **Advocate for More Funding Options** – MassBio should work with the Commonwealth of Massachusetts to expand the funds available to early-stage companies through the Massachusetts Life Sciences Center. In addition, MassBio should continue to advocate for increases in NIH funding. Government leaders must not underestimate the importance of research institutions. They are a critical resource to attract industry partners and serve as an engine for the Massachusetts economy.
5. **Promote the Massachusetts Life Sciences Cluster** – With capital at a premium and escalating pressure to demonstrate value, companies and investors across the United States and worldwide will be searching for the best place to start and operate a life sciences company. Industry, state, and local agencies should come together to ensure that companies and investors are aware of what Massachusetts has to offer.



## Joining Forces to Advance Massachusetts' Leadership in Life Sciences

**"If anyone can do well in this difficult environment, it is Massachusetts. They have all the pieces." – California Biotechnology Executive**

Despite all the turmoil in healthcare and the uncertain outlook for drug discovery and research, clusters across the United States, Europe, and Asia are intently focused on building their own version of the life sciences ecosystem found in Massachusetts. Captured below are several of the notable investments and partnerships that are underway.

- **China:** Five-year, \$300 billion plan to develop the biotechnology sector between 2011 and 2015. Includes plans to sponsor more than 160 drug development programs and create 1 million jobs.<sup>9</sup>
- **New York City:** Several \$100 million+ public-private partnership investments in biotech, e.g. \$140 million raised as of early 2014 for New York Genome Center through institutions, philanthropies, and government grants.<sup>10</sup>
- **Houston, Texas:** University of Texas M.D. Anderson Cancer Center launched 10-year "Moon Shots" campaign in late 2012, aiming to invest \$3 billion to attain ambitious goals in the prevention, detection, and treatment of various cancer types.<sup>11</sup>



For life sciences companies today, Massachusetts is the place to be, but the environment can change quickly. Well-funded venture firms see an advantage to keeping their early companies close to their research roots and close to their local offices. Kendall Square is the hub, but prices are rising, space is at a premium<sup>12</sup>, and transportation infrastructure is stretched.

Massachusetts should compete for companies across the lifecycle spectrum. Maintaining the Cambridge core is essential, as is providing opportunities for companies across the state at more competitive price points. In competition with other regions that often have lower costs and greater incentives, Massachusetts needs to tell its story of qualitative benefits convincingly—and proactively.

Anchor companies provide stability to a cluster and spin-off experienced executives who will lead future generations of companies. The impact of successful anchors can be seen by looking at legacy effects when "graduates" of anchor companies like Genzyme or Biogen Idec bring their expertise to new companies. This legacy is the hardest asset for emerging clusters to replicate and it also requires that we continue to build and retain anchor companies.



To ensure the future vitality of the Massachusetts life sciences cluster, we must build a robust industry presence, including fully integrated companies with more activities located in Massachusetts.

Impact 2020 **recommends** the following to **recruit and retain** companies further down the value chain:

1. **Call for Reauthorization the Massachusetts Life**

**Sciences Initiative** – While there are many lessons to be learned from the implementation of the initial authorization, the clear consensus from industry and other stakeholders is that the \$1 billion commitment sent an important message that Massachusetts does value the life sciences industry and is committed to ensuring its future.

2. **Work with State and Local Agencies on Incentives for Anchor Companies**

– Keeping companies in Massachusetts as they grow into more fully integrated companies with manufacturing and commercial operations has many benefits. Minimizing impediments to business operations is critical to communicating a welcoming message. In its programming, MassBio can feature some of the state’s downstream assets to help support the message.

3. **Proactively Market the Cluster and Close**

**“Wins”** – Stakeholders tout Bristol-Myers Squibb’s decision to build facilities in Devens and Shire’s decision to build out a campus in Lexington as examples of how the State has effectively mobilized resources to win companies to Massachusetts. The perception is that this proactivity and urgency has waned in recent years. The BioLeads initiative, which includes MassBio and multiple state agencies cooperating in lead development, is unique, successful and should be continued, but increased efforts should be made in proactive outreach to companies on the rise within Massachusetts and beyond its borders. Determining which state agency is singularly responsible for such outreach and which authority is empowered to extend incentive proposals (which should not be limited to MLSC programs) to promising prospects would be a major step forward.

4. **Expand University-Industry Collaboration through the Massachusetts Life Sciences Education Consortium (MLSEC)**

– Commitment to STEM education is critical for this industry and there is a significant opportunity for closer ties between universities and industry. UMass, Worcester Polytechnic Institute, Northeastern University and other institutions are already collaborating with companies on training. The MLSEC (led by MassBio & MassBioEd) should be the go-to resource for companies and universities seeking to collaborate on workforce training.

5. **Lead Efforts to Develop a Massachusetts Life Sciences Job Forecasting Study**

– Both companies and universities point out that the lack of a reliable, ongoing source of data on job demand in the life sciences industry creates challenges for both parties around workforce training and planning. MassBio and MassBioEd can convene industry and education leaders to develop an action plan to create this resource and they can reach out to companies to gather ongoing data for the benefit of all stakeholders.



# Massachusetts: The Hub for Life Sciences IT

**“The other threat I see is that we [Massachusetts] do not become the center of information technology and advanced analytics. As we become more reliant on data analytics, things could start shifting to the West Coast.”**

**– George Scangos, CEO, Biogen Idec**



Dramatic improvements in information technology are transforming many industrial sectors, and the life sciences industry poses special challenges due to the complexity and length of the development process, the variability of patient circumstances, and the fragmentation of decision-making. New tools for capturing data, conducting sophisticated analytics, integrating data, and enhancing personal connectivity developed elsewhere should provide a springboard to address many problems faced in the life sciences industry.

Catalyzed by the Affordable Care Act, Watertown-based athenahealth is an industry leader in the development of cloud-based electronic health records (EHRs).<sup>13</sup> Beth Israel Deaconess Medical Center and Partners HealthCare are leaders in adopting EHRs. Massachusetts is also leading the way in the development of a program that connects provider EHRs across the state through the Mass Health Information Highway.<sup>14</sup> eClinicalWorks, Ubiqi Health, Paradigm4, ZappRx and many other health IT startups are here in Massachusetts.


The future is bright.

The potential impact of IT on drug research, development, and marketing is already evident. Longitudinal data covering the entire patient experience from diagnosis to outcomes, with visits, procedures, and costs captured at all stages and in all settings, will eventually be available. In the future, this information will be linked to patient registries, individual genomic profiles, disease biomarkers, and personal monitoring technology so that caregivers can rapidly monitor and evaluate various disease management techniques and interventions.

For life sciences companies, the availability and effective application of these tools will be transformative. Already, research institutions like the Broad Institute are employing informatics tools for basic research. These tools are starting to make their way into startup companies. Eventually, using detailed patient data will be routine in assessing stage of disease, detailing characteristics of tumors and tissue changes, selecting patients for clinical trials, and assessing their outcomes in-silico against a standard set of data.








In life sciences information technology (LSIT), Massachusetts can and should be the leader. To exploit this opportunity, the Massachusetts cluster should seek opportunities to cross-fertilize these two powerful, innovative, and entrepreneurial sectors:

1. **Collaborate with MassTLC to Launch an LSIT Program** – Work with the Massachusetts Technology Leadership Council (MassTLC) to create an integrated and focused program for LSIT to cultivate cross-sector relationships between IT and life sciences companies. This program can leverage the planning resources of the two organizations to develop a set of events for the community that can bring attention to the growing LSIT opportunity and share information on technologies, emerging companies, and industry needs and challenges.
2. **Support Efforts Underway by MassTLC to Bring Focus to LSIT Talent Development** – MassBio and MassBioEd can help by convening life sciences companies, IT companies, and academia to dialogue on how to attract and retain IT talent in Massachusetts. The organizations can work with the group to define IT-focused, life sciences career paths that can be publicized to the industry.
3. **Establish an LSIT Resource Center** – Curate a centralized set of resources, such as LSIT company directories, LSIT job postings, and updates on local LSIT initiatives for members.

With an investment to more closely connect the life sciences and IT sectors, Massachusetts has an opportunity to build a new unique industry sector that could grow well into the future.



# Summary of Key Messages and Recommendations

Impact 2020 – Recommended Initiatives for MassBio				
<b>Impact 2020 Vision</b>	To advance Massachusetts' leadership in the life sciences industry, championing innovation in order to bring value to the global healthcare system and make meaningful impact on patients' lives.			
<b>Strategic Priorities for the Cluster</b>	Demonstrate the value of innovation for the healthcare system and ultimately for patients	Maximize access to capital and other enabling resources for early-stage life sciences companies	Support company expansion down the value chain	Capitalize on information technology to advance the life sciences
<b>MassBio Initiatives:</b>	<b>Value and Patient-Centered Initiatives</b>	<b>Company Formation Initiatives</b>	<b>Company Expansion Initiatives</b>	<b>Life Sciences Information Technology Initiatives</b>
<b>Convene Key Groups</b>	<ul style="list-style-type: none"> <li>❑ Convene a high-profile Value-Based Healthcare Working Group 2-4 times per year</li> <li>❑ Engage payers and providers on MassBio strategic priorities, e.g. Board seats</li> </ul>	<ul style="list-style-type: none"> <li>❑ Rally agencies to promote the Massachusetts life sciences cluster and attract global resources</li> <li>❑ Organize regular startup CEO forums to share best practices</li> </ul>	<ul style="list-style-type: none"> <li>❑ Through MassBioEd and the MLSEC, convene industry and university to expand workforce collaborations</li> </ul>	<ul style="list-style-type: none"> <li>❑ Collaborate with MassTLC to launch an LSIT Program</li> <li>❑ Bring focus to LSIT talent development</li> </ul>
<b>Advocacy Efforts</b>	<ul style="list-style-type: none"> <li>❑ Articulate value arguments for life sciences products and build awareness with government officials and agencies</li> <li>❑ Communicate to the public on the value of life sciences innovation for patients</li> </ul>	<ul style="list-style-type: none"> <li>❑ Advocate for more seed-stage funding options through the MLSC and other sources</li> <li>❑ Advocate for NIH funding</li> </ul>	<ul style="list-style-type: none"> <li>❑ Support renewal of the LSI</li> <li>❑ Advocate for enhanced state incentive programs and external marketing and prospecting</li> <li>❑ Promote Massachusetts as a range of optimal locations for life sciences companies across the business lifecycle.</li> </ul>	<ul style="list-style-type: none"> <li>❑ Support MassTLC in its efforts to bring government attention to life sciences IT opportunities</li> </ul>
<b>Programs and Events</b>	<ul style="list-style-type: none"> <li>❑ Establish a value resource center</li> <li>❑ Develop and promote value-based training and education for life sciences companies</li> <li>❑ Highlight more patient successes and opportunities in programs and events</li> </ul>	<ul style="list-style-type: none"> <li>❑ Expand MassCONNECT and its role in company formation</li> <li>❑ Maximize access to funding and enabling resources</li> </ul>	<ul style="list-style-type: none"> <li>❑ Enhance visibility for biomanufacturing assets and commercial talent</li> <li>❑ Develop and implement a state-wide, biannual job forecasting study</li> </ul>	<ul style="list-style-type: none"> <li>❑ Create forums and events under LSIT program that enable cross-sector relationship development</li> <li>❑ Identify and publicize LSIT career paths</li> <li>❑ Establish an LSIT resource center for members</li> </ul>

While MassBio is prepared to take on these initiatives, there are areas where leaders of other healthcare sectors can engage. Impact 2020 asks the leaders of local payers and providers groups to:

- Engage with MassBio and industry leaders on a dialogue around the required data, systems, metrics, and processes that can enable a model of value-based healthcare;
- Pursue experiments and pilots on sharing high-quality data among groups so that a stronger understanding of the patient experience, and all its costs and outcomes, can be attained.

MassBio is prepared to work with leaders of these groups and their associations on these areas.

Impact 2020 holds several key messages for policymakers and stakeholders in the life sciences industry, and identifies several areas where MassBio members and industry as a whole can engage. The tables on the next page lay out how stakeholders can help further the efforts to achieve the goals laid out by Impact 2020.

Impact 2020 - Key Messages for Local, State, and National Policymakers	
Primary Themes	Key Messages
Value – Impact on Innovation	<ul style="list-style-type: none"> <li>Value-based healthcare is more than just price controls; any value-based system must achieve a balance with ensuring a reward for innovation, or patients will lose</li> <li>Massachusetts is in a unique position to convene stakeholders across healthcare in a productive dialogue around value; local initiatives can have national influence</li> <li>Patients must be involved in any discussions around value-based healthcare</li> </ul>
Support for Company Formation	<ul style="list-style-type: none"> <li>While 2013 has been strong for the industry, life sciences is inherently risky and fragile, and highly vulnerable to a reduction in funding support</li> <li>NIH funding is critical to seeding future generations of technologies and companies, and must be preserved</li> <li>Re-authorization of the Massachusetts Life Sciences Initiative will, once again, send a very important message to the life sciences industry that it is valuable to the state, especially as other clusters are investing aggressively to compete</li> <li>Active dialogue with industry around key topics, e.g. reimbursement, will help mitigate the negative impact that regulatory uncertainty has on investment</li> </ul>
Support for Company Expansion	<ul style="list-style-type: none"> <li>Favorable business policies and incentives to encourage companies to grow into maturity in Massachusetts will help blunt the aggressive efforts evident in other clusters</li> <li>Massachusetts has significant capabilities downstream from R&amp;D, particularly in biomanufacturing, that should be recognized and supported</li> <li>These capabilities leverage talent in the broader state, accruing benefits beyond the Boston/Cambridge center</li> </ul>
Life Sciences Information Technology Opportunity	<ul style="list-style-type: none"> <li>Information technology can enable a broad range of solutions for problems in healthcare and the life sciences</li> <li>Across Massachusetts there is a wide array of initiatives underway, but they are fragmented</li> <li>Government cooperation and support for cross-industry initiatives will stimulate a 'life sciences information technology' hub and give Massachusetts a unique competitive advantage</li> </ul>

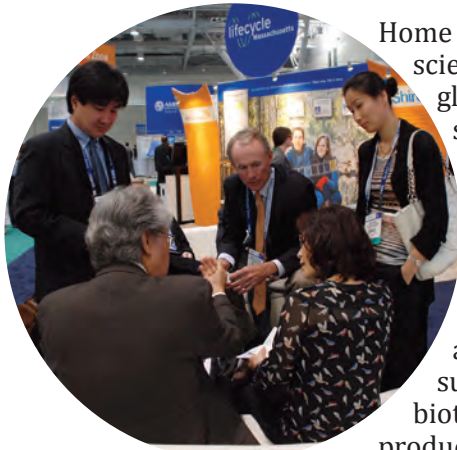
Impact 2020 – Key Areas of Engagement for Stakeholders	
Stakeholders	Key Areas to Engage
Large Pharmaceutical Companies	<ul style="list-style-type: none"> <li>Seek opportunities to work across traditional boundaries with payers and providers in MA</li> <li>Support local initiatives to ensure funding, space, and support for startup companies</li> <li>Commit senior executive time to critical local issues that require visible industry support</li> <li>Engage with MassBio in communicating patient stories and benefit</li> </ul>
Established Biotech Companies	<ul style="list-style-type: none"> <li>Commit to collaborative high-level leadership around local infrastructure, policy, and workforce issues</li> <li>Actively participate in senior leadership forums to address critical questions around value-based healthcare and life sciences information technology</li> <li>Engage with MassBio in communicating patient stories and benefit</li> </ul>
Early-Stage Companies	<ul style="list-style-type: none"> <li>Participate in MassCONNECT to ensure efficient access to funding sources, space, and other resources</li> <li>Participate and support startup CEO forums to exchange lessons learned</li> </ul>
Universities and Research Centers	<ul style="list-style-type: none"> <li>Consider opportunities to provide more seed resources and/or funds for promising research</li> <li>Engage with MassCONNECT as it expands programming for new companies</li> </ul>
Investors and Funding Sources	<ul style="list-style-type: none"> <li>Work with MassBio on programming to enhance early-stage company understanding of reimbursement and the value-based healthcare debate</li> <li>Assist MassCONNECT in advising and mentoring early-stage companies</li> <li>Encourage portfolio companies to join MassBio and engage in industry dialogues</li> </ul>
CROs, CMO's and Service Providers	<ul style="list-style-type: none"> <li>Continue to work with MassBio to build visibility for available resources, to expand resources, and to ensure a strong talent pool</li> </ul>

Finally, Impact 2020 puts forth a strong call for industry leaders to step up and provide leadership to the cluster on the critical issues that have been identified. MassBio will enable the cultivation of cluster leadership through an annual or biannual leadership forum, mentoring, and recognition of contributions.

The Massachusetts life sciences cluster is in a strong position, but with success comes responsibility. Impact 2020 calls for MassBio to elevate its role, forge cross-sector relationships, educate the public and its representatives, stimulate local development efforts, and enhance services for members. MassBio will continue to be the greatest advocate for the Massachusetts life sciences cluster, for innovation, and ultimately for patients. MassBio and its Board of Directors are prepared to provide leadership, champion innovation, and ultimately help the cluster deliver solutions with meaningful impact on patients' lives.

# Massachusetts Life Sciences: The State of the Cluster

The Massachusetts life sciences cluster is in a strong position, but with success comes responsibility. Impact 2020 calls for MassBio to elevate its role, forge cross-sector relationships, educate the public and its representatives, stimulate local development efforts, and enhance services for members. MassBio will continue to be the greatest advocate for the Massachusetts life sciences cluster, for innovation, and ultimately for patients. MassBio and its Board of Directors are prepared to provide leadership, champion innovation, and ultimately help the cluster deliver solutions with meaningful impact on patients' lives.



Home to many of the nation's top hospitals, research universities, life sciences companies, and healthcare investors, Massachusetts has built a global leadership position among life sciences clusters. Its universities spin out novel technologies year after year, committed investors and entrepreneurial talent translate these technologies into products, and experienced leaders successfully steer these products to market. All of this happens within a vibrant and collaborative ecosystem.

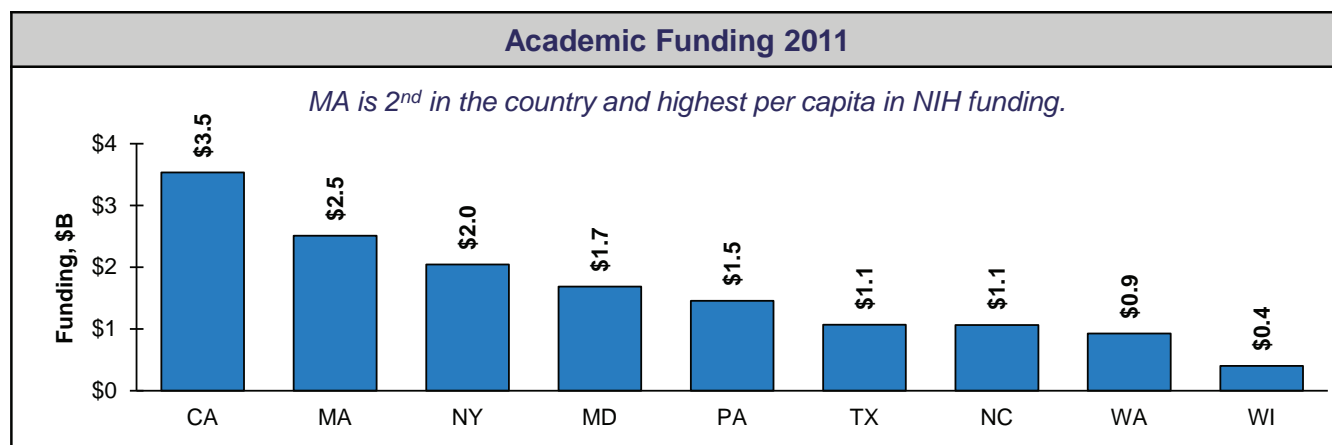
This ecosystem has been built through generations of entrepreneurship. As companies are founded, grown and acquired, leadership is developed and redeployed to nurture the next generation of companies. The recent success of the Massachusetts cluster is apparent in the continued growth of biotech jobs, new companies, and new products. When companies and their products succeed, the cluster succeeds.

At the same time, anything that threatens innovation, threatens the cluster. The life sciences industry is facing significant challenges from regulators and payers. Growing reimbursement and market pressures are deterring some investors from the industry, making early-stage capital harder to access. If Massachusetts is to remain a wellspring for life sciences innovation, it must attend to the fundamentals of innovation and address threats facing the industry.

## Robust Fundamentals, Special Enablers

Technology, capital and talent are fundamental to the success of a life sciences cluster. Technology springs from the efforts of researchers, and Massachusetts is home to 30 public and 94 private universities<sup>15</sup> and attracts the second highest level of NIH funding among states [Figure 1]. More telling than research dollars are the numbers of patents, licenses and startups that are generated by universities. As Robert Beall, CEO of the Cystic Fibrosis Foundation, said, "You need institutions that do more than invest in basic research, but that are committed to getting the ideas and IP out to the market." AUTM metrics indicate that Massachusetts universities are highly productive in technology transfer [Figure 2], an accomplishment that can be credited to not only strong research but also strong industry orientation at universities—nimble tech transfer offices, collaborations with industry, and faculty incentives rewarding patents and products.

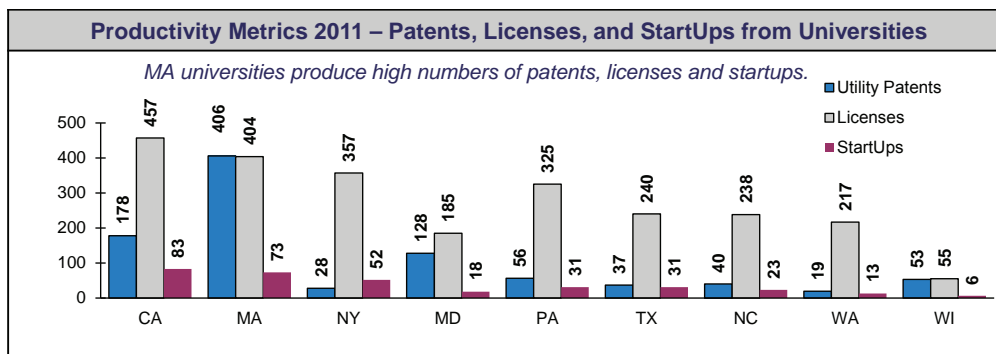
Figure 1



Source: Health Advances analysis, NIH.



Figure 2



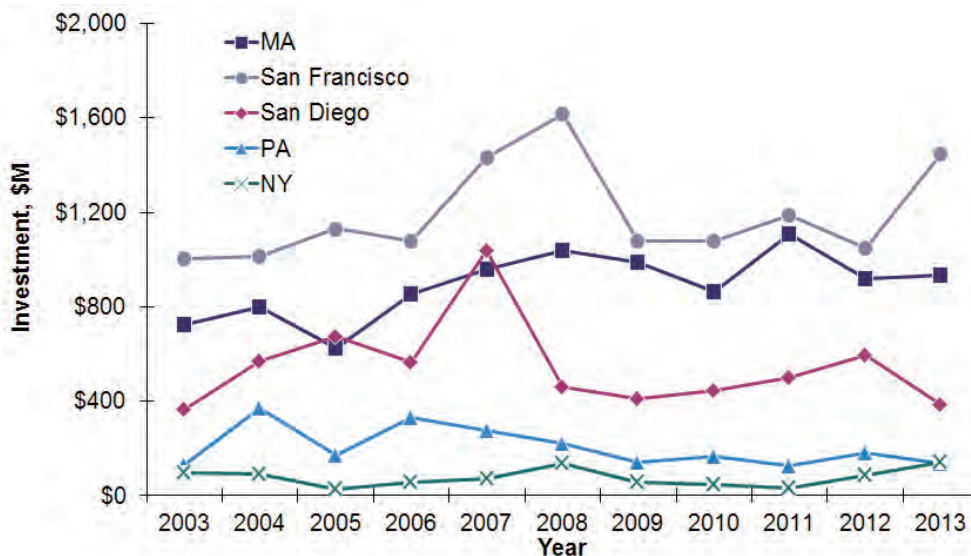
Source: Health Advances analysis, NIH RePORT, AUTM STAT – data is across all sectors, as AUTM does not track at this level; hence productivity should be taken as directional for all sectors.

Massachusetts is also fortunate to have strong venture capital firms seeding companies spun out of university labs. Several of the most active life sciences venture capital firms are based in Massachusetts, including Atlas Venture, Flagship Ventures, HealthCare Ventures, MPM Capital, Polaris Venture Partners and Third Rock. Over the past 10 years, the New England region has consistently seen between \$800 million and \$1.1 billion in venture capital investments, higher than every other cluster except the San Francisco Bay Area.

Figure 3

### Biotech VC Investment

All Stages, 2003 - 2013



Source: Health Advances analysis, PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report, Data: Thomson Reuters.

A strong percentage of Massachusetts-based VC firms focus on life sciences investing, compared to firms in most other regions [Figure 4]. While San Francisco has nearly double the number of VC firms that do biotech investing, one San Francisco biotech executive remarked: “The benefit in Boston is that the big VCs stick with the life sciences. In other geographies, more investors straddle between life sciences and information technology, shifting dollars in and out of the sector.”



