Article

Creating Communities of Life Science Innovation in the US: History of Critical Factors That Helped the BioHealth Capital Region Emerge

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ABSTRACT

Art is 'I': Science is 'We'

Claude Bernard, French Physiologist, 1813-1878

Background: Advancements in biotechnology are recognized as one of the most important scientific achievements of the 20th Century. The emergence of biotechnology profoundly impacted the health of the world, and the economic vitality of regions where bio clusters and bioresearch parks grew. This article explores some of the historical and policy implications undergirding this development in the United States and the importance of alignment of life science research activity, public policies, and leadership to build place-based communities of biotechnology innovation.

Discussion: The real scientific advances in biotechnology research are beyond the scope of this paper. Instead, this paper will review the growth of team science, the historical factors supporting the growth of the technology sectors with an emphasis on biotech clusters and bioresearch parks, and policies and programs in the 20th Century that helped launch the 21st Bio Century. We conclude with a ranking of the leading biotech clusters in the US, the factors supporting bio clusters, with a case study of the emergence of the multi-jurisdictional BioHealth Capital Region in Maryland, the District of Columbia, and Virginia.

Conclusion: Regions that coordinate life science research at anchor institutions, take advantage of supportive federal policies, spur local bio innovation incentives, and foster private leadership will be those that advance faster and farther in bio health economic development. Beyond the advantages of local economic development, an agile and responsive biohealth cluster can spur global health solutions. The unprecedented speed and international cooperation, as the responses to the need for Covid19 vaccine development, and distribution have demonstrated to the world, can be applied more broadly for other health needs and broadter technology solutions.

Learning from successful case studies of leading regional biohealth clusters, particularly the Capital Region BioHealth cluster, should be of interest to policymakers, public health officials, and economic development practitioners across the United States.

Journal of Commercial Biotechnology (2021) 26(1), 27–13. doi: 10.5912/jcb966

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INTRODUCTION

Technology clusters have been of interest to researchers for many years. Darmody and Bendis participated in a National Research Council Symposium, *Clustering for 21st Century Prosperity,* Washington DC., 2012, which included speakers from the US Small Business Administration (SBA), National Institute for Standards and Technology (NIST), the U.S. Economic Development Administration (EDA) and the State Science and Technology Institute (SSTI). The symposium emphasized the need for sustained investment and coordination of federal, state, and local actors with anchor institutions, including universities, corporate research centers, research parks, hospitals, and others to build effective technology clusters.

In particular, biotechnology clusters offer communities local economic development opportunities and advances in human and animal health worldwide. But not all communities have these advantages. The cost of wet lab space, the presence of anchor universities or hospitals, the need for trained bioscience researchers and technicians, regulatory hurdles, and the longer maturation time for life science innovations necessarily limit world-class growth biohealth regions. Even with these assets, some biohealth clusters will underperform due to a lack of strong biotech alignment.

In terms of biotechnology alignment regionally, public/private innovation intermediaries are a critical factor. BioHealth Innovation (BHI), a public-private partnership life science innovation intermediary, was formed in 2011 in the BioHealth Capital Region to accelerate the growth of life scientists, entrepreneurs, and businesses to the resources, networks, collaborators, and investors they need to grow.

Rich Bendis, the founder of BHI, has identified six factors for strong biohealth alignment in regions:

1. strong leadership,
2. significant industry engagement,
3. talent,
4. access to capital,
5. research assets and facilities, and
6. marketing and brand awareness.

The application of these factors to the BioHealth Capital Region will be explored at the conclusion of this paper. Additionally, the region's response to the COVID-19 Pandemic in attracting research funding for vaccine research and other pandemic responses shines a light on pre-existing networks' importance to respond to unexpected opportunities.

DISCUSSION:

Increasing Importance of Team Science

Science increasingly is collaborative, and the efficiency and effectiveness of science geographically clustered in recognized. This is especially true of bioscience given the increased cost of wet lab facilities, a longer time for maturation of technologies, clinical trial design, government regulatory hurdles, reimbursement strategies, and other factors.

According to the National Research Council:

Ninety percent of all science and engineering publications are authored by two or more individuals. The size of authoring teams has expanded as individual scientists, funders, and universities have sought to investigate multifaceted problems by engaging more individuals. Most articles are now written by 6 to 10 individuals from more than one institution. See, *Enhancing the Effectiveness of Team Science.* Washington, DC: The National Research Council 2015. National Academies Press. https://doi.org/10.17226/19007.

Nearly all Nobel prizes are now awarded to teams. The time of the solo scientist is long past. The last sole winner in Physics, for example, was in 1992. There have been only four sole winners of the Nobel Prize in Medicine since 1973. Research parks and bioclusters historically have helped facilitate connections among scientists and engineers, along with industry, through place-based informal and formal interactions.

