

Acknowledgements

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Fourth Economy Consulting conducted the analysis and report development in partnership with Warner Advisors during the summer of 2016. This report is meant to inform key Pittsburgh regional stakeholders about the assets and opportunities that exist in the life sciences industry sector and highlight areas of future focus.

For additional information please contact:

Rebecca Bagley

Vice Chancellor for Economic Partnerships University of Pittsburgh bagley@pitt.edu 412-624-5530

Or

Jerome Paytas, PhD

Vice President, Research & Analytics Fourth Economy Consulting jerry.paytas@fourtheconomy.com 412-325-2457

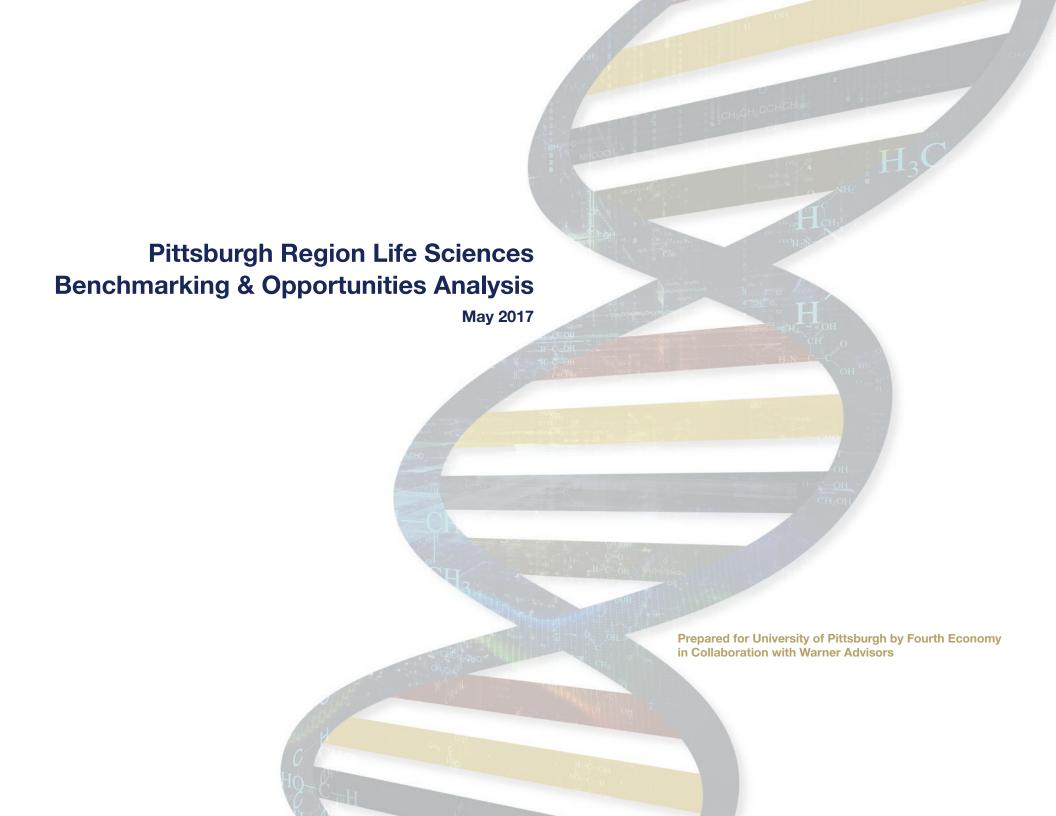


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Executive Summary

About

The following analysis was conducted by Fourth Economy, a Pittsburgh based economic development consulting firm in partnership with Warner Advisors, a Silicon Valley based life sciences strategy firm. The analysis included:

- One on one interviews with 33 life sciences leaders representing academic, industrial, financial and non-profit components of the life sciences cluster
- Primary data collection and analysis
- Secondary desktop research regarding industry trends and benchmarking information
- Focus group discussion to validate and refine findings

These sets of activities were performed from May-July 2016 and the resulting findings are presented in this report and a companion slide deck.

Context

To begin to assess and identify regional ecosystem opportunities for the development and expansion of a life sciences cluster in the Pittsburgh region we must start by putting this inquiry into some context. Pittsburgh is a leader in life sciences research, and, with more resources and investment, it can become a national leader in life sciences industry.

The life sciences sector continues to hold the promise of significant growth potential for many locations throughout the United States. For the purposes of this benchmarking and opportunities analysis we are working with a definition of life sciences that includes "core" and "expanded" characteristics. The core is defined as the life sciences sector that has been analyzed and reported on over the past 15-20 years by groups like BIO and their contracted agent TEConomy Partners (formerly Battelle Technology Partnership Practice). The expanded life sciences sector recognizes that there is a growing array of companies and activities that no longer fit neatly into the core definition. The convergence of technology and sectors is creating

an environment that does not allow for the same way of measuring the industry and a new approach has not yet emerged. Health-related Information Technology is one such area that can be classified as either life sciences or information technology.

U.S. Bioscience Establishment and Employment Data, 2014 and Percent Change, 2001-2014 and 2012-2014

	Establishment Data			Employment Data		
Bioscience Industry & Subsectors	Count, 2014	Change 2001-2014	Change 2012-2014	Count, 2014	Change 2001-2014	Change 2012-2014
Agricultural Feedstock & Chemicals	1,811	5.2%	2.2%	77,545	0.0%	1.5%
Bioscience-related Distribution	37,833	3.4%	2.8%	452,325	8.8%	2.3%
Drugs & Pharmaceuticals	3,301	26.4%	8.0%	293,353	-4.2%	3.2%
Medical Devices & Equipment	7,636	22.6%	5.5%	349,045	1.3%	-0.1%
Research, Testing, & Medical Laboratories	26,702	79.0%	10.2%	483,412	32.4%	3.4%
Total Biosciences	77,283	24.5%	5.7%	1,655,680	9.7%	2.2%

Source: TEConomy Partners analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN Group. The national core life sciences sector has continued to grow with a 9.7% increase in employment in the 2012-2014 time period according to the analysis released in June 2016 by TEConomy Partners and BIO.¹ The continued decrease in Drugs and Pharmaceutical employment and increase in Research, Testing & Medical Laboratories confirm previous Fourth Economy work noting that the larger Drugs and Pharmaceutical companies are pursuing more of their development through contractual relationships with Contract Research Organizations and lowering their overall headcount.

Pennsylvania's life sciences industry demonstrated a 1.5 percent employment loss during the 2012-2014 period. This overall decrease was driven by an 8.3 percent loss in employment in Drugs and Pharmaceuticals and a slight decrease in Medical Device related employment.² Nationally and in the region, manufacturing has struggled, but Pittsburgh's employment in NAICS 334510 electromedical apparatus manufacturing has grown by 56 percent from 2010 to 2015, an increase of nearly 740 jobs. The convergence of life sciences with Pittsburgh's traditional manufacturing base can be a powerful driver of growth.

Evolving Industry

There are four categories of macro economic trends affecting Pittsburgh's opportunity:

Macro Economic and Care Model Trends in Life Sciences

- Financial risk shifting to all sectors of the life sciences value chain creates an opportunity for regions that can span that value chain from bench to bedside.
- The focus on consumers and longitudinal care management requires more real-time information interchange that blends biomedical and IT expertise.
- The broadening spectrum of pre- and post-care solutions will need to leverage a large and diverse clinical base that can encompass the care model.
- Take-away for Pittsburgh
- Macro market changes are driving more integration of science and IT/data solutions that will
 require new business and operational models that can leverage the biomedical expertise of the
 University of Pittsburgh and computer science expertise of Carnegie Mellon University.

Health IT and Automation Clinical Care and Operational vs. Operations Advances

- Care shifts create need for longitudinal big-data from multiple locations and sources
- Move to cloud/platforms, customized mobile apps in "rapid cycle development"
- Investment attracted to new multi-component solutions blending Internet of Things (IoT) emergence, 3rd party developers, machine/auto generated data
- Linking of automation, including robotics, to data sets to provide continuum of care management
- Takeaway for Pittsburgh:
- Creates opportunity for new solutions requiring Pitt regional care model and technical expertise

Life Sciences R&D and Commercial Market Forces

- More R&D and investment is moving to high cost chronic and specialty disease therapeutics categories in fields such as oncology, rheumatology, and infectious diseases.
- Investment is also increasing in new frontiers such as regenerative medicine as well as neuro/behavioral medicine.
- Large life sciences companies are expanding their breadth of product and service types, but they are increasingly relying on start-ups as their R&D engines.
- Takeaway for Pittsburgh
 - Research advances require more cross-discipline collaboration between biomedical science, computation, design, engineering, materials and manufacturing
 - Building unique expertise and infrastructure that encompasses intersecting and converging disciplines can attract more R&D locations in life sciences.

Life Sciences and Health IT Funding and Value Creation, Value Creation Development

- Markets are now under price pressure from competition, consumers, insurers and
 regulators, which has begun to significantly shift funding to higher risk/higher return
 biologics and specialty therapeutics and away from devices and diagnostics which face
 longer development times, greater regulatory barriers and more price pressures.
- Investors remain excited about the Health IT segment but there is greater emphasis on solutions that address operational quality and cost applications driven by big data and enhanced automation.
- Venture funding for much of life sciences is moving toward later stages and increasingly with deals including a syndicate of multiple investors.
- Takeaway for Pittsburgh
- Non-VC investors are required early and from various sources to succeed
- The intellectual property must be rigorously vetted to validate solutions, segments and alignment with value chain in the face of so many market shifts.

Pittsburgh Region Opportunity Analysis Challenges and Gaps for Pittsburgh Life Sciences

The benchmarking analysis identified several gaps that must be addressed for Pittsburgh to capitalize on the opportunity in Life Sciences:

The Ecosystem

The Pittsburgh life sciences ecosystem is not geographically concentrated with pockets of activity throughout the city and the larger region. This is both a factor of the small size of the industry and lack of a primary geographic location that has evolved or been designated as the life sciences hub.

Research Base

The majority of the research and development seems to be occurring at the basic research level as academic researchers work to solve early stage technology challenges. There is limited NIH backed research and development that is being conducted by corporate partners or which translates into commercial opportunities.

Pittsburgh receives \$266 per capita in NIH funding compared to a U.S. average of \$65.

Pittsburgh has a few large private life sciences firms that are conducting research and development in the region, but it is not linked to the Universities or startups in a significant way (see discussion on page 15 for more). Venture-backed research and development is also occurring on an increasing scale, but the region is lagging its peers in the overall funding levels and average deal size (see Investment on page 37 for more).

Commercialization and Startup Activity

The region is not turning research into commercial activities and is specifically underperforming in generating regional startups and high growth companies. Given that it is more difficult and takes longer to develop and grow firms in the life sciences versus other clusters, these challenges represent a more significant gap for this sector.

Over time the Entry Rate has slowly fallen from a peak of 14 new firms per 100 in 1977 down to 8 firms per 100 in 2013. Fewer than six seed stage deals are being funded in life sciences per year in the region.

Investment

The Pittsburgh region is realizing better investment trends relative to a decade ago but the numbers are still low. There is also a lack of resident capital that can support a larger crop of life sciences startups OR even assist the current group as they continue to mature.

Life science venture deals in Pittsburgh average \$6.4 million compared to \$18.6 million in the benchmark regions.

Industry Base and Cluster

The region has a very diverse base of life sciences firms, most of which are very small. There are few large firms that bring national attention and market reach that are based in the region. The region does not appear on any national rankings of life sciences industry activity.