## Massachusetts At A Glance (2013)

**900+**  
biopharma and  
medtech companies

Home to R&D centers  
of **8** of the top **10**  
pharmaceutical  
companies

**~56,000**  
employed in biopharma

**1,200** drugs in trials

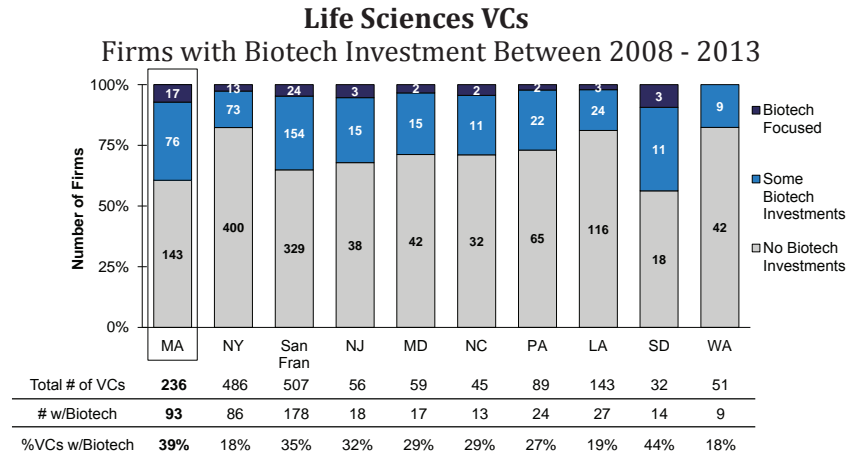
**1<sup>st</sup>** breakthrough  
designated drug

**93** venture capital  
firms investing in  
life sciences

**Highest NIH funding**  
per capita

**6** of the top **10**  
NIH-funded hospitals

Figure 4



***"The benefit in Boston is that the big VCs stick with life sciences. In other geographies, more investors straddle between life sciences and information technology, shifting dollars in and out of the sector." – SF Biotech Executive***

Source: Health Advances analysis, ThomsonONE. 'Biotech Focused' means the firm has invested 60% of its investment portfolio in Biotech or Medical/Health Focused. 'Some Biotech Investment' means at least one investment in a biotech firm over a five year period. 'No Biotech Investments' means no biotech investments over a five year period.

Massachusetts has a diverse set of investors beyond venture capitalists, from bridge investors and late-stage money management firms such as RA Capital and Brookside Capital, to angel investors and family foundations. "In Boston, more angels are former life sciences executives versus other towns where they are paper or oil magnates," remarked one local biotech executive. In recent years, institutional investors have been supplemented by increasingly active corporate funds, the majority of which have a presence in Massachusetts. The diversity of investors in the cluster creates a more resilient capital base for the life sciences, mitigating fluctuations in VC investing.

A final foundational component required for a strong life sciences cluster is talent. With its high density of universities, Massachusetts graduates more life sciences Ph.D.'s per capita than any other cluster<sup>16</sup>. These students provide the scientific expertise required in a life sciences company. In addition to scientific talent, companies need experienced leadership and functional skills. Here, Massachusetts benefits from a vast network of experienced industry professionals, derived from several generations of companies. Using Genzyme as an example; more than 50 companies have been built by former Genzyme employees who since started or led new ventures [Figure 5].

Figure 5



Source: Health Advances analysis, LinkedIn.

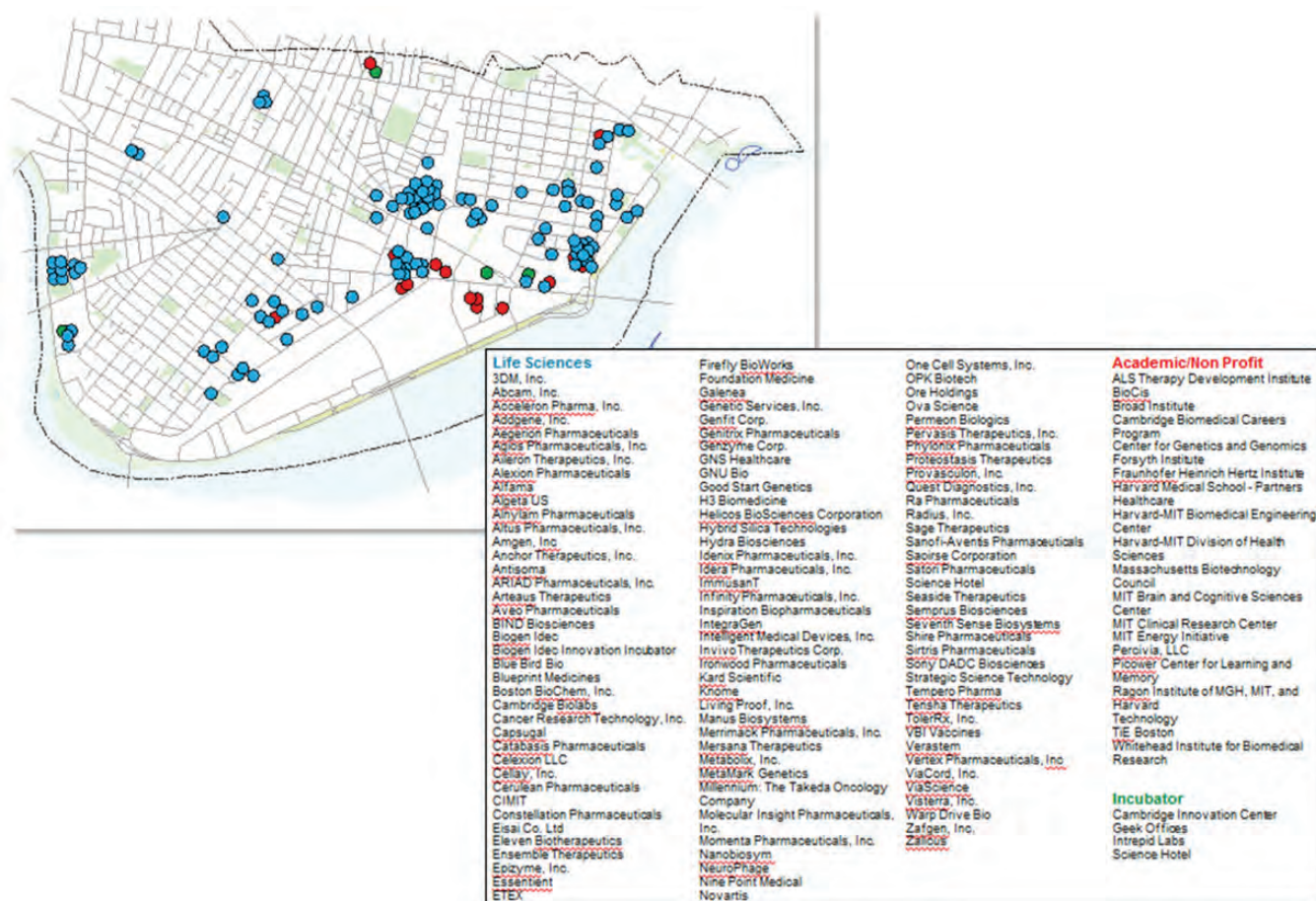
Exploiting this network effect, new Massachusetts companies gain competent advisors to navigate the complexities of drug development. Investors and executives build trust over several company experiences. As business is built upon relationships, the local cluster is primed for deal making and company formation. “People go from job to job; we see each other socially; we live in the same towns...there is a lot of relationship building and in the end, people do deals with people they know and like,” said Deanna Peterson, VP of Business Development at Shire.

Many of the parameters that have been discussed show Massachusetts doing well, but also show California, in particular the Bay Area, doing as well or better. However, the perception of stakeholders in both clusters is that Massachusetts is gaining the edge. Luke Timmerman, previously at Xconomy, showed that Boston ranks number one when measuring the number of life sciences companies with over \$100 million in cash and short-term investments (37 in 2013 compared to 26 in San Francisco).<sup>17</sup> Metrics aside, stakeholders point to two distinct advantages for Massachusetts. The first is the stronger presence of big pharma R&D centers. The second is the unique concentration of the Massachusetts cluster.

This second point, in particular, came up repeatedly in conversations. Cambridge’s Kendall Square is heralded for its unique density of life sciences companies, academic universities, investors, and service providers. A previous analysis showed that Kendall Square’s density of technology companies (life sciences plus information technology), at 163 companies per square mile, is unparalleled; the next densest cluster, Palo Alto, CA, has 36 technology companies per square mile. For biotech specifically, Kendall Square has 48 companies per square mile compared to Palo Alto’s 13.<sup>18</sup>

**Figure 6**

### Kendall Square’s Unparalleled Density ~50 biotech companies per square mile



Source: Cambridge City Council 2014.



“Within five minutes of my office,” said George Scangos, CEO of Biogen Idec, “I can visit so many companies and institutes, just by walking. This concentration just does not exist in the Bay Area. It creates more intensity and more community spirit.” A leader from another cluster remarked, “The beauty of Massachusetts is that it has such a concentration in Kendall Square. This has created more of a culture of working together and being part of a club.”

This “club” and its elements of collaboration, leadership, and entrepreneurship are the unique drivers behind the Massachusetts cluster’s success. It fosters a culture supportive of growth and a vibrant network of people and resources that sustain this growth. It is critical to connecting fundamental inputs to build companies and products that succeed.

## Metrics of Success

The continued success of the Massachusetts cluster can be seen in its expanding industry footprint, jobs growth, and product success.

Today, over 900 biopharma, medical device, and diagnostics firms are located in Massachusetts.

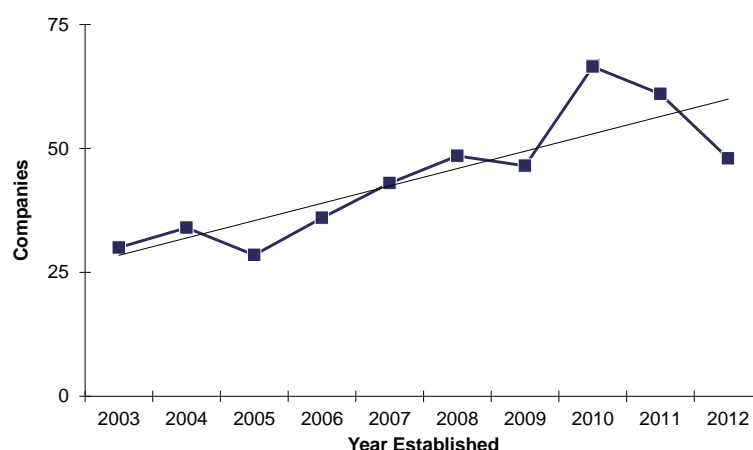
<sup>19</sup> Seven of the world’s top ten pharmaceutical companies have an R&D presence. Of the top five biotechnology companies on the basis of market value, three have a presence in Massachusetts,

and one, Biogen Idec, is headquartered in Cambridge.<sup>20</sup> At the same time, dozens of new ventures are being formed each year, with many focused on cutting-edge science from Massachusetts’ universities. Data suggest that between 40 and 60 new companies have been formed per year over the past five years in Massachusetts. Several companies are already renowned for the strength of their scientific platform, management teams, and pipeline. Bluebird bio and Epizyme are two examples [See Case Studies - P].



Figure 7

Number of New MA Life Sciences Companies  
2003 - 2012

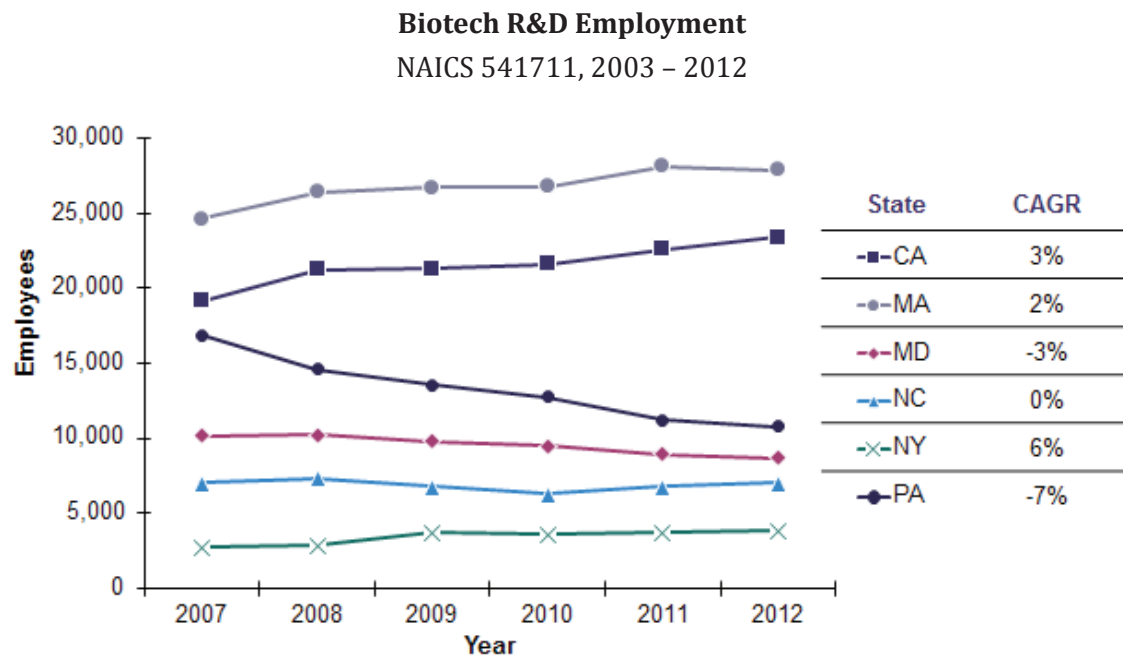


Source: Health Advances analysis, ThomsonONE, Dun & Bradstreet

Company growth means jobs growth, and Massachusetts leads the nation in biotech R&D employment. In 2012, Massachusetts employed about 28,000 biotech R&D employees.<sup>21</sup> Despite an economic downturn, these jobs have grown at a 2% compound annual growth rate between 2007 and 2012. The critical mass of life sciences companies and institutions in Massachusetts is a strong draw for industry talent. The diversity of employers provides strong career flexibility. People can move from a startup to a large biotech, or from a research institute to a pharma R&D center, without relocating. And professionals are more willing to move their families to Massachusetts knowing that there are many career options available once they do relocate.



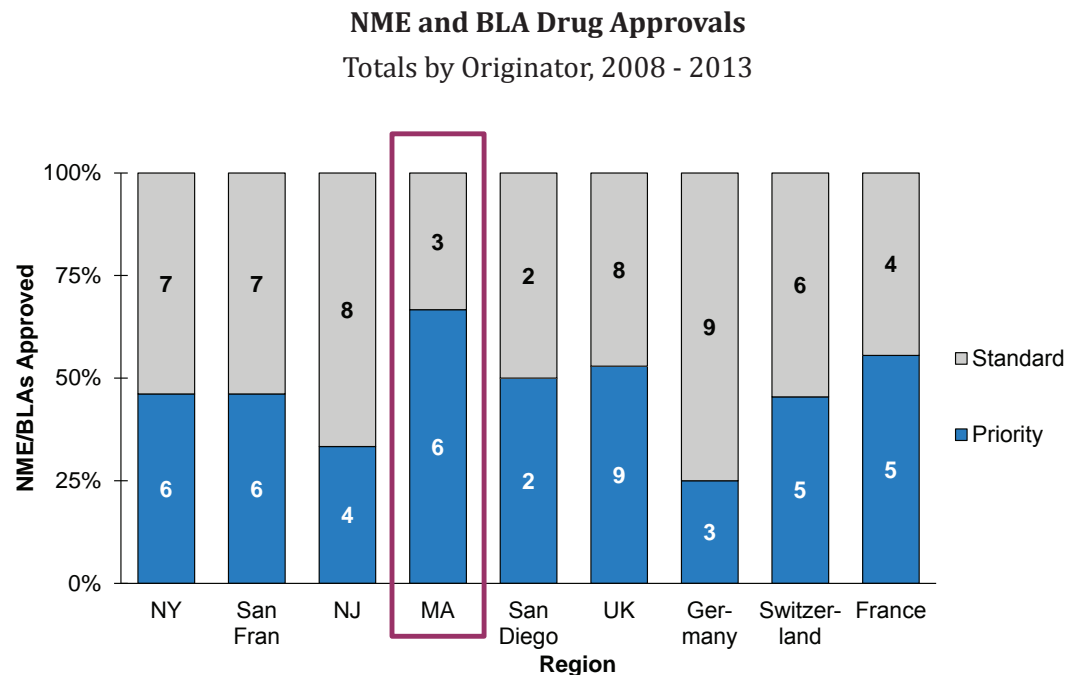
Figure 8



Source: Health Advances analysis, U.S. Bureau of Labor Statistics.

Ultimately to sustain jobs growth, companies must be successful, bringing new products to market and delivering shareholder value. Here big pharma hubs, such as the United Kingdom, New York, New Jersey, and San Francisco, lead in total number of FDA approvals. However, Massachusetts-based companies produce a disproportionate number of priority review approvals. Priority reviews are granted to products providing a significant treatment, preventive or diagnostic therapeutic advance.<sup>22</sup> Recent priority review approvals include Kynamro (Genzyme), Kalydeco (Vertex), and Tecfidera (Biogen Idec). [See Sidebar - P ]

Figure 9



Source: Health Advances analysis, FDA, Pharmaprojects.

## *Recent Major Products Developed by Massachusetts Companies Address Critical Unmet Needs for Patients*



**genzyme**  
A SANOFI COMPANY

**Genzyme's Kynamro (mipomersen) for Homozygous Familial Hypercholesterolemia (HoFH)**

- HoFH is a rare inherited condition where the body is unable to remove LDL-C, leading to abnormally high levels of circulating LDL-C
- Patients with HoFH often suffer heart attacks and death before age 30
- Kynamro is a novel weekly injection that works with other lipid-lowering medications and diet to impair the creation of LDL-C
- The product is based on Isis Pharmaceutical's antisense technology
- Kynamro was approved under Orphan Designation in January 2013, providing a new option for patients to manage a fatal disease



**VERTEX**

**Vertex' Kalydeco (ivacaftor) for Cystic Fibrosis**

- Cystic fibrosis is a rare inherited disease where a defective gene leads to abnormal secretory fluids that obstruct the lungs and digestive organs
- Kalydeco is the first approved treatment that addresses gene defects and not just symptoms, improving lung function in patients with the G551D mutation (4% of the CF population)
- Kalydeco was approved under Orphan Designation in January 2012
- The product brings hopes to patients with the mutation, and symbolizes the promise of personalized medicine, targeted drugs that treat patients with specific genetic makeups



**biogen idec®**

**Biogen Idec's Tecfidera (dimethyl fumarate) for Multiple Sclerosis**

- Multiple sclerosis is a chronic autoimmune disease of the central nervous system, affecting more women than men
- Multiple sclerosis can impair movement, sensation, and cognition, significantly hindering patients' quality of life
- Tecfidera is a novel oral medication for the treatment of relapsing forms of MS, approved in April 2013
- Tecfidera showed better efficacy than current front-line options with a relatively mild safety profile, providing a promising new option for patients
- In its first months of launch, demand for the drug beat many analysts' expectations

## Company Profiles : Innovative Massachusetts Companies on the Rise



Epizyme (NASDAQ: EPZM, Cambridge, Mass.) began very quietly in 2007 and quickly roared into the public markets in 2013 with an \$89 million IPO and a \$107 million follow on offering in early 2014. With an experienced team led by CEO Robert Gould, previously at the Broad Institute and at Merck, President and CFO Jason Rhodes, previously at

Alnylam, CSO Robert Copeland, previously at GSK, and CMO Eric Hedrick, previously at Pharmacyclics, the company has carefully crafted a strategy that uses multiple financing options and partnerships to realize the potential of its technology for patients and shareholders.

With a world-renowned team that included co-founders Yi Zhang, then a professor at University of North Carolina at Chapel Hill and now a professor of genetics at Harvard Medical School, Nobel Laureate H. Robert Horvitz of MIT, and Kazumi Shiosaki, MPM capital's managing director and the founding CEO, a new biopharmaceutical company was born in 2007 with the goal of discovering personalized therapeutics for patients with genetically defined cancers. And what the company's research found was that many disease-causing genetic alterations occur in the enzymes that control gene expression via a regulatory mechanism called epigenetics.

Epizyme operated in stealth mode for the next two years, creating a product platform targeting a class of epigenetic enzymes, histone methyltransferases (HMTs), and demonstrating that these enzymes drove specific cancers and could be drugged with novel small molecule inhibitors. In 2008, the company raised a \$14 million Series A round and in 2009, the company raised a \$40 million Series B round. These venture rounds and the company's rapid scientific progress positioned Epizyme for vital strategic collaborations soon afterwards.

In 2011, Epizyme entered collaborations with GlaxoSmithKline, Eisai, the Leukemia & Lymphoma Society (LLS) and the Multiple Myeloma Research Foundation (MMRF). In parallel, the company continued to make rapid R&D progress and published the first in vivo efficacy data in the entire HMT field. In 2012, Epizyme began an award-winning partnership with Celgene that brought in \$90 million upon signing and allowed Epizyme to retain 100% of US rights on its lead clinical program, EPZ-5676, a novel therapeutic candidate to treat genetically defined acute leukemias. Together, these therapeutic collaborations have provided Epizyme with approximately \$171 million in non-equity funding to date, with the potential for more than \$1 billion of milestone payments and royalties or profit sharing on product sales. In December 2013, Epizyme earned a \$25 million payment in the Celgene collaboration for the achievement of a clinical proof of concept milestone.

As CEO Robert Gould said, "We are building a new leading biopharma company, and our scientific, business, and financing strategies work hand in hand to realize this potential. With the strong foundation of our strategic partnerships, Epizyme was ready to go when the IPO markets opened in 2013, accessing capital that provides us with the fuel to pursue our vision."





## Company Profiles : Innovative Massachusetts Companies on the Rise



bluebird bio, inc (NASDAQ: BLUE, Cambridge, Massachusetts) is attempting to turn 20 years of gene therapy research into a clinical reality for patients suffering from hereditary diseases.

For several inherited diseases, patients require lifelong and/or burdensome treatments, and often, these interventions are not enough. For example, in the case of adrenoleukodystrophy (ALD), a rare and lethal neurological disorder, patients require stem cell transplantation from a matched donor. Without such a donor, patients progress into a vegetative state and ultimately death.

However, with gene therapy, it is possible to directly address and correct the underlying cause of ALD, a mutated form of the ABCD1 gene. bluebird's lead therapy is a lentiviral delivered functional copy of the ABCD1 gene. The lentivirus containing the ABCD1 gene is used to transform blood stem cells taken from an ALD patient. Once transformed, these cells are transfused back into the patient, now with the functional copy of the gene. In 2009, in collaboration with a French group, bluebird treated several ALD patients, and at the time of this publication, these patients continue to have stable ABCD1 expression and demonstrate therapeutic progression, remarkable evidence of the potential for gene therapy.

According to Nick Leschly, bluebird's CEO, "bluebird is a company that could have only happened in a place like Massachusetts." Being in Massachusetts allowed the company to recruit top scientific talent and be close to prominent life sciences investors. Leschly himself comes from a former Massachusetts success, Millennium Pharmaceuticals, and was part of the founding team at Third Rock Ventures. Since Leschly joined the company, bluebird has raised \$139 million through four VC financings and grant awards, and has established a development partnership with Celgene.

Leschly acknowledges that timing is a big component to success, and it appears now is the time for gene therapy. In June 2013, bluebird bio raised \$116 million during its IPO, from which the company plans

to fund a Phase II/III study for childhood cerebral ALD in 2014. Though there is still technological and regulatory/reimbursement risk ahead, bluebird has demonstrated that gene therapy can accomplish disease modification and has the potential to replace years of expensive chronic therapy. Should bluebird succeed, it will be exciting to watch this local company pioneer a new paradigm in care and bring lifesaving therapies to patients.





## Sustaining Success

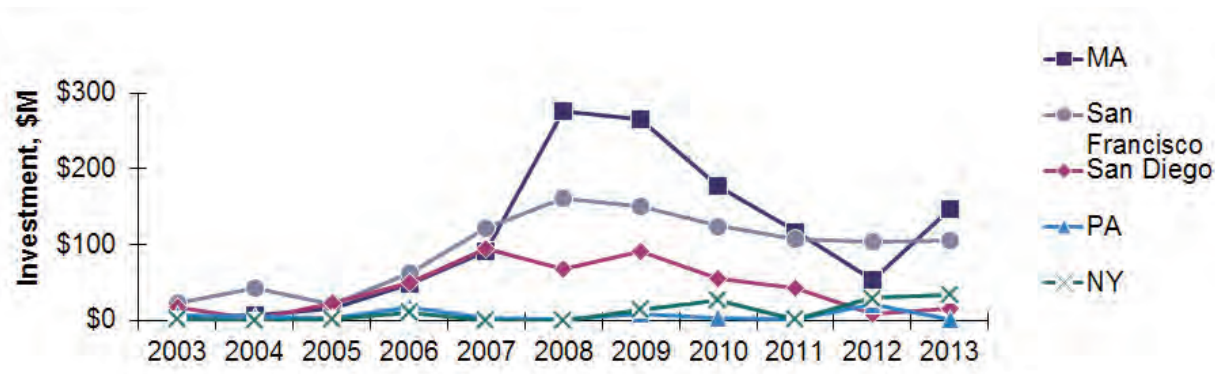
To sustain its success, the Massachusetts life sciences cluster must protect what has made it the cluster it is today while addressing emerging areas of vulnerability.

### *Company Formation – Seed-stage Financing Challenges*

Looking more closely at venture capital data shows a trend of declining seed-stage investment since record-high seed funding in 2008 [Figure 10]. While local investors remarked that they are still investing in seed-stage ideas, conversations with entrepreneurs reflected a different perception. The disconnect may be attributed to a shift in early-stage investing by VC firms to a model of ‘venture creation,’ whereby novel science is being proactively identified and spun out into companies by the VCs themselves. This has left a more challenging path for less established entrepreneurs, who need to connect a variety of other funding sources to keep their ventures alive.

**Figure 10**

**Biotech VC Investment – Seed-stage 2003-2013**



Source: Health Advances analysis, PricewaterhouseCoopers/National Venture Capital Association MoneyTree™ Report, Data: Thomson Reuters.

While this shift may create an even more Darwinian climate for the most promising technologies to emerge, it is inherently challenging to “pick the winners” early. Enabling a larger set of ideas and technologies to move forward to proof of concept is likely better for the ecosystem at large.

With this in mind, leaders in the Massachusetts cluster will need to address the recent decline in seed-stage funding. Corraling a diverse set of investors—angels, family and disease foundations, the “crowd”— to provide seed capital, advocating for government support, and providing low-cost space, are all tactics that will be required to keep the vibrancy of entrepreneurship alive. These ideas are discussed in more detail in the Financing Life Sciences Innovation Chapter.