Agglomeration Theory

Why do technology firms, including biotech firms, locate near each other? According to Economist Alfred Marshall (1842-1924), firms receive increasing returns from a trinity of agglomeration economies: 1) a local pool of skilled labor, 2) local supplier linkages, and 3) local knowledge spillovers. Marshall famously posited the theory of intellectual spillovers by arguing that in industrial clusters, "the mysteries of the trade become no mystery, but are, as it were, in the air." That is why there are clusters of tech companies in Silicon Valley, auto manufacturers in Detroit, and financial services in New York.

Agglomeration benefits regions and residents by better job matching, higher wages, and more opportunities for civic engagement. Growing clusters in a region and creating a sense of place is the goal for many cities and regions.

Early knowledge clusters and business clusters

Libraries and Universities as Knowledge Centers:
Knowledge clusters are as old as history and started with institutions that recorded knowledge. One of the first knowledge institutions was the library. One of the earliest libraries was formed in the city of Nineveh, located near the current Mosul in Iraq. Over 30,000 clay tablets from the Library of Ashurbanipal have been discovered at Nineveh, probably from the 7th Century BCE. Many other libraries, such as the Great Library of Alexandria in Egypt, followed.

Later, universities became centers of knowledge, such as the University of Bologna (1088), the University of Paris (1150), and the University of Oxford (1167). Much later, universities would become important research centers that helped launch the biotech revolution in the 20th Century.

Considered the first research university in the U.S., Johns Hopkins University would integrate teaching and research, borrowing the concept of graduate education from Germany's Heidelberg University. Later, Johns Hopkins University would create Johns Hopkins Medical School and Hospital, widely noted as one of the world's best medical complexes. The JHU model of graduate education and research would be adopted by research universities across the U.S.

Business Clusters:
In Istanbul, the Grand Bazaar is just one example of ancient meeting places that focused exchange of goods and were precursors to modern cities and business clusters. Long before Starbucks, coffee shops played an important role as business clusters allowing all sorts of classes of people to meet and discuss. In the late 17th century, more than 80 coffee shops in London were centers where businesses and entrepreneurs traded information. The London Stock Exchange (LSE) was founded in Jonathan's coffee shop in 1698 when broker John Casting began posting stocks and commodities' prices, a popular meeting place for businessmen to conduct trades. A similar pattern at Lloyd's Coffee shop in Tower Street in London followed where the underpinning of Lloyd's of London Insurance was formed by posting information about shipping out of England's ports.

The eternal human need for having accessible places where people could gather to share information and knowledge would be replicated in creating bioclusters and bioresearch parks.

Later Policy and Program Developments in the US:

A series of path-breaking private, academic, and government biological research efforts, policy initiatives, entrepreneurial drive, and industry organizations' development helped spur the creation of bio clusters and bioresearch parks in the U.S. in the 19th and 20th centuries.

1862: Land Grant Act and Strong Patents

One of the first federal tech transfer acts was the Land-Grant College Act of 1862 or Morrill Act, which provided grants of federal land to states to finance the establishment of colleges specializing in the agriculture and mechanical arts. Sponsored by Vermont Congressman Justin Morrill (1810-1898), the legislation provided land to the states, the sale of which provided funds to create or support mostly public colleges. (MIT is a Massachusetts land grant university along with the University of Massachusetts. Cornell is the original land grant for the state of New York.) Among other benefits, the legislation spurred the creation of more engineering departments, the 'mechanical arts" that would later benefit the United States in its economic growth.

Abraham Lincoln signed the Land Grant legislation during the Civil War. Abraham Lincoln would also help promote the patent system that would be critical to the launch of the biotech revolution by becoming the only President to be awarded a patent in 1849.

While running for office in 1859, he made his famous comment that the patent system 'secured to the inventor, for a limited time, the exclusive use of his invention; and thereby added the fuel of interest to the fire of genius, in the discovery and production of new and useful things.'

Nearly all observers recognize that strong patent protection available historically in the US has been a mainstay for the growth of biotech companies in the US.

The Land Grant system that Lincoln helped create would benefit the looming biotech revolution by creating agricultural experiment stations—experimental farms—in 1887. Later in 1914, Congress would fund the cooperative extension service whereby trained experts from land grant universities would work with the leading economic sector—agriculture—to provide scientific expertise on improving crop yields and eventually helping the US feed the world. In later years, some of these agricultural experiment stations would be the catalysts for research parks. The portions of the land that universities acquired or the experimental stations would be transformed into research parks and innovation hubs.

Current NIH campus, Bethesda, Maryland

More importantly, the tradition of land grant universities working with their local industry partners through the extension service would continue as new technologies evolved, including information and biotechnologies. This experience would lead many universities to help form biotech spinouts when the technology advances and policy reforms later in the century encouraged this activity, as discussed below. This, in turn, led to the founding of AUTM, an international organization of technology commercialization professionals that has been critical to the advancement of bioscience commercialization activities.