U.S. cluster rankings

Rank	Cluster	Weighted score	Rank	Cluster	Weighted score	Life sciences employment concentration: Weight: 25.0% Measured as the percent of industry employment
1	Greater Boston Area	72.5	10	Seattle	40.8	against total metro private employment.
2	Raleigh-Durham	66.4	11	Denver	38.5	Life sciences employment growth: Weight: 10.0%
3	San Francisco Bay Area	64.3	12	New Jersey	35.8	Life sciences establishments concentration:
4	San Diego	63.1			100	Weight: 10.0%
5	New York City	60.3	13	Suburban Maryland/Metro DC	35.5	Measured as the percent of industry establishments against total metro private establishments.
6	Los Angeles/Orange County	58.3	14	Westchester County	31.9	Life sciences venture capital funding:
7	Philadelphia	50.3	15	Central & Southern Florida	30.3	Weight: 20.0% Life sciences National Institute of Health funding
8	Long Island	48.2	16	Indianapolis	29.6	Weight: 20.0 %
9	Minneapolis	43.5	17	Chicago Metro	27.5	Life sciences patents: Weight: 15.0%



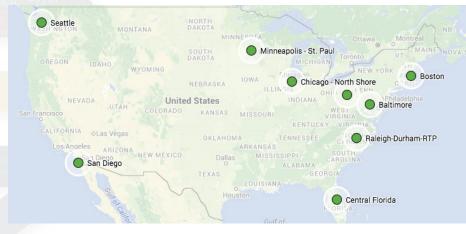
Lessons from Benchmark Locations

The Fourth Economy team performed a national scan to identify the lead life sciences communities and others that are similarly positioned to the Pittsburgh region. The final set of nine benchmark communities included:

- Boston, MA
- Raleigh-Durham, NC
- San Diego, CA
- Minneapolis, MN

- Seattle, WA
- Baltimore, MD / Washington D.C.
- Orlando / Central Florida
- Chicago, IL

Figure 1: Benchmark Regions



Each of the benchmark locations has highlighted the life sciences sector as a significant economic development driver and in varying degrees is working to support and promote its success. The most significant lessons learned include:

- The communities that have had historic success due to a concentration of large life sciences companies are seeing declines as a result of industry transformation.
- Several areas (Boston, Raleigh -Durham, Central Florida, Seattle) have been helped
 by a confluence of catalyzing forces in place, including philanthropy and government
 funding. Significant and sustained private and public investment focused on a portfolio of
 needs ranging from life sciences infrastructure to services and venture capital is the most
 important catalyst to growth.
- Having a local champion and hive for the industry is critical to its success by providing a
 focal point, connecting the pieces of the industry and providing programming to advance
 opportunities.
 - Baltimore BioHealth Innovations
 - Boston Mass Bio & Massachusetts Life Science Center
 - Chicago Chicago Life Sciences Consortium and Matter
- Orlando Enterprise Florida and more recently IQ Orlando
- Raleigh-Durham NC Biotech Center and Research Triangle Park
- San Diego BioCom and UCSD Connect
- Seattle Washington Biotechnology and Biomedical Association

- In addition having state and/or local economic development support is critical as some highlights note:
- Florida has risen in the rankings over the past decade as a result of significant capital investment by the state and often matched locally. Estimates show that over \$816 million has been invested in the life sciences industry during that period.³
- Massachusetts and specifically Boston is benefiting from a \$1 billion investment pledge made in 2008.
- Matter (Chicago) received over \$4 million in state grants that were matched by \$4 million in private support to launch in 2015.
- San Diego and Raleigh-Durham's efforts have significantly benefited from state investment in life sciences research infrastructure.
- Urban environments are attractive locations for life sciences companies to flourish –
 Boston, Durham, San Diego and now Chicago are all demonstrating this
- Other than Boston and San Francisco (not profiled), there are really no break-outs today, although some (San Diego, Seattle) are continuing to have strong growth from start-ups, and others (Minneapolis, Chicago, Raleigh-Durham) are seeing growth from the legacy mainstay companies, with a few start-ups, but no major new success stories outside of the established, legacy firms.

Outside of the United States, other major locations such as Israel, Germany, and many regions in Asia are in some ways "leapfrogging" the competition with major new infrastructure, funding sources, talent capture and recruitment. The intensity of need to "get going now" is amplified or this window of opportunity will close quickly.



Opportunities for the Pittsburgh Life Sciences Cluster

Throughout the interviews and analysis conducted by the Fourth Economy team several themes emerged regarding the approach that should be undertaken to grow the life sciences cluster. Despite some gaps identified, the general consensus is that Pittsburgh is poised to make substantial progress because many critical components exist in the life sciences ecosystem including:

World-class research

BASE OF

START UP

- Base of start up companies
- Handful of larger life sciences corporations
- Base of lab space and growing office portfolio
- · Core of specialized, advanced manufacturing

WORLD-CLASS RESEARCH NIH + 1,000 Pl's **BASE OF LAB** SPACE AND GROWING venture Concentrated in and angel **OFFICE COMPANIES** firms with **PORTFOLIO** North Side and nearly Shadyside \$1B invested DYNAMIC MIX OF LARGE AND SMALL FIRMS

The research conducted started to identify a set of parameters or considerations that the community should use to articulate a life sciences strategy, these include:

- Based on analysis of market trends, meaningful shifts in products and a solutions focus
- Matched with overall aspirational appetite of regional players; "go-big and differentiate"
- · Focused on existing sets of expertise, commercialization potentials, resources and capacity that can be made available
- Differentiated from other regions with a recognizable distinct focus
- Enabled by significant resource, skills, infrastructure investment (local and national)
- Led by a strategic innovation plan, that provides both physical and organizational "gravitational force" such as a physical location with a strong life sciences lead
- · Marketed and promoted by all participants in region industry, government, and universities

Pittsburgh has four opportunities to grow its life sciences industry cluster. These opportunities are summarized below but they explored in more depth in the Pittsburgh Life Sciences Ecosystem beginning on page 40.

- 1. The region has distinct strengths in research spanning several disciplines that converge with market trends to provide a platform for global leadership in life sciences industries.
- 2. The region has accelerated its capacity to translate research to market, and can make further improvements in these processes by dedicating resources and personnel to commercialization initiatives.
- 3. Continued research collaboration, the establishment of an innovation district, and increased coordination amongst sector leadership, generates momentum that can create a central hub for the sector.
- 4. Following the models of other regions, the designation of a convening cluster organization or initiative will accelerate development and commercialization.

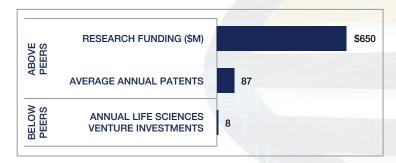
Opportunity 1: The region has distinct strengths in research that spans several disciplines that converge with market trends to provide a platform for global leadership in life sciences industries.

The University of Pittsburgh is widely recognized as a leader in life sciences research, UPMC is a top-ranked hospital system and Carnegie Mellon is a leader in computer science and engineering. This recognition can be leveraged to increase the region's national and global connectivity with the commercial life sciences sector. Increasingly companies are co-locating research facilities in proximity to academic research and the region can leverage our research reputation to recruit companies for co-location and collaboration in the city.

Increasing the level of corporate partnerships and sponsored research activity can serve two purposes: first, bringing more life sciences research capacity into the community and second, introducing private companies to the Pittsburgh life sciences ecosystem. There must be a much stronger effort focused on engaging the corporate partners and facilitating their interaction with the research community to eliminate the

barriers to cooperation. A good example is UPMC's recent partnership with IBM Watson and the formation of startup, Pensiamo, which will be based in Pittsburgh to use cognitive analytics to improve supply chain performance in hospitals.

Recruiting corporate partners will also attract top-level research and management talent that the region needs to build its startup community. One of the barriers to recruiting talent to local startups is the lack of backup employment options if the local startup does not succeed. Corporate partners will bring the talent with them and make it easier for startups to recruit as the depth of employment offerings will increase. This external talent also brings with it connectivity to national and global markets and investors that can further fuel the growth of the startup community and improve the retention of startups that are created as they move through life cycle.



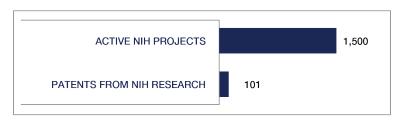
Opportunity 2: The region has accelerated its capacity to translate research to market, and can make further improvements in these processes by dedicating resources and personnel to commercialization initiatives.

Interviews with stakeholders emphasized the need for the University of Pittsburgh, specifically to continue to increase its capacity for validating and packaging the intellectual property (IP) it produces. As the volume of activity increases, this investment will need to rise. Conducting more research on the competing technologies and patents from a legal and market perspective will provide potential investors and entrepreneurs with a better sense of the commercial opportunity the IP can provide. This effort will further encourage a greater understanding of commercialization throughout the research enterprise so that more researchers bring commercial understanding to the output of their efforts and even creating an initial business plan.

In addition to translating research to market, the University of Pittsburgh can leverage its substantial, high-level alumni contacts with the region's diverse research assets to attract life sciences companies. These larger firms will increase partnerships with academic researchers as well as the region's life science entrepreneurs. They will also deepen the pool of talent – the lack of which has contributed to several recent exits. Each of the Benchmark regions had some form of entity, ranging from economic development organizations to trade associations, serving this purpose. Developing a pitch book that sells the Pittsburgh life sciences story – with its top tier research expertise and growing entrepreneurial culture – will provide a simple but effective resource for attraction efforts.

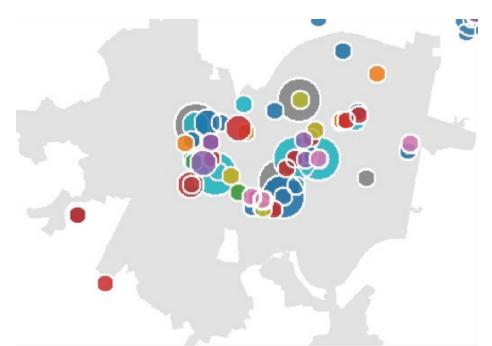
Engaging corporate partners will also help to promote internal commercialization efforts. At the very start of these relationships, there must be an increased capacity on the business development effort to engage corporate partners around identifying and solving critical health

problems that leverage the university's research expertise into markets aligned with the corporate partner. Given the funding trends in national investment markets, the region must identify more resources for pre-seed due diligence and venture development. External capital will play a role for the foreseeable future. The region must support and expand regional networking with national venture networks so that local startups are in a better position to syndicate deals and get the capital they need to grow.



Opportunity 3: With improved research on innovation corridors and increased coordination amongst sector leadership, there is an opportunity to create a central place of gravity for the sector.

The region needs to establish a central location or hub for life sciences activity in the region. Space in Oakland is currently at a premium but the creation or repurposing of facilities for commercial collaborations with wet lab capacity located in proximity to the university will enable more interaction and collaboration between academic researchers, corporate partners and the startup community. The region also needs to develop and maintain a directory of life sciences firms in the region and an inventory of laboratory space. These elements will support a more coordinated network of researchers, entrepreneurs and investors.



Opportunity 4: Continued research collaboration, the establishment of an innovation district, and increased coordination amongst sector leadership, generates momentum that can create a central hub for the sector.

Success in Benchmark regions has been due in part to the existence of a convening cluster organization, which accelerates growth in the sector. The regional support system includes organizations that are either focused on a narrow function related to life sciences, or which include life sciences as part of broader portfolio of industry sectors. This results in a situation where no single organization has responsibility to address the spectrum of needs and barriers that face the sector. Creating a platform for coordination and providing a clear and unifying growth strategy that aligns and leverages these efforts will advance Life Sciences as an industry in the region.

This analysis has identified four critical opportunities that must be

aligned with existing or new organizations, along with the capacity and resources to address those challenges. There needs to be an organization or initiative that provides a clear focal point for retention, expansion and recruitment, marketing and translational research that integrates the resources and expertise of a variety of partners spanning regional academia, corporations and economic development organizations. This organization should promote regular convening within and between areas of specialization that can generate a new collision of ideas and the convergence of new opportunities. The region will need to speak with one voice so that it can effectively develop and disseminate cluster information on technologies, researchers and companies to a global audience.

Pittsburgh Life Sciences Ecosystem Today



FOUNDATIONS, ANGEL INVESTORS, VENTURE CAPITAL, GOVERNMENT AGENCIES



McCUNE





Accelerator Fund









Vision / Growth Platforms

The Pittsburgh region will need to rally around a big vision for the life sciences. This vision should be built on the region's core competencies in life sciences and related fields that create unique opportunities to develop market leading life sciences solutions. The region can provide a comprehensive platform of life sciences research, development and commercialization that leverages leading research disciplines in life sciences, engineering and computational sciences with the infrastructure for clinical trials and clinical applications as well as the design and manufacturing expertise to take technologies from bench to bedside or other market end users.







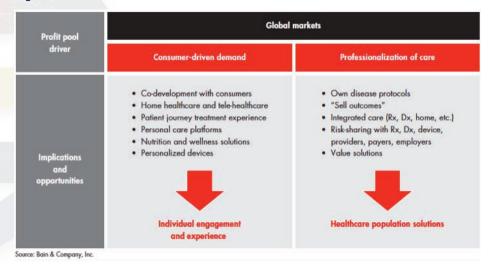


The Global Life Sciences Industry: Trends and Observations

The analysis of industry trends began with a literature scan of the existing market analyses on life sciences. The objective of this scan was to identify the major trends that would impact Pittsburgh's build-out of the life sciences cluster.

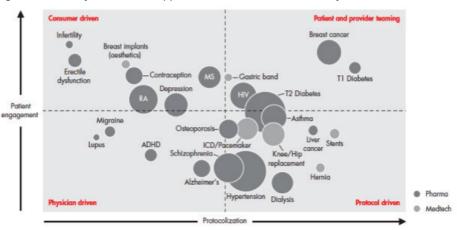
Bain and Company segmented the market into two primary segments – consumer driven demand and the professionalization of care (see Figure 2).