### *Company Expansion - Attracting Anchor Companies*

The presence of strong anchor companies is critical to sustaining the future of a cluster. Companies that are independent and have marketed products in addition to robust pipelines help drive the growth of the cluster economy. Furthermore, these companies give back to the community; their leaders engage with other local leaders, champion important local issues, and encourage the building of local communities. Indeed, Massachusetts’ roots can be traced back to early biotech leaders, including Genetics Institute, Genzyme, Millennium, and Biogen Idec, who had strong interest in building the cluster.



But of these historic biotech leaders, only one now remains independent. In looking to the future of the cluster, nurturing the next anchors and the next generation of committed leadership is critical. This will require coordinated efforts by the state and the local industry to both incentivize companies to keep operations in Massachusetts as they expand and to attract fully integrated companies to Massachusetts. While the cluster is a magnet for R&D activity, it is less considered for biomanufacturing or corporate function operations. But, as George Scangos, CEO of Biogen Idec, stated “being close to R&D operations provides advantages.” Cross-functional teams are necessary to optimize program development; early biomanufacturing and commercial input can ensure market success.

Shire’s expansion in Lexington, Massachusetts is an exceptional example of the Massachusetts state government working with industry to bring an important new anchor to the cluster. **[See Case Study - P.]** Through further economic development and workforce development, the cluster can continue to build an even stronger and more diversified industry base.




## Leveraging Leadership for Impact

As a leading cluster, Massachusetts is in a position to address critical opportunities and threats facing the life sciences industry across the globe. In the face of an evolving healthcare system, Massachusetts is primed to help navigate the industry through the shifts.

### *The Question of Value*

Globally, healthcare systems are facing cost pressures; in the U.S., healthcare reform has taken the national stage with the rollout of the Affordable Care Act. The consistent theme from policymakers is that healthcare systems need to see greater value from care, i.e. increased quality or outcomes with equal or lesser costs. As a stakeholder in the system, life sciences companies need to be part of the solution by demonstrating the value of their products. Beyond showing efficacy and safety, companies need to show how their products increase quality or outcomes without adding significant costs to the system.

In order to demonstrate value, companies will need to work with providers, government, and payers to design studies, access real-world data, and produce meaningful evidence. It is difficult for any one company to drive these efforts, but having a consortium of companies, providers, and payers dialogue on these issues can help define a path forward for the industry.



Massachusetts is an optimal place to drive this effort, as it has been an incubator for several aspects of reform, from universal coverage to accountable care organizations. Massachusetts-based companies like Foundation Medicine are creating their own data portals to build evidence for value, while organizations such as Optum Labs are creating cross-sector partnerships to incubate ideas that will make value-based healthcare a reality. These ideas and initiatives are further explored in the Rewarding Innovation and Delivering Value chapter.


### ***Life Sciences Information Technology: The Implications of Big Data***

Capturing, analyzing, and applying data is a critical competency for life sciences companies, now more than ever. Whether it is applying Bayesian algorithms to analyze multi-omic data for R&D or analyzing millions of clinical records to generate value evidence, companies need health IT talent and technology to compete in the future.

Massachusetts is home to several leaders in the health IT space, including athenahealth, and eClinicalWorks, and the state has many local venture firms working on various aspects of connecting providers, patients and payer to medical data. The Mass Technology Leadership Council estimates that “Big Data” employs nearly 70,000 people in the state, including vendors and data scientists or managers in end industries, and that this number could increase to 120,000 by 2018.<sup>23</sup> This creates a strong opportunity for life sciences companies to engage and experiment with applying new IT applications and accessing robust datasets.

That said, Silicon Valley has a stronger base of IT talent and stronger venture activity in the space.<sup>24</sup> One biotech CEO shared that in his company’s efforts to recruit high level IT talent, prospects encouraged the firm to locate its IT initiative in the Bay Area. Massachusetts will need to proactively attract life sciences IT to the cluster, showing these companies how locating near its constellation of life sciences companies, universities, hospitals, and research institutes can provide a market incubator for products and accelerate success.

The future is bright for the Massachusetts cluster, if it continues to nurture its members, attract new companies, and address industry challenges and opportunities. The next chapters expand on key issues and provide an action plan for 2020.





## Lessons from Other Clusters

New York, Seattle, Houston, Germany, and China — every one of these clusters would like to achieve the level of industry success seen in Massachusetts. Promising new companies, cutting-edge technology, an educated well-paid workforce, deep-pocketed pharmaceutical companies-- why wouldn't they attempt to follow?



### New York City:

#### **Public-Private Partnerships to Spur Development**

New York has many advantages. It has a wealth of academic research institutions and teaching hospitals. It has been the headquarters of Pfizer and is a short train-ride from Merck, Bristol-Myers Squibb and Novartis in New Jersey. It also has exceptionally broad and deep financial resources at every point in the value chain. But the key challenge in New York is for new companies to find the necessary space and financing to overcome the cost of living and doing business in the city.

Recently, state and local agencies along with private organizations have collaborated on a number of initiatives to jumpstart the cluster. Examples include the NY Genome Center, BioAccelerate NYC, and the NYC Bioscience Initiative. These initiatives are raising significant dollars. Over \$140 million was raised as of late 2013 for the NY Genome Center from philanthropists, institutions, and government agencies.<sup>25</sup> These public-private partnerships and grassroots efforts are providing creative solutions to the problem of providing reasonably-priced space for early-stage biotech companies. While early, Massachusetts should monitor these experiments in New York to see if they make progress in creating affordable space for startups.



### Seattle:

#### **Local Business Leaders Making a Difference**

The University of Washington is one of the top academic medical centers in the country and receives the third largest pool of NIH funds<sup>26</sup>. Historically it has been a rich source of biotech innovation, spawning and supporting local companies like Seattle Genetics and Dendreon, and the now-acquired Zymogenetics, Immunex and Corixa. However, the academic life sciences research base drops off dramatically beyond the University of Washington and skilled talent can be hard to access. Also, venture capital is tight compared to other clusters.

Recognizing these challenges, the Washington Biotechnology and Biomedical Association (WBBA) has become a very active group of more than 500 biotech companies.<sup>27</sup> Because each new company is so important to the cluster, WBBA concentrates its efforts on bringing them each one into the network. Other institutions are ready and willing to collaborate in these efforts, and this attracts industry. Chris Rivera, WBBA's President, shared a comment from Novo Nordisk: "The WBBA's support for Novo Nordisk and networking played a key role of our second expansion decision over Boston. The integration with the local biotech community has been deemed quite successful, and the collaborative nature of Washington's biotech sector as sort of "coopetition" where pharma, academia and non-profit players interact closely with main focus on long term patients solutions and not short term financial gains are important to Novo Nordisk and our future strategic growth."

Seattle has also benefited from the philanthropic and investment interests of Microsoft founders Bill Gates and Paul Allen. The Gates Foundation is well-known for its life sciences interests. Paul Allen has invested in several biotech companies. Massachusetts has its own cadre of wealthy investors and philanthropists with interests in life sciences, who could offer additional vital sources of new funding if they are engaged in a more systematic manner.



### Texas:

#### **Doubling Down in Cancer Research**

Baylor College of Medicine has for many years been one of the more aggressive centers for commercially-oriented technology transfer and the University of Texas, MD Anderson is one of the top cancer research and clinical centers in the country. The State of Texas and MD Anderson have initiated programs to build on these strengths in cancer research. The "Moon Shots" initiative by MD Anderson<sup>28</sup> and the state-funded Cancer Prevention & Research Institute of Texas (CPRIT) set ambitious goals in the prevention, detection, and treatment of various cancer types. Bolstered by Texas' business-friendly policies, these \$3 billion initiatives aim to attract researchers and companies to the state. Examples of companies that have benefitted from CPRIT grants include several Texas-based firms—Caliber Biotherapeutics, Peloton Therapeutics, Molecular Templates, Mirna Therapeutics—as well as UK-based Cell Medica, which has since opened an office in Houston.<sup>29</sup> With aspirational "big picture" goals, MD Anderson and the state of Texas have rallied numerous stakeholders and helped focus vast amounts of capital to achieve progress. As more talent and technology flow to the region, these initiatives will show how calls to action can inspire cluster development.



## Lessons from Other Clusters

While other clusters do not pose an imminent threat, Massachusetts must not rest on its laurels. Other clusters don't have the same riches today, but that may make them even more hungry, more creative, more collaborative, more committed, and more determined. Analyzing efforts to build even a modest version of the life sciences infrastructure we have in Massachusetts may provide invaluable lessons.



### China:

#### **Enormous Government Support Laying the Foundation**

The Chinese government has made a big bet on biotech, pledging \$300 billion in a five-year plan to build sprawling new research parks and manufacturing plants, add 1 million new jobs, and spur significant industry growth by the end of 2015.<sup>30</sup> At the same time, the country's healthcare system is expanding access to care for its 1.3 billion citizens. These dynamics are attracting talent and capital to the region. Western-trained Chinese citizens are returning to China, rather than settling in the U.S. or Europe. U.S. investors such as Fidelity Biosciences and Vivo Ventures are funding or starting companies in China to develop drugs for the Chinese market.<sup>31</sup> Big pharma companies like Merck, Pfizer, and AstraZeneca are forming joint ventures with Chinese companies for R&D.

These efforts will take time to produce successful results, and challenges remain around navigating regulatory requirements and cross-cultural dynamics. However, significant groundwork is being laid and in the future China could become a formidable force in the life sciences. Establishing strong working relationships with the China cluster will be important. Massachusetts cluster leaders should broker collaborations with China-based firms and investors to create mutually beneficial exchange and investment.



### Germany:

#### **Investments Wane When Innovation is Not Rewarded**

"Health Made in Germany"<sup>32</sup> may be the local trade organization model, but stimulating biotech investment has been an uphill battle in a market that has been one of the most aggressive at developing drug pricing controls. Germany can claim to be a birthplace of the pharmaceutical industry with notable leaders such as Boehringer Ingelheim, Bayer, and Merck. Over the years, the national and local governments have pursued many initiatives to support biotech industry formation, but the results have been modest at best. Strong government effort to pursue price controls for drugs is a hindrance to pharmaceutical and biotech investment. Many biotech industry experts point to the German Institute for Quality and Efficiency in Healthcare's (IQWiG) cost control initiatives as evidence of an unfriendly investment environment. Aggressive downward pressure on pharmaceutical pricing is a factor in attracting local investment. As policymakers push forward in the U.S. with healthcare reform and cost-effectiveness initiatives, they should heed the lessons of Germany and recognize that lack of reward for innovation could be the biggest threat to the Massachusetts cluster.



### Lessons for Massachusetts:

Other clusters will continue to invest and compete for their own version of Kendall Square. Massachusetts must learn from their experiments in order to preserve the bastion of innovation and industry leadership that has been cultivated over many years. Forging effective partnerships between public and private organizations can address funding and infrastructure challenges that stymie growth. Rallying investors outside the life sciences to the industry, through aspirational programs with personal relevance, will expand the pool of funding for startup companies. Massachusetts should be seen as a "global beachhead" to draw foreign investors, talent, and companies to Massachusetts to participate in world-class R&D efforts. Finally, defending the basic systems that reward innovation as governments seek to manage rising healthcare costs is critical to safeguarding the very foundation of the cluster.

# Rewarding Innovation and Delivering Value in Life Sciences

**“The greatest threat to the Massachusetts life sciences cluster is a diminished reward for innovation. If healthcare reform undermines that incentive, this entire cluster could disappear overnight.” – Vicki Sato, Professor, Harvard Business School**

Whereas previous strategic reports on the Massachusetts life sciences sector have focused on regional challenges, state government initiatives, and local partnerships, it is a global issue—specifically healthcare cost containment—that is most likely to shape events over the next decade for the industry. Nearly every stakeholder interviewed for Impact 2020 referred to national health policy, cost containment and drug price reform as major threats to the ecosystem and the primary strategic issue for their business.

As this report is prepared in early 2014, the Massachusetts cluster is doing well, the biotech IPO market is the most active that it has been in years, and several major breakthroughs are imminent in gene therapy, personalized medicine, and orphan diseases. However, many executives are concerned that this industry faces a perilous future. Every day, headlines in the industry press highlight another initiative to control spending on drugs and limit access to new therapies.

Massachusetts may be in a better position than other clusters to survive the emergence of a new model for the payment and delivery of healthcare. However, because it is so dependent on this sector, the cluster is also more vulnerable, unless it takes action. Therein lies the opportunity for Massachusetts.

With strong local leadership in all relevant sectors of the life sciences ecosystem and a track record for finding creative solutions, Massachusetts can be a vanguard in enabling change. Today, most discussions regarding the value of new therapeutic options are taking place in the trenches, with marketing executives on one side and formulary committees, pharmacy benefit managers (PBMs), and purchasing groups on the other. Their conversations focus on tactical decisions regarding formulary acceptance, tiering, and co-payments for a specific drug. Cost-benefit arguments offered by big pharma are received with skepticism. The result is a zero-sum debate of the cost-benefit of an individual drug, device, or service.

Interviews with stakeholders from across all sectors voiced the same need: to elevate the discussion regarding value-based care to a higher level. Massachusetts must bring together senior leaders from product companies, payers, providers, and government to discuss an appropriate system for evaluating trade-offs, to develop a set of metrics to balance various interests, and to adopt systems that ensures adequate access to high quality care for patients at a reasonable cost. Viewed in the context of the patient, the interests of otherwise opposing parties align, and enable a path forward toward a workable solution.

**“When value is measured in terms of our patients and their outcomes, we are all on the same side of the table.” – Gary Gottlieb, CEO, Partners HealthCare**

“Boston/Cambridge is a close-knit community where all the local leaders know each other. It seems that it should be the right environment to bring together all the relevant parties in a productive discussion.”  
– California Biotechnology Executive

## ***Healthcare Reform: Local Leadership in a Global Debate***

The Affordable Care Act (ACA) and resulting efforts to bend the healthcare cost curve were starting points for many stakeholder conversations, but all agreed—regardless of what happens in Washington DC—the movement toward more aggressive cost containment measures and pricing restrictions will accelerate. Private initiatives led by insurance companies and employers will force life sciences companies to clearly demonstrate not only efficacy and safety of new products, but also the impact on system economics and patient outcomes.

For drug companies, cost containment is a global phenomenon that has been unfolding in Europe for many years. Dominated by single-payer systems, European pricing policies, particularly in the United

Kingdom, France, and Germany, have instituted aggressive cost containment and drug reimbursement reviews. Approval dossiers detailing the cost-benefit arguments for a given drug are standard practices for pharmaceutical companies launching products in Europe. Arguably, obtaining favorable reimbursement has become more critical than regulatory approval. While the United States is not yet moving toward a single payer system, the U.S. government does account for almost 40 percent of drug spending<sup>33</sup>. Increasingly, marketing executives planning for new products, business development executives conducting due diligence on assets to in-license, and investors evaluating funding options for life sciences companies focus intently on pricing flexibility, tangible product differentiation, and persuasive value arguments for payers.

The next five years will be characterized by a wide range of experiments as those advocating for price controls and those advocating for innovation debate the issues. But, as industry participants in an Impact 2020 focus group on value said, pricing does not equal value. Inevitably, the hurdle for demonstrating meaningful life sciences innovation will be higher. Value will take into account the full continuum of disease management from diagnosis to final outcome. It must reflect an assessment of individual patient needs as well as population statistics. It must address near-term and longer term impact on providers and payers.

Two critical questions will frame the future debate. First, from a public policy perspective, how far will regulators go in restricting access to new technology? And how will future restrictions on technology utilization be implemented? Local life sciences companies and investors cannot afford to be passive in this debate. They must be actively engaged in influencing the answers those questions.

Is Europe a model for what the U.S. will eventually become? A senior industry executive recently based in Europe shared his view that if the U.S. were to adopt an aggressive stance on restricted access and reimbursement as has occurred in the UK and Germany, it would be the single greatest threat to life sciences innovation in the U.S. European policymakers have been able to implement restrictive policies because the U.S. continues to invest in healthcare research and development. But the evidence is clear: life sciences venture capital has largely abandoned Europe<sup>34</sup>, European startups are looking to the U.S. for their opportunity and European pharmaceutical companies are questioning whether building additional infrastructure in such a restrictive environment makes sense.

In Massachusetts, the impact of policy reform is starkly evident in the field of regenerative medicine. Regenerative medicine is on the verge of major breakthroughs in heart disease, ophthalmic diseases, diabetes and many other disorders and Massachusetts has helped to pioneer the field and should remain a leader.

At the same time, two companies in the regenerative medicine field are struggling to preserve a viable business model. Organogenesis and Shire marketed the only two FDA-approved, advanced skin substitutes manufactured using novel cellular therapy techniques (Apligraf and Dermagraft, respectively). In November 2013, CMS dramatically cut reimbursement for these living cell-based products.<sup>35</sup> Immediately, treatment centers around the country were forced to reconsider their use of these products, and these two companies, after years of development and multi-hundred million dollar investments, needed to re-evaluate their strategies. For many elderly patients with diabetes who suffer from ulcerated lesions, access to these therapies is critical but is now uncertain. Shire chose to exit the field, selling Dermagraft to Organogenesis, leaving one company to fight the reward-for-innovation battle.<sup>36</sup>

The concern about whether there will be a reward for innovation is real. The investors, fund managers, stockholders, and employees, who are betting on the life sciences industry, are prudently reassessing whether the rewards justify the risk. As is well documented elsewhere, drug products in the early planning stage today will not be available for patients for a decade or more. Companies and investors need more certainty about the potential return on their investment. They need to know that there will be a reward for innovation and recognition for value created. Otherwise, the risk is too high. Many U.S. venture firms have already backed away from the risk inherent in life sciences, redeploying dollars toward high tech and consumer products. With an enormous investment at stake and a high level of uncertainty and a long time horizon for a payback, the life sciences industry and the Massachusetts cluster could face a bleak future.



## ***Call to Action for Key Stakeholders***

For the life sciences industry and the local cluster, there is an opportunity to influence the future and hopefully ensure the cluster's vitality for years to come. Impact 2020 calls on industry and other key healthcare sectors to embrace value and to collaborate to determine the best solutions:

**Embrace Value Arguments:** Not long ago, pharmaceutical companies such as Merck and Pfizer populated the lists of the most admired companies. They were the “blue chip” stocks that investors sought out. Now they are companies that, as one executive said, are “easy to dislike.” Pricing and promotional practices have sullied reputations. Many stakeholders voiced a desire for the industry to re-examine and police its own practices.

Stakeholders strongly suggested a need for life sciences companies to engage and lead a higher-level discussion of how to measure and reward value for novel life sciences products and assess outcomes. “Pharmaceuticals should be part of the solution to excessive growth in healthcare spending and not the cause.” “Personalized medicine should lead to more effective, more targeted and more cost-effective care.” “Novel delivery systems should reduce hospital stays and enable out-patient management.” All these observations are theoretically true, but will only become reality if industry collaborates and makes the case for its potential contribution to medicine, to curbing healthcare spending, and to improving patient lives. Zero-sum arguments on a product-by-product basis are not sufficient. Industry leaders must be present at the table, avoid the temptation to prioritize short-term solutions, leverage their collective financial resources to investigate new algorithms, and direct talented managers to advance the effort.

Foundation Medicine is an example of a local company that is embracing the challenge of demonstrating value **[See Case Study - P ]**. The company's first diagnostic test, FoundationOne, allows physicians to access a report describing the pattern of genomic alterations found in a patient's tumor sample and highlighting potentially beneficial therapies and clinical trials. However, Foundation Medicine and others pursuing reimbursement for NGS-based diagnostic tests have encountered a complex and time-consuming process. In response, the company has made significant investments to capture data on how patients fare on therapies selected by oncologists based on their FoundationOne report. As Foundation Medicine's Chief Commercial Officer Kevin Krenitsky says, “There is a need to improve data transfer between payers and companies in order to open communication and demonstrate value.”

**Encourage Local Collaboration:** In discussions, many dismissed these cost containment threats as national and global issues that cannot be solved at the local level. Interestingly, those outside Massachusetts were more optimistic and, in fact, look to Massachusetts for leadership on these topics. Massachusetts has led the way before; ensuring health insurance coverage for all its citizens with an approach that became a model for the national system. In a complex, highly fragmented healthcare environment with many diverse and conflicting perspectives, many believe that Massachusetts is in the best position to conceive of a system that balances an intense commitment to research and development with economically responsible patient care.

Others are skeptical that this will really happen. However, as part of this project, MassBio has been able to engage representatives from payers, providers, academic institutions, large and small drug companies, state government, and venture firms to come together to share ideas, through interviews and participation on the MassBio Impact 2020 Advisory Board. And one local organization, Optum Labs, is seeking to develop collaborative solutions to healthcare problems in order to improve outcomes and quality of care and to better define value. Optum has brought together multiple stakeholders involved in healthcare delivery and innovation, including patient groups like AARP, pharma companies such as Pfizer, academic researchers including Boston University, providers and clinician organizations such as Tufts Medical Center, the American Medical Group Association, and many more. **[See Case Study - P].**



## *Recommendations for MassBio*

Among all the issues, concerns, and opportunities highlighted in this report, none is as important as promoting a suitable reward for innovation. The next five years in healthcare will be characterized by a nearly complete disruption of the industry. The future will be characterized by rising consumerism, delivery-model transformation, proliferation of data solutions, and system integration. While strong today, the Massachusetts life sciences cluster could be rapidly undermined by the adoption of a system that does not appropriately measure value. MassBio, as the representative of this cluster, must continue to advocate, educate, and elevate the discussion around these issues of value for innovation.

- 1) **Convene a Value-Based Care Working Group:** MassBio can elevate the dialogue on value by engaging trade associations and business groups across the healthcare spectrum, including the Network for Excellence in Health Innovation (NEHI), MassMEDIC, Massachusetts Association of Health Plans (MAHP), the Conference for Boston Teaching Hospitals, and Massachusetts Life Sciences Center (MLSC). Two or three Board members or senior executives from each group should come together to formulate views on how value should be defined, measured, and implemented in the broader healthcare environment. The group can work toward publishing white papers on these topics, engaging directly with policymakers, and participating in national forums on healthcare reform, ultimately becoming a highly visible resource for local, state, and national leaders.
- 2) **Engage Payers and Providers:** MassBio, its President and its Board should seek out opportunities to involve representatives from payers and providers in an ongoing discussion of the local opportunities. Several senior executives from payers, providers, investors and industry acknowledge minimal cross talk with leaders in other sectors. MassBio should consider adding a payer representative and a provider representative to its Board of Directors as a first step toward bridging the gap in communication. Not only do the groups need to learn more about each other, the hope is that they will realize many shared interests and challenges.
- 3) **Advocate for the Value of Innovation for Patients:** MassBio should continue to work with national and state legislators and government officials to build awareness for how value is created by local companies, the importance of the life sciences sector overall, and how policy initiatives may hinder innovation. MassBio should communicate to the public the value of innovation for patients. MassBio must demonstrate leadership by ensuring continual awareness around issues of value in life sciences solutions as measured in patient outcomes. MassBio should keep patients, patient needs, and patient value front and center with all its various stakeholders.
- 4) **Develop More Value Programming and Education:** MassBio should continually inform its members on reimbursement initiatives and provide a curated resource center to educate companies on payers and providers, their interests and incentives. At the programmatic level, MassBio has an opportunity to help the smaller biotech companies to “speak value,” through MassCONNECT mentorship and MassBioEd’s Biotech Learning Center curricula. While these companies are a long way from launching products into the market, making a persuasive argument to investors and partners supporting the value of their preclinical or early clinical program must reflect a more sophisticated understanding of how payers make decisions. Programs and events should also incorporate patient experiences, and stories of successful innovation.

## Case Study - Foundation Medicine



Foundation Medicine (NASDAQ: FMI, Cambridge, MA) is bringing comprehensive precision medicine into routine care in oncology. Companion diagnostic testing for certain targeted therapies has been adopted for a handful of tumors and therapies. Foundation Medicine was founded in 2010 by

scientists at the Broad Institute, Dana-Farber Cancer Institute, MIT, and Harvard based on the premise that utilizing next generation sequencing (NGS) to assay the entire genomic profile of a patient's tumor, rather than a single gene, would more reliably identify all the available targeted therapeutic options.

Shortly after founding, the company launched its first diagnostic test, FoundationOne, a fully informative genomic profile based on several hundred known cancer genes. Physicians access a report describing the pattern of genomic alterations found in a patient's tumor sample and highlighting potentially beneficial therapies and clinical trials. With the launch of FoundationOne, this type of approach is now available to physicians practicing within and outside major cancer centers.

Immediately, NGS delivers value to patients, making it possible to replace multiple expensive diagnostic tests, accelerate the time to a treatment decision, and reduce biopsy sample requirements. The future value of NGS is even more compelling, as Foundation Medicine's products will enable physicians to look at one patient's profile in the context of thousands of other similar patients and treatment experiences. The company has committed to open access to the largest oncology genomic data set in the world, and is also planning to enhance their physician interface, Interactive Cancer Explorer™, in order to capture data on how patients fare on therapies selected by oncologists based on their FoundationOne report. Not only will open access to this data provide outcomes-based evidence for patients, providers, and payers, but it will also allow others to continue to push research forward and find even better therapies for cancer patients in the future.

Foundation Medicine and others pursuing reimbursement for NGS-based diagnostic tests have encountered a complex and time-consuming process to obtain reimbursement. Foundation Medicine is investing millions of dollars to provide clear tangible evidence that FoundationOne's \$5,800 price tag is justified. As Foundation Medicine's Chief Commercial Officer Kevin Krenitsky says, "There is a need to improve data transfer between payers and companies in order to open communication and demonstrate value." Foundation Medicine offers a valuable proof case for why a dialogue among companies, payers, and providers on how to assess and measure value is necessary today. Without this dialogue, the risk may be too great for entrepreneurs and investors considering the next Foundation Medicine.



## Case Study – Optum Labs



In early 2013, Optum and Mayo Clinic established Optum Labs, an open center for collaborative research and innovation, providing unique data and analytic resources that enable stakeholders from across the healthcare ecosystem to drive advances that will lead to improved patient care and patient value. Cambridge was chosen as the site for this new collaboration because as Paul Bleicher, M.D., Ph.D., CEO of Optum Labs, explained, “many of the leading healthcare institutions, biotech, and pharma companies had decided to locate here – it felt like a great concentration of healthcare stakeholders existed in and around Cambridge and the greater Boston area.”