1930: The Ransdell Act and Creation of the National Institutes for Health

The Act changed the name of the federally supported Hygienic Laboratory located in downtown Washington DC to the National Institute of Health. It moved it to its present site in Bethesda, Maryland. The Hygienic Laboratory was originally located on Staten Island as a single room bacteriological lab for sick and disabled sailors. The lab moved to Washington DC in 1891, and its workload increased when Congress passed the Biologics Control Act in 1902 as a result of the need for testing of vaccines for purity and potency, a topic of much interest currently (The FDA would gain this vaccine regulatory authority in 1972 from the NIH).

As improvements in bio health research evolved in the middle part of the 20th Century with the War Against Cancer and other initiatives, Congress increasingly looked to the NIH to supply research-based solutions to health issues facing the nation, creating more NIH institutes and providing more funding to NIH.

The creation of the small one-room hygienic lab originally on Staten Island at the end of the 19th century would, with funding by Congress and US taxpayers, grow by 2000 into the world's largest biomedical institution in Bethesda, Maryland and fund billions of dollars of bioresearch at universities and firms across the country as well as its own researchers on its campus in Maryland. (*See,* Steve Furgenson's history of NIH, in this publication, *infra)*

1945: World War 2 and The Endless Frontier

Seventy-five years ago, Vannevar Bush, an electrical engineer who directed government research during the Second World War, authored *Science—The Endless Frontier.* His report called for a centralized approach to government research, which led to the creation of the National Science Foundation in 1950 and is credited as a path-breaking roadmap for US science policy.

Over the next 75 years, the federal government invested billions of dollars of research through NIH, DOD, Department of Energy, the National Science Foundation, and others, creating the world's leading research universities in the United States based on research funds competed.

1951: World's First Research Park at Stanford University

In 1951, Stanford University, in cooperation with the city of Palo Alto, created the Stanford Industrial Park, with Varian Associates and Hewlett-Packard as early tenants. This is arguably the world's first research park. Stanford University Provost and Dean of Engineering Frederick Terman proposed the park to bring industry closer to Stanford University, emerging as an internationally known research university. Several orchards adjacent to the university formed the research park site, eventually seeding the development of Silicon Valley in the 1960s-1980s.

1958: Growth of the Venture Capital Sector Financing Innovative Companies

In 1958, Congress passed the Small Business Investment Act that allowed the US Small Business Administration (SBA) to license Small Business Investment Companies (SBICs) to help finance and manage small entrepreneurial businesses. This law helped to launch the private equity sector. A later change in 1974 through the Employee Retirement Income Security Act (ERISA), which allowed corporate pension funds to invest in private equity, helped spurt the modern venture capital industry that would provide funding for information technology companies and biotech companies in the 1970s through today.

The angel investing movement, a related way to support start-up firms, would grow, allowing high net worth individuals to invest their funds into private firms and angel investing clubs' growth. Federal Securities and Exchange Commission (SEC) reforms in later years would allow more individuals to take part in private investment that earlier would have required high net worth.

These financing initiatives would help support the growth of the biotech industry in the years following their enactment. Some states and localities would enact bio financing incentives as well, such as the state of Maryland and Montgomery County Maryland bio investment tax credit.

1959: Incubators Launched: Later Emergence of Biotech Incubators

In 1959 the city of Batavia in New York had lost its major industry partner. This Massey-Harris harvester company had a huge warehouse with no corporate tenants willing to take up leasing the entire facility. One of the city's leading business families acquired the space, rebranded it the Batavia Industrial Center, and offered what would become offerings for many technology incubators: short term leases, smaller spaces, shared secretarial service and office supplies, mentoring services, and financing help for companies. It leased space for chicken coops from the nearby Mount Hope Hatchery, creating one of the first incubator spaces in the U.S.

The concept of incubator space and accelerators for start-up companies would grow with organizations such as Y Combinator, and the International Business Innovation Association (iNBIA) would be formed to represent these organizations. iNBIA estimates there are now more than 7,000 incubators worldwide. Specialized biotech incubators with high-cost wet lab space would be launched, such as JLabs, part of Johnson and Johnson Innovation in 13 bio incubator locations worldwide.

1980: Bayh Dole Act, the Cohen Boyer Patent and Genentech Initial Public Offering

In 1980 President Carter signed into law the Patent and Trademark Law Amendment Act, better known as the Bayh-Dole Act. That law gave universities and other organizations the right to take title to intellectual property created with federal research funding. This law gave rise to university technology transfer offices and spurred new drugs and biotech companies.

That same year two investors, Stanley Cohen of Stanford and Herbert Boyer of UCSF were awarded a patent for their work in 1974 studying the process of recombinant DNA, which would be a platform for further bioscience research in the 1980s and beyond. Advances in bioresearch had been taking place decades earlier.

Finally, that year Genentech, a four-year-old company that produced human proteins made by bacteria into which human proteins had been slipped using recombinant DNA, had its public offering on the New York Stock Exchange. Genentech benefited from the venture capital sector advanced by Congress, and many follow-on biotech companies would go public in the months and years after the Genentech filing.