Figure 2: Global Markets



However, within these large segments, there are many shades that distinguish opportunities as they relate to specific diseases and specific applications. The interplay between the role of the consumer, the physician, treatment protocols and patient-provider relationships varies greatly (Figure 3).

Figure 3: Trends by Disease and Application Create Distinct Market Dynamics



Note: We determined the placement of diseases or conditions in this figure by assessing the number of protocols available, adjusted for prevalence and total spending on that condition for consumerization, we measured online presence and also adjusted for prevalence. Sources: International Guideline Characteristical Guideline Characteristics (Alchimateristics) and the protocol of the protocol of

The development of new technology, shifts in the regulatory infrastructure and mechanisms for payment have begun to disrupt existing business models and create a new landscape in which new players and business models can emerge (Figure 4).

Figure 4: Summary of Disruptive Forces



Source: Accenture. Healthcare Disrupted.

Categories of Macro Economic Trends Affecting Pittsburgh's Opportunity

This market scan identified four major trend categories that will impact planning for Pittsburgh's life sciences future.

- 1. Macro Economic and Care Model Trends in Life Sciences
- 2. Health IT and Automation Clinical Care and Operational vs. Operations Advances
- 3. Life Sciences R&D and Commercial Market Forces
- 4. Life Sciences and Health IT Funding and Value Creation, Value Creation Development

Macro Economic and Care Model Trends in Life Sciences

The current care model is based on addressing specific episodes of illness, injury or other adverse health conditions by providing (and paying for) specific procedures to address those episodes. The treatments and procedures are priced the same regardless of their effectiveness and procedures may even be driven by patient demands, the desire to avoid lawsuits or treatment protocols. Value based care seeks to address the inefficiency and cost of the current model. In value based care the providers are paid for maintaining and/or improving patient health, which requires evidence of positive outcomes, as well as requiring more information about baseline conditions for the individual and groups of individuals. The episode or procedure model is discrete with defined interventions and end points, whereas the value-based model is continuous and shifts the financial risk to all sectors of the life sciences value chain.

The continuity of the value based model impacts clinical care provision as well as nearly all new life sciences research and development for drugs, devices and treatments that forces a re-thinking of innovation and product commercialization models. The value-based model requires a more interactive interchange of information with consumers, clinicians and all of the treatments and tools applied to a system of longitudinal care management. Rather than discrete treatments, there must be a systems approach that manages pre-intervention, intervention and post-care for all market solutions in a way that effectively erases pre-care and post-care distinctions. This change in focus from a procedure or product to continuum solutions and systems creates opportunities for blending solutions across industry sectors, specifically integrating biomedical science with IT/data solutions.

Health IT and Automation Clinical Care and Operational vs. Operations Advances

The care shifts represented by the value-based model create the need for longitudinal big-data that combines multiple data sets from a variety of locations and sources. Protocols for standardizing and integrating the data will impact the requirements for data capture and integration for workflow decisions. Developing, testing and validating these solutions creates opportunities to leverage Pittsburgh's integrated regional care model and technical expertise that spans biomedical, clinical and computational disciplines.

Cloud-based systems and platform as well as customized mobile apps are already in development with many new technology entrants taking new approaches and escalating change. The increasing use and integration of sensors and machine or automatically generated data is attracting large investments in multi-component solutions in an emerging Internet of Medical Things (IoMT) that links automation, including robotics, to data sets to provide a continuum of care management that breaks down traditional silos of healthcare.

Life Sciences R&D and Commercial Market Forces

Expiring patents, competition from generics and greater pressure to regulate or contain drug and treatment costs have limited the returns of many mass-market drugs and devices. Research and investment is shifting to new areas where the higher risk is balanced by the potential for higher returns resulting in a move to high cost chronic and specialty disease therapeutics categories such as oncology, rheumatology, and infectious diseases. As the R&D focus has shifted there is increased use of "precision" science for targeting of products.

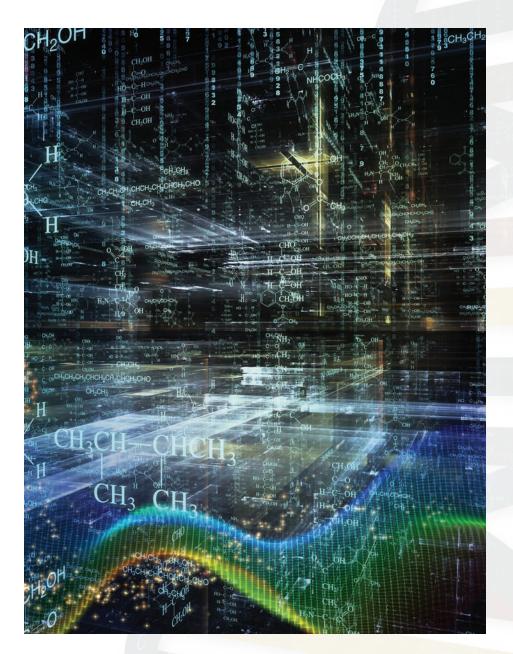
Investment is also increasing in new frontiers such as regenerative medicine and neuro/behavioral medicine. Regenerative medicine combines biology, biomaterials and engineering to maintain or restore tissues and organs. Often used interchangeably with tissue engineering, regenerative medicine currently has limited patient treatment applications but potential uses range from various stem cell therapies to rebuilding damaged cartilage to regenerating damaged kidneys. The approaches are experimental and costly but they hold great potential. Regenerative medicine combines a variety of disciplines from biology to materials to engineering and is increasingly including biosensors that could be linked into the emerging loMT.

Startups are becoming the engines of R&D as large corporations confront market uncertainties and the complexity of evolving care models. The large life sciences firms are expanding their breadth of product and service types by investing or acquiring these startups. For the startups and their investors the end goal of the initial public offering (IPO) has been replaced by the exit by acquisition. These acquisition events can trigger a wave of new startups as researchers, management and investors from the acquisition target take their exit earnings and reinvest in new startups. The ability to build unique and interdisciplinary expertise can increase the chance that a region will retain the second and third generation startups.

Life Sciences and HIT Funding and Value Creation, Value Creation Development

Markets are now under price pressure from competition, consumers, insurers and regulators, which have begun to significantly shift funding to higher risk/higher return biologics and specialty therapeutics. This move is targeting specific applications for subsets of patients based on unique characteristics of the individual or the condition, which distinguishes products from one another and limits competing and alternative therapies, which can reduce the price pressure on the life sciences firms. Investors are shying away from devices and diagnostics because they are subject to longer development times, greater regulatory barriers and more price pressures from all sources.

Investors remain excited about the Health IT segment but there is greater emphasis on solutions that address operational quality and cost applications driven by big data and enhanced automation. The lack of big exits in the HIT segment could cool that enthusiasm. Venture funding for other segments of life sciences is moving toward later stages and increasingly with deals including a syndicate of multiple investors. Non-VC investors such as Angels and public-private economic development funds are taking a greater role in seed and early stage funding. There is also an emerging trend of philanthropy funding large-scale focused efforts, known as Moonshots, on specific diseases.



Benchmarking Peer Life Sciences Communities

The Fourth Economy team executed a data scan to identify recognized life sciences clusters located in the United States. This work identified eight (8) areas for benchmarking and analysis detailed in the following section.

About the Labor Force Data

Each of these communities defines the life sciences cluster in their own way in terms of their methods for counting firms and jobs as well as the geographic breath of the cluster. This analysis used a normalized approach with a common core set of NAICS codes for the metropolitan area for each location. This approach allows for a standardized comparison of the relative size of each location even though Pittsburgh's numbers may not match what these benchmark clusters are reporting.

About the Venture Capital Data

The life sciences industry relies significantly on venture capital to take ideas to commercial products. In some areas such as biotechnology these are high risk, high reward propositions while in other subsectors such as Health IT there is a lower barrier to entry for new products. We have provided venture data from 2000-2014 in order to normalize any significant peaks and valleys of investment caused by overall economic fluctuations. Angel investment will only include angel investment from an organized angel network but the location and details of individual investors is typically not disclosed. We have also analyzed the variance between companies in the benchmark region attracting capital from regional and external investors and how much capital in the benchmark region is flowing out of the region in search of life sciences investments. Analysis of the investment flow data shows that capital exists but there aren't enough local deals to capture the investments.

Research Scan

In addition to our own work we also researched how other groups are characterizing each of these locations and identified a few comparative resources. The following image is from Jones Lang LaSalle's "Life Science Outlook 2015: United States" report and provides an approach to ranking each of the life sciences clusters based on size, size compared to other sectors, research and development inputs and outputs and venture capital funding.

U.S. cluster rankings

Rank	Cluster	Weighted score	Rank	Cluster	Weighted score
1	Greater Boston Area	72.5	10	Seattle	40.8
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3	San Francisco Bay Area	64.3	12	New Jersey	35.8
4	San Diego	63.1	13	Suburban Maryland/Metro DC	35.5
5	New York City	60.3	1000 C	Management of the state of the	20000
6	Los Angeles/Orange County	58.3	14	Westchester County	31.9
7	Philadelphia	50.3	15	Central & Southern Florida	30.3
8	Long Island	48.2	16	Indianapolis	29.6
9	Minneapolis	43.5	17	Chicago Metro	27.5

Source: http://www.us.jll.com/united-states/en-us/Documents/Life-Sciences/JLL-US-Life-Science-Outlook-2015.pdf

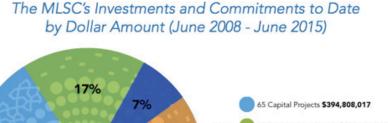
Boston, MA

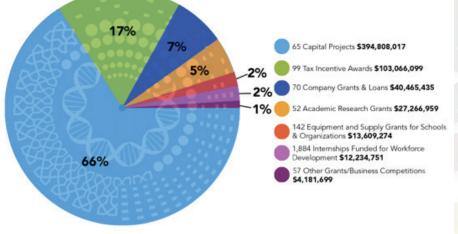
Background

The Boston area is a mature, stable and evolving life sciences market that ranks near the top of every life sciences category from research to patents and from VC funding to IPOs. The sector is supported by significant private, public and academic investments that have a self-reinforcing cycle of investment and commercialization. Areas of focus include biotechnology, pharmaceuticals, medical devices, diagnostics and bioinformatics. The roots of the industry in Boston and specifically Cambridge date back to 1976 with the discovery at MIT of recombinant DNA. The region has been pioneering ever since.

The Boston area has benefited significantly from the \$1 billion commitment made in 2008 by the Governor and Legislature to the Massachusetts Life Science Center. ⁴ This investment supports what is regarded as the most comprehensive set of programs to support the industry. It allows for proactive and collaborative strategies that have kept the state and the Boston area ahead of the industry curve. Added to this is the strength of MassBio, the industry trade association that was founded in 1985, one of the first such life sciences sector specific trade groups to form. As of June 30, 2015 the MLSC has invested over \$585 million of that commitment across seven types of investments as illustrated on the image at right from their 2015 Annual report.

These investments seem to be catalyzing the growth of the life sciences sector with a significant number of startups continuing to make progress and established firms locating operations to be near all of the life sciences activity. The community is now citing a "life sciences stampede" that is occurring following some major announcements late last year including Shire Pharmaceuticals relocating their U.S. headquarters (500 jobs) to Boston from the first location in eastern Pennsylvania as well as the much discussed General Electric headquarters deal which includes health related divisions.





4http://www.masslifesciences.com/

Dashboard

The life sciences sector labor force in the Boston MSA has shown moderate gains over the past three years. Significant increases are demonstrated in the areas of Drug and Pharmaceuticals and Research, Testing and Medical Labs. These increases have been tempered somewhat by losses in the Agricultural Feedstock and Chemicals, which is the region's smallest subsector, as well as Medical Device and Equipment, which is in decline nationally.

Boston, MA Life Science Sector Employment			
Sub Sector	2011	2014	Change 2011-2014
Agricultural Feedstock & Chemicals	1,318	1,071	-19%
Drug & Pharmaceuticals	7,616	9,589	26%
Medical Device & Equipment	16,352	15,247	-7%
Research, Testing and Medical Labs	17,674	18,876	7%
Totals	42,960	44,783	4%

The 2016 Genetic Engineering and Biotech News Rankings show Boston with:

- 5,634 patents; 2nd to San Francisco Bay Area
- \$519 million NIH funding (#1)
- 16.7 million SF of Lab Space (#1)

Venture Capital Investment

During the time period analyzed Boston has attracted a \$2.5 billion net flow of investment capital into the region to support the life sciences sector. These funds have supported an average of 71 deals per year during this period.