Problems in health care are multifaceted. Definitions of value can be complex, but most focus on the “Triple Aim” which defines value as improving outcomes and the patient experience of care, while reducing the per capita cost of healthcare. This system definition of value requires stakeholders, who have historically sat at different tables, to come together and sit at the same one. Optum Labs seeks to develop collaborative solutions to healthcare problems in order to improve outcomes and quality of care and better define value. The center has brought together diverse stakeholders of the healthcare ecosystem involved in healthcare delivery and innovation. These include consumer advocacy organizations like AARP, pharma companies such as Pfizer, academic research institutions including Boston University, providers and clinician organizations such as Tufts Medical Center and the American Medical Group Association, and many more.

Optum Labs works on problems that affect the system of care and that are of shared interest to all its stakeholders. The center’s co-founding partner, Optum, has a life sciences group with more than 150 health-effectiveness and outcomes researchers who study and review whole classes of drugs. Optum brings innovative analytical tools, and a proprietary database that includes administrative data covering approximately 150 million lives, spanning more than 20 years of health records. Co-founding partner Mayo Clinic brings clinical data on roughly 5 million patients and patient-focused research expertise. When Optum purchased Cambridge-based Humedica, 37 million EHR patient data sets were also included. The key to success for Optum Labs will be enabling its diverse partners to mine this rich, longitudinal dataset with leading-edge analytics to develop insights into populations and the people within them. In addition, Optum Labs will be growing its data resources through partnerships with providers, life sciences companies, and other organizations. By linking the output of the research to the clinical environment via Optum Labs and partner care settings, the goal is to implement new knowledge that improves healthcare delivery and patient outcomes.

While Optum Labs strives to conduct research that translates to improved patient care, it also seeks to influence policy holders based on the analyses and insights of its diverse group of partners. Unlike many other big data efforts in healthcare, research findings are open and available. By publishing data, Optum Labs believes its efforts will more fully benefit patients. Historically, research efforts like this were done internally by HEOR groups inside of pharma or payer organizations in order to negotiate pricing. Today, this research must be done collaboratively in order to understand the continuum of care across multiple interventions and settings, so that in the end, patients get the best care possible.





# Financing Life Sciences Innovation: Growing Challenges in Seed Financing

## Declines in Life Sciences Venture Capital

Access to high-risk, early-stage venture capital (VC) is the fuel that has driven innovation in the Massachusetts life sciences cluster since the early days of Genetics Institute. Massachusetts is fortunate to have a group of highly successful venture funds committed to the life sciences. These funds have continued to invest through economic cycles and have played a pivotal role in shaping the industry.

In the broader VC industry, however, suboptimal biotech returns have caused many funds to exit the space. Silicon Valley Bank's data suggests that there was a 54% decline in venture dollars raised for life sciences between 2007 and 2012 [Figure 1]. Limited Partners are rethinking their allocation toward venture investing. CalPERS, the \$250 billion California Public Employees' Retirement System, has committed substantial investments to life sciences through funds such as Aisling Capital, Alta, Clarus Lifesciences, Essex Woodlands and TPG. CalPERS has announced that, over the next five to 10 years, they will cut venture capital from 7% of its portfolio to 1% of its portfolio, a drop of \$15 billion, due to concerns over disappointing returns.<sup>37</sup> The National Venture Capital Association (NVCA) and Medical Innovation and Competitiveness (MedIC) Coalition call the current life sciences venture landscape "extremely troubling," stressing that "we risk destroying an innovation ecosystem that has generated high-quality jobs and growth for the U.S. economy for decades."<sup>38</sup>

**Figure 1:**

**Recent Declines in U.S. Venture Capital Raised (\$M) for Life Sciences Investing**



Source: Silicon Valley Bank.

Several established VC firms have shifted more attention to "venture creation," where cutting-edge research is identified by fund principals, incubated in their offices, nurtured by executives-in-residence, linked into the network, and then funded. New companies have been started to address orphan diseases, cellular therapy, and gene therapy, all by venture capitalists themselves. Other firms have moved downstream, investing in public companies with late-stage assets or approved products. What do these shifts imply for entrepreneurs? In the past, entrepreneurs could write a business plan and take it on a road show to 25 or 30 VC firms, leading to a series of syndicated funding rounds. Now, there is too much uncertainty with the entrepreneur, the intellectual property, the development plan, and the interests of other investors for VCs to invest in this model.

This has led to a wider "valley of death," where the hurdle to get from a seed to a Series A or B event is much higher. Silicon Valley Bank data also indicates that the dollars invested in Series A, taking into account all funding rounds exceeding \$2 million declined by approximately 50%. Research by Iain Cockburn from

Boston University and Josh Lerner from Harvard University addresses the grave concerns facing the industry based on an evaluation of risk and cost of capital and the implications for lower investment.<sup>39</sup> The future poses more risk, not less. If an entrepreneur is unable to attract the deeper-pocket VCs, as this data suggests, raising small amounts of capital will be more difficult. The result is a much more Darwinian ecosystem.

Some argue a more demanding investment climate means we will avoid the overinflated, capital-inefficient mistakes of the past and the free-market will enable the best ideas get to move forward. They suggest companies that do obtain funding should be stronger and that this is the best outcome for the industry. Others worry that many good ideas could be lost, and that this is a “shots-on-goal” issue. They observe that many promising ideas may die due to the lack of a small amount of capital necessary to sharpen the storyline or bring in the right team. They question whether, in this more selective investment environment, picking winners is really possible.

It is clear that venture funding for the life sciences is down. In the face of this, significant efforts outside of venture capital must be focused on the early-stage industry. This means connecting startups to a diverse network of funding sources, advisors, and enablers as early as possible. MassBio can play a central role in connecting entrepreneurs to the resources they need to pressure test and shape their ideas. From angel groups to family foundations to crowdfunding, there are diverse funding sources that can provide seed capital to promising startups. Early access to advisors or mentors can help entrepreneurs focus their efforts. Leveraging external resources like incubators and contractors can enable lean businesses operations. The cluster’s network can provide all of these elements and MassBio can serve as the central link.

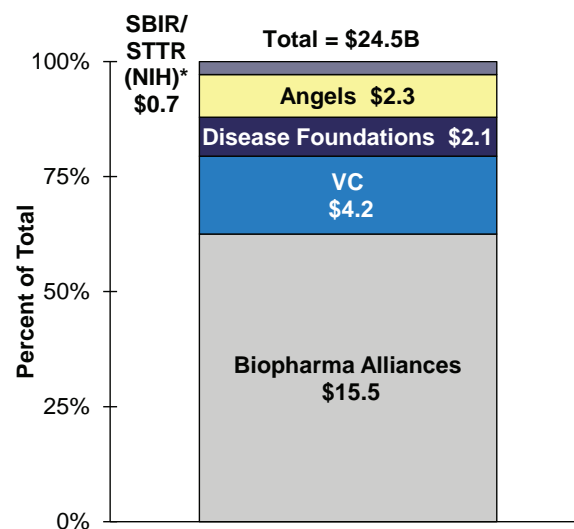
The following sections describe important seed-stage resources and how they can be made more accessible to startups in need.

## Corralling Alternate Funding Sources

In recent years, alternate sources of funding have equaled or exceeded venture capital dollars [Figure 2]. These sources have advantages, disadvantages, and their own learning curves.

Figure 2:

**Total Capital Invested in Biotech, U.S., 2012**



## Angels and Angel Groups

With less institutional venture capital available, raising money from friends, family, and other individual investors has become more common. Massachusetts has a large number of technology-oriented veterans who can qualify as angels and collectively they can help offset the growing funding gap. Many angels are already organized into networks or groups, and several in Massachusetts focus on the life sciences.

### Massachusetts Life Sciences Angel Groups



Angels are a valuable source of capital for the right companies. Angel money can fund a few experiments, important hires, and patent filings, supplementing the founder's personal funds and sweat equity. Investment opportunities that fit best are efficient development programs that can quickly lead to value-creating events. Jim Jenson, previously at Dicerna Pharmaceuticals, is funding his new company Sabik Medical with angel money. The company is based on a novel approach for diagnosing and treating prostate cancer, and Jenson has prepared a tightly-focused plan to achieve proof-of-principle.

As another example, Lexington-based Avaxia Biologics is funded by several angel groups, including Massachusetts-based Launchpad Venture Group and Mass Medical Angels **[See Case Study]**. The company is developing an orally-administered anti-TNF for inflammatory bowel disease. As injectable anti-TNF molecules are already approved for IBD, Avaxia's novel approach does not need to validate the basic science, enabling a very efficient startup model.

Entrepreneurs must be prepared for some challenges with angel funding. First, the amount of capital available from an individual is limited, so often a larger number of investors are needed to reach a critical mass. Tranches of \$20,000 to \$100,000 are common, so a \$2 million raise could involve 20 or more investors, posing communication and management challenges. Furthermore, subsequent capital needs often require other funding sources, diluting those early investors.

These concerns aside, angel money can help companies achieve significant strategic deals and exits. Barbara Fox, CEO of Avaxia remarked, "These angel groups are smart, they do their diligence and I need to emphasize communication, but pharmaceutical companies don't care where the early-stage investment comes from." In another example, Merck bought Beverly-based SmartCells for upfront and milestone payments of ~\$500 million in December 2010. Started in 2004, SmartCells was able to achieve this sizable exit with modest fundraising from NIH grants and angel groups, totaling just under \$10 million.<sup>40</sup>



## Case Study: Avaxia Biologics



Creativity and tenacity have allowed Avaxia Biologics, Inc. (Lexington, MA) to bring their flagship compound AVX-470 through Phase I clinical trials, secure patent protection, and position the company for future development.

AVX-470 was developed using Avaxia's propriety technology platform, based on gut-targeted polyclonal antibody therapeutics. Initial validation of the compound for treatment of oral mucositis was

achieved through collaboration with Watertown-based CRO Biomodels LLC, a leader in the study of cancer treatment-related mucosal injury. Riding on that success, Avaxia looked at AVX-470 in Inflammatory Bowel Disease (IBD), which emerged as its lead indication.

Avaxia's fundraising began with a Phase I Small Business Innovation Research (SBIR) grant to pursue oral mucositis. As Avaxia's CEO Barbara Fox stated, "The support of the NIH provided both the funding we needed to advance the development of this much needed therapeutic, and critical scientific validation of our approach." Additional SBIR grants were awarded over the next three years, totaling approximately \$1.5 million.

Based on clinical success in IBD, Avaxia was able to raise \$4.1 million in a Series A financing round which closed in early 2012 from Northeast-based angel investors, including Beacon Angels, Launchpad Venture Group, Mass Medical Angels, Cherrystone Angels and Maine Angels, as well as other individual investors. Fox herself recognized the important role of angels in their success, stating, "Having broad support from the New England angel community demonstrates the important role that individual investors are playing in funding early-stage biotech companies."

In February 2013, Avaxia began its Phase I clinical trial for AVX-470 in IBD. To fund the trial, the company was able to secure a Series B round of \$11. million from both existing and new angel investors. Notably, AbbVie, which markets anti-TNF Humira, provided funds in this round. For their commitment they receive a board seat, but no rights to AVX-470.

Managing a large number of angel investors may be a challenge, but one that Fox welcomes. Avaxia's story illustrates another model for creative execution, careful deployment of resources, and building a story that can ultimately attract a deep-pocket pharmaceutical partner and successful exit.



## Family Foundations

Wealthy philanthropists and family foundations have a long history of investment in healthcare, supporting hospitals, research institutes, and disease foundations. In recent years, many have realized that funding basic research, while essential, is not sufficient to make progress for patients. The Gates Foundation, the Paul G. Allen Family Foundation, the Helmsley Trust, and the Pritzker Family have all invested in the life sciences. Thomas Flatley, who owned one of the largest real estate firms in the Northeast, founded the Flatley Foundation which formed a not-for-profit in 2008 for cystic fibrosis drug research.<sup>41</sup> The Wellcome Trust is a UK-based charitable organization that is expanding its global reach. With an endowment of around £17B, the Trust is one of the largest funders of global biomedical research, and is increasingly funding early-stage companies [See Case Study].

A recent example of success in family foundation funding is Acetylon, which experience a banner year in 2013. [See Case Study]. The company concluded a \$1.7 billion partnership deal with oncology leader Celgene, reaching that milestone without any traditional venture capital. Instead, Acetylon raised angel money and received support from the Kraft Family Foundation. Bob Kraft, known locally for his ownership of the New England Patriots, grew up in Brookline, Massachusetts, received an MBA from Harvard Business School, and built International Forest Products, one of the largest paper and packaging companies in the world. The Kraft Family Foundation has a long-standing relationship with the Dana-Farber Cancer Institute. This model worked to move Acetylon along, and many executives are eager to explore this new way of raising funding.

While there is a large philanthropic interest inspiring these investments, frequently influenced by personal experiences or associations, the leaders of these foundations are also sophisticated business executives. Before approaching these foundations, companies need to have not only programs with high potential to impact patients' lives, but also efficient business models and strong management teams.

### Case Study: Acetylon



Acetylon Pharmaceuticals (Boston, MA) has been able to advance their lead compound, ricolinostat, an oral, small molecule, selective HDAC6 inhibitor, into multiple clinical trials using a variety of funding sources including wealthy individuals, a Massachusetts family foundation, an international nonprofit disease organization, corporate equity investment, and a major corporate partnership.

Acetylon's foundational technology emerged from a local connection between the Dana-Farber Cancer Institute and the Broad Institute, based on HDAC inhibitor research. Dr. Stuart Schrieber's lab at the Broad Institute was one of the first to discover the structure and biological function of HDAC enzymes and had been developing novel "probe" compounds that could selectively inhibit HDAC6. Dr. Kenneth Anderson's lab at DFCI had developed and validated multiple myeloma in vitro and animal models and for many years, assessed compounds for industry. Dr. Anderson was involved in the early stages of both Celgene (Thalomid and Revlimid) and Millennium: The Takeda Oncology Company (Velcade) in preclinical and clinical research of successful new drugs. When the two labs collaborated to test the potential of these selective HDAC6 inhibitors in multiple myeloma models, the opportunity for an effective therapy was demonstrated and additional translational research was undertaken. Acetylon was subsequently formed to develop a druggable compound and advance the technology into clinical trials.

Acetylon's fundraising began in late 2008, at the height of the 2007-09 recession, a particularly difficult time to raise money from venture funds. In July 2009, the company raised \$7.25 million from a group of private investors, including the Kraft Family Foundation. Robert and Myra Kraft were well-known benefactors of Dana-Farber Cancer Institute and through the Institute became connected with the young startup. Several other high-net worth individuals invested through similar connections. As Acetylon's CEO Walter Ogier said, "Having Harvard and MIT present in Massachusetts, which makes possible connections with institutions like DFCI and the Broad Institute, is a big help when securing funding. Key opinion leaders' endorsement is important when raising money from high-net worth individuals who may not routinely invest in biotech."

During the next two years, Acetylon made progress on qualifying their HDAC6 compound, winning grant money from the NIH and IRS, and receiving \$2 million in additional financing from private investors. Promising preclinical data on ricolinostat enabled Acetylon to raise \$26 million in a Series B financing and secure \$5 million in non-dilutive funding from the Leukemia and Lymphoma Society to advance ricolinostat into clinical development.

Acetylon's early clinical trial data attracted the attention of Celgene, which in early 2012 invested \$15 million to support the expansion of ricolinostat clinical development.<sup>49</sup> Then in 2013, Celgene and Acetylon announced an exclusive strategic collaboration, with an upfront \$100 million payment by Celgene and a potential total deal value of \$1.7+ billion dollars.<sup>50</sup>

Acetylon's story demonstrates the powerful connections within the Massachusetts life sciences cluster, the diversity of capital sources that are available, and the resilience of entrepreneurs. However, it also demonstrates how many different elements have to align to propel a company forward.

## Case Study: Wellcome Trust



As the funding gap widens for entrepreneurs, one charitable foundation has developed a novel investment approach for early-stage life science companies and is taking steps to expand its geographic presence. The London-based Wellcome Trust is increasingly funding research and development projects to help transition them to a point where they are

attractive to later-stage investors or acquirers. While historically the majority of funds have gone to universities, about 40% are currently invested in companies and this is an area that Keith Spencer, Business Analyst at the Trust, says will continue to grow. "Earlier is where the interesting science can be found. We would love to work on more pre-clinical projects," says Spencer.

The Wellcome Trust's Technology Transfer Division" offers several mechanisms for funding projects, including their "Seeding Drug Discovery Award" for early-stage small molecule drugs, and their "Translational Fund Award" for other R&D projects meeting an unmet clinical need, including biologic drugs and diagnostics. Projects are evaluated based on the quality of science and research as well as the level of unmet medical need. The Trust strives for reasonable terms of investment, with the typical terms for companies being a convertible loan with a 20% discount rate at a future fundraising round. Standard templates for funding terms are published on the Wellcome Trust website: "Our overriding priority is curing disease not financial return," says Spencer.

The Trust is able to add valuable resources beyond capital invested. A research steering group with extensive industry and academic experience meets quarterly to help oversee and strategically manage the project. Citing a 50% reinvestment rate as a project progresses on its development path, the Trust is able to double down on its successes. Early-stage drug discovery projects may receive £1-2MM GBP, while later stage drug discovery projects may receive £4-5MM GBP. These dollars can make an incredible difference for a nascent project.

Some of the Trust's most recent investments in the US include Pennsylvania's VenatoRx Pharmaceuticals – developing novel anti-infectives to antibiotic resistance, New Jersey's PTC Therapeutics – focused on RNA based oral treatments (projects funded are for glioblastoma and drug-resistant infections), and San Francisco-based Achaogen – developing novel aminoglycosides for treatment of multi-drug resistant gram-negative bacteria. "There is no question we are seeing more applications. In Seeding Drug Discovery, we have more than doubled the applications received since we moved to Early and Late awards" says Spencer. The Wellcome Trust team believes there is a lot of great science to be funded and is excited to increase its role as traditional capital sources decline.



## Crowdfunding

Crowdfunding has emerged as an investment vehicle only in the last few years. The JOBS Act (Jumpstart Our Business Startups Act), signed into law by President Obama in April 2012, opened the door to an entirely new approach to raising private investments **[See Sidebar]**. Platforms like Poliwoogg, MedStarter, and HealthiosXchange are already testing the model.

Is crowdfunding a realistic option for life sciences companies? Skeptics believe that companies will be unable to raise enough money, that less-informed investors will quickly become disillusioned by failures, and that the logistics of managing a diverse group of investors will be unwieldy. Bruce Booth from Atlas Venture shared a more optimistic view of what crowdsourcing may mean. He believes that across the U.S., and particularly in Massachusetts, there is a tremendous amount of wealth sitting on the sidelines that could be deployed into private companies if there was an efficient vehicle. Crowdfunding may provide an opportunity for those companies to gain visibility. For companies with modest funding requirements and compelling concepts, the model is intriguing.

Greg Simon, CEO of Poliwoogg, is an evangelist. His organization will manage investments in private companies on behalf of individual investors and create index funds that follow private investments. Greg believes that crowdfunding will “democratize and disintermediate life sciences investing. It is a disruptive model that will allow the American people to invest in ideas that they are passionate about.” If Greg Simon’s vision becomes reality, private investing by individuals in the future may look a lot like public markets today.

Many questions do remain. Will crowdfunding attract mainstream life sciences companies or will it be a fringe opportunity for a narrow group of companies that cannot be otherwise funded? Will investors find the companies and the returns sufficiently attractive to stay in the game? We are at the early stages of this experiment, but for the Massachusetts cluster it bears watching.

### Sidebar: U.S. JOBS Act and the Birth of Crowdfunding

Most early-stage entrepreneurs do not have an existing network of high-net worth individuals. Just finding these potential investors can be incredibly difficult, let alone convincing one to invest in a new company. But with the passage of the JOBS Act, fundraising may become more feasible for entrepreneurs in search of an investor base.

The JOBS Act was signed into law by President Obama in April 2012, and in 2013, the U.S. Securities and Exchange Commission proposed several rules on provisions of the Act enabling companies to seek investment through crowdfunding mechanisms. These included modifications to the General Solicitation provision, now allowing public advertisement of private offerings. Updates to Regulation A raise the limit for private placements with accredited investors from \$5 million to \$50 million. The Crowdfunding Provision, part of Title III, creates rules and a path for non-accredited investors to begin investing in companies. As of this writing, several of these rules proposed by the SEC are still open for public comment and are subject to change prior to formal approval, though many believe approved rule changes will significantly increase available capital for early-stage life sciences companies.<sup>51</sup>

Startup companies can now generally solicit investment from accredited investors through crowdfunding portals such as AngelList, Poliwoogg, VentureHealth, and HealthiosXchange. These new platforms have begun to actively recruit companies and raise money from private investors. AngelList has demonstrated early success, boasting \$2.4 billion of capital raised for 4,000 companies over two years.<sup>52</sup> VentureHealth, a life sciences crowdfunding site, has had successful exits with companies that raised money through the site, including Nfocus Neuromedical (purchased by Covidien) and BodyMedia (purchased by Jawbone).<sup>53</sup> These early examples demonstrate that there is investor appetite for crowdfunding and potential to fund companies to an exit.

With more than five million households having a net income greater than \$200,000<sup>54</sup>, there is considerable opportunity for new sources of capital here in the U.S. If just a fraction of this population participates in crowdfunding as an opportunity to invest, there would be billions of dollars available for life sciences.

There are major questions regarding how the JOBS Act will be implemented. Will it attract a significant number of quality deals? Will capital resources be sufficient to support life sciences ventures? Will the logistics of managing large number of investors restrict use? Undoubtedly adoption will be faster outside of life sciences and use of this new approach to accessing private capital will evolve in structure. It is unlikely that crowdfunding can fill the gap in early-stage life sciences capital, but for certain ventures it could present an important new option.

A summary of the relevant proposed provisions of the Act<sup>55</sup>:

- **Title II - General Solicitation** (SEC approved July 2013)
  - Revise Rule 506 of Regulation D under the Securities Act of 1933 (Securities Act) and allows general solicitation or advertising for companies offering or selling securities
  - Only accredited investors can invest in these companies
    - Companies are required to verify investors are accredited or face ban from fundraising for one year
    - Investors are considered accredited with \$1 million in net worth, or making \$200,000 a year for the past three years
- **Title III - Crowdfunding Provision** (Open to public comment through February 2014)
  - Amends Section 4 of the Securities Act to allow companies to raise up to \$1 million per year from non-accredited investors, but not exceeding certain individual thresholds
    - In 2013, SEC proposed rules on thresholds the Act called for, including:
      - Individuals can invest up to \$2,000 or 5% of their annual income or net worth (whichever is greater), if both their annual income and net worth are less than \$100,000
      - Individuals with an annual income or net worth of more than \$100,000 can invest up to 10% of their annual income or net worth (whichever is greater)
  - Requires issuers to use an intermediary that is either a broker registered with the SEC or a “funding portal” registered with the SEC (such as a crowdfunding website)
- **Title IV - Increasing Private Placements** (Open to public comment through March 2014)
  - Revises Regulation A of the Securities Act and raises the exemption for small security offerings from \$5 million to \$50 million during a 12-month period
    - Applies to accredited investors
  - Proposed preemption, currently requiring companies to register offerings in each state where made available



## ***Disease Foundations***

Not-for-profit disease foundations are key stakeholders in the Massachusetts life sciences cluster. Not only do disease foundations offer funding, but they also have strong connections with key opinion leaders, regulators, and patients. Their commitment to their fields and their vision across the value chain, from scientific knowledge on targets and pathways, to clinical trial expertise, to patient insights, makes them valuable partners. Examples of successful disease foundation and industry partnerships include:

- Vertex and Cystic Fibrosis Foundation (CFF) collaboration to develop Kalydeco<sup>42</sup>
  - CFF provided \$75M, as well as scientific and clinical support for Kalydeco development
- Pfizer's Centers for Therapeutic Innovation and Juvenile Diabetes Research Foundation collaboration on Type 1 Diabetes research<sup>43</sup>
  - Relationship combines funding and scientific expertise of both organizations
- The Jackson Laboratory and Michael J. Fox Foundation's Biomarker Initiative<sup>44</sup>
  - MJFF providing funding to Jackson Labs to distribute Parkinson's Disease mouse models

Entrepreneurs and investors are increasingly reaching out to these organizations as part of their portfolio planning and fundraising strategies. As disease associations become more involved with the industry, questions arise as to how their funding models will evolve. Historically, these organizations provided non-dilutive grants to companies. However, as these foundations have begun funding clinical trials or critical proof-of-concept studies, they have sought royalties or equity. Securing returns on their investments help access dollars for future investments, and therefore fits the mission of serving patients. That said, most stakeholders expressed the view that not-for-profit organizations should take on investments or programs that for-profit organizations will not. Balancing risk across a portfolio is important for any investor, for-profit and not-for-profit, but the not-for-profit balance should be shifted toward higher risk. Robert Beall, CEO of the Cystic Fibrosis Foundation, explained, "Disease foundations have an important role to play, but we have to be careful that too many foundations don't ask for too much too early."

A growing stake in investments by disease foundations raises other questions related to intellectual property ownership, continuation language in agreements, and governance. Particularly for companies, but also larger companies, disease foundations will become a more frequent partner and these issues in partnership structure will need to be resolved.

## ***University and Teaching Hospital Funds***

NIH funding is down due to federal budget cuts. Universities and teaching hospitals are seeking ways to supplement research funding and industry has become an important source. Sponsored research agreements and other industry collaborations have bridged some of the gap that declining grant money has created. With this shift, institutions realize that to obtain greater returns on their discoveries and preserve the flexibility to pursue their own interests, they need to have more skin in the game than just the IP and the scientist.

Boston University, Harvard University, and many other institutions have explored and experimented with early-stage investing with various levels of success. Sustained commitment and political influence can complicate the investment decision process. However, with a new healthcare environment and the escalating challenge for bridging the valley of death, organizations should streamline decision-making and leverage their endowments and networks to make funds available.