1986: Association of University Research Parks Formed

After its founding, the Stanford Research Park model would be emulated in many places across the U.S. and

increasingly worldwide. University City Science Center, one of the first urban research parks, was formed in 1963 in Philadelphia around the University of Pennsylvania, Drexel, Temple, and others. Research Triangle in North Carolina was growing after a slow start.

In 1986, research park directors from Stanford Research Park, Central Florida Research Park, Arizona State University Research Park, Oakland University, RPI in New York, Texas A&M. Research Triangle Park, and Edmonton Canada Research Park Authority met in Arizona to form the Association of University Research Parks (AURP).

The growth of university tech transfer offices spurred by the Bayh Dole Act, more start-up companies financed by venture and angel capital, and advances in biotech research helped to promote the use of research parks as places to grow university public-private partnerships. Specialized parks in biotechnology were formed in San Diego, Baltimore, Boston, and San Francisco. AURP would form an AURP Bio Health Caucus to represent the unique opportunities and challenges in bio health research, including the higher cost of wet lab facilities, longer maturation time for life science technologies, and clinical trial strategies.

1993: BIO Organization formed: State Affiliates Follow

In 1993 two small bio trade groups—the Industrial Biotechnology Association (IBA) and the Association of Biotechnology Companies (ABC)—merged to form a single organization called the Biotechnology Industry Organization (BIO). Initially uniting 503 biotech companies, the new organization would grow to become the largest bio trade organization representing more than 1,100 biotech firms, research universities, state biotechnology centers in the US, and more than 30 countries. The organization would later rebrand itself as the Biotechnology Innovation Organization.

State organizations related to BIO would be formed to build regional bio clusters, such as Virginia BIO, California Life Science Association, and the Maryland Tech Council. https://www.bio.org/csba These organizations would be critical state-based organizations to advocate on behalf of bio institutions and clusters in their jurisdictions, working on state and local programs to support this sector of the innovation-based economy.

2017: National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL)

In 2017 a $70 million award was made by the National Institute for Standards and Technology (NIST) to create NIIMBL, headquartered at University of Delaware Research Park with a national consortium of university and industry partners. NIIMBL's mission is to accelerate innovation in biopharmaceutical manufacturing, support the development of standards to enable more efficient and manufacturing capabilities, and train a world-leading workforce to support an industry sector supplying medicines worldwide. The Association of University Research Parks (AURP) awarded NIIMBL its COVID19 Excalibur Award for Response and Resiliency in 2020 to coordinate biomanufacturing research during the Pandemic.

NIIMBL is a Manufacturing USA member, a national network of linked manufacturing institutes, and joins BioFab USA of Manchester, New Hampshire and BioMADE (Bio Industrial Manufacturing and Design Ecosystem) of St. Paul Minnesota as other bio-related manufacturing institutes sponsored by NIST and the Department of Defense. With the growing interest of ensuring medical supply lines are robust in the US, more funding of biomanufacturing initiatives is expected in the future.

There are no such things as applied sciences, only applications of science
Louis Pasteur, 1822-1895

COLLABORATIVE RESEARCH IN BIOTECHNOLOGY:

The Organization for Economic Co-operation and Development (OECD) defines biotechnology as "*the application of science and technology to living organisms as well as parts, products, and models thereof, to alter living or nonliving materials for the production of knowledge, goods, and services.*"

Biotechnology companies are often located close to anchor institutions—major universities, hospital systems, and research centers—and can be associated with supportive, more prominent companies interacting with smaller bio enterprises spun out from anchor institutions. Biotech firms are often located in bio parks, such as UMB Bio Park in Baltimore, UCSD in San Diego, California, or Research Triangle Park in North Carolina. Even in downtown Manhattan, high rise office buildings are being repurposed into wet lab space.

Modern biotechnology harnesses cellular and biomolecular processes to develop technologies and produce to improve our lives and our planet's health. Biotechnology includes industrial use of recombinant DNA, cell fusion, and novel bioprocessing techniques. Advances in the biosciences have blurred the boundaries between historically separate disciplines and overlapping with other fields, such as medicine, artificial intelligence, chemistry, informatics, quantum computing, and physics, thereby increasing the need for interdisciplinary research and bringing different industries closer to each other. The biotechnology sector also makes extensive use of external services in R&D—testing, financing, and marketing—which also tend to be located nearby.

Counterintuitively, international connections are also critical to the local growth of bioclusters as much bioscience involves researchers from many countries. Accordingly, proximity to international airports and transportation hubs is an essential element of building robust biotech clusters.

Biotechnology is a science-driven business, which means that clustering often occurs in proximity to crucial knowledge centers, usually universities or public research institutes conducting top-level research. Because this knowledge is often tied to individual researchers or research groups, effective utilization requires close interaction between actors and multilevel partnerships. Also, anchor institutions are now looking at ways to connect with the community, whether it is workforce housing, childcare, biotechnician training programs attracting clients from the local community, and other connecting activities. Specialized labs, such as CGMP (Current Good Manufacturing Practices) that meet FDA regulations are sometimes needed as part of the local bio innovation ecosystem.