Boston: 2000-2014 Venture Capital Investments - All Stages							
	Incoming	Number	Outgoing	Number	Net Investment		
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark		
Health	\$5,500,000,000	268	\$5,740,000,000	262	\$(240,000,000)		
BioTech	\$15,770,000,000	724	\$13,030,000,000	591	\$2,740,000,000		
Total	\$21,270,000,000	992	\$18,770,000,000	853	\$2,500,000,000		

Key Lessons

While it is difficult to see comparisons between Pittsburgh and Boston in the area of life sciences it is worthwhile in contemplating some of the key attributes that set them apart:

- Aggressive and sustained focus on the industry. Of course success is a great case for
 doing more of the same but throughout economic and political cycles there have been
 strong partnerships between private industry, academia and government that have
 allowed for a continued focus on the life sciences as a key economic driver of the Boston
 region.
- A portfolio of investments. From research and research infrastructure to early stage
 capital and existing industry incentives, the Boston region has a balanced level of effort
 that has supported sustained growth despite life sciences sector transformation.
- Leadership from MassBio and the Massachusetts Life Science Center has allowed for a continued proactive strategy to be developed and supported.
- Massachusetts' investment of \$1 billion was ten times the commitment that Pennsylvania made to the statewide Life Science Greenhouse program.

What's Next

The 'life sciences stampede' may be a real thing – at least for the time being. A unique convergence of a desire for urban live-work environments combined with significant development/ redevelopment in Boston has generated significant interest in the community in general. Because of the community's life sciences pedigree that interest is even more significant in the sector. The larger corporate relocation 'wins' over the past two years will drive even more interest.

With the \$1 billion 10 year strategy on year 8 it will be interesting to see how the community begins to contemplate the next steps and what's next from the public sector in support of the industry.

Central Florida

Background

Central Florida's leap into the development of a life sciences cluster began with a 2006 Milken Institute Study estimate that the UCF College of Medicine, along with a life sciences cluster could create over 25,000 jobs within 10 years.

Central Florida has pursued a ground up strategy first focussed on building out the healthcare infrastructure including the following that have received investments since:

- Sanford Burnham Prebys Medical Discovery Institute at Lake Nona
 - Lured by \$350 million in local and state incentives in 2006 but as of 2016 has decided to leave
 - University of Florida is planning to take over operations with an expected transfer of assets but the plan has to be approved.⁵
- M.D. Anderson Orlando Cancer Research Institute
- University of Central Florida College of Medicine
- Nemours Children's Hospital

Areas of Focus

The Central Florida cluster is focused on Clinical Trials including drug and vaccine research, Healthcare Delivery, Medical Device and Diagnostics, Specialty Pharma and Pharmaceuticals, Sports Innovation and Performance.

Dashboard

Central Florida has demonstrated relatively stable job growth overall and significant growth in the area of medical devices and equipment but the size of this sector and of the life sciences industry in Orlando remains among the smallest of all the benchmark regions.

Central Florida Life Science Sector Employment			
Sub Sector	2011	2014	Change 2011-2014
Agricultural Feedstock & Chemicals	305	495	62%
Drug & Pharmaceuticals	795	737	-7%
Medical Device & Equipment	1,639	2,401	47%
Research, Testing and Medical Labs	3,329	2,722	-18%
Totals	6,067	6,356	5%

Venture Capital Investment

Central Florida is a net importer of venture capital investment although with an average of 1 deal per year, they are a small player in the overall life sciences venture capital scene.

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Central Florida/ Orlando: 2000-2014 Venture Capital Investments - All Stages							
	Incoming	Number	Outgoing	Number	Net Investment		
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark		
Health	\$257,310,000	11	\$11,000,000	2	\$246,310,000		
BioTech	\$5,200,000	2	\$82,000,000	6	\$(76,800,000)		
Total	\$262,510,000	13	\$93,000,000	8	\$169,510,000		

⁵See http://www.orlandosentinel.com/health/os-uf-sanford-burnham-deal-details-story.html.

Key Lessons

The recent Sanford Burnham departure raises questions that are not yet answered but it does point to the risks of relying on attracting one large single purpose entity whether it is public or private.

As with Boston, the Central Florida life sciences cluster has demonstrated a sustained commitment to investing in a significant way. While most of this effort has been focused on building infrastructure it is clear that the sector is in an early stage of development with an emphasis on building research infrastructure and activity and evolving to focus more on company creation.

Unlike some other benchmark regions that need to retrofit communities to provide live, work, play opportunities in an urban environment, Central Florida is building from scratch which allows for a more expedited process if enough capital is available.

What's Next

Central Florida is working to create the Florida Hospital Health Village. This development is being designed as a 172-acre mixed-use transit oriented development. The development includes a life sciences research center, hospital cluster and is the hub for new companies. Institutional partners include the Florida Hospital Diabetes Institute, Translational Research Institute for Metabolism and Diabetes and three planned Bioresearch Centers including office and lab space (wet and dry labs)

They have recently created a new 'front door' called IQ Orlando (http://iqrlando.com/). The IQ Orlando mission is "Harnessing Orlando's best resources to invent the future of healthcare". The big challenge for Central Florida will depend on how it handles the transition of Sanford Burnham and its ability to invest in other elements of the ecosystem besides the research.

San Diego

Background

Today the life sciences industry in San Diego is a major economic force with over 1,100 companies and 80 research institutes. This fact is due to the history of the life sciences cluster in the City, which starts back in the 1950s-60s with the founding of the Salk Institute, Scripps Research Institute, and the University of California San Diego. The region's biotechnology industry began in the late 1970s with the formation of Hybritech, a company that pioneered commercial use of monoclonal antibodies. Hybritech itself was purchased by pharmaceutical giant Eli Lilly, but key personnel from the firm went on to start their own biotechnology businesses. Hybritech alumni reportedly have produced more than 40 biotech start-ups in the San Diego metropolitan area in the past 15 years.

The development of the industry has been catalyzed by the UCSD's Connect program, founded in 1985, which encourages networking among biotech researchers and businesses. Area biotech pioneers have become serial entrepreneurs, and the fortunes they built in the 1980s have helped form venture capital funds to fuel successive rounds of start-ups. This circle of talent, ideas and capital fuels the San Diego Life Sciences Cluster today

The industry is supported and represented by BioCom one of the best-known life sciences trade groups in the country.

According to JLL "San Diego saw \$43.8 billion in M&A Transactions from 2011-2014. Large pharmaceutical companies are purchasing biotechs to fill their R&D pipelines." 6

⁶http://www.us.jll.com/united-states/en-us/Research/US-San-Diego-Life-Science-Outlook-2015-JLL.pdf?94aff3a3-89ae-4db2-9203-276480017674

Dashboard

With 15% growth in the period analyzed San Diego is on top of the benchmark life sciences clusters. With growth in all subsectors except small job losses in Agricultural Feedstock and Chemicals it is clear that San Diego has a strong and diverse base of companies operating in the life sciences space.

San Diego, CA Life Science Sector Employment			
Sub Sector	2011	2014	Change 2011-2014
Agricultural Feedstock & Chemicals	474	405	-14%
Drug & Pharmaceuticals	5,317	6,349	19%
Medical Device & Equipment	7,283	7,927	9%
Research, Testing and Medical Labs	20,196	23,422	16%
Totals	33,270	38,103	15%

The 2016 Genetic Engineering and Biotech News Rankings show San Diego with:

- 2,644 patents (#4)
- \$90.9 million NIH funding (#7)
- 9.5 million square feet lab space (#5)

Venture Capital Investment

San Diego sees a significant amount of venture capital invested in its companies with an average of 32 companies receiving investment during the period reviewed. The majority (9 to 1 ratio) of this investment is being attracted to companies classified as BioTech.

Key Lessons

The history and culture of San Diego is what most cite as the reasons for success. The Hybritech story is one that illustrates the power of growing technology companies and realizing the direct benefits of their growth and the indirect benefits as they spin out talent to form new companies.

San Diego: 2000-2014 Venture Capital Investments - All Stages							
	Incoming	Number	Outgoing	Number	Net Investment		
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark		
Health	\$793,400,000	49	\$354,510,000	21	\$438,890,000		
BioTech	\$9,400,000,000	404	\$1,490,000,000	70	\$7,910,000,000		
Total	\$10,193,400,000	453	\$1,844,510,000	91	\$8,348,890,000		

Connect has been a significant resource for the growth of the life sciences industry and even today has a diverse set of programs from financial to technical assistance that support younger companies in the industry.

The culture is described as collegial and collaborative as compared to peer communities and as a result it is a place that people come together to solve science challenges. San Diego had both the unique challenge and advantage that it developed the university at the same time as the industry so that the culture of both the academic and the commercial sectors emerged and formed in interaction with each other, with the success of one feeding the success of the other.

What's Next

BioCom and a group of life sciences executives recently adopted a vision⁷ for what is next which include:

- Becoming the globally recognized leader in genomics
- The leading U.S. portal to Japan's life sciences companies BioCom has opened a Tokyo office and a direct flight now exists between the two communities.
- Being the home to the largest, most diverse contract research organization industry significant industry growth expected and already San Diego is home to 85 CROs
- Becoming more regional by including Los Angeles as part of a regional life sciences cluster

The San Diego region has developed a big vision, backed by a clear strategy that focuses on core strengths and targeted areas of market opportunity.

⁷http://www.xconomy.com/san-diego/2016/05/04/a-vision-for-boosting-the-life-sciences-in-san-diego-and-beyond/

Minneapolis / St. Paul, Minnesota Background

The Minneapolis/St. Paul life sciences sector is another example of an established cluster. Most sources identify the 1950s as the period when the region established leadership in the field of medical device discoveries. Today over 700 companies have headquarters or major operations in the area. One of the oldest and still very much a leader Medtronic drives a lot of activity in the region and throughout the state.

According to the Medical Valley Association the Pharmaceutical/biotechnology cluster has grown 58% in the last 10 years. Key companies leading the cluster include Upsher-Smith Laboratories, Perrigo, ANI Pharmaceuticals, and Bio-Techne/R&D Systems.

Other highlights from the Medical Valley Association:

- Drug-delivery therapies from Medtronic, Mayo Clinic, and the University of Minnesota.
- Currently 26 companies in active clinical development with the FDA, accounting for 3,296 ongoing clinical trials
- It leads the nation in cumulative premarket approvals granted by the FDA 33% of all PMAs between 1960-2014
- In 2015 formed the Minnesota Medical Manufacturing Partnership and were awarded IMCP designation from the Economic Development Administration

The development of the life sciences cluster in Minneapolis/ St Paul is best characterized as slow and steady as existing companies gradually invest in their own growth potential with little government or outside capital stimulus. Efforts over the past decade to get the state more engaged in life sciences related economic development have largely failed.

The statewide life sciences trade association became known as Medical Alley Association early in 2016 as it wanted to refocus efforts on the Health Technology sector which includes medical device, biopharmaceutical, diagnostics and digital health sectors. The group provides advocacy and research services for the industry.

Dashboard

Other than strong growth in the Research, Testing and Medical Labs subsector the overall life sciences cluster demonstrated job loss during the period analyzed.

Minneapolis/ St. Paul, MN Life Science Sector Employment					
Sub Sector	2011	2014	Change 2011-2014		
Agricultural Feedstock & Chemicals	808	688	-15%		
Drug & Pharmaceuticals	3,377	2,869	-15%		
Medical Device & Equipment	27,962	27,051	-3%		
Research, Testing and Medical Labs	3,874	4,493	16%		
Totals	36,022	35,101	-3%		

JLL notes in their 2016 Market Outlook

- 1,408 patents
- \$32.9 million NIH funding
- 12.7 million SF of Lab Space

⁹https://www.medicalalley.org/library/research/minnesotas-pharmaceutical-industry-today/

⁹This is an example where the data and definitions used by local organizations yield dramatically different trends and performance.

Venture Capital Investment

The Minneapolis/ St Paul community attracts slightly more incoming venture capital compared to the outgoing investment from local venture sources funding deals outside the region.

Minneapolis/ St. Paul: 2000-2014 Venture Capital Investments - All Stages						
	Incoming	Number	Outgoing	Number	Net Investment	
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark	
Health	\$1,210,000,000	66	\$1,100,000,000	48	\$110,000,000	
BioTech	\$447,240,000	26	\$444,000,000	25	\$3,240,000	
Total	\$1,657,240,000	92	\$1,544,000,000	73	\$113,240,000	

Key Lessons

The Minneapolis/ St. Paul life sciences cluster is very much driven by large corporations with companies like Medtronic, Boston Scientific, Smiths Medical, Bayer all driving the historic success.

The state enacted an Angel Investment Tax Credit in 2010 and the life sciences sector in the Minneapolis St. Paul community has received the majority of the benefits with over \$6.7 m in credits in 2015 alone. 10

What's Next

The University of Minnesota received a \$3M grant from NIH and was named one of three new Research Evaluation and Commercialization Hubs(REACH¹¹) nationally. The focus of the commercialization activities includes diagnostic tools, medical devices and preventative medicine.