Partners Innovation Fund was founded in 2007 with \$35 million from Brigham and Women's Hospital and Massachusetts General Hospital to address the gap in seed funding. On its website, the fund explains, "Due to changes in the investment environment, there is a dearth of funding support for translational research between discovery and proof of concept. By focusing on this capital gap, the Fund can advance projects of high commercial potential to a stage where more traditional investment sources are attracted to underwrite the risk." The Fund has laid out four major goals:



- Capture more value from the Partners HealthCare research portfolio.
- Bridge the capital gap between discovery and clinical trials.
- Attract external capital by demonstrating institutional commitment.
- Generate a return on investment to refresh capital for additional technology investments.<sup>45</sup>

In 2013, one of Partners Innovation Fund's portfolio companies, CoStim Pharmaceuticals, was acquired by Novartis, providing a successful exit.<sup>46</sup>

## Sidebar: NIH Support for Academic Research: Without Fuel Will The Massachusetts Engine Sputter?

In 1961, Orrie Friedman, Professor of Biochemistry at Brandeis University left academia to form the first biotech company in Massachusetts, Collaborative Research. Dr. Friedman's fledgling company eventually became Genome Therapeutics and subsequently Oscient. In 1967, the Harvard Faculty of Arts and Sciences approved the formation of a separate department of Biochemistry and Molecular Biology. Researchers in that department would go on to found Biogen (Dr. Walter Gilbert) and Genetics Institute (Dr. Mark Ptashne and Dr. Thomas Maniatis).<sup>56</sup>

Since those early days of biotech, the Massachusetts cluster has been on a wild ride, leveraging the powerful research engine of our academic institutions and teaching hospitals to generate an amazing flow of life sciences advancements from insulin and angiogenesis to stem cells and next generation sequencing. Intellectual property from the institutions has formed the foundational value of nearly all our local life sciences companies for nearly 50 years. Research faculty and the Ph.D.'s from their labs are the training ground for industry R&D.

The number one reason why life sciences companies and investors come to Massachusetts and stay in Massachusetts is to access the science, the IP and the talent emanating from our research institutions. Nearly every stakeholder articulated in one way or another the same sentiment, while the cost of doing business in Massachusetts is higher, there is no place on earth where you can part of such a rich environment if you are in biotech. In our conversation with Henri A. Termeer, former CEO of Genzyme, for this project, continued public support for basic research funding was his top concern for the cluster. "We must nurture this vital research and clinical asset. We are taking it for granted. Unfortunately the government is hesitating to support it."

On January 13, the bipartisan bill from the House Appropriations Committee in Congress recommended 2014 funding for NIH at the level of \$29.9 billion. At \$1 billion higher than the post-sequestration funding for 2013, some legislators touted this as a win. This funding level is nearly \$714 million below the approved 2013 level and NIH will receive \$950 million less than in 2012.<sup>57</sup> Until last year the NIH budget had been growing but at a slower rate than in the past. However, in real dollars Federal Government investment in research has been declining since 2003 and it is declining as a percentage of GDP. NIH Director Dr. Francis Collins endorsed the findings saying, "It is my hope that this thoughtful, unflinching report of those [spending] trajectories will attract enough attention to help us realize that our dominance of biomedical research cannot be taken any more as a given."<sup>58</sup> That was before the sequester cuts.

Massachusetts receives more NIH funding than any other state on a per capita basis, but the Massachusetts cluster is also more vulnerable to a decline in funding.

Reduced funding for Massachusetts research institutions will have a detrimental effect on the flow of new technology. Academic institutions rely on NIH RO1 grants to fund scientists and provide infrastructure. Application success rates for RO1 grants from NIH have fallen to an all-time low. The average age for a successful, first time grant recipient is 42.<sup>59</sup> And to be successful at receiving a grant, an investigator must have some data to support his or her idea. For the Ph.D. or Post-doctoral student in their late 20's or early 30's there is an ever-widening gap and a nearly impossible path to a successful career in academic research.

To attract, retain and support the best of these scientists until they can compete for external funding, the research institutions must provide support.

Philanthropy and endowment funds help, but, as has always been the case, funding of academic research has to compete in universities with investments in the educational mission. In teaching hospitals, executives must make hard decisions between underwriting patient care and indigent care versus funding research. As one hospital executive stated, “We must consider what is the value of conducting research in the context of a new healthcare delivery infrastructure? We will be forced to decide between a focus on better and cheaper care and a fascination with research and being a teaching hospital.”

Unfortunately, academic researchers are getting the message. The number of bench level scientists is shrinking. Smart faculty members are shifting attention away from basic research and toward translational and clinical research. Young scientists are weighing tough decisions as to whether they can stay in academia. For a 30-year old, burdened with school debt and a young family to support, an academic career track may not be viable.

This is the trend and it is occurring at a time when many foresee the most dramatic advances in life sciences research. Genomics, proteomics, personalized medicine, CNS research, healthcare information technology and data processing skills are all coming together to create truly disease-modifying therapies. The question that remains is, will we find a way to pay for innovation? Other parts of this report focus on value and reimbursement for novel products. As is evident in the quotes from Francis Collins, Henri A. Termeer, and executives from local research institutions, if we do not change the apparent direction of the national policy and provide adequate funding for basic research in the life sciences, the flow of novel products will decline precipitously and patient care will suffer.

This is a national issue, but one in which Massachusetts has a lot to lose. Massachusetts must find ways to exert influence on the national debate and make the case for public funding. Our legislative representatives must fully internalize what is at stake for our local research institutions, companies, and patients.

### ***Corporate Venture Capital***

Pharmaceutical company venture arms were originally started to gain a window into novel technologies and ensure a pipeline. The model has shifted as corporations and their funds have struggled with the balance between financial returns and strategic interests. The result is that corporate venture capital has largely evolved to an institutional model, focused on optimizing financial returns. Corporate investors are now part of the mainstream funding options, leading deals and co-investing with VC firms. Recent statistics from the National Venture Capital Association indicate that corporate VCs were involved in about 15-20 percent of all life sciences venture deals. They report that 53 corporate VC funds are investing in life sciences and committed \$646 million, or nearly 10 percent of all venture dollars in 2012.<sup>47</sup>

In addition, life sciences companies continue to explore new models for investing in early-stage life sciences. Cambridge is one of three locations worldwide for a Johnson & Johnson Innovation Center. Robert Urban, the head of the Cambridge Center shared the J&J vision. The Innovation Centers are central hubs for coordinating efforts with the local community and internal J&J functions including the operating divisions of J&J, venture capital group – J&J Development Corporation, and various business development groups.

H3 Biomedicine offers another industry experiment designed to leverage substantial cash flow to access external technologies and transform R&D. Founded out of the Broad Institute, H3 received a commitment of \$200 million over 10 years from Japanese pharmaceutical company Eisai to develop a novel drug discovery platform leveraging patient genomics, tumor biology and advanced synthetic chemistry.<sup>48</sup>

### ***Government Funds***

The U.S. government’s National Institutes of Health, Small Business Innovation Research, and Department of Defense programs provide critical non-dilutive funds that advance early science. Cuts in these programs have significant and long-term repercussions on the productivity and pace of innovation. As the ultimate seed funder of the life sciences industry, the federal government must keep up its commitment to ensure future growth and progress.

State government support has become increasingly important across many clusters, where local governments are committing funds to accelerate early-stage company formation and to attract existing companies. From the \$3 billion California Institute for Regenerative Medicine to the State of Texas' \$3 billion pledge for cancer prevention, states are investing significant dollars to seed industry growth.

In Massachusetts, the \$1 billion, 10-year Massachusetts Life Sciences Initiative (LSI), established in July of 2008 by Governor Deval Patrick, showed that the state embraces the life sciences industry. The support offered in 2008 will be even more important in 2018. Key elements of the LSI are important for the vitality of this sector and should be expanded. Particularly for early-stage companies, accelerator programs for space and seed funding are critical. Other states have developed models, such as QB3 in California or Connecticut Innovations, which should be considered by the Commonwealth [See Sidebar].

## Sidebar: Massachusetts Life Sciences Center



Investing in the State of Innovation

Proposed in 2008 and signed into law in 2009 by Governor Deval Patrick, the \$1 billion, 10-year Massachusetts Life Sciences Initiative (LSI) sent an important, and in many people's opinions, long overdue message that the Commonwealth of Massachusetts embraces the life sciences industry. The initiative solidified the state's message that it was willing to work with life sciences companies and build infrastructure, that it is serious

about ensuring the best workforce possible, and that Massachusetts would not sit idly by as other clusters aggressively pursued its growing companies.

Five years later, the Commonwealth's investment has paid off. According to an independent evaluation by The Boston Foundation published in 2013, Massachusetts life sciences employment outperformed the nation 2:1, showing 27.3% ten-year jobs growth versus 11.9% nationwide. The LSI created 2,500 jobs, generating \$266 million in wages and salaries over five years, and \$93 million in state personal income and sales taxes during that period. Overall, for every tax incentive dollar invested, \$1.66 will be returned.<sup>60</sup>

Impact 2020 strongly endorses the re-authorization and expansion of the LSI. The observations of this report regarding reimbursement concerns and threats to innovation, reduced NIH support, intensifying competition from other clusters and escalating hurdles for starting new life sciences ventures, make the case that an unambiguous message of support offered by the State in 2018 will be even more important than it was in 2008.

## Sidebar: Public-Private Investments to Accelerate Seed-Stage Companies - Two State Examples



QB3, or the California Institute for Quantitative Biosciences, is a public-private life sciences incubator originally founded in 2000 as one of four Governor Gray Davis Institutes for Science and Innovation. The State of California pledged \$100 million for each of the four institutes, with the goal to match every state dollar with two dollars in non-state funding. QB3's mission is "to stimulate innovative life science to keep us healthy, sustain our environment, and grow the economy."<sup>61</sup>

The institute has programs spanning the stages of company formation, including educational programs, research facilities, internships, mentoring, incubators, and a seed-stage venture fund. Notable programs include:

- The Bridging-the-Gap Award – grants \$100,000 per year to promising ideas that are one to three years from seeding a company
- Startup in a Box – provides legal services and business advice to help entrepreneurs set up companies
- Mission Bay Capital – seed-stage venture capital fund operated by QB3 that invests in University of California startups<sup>62</sup>



Since its founding, QB3 has started 62 companies that have collectively created more than 280 jobs and attracted more than \$230 million in investment. More than 20 of these companies are University of California spinoffs. San Francisco Mayor Edwin M. Lee has stated “QB3 is an engine for new company creation which is driving job growth and economic activity in the city.” QB3 Associate Director Douglas Crawford remarked, “This has been an unqualified success...These incubators have enabled us to bridge the gap between great university science and commercial success.”<sup>63</sup>



In 1989, the State of Connecticut formed **Connecticut Innovations (CI)** to be the leading source of financing support for early and innovative technology companies in the state. CI provides grants, venture capital, flexible loans, advisory services, and business connections to participating companies. Since 1995, the program has invested almost \$250 million in 190+ companies and has recruited 25 companies to the State. CI estimates that it has helped bring \$4 billion in financing to Connecticut companies and has created more than 26,000 jobs.<sup>64</sup>

On September 4, 2013, recognizing the declines in NIH funding and the growing “valley of death” in the life sciences, Governor Daniel P. Malloy established the \$200 million Connecticut Bioscience Innovation Fund, a 10-year evergreen fund underwritten by the State Bond Commission. The initiative seeks to finance commercializable programs that will “improve healthcare coordination, quality or efficiency; reduce healthcare costs; and increase job growth.” The \$200 million fund is part of a broader economic development strategy to catalyze the life sciences industry in Connecticut. Previous investments include the 2011 \$864 million Bioscience Connecticut initiative, which called for significant renovations of University of Connecticut health facilities to increase research productivity; the 2012 \$291 million investment in Jackson Laboratory’s research center in Farmington CT; and the June 2013 \$2 billion in funding to upgrade STEM programs at UConn.<sup>65</sup>

These investments aim to achieve Governor Daniel Malloy’s vision: “By becoming a leader in bioscience, Connecticut can again be at the forefront of an economic renaissance. By capitalizing on existing assets, and by attracting new ones, Connecticut can lead the new economy in a way that will make us an attractive place to do business, and a state that retains and attracts top-flight, national talent.”<sup>66</sup>

## Case Study: Kendall Square

Massachusetts has the greatest density of biotechnology companies in the world. This density is a significant enabling component of the cluster’s resiliency. The greatest concentration of biotech companies in the state is centered in East Cambridge, notably around Kendall Square. Of course Cambridge is not the only focus of biotech in Massachusetts, as there are hundreds of companies in Boston and surrounding towns such as Watertown, Framingham, Waltham, Woburn, Lexington, and Worcester. But because 150 life sciences companies are in Cambridge<sup>67</sup>, clustered most densely in Kendall Square, it is considered to be the heart of Massachusetts life sciences cluster.

Many executives view having a life sciences company located within the 6.4 square miles of Cambridge as being critical to success. Considered the epicenter of Massachusetts’ biotech scene, Kendall Square and the greater East Cambridge area contain roughly 6 million square feet of lab space<sup>68</sup> and is home to approximately 100 biotech companies, including Biogen Idec and Genzyme/Sanofi and R&D centers from Novartis, Amgen, Pfizer, and Johnson & Johnson.<sup>69</sup> These companies have been locating in this industrial neighborhood of Cambridge to be near MIT and the burgeoning startup community. Over 30 years, the area’s industrial warehouse landscape has been transformed by developers to create accessible urban walking space for tech and life sciences companies. The area is easily accessible by public transportation and is friendly to a growing bicycle population. However, urban accessibility combined with the desire to be in such close proximity to MIT and other companies has made Kendall Square real estate in increasingly high demand, resulting in escalating prices.

Consistent and increasing demand and limited supply of lab space have made rents in East Cambridge some of the highest in Massachusetts. Triple-net rates for lab space in Cambridge have risen to a historically high range of \$50–60 per square foot.<sup>70</sup> Even at these prices, desirable space is increasingly harder to find, especially for small, startup operations. Developers indicate that they will build properties along with demand. Larger companies looking to move to Cambridge have opted to do just that, and have announced several projects to build their own space including Novartis, which is expanding its footprint by 550,000 square feet by 2015, and Pfizer, which is building an additional 180,000 square feet of space on land owned by MIT.<sup>71</sup>

Building new facilities is not an option for startup companies, and instead, flexible lease options are highly desirable. As a result of the building boom, affordable, small footprint lab space is scarce in Cambridge, yet it is a critical ingredient if Massachusetts is to preserve the entrepreneurial ecosystem. Stakeholders expressed concern should Kendall Square risk losing its startup culture.

Addressing the small space crunch will likely mean a collection of expanded options for companies:

**Incubators and Accelerators:** Incubators and accelerators play a critical role for growing companies. Lab Central is a fully functional, flexible lab and office space that provides facility and administrative services, along with all the permits, waste handling, and equipment commonly required in many biotech lab spaces. This model allows companies to establish a strong local presence while not worrying about the high startup costs building out a new space would require. Lab Central's 27,000 square foot facility can accommodate up to 65 entrepreneurs and biotech startups with lab space in units ranging from a single bench to a private suite, all available for monthly leasing. Funding provided by the Massachusetts Life Sciences Center was critical to the establishment of Lab Central and additional investments in this area would further address the issue.<sup>72</sup>

**Small Footprint Incentives and/or Mandates:** Encouragement and support from state and local agencies and other partners may be an important component for creating additional ready-to-use lab spaces for startup companies. MIT recently agreed with the City of Cambridge to set aside 10 percent of its planned redevelopment for startups and smaller companies in the 1 million square feet of commercial development permits the school received.<sup>73</sup> One executive suggested that local and state leaders should explore a mandate similar to the state's affordable housing policy, arguing that it is in the best interests of the big tenants to provide for the smaller tenants.

**Subleases:** More established companies also need to provide for future growth. Moving is costly and interrupts business flow so larger companies sometimes take on more space than is initially needed and sublease until they need the space. Subleasing unused lab space from larger companies can be a great opportunity for young companies. However, the availability of these opportunities can be difficult to ascertain and often occur as off-market transactions through personal connections.

**Non-Cambridge Options:** Given space constraints and soaring rents, many companies are finding it easier to set up operations in other cities and towns throughout the Commonwealth. Cities and towns such as Watertown, Framingham, Waltham, Woburn, Lexington, and Worcester have a strong and growing biotech presence. Immediate access to MIT and Harvard may not be necessary or worth the investment for every company. One example is Worcester's Massachusetts Biomedical Initiative, which includes three properties and is home to 20 companies. MBI provides not just the physical space companies need, but also offers events, programs and support services that have resulted in a strong life sciences community in Worcester.<sup>74</sup> Worcester Polytechnic Institute and UMass Medical Center's strong commitments to collaborate are also underlying the Worcester cluster's success.

A more concerted effort to identify and catalog space options for startups would enable these companies to start faster, concentrate on R&D and either grow or fail quickly. Municipal and state support through tax incentives or other supportive measures like Cambridge's agreement with MIT should be encouraged in order to maintain an accessible supply of space for young companies.

Locating in Cambridge is not a requirement for larger, more established companies and presents a significant opportunity for Massachusetts. Boston's thriving Innovation District is an example of a focused investment with anchor company Vertex Pharmaceuticals consolidating their operations to a brand new 1.1 million square foot building.<sup>75</sup> They join several smaller companies in the area, and will serve as an important life sciences mini-cluster for the Boston life sciences sector. Three Massachusetts firms with a 2013 IPO were based in the suburbs: Watertown (Enanta and Tetrphase) and Natick (Karyopharm Therapeutics). As some Cambridge startups have grown, many, including Cubist and T2 Biosystems, have opted to move out of Cambridge into Lexington where space is more available and rents are substantially lower. International pharmaceutical companies coming to Massachusetts have also chosen suburban locations, including AstraZeneca's R&D facility in Waltham and Shire's headquarters in Lexington.



As part of MassBio's economic development work, 76 communities have been identified as BioReady, meaning they are supportive and attractive locations for life sciences companies. These municipalities have adopted pro-biopharma public policies in order to ease the pathway for renovation or new construction. The BioReady Communities Guide can serve as a resource for companies seeking to locate in Massachusetts. Access to a centralized resource for life sciences properties and a coordinated effort by state and industry stakeholders to guide companies through the options and logistics will facilitate future growth in the sector.<sup>76</sup>

Currently, demand for life sciences space is at a peak. Investment is strong and growth is the priority but the industry is cyclical. Preserving space for small companies is essential to seed future growth. Attracting and keeping anchor tenants and incentivizing them to build out commercial operations and headquarters here in Massachusetts is a tremendous opportunity.



## Recommendations for MassBio

Several important themes emerged from conversations with early-stage companies utilizing alternate sources of capital, highlighting what can be done to ensure effective use of these resources.

- 1. Expand MassCONNECT** – This experimental program sponsored by industry through MassBio has proven to be a valuable vehicle for mentoring entrepreneurs. Connecting entrepreneurs with seasoned business leaders in the life sciences industry as early as possible can help good ideas move forward efficiently and bad ideas get killed early. The MassCONNECT program is a model for making this happen and expanding this program to reach more startups would be valuable for the cluster. Beyond mentoring, MassCONNECT can become a central hub for accessing space, talent, and other external resources to support a capital efficient early-stage business model.
- 2. Maximize Access to Existing Funding Options** – The “valley of death” from seed funding to Series A has expanded. Many startup CEOs developed their funding strategies through a more-or-less haphazard, time-consuming, and exhausting networking process. They would all support efforts to increase awareness for these options and develop more systematic access to decision-makers. MassBio can maximize access to existing funding options, collect information on alternative sources and connect entrepreneurs with a diverse range of investors. More forums that provide startups exposure to and interaction with key decision makers at diverse funding groups would be invaluable.
- 3. Convene Startup CEOs in Small Group Forums** – Each funding source has its own learning curve. Startup CEOs are eager to learn from each other, to determine which models might work best for their businesses, and to quickly adopt best practices for pursuing funds, convincing decision-makers, and managing investors. Sharing information and best practices on alternate financing could be achieved through more startup CEO group forums.
- 4. Advocate for More Funding Options** – MassBio should work with the State of Massachusetts to expand the funds available to early-stage companies through the MLSC. In addition, MassBio should continue to advocate for increases in NIH funding. Government leaders must not underestimate the importance of research institutions. They are a critical source to attract industry partners and serve as an engine for the Massachusetts economy. Legislators and state officials themselves must be strong advocates for sustained increases in federal funding of basic research.

Many teaching hospitals, academic research centers, disease foundations, and other organizations are actively funding or exploring funding for emerging life sciences concepts. Experienced advisors from industry and investor groups should encourage these efforts, but also provide guidance on investment parameters that will effectively de-risk ideas and facilitate access to deeper-pocket investors.
- 5. Promote the Massachusetts Life Sciences Cluster** – With capital at a premium and escalating pressure to demonstrate value, companies and investors across the United States and worldwide will be searching for the best place to start and operate a life sciences company. Massachusetts’ breadth and depth of resources, particularly its basic and clinical science, workforce, and executive talent should be a magnet. Industry, state and local agencies should come together to ensure that companies and investors are aware of what Massachusetts has to offer.



# Enabling Strong Anchor Companies: Biomanufacturing and Workforce Development

“Six Degrees of Separation,” the classic game of connections, quickly reaches exponential proportions in the Massachusetts life sciences community. Start with the region’s flagship companies—Millennium, Genzyme, Biogen Idec or Genetics Institute—and the legacy of those companies becomes strikingly apparent. Many current business leaders learned and honed their skills at one of these companies. The Massachusetts cluster owes much of its growth to these historic anchors. Successful, fully-integrated companies generate talent and experience that propel the next generation of companies. For these reasons, Massachusetts must invest in attracting and supporting anchor companies as they mature and ensure they have the resources they need.

As companies like Biogen and Genzyme expanded beyond product development into commercial operations, their contribution to the Massachusetts economy grew dramatically. They added (and continue to add) jobs but more importantly, they added diversity through new functional requirements and new business segments. As companies grow, they require additional skills and capabilities and, as a result, Massachusetts has an exceptionally strong cadre of experienced regulatory, medical, and sales and marketing talent.

For example, many in the industry point to Genzyme as the pioneer of the orphan disease business model. Orphan markets have a limited number of treatment centers and only hundreds or thousands of patients, requiring high levels of customer support and close relationships with the patient community. The commercial model requires very different skills across functions than traditional pharmaceutical sales and marketing. Genzyme has provided a template for how to service an orphan disease market. New companies like bluebird bio or Aura Biosciences, which are developing the next generation of orphan therapies, follow the Genzyme model. At bluebird bio, Nick Leschly and his team will break new ground as they negotiate reimbursement structures with payers for their gene therapy products. Genzyme, meanwhile, has expanded into oncology and multiple sclerosis and now serves as the major U.S. center for multinational owner, Sanofi.

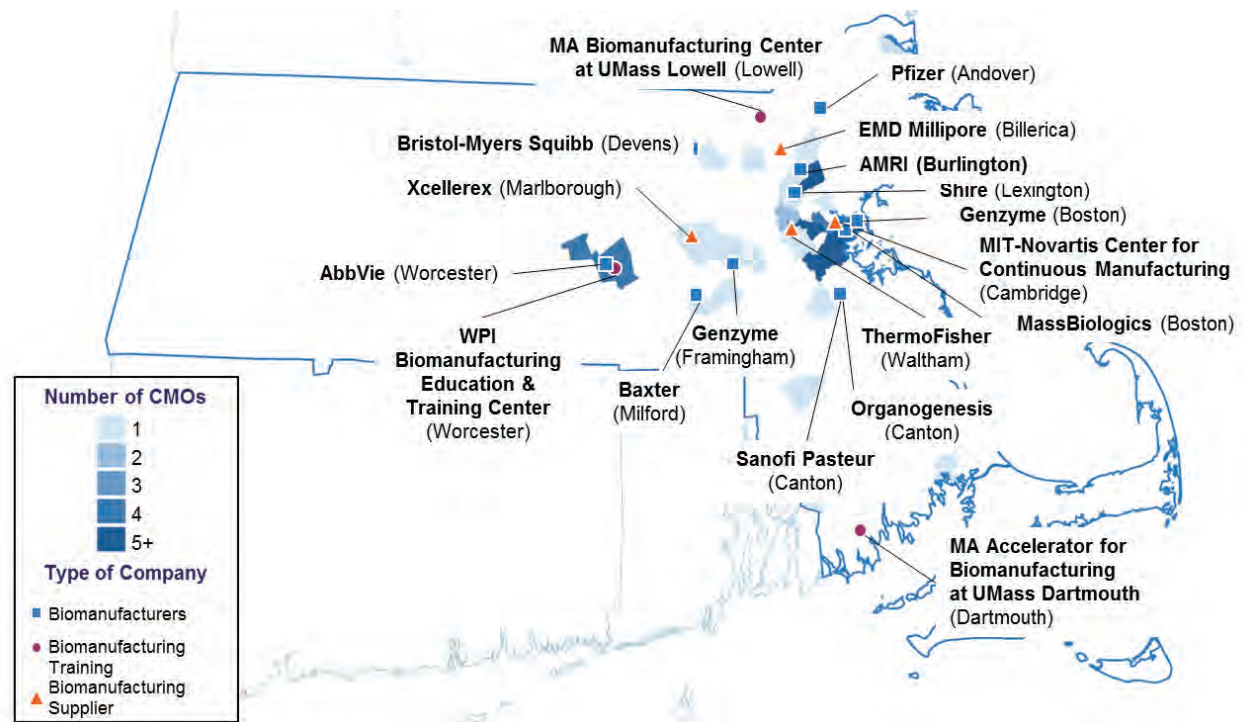
Growing anchor companies is a big opportunity for Massachusetts. Building a manufacturing base and providing a trained workforce are both important needs that will need additional attention and investment in the next several years.

The state may be known for its world-class research institutions, which have attracted big pharma and generated hundreds of startups to date. But Massachusetts also has impressive capabilities further down the value chain, particularly in highly specialized biologic manufacturing. Building these capabilities will ensure broader industry growth into the future.