WHERE ARE THE LEADERS IN BIOHEALTH? INDUSTRY BIO REGION RANKINGS:

Listed below are recent rankings from Genetic Engineering and Biotech News (GEN), CBRE, and JLL, three of the most respected life science industry observers. There is some variation of the rankings of bio regions depending on how the region is defined— is New Jersey included in New York? for example— and the criteria being measured (NIH grants, amount of wet lab space, number of patents, venture capital, jobs, etc.)

GEN

Genetic Engineering and Biotech (GEN) Ranking

1. Boston-Cambridge
2. San Francisco Bay Area
3. New York/New Jersey
4. BioHealth Capital Region: Md/DC/Va
5. San Diego
6. Greater Philadelphia
7. Los Angeles/Orange County
8. Raleigh/Durham North Carolina
9. Seattle
10. Chicagoland

CBRE

CBRE Ranking

1. Boston-Cambridge
2. San Francisco Bay Area
3. San Diego
4. New Jersey
5. Raleigh/Durham North Carolina
6. DC-Baltimore
7. New York City
8. Philadelphia
9. Los Angles
10. Chicagoland

JLL

JLL Ranking

1. Greater Boston
2. San Francisco Bay Area
3. San Diego Metro Area
4. Maryland (BHCR)
5. Raleigh Durham Metro Area
6. Philadelphia Metro Area

7. New York Metro Area
8. Los Angeles/Orange County
9. Seattle Metro Area
10. New Jersey

The following city snapshots of bio clusters from the East Coast are from *Genetic Engineering News* review of top biotech clusters for 2019 to provide some context of local factors supporting the growth of these clusters:

Boston/Cambridge

Rather than rest on its laurels, the nation's largest biopharma cluster seeks new avenues for growth and thinks it has found one in digital health. Addressing a Massachusetts Biotechnology Council (MassBio) conference on September 9, Gov. Charlie Baker (R) committed the Bay State to advancing digital health by creating a digital health record database, citing McKinsey's estimate the industry will grow to more than $350 billion by 2025. Another new avenue is gene editing: In March, Cambridge-based Beam Therapeutics, co-founded by CRISPR pioneer Feng Zhang, Ph.D., raised $135 million in Series B financing, bringing its total capital raised to $222 million in less than a year. Longtime strengths like top-tier universities and talent have fueled an increasingly robust start-up ecosystem. On September 13, a team of industry veterans and academic researchers—including George Church, Ph.D., of Harvard Medical School—opened Petri, a start-up accelerator offering a 12-month program for translating research ideas into commercial success; its tools include $250,000 or more in capital and access to the team's expertise. However, the region's clogged highways and Massachusetts Bay Transportation Authority—plagued by two train derailments in June—must improve, or biopharma job growth cannot continue, MassBio's Elizabeth Steele told *The Boston Globe*. The region ranks lowest at third in employment with 95,209 jobs (JLL), while MassBio recorded 74,256 biopharma jobs last year. Boston/Cambridge is second in patents (7,935), and leads the nation in lab space (figures range from 30 million [Colliers|Boston] to 23.9 million [JLL]), NIH funding

(5,004 awards totaling $2.627 billion), and VC funding ($6.789 billion in 174 deals).

Greater Philadelphia

University City Science Center plans to join developer Wexford Science + Technology and Chicago real estate investment trust Ventas to develop One uCity Square. The 389,000-square-foot, 13-story office-lab-retail building, is slated for completion in the fourth quarter of 2021. At the center, the new Launch Lane accelerator will begin accepting applications in October; up to 12 start-ups will be accepted early next year. In February, the Science Center welcomed Cranbury, NJ-based Amicus Therapeutics, which is creating a Global Research and Gene Therapy Center of Excellence, bringing 200 jobs to 3675 Market St. The region houses 30+ cell and gene therapy developers, including Spark Therapeutics. The spinout of Children's Hospital of Philadelphia has found a buyer in Roche, but the planned $4.8 billion acquisition had been delayed for months while the companies try to resolve competitiveness concerns raised by the U.S. Federal Trade Commission and U.K. regulators. In suburban Montgomery County, Thomas Jefferson University has opened the $7 million Jefferson Institute for Bioprocessing in collaboration with the Dublin, Ireland-based National Institute for Bioprocessing Research and Training. In Harleysville, PA, Colorcon on September 17 created the $50 million Colorcon Ventures VC fund to invest in companies across manufacturing, the supply chain, and delivery of pharmaceutical products and services. The "City of Brotherly Love" and suburbs remains a consistent sixth in VC ($806 million in 37 deals), NIH funding (2,340 awards totaling $1.108 billion), lab space (10.6 million square feet), but is seventh in patents (1,912) and jobs (54,709 according to JLL; 49,000 according to Select Greater Philadelphia).