Chicago

Background

Chicago ranks in the top 10 in most life sciences industry rankings including holding on to the 10th spot in the 2015 and 2016 Genetic Engineering & Biotechnology Ranking of the Top 10 U.S. Biopharma Clusters. Chicago's strength comes from a combination of:

- World class medical research: Northwestern University
- Focus: home to one of the highest concentrations of the biopharmaceutical industry in the U.S.
- Capital: as a financial center there is ample investment capital to fuel company growth
- Real Estate: both in the city and at the 23-acre Illinois Technology and Science Park a facility specifically designed for biosciences, nanotech and medical device companies.

A couple of organizations to note include the Chicago Life Sciences Consortium (CLSC), a non-profit organization committed to serving as a key driver for the Chicago area life sciences industries and Matter. ¹² Matter is a health tech incubator that opened in 2015 and as of early this year reported 125 companies collaborating in its space. In January they signed a partnership deal ¹³ with Abbott who wants to help commercialization health technologies. Matter's focus on bridging the gap between health-related tech and the physician and user community is resonating well in the marketplace and creating growing interest in the life sciences startup scene in Chicago.

¹⁰https://www.leg.state.mn.us/docs/2016/mandated/160379.pdf

¹¹http://mn-reach.umn.edu/

¹²http://www.chicagobusiness.com/article/20140211/BLOGS11/140219941/the-formation-of-matter-chicagos-new-health-tech-incubator

¹³http://hitconsultant.net/2016/01/28/health-tech-incubator-matter-abbott-partner-to-support-healthcare-innovation/

Dashboard

The Chicago life sciences industry employment cohort saw nominal growth in the period analyzed with the largest segment coming in the area of Research, Testing and Medical Labs. The majority of these jobs are in larger corporations and companies related to the significant federal lab presence that exists in the Chicago market.

Chicago, IL Life Science Sector Employment			
Sub Sector	2011	2014	Change 2011-2014
Agricultural Feedstock & Chemicals	1,470	1,933	31%
Drug & Pharmaceuticals	16,669	17,119	3%
Medical Device & Equipment	13,947	13,857	-1%
Research, Testing and Medical Labs	13,778	14,741	7%
Totals	45,864	47,650	4%

The 2016 Genetic Engineering and Biotech News Rankings show Chicago with:

- 1,204 patents (9th)
- \$110 million NIH funding (10th)
- 1.5 million square feet in lab space (12th)

Venture Capital Investment

Chicago is a global financial center, therefore it is not surprising that capital would flow from the region. With a net of over \$3.4 billion flowing to investments outside of Chicago, there is a significant gap or mismatch in the Chicago ecosystem. While most regions in the middle of the country are cash starved it seems that Chicago has investment capital but not enough deals to satisfy it's local appetite.

Chicago, IL: 2000-2014 Venture Capital Investments - All Stages						
	Incoming	Number	Outgoing	Number	Net Investment	
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark	
Health	\$229,220,000	22	\$744,000,000	62	\$(514,780,000)	
BioTech	\$566,760,000	28	\$3,530,000,000	131	\$(2,963,240,000)	
Total	\$795,980,000	50	\$4,274,000,000	193	\$(3,478,020,000)	

Key Lessons

With an average of only 3 deals per year in the life sciences during the period reviewed we wonder why no one has tried to tackle this issue previously. The \$4.2B invested outside of the region in life sciences by local venture firms represents an incredible missed opportunity. Chicago investors are finding nearly five deals outside the region for every deal they fund in the region.

Matter was formed because a group of industry sector friends recognized that what is missing in Chicago was a 'collision space' where capital and ideas can meet up and where those good ideas can tap into a network of mentors that help push them along. It is not clear yet whether this effort can provide the deal flow to absorb Chicago's outgoing life sciences venture investment.

What's Next

Matter, in a very short time is changing the life sciences startup dynamic in Chicago. What remains to be seen because of the lack of time that has passed since they launched is what number of the 125 startups will see commercial daylight. Matter recently formed a partnership with Abbott one of the region's and nation's biggest health technology companies that will certainly provide an acceleration path for some promising technologies.

The relative balance between three of the life sciences sub sectors should bode well as the overall industry continues to evolve.

Raleigh - Durham, North Carolina

Background

The Raleigh- Durham region includes Research Triangle Park (RTP) and concentrated areas of life sciences activity in west Raleigh and downtown Durham. In recent years RTP has been looking to reinvent itself from a suburban office park feel to a more urbanized environment that includes related cultural and recreational amenities. The majority of the region's life sciences lab space has historically been located at RTP and included facilities for several agri-bio firms. Durham has seen significant growth in the amount of life sciences activity underway.

The region caters to a diverse set of life sciences industries including

- Pharmaceuticals
- Human Biotechnology
- Agricultural Biotechnology
- Medical Instruments
- Diagnostics
- CRO
- Advanced Medical Care

The sector is supported by the North Carolina Biotechnology Center located in RTP. While this is a statewide organization, the majority of the NC Biotech Center focus is in the concentrated areas of activity as described above and it is geographically focused on the RTP region. The NC Biotech Center is supported by the state and provides an array of services including loans, grants, training opportunities and events to grow the sector. In addition the Raleigh and Durham Chambers work to promote the industry and support company expansions and relocations.

Dashboard

Raleigh- Durham has been impacted during the 2011-2014 period by consolidations and layoffs as a result of the region's location for several larger life sciences companies. The hardest hit sub sector has been the Research, Testing and Medical labs category.

Raleigh-Durham, NC Life Science Sector Employment					
Sub Sector	2011	2014	Change 2011-2014		
Agricultural Feedstock & Chemicals	1,196	1,000	-16%		
Drug & Pharmaceuticals	3,669	4,193	14%		
Medical Device & Equipment	3,005	3,078	2%		
Research, Testing and Medical Labs	7,777	5,206	-33%		
Totals	15,646	13,478	-14%		

Rankings from the 2016 Genetic Engineering and Biotechnology News "10 U.S. Biopharma Clusters" (2015)

- \$102.6 million in NIH funding (#6)
- 6.64 million in lab space (#6)
- 816 patents (#11)

Venture Capital Investment

The Raleigh-Durham market is a net importer of capital with a significant uptick activity in recent years in the Durham submarket.

Raleigh- Durham, NC: 2000-2014 Venture Capital Investments - All Stages						
	Incoming	Number	Outgoing	Number	Net Investment	
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark	
Health	\$790,500,000	20	\$277,350,000	15	\$513,150,000	
BioTech	\$3,320,000,000	158	\$2,020,000,000	94	\$1,300,000,000	
Total	\$4,110,500,000	178	\$2,297,350,000	109	\$1,813,150,000	

Key Lessons

The Research Triangle Park is now a classic example of a 'build it and they will come strategy' and one that is instructive in having a long view to manage towards success. Patient and sustained investment over five decades (founded in 1959) has sustained long-term growth for the state and regional economy. The RTP and overall Raleigh-Durham region has maintained a broad technology-based economic development focus and the life sciences sector is one of several identified industry sector priorities.

Recruitment of many satellite operations of domestic and global life sciences companies demonstrates the strength of the talent pool, facilities and network but as the industry continues to transform these larger more established companies are in flux and are looking to innovate and become even more operationally nimble.

The combination of a strong entrepreneurial ecosystem combined with leadership from academic and business trade groups has served the life sciences industry well.

What's Next

Downtown Durham will continue to thrive as a location for technology in general but with a focus on life sciences as a result of Duke University and Duke Medicine acting as co-anchors on a 1 million SF office and lab space development called Durham ID (Innovation District). 14, 15

A scan of recent life sciences news highlights that the job losses of the past few years seem to be continuing as layoff announcements have continued in 2016 with BASF (190 jobs) and IBM Life Sciences (undisclosed). These losses may be counterbalanced by significant startup activity and follow on funding to a crop of smaller companies.

The significant crop of life sciences startups in the community may balance industry job losses in the future but it will be a question of which trend accelerates faster first.

Baltimore

Background

For this analysis we wanted to look at Baltimore and not the larger Baltimore-Washington corridor. The Baltimore region is unique due the proximity to the nation's capital and the large federal life sciences complex associated with the National Institutes of Health, Food and Drug Administration and other agencies that invest and regulate the industry.

Over the past few years the region has launched the BioHealth Innovation as an effort to spur a startup community in the region.

Dashboard

As compared to the other benchmark locations the private labor force in the life sciences in Baltimore is very small and over the period analyzed shrinking significantly. Further analysis may reveal that much of this loss is due to the relationship between these companies and federal agencies and the federal budget issues that occurred during this time period.

Baltimore, MD Life Science Sector Employment						
Sub Sector	2011	2014	Change 2011-2014			
Agricultural Feedstock & Chemicals	401	329	-18%			
Drug & Pharmaceuticals	1,482	1,399	-6%			
Medical Device & Equipment	1,682	1,672	-1%			
Research, Testing and Medical Labs	6,373	4,210	-34%			
Totals	9,937	7,610	-23%			

¹⁴http://durhamid.com/

¹⁵http://stewartinc.com/portfolio-post/durham-innovation-district/

Rankings from Genetic Engineering and Biotechnology News "10 U.S. Biopharma Clusters" (2015)

- 3,531 patents (#3), just over half of which (1,798 or 51%) are held by the U.S. Department of Health and Human Services
- 11.1 million square feet in lab space (#3)
- \$133.5 million in NIH funding (#5), of which Johns Hopkins University accounted for 71% or \$94.867 million;
- Home region of the NIH, FDA, and CDC

Venture Capital Investment

As with the employment counts, the venture capital activity in Baltimore is very low and the region is a net exporter of capital.

Baltimore, MD: 2000-2014 Venture Capital Investments - All Stages						
	Incoming	Number	Outgoing	Number	Net Investment	
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark	
Health	\$100,000	1	\$262,750,000	7	\$(262,650,000)	
BioTech	\$158,450,000	18	\$616,920,000	22	\$(458,470,000)	
Total	\$158,550,000	19	\$879,670,000	29	\$(721,120,000)	

Key Lessons

Proximity to federal agencies seems to limit startup activity rather than support it as demonstrated by Baltimore and also seen in Chicago. An entrepreneurial culture does not spring organically from a research base, but requires dedicated resources and collaboration.

What's Next

BioHealth Innovation has noted in a recent report some of the areas that must be tackled in order to create a more successful life sciences environment.

- Requires a more robust entrepreneurial culture
- Universities in the area issue fewer patents and launch fewer startups and earn less income through licensing technology compared to universities in peer markets.
- Overall venture capitalists invest less in the region than elsewhere \$1 billion in 2014. The analysis provided above shows that little of those funds go to life sciences companies.

These are areas that BioHealth and its partners are working to transform to better prepare the region for life sciences growth.

Seattle

Background

Seattle has blossomed in the last few years thanks to a significant increase in research and development investment and commercial activity in the area. A recent article¹⁶ summed up Seattle's life sciences rise to top ten lists by highlighting the key drivers.

The Bill and Melinda Gates Foundation has the highest profile globally, serving as a catalyst for billion-dollar global vaccination and treatment programs. Gates Foundation Venture Capital's whip smart Charlotte Hubbert was on hand to talk about their direct investment strategy and to receive a nod from the LSINW Women in Life Science Award.

The Seattle Children's Research Institute (SCRI) is now among the top 5 pediatric research hospitals in the US. Dr. Elizabeth Aylward was on hand to discuss industry partnerships for their researchers. SCRI attracts hundreds of millions in research—much of it for clinical trials of pharmaceutical treatments previously untested for kids.

The University of Washington and the Fred Hutchinson Cancer Research Centre (AKA FredHutch) also have a sophisticated approach to cultivating research-industry partnerships. On the venture side, dozens of VC funders and pharmaceutical company strategic investors were there to find the next Seattle Genetics. Some of the novel ventures spun off from these partnership, have grown into textbook success stories:

Juno Therapeutics, founded in 2013, which has raised almost \$700 million, and forged a 10 year partnership with Celgene, valued at \$1 billion to commercialize a new cancer treatment that uses T-Cells to attack cancer cells.

The Infectious Disease Research Institute, known as IDRI which has trialed tuberculosis, leishmaniasis and pandemic flu vaccines. IDRI is home to the Global Health Vaccine Center of Innovation, a Sanofi Pasteur partnership. Sanofi Pasteur and the Gates Foundation hope that the partnership will speed up vaccine development, innovation and distribution, particularly in the face of rapid, emergent infectious diseases.

These drivers combined with a robust venture environment has spurred strong increases.

Dashboard

The labor force figures for Seattle show a 10% overall growth total for the life sciences sector.