## ***Biopharmaceutical Manufacturing – A Lesser Known Advantage***

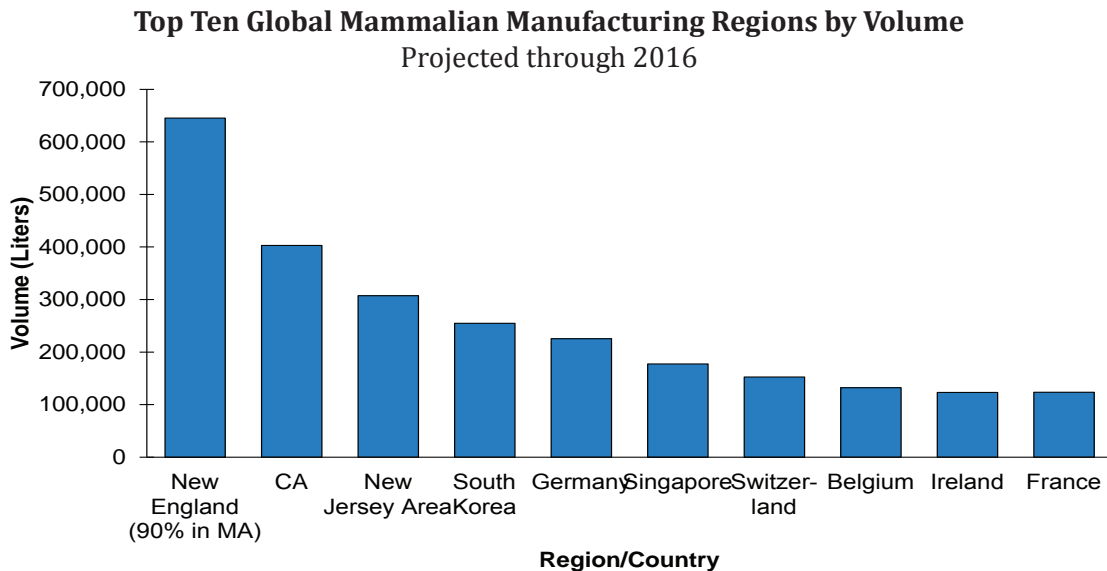
The biomanufacturing footprint in Massachusetts is striking **[Figure 1]**. As of 2013, Massachusetts had 600,000 liters of mammalian cell culture manufacturing capacity, the most anywhere in the world **[Figure 2]**. Large biopharma companies own a significant part of this capacity, including Bristol-Myers Squibb (Devens), Genzyme (Boston and Framingham), Shire (Lexington), Pfizer (Andover), and AbbVie (Worcester). Surrounding these companies is a vibrant ecosystem of suppliers, contract manufacturing organizations (CMOs), and training centers. Leading biomanufacturing suppliers, including EMD Millipore, Xcellerex, and Thermo Fisher, are innovating the next generation of manufacturing technologies. Dozens of CMOs support early-stage companies as they develop critical manufacturing processes and protocols. Finally, contract and training facilities at WPI and UMass provide companies with on-demand support in building out manufacturing capabilities.

**Figure 1: Massachusetts' Biomanufacturing Footprint**



Source: PriceWaterhouseCoopers, Massachusetts Manufacturing Report, 2013.

**Figure 2: Massachusetts' Biomanufacturing Capacity**



Source: Reynolds, E. (2011). Massachusetts biomedical roundtable update. Cambridge, MA: MIT Industrial Performance Center.

Massachusetts' robust biomanufacturing ecosystem is supported by a skilled workforce of over 9,000 personnel. The complex nature of biomolecules requires specialized skills to develop and control production processes, which directly influence the efficacy and safety of final products. These skills are honed through years of training and operating experience. Bill Aitchison, Head of Global Industrial Operations of Genzyme, remarked, "We come to Boston because people that know biomanufacturing exist here. They don't exist in Singapore or India. There are few places in the world where you find the right people for biomanufacturing."

In recent years, Massachusetts has supported new accelerators and biomanufacturing training centers with funding from the Massachusetts Life Sciences Center. Worcester Polytechnic Institute's

Biomanufacturing Education & Training Center, a site that offers hands-on training and retraining in state-of-the-art manufacturing techniques, has partnered with dozens of leading biopharma companies to train staff. The Massachusetts BioManufacturing Center at UMass Lowell and the Massachusetts Accelerator for Biomanufacturing at UMass Dartmouth provide industry with staff and capacity to test new biomanufacturing processes, while training future workers. These centers confer a strong advantage in developing a more competitive workforce.

With robust capacity and skills in place, Massachusetts should capitalize on future shifts in biomanufacturing. New cell therapies, vaccine technologies, and complex gene therapies currently being researched and developed in Massachusetts will all require unique manufacturing solutions that are closely integrated with R&D operations. Both single-use and continuous manufacturing technologies will not only enable production of new therapies, they will also make it more economical for necessary small-batch production of targeted medicines **[See Sidebar]**. Local companies are developing these technologies and local CMOs are gaining early experience with these innovations. There is a tremendous opportunity to support regional CMOs and training centers, connect them with biopharmaceutical partners, and convene leaders to discuss best practices in new manufacturing technologies in order to make Massachusetts the world leader in biomanufacturing.

As illustrated by Shire's decision to co-locate R&D and manufacturing in Lexington, followed by commercial capabilities and then worldwide headquarters **[See Case Study]**, Massachusetts' R&D strengths provide leverage in downstream expansion. Proximity of scientists and manufacturing engineers enables faster and more effective process troubleshooting, which is invaluable during early development. Second, supporting local CMOs can help retain jobs as companies move into commercial production. Mark Bamforth, CEO of Gallus BioPharmaceuticals pointed out, "If a CMO can win a contract for Phase III clinical production, they're likely going to remain the preferred manufacturing partner through commercial launch."

## **Sidebar: Biomanufacturing Innovations in Massachusetts**

### ***Single Use Platforms***

A paradigm shift is underway in biomanufacturing as expensive, fixed infrastructure—the big stainless steel tanks that have to be thoroughly cleaned after each use—are replaced by single-use disposables. Single-use manufacturing platforms are being developed and piloted by companies in Massachusetts. The most often cited reasons for adopting disposable technologies are the elimination of cleaning requirements, the reduced risk of cross-contamination, the increased convenience and flexibility of disposable technologies, and the reduced time for a new facility to become operational.<sup>80</sup> Over the past seven years, single-use bioreactor utilization has grown by a compound annual growth rate of approximately 20 percent.<sup>81</sup> This trend is indicative of the rapid adoption of single-use technologies. Massachusetts stands to be a leader in these single-use manufacturing based on the companies pioneering development of these new technologies including GE Healthcare's FlexFactory, Thermo Fisher's Hyperforma, and EMD Millipore's Mobius.<sup>82</sup>

### ***Continuous Manufacturing Technologies***

Today, most biomanufacturing requires batch production, which is inflexible and time consuming. Continuous manufacturing, on the other hand, enables an end-to-end enclosed production line, whereby once all initial starting materials are added to the system, the only output is final product. Paired with new sensing technology for in-process monitors and real time data collections and in-process controls, quality will improve and waste will decline.

Massachusetts is also pioneering new continuous manufacturing platforms. Early in 2013, Genzyme scientists published two technical papers, outlining a process for continuous biomanufacturing, essentially connecting a small bioreactor to a type of chromatograph that continuously separates protein from surrounding liquid.<sup>83</sup> In another example, through a joint effort which began in 2007, MIT and Novartis have been working together to advance manufacturing technology for biopharmaceuticals via the Novartis-MIT Center for Continuous Manufacturing. The Center has received funding from Novartis and the federal Defense Advanced Research Projects Agency (DARPA), to produce an end-to-end continuous production technology for biopharmaceuticals.<sup>84</sup> Rapid biomanufacturing via continuous production will make it possible to produce more types of drugs, scale production quickly, reduce costs, and produce small volume products at a lower cost.

## Workforce Development – Door-to-Floor Preparation Through University-Industry Collaboration

Ensuring a pipeline of future talent that is well prepared for the requirements of industry jobs will require coordinated efforts between companies and secondary and higher education institutions. It is virtually impossible to overcome the lag between industry advances and new training programs for the skills that these advances may require. But closer coordination efforts and ongoing communication between the industry and the educational sector can make the lag shorter and less problematic.

Massachusetts colleges and universities are known as some of the strongest in the nation, with a history of successful life sciences programs. Employers, however, increasingly demand even more experience and a better prepared workforce. A well-trained workforce starts with strong, foundational science, technology, engineering and math (STEM) programs, which must continue. However, Impact 2020 discussions and interviews revealed additional insights into the needs of companies and how collaborations with universities might better address industry needs.

There are many lessons to learn from existing programs and even more opportunities to dialogue on creative education and training approaches. Below we cite a number of ways MA schools have differentiated, and can continue to differentiate themselves, in order to position their graduates as leaders in the life sciences space. MassBioEd has done significant work in advancing academic-industry alignment with the Massachusetts Life Sciences Education Consortium and a program of endorsing academic programs proven to meet industry needs **[See Sidebar]**.

### ***Business and Industry Knowledge for Scientists***

A basic science education is an essential foundation, but to succeed in an industry based on the principles of entrepreneurship and innovation, in an increasingly challenging regulatory and commercial environment, today's graduates need more practical business knowledge. Scott Gillis, CEO of Onsite Therapeutics, shared a relevant observation: "The science department thought you could teach students to do biological experiments in a lab and they could get cool biotech management jobs. The reality is, if you want a management job in the life science industry, you also should have some business related education to include FDA regulations, managing people and budget/ financial controls."

Integrating management, regulatory, and finance classes into a biotech curriculum will better prepare graduates to understand their place in a company ecosystem and allow them to take on leadership roles. Through conversations with industry stakeholders, local schools are beginning to make this realization and several now offer a unique program called the "Professional Science Masters" or PSM, as well as mandating business courses as part of a traditional biotech curriculum.

### **Sidebar: The Massachusetts Life Sciences Education Consortium (MLSEC)**



The Massachusetts Life Science Education Consortium (MLSEC) is a joint initiative between the MassBioEd Foundation and MassBio with the mission to "promote a coordinated approach to the development of the Massachusetts life sciences workforce through a partnership between the life sciences industry and higher education." The MLSEC has identified four key areas of focus:

- Connect the industry and higher education through an effective communications strategy
- Validate, guide, and review the relevance of programs and curricula intended to prepare students for careers in the life sciences
- Endorse higher education/industry talent development best practices or government programs aimed at supporting talent development
- Advocate for initiatives that will enhance the ability of Massachusetts to meet the future employment needs of the industry.<sup>85</sup>



The MLSEC has made progress on validating community college programs in the life sciences. It has developed a set of criteria based on core competencies required in biotechnology education. Those meeting all competencies are awarded gold or silver ratings, with established internship or cooperative experience distinguishing the gold rating holders.

Moving forward, the MLSEC will focus on areas identified by Impact 2020, specifically around industry and higher education collaboration in best practices development and job demand forecasting.

## Case Study: PAREXEL International Corporation



In clinical research, just as in any field, there are job requirements that are not taught in a broad university curriculum. For example, how does one apply biostatistics to clinical trial results? Or how does basic biology contribute to processes during clinical research? Recognizing these gaps, PAREXEL International Corporation has invested in a workforce

training division known as the PAREXEL Academy, with branches abroad in Europe and Asia, and location close to its Massachusetts headquarters. "We recruit university graduates with strong sciences skills and knowledge, and we invest special training to enable them to contribute to clinical research management," said Albert Siu, VP of the PAREXEL Academy. PAREXEL has joined forces with Salem State University to design a post-graduate certificate program in clinical research management. Initially launched as a seven-week intensive pilot program, it has now evolved to become a six-month program that combines online learning with weekend class time to accommodate working individuals. The program modules are taught by experts in the field who have significant industry experience and academic credentials. When asked why they paired with a university, Siu said "Universities give us access to talent, facilities and faculty expertise. We are interested in partnering with institutions that commit to excellence in education and the development of students possessing critical job skills. Clinical research management requires a right blend of sciences, management and people skills. I believe an academic setting is designed to address these needs." Siu is complimentary of Salem State's approach to effecting quality educational outcomes for students, and explains why it is a strong choice as a partner. "The administration focuses on getting things done. I like this action-orientation approach. And they also have a Nursing School that produces a fair number of graduates every year."

A company's leadership is critical in effective training and making workforce development a priority. "Training is affected greatly by senior leaders. At PAREXEL, we know how effective training can impact business results," said Siu. "PAREXEL has a strong vision and commitment to make training investments happen." A company must believe that workforce development is an investment. It creates an employment value proposition, builds employee engagement, through which quality client-centric services are delivered."

Time to productivity is a metric that Siu's group uses to measure the success of his training and university partnership programs. "We have reduced the training time for our newly hired Clinical Research Associates (CRA) by more than a third." Siu reflected. "This allows the CRAs to begin applying their training and working on behalf of our clients to bring new treatment options to market even faster." Job offers and placements for graduates into companies as fulltime employees are another strong metric of success. "Of the 17 people graduated in last year's certificate program with Salem State, 16 were offered positions - that's a 94% offer rate."

Massachusetts universities and life sciences companies are already doing a lot to address workforce requirements and improvements in "door-to-floor" time. But there is a lot more that can be done. In multiple meetings with companies and academic institutions including a joint brainstorming forum numerous ideas were raised. Several are described below.

**Company Sponsored Degrees:** More than half of the R&D job postings for biotech jobs in Massachusetts require a graduate or professional degree. At the same time, companies often struggle to retain young recent graduates who look to continue their education or increase professional development opportunities at other firms after a few years in a company. By sponsoring career-relevant graduate degrees for their employees through partnerships with local universities, local biopharma companies can improve their employee retention, job satisfaction, and build internal leadership and expertise for the future of the company.

In engineering, Raytheon has been doing this for some time in partnership with UMass, sending employees to the UMass system for a master's degree. Some are even able to accomplish their studies online. "They have grown a lot of talent in-house," said Sanjeev Manohar, Associate Dean at UMass Lowell. University leaders believe such programs would be worthwhile in the life sciences sphere and shared that a few local biopharma firms have hinted at interest.

**Easy Access to Continuing Education Programs:** Biopharma is a fast moving and quickly evolving industry. Technologies available to scientists, regulations around drug approval, and the commercial and reimbursement landscape are changing practically on a daily basis. The dynamic nature of this field requires access to tools to better understand these changes and their effect on the drug development ecosystem. MassBioEd currently offers a Biotech 101 course to help educate non-science employees of biotech companies about the technologies and scientific principles of biotech discovery and development today. A similar need exists to educate the science staff about clinical, regulatory, and commercial issues.

For employees living in a busy world, access to on-demand, on-line courses and curricula are ideal to enable industry members to learn on their own time. The last few years have seen a boom in Massive Open Online Courses (MOOCs), pioneered by two local universities, MIT and Harvard, in the development of the EdX program. Many such courses already cover current topics such as genomics, principles of drug development, and clinical trials. A collaboration with local (or other national) universities could help MassBioEd offer a broad array of up-to-date and relevant materials for the industry to keep companies abreast of the rapidly changing environment.

**Industry-Faculty Links:** In our focus session with industry, representatives from several companies acknowledged that one of their greatest concerns is that the professors are not in-tune with company needs and the latest technology because the industry is evolving so quickly. Industry externships to academia would help infuse academic programs with insight into industry and provide interesting opportunities for industry staff. Similarly, while student internships are helpful, faculty internships with industry may be even more helpful. University representatives confirmed that professors with greater industry exposure are likely to be in highest demand among students.





## Case Study: Shire



To be as brave as the people we help.

For Shire Pharmaceuticals, the decision to expand its operations in Massachusetts was multi-factorial and the lessons learned should be used to attract other large biopharma companies to the Commonwealth. With more than 5,000 employees worldwide and a market cap of \$30 billion as of March 25, 2014, Shire is an important anchor to the local cluster.<sup>79</sup> Anchor

companies bring tangible benefits to the Massachusetts cluster, increasing jobs across the value chain as well as intangible benefits of economic stability and bolstering the cluster's reputation as a global leader.

For Shire, locating its R&D group in Massachusetts made sense after its 2005 buy-out of Transkaryotic Therapies, whose facilities were located in Kendall Square. But for a company with commercial products and manufacturing operations, Massachusetts—and particularly Cambridge—is an expensive place to operate.

In 2005 and 2006, when Shire was debating its options, Massachusetts' life sciences legislation was still in development. "North Carolina was aggressively wooing us, since they had just lost Bristol-Myers Squibb's expansion project to Fort Devens [Massachusetts]," says Bill Ciambrone, Executive VP of Technical Operations at Shire. Ultimately, through negotiations with the governor and state legislators, with strong support from MassBio, Shire secured \$40 million in tax incentives from the Commonwealth. While still lower than what other clusters could offer, Massachusetts held two distinct advantages that outweighed the difference.

1) Access to Talent: "There was a pipeline of talent here like nowhere else and that's huge," says Ciambrone. Massachusetts touts impressive biomanufacturing capacity and has legions of experienced technicians and operators. Shire now gives back to further the talent pool, by taking an active part in local workforce development and partnering with institutions across the education spectrum: Minuteman Regional High School, a local high school; several community colleges, including Quincy, and Middlesex; and universities such as WPI, UMass, and Tufts. These partnerships are working well for Shire by providing well-trained, top-tier talent.

2) Proximity of Manufacturing to R&D: "We are a small-volume, multi-product company and our manufacturing group uses the same disposable technology as our R&D group so having them nearby to troubleshoot and brainstorm was invaluable," Ciambrone says. Shire caught a lucky break when they found that the Lexington site (formerly occupied by Raytheon) was already permitted for manufacturing. Uniting various functions on one site created a sense of community, Ciambrone says.

For a more mature company, locating outside of Kendall Square, but still within the radius of talent in Eastern Massachusetts, is both cost-effective and smart. "Our employees can live in Lexington, but they can also commute from Cambridge, or even from Worcester," Ciambrone remarks.

Ciambrone is vocal about the need to attract more companies with manufacturing capabilities to Massachusetts, specifically in using incentives to do so. Expansion of such companies toward the I-495 corridor and toward Worcester will have strong impact on Massachusetts economics growth. "The talent is here. High-labor manufacturing will always be cheaper somewhere else, but here the proximity to R&D and to technical talent is a huge plus for low-labor content jobs where cGMP is vital," he says.

Shire is excited that they could make the Massachusetts move work for them and has already seen the benefits of their decision. Shire now employs approximately 1,650 employees at the Lexington site, more than a quarter of their total workforce.



## Sidebar: WPI: A Model for Industry Collaboration

Industry Partnerships and Experiential Learning: The MQP



Just 50 miles outside of Boston, one area school is hitting all the right notes to promote a life sciences career-focused track for its graduates. Worcester Polytechnic Institute (WPI) is living up to its motto of “theory and practice” through its strong dedication to industry partnerships and its commitment to project-based learning through the MQP (Major Qualifying Project), a thesis-like research project required of every

student in order to graduate. WPI administrators tout that being career-driven, wanting to make a tangible impact on industry, and problem solving is “in the DNA of WPI undergrads.”

The MQP guarantees that all students have at least a year of lab work. “Many students are doing master’s or Ph.D.-level work, learning the value of trial and error, experimental design, and real success rates,” says Joseph Duffy, Department Head of Biology and Biotechnology. WPI meets with industry firms to understand what their interests are and what projects they want done that they just don’t have internal capacity for. Project plans are developed and students with academics interest in those areas are paired with companies. Students take paid internships over the summer of their junior year to understand the underlying problem for the project and to get a sense of industry work environment. At the end of the summer, they take the project back with them to the university, where they work with a faculty advisor who serves as a liaison between student and company.

Companies currently involved in MQPs include: Roche, Pfizer, and Abbott. On several occasions, students completing MQPs were offered full-time positions at respective employers. “The fact that students get to train in their environment is great - and the company benefits because it’s like one long interview,” highlights Duffy.

### Central Point of Contact

When students or faculty want to reach out to industry or when companies are interested in partnerships or opportunities, they all know whom to call. Rachel LeBlanc serves as the Director of Corporate and Professional Education and is the centralized point person for industry interactions. Her office and staff do a fair amount of outreach to understand company and industry needs. “The dialogue is frequent,” she says. Her colleagues commend her efforts and laud the centralized system, which means there is never confusion about whom to call. “One benefit is that we are small enough to avoid an overabundance of faculty governance - it makes us nimble,” LeBlanc remarks.

### Biomanufacturing Education and Training Center

To further connect with the needs of industry, WPI has developed a comprehensive biomanufacturing training program at the newly established BETC (Biomanufacturing Education and Training Center). “Our center is not only training students from WPI; its major aim is to help in workforce development for biomanufacturing industry here in MA and beyond,” said Kamal Rashid, director of the newly established center. Companies are able to design tailored programs for their employees or send them to already established “101” type courses. The purpose of these programs is to shorten the period of time to productivity for these employees.

Many local companies have already taken advantage of BETC’s open enrollment training offerings, including Shire, Biogen Idec, Genzyme, and Bristol Myers Squibb. To stay up-to-date with industry needs, WPI has proactively pursued partnerships with leading suppliers to the manufacturing industry, such as Eppendorf North America and EMD Millipore. WPI is excited about the role its training center can play in creating a top-tier biomanufacturing talent pool.



## Sidebar: UMass: Investing LSI Dollars to Develop World-Class Life Sciences Education



Part of the Massachusetts Life Sciences Initiative (LSI) Act signed by Governor Patrick in June of 2008 provides \$500 million for the Massachusetts Life Sciences Investment Fund (MLSIF), of which over \$200 million is earmarked for the University of Massachusetts (UMass). Since 2008, UMass has made significant strides in growing its internal Life Sciences capabilities as well as positioning itself as a financial supporter for external ventures.

UMass began its endeavor with a mission to “provide affordable and accessible education of high quality and to conduct programs of research and public service that advance the knowledge and improve the lives of people of the Commonwealth, the nation and the world.” A subsequent task force that was formed had a number of initiatives to support

this mission, with three primary goals: attract talent, invest in existing university research, and develop infrastructure to support innovation.<sup>86</sup>

**Talent:** In 2008, MassBio, MassBioEd, the Massachusetts Life Sciences Center (MSLC) and UMass launched the Massachusetts Life Sciences Talent Initiative study, which reiterated that a talented workforce is the backbone of a successful life sciences ecosystem.<sup>87</sup> In response, the Boston campus opened the Student Success Center in 2008 to provide career guidance to individuals in the College of Science and Mathematics.<sup>88</sup> Later, a Baccalaureate-MD pathway program was developed to better help guide those with an interest in careers in medicine, and in 2010 a new undergraduate degree program in bioengineering was established to help expand potential post-graduate opportunities. Additional focus was placed on attracting talented graduate students as well, and the University began expanding its program offerings to include graduate degree programs in Clinical Investigation, Biomedical Engineering, and the Pharmaceutical Sciences.

**Research:** Starting in 2008, the University made a concerted effort to support the innovative life sciences research occurring within its campuses. Since the MSLIF was launched, UMass’ R&D expenditures in the life sciences have grown by more than eight percent. Much of this was allocated toward establishing specific research centers to address a variety of clinical unmet needs. For example, in an effort to address the growing need for personalized therapy in oncology, the university collaborated with Dana-Farber Cancer Institute to establish the Center for Personalized Cancer Therapy in 2011, with the goal of developing cost-effective, reliable tests to determine different sub-types of all common cancers. In addition, the university has helped to support industry achieve clinical success through licensing agreements, including the licensing of a monoclonal antibody to Merck for treatment of *C. Difficile* infection in 2009.<sup>89</sup>

**Innovation:** Looking to support innovation across the state, UMass has used some of its resources to fund initiatives outside the university as well. In 2011, it developed the Massachusetts Medical Device Development Center, an incubator for small medical device companies at the UMass Lowell campus. A year later, the center housed twelve companies and assisted them in raising more than \$4.6 million in grants and \$9 million in private venture funding.<sup>90</sup> Other support for the startup community has included establishment of the Venture Development Center at UMass Boston, the Massachusetts Accelerator for Biomanufacturing at UMass Dartmouth, and a big data center in the life sciences – the Massachusetts Green High Performance Computing Center (MGHPCC). MGHPCC is a platform for collaborations across member universities and industry partners around computationally based research. Located in Holyoke, the MGHPCC hosts eight acres of computer servers for big data storage and analytics, which will enable small to mid-sized life sciences company to access specialized computing capabilities.<sup>91</sup>

UMass’ support of the life sciences through talent development and strategic investments is a prime example of a highly motivated institution with vast resources, committed to helping the state of Massachusetts remain a leader in the field.