New York/New Jersey

Manhattan's lab space inventory should nearly double in two years as another 1.5 million square feet is built, according to commercial real estate firm CBRE. Leading the way is Alexandria Real Estate Equities, now constructing a third building—the 550,000 rentable-square-foot North Tower—at Alexandria Life Science Center-New York City in Manhattan. Across the East River in Long Island City, Alexandria, last year bought The Bindery, a 175,000-square-foot building, for a reported $75 million, then spent $25 million in July for a site across the street. Alexandria also plans to expand its LaunchLabs® accelerator to a second Big Apple location at Columbia University's Lasker Biomedical Research Building. Deerfield Management this month closed on financing to acquire 345 Park Avenue South for conversion into life-sci space, while Larry Silverstein's Silverstein Properties and Taconic Investment Partners have converted 619 West 54th Street into The Hudson Research Center. North of NYC, BioMed Realty, on August 29, plans to renovate two buildings totaling 97,000 square feet for smaller biotechs at Ardsley (NY) Park. In New Jersey, Gov. Phil Murphy (D) enacted a doubling of the

state tax credit for angel investors in July. The Garden State has 60% of the region's jobs, in which the two-state tandem ranks first (127,376, according to JLL). NY-NJ is second in lab space (figures range from 30.33 million square feet [JLL] to roughly 20 million square feet [CBRE]), as well as NIH funding (4,525 awards totaling $2.16 billion). However, the region places fourth in venture capital ($1.512 billion in 40 deals, up 40.5% from a year ago) and fifth in patents (4,539).

BioHealth Capital Region [Maryland/Virginia/Washington, D.C.

The Maryland/Virginia/Washington, DC "BioHealth Capital Region (BHCR)" has won over numerous employers as it strives to grow into a top-three cluster by 2023. Kite, a Gilead Company, chose Maryland's Frederick County to build a 279,000-square-foot manufacturing site for CAR-T therapies, including its marketed Yescarta® (axicabtagene ciloleucel). Also, in April, Paragon Bioservices (since acquired by Catalent) opened a 151,000-square-foot commercial manufacturing center in Harmans, MD. AveXis, a Novartis Company, agreed to use Harmans as a manufacturing site for the recently-approved gene therapy Zolgensma® (onasemnogene abeparvovec-xioi). A month later, Gaithersburg, MD-based Viela Bio filed for a $150 million IPO; the company spun out last year from AstraZeneca, a regional anchor since 2007 when it acquired MedImmune (a name retired in February). French diagnostics developer HalioDx, a Qiagen spinout, opened its first North American lab in Richmond at Virginia Bio+Tech Park, which is partnering with Activation Capital to develop additional space for expansion-stage companies. Regional anchors also include the NIH, FDA, and Johns Hopkins University, which won 40% ($648.971 million) of the region's $1.6 billion (3,272 awards) in NIH extramural funding, ranking it third; the agency also devotes about 10% of its $39.234 billion FY 2019 budget to intramural research. BHCR is third in NIH fund ing (3,272 deals totaling $1.608 billion) and patents (5,367), and fourth in lab space with 22.8 million square feet according to Rockville, MD-based Scheer Partners, which measures the entire region [JLL counts 12.95 million for Northern Virginia/Suburban Maryland/Baltimore). In VC, JLL records $1.229 billion, good for fifth (and better than the $750 million counted by PwC/CB Insights). BHCR's 55,882 jobs (JLL) ranks the region sixth.

Profiles from Genetic Engineering News https://sciencecenter.org/news/top-10-u-s-biopharma-clusters-2

APPLYING SIX FACTORS SUPPORTING GROWTH OF BIO CLUSTERS TO THE BIOHEALTH CAPITAL REGION:

The BioHealth Capital Region (BHCR), comprised of Maryland, Washington, DC, and Virginia, is perhaps a surprising entrant on leading biotech clusters in the US. Unlike Greater Philadelphia, with its ties to Delaware and New Jersey, the DMV (DC, Md, and Virginia) does not have a history of multi-jurisdictional cooperation.

Also, until 2015 the region did not have a recognizable science brand. Still, leaders at Astra Zeneca—a leading biotech company headquartered in the region— and BHI thought it was time to consider new names. Over six months, 150 regional leaders met to evaluate the need for a brand, and *The BioHealth Capital Region* term and brand emerged.

The brand's rationale was that names such as 'biotechnology' and 'life sciences' were too limiting when drug development, biotechnology, medical devices, computing advances, diagnostics, vaccines, healthcare cybersecurity, and other technologies were becoming interdependent on one another. Second, the term 'capital' had a double meaning with the Nation's Capital as the jurisdiction with existing international awareness, coupled with the need for financing 'capital' to grow the industry. Third, 'region' was used to intentionally eliminate artificial state, county, and city boundaries to find ways to work together regionally. Since that time, BioHealth Capital Region has been increasingly accepted locally, nationally, and internationally as a science brand for the area.

With a deep bench of federal labs, universities, and private industry and BioHealth Innovation-a critical intermediary organization to bring jurisdictions together – the BHCR region has jumped two spots in GEN's rankings in the last five years. The region's strengths include more than 800 biohealth companies, proximity to NIH and FDA, a network of bio-oriented research parks and research universities, and a strong bio patent portfolio.