Seattle, WA Life Science Sector Employment			
Sub Sector	2011	2014	Change 2011-2014
Agricultural Feedstock & Chemicals	283	380	34%
Drug & Pharmaceuticals	1,324	2,623	98%
Medical Device & Equipment	7,100	6,551	-8%
Research, Testing and Medical Labs	5,293	5,781	9%
Totals	14,000	15,335	10%

Seattle, WA: 2000-2014 Venture Capital Investments - All Stages									
	Incoming	Number	Outgoing	Number	Net Investment				
Sector	Investment	of Deals	Investment	of Deals	Flow to Benchmark				
Health	\$1,220,000,000	75	\$454,080,000	38	\$765,920,000				
BioTech	\$3,290,000,000	178	\$2,060,000,000	99	\$1,230,000,000				
Total	\$4,510,000,000	253	\$2,514,080,000	137	\$1,995,920,000				

¹⁶http://ayogo.com/blog/life-science-innovation/

Key Lessons

Philanthropic investment in specialized research areas can have a significant impact on a region's life sciences sector.

In 2015 the region lost Amgen and its 650 workers (not reflected in the data above), which has generated some reflection by the community and spurred the launch of a strategic effort.

Seattle has a strong investment community and an established startup culture, but it has struggled to create and sustain job growth. State and local efforts have not achieved the scale of Massachusetts or the strategic and geographic focus of North Carolina.

What's Next

The Amgen loss has provided catalyst to pursue a diverse strategy. Many leaders in the region now want to focus on small and medium companies with lots of research. Concerns have been raised that a broad base of companies is needed to retain talent by providing more depth of job opportunities – the second and third jobs that would provide more of a career path don't exist in sufficient numbers in the region.

"Seattle is one of the few cities in the world with a dense confluence of biotechnology, medicine, information technology, and public health expertise, and a footprint small enough to encourage intense collaboration between the sectors. From that mix come new ideas, products, and organizations that aim to change the way new therapies are created and how people in the U.S. and around the world get their healthcare." As a result the Washington Biotech Business Association has launched Convergence as described below.



Convergence is a WBBA initiative to rally healthcare enterprise stakeholders, innovators, and industry leaders around a shared ambition to create next generation healthcare. Healthcare that is patient and person-centric, precise, and affordable.



 $^{^{17}} http://www.xconomy.com/seattle/2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-life-science-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disruptors-2016/03/01/xconomys-exome-presents-seattles-disrupto$

Each of these benchmark locations benefits from public and private interest aligned to support the life science industry. This support comes in different forms including trade associations, economic development initiatives and entrepreneurial support organizations. The following chart highlights a handful of these groups and illustrates the core functions they serve in their community.

Benchmark	Life Science Entrepreneurial Development Organization Examples	Year Founded	Annual Budget Est	Grant	Loan/ Equity	Mentoring	Funding for Facilities	Executive Coaching	Purchasing	Events	Advocacy	Membership Dues
Boston	Massachusetts Life Science Center	2004	~\$65M	•	•		•			•		
	MassBio	1985	\$5.2 M						•	•		•
San Diego	Connect	2005	\$3.4 M	•	•	•		•		•	•	•
	BioComm	1992	\$4M						•	•	•	•
Seattle	Washington Biotechnology and Biomedical Association	1990	\$2.4M	•	•	•		•	•	•	•	•
Chicago	Matter	2015	\$3M			•	•	•		•		
	Chicago Life Sciences Consortium	2014	N/A							•	•	
Central Florida	IQ Orlando	2015	New							•		
Minneapolis	Medical Valley Association	1987	\$2M						•	•	•	•
North Carolina	North Carolina BioTech Center	1984	\$18M	•	•		•			•		
Raleigh-Durham	Durham Chamber	1939	\$1.3M							•		•
	BioHealth Innovation	2012	\$2.8M			•		•		•		

Pittsburgh Life Sciences Ecosystem

Geographic Overview

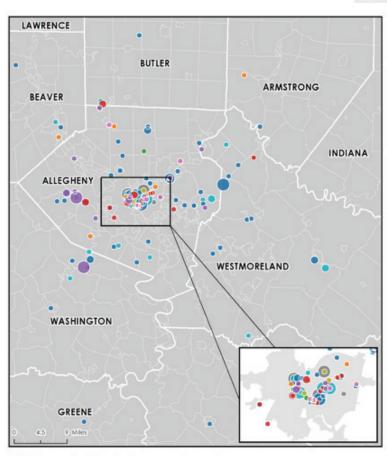
There is a great deal of research and opinion in the field of innovation-based economic development that highlights how a concentration of performers in a similar industry sector contributes to accelerated development and growth of products and companies. This is the motivation for technology parks and the recent push to form Innovation Districts as described by the Brookings Institute. This concentration allows for 'collision spaces' where ideas, researchers, capital, industry and service providers can connect. There are several geographic clusters of firms and activity in Life Sciences in the Pittsburgh region. Within the City of Pittsburgh itself there are pockets of activity on the North Shore, Downtown, Uptown, Almono, the South Side, Oakland, Shadyside and East Liberty.

Interviews with entrepreneurs, researchers and university officials did not yield a clear perspective on the need for life sciences facilities in the region. Some expressed the need for more incubator or accelerator space, while others felt that was a lower priority. Perspectives also differed on the availability of lab space. The university has a significant amount of lab space but various legal requirements associated with how those labs were financed render it unavailable for commercial research and for the development of startup companies.

"There is underutilized space in the universities that we could untangle, but there is plenty of other lab space available. You can find space if you ask around."

What is the opportunity?

The region does not have a geographic center or a hub for life sciences activity. Oakland is the natural hub for research, but there is limited corporate lab space and significant build-out so companies have dispersed to various other locations. Recent analysis commissioned by the University of Pittsburgh has identified the potential for one million square feet of new lab space near the University.



Pittsburgh Life Science Assets



Research Base

First and foremost, the life sciences sector in Pittsburgh is built on an outstanding, world-class research base that is anchored by the two largest universities, University of Pittsburgh and Carnegie Mellon University. Between these two universities there are 24 academic programs related to our core strengths in life sciences that are in the top 20 as ranked by U.S. News and World Report.

Table 1: Top 20 Academic Program Rankings

University of Pittsburgh	Carnegie Mellon University
Top 20 Academic Program Rankings	Top 20 Academic Program Rankings
1st in Physical Therapy	1st in Computer Science
4th in Clinical Nursing	2nd in Computer Engineering
4th in Nursing Anesthesia	2nd in Artificial Intelligence
4th in Occupational Therapy	5th in Engineering
5th in Women's Health	8th in Electrical Engineering
7th in Psychiatry/Psychology	8th in Mechanical Engineering
7th in Speech Language Pathology	9th in Cognitive Psychology
8th in Drug and Alcohol Abuse	9th in Statistics
9th in Pediatrics	11th in Materials Engineering
9th in Pharmacy	
10th in Geriatrics	
11th in Clinical Psychology	
16th in Medical Research	
18th in Biomedical Engineering	
18th in Clinical Medicine	

Source: The Brookings Institution, TEConomy Partners, and the U.S. News and World Report Rankings

"The University of Pittsburgh ranks fifth in funding from the National Institutes of Health (NIH) and is a leader in new fields such as Quantitative Systems Pharmacology, Personalized Medicine, and Drug Discovery." The region is also home to leading institutes in regenerative medicine, brain research and cancer research. There are ten disciplines in which the region is in the top fifteen for active NIH projects:

Table 2: Active NIH Projects in Pittsburgh by Discipline

Discipline	Rank in Active Projects	Active Projects		Active Funding
Bioengineering	8		21	\$7,734,506
Brain Disorders	15		12	\$2,841,855
Genetics	12		419	\$174,167,175
Neuroscience	5		52	\$15,119,175
Pediatrics	4		120	\$56,142,274
Regenerative Medicine	2		49	\$16,873,894
Robotics	6		7	\$1,642,530
Surgical	5		116	\$58,081,312
Therapeutics	3		163	\$75,676,779
Women's Health	5		166	\$96,539,787

Source: Fourth Economy analysis of NIH grant awards 2012-2016.

The University of Pittsburgh is the primary local engine for the life sciences research and development funded by the NIH.

Table 3: Top NIH Recipients - Active Grants (July 2012 - May 2016)

Recipient	Projects	Sum of Direct Costs
University of Pittsburgh	1366	\$441,399,834
Magee-Women's Research Institute and Foundation	64	\$42,123,570
Carnegie-Mellon University	67	\$16,796,287
NSABP Foundation, Inc.	3	\$9,143,912
Steelworker Charitable/Educational Organization	5	\$6,110,071
Duquesne University	18	\$4,417,414
Institute for Transfusion Medicine	2	\$3,707,453

Source: Fourth Economy analysis of NIH grant awards 2012-2016.

The NIH also tracks patents from their grants. The region has been awarded 101 patents from more than 1,500 active grants, about seven percent of the total. Given the nature and pace of life sciences research, there are not likely to be a large number of patents from active projects. Adding in patents awarded from research conducted since 2008 yields another 48 patents. Most but not all of the patents are held by organizations based in the region but approximately one out of every ten patents goes to an outside organization, which reduces the opportunity to create a company in the region.

Table 4: Patents from Active NIH Grants (101 Total)

Institution	Patents
University of Pittsburgh	74
Carnegie-Mellon University	13
Duquesne University	3
Oregon Health & Science University	3
University of Michigan	2
Colorado State University	1
Northwestern University	1
University of California San Francisco	1
University of Florida	1
University of Texas Health Science Center	1
Vanderbilt University	1

Source: Fourth Economy analysis of NIH grant awards 2012-2016.

There have been nine companies with active NIH grants in the region from 2012-2016. One company, PNA Innovations, has relocated to Massachusetts but the other eight remain in the region. In total, private firms in the region account for less than \$4.3 million in active NIH grants with an average award of less then \$330,000. None of the private firms have reported any patents linked to their NIH projects during this time period.

Table 5: Top Private NIH Recipients - Active Grants

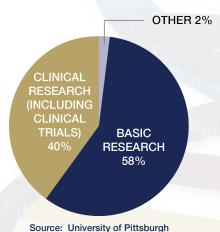
Recipient	Projects	Sum of Direct Costs
Lipella Pharmaceuticals, Inc.	5	\$1,232,935
Ension, Inc.	2	\$1,105,704
Cernostics, Inc.	1	\$624,917
Mosaix Software, Inc.	1	\$499,395
Cognition Therapeutics, Inc.	1	\$298,527
Schell Games, LLC	1	\$224,637
Pinmed, Inc.	1	\$149,998
Neuro Kinetics, Inc.	1	\$149,794

Source: Fourth Economy analysis of NIH grant awards 2012-2016.

NIH funding to all institutions in Pittsburgh is concentrated in basic research (58%) and in clinical research and trials (40%). This data corresponds with Fourth Economy's analysis of active NIH projects in the region as well as interviews with regional and national researchers, entrepreneurs and investors indicated that Pittsburgh is more focused on early stage research.

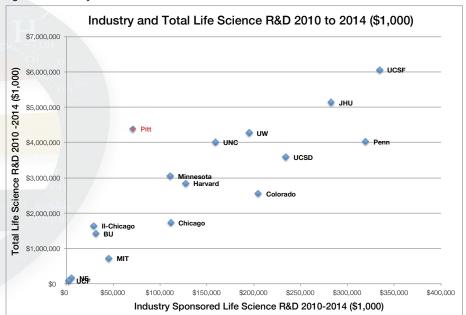
Figure 4: University of Pittsburgh Health Sciences FY 2016 Budget

HEALTH SCIENCES BUDGET FY2016



Regardless of the stage of R&D, the fact that the NIH contributes the majority of the region's life sciences R&D, and that it is conducted primarily by academic institutions, contributes to the lack of connection with commercial partners. The majority of life sciences R&D in the Pittsburgh region is conducted by the University of Pittsburgh but only two percent of the R&D in Biological Sciences, Medical Sciences, Other Life sciences was funded by industry sources.

Figure 5: Industry and Total Life Sciences R&D 2010 to 2014



Source: National Science Foundation. The chart excludes several outliers such as Duke on the high end, as well as Boston College and University of Massachusetts Boston.

Duke generates more than \$1.3 billion in industry R&D, which is 26 percent of its life sciences R&D. The average for the institutions in the benchmark regions is seven percent. The University of Pittsburgh's nearly \$71 million in industry-funded R&D ranks 12 out of the 19 institutions and well below the average of \$189 million. If the University of Pittsburgh attracted an average level of industry R&D in life sciences, it would generate nearly \$310 million in R&D.

Table 6: Industry Financed and Total Life Sciences R&D 2010 to 2014.