## Case Study: UMass Lowell

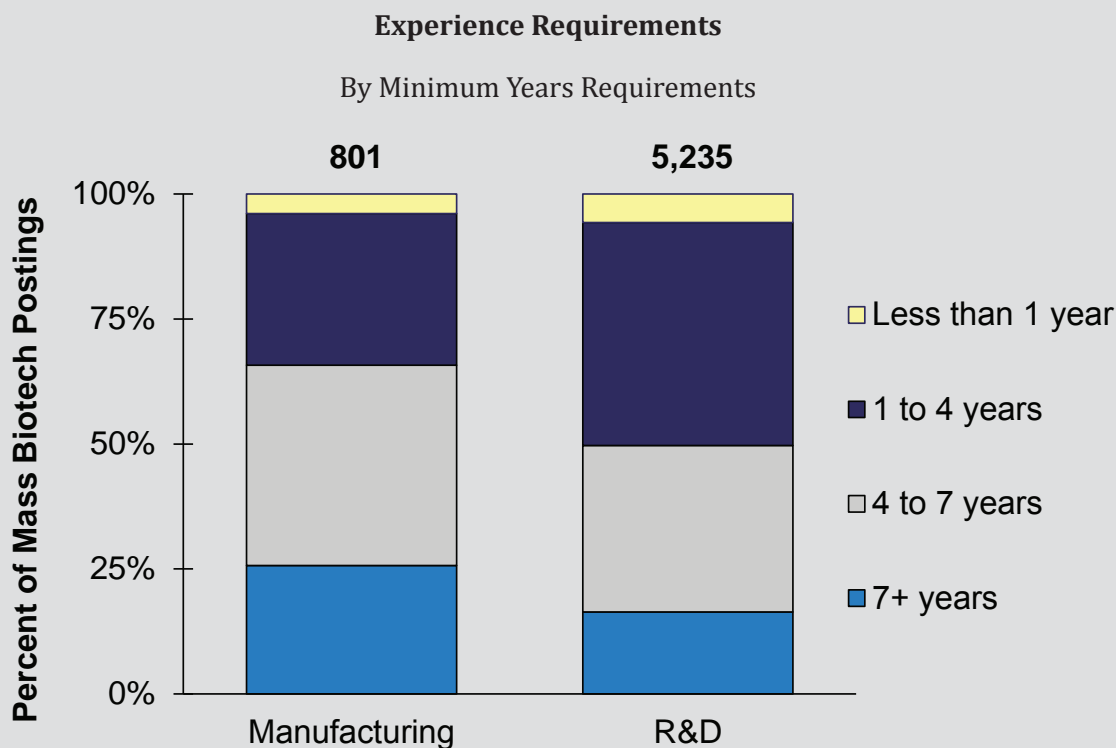


In 2013, three area universities (Brandeis, Northeastern, and UMass) offered PSM programs in the biotech and/or life sciences space. While the program in Massachusetts was pioneered by Northeastern, UMass Lowell currently offers the widest array of PSM programs including programs in Applied Biotechnology, Clinical Lab Sciences, Pharmaceutical Biochemistry, and

Project Management in Life Sciences. “It’s like a master’s program on steroids with business courses layered on top, and a mandatory internship,” said Sanjeev Manohar, Ph.D., Associate Dean at UMass Lowell’s College of Engineering. The PSM is a two-year, non-thesis, degree option that consists of eight core science courses, three professional MBA-type courses in leadership, communication, or project management, and a paid internship or professional development project, to reflect the skills that employers are seeking. “In the past, master’s programs were like a filter for Ph.D.’s but these really stand on their own and are career oriented,” Manohar said. “Placements have been great!”

### Experiential Learning

In 2012, approximately 95% of the job postings in Massachusetts for manufacturing and R&D required at least a year of experience, with the majority requiring more than four years. Multiple companies who participated in this planning process shared their intentional focus on reducing what they call “door-to-floor time”—the time it takes for new employees entering their organization to become productive—by one-third. Experiential learning is the best solution, but for recent graduates, this may seem like an insurmountable prerequisite.



Source: Health Advances analysis, Burning Glass Technologies Database, Accessed March 2014.

The most successful life sciences graduates are able to demonstrate relevant work experience and laboratory skills to prospective employers. At the entry level, internships and co-op programs are some of the best ways students can be exposed to the industry. Industry leaders cite a desire for entry-level employees who are relatively self-sufficient, understand the basics of working in industry and not just an academic lab, and who have exposure to the laboratory techniques they will utilize on the job.

## Case Study: Northeastern University



### Northeastern University

For decades, Northeastern University has been at the forefront of the experiential learning movement through its highly successful co-op program, which places students in six-month, full-time, paid positions in their field of choice two or three times over their

college career. The program alternates semesters dedicated to academic study and co-op semesters allowing students to become fully immersed in a professional work environment. Co-op coordinators manage relationships with area employers and centralize job postings through a Northeastern online portal. Biopharma executives throughout the Boston area are very familiar with this program and commend the University for providing its graduates with hands-on experience. Currently, about 300 life sciences students at Northeastern seek a co-op position annually, and 70 local hospitals and biopharma companies host positions. Local employers include Genzyme, Cubist, Vertex, Dyax, Millennium, and Infinity Pharmaceuticals. Frequently, students are able to return to their co-op organizations for full-time employment after graduation, or are able to explore a broader range of positions due to their strong backgrounds. Employers benefit by hiring their former co-ops full-time since they have undergone an extended training and “trial” period. Educators and industry experts have called for a significant increase in internship and co-op programs across the life sciences field.

#### Targeted Certificate Programs

Life sciences executives lament that a general associate or bachelor’s degree in biology is often not sufficient or relevant to the positions available in industry; a more specialized education is required. The fact is, however, that many different companies require very specific areas of expertise that may not always be universally applicable. Some examples include animal work for preclinical studies, clinical trial management, and cell culture techniques. Gaps in education in such specialized areas may be filled by targeted certificate programs that are developed by industry companies in concert with local schools. MassBioEd should continue the work of the MLSEC to best align industry and academia and fill these gaps in a manner that is efficient for the companies and the academic institutions.

## Recommendations

Keeping companies in Massachusetts as they grow into more fully integrated companies with manufacturing and commercial operations has many benefits. The high cost of doing business often comes up as a barrier to expanding company activities in Massachusetts. The state must provide incentives to attract and retain companies, but often, costs are only part of the equation. Equally important are elements that reduce time and uncertainty – e.g. permits, zoning – which the state can address. Companies also value having access to talent and co-locating activities to allow cross-fertilization between functions. By proactively courting company prospects, ensuring business-friendly policies, and investing in workforce development, Massachusetts can build a broader and more diverse industry footprint, benefitting the cluster for years to come.

- 1. Call for Reauthorization of the Massachusetts Life Sciences Initiative:** While there are many lessons to be learned from the implementation of the initial LSI, the clear consensus from industry and other stakeholders is that the \$1 billion commitment sent an important message that Massachusetts does value the life sciences industry and is committed to ensuring its future. Shire's decision to expand in Lexington is just one example of a "win" as a result of the Initiative. However, other regions (domestic and international) have grown increasingly more aggressive in courting industry in the last five years, and Massachusetts must continually reiterate its support.
  - a. Support STEM by investing in proven STEM programs:** The LSI's funding support for STEM education is critical. LSI has provided valuable grants to many schools. Often, grants are most effective when they are complemented with training and hands-on support. LSI should fund programs that have proven to be effective in this regard.

MassBio's BioTeach program has been an effective model for boosting life sciences training at high schools. Since 2005, the program has trained more than 750 science teachers and taught thousands of students at 189 public high schools. The program not only provides lab equipment, but also curricula training, teacher support and student career exploration opportunities.<sup>77</sup>
- 2. Work with State and Local Agencies on Incentives for Anchor Companies:** Keeping companies in Massachusetts as they grow into more fully integrated companies with manufacturing and commercial operations has many benefits. Biomanufacturing is a core skill and there are more resources in Massachusetts than is immediately apparent. As companies mature, tax incentives and infrastructure investments become more important than academic links. Minimizing impediments to business operations is critical to communicating a welcoming message. In its programming, MassBio can feature some of the state's downstream assets to help support the message.
- 3. Proactively Market the Cluster and Close "Wins":** Stakeholders tout BMS' decision to build facilities in Devens and Shire's decision to build a campus in Lexington as examples of how the State has effectively mobilized resources to win companies to Massachusetts. A recent example is the ability of uniQure, a Dutch-headquartered gene therapy company, to secure local real estate tax incentives, lease a facility in Lexington and receive a tax benefit award from the MLSC within just a four month period.<sup>78</sup> Nonetheless, a perception persists that the State could be more proactive and better coordinate "closing" prospect leads. The BioLeads initiative, which includes MassBio and multiple state agencies cooperating in lead development, is unique, successful, and should be continued, but increased efforts must be made in proactive outreach to companies on the rise within Massachusetts and beyond its borders. Determining which state agency is singularly responsible for such outreach and which authority is empowered to extend incentive proposals (which should not be limited to MLSC programs) to promising prospects would be a major step forward.
- 4. Expand University-Industry Collaboration through MLSEC:** Commitment to STEM education is critical for this industry. However, there remains a significant opportunity for closer ties between universities and industry. UMass, Worcester Polytechnic Institute, Northeastern and other institutions are already collaborating with companies on training. MassBio and MassBioEd's Massachusetts Life Sciences Education Consortium (MLSEC) should be the go-to resource for companies and universities seeking to collaborate on workforce training. The MLSEC should document, publicize, and share best practices in these collaborations, and explore new efforts for dedicated and industry-wide training programs to build a highly-skilled and productive workforce.
- 5. Lead Efforts to Develop a Biannual MA Life Sciences Job Forecasting Study:** Both companies and universities point out that the lack of a reliable, ongoing source of data on job demand in the life sciences industry creates challenges for both parties around workforce training and planning. Creating such a resource would require coordination among companies in the industry to submit job hiring, vacancy, and turnover data that can be aggregated and analyzed to provide valuable insights for education and training managers. MassBio and MassBioEd can convene industry and education leaders to develop an action plan to create this resource and they can reach out to companies to provide ongoing data for the benefit of all stakeholders.



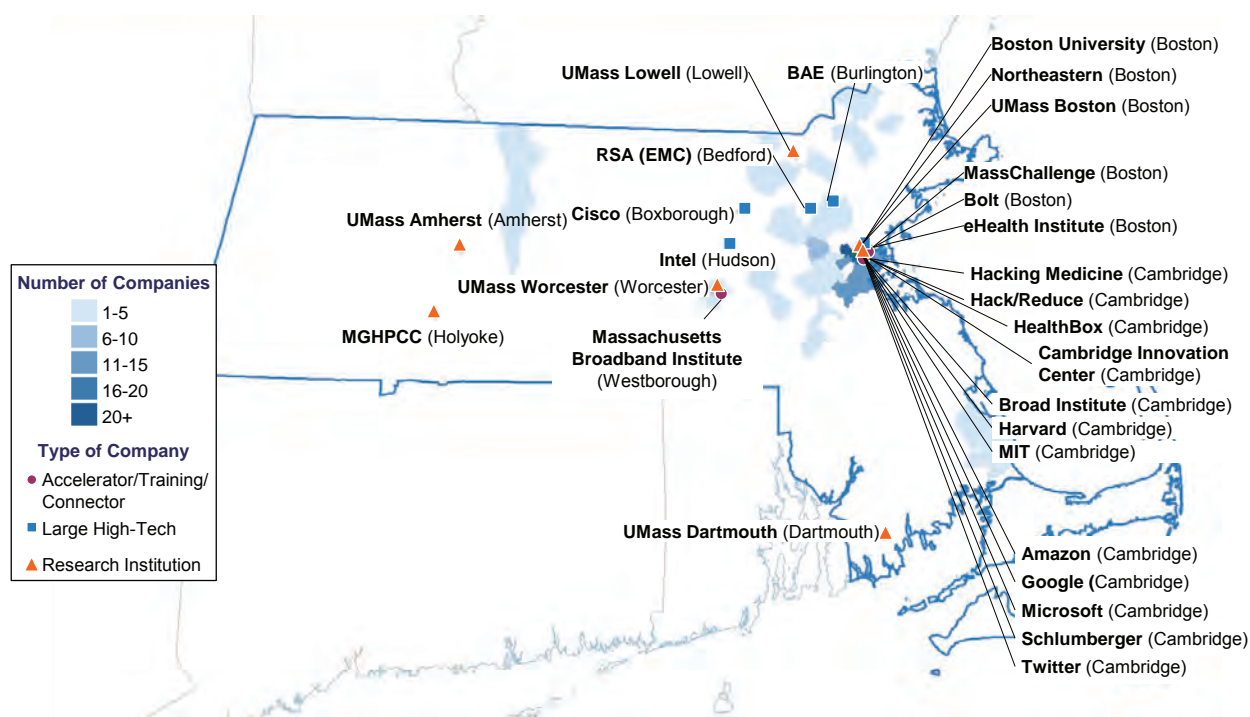
# Massachusetts, the Life Sciences Information Technology (LSIT) Hub

At the December 2013 Forbes Healthcare Summit in New York, Matthew Herper from Forbes asked a panel of healthcare luminaries whether big databases could eventually replace randomized controlled clinical trials. Rather than running multiple trial arms designed to minimize risk of bias, existing data on natural history of disease, treatment patterns, and outcomes for the selected cohort of patients would be the control. Panelists Susan Desmond-Hellmann, the Dean at University of California San Francisco and formerly head of development at Genentech, and Jonathan Bush, founder and CEO of electronic health records provider athenahealth, both said yes.<sup>92</sup> Imagine how that one possibility would transform clinical trial design, reduce cost, and shorten development time frames, bringing more novel therapies to patients faster.

Clinical trial design is just one example of how information technology (IT) will transform drug discovery and development, and the entire life sciences sector. In the context of this report, IT will be a critical enabling tool that is essential to address the three other key themes, facilitating new company formation, assessing and measuring the value of innovation, and delivering that value to patients.

However, to maximize this opportunity, we must bridge major divides that exist in communication, content knowledge, and talent development. Massachusetts has an impressive IT footprint, with several major IT companies, accelerators and incubators, and leading universities [Figure 1]. But Massachusetts must be more intentional in breaking down silos, encouraging collaboration, highlighting key needs, and bringing together a very fragmented set of life sciences needs and IT resources, in order to grow as a world-leader in life sciences IT (LSIT).

**Figure 1: Massachusetts' IT Footprint**



**Source:** Boston Business Journal: Mass High Tech Life Sciences Directory.

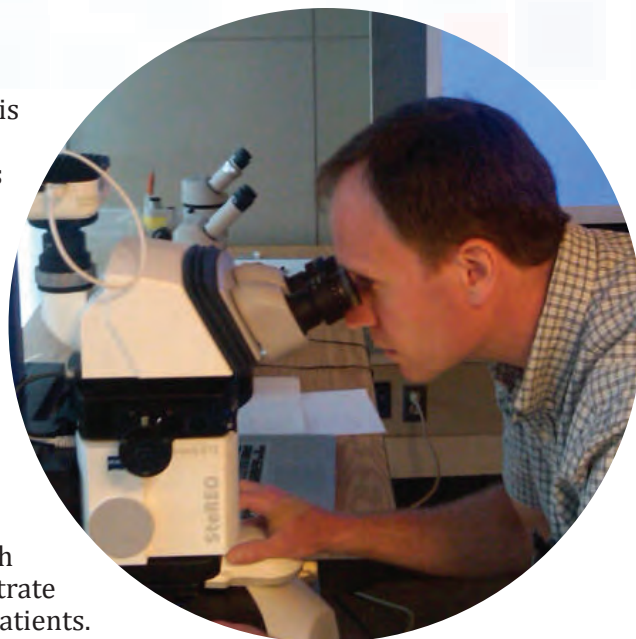
## Catching the IT Wave

From megabytes to gigabytes to terabytes and now petabytes, data collection and analysis are exploding. IT advances are already transforming other industries. High-powered computing has made it possible to discover the make-up of subatomic particles.<sup>93</sup> Big data analytics give city managers the ability to predict crime, fires, traffic patterns, and manage municipal services more cost effectively.<sup>94</sup> High-speed data networks of fiber optic cable now connect much of the globe and new advances in cable speed now make it possible to transfer data at 10 terabytes (~1,000 gigabytes) per second.<sup>95</sup>

IT is rapidly moving into healthcare, creating digital connections among patients, providers and payers,

enabling more reliable data collection, and facilitating data analysis and informed decision-making. Watertown-based athenahealth [See Sidebar] reports more than 50,000 providers have joined its web environment, AthenaNet.<sup>96</sup> While AthenaNet is a valuable management tool for providers, the long-term value being built is in the data set. Data produced from electronic health record (EHR) systems will make it possible for providers and payers to communicate in richer and more objective terms. EHR data has the potential of being incredibly more descriptive than current payer claims data because of the possibilities to connect multivariate patient outcomes (e.g. lab tests and clinician observations) with costs, regardless of the treatment setting.

Another local company, Ubiqi Health, has created a platform to enable disease tracking and capture outcomes data. Incredibly rich EHR datasets will enable biopharma companies to better demonstrate the value of their interventions in an individual or population of patients.

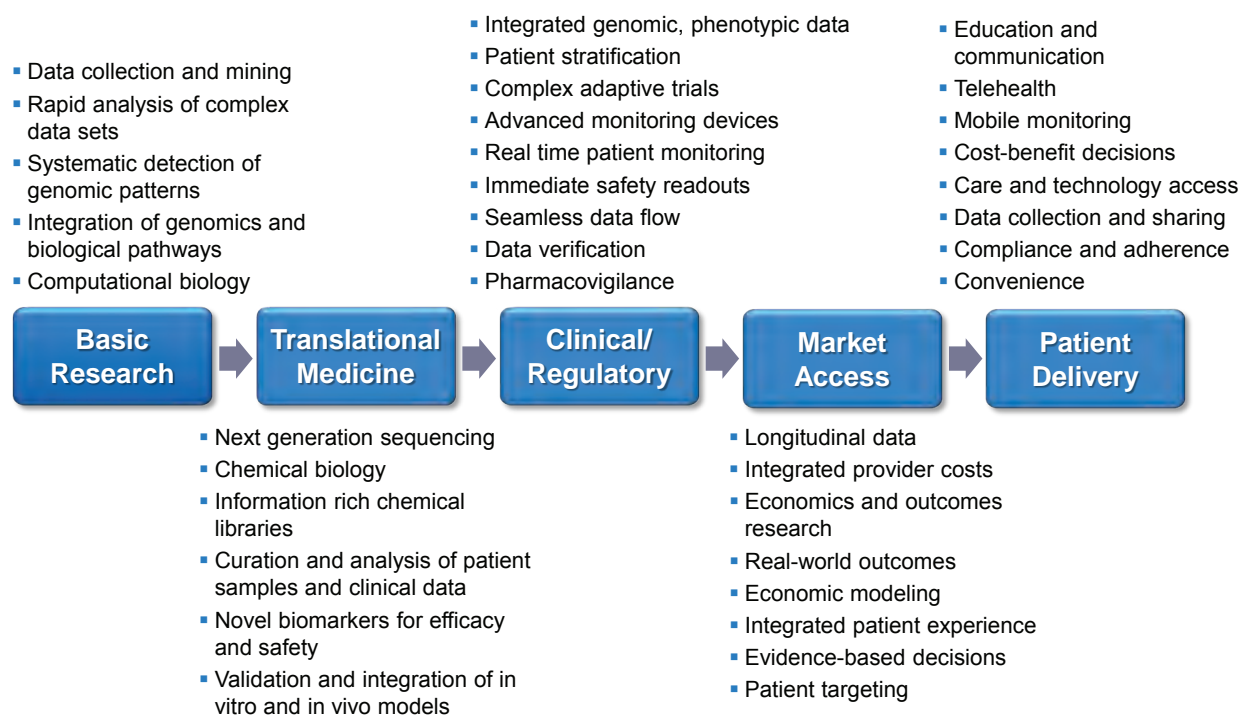


### Connecting IT and Life Sciences in Massachusetts

Research productivity, reproducibility, and transparency are persistent issues faced by academic and for-profit research institutions. Drug discovery and development will need to become more efficient as access to capital, at all levels, becomes more uncertain. Payer organizations must better manage risk and financial resources to ensure that their covered patients can have access to the best therapies and care. Hospitals and healthcare providers need to manage delivery of care with more consideration of costs as they increasingly take on financial risk in the era of healthcare reform. Increasingly, providers will look to industry to share the risk of high-priced therapies. Perhaps most transformative will be the cost/benefit decisions patients will make as they take on more financial responsibility for their healthcare.

At every level of the life sciences value chain there are opportunities for transformative solutions enabled by information technology [Figure 2].

**Figure 2: LSIT Applications Across the Product Development Value Chain**

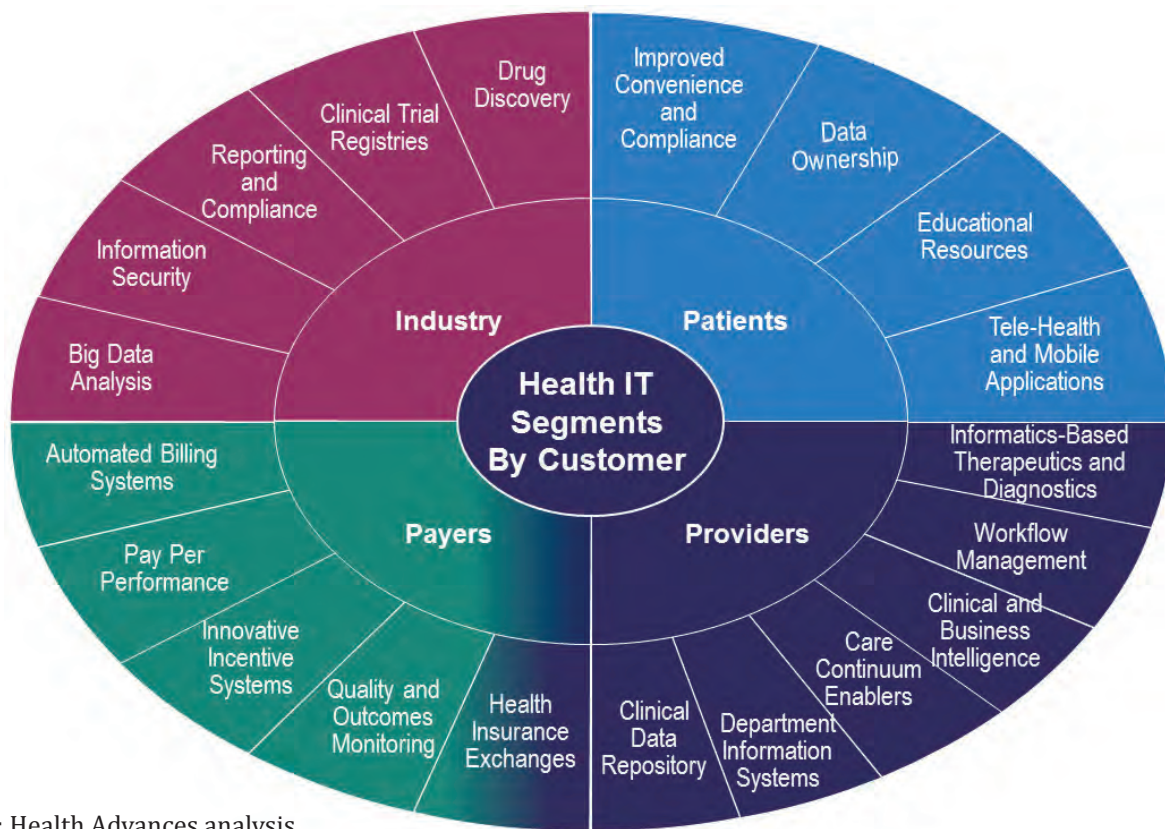


Source: Health Advances analysis

Most will acknowledge that California is the leader in IT broadly, with behemoths like Google, Facebook and hundreds of smaller IT companies based there. Like Massachusetts' strengths in life sciences, California has the entire package—a heritage of IT innovation, talent at the “bench-level” and at the executive level, and dedicated, long-term investors.

However, Massachusetts does have a strong, albeit fragmented, IT platform of its own. With its breadth of research activities and deep content knowledge, Massachusetts has the opportunity to be the leader in life sciences-related IT as outlined in the Industry quadrant of the Life Sciences IT diagram [Figure 3].

**Figure 3: LSIT in Broader Health IT Context**



Source: Health Advances analysis

Below are just a few examples of the IT resources, efforts, and experiments in the state:

- The Massachusetts Health Information Highway (Mass HIway) – a state-driven effort to secure statewide health information exchange, the most advanced in the nation, through facilitating data sharing among provider systems to enable seamless coordination of care.<sup>97</sup>
- Influx of companies from the West Coast setting up facilities in Massachusetts, including Google, Microsoft, Amazon, Twitter, Intel, Cisco, and others.
- Expansive fiber optic network throughout the state and connected to main trunk lines to New York and across the Atlantic enabling high speed transfer of data globally.
- High-power computing required to perform big data analytics such as the Massachusetts Green High Power Computing Center (MGHPCC) in Holyoke, MA, a cooperative effort between MIT, Harvard, UMass and Cisco, with opportunities for the life sciences industry.<sup>98</sup>
- Data driven genomics and systems biology based efforts at Harvard, MIT, and most notably the Broad Institute focused on better understandings of disease such as oncology and rare conditions.
- Dr. David Altshuler from the Broad Institute, Harvard and MIT has been instrumental in the formation of the Global Alliance for Genomics and Health, an alliance of 151 members,



working with Google Genomics, committed to collaborating and sharing genomic and clinical data.<sup>99</sup>

- Optum Labs based in Waltham, a division of United Health and unique partnership model employing a rich pool of de-identified data and advanced analytics to address comparative effectiveness questions, quantify variability in treatment response, better understand patient needs, and develop evidence to support novel treatment paradigms **[See Case Study]**.<sup>100</sup>
- Baystate Health's Technology Innovation Center in Springfield leveraging data from 80 medical groups and three hospitals including Tufts University Medical Center and a health insurance provider with 100% EHR adoption that is available to investigate patterns of care in a longitudinal, multigenerational data set.<sup>101</sup>

## Leading in LSIT

Dr. Michael Rosenblatt, Chief Medical Officer of Merck, remarked, "The products of pharmaceutical research and development are only useful when surrounded by information on how to use (and how not to use) them. Big data will generate insights that could not be obtained previously, if we use quality data and analyses so that we do not come to precisely the wrong conclusions." Bioinformatics are being employed at nearly every step in the drug discovery and development process. Combining genomic, phenotypic, and longitudinal data will allow for more effectively designing and more efficiently managing clinical trials. Cross-functional access, manipulation and integration will allow for patient stratification and targeted data collection. Advanced measuring devices for detecting and recording along with nearly instantaneous analysis will allow for real-time patient monitoring to improve safety. And as was earlier described, sophisticated, highly selective, and detailed data sets that map disease progression in specific patient populations could transform randomized, controlled clinical studies.

Those who are working at the leading edge of applying IT technology to drug discovery and development are already anticipating some of the great challenges. As Dr. Stephen Cleaver, Executive Director of Informatics Systems at Novartis Institutes for BioMedical Research, said, "Without the analysis piece, the data is meaningless." He went on to say that this new approach to research will require a new breed of "data scientist" who will need to work hand-in-hand with biologists and chemists.<sup>102</sup>

Unfortunately research by the Massachusetts Technology Leadership Collaborative (MassTLC) shows a shortage of IT talent available in Massachusetts<sup>103</sup>, and that shortage is already being reported by life sciences companies looking for talent. The best talent from MIT, Harvard, and other local universities is being drawn to other industries, with faster development cycles, or other clusters. Massachusetts' IT and life sciences industries must work together to retain talent.