BHI CEO President Rich Bendis has identified six factors critical for success in the BHCR and other regions in the country:

#1: STRONG LEADERSHIP

Strong leadership is always critical to a cluster's development, expansion, and sustained success. A cluster's growth can be spearheaded by various sources, including academia, political leaders, industry, and others.

"I was involved with building the Philadelphia biohealth cluster led by academia with support from the mayor, governor, and industry. The President of the University of Pennsylvania, Judith Rodin, was the primary driving force," stated Bendis.

"Leadership in building a cluster comes in many different flavors," he added. Bendis noted that other major clusters have been led by politicians, technology, talent, and other influencers. As an example, the Boston cluster has largely been driven by technology and talent emerging from Harvard and MIT. According to Bendis, the BHCR cluster has been led by industry, with MedImmune (now AstraZeneca) and other supporting organizations like BHI as the primary driving forces in the cluster's rise to prominence.

"I think the potential to last the longest would be an industry-driven cluster rather than a government one, which is subject to changes in administrations and priorities. It is not necessarily "all for one" when it comes to academic and government cluster leadership. Industry-led clusters have more potential for the stability of vision and action," according to Bendis.

"Industry is a predictable driver of growth. It will always be driven by the market; you have to create products that the market needs, and that will drive the economy," stated Bendis.

About six years ago, Medimmune examined what it needed to do to support its own growth within the region and took the lead, partnering with BHI and other organizations to create a regional brand and the infrastructure it needed to thrive. While AstraZeneca has absorbed the Medimmune brand, multiple companies are emerging as new industry cluster leaders.

AstraZeneca has recommitted to supporting the BHCR cluster, and homegrown companies like Emergent Biosolutions, Macrogenics, United Therapeutics, and Supernus, among others, have grown substantially. What's more, international biohealth companies like GSK, Qiagen, Kite, Autolus, and Janssen (who acquired Beniver) see the value in keeping or establishing a presence in the region.

From an industry leadership standpoint, the BHCR is in a strong position with homegrown companies thriving and international companies increasingly planting roots in the BHCR.

#2: SIGNIFICANT INDUSTRY ENGAGEMENT

Bendis believes that significant industry engagement—above and beyond engagement focused only on a company's benefit—is critical to creating a top-tier biohealth hub. This means an industry-led, industry-funded, and market-driven effort to cluster building and growth.

According to Bendis, government, economic development organizations, associations, and other loosely connected membership organizations are not enough to build a top-tier cluster. Industry must be directly engaged with strong, committed cluster leaders and supported by organizations with experienced professionals with business and entrepreneurial experience. Building an elite biohealth cluster is about bringing various forces together behind industry-driven and funded programs designed to maximize the return on the region's growth assets. Bendis sees the ascension of the BHCR as a product of this type of collaboration.

MedImmune/AZ was the first major industry player, led by Jarrod Borkat, to commit to building the cluster. It took an even bolder step forward when it gave up control, showing they were not purely motivated by self-interest. Over the past five years, dozens of other companies have become more engaged in the region, such as GSK, Emergent BioSolutions, Emmes Corporation, Qiagen, REGENXBIO, and American Gene Technologies (AGT).

AGT's CEO, Jeff Galvin, has become one of the region's most vocal supporters. He invests his time every month to engage in various ways with the ecosystem, from supporting STEM education programs or hosting events for postdocs at their facility to visiting other local companies and even writing about other Gene Therapy companies in Maryland on their blog.

"At BHI, which serves as an innovation intermediary for the region, we contributed to bringing industry, academia, government, and other forces together by helping these groups better manage what we call the three "Cs" of ecosystem building: cash, control, and credit," stated Bendis. "Who gets the cash? Who is in control? And who gets the credit…the cash is really the driving factor. The next is control. Who controls what? The cash, budgets, programs, and venues? Finally, it is credit. Everyone wants credit when someone succeeds. If everyone can understand these drivers and get their egos out of the way, we can succeed together."

Collaboration, the fourth "C," can only be achieved when key influencers decide to work together for the greater good of the biohealth cluster. The spirit of true collaboration for universal benefit is a critical factor in sparking the right kind of industry engagement for cluster growth. Bendis believes in a balanced and measured approach to cluster building and that this collaborative *esprit de coeur* is growing here in the BHCR.

#3: TALENT

Developing, attracting, and retaining life science talent at all levels is another key driver to biohealth cluster success. Each of the top four clusters has a significant and diverse pool of local talent, the strong companies to attract new talent, job mobility potential without relocating, and a desirable lifestyle.

"Scientific talent has never been a problem in the BHCR," stated Bendis. "I've been talking to a number of CEOs at emerging biohealth companies, and they tell me they can generally build their core team with talent from the region—that is to say about 75-80% of the talent they need is right here," added Bendis.

The BHCR has the highest concentration of PhDs and master's Degrees in the life sciences in the world. The region's scientific talent pool exists because of its robust university system and government presence.