Institution	Industry (\$M)	Total (\$M)	Share
Boston College (BC)	\$0.4	\$50.2	1%
Boston University (BU)	\$31.5	\$1,414.3	2%
Duke University (Duke)	\$1,325.1	\$5,095.7	26%
Harvard University (Harvard)	\$127.3	\$2,846.5	4%
Johns Hopkins University (JHU)	\$282.8	\$5,127.0	6%
Massachusetts Institute of Technology (MIT)	\$45.4	\$714.0	6%
Northeastern University (NE)	\$5.7	\$150.3	4%
University of California, San Diego (UCSD)	\$234.2	\$3,582.1	7%
University of California, San Francisco (UCSF)	\$334.2	\$6,056.8	6%
University of Central Florida (UCF)	\$2.5	\$83.1	3%
University of Chicago, The (Chicago)	\$111.3	\$1,721.3	6%
University of Colorado (Colorado)	\$204.9	\$2,553.0	8%
University of Illinois at Chicago (Il-Chicago)	\$29.4	\$1,638.4	2%
University of Massachusetts Boston (U Mass-Boston)	\$0.3	\$54.1	1%
University of Minnesota (Minnesota)	\$110.9	\$3,042.3	4%
University of North Carolina at Chapel Hill (UNC)	\$159.1	\$4,009.3	4%
University of Pennsylvania (Penn)	\$319.5	\$4,021.0	8%
University of Pittsburgh (Pitt)	\$70.8	\$4,384.0	2%
University of Washington (UW)	\$195.0	\$4,265.7	5%

What is the opportunity?

Both interviews and data suggest that the majority of the research and development is focused on early stage technology challenges. There is limited NIH backed research and development that is being conducted by corporate partners and limited industry support for the life sciences R&D conducted in the region, which limits the region's ability to translate that research into commercial opportunities.

Pittsburgh has a few large private life sciences firms that are conducting research and development in the region, but those activities are not linked to the Universities or startups in a significant way (see discussion on page 46 for more). Venture-backed research and development is also occurring on an increasing scale, but the region is lagging its peers in the overall funding levels and average deal size (see Investment on page 9 for more).

Commercialization and Startup Activity

Overall technology sector data from Brookings & TEConomy Partners demonstrates that the region's strength in inventions does not always translate into startups. Compared to the rest of the nation the region has a high rate of invention disclosures, licenses and options but the region does not convert that research into patenting and startups. Interview respondents suggested that much of the research activity is too focused on basic research so it does not have strong commercial potential. This also explains the gap between our levels of research funding, invention disclosures and startup activity. The region performs above the AUTM university average, but this includes many schools with far less research activity than Pittsburgh.

Table 7: Commercialization Gap

	Pittsburgh Index	AUTM University Average
Invention Disclosures	5.53	3.81
Startups	0.17	0.15
Patents	1.05	1.04
Licenses and Options	2.51	1.09

Source: The Brookings Institution and TEConomy Partners

The story in Pittsburgh is one of "missed opportunities." The region has more than 4 times as much NIH funded R&D per capita as the U.S., but only our employment in electromedical apparatus manufacturing is comparable. On other measures of life sciences employment, the region is well below the level of our research activity. The region employs one-tenth of the expected employment in pharmaceutical

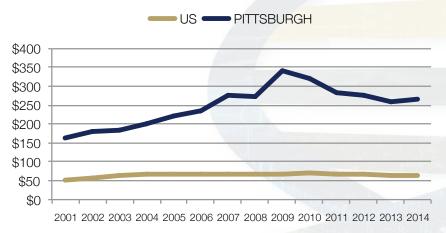
preparations. In other words we have the research, but we lack the industrial base to support its translation to commercial products within the region.

Figure 6: Research Specialization and Industry Employment

	Pittsburgh to US Average
NAICS 334510 Electromedical apparatus manufacturing	4.13
NIH Funding per Capita	4.09
NAICS 54171 Physical, engineering and biological research	1.37
NAICS 33911 Medical equipment and supplies manufacturing	1.09
NAICS 3254 Pharmaceutical and medicine manufacturing	0.1

Figure 7: Increasing Research Funding

NIH FUNDING PER CAPITA



Source: http://officeofbudget.od.nih.gov/spending_hist.html.

"Pittsburgh has been increasing its NIH-funded research activity well above the U.S. average, but the region has not made the same gains in startups, venture investment or employment the commercial life sciences activity."

Interviews with local researchers and entrepreneurs also found a sentiment that companies are leaving the region. From the current startup community, our research has identified only seven firms that started here and left since 2011. There seems to be a false sense that the region has experienced an exodus of startups in the life sciences motivated by a few significant losses.

Figure 8: Life Science Firms Leaving/Not Operating in Pittsburgh Region (2011-2016)



"According to data from The Brookings Institution and TEConomy Partners, overall the region has fewer technology starts compared to select metropolitan regions."

Analysis of establishment Entry and Closing rates for all sectors from 1977 to 2013 shows that the region experienced spikes of new firm formation in the 1980s after the collapse of the steel industry. At that time a number of new programs began to diversify the economy and spur entrepreneurial growth. Over time the Entry Rate has slowly fallen from a peak of 14 new firms per 100 down to 8 firms. The region has also reduced the rate of closings so that only 4.7 firms per 100 were closing by 2013.

Figure 9: Firm Entry and Closing Rates, 1977 to 2013



This data largely agrees with data from the Kauffman Index where Pittsburgh is below our peers in terms of startups, the rate of business owners and the density of high-growth companies. But **the region is doing better in maintaining our small businesses**, which is reflected in the decreasing rate of Closings and our above average score for Established Small Business Density. The region also scored better than our life sciences peers in the Share of Scaleups – which are firms growing to fifty or more people by their tenth year (which means they have to still be in business). The region has been building an entrepreneurial culture almost from scratch. Over time it has started to develop a base of entrepreneurial firms and talent that can seed and generate additional startups and entrepreneurial firms, but it has been a long process of creating that foundation for growth.

Table 8: Select Indicators from the Kauffman Index 2015

		Below Peers	Above Peers			
	Rate of	High-Growth	Rate of	Established		
	Startup	Company	Business	Small Business	Share of	
Location	Growth	Density	Owners	Density	Scaleups	
Pittsburgh	54.4%	62.9	5.1%	1,166	2.1%	
Peer Average	67.3%	144.6	6.2%	1,055	1.7%	
Boston	74.3%	138.7	6.1%	1,267	2.1%	
Chicago	47.8%	102.5	5.4%	1,057	1.3%	
Minneapolis	54.7%	119.0	6.2%	1,118	1.8%	
Orlando	37.3%	117.2	6.2%	880	1.0%	
San Diego	73.0%	162.1	7.4%	953	1.6%	
Seattle	67.0%	101.2	6.1%	1,112	1.5%	
Washington	116.9%	271.5	6.2%	997	2.3%	

Source: Kauffman Index 2015, select indicators from Growth Entrepreneurship Index and Main Street Index. Raleigh Durham is not ranked in the Kauffman Index.

Factors Driving Life Sciences Startup Activity Demographics

One of the factors is the region's entrepreneurial culture and talent base is rooted in our demographics. The region has spent decades trying to recover from the population losses of the 1980s. The region has seen some recent growth in the 25 to 34 age group that is well above the U.S. average, which is a significant turnaround in a demographic that had been declining for some time. The region saw a decrease however in the 35 to 44 age group, which is the primary demographic for new entrepreneurs. We also lost significant population in the 45-54 age group, possibly losing experienced talent. These demographics may explain some of our continued inability to generate more startup activity, but there is also a positive sign for the future if the region is able to retain and grow the 25 to 34 segment over the next decade.

Entrepreneurial Linkages

The Pittsburgh region has also seen more entrepreneurial linkages within the startup community in the life sciences. A significant amount of the currently active startup portfolio is centered on the University of Pittsburgh and Carnegie Mellon University. The region is seeing the emergence of a few local anchors that are generating their own startup networks forming around Phillips Respironics, Thermo Fisher, and McKesson Automated Healthcare (now Omnicell). Research the Carnegie Mellon Center for Economic Development conducted in 2002, found that the life sciences startup ecosystem was then centered on only the Universities and there were few second or third generation linkages.

Attracting Talent

The region has also succeeded in bringing in executive talent from large organizations based outside the region such as Boston Scientific, the University of Houston, Quest Diagnostics, Silicon Valley Bank and Los Alamos National Laboratory.

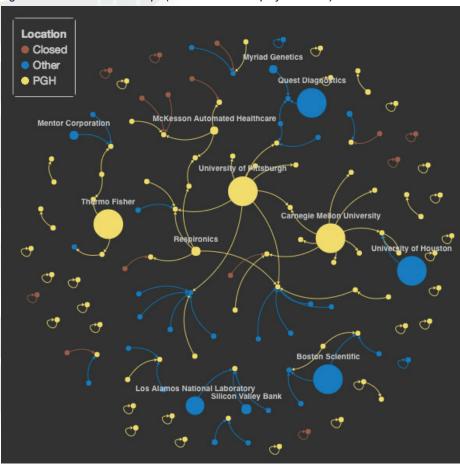


Figure 10: Life Sciences Startups (Size = Relative Employment Size)

Source: Fourth Economy Analysis of the employment linkages of C-Level Executives in current Pittsburgh Life Sciences Startups

Note: Certain names, such as McKesson Automated Healthcare and Respironics have not been updated, but reflect the legacy references that have more local meaning.

"Pittsburgh needs experienced entrepreneurial talent in the life sciences space who have gone through the whole cycle of raising capital through the **big** exit." – Life Sciences Investor

What is the opportunity?

The region is not turning our research into commercial activities and specifically underperforming in generating regional startups and high growth companies. Given that it is more difficult and takes longer to develop and grow firms in the Life Sciences, these challenges represent a more significant gap for this sector.

Investment

Overall Venture Capital investment has generally tracked the U.S. in terms of annual trends. Only four percent of the venture investment have been in seed stage investment and only eighteen percent in early stage investments. Interviews with regional stakeholders emphasized the importance of angel investment and economic development investment for the seed and early stage firms. The economic development investments from InnovationWorks and the Pittsburgh Life Sciences Greenhouse are generally captured in this data, but angel investments often are not, so this data may underestimate the total investment in seed stage firms.

The investments in later stage firms account for 57 percent of the total invested in Life Sciences in the region, but that amount is dominated by two significant deals (Hellomics and Redpath Integrated Technology). Another significant later stage investment (Cohera Medical) left the region in 2015 after a \$50M financing round.

Table 9: Venture Investment in Life Sciences 2005-2015

Total 2005-2015 by Stage (\$M)					
	Seed	Early Stage	Later Stage	Expansion	Total
Biotechnology	\$41	\$147	\$452	\$152	\$792
Health	\$0	\$19	\$84	\$51	\$155
Total	\$41	\$166	\$536	\$203	\$947
Share 2005-2015 by Stage (\$M)					
	Seed	Early Stage	Later Stage	Expansion	Total
Biotechnology	5%	19%	57%	19%	100%
Health	0%	12%	54%	33%	100%
Total	4%	18%	57%	21%	100%

Source: Innovation Works; PricewaterhouseCoopers/National Venture Capital Association, MoneyTree™ Report, Data: Thomson Reuters; Pittsburgh Investments in Life Sciences 2005-2015.

Pittsburgh's venture investment is more diversified in a variety of industry sectors that reflects a deliberate effort beginning in the 1980s to diversify its economy. In that regard the economic strategy has succeeded but it has made more difficult the development of depth and "bench strength" in any individual industry sector.