Altering the drug discovery process to integrate IT will also pose cultural challenges. As Dr. Todd Golub from the Broad Institute points out, these two high tech cultures, information technology and life sciences research, run at different paces. IT culture moves at a very fast pace and researchers are used to short development timelines and quick decision making. If IT is a sprint, pharmaceutical R&D is a marathon, which may be less attractive to young IT talent.

Integration of the various data sets necessary to enable some of these sophisticated analyses will require transparency, and the pharmaceutical industry has been resistant to open source data. That view is short-sighted; the market is going in a new direction, driven by patients who are willing to take on the risk of sharing their own data to enable a cure.

Life sciences IT success will also require a level of cross-silo cooperation that has not historically been the practice in healthcare or in the pharmaceutical industry. In healthcare IT, the barriers are eroding. Consolidation of providers and payers will enable data integration. But while that enables an organization like Kaiser Permanente, a large healthcare provider, to have a more comprehensive data set, it is also held captive by a private company. This is why public projects like the Mass Hlway are an valuable experiment and why collaborative health IT efforts in Massachusetts are also important. The data integration and analysis task is bigger than one organization can afford to take on by itself. It will require collaborations between companies, with universities, with providers, and with payers at all levels to ultimately demonstrate value through patient outcomes.



## Recommendations for MassBio

To support the growth of an LSIT sector in Massachusetts, MassBio should pursue the following recommendations:

1. **Collaborate with MassTLC to Launch an LSIT Program** – Work with the Mass Technology Leadership Council (MassTLC) to create an integrated and focused program for LSIT to cultivate cross-sector relationships between IT and life sciences companies. This program can leverage the planning resources of the two organizations in order to develop a set of events for the community that can bring attention to the growing LSIT opportunity and share information on technologies, emerging companies, industry needs, and challenges.
2. **Support Efforts Underway By MassTLC to Bring Focus to LSIT Talent Development** – MassBio and MassBioEd can help by convening life sciences companies, IT companies, and academia to dialogue on how to attract and retain IT talent in Massachusetts. Work with the group to define IT-focused, life sciences career paths that can be publicized to the industry.
3. **Establish an LSIT Resource Center** – Curate a centralized set of resources, such as LSIT company directories, LSIT job postings, updates on local LSIT initiatives for members.

There is a real and unique opportunity for Massachusetts to build off its strength in research and development to capture a segment of the increasingly active and important life sciences IT sector, and increased collaboration and effort between industry organizations will position the Commonwealth to take advantage of the opportunity.


## Case study: athenahealth



Athenahealth (NASDAQ:ATHN, Watertown, MA) is the leading provider of electronic health record (EHR), practice management, and care coordination services to medical groups and health systems. Founded and based in Watertown, MA, athenahealth is developing solutions to help providers meet the goals of pay-for-performance medicine and healthcare reform.

The company was founded by current CEO, Johnathan Bush in 1992.<sup>104</sup> Athenahealth has and will continue to be an important anchor for Massachusetts' young and growing health IT scene. The company's EMR system, athenaClinicals, was ranked #1 in 2013 by KLAS<sup>105</sup> (which provides impartial ratings of healthcare technology to help providers make informed decisions) for usability, efficiency, and effectiveness. Consistent in their ambition to offer the best EMR product in the industry, athenahealth has a long history of working with companies who have developed solutions that would augment or add additional features to their EMR system. In 2013, the company partnered with iTriage, an app designed to let patients look up symptoms they might be having, find more information, and be directed to a healthcare provider nearby who might be helpful.<sup>106</sup> Earlier in the year, the company purchased Epocrates, an app providing clinical content to physicians. Athenahealth's commitment to collaboration should not only attract other companies to the Commonwealth, but should also allow for company alumni to be successful in new startup endeavors.

Just as we've seen employees of biopharma companies leave Genetics Institute, Biogen Idec, and Genzyme spinning out into new companies, there is already evidence of athenahealth alumni developing new solutions within their own startups here in the Commonwealth. Former athenahealth employee Zoe Barry founded ZappRx, a mobile prescription platform that allows physicians and patients to better coordinate complex prescription management. Another alumnus, Yechiel Engelhard, created GeckoCap, an intuitive device that allows parents to track and monitor their children's asthma medication usage through mobile devices. The talent base athenahealth is creating in Massachusetts will be a key resource for the young health IT cluster developing here.



Since its founding, athenahealth has been incredibly successful and has planted a flag in Watertown as the site for further expansion of its presence in Massachusetts. In 2013, the company announced plans to develop a converted World War I gunpowder arsenal into a 21<sup>st</sup> century, state-of-the-art, health IT campus, akin to Google's prolific Mountain View campus.<sup>107</sup> In 2011 and 2012, athenahealth was voted best place to work in Massachusetts by *Boston Business Journal*. The company wants to build upon that reputation by installing all the amenities of a modern tech company including on-campus chefs, pubs, and unique workspaces that allow for creative thinking in their expanded facilities. Athenahealth foresees their Watertown campus as an opportunity to not only expand the rapidly growing company, but as space for new health IT companies to grow and collaborate with athenahealth to create the best solutions to problems facing all stakeholders in healthcare.

# Leadership in the Massachusetts Cluster



In conversations with stakeholders about the vulnerabilities of the Massachusetts life sciences cluster, one concern raised by several people was whether future leaders would step forward to fill the shoes of Henri A. Termeer (Genzyme), Joshua Boger (Vertex), or Jim Vincent (Biogen). It is ironic that at a time when the local life sciences industry is experiencing its strongest growth in years, many are worried about who will step forward as vocal advocates and stewards of this unique industry cluster.



Stakeholders are all quick to observe that there are many passionate, community-minded, bright, energetic people leading companies and investor groups who have had great success and have much to contribute. Many serve on the MassBio Board of Directors and others have generously donated their time to provide input in the Impact 2020 research process. But who among them will have the stature, experience, interest, and base of credibility to rally the industry when needed?



What is behind this concern is that as the life sciences industry is going through a dramatic transformation and fewer leaders have the opportunity to rise to the same level as earlier industry icons. Building large, fully integrated companies with thousands of employees is increasingly rare as successful companies are quickly acquired by large pharmaceutical companies. Few companies will survive as independent organizations long enough to build out full commercial operations and mature their management team with home-grown talent. While the influx of big pharma research groups into Massachusetts adds a lot to our cluster, the leaders of these groups do not have deep roots in this area and leadership changes frequently. As our cluster expands, will executives see the need and be willing to take time from their company responsibilities to invest in the future of the cluster? Analysis of other clusters indicates that smaller clusters have a greater sense of urgency and possibly greater unity.



At times, it is necessary for MassBio and others to “gather the troops” and exert leverage. One message that came through more than all others in this report, and that is “we cannot rest on our laurels.” Multiple interviewees cited the rise and fall of Route 128, the Technology Highway of the 1970’s and 1980’s. The life sciences industry could easily go the way of Digital, Wang and other technology companies without careful care and nurturing.

Several local executives mentioned that the renovation process for the Longfellow Bridge connecting Boston and Cambridge has caused them unending consternation and inconvenience for their employees leading them to question, “Did anyone think through the impact on all the Cambridge companies?” Yet when the renovation was in the planning stages, when there was opportunity for input, industry leaders were largely absent. The local life sciences industry and its 56,000 employees<sup>108</sup> should be able exert some influence. Many of the recommendations outlined in Impact 2020 require industry leaders to step forward. Facing many headwinds, industry leaders must be a force in galvanizing support around key issues.

There are ways that MassBio can facilitate efforts but success will require industry leaders to step forward and lead:

- **Massachusetts Life Sciences Industry CEO Forum:** CEOs of major life sciences companies in the cluster should commit to participate in and support a biannual forum hosted by MassBio to agree on future issues, to outline an action plan for each key issue, and designate which executive(s) will take leadership on each issue. The chair of the MassBio Board can chair this forum. This report frames a series of opportunities around government policy, workforce, company formation, and healthcare reform that can inform the initial agenda.
- **Young Leaders Mentoring:** Each year, as part of the forum, each senior executive should commit to mentoring a promising young leader, encourage their participation in the forum and schedule periodic meetings to work together on one big issue.

# Impact 2020: Call to Action

The Massachusetts life sciences cluster is at a critical juncture. The cluster has experienced many successes. Advances in cutting-edge science, progress in information technology, and renewed enthusiasm in the public markets have generated more opportunity than ever before. But this potential, and the future of the cluster, are facing threats from regulatory and reimbursement shifts that are creating uncertainty for companies and investors and casting a negative light on the industry.

The Massachusetts cluster will not only survive but thrive if its leaders are prepared to meet the challenges ahead and respond to these shifts with urgency. In order to achieve the vision of Impact 2020, this report has laid out the following strategic priorities for the cluster:

- Demonstrate the value of innovation for the healthcare system and ultimately for patients
- Maximize access to capital and other enabling resources for early-stage companies
- Support life sciences company expansion down the value chain
- Capitalize on information technology to advance the life sciences
- Articulate the industry's patient focus

Each of these areas has implications for local, state, and national policy. Impact 2020 calls for policymakers to ensure that value-based healthcare is informed by all stakeholders, including patients, and that it balances reward for innovation to avoid any unintended consequences. This report asks for recognition and support of the life sciences information technology opportunity. Finally, Impact 2020 calls for policymakers to support life sciences company formation and expansion in Massachusetts, specifically through NIH funding increases, LSI renewal, and business-friendly tax and permit policies. These messages are detailed further in the table on the following page.

## Impact 2020 - Key Messages for Local, State, and National Policymakers

Primary Themes	Key Messages
<b>Value – Impact on Innovation</b>	<ul style="list-style-type: none"><li>• Value-based healthcare is more than just price controls; any value-based system must achieve a balance with ensuring a reward for innovation, or patients will lose</li><li>• Massachusetts is in a unique position to convene stakeholders across healthcare in a productive dialogue around value; local initiatives can have national influence</li><li>• Patients must be involved in any discussions around value-based healthcare, they deserve a seat at the table and their interests must be heard</li></ul>
<b>Support for Company Formation</b>	<ul style="list-style-type: none"><li>• While 2013 has been strong for the industry, life sciences is inherently risky and fragile, and highly vulnerable to a reduction in funding support</li><li>• NIH funding is critical to seeding future generations of technologies and companies, and must be preserved</li><li>• Re-authorization of the Massachusetts Life Sciences Initiative will, once again, send a very important message to the life sciences industry that it is valuable to the state, especially as other clusters are investing aggressively to compete</li><li>• Active dialogue with industry around key topics, e.g. reimbursement, will help mitigate the negative impact that regulatory uncertainty has on investment</li></ul>
<b>Support for Company Expansion</b>	<ul style="list-style-type: none"><li>• Favorable business policies and incentives to encourage companies to grow into maturity in Massachusetts will enhance the cluster's ability to appeal to companies across the business lifecycle</li><li>• Massachusetts has significant capabilities downstream from R&amp;D, particularly in biomanufacturing, that should be recognized and supported</li><li>• These capabilities leverage talent in the broader state, accruing benefits beyond the Boston/Cambridge center</li></ul>
<b>Life Sciences Information Technology Opportunity</b>	<ul style="list-style-type: none"><li>• Information technology can enable a broad range of solutions for problems in healthcare and the life sciences</li><li>• Across Massachusetts there is a wide array of initiatives underway, but they are fragmented</li><li>• Government cooperation and support for cross-industry initiatives will stimulate a life sciences information technology hub and give Massachusetts a unique competitive advantage</li></ul>



Impact 2020 broadens the focus for MassBio, more than previous strategic plans, beyond its current life sciences company membership to other key healthcare stakeholders. To steward the cluster through the challenges of the next five years, MassBio will need to join forces with other sectors – providers, payers, research centers, information technology firms – to broker critical dialogues that enable collaborations and inform policymaking. Impact 2020 provides a set of priorities and initiatives for MassBio that capitalize on its strengths in convening groups, advocating for the industry, and developing effective programs and events for stakeholders.

- **Convene Key Groups Across Sectors** – As a trade organization for life sciences companies, MassBio is in a position to represent the industry, to reach across the table, to convene other groups, and to organize critical discussions and forums. But this is not just an organizational role, it is a leadership role, and one that is urgently needed. On behalf of the multitude of life sciences companies, MassBio can bring together leaders to address challenges that need cohesive and convergent solutions. The key issues facing the cluster that this report has highlighted will require cross-sector dialogue and collaboration.
- **Advocate for the Industry with Policymakers and the Public** – The life sciences industry has come under scrutiny for the value of its products, creating misperceptions in the public and policies that could have unintended consequences. There are numerous ways that medical advances have benefited patients and there is still significant unmet need across many conditions. MassBio can educate the public and policymakers not only on how medical technology benefit patients, but also on what is required for development efforts to produce transformative therapies and cures. Policymakers need to show their support for the industry, and there are numerous ways that this can occur, from renewing the LSI, to increasing NIH funding, to ensuring business-friendly policies.
- **Focus Programs and Events around Priority Areas** – MassBio can focus its programs and events to address critical issues facing the cluster. To help prepare companies for an era of value-based healthcare, MassBio can provide education around reimbursement and system economics to ensure all companies can “speak payer.” To address the early-stage financing climate, MassBio can expand MassCONNECT to ensure any life sciences startup can be connected to a diverse range of investors and enabling resources. MassBio can continue to support state and local agencies on developing incentive packages and business-friendly economic policies. Through MassBioEd, the organization can bring companies together with secondary and higher educational institutions to develop effective training programs and build resources that will advance workforce planning.



The table on the following page details the key initiatives Impact 2020 recommends for MassBio to support the strategic priorities for the cluster and help achieve the vision set for Massachusetts life sciences in the years ahead.

## Impact 2020 – Recommended Initiatives for MassBio

Impact 2020 Vision	To advance Massachusetts' leadership in the life sciences industry, championing innovation in order to bring value to the global healthcare system and make meaningful impact on patients' lives.			
Strategic Priorities for the Cluster	Demonstrate the value of innovation for the healthcare system and ultimately for patients	Maximize access to capital and other enabling resources for early-stage life sciences companies	Support company expansion down the value chain	Capitalize on information technology to advance the life sciences
MassBio Initiatives:	Value and Patient-Centered Initiatives	Company Formation Initiatives	Company Expansion Initiatives	Life Sciences Information Technology Initiatives
Convene Key Groups	<ul style="list-style-type: none"> <li>Convene a high-profile Value-Based Healthcare Working Group 2-4 times per year</li> <li>Engage payers and providers on MassBio strategic priorities</li> </ul>	<ul style="list-style-type: none"> <li>Rally agencies to promote the Massachusetts life sciences cluster and attract global resources</li> <li>Organize regular startup CEO forums to share best practices</li> </ul>	<ul style="list-style-type: none"> <li>Through MassBioEd and the MLSEC, convene industry and university to expand workforce collaborations</li> </ul>	<ul style="list-style-type: none"> <li>Collaborate with MassTLC to launch an LSIT Program</li> <li>Bring focus to LSIT talent development</li> </ul>
Advocacy Efforts	<ul style="list-style-type: none"> <li>Articulate value arguments for life sciences products and build awareness with government officials and agencies</li> <li>Communicate to the public on the value of life sciences innovation for patients</li> </ul>	<ul style="list-style-type: none"> <li>Advocate for more seed-stage funding options through the MLSC and other sources</li> <li>Advocate for NIH funding</li> </ul>	<ul style="list-style-type: none"> <li>Support renewal of the LSI</li> <li>Advocate for enhanced state incentive programs and external marketing and prospecting</li> <li>Promote Massachusetts as a range of optimal locations for life sciences companies across the business lifecycle</li> </ul>	<ul style="list-style-type: none"> <li>Support MassTLC in its efforts to bring government attention to life sciences IT opportunities</li> </ul>
Programs and Events	<ul style="list-style-type: none"> <li>Establish a value resource center</li> <li>Develop and promote value-based training and education for life sciences companies</li> <li>Highlight more patient successes and opportunities in programs and events</li> </ul>	<ul style="list-style-type: none"> <li>Expand MassCONNECT and its role in company formation</li> <li>Maximize access to funding and enabling resources</li> </ul>	<ul style="list-style-type: none"> <li>Enhance visibility for biomanufacturing assets and commercial talent</li> <li>Develop and implement a state-wide, biannual job forecasting study</li> </ul>	<ul style="list-style-type: none"> <li>Create forums and events under LSIT program that enable cross-sector relationship development</li> <li>Identify and publicize LSIT career paths</li> <li>Establish an LSIT resource center for members</li> </ul>

While MassBio is prepared to take on these initiatives, there are areas where leaders of other healthcare sectors can engage. Impact 2020 asks the leaders of local payers and providers groups to:

- Engage with MassBio and industry leaders on a dialogue around the required data, systems, metrics, and processes that can enable a model of value-based healthcare;
- Pursue experiments and pilots on sharing high-quality data among groups so that a stronger understanding of the patient experience, and all its costs and outcomes, can be attained.

MassBio is prepared to work with leaders of these groups and their associations on these areas.

Impact 2020 identifies several areas where MassBio's direct membership can engage. The table below summarizes key recommendations for member groups on how they can help further the efforts to achieve the goals laid out by Impact 2020.

## Impact 2020 – Key Areas of Engagement for Stakeholders

Stakeholders	Key Areas to Engage
<b>Large Pharmaceutical Companies</b>	<ul style="list-style-type: none"> <li>• Seek opportunities to work across traditional boundaries with payers and providers in MA</li> <li>• Support local initiatives to ensure funding, space, and support for startup companies to secure future in-licensing and acquisition opportunities</li> <li>• Commit senior executive time to critical local issues that require visible industry support</li> <li>• Engage with MassBio in communicating patient stories and benefit</li> </ul>
<b>Established Biotech Companies</b>	<ul style="list-style-type: none"> <li>• Commit to collaborative high-level leadership around local infrastructure, policy, and workforce issues</li> <li>• Actively participate in senior leadership forums to address critical questions around value-based healthcare and life sciences information technology</li> <li>• Engage with MassBio in communicating patient stories and benefit</li> </ul>
<b>Early-Stage Companies</b>	<ul style="list-style-type: none"> <li>• Participate in MassCONNECT to ensure efficient access to funding sources, space, and other resources</li> <li>• Participate and support startup CEO forums to exchange lessons learned</li> </ul>
<b>Universities and Research Centers</b>	<ul style="list-style-type: none"> <li>• Consider opportunities to provide more seed resources and/or funds for promising research</li> <li>• Engage with MassCONNECT as it expands programming for new companies</li> </ul>
<b>Investors and Funding Sources</b>	<ul style="list-style-type: none"> <li>• Work with MassBio on programming to enhance early-stage company understanding of reimbursement and the value-based healthcare debate</li> <li>• Assist MassCONNECT in advising and mentoring early-stage companies</li> <li>• Encourage portfolio companies to join MassBio and engage in industry dialogues</li> </ul>
<b>CROs, CMOs and Service Providers</b>	<ul style="list-style-type: none"> <li>• Continue to work with MassBio to build visibility for available resources, to expand resources, and to ensure a strong talent pool</li> </ul>

Finally, Impact 2020 puts forth a strong call for industry leaders to step up and provide leadership to the cluster on the critical issues that have been identified. MassBio will enable the cultivation of cluster leadership through an annual or biannual leadership forum, mentoring, and recognition of contributions.

The Massachusetts life sciences cluster is in a strong position, but with success comes responsibility. Impact 2020 calls for MassBio to elevate its role, forge cross-sector relationships, educate the public and its representatives, stimulate local development efforts, and enhance services for members. MassBio will continue to be the greatest advocate for the Massachusetts life sciences cluster, for innovation, and ultimately for patients. MassBio and its Board of Directors are prepared to provide leadership, champion innovation, and ultimately help the cluster deliver solutions with meaningful impact on patients' lives.

## The Impact 2020 Effort

The Impact 2020 Report is the culmination of nearly nine months of meetings, discussions, interviews, and online and in-person focus-sessions with the broadest definition of industry stakeholders. We would like to express our gratitude for all the assistance, support, and time that many individuals have contributed to this effort. We thank members of the MassBio Board of Directors and particularly the Steering Committee who have challenged our thinking and guided the effort. The Impact 2020 Advisory Board is an impressive group that is full of energy and ideas but also has many demands on their time. Their willingness to carve out time for us demonstrates a sincere devotion to solving the issues that we face. Well over 100 people from across all sectors contributed input to this analysis and every observation has been seriously considered. We appreciate their time and in the appendix we have noted as many of you as possible. Thank you also to the team from Health Advances LLC and MassBio. Their day-to-day intimacy with the global industry, their relationships with executives at local companies and their knowledge of the issues and challenges that we face have been critical for this undertaking.

## Stakeholders Interviewed

### Life Sciences Companies

William Aitchison, Genzyme Corporation  
Bruce Barclay, Formerly at Cubist  
Zoe Barry, ZappRx  
Kees Been, Lysosomal Therapeutics Inc  
William Ciambone, Shire Pharmaceuticals  
Michael Cardone, Eutropics Pharmaceuticals  
Donald Corcoran, AstraZeneca  
Douglas Fambrough, Dicerna Pharmaceuticals  
Steven Fawell, AstraZeneca  
Jay Foley, Sanofi/Genzyme  
Barbara Fox, Avaxia Biologics, Inc.  
Geoff Gallo, AstraZeneca  
Robert Gould, Epizyme  
Alaa Hamed, Sanofi/Genzyme  
William Heiden, AMAG Pharmaceuticals  
James Jenson, Sabik Medical  
Christopher Kiritsy, Arisaph Pharmaceuticals  
Kevin Krenitsky, Foundation Medicine  
Ivana Magovcevic-Liebisch, Teva Pharma  
Nagesh Mahanthappa, Scholar Rock, LLC  
David Meeker, Sanofi/Genzyme  
Walter Ogier, Acetylon  
Michael Pellini, Foundation Medicine  
Edward Pesicka, Thermo Fisher Scientific  
Anna Protopapas, Millennium/Takeda  
John Ripple, Permeon Biologics  
George Scangos, Biogen Idec  
David Schenkein, Agios Pharmaceuticals  
Anshuman Sharma, Ubiqi Health  
Henri A. Termeer, Genzyme, Board of Directors  
Steven Tregay, FORMA Therapeutics  
Robert Urban, Johnson & Johnson  
Michael Webb, Allegro Diagnostics  
Howard Weisman, Seventh Sense Biosystems  
Craig Wheeler, Momenta Pharmaceuticals  
Jeffery York, Millennium/Takeda

### Investors

Janice Bourque, Hercules Technology Growth Capital  
Greg Brown, HealthCare Royalty Partners  
William Clifford, Oberland Capital  
Marc Goldberg, BioVentures Investors  
Clark Hayes, Silicon Valley Bank  
Steven Knight, Fidelity Biosciences  
Peter Kolchinsky, RA Capital Management  
Jonathan Norris, Silicon Valley Bank

Lauren Silverman, Novartis Venture Funds  
Greg Simon, Poliwoog  
Keith Spencer, Wellcome Trust  
Daphne Zohar, PureTech Ventures

### Service Providers

Tom Andrews, Alexander Real Estate Equities  
Mark Bamforth, Gallus Biopharmaceuticals  
Michael Barron, Bingham McCutchen  
Casey Bolger, Kevin P. Martin Associates  
David Brook, Hamilton, Brook, Smith and Reynolds  
Heidrun Bruchmann, PAREXEL International  
Dan Cordeau, Alexander Real Estate Equities  
Daniel Davis, Accounting Management Solutions  
Glen Giovannetti, Ernst & Young  
Laurie Halloran, Halloran Consulting Group  
Mike O'Hara, Deloitte  
Chris Otey, Alexander Real Estate Equities  
Chris Palatucci, Palatucci Executive Search  
Albert Siu, PAREXEL International  
Ramani Varanasi, Avillion

### Associations, Government, and Nonprofits

Margaret Anderson, Faster Cures  
Robert Beall, Cystic Fibrosis Foundation  
Richard Bendis, BioHealth Innovation  
Valerie Fleishman, New England Health Institute  
Paul Guzzi, Boston Chamber of Commerce  
Tom Hopcroft, Mass Tech Leadership Council  
Gail Maderis, BayBio  
Pamela Norton, Massachusetts Life Sciences Center  
Kevin O'Sullivan, Massachusetts Biomedical Initiatives  
Lora Pellegrini, Massachusetts Association of Health Plans  
Chris Rivera, Washington Biotechnology and Biomedical Association  
Thomas Sommer, MassMEDIC  
Todd Sherer, Michael J. Fox Foundation for Parkinson's Research  
Melissa Stevens, Faster Cures  
Susan Windham-Bannister, Massachusetts Life Sciences Center

### Academia, Providers, and Payers

Cynthia Bainton, Northeastern University  
Doug Banks, UMass President's Office  
Abi Barrow, Massachusetts Technology Transfer Center  
Edward Benz, Dana-Farber Cancer Institute  
Eric Beyer, Tufts Medical Center  
Bill Brah, UMass Boston  
John Brooks, Joslin Diabetes Center  
Jim Capistran, UMass Amherst

Thomas Chmura, UMass President's Office  
John Ciccarelli, UMass Boston  
Chris Coburn, Partners HealthCare  
Michael Collins, UMass Medical Center  
Joseph Duffy, Worcester Polytechnic Institute  
David Easson, Worcester Polytechnic Institute  
Sandra Fenwick, Children's Hospital Boston  
Omid Farokhzad, Brigham & Women's Medical Center  
Lynn Griesemer, University of Massachusetts  
Nate Hafer, UMass Medical School  
John Halamka, MD, Beth Israel Deaconess Medical Center  
Vanecia Harrison-Sanders, Northeastern University  
Rachel LeBlanc, Worcester Polytechnic Institute  
James Leung, Northeastern University  
Michael Malone, UMass Amherst  
Tony Mangano, Worcester Polytechnic Institute  
Sanjeev Manohar, UMass Lowell  
Lita Nelsen, Massachusetts Institute of Technology  
Dick Nesto, Lahey Clinic  
Kamal Rashid, Worcester Polytechnic Institute  
Jonathan Soderstrom, Yale University  
Kevin Tabb, Beth Israel Deaconess Medical Center  
Ralph de la Torre, Steward Health  
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