However this diversity can also be a source of adaptation and new opportunity as the life sciences industry converges with other innovative and legacy sectors. Given the larger industry and market trends the strengths of the region in these other sectors can be a source of strength and opportunity. Pittsburgh has also been successful in attracting outside capital in life sciences where nearly \$6 out of every \$10 invested has come from outside the region.¹⁸

Table 10: Pittsburgh Venture Investment 2011-2015 in Life Sciences and Related Sectors

		111111111111111111111111111111111111111
Amount 2011-2015	Percent of Total	Annual Average
\$1,700,000,000	100%	
\$477,700,000	28%	\$95,540,000
\$294,100,000	17.30%	\$58,820,000
\$129,200,000	7.60%	\$25,840,000
\$27,200,000	1.60%	\$5,440,000
\$27,200,000	1.60%	\$5,440,000
\$192,100,000	11.30%	\$38,420,000
\$141,100,000	8.30%	\$28,220,000
\$119,000,000	7.00%	\$23,800,000
	\$1,700,000,000 \$477,700,000 \$294,100,000 \$129,200,000 \$27,200,000 \$27,200,000 \$192,100,000	\$1,700,000,000 100% \$477,700,000 28% \$294,100,000 17.30% \$129,200,000 7.60% \$27,200,000 1.60% \$27,200,000 11.60% \$192,100,000 11.30% \$141,100,000 8.30%

Source: Innovation Works, Ernst & Young: A snapshot of Pittsburgh's technology investment landscape, 2011-2015

One of the primary gaps in the regional investment landscape is that the life sciences venture deals in Pittsburgh average \$6.4 million compared to \$18.6 million in the benchmark regions. Given the larger capital requirements in life sciences, it will be very difficult to sustain growth at these levels of investment. The region has few investors that are focused on life sciences or that could lead the kind of

¹⁸Analysis of venture capital flows in biotechnology and health from venturecapitalflows.com.

syndicate deals that are happening in other regions. There has been an ongoing debate about the need for more capital, but it is not clear how much of that capital should be local or how this gap should be filled and what the balance should be between local and national investors. Stakeholders interviewed expressed mixed opinions on whether we can continue growing as a life sciences hub with only outside capital. However Pittsburgh investors have also been investing in life sciences firms outside the region with more than \$250 million invested outside the region between 2000 and 2014.¹⁹

"Good deals find money and money finds good deals"

There is a chicken and egg problem with the Pittsburgh region's venture investment climate. Venture investors will seek out good deals and Pittsburgh firms have been successful in raising funds from local and national sources, but the region has not been able to raise the kind of money to really accelerate growth in the sector. Big successes and "home runs," deals that generate large returns can greatly increase the amount of venture dollars attracted to the region. These big returns are becoming more difficult as the life sciences shift from IPOs to mergers and acquisitions, but the ability of a region to consistently generate any of these large, profitable exits provides a major draw for investors.

Table 11: Pittsburgh Exits, IPOs and Deals

Company	Exit /IPO	Exit Year	Amount	Status
Automated Healthcare	McKesson	1996	\$65M	Active, Region
Nurel Therapeutics	Diamyd	2005	\$1.5M	Active, Region
Medrad	Bayer	2006	ND	Active, Region
Renal Solutions	Fresenius	2007	\$200M	Active, Moved (2014)
Respironics	Phillips	2008	\$4B	Active, Region
StageMark / Cellatope	Cypress Bioscience	2009	\$2 M plus milestone options	Inactive
Perioptimum	Steris	2010	Undisclosed	Active, Region
Agentase	FLIR	2010	\$274M	Active, Region
Cellumen	Apredica	2010	ND	Active, Region
Knopp Biosciences	Biogen IDEC	2010	\$345M licensing deal	Active, Region
MedSage Technologies	Phillips Respironics	2011	ND	Active, Region
Applied Computational Technologies	Varian	2013	ND	Inactive
Blue Belt	Smith & Nephew	2015	\$275M	Active, Region
Evolent	IPO	2015	\$845M (est market cap Q2-2016)	Active, Moved
McKesson	Aesynt	2013	ND	Sold to Aesynt
Aesynt	Omnicell	2016	\$281M	Active, Region

¹⁸Analysis of venture capital flows in biotechnology and health from venturecapitalflows.com.

Pittsburgh has generated few of these large exits and many of the successes are older and the attractive power tends to diminish over time. Since 2010 the region has generated five exits of more than \$250 million, but the largest was the IPO of Evolent, which has a 2016-Q2 market capitalization of \$845 million but it is now based in Virginia. Evolent was recently recognized by Forbes magazine as the 12th most promising companies and currently has an employee count of 735.²⁰ It is not clear whether future investors will consider this deal in terms of whether they will invest in Pittsburgh. The creation and launch of Evolent could have been one of the biggest recent life sciences successes, and while it has generated some return for UPMC and as many as 150 subcontract jobs in the region, this is essentially a missed opportunity.²¹

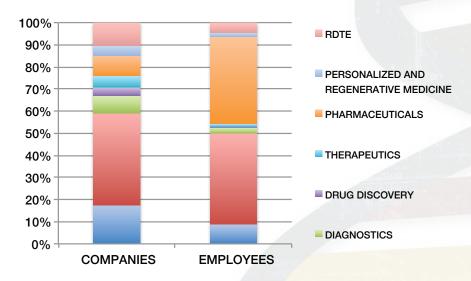
Where is the opportunity?

Investment trends in the Pittsburgh region are improving relative to a decade ago but the numbers remain low and there is a lack of resident capital that can syndicate and support a larger crop of life sciences startups and even to assist the current group as they continue to mature.

Industry Base and Regional Cluster

The life sciences sector is rapidly changing and very hard to categorize based on traditional industry codes such as NAICS. In order to really understand the Pittsburgh ecosystem, Fourth Economy identified life sciences firms from multiple sources and then verified their current location, product and market portfolio, and status of operations. This information provided the basis for classifying the firms and employees currently active in the Pittsburgh region. There are 154 firms and more than 15,000 employees in the sectors defined as life sciences in Pittsburgh. Only seven firms have more 1,000 employees in the region and 62 percent have fewer than twenty employees.

Figure 11: Pittsburgh Life Sciences Firms (154 Firms and 15,000 Employees)



Source: Fourth Economy analysis of firms from multiple sources; the life sciences portfolios of Innovation Works and Pittsburgh Life Sciences Greenhouse; firms reported by the Pittsburgh Regional Alliance; DatabaseUSA; Fortune Inner City 100; LaunchPGH; Crunchbase; NIH.

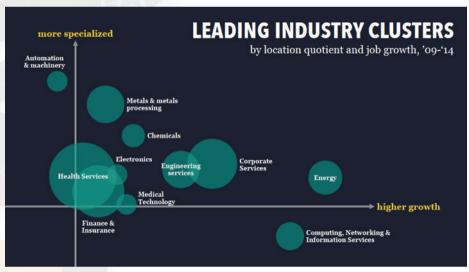
The traditional base in Medical Devices is apparent in the share of firms and employees. Two larger firms, Mylan and Bayer, dominate pharmaceuticals employment. There is a growing base of firms in Healthcare IT and Automation (HITA) as well as a collection of smaller firms in Personalized and Regenerative Medicine, Therapeutics, Drug Discovery and Diagnostics.

Framing life sciences in the context of other regional clusters, it is clear that the Health Services and Medical Technology clusters are both more specialized and higher growth than many other sectors, but they lag the other leading clusters in the region.

²⁰See http://www.forbes.com/companies/evolent-health/

²¹See http://www.upmc.com/media/NewsReleases/2015/Pages/evolent-ipo.aspx

Figure 12: Pittsburgh Leading Industry Cluster



Source: The Brookings Institution and TEConomy Partners

What is the opportunity?

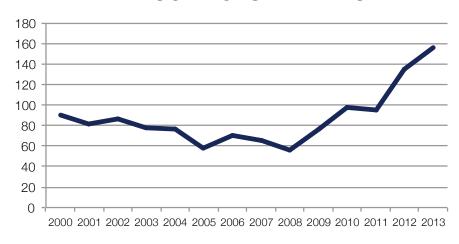
The region has a very diverse base of life science firms, most of which are very small. There are few large firms that bring national attention and market reach that are based in the region.

Convergence

These clusters represented in Figure 12 are defined by NAICS industry groups that do not reflect emerging fields such as Healthcare IT and Automation. Figure 12 also demonstrates the potential for convergence within the region's leading clusters. The emerging HITA cluster is a combination of assets and expertise based in Computer Networking & Information Services, Health Services, Medical Technology and Automation & Machinery. Other sectors in life sciences are also outgrowths of regional specialization in multiple fields and disciplines.

Figure 13: Life Sciences Patents in the Pittsburgh MSA 2000-2013

LIFE SCIENCES PATENTS



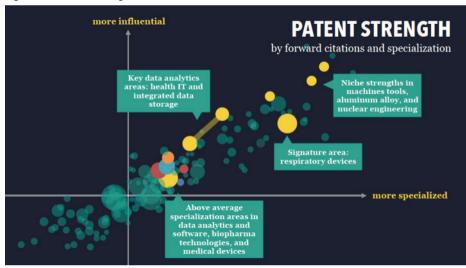
Source: US Patent and Trademark Office, Patents by Class, Analysis by Fourth Economy

"Pittsburgh is one of the few regions with a top-ranked medical research school, a top-ranked integrated healthcare system, a top ranked computer science school and a supercomputer"

- Serial Life Sciences Entrepreneur

The Pittsburgh region has had a strong core of academic R&D in the life sciences that is beginning to spill over into other industry sectors and traditional sectors of economic strength in manufacturing as well as information technology, software and computers. Analysis by The Brookings Institution and TEConomy Partners revealed converging patent strengths in health IT, integrated data storage, data analytics, biopharma technologies and medical devices.

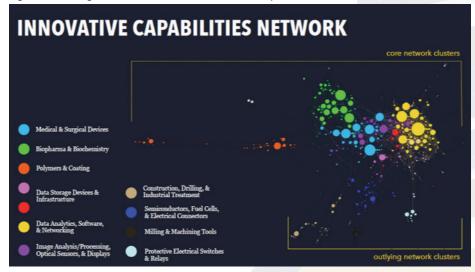
Figure 14: Patent Strength



Source: The Brookings Institution and TEConomy Partners

This convergence is apparent in areas of patent specialization and the synergies between industry clusters (Figure 15). Analysis of the patent citations by TEConomy Partners reveals the synergies between medical and surgical devices, biopharma and biochemistry, data analytics and image analysis.

Figure 15: Linkages in Patent Citations Between Disciplines

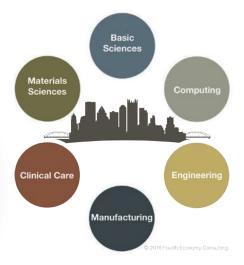


Source: The Brookings Institution and TEConomy Partners

The research into the region's life sciences ecosystem revealed the opportunities and challenges related to converging industry sectors. The Brookings Institution and TEConomy Partners analyzed the region's opportunities more broadly, not focused on Life sciences, however their analysis independently arrived at similar conclusions. Their analysis identified cross-cutting competencies in image analysis techniques, image data storage, materials analysis and optic sensing technologies as well as synergies that could be exploited that would better integrate academic and industrial assets. They identified medical filters and prosthetics, image analysis, diagnostic sensors and pattern recognition, all of which leverage resources and expertise based in Life sciences.

Figure 16: Converging Expertise

Multidisciplinary Converging Fields of Expertise



Pittsburgh Potential for Developing Life Sciences Differentiation

What is the opportunity?

The industry base is smaller than peers and diversified across a spectrum of life sciences. Current market and regulatory trends will depress growth in the traditional subsector base of Medical Devices for the near future. Building depth and strength will require a significant and long-term strategy.

"There are many complementary assets, such as Carnegie Mellon University, but the University of Pittsburgh is the anchor in life sciences and it will be the engine that drives it forward, or not."

- Anonymous





Interviews (alphabetical by last name)

Michael Annichine, Magee-Womens Research Institute and Foundation

Christian Manders, Promethean

Don Taylor, PLSG and Pitt Plastic Surgery and McGowan

Lynn Banaszak Brusco, Carnegie Mellon University

Patricia Beeson, University of Pittsburgh

Herb Boyer, Genentech

Neil Campbell, Helomics

Sam Collela, Versant Ventures

Rory Cooper, Human Engineering Research Lab

Pete DeComo, ALung

Kent Engelmeier, UPMC Opthamology - Fox Center

Max Fedor, University of Pittsburgh

David Goldberg, Allegheny Health Network

John Kuzmishin, UPMC

Debra Lam, City of Pittsburgh

Art Levine, University of Pittsburgh

Tom Link, URA

Rich Lunak, Innovation Works

Marc Malandro, University of Pittsburgh

John Manzetti, Pittsburgh Life Sciences Greenhouse

Keith Marmer, SG3 Ventures

Sean McDonald, Adams Capital Management

Tim McNulty, Carnegie Mellon University

David Motley, Headwaters SC

Mark Redfern, University of Pittsburgh

Steven Reis, University of Pittsburgh

Brent Saunders, Allergen

Dietrich Stephan, University of Pittsburgh

Lansing Taylor, University of Pittsburgh

Nathan Urban, University of Pittsburgh

Bill Wagner, McGowan Institute for Regenerative Medicine

Michael Wells, Princeton Biopharma

Dennis Yablonsky, Allegheny Conference

Definitions for the Kauffman Index Indicators

Rate of Startup Growth: Measures how much startups have grown as a cohort, on average, five years after founding - measured by change in employment.

Share of Scaleups: Measures the number of firms that started small but grew to employ fifty people or more by their tenth year of operation as a percentage of all employer firms ten years and younger.

High-Growth Company Density: Measures the number of private businesses with at least \$2 million in annual revenue reaching three years of 20 percent annual revenue growth normalized by total business population.

Rate of Business Owners: Measures the percent of adult population of a given area that owns a business as their main job.

Established Small Business Density: Number of established small businesses per 100,000 resident population. Established small businesses are defined as businesses over the age of five employing at least one, but less than fifty, employees.