However, the region does have its challenges, particularly in the area of finding local sales, marketing, and commercial talent. Because many BHCR companies are pre-market and pre-commercial, these professionals' regional talent pool is less robust than some bioclusters. In addition, Bendis sees a need for more c-level and entrepreneurial talent in the region but does not view this as a major obstacle to its development.

Bendis believes attracting this talent is not too challenging for the BHCR given the number of high-profile companies in the region and its attractive lifestyle. The cost of living in biohealth clusters like Boston, the San Francisco Bay Area, and New York/New Jersey is very high. It is altering migratory talent patterns, putting the BHCR in a strong position for talent acquisition and retention.

"What we are seeing is talent migrating south. The cost of living tends to decrease the further south you go. The BHCR is not the least expensive, but we do offer a great quality of life, outstanding schools, and the security that comes with strong industry, academic, and government opportunities to move jobs if needed," stated Bendis.

Bendis believes talent is one of the BHCR's greatest assets and that the region is well-positioned to build on this key biocluster element.

#4: ACCESS TO CAPITAL

Whether angel investment, seed capital, pre-series A, Series A/B, or non-dilutive funding, access to capital or lack thereof, is a key driver of biocluster development, growth, and sustainability.

Silicon Valley's Sand Hill Road area is the poster child for concentrated venture capital driving growth and innovation. And clusters like Boston, San Francisco, and New York/New Jersey simply have a higher concentration of capital opportunities than the BHCR, though that is starting to change.

"There are a lot of wealthy, high net worth individuals within the BHCR. The venture capital environment is just not as formalized here as it is in other clusters. The people that can fund companies come from lower risk, non-entrepreneurial backgrounds and tend to be reluctant to jump into high risk biohealth investing," stated Bendis. "There seems to be a leadership gap in organizing the many high net worth people able to fund deals."

Access to early-stage capital is a challenge in the BHCR, particularly in the 500K to $5M space.

Regionally, the average round in 2018 was about $14M, up from $11.5M in 2017. These larger funding levels mirror a national trend where venture capital firms are investing higher amounts in fewer companies, thus creating a gap in that early-stage funding strata.

There is good news for start-ups and early-stage companies seeking funding: The region sits at the center of non-dilutive funding opportunities via the Small Business Innovation Research (SBIR) program. $3.5B in SBIR funding is available each year nationally, flowing through 11 agencies. Many SBIR funding opportunities come via the NIH and other entities located in the BHCR. While proximity to agencies with SBIR funding is not a determining factor in who gets selected, companies in the region certainly can benefit from being closer to these agencies.

"SBIRs are the purest form of capital that exists. You don't have to mortgage your house, you don't give up any equity, and you don't have to pay it back," stated Bendis. "We are not yet at our' bodyweight' in the region regarding SBIR funding," added Bendis.

The region has its strengths and weaknesses when it comes to funding. SBIR and non-dilutive opportunities abound while early-stage funding opportunities are growing but remain a challenge. Initiatives like the annual BioHealth Capital Investment Forum, which allowed 95 companies to connect with over 30 investors, including JP Morgan, is a step in the right direction for increasing venture capital opportunities. The second annual BioHealth Capital Investment Forum is scheduled for October 15th and 16th at AstraZeneca.

"If you take a look at our major financings recently, it represents a significant upward trend of attracting new investors from outside the region," stated Bendis.

#5: RESEARCH ASSETS & FACILITIES

A concentration of research assets and available facilities, particularly when it comes to wet lab space, is an

essential building block for a robust bioscience cluster. Strong cluster research assets produce a steady stream of talent and tech transfer opportunities that foster sustainable growth. And ample wet lab space and cutting-edge facilities help this talent bring new technologies to commercialization.

The BHCR has an unrivaled research asset infrastructure already in place. Johns Hopkins University (JHU) and the University System of Maryland (USM) generate $3.5B in combined, annual R&D investment; the NIH's intramural program employs 6,000 scientists and has a $3.5B annual research budget; and the Federal Research R&D investment in 59 Maryland labs—the most labs in any state— totals $12B annually.

From a facilities standpoint, the BHCR is ranked #4 in wet lab space with 22.5M square feet spread across a multitude of centers and institutes across the region. "We are ranked 4th in research, but when you add the 6,000-intramural scientist at NIH, the BHCR annually generates $5.5B in research, and no other cluster even comes close to that," stated Bendis.

#6: MARKETING & BRAND AWARENESS

Having a strong cluster is one thing; national or global awareness of this strength is another. Many top-tier biohealth clusters actively promote their regional brands and have strong brand recognition in the U.S. and across the globe. The BHCR has many strengths, but self-promotion and regional brand evangelism is not yet one of them.

"We are not self-promotional. This is not a marketing-driven cluster. People generally are not as extroverted about promoting their successes publicly," stated Bendis. "Brand awareness is extremely important. If we do not talk about ourselves, if everyone does not become an ambassador for their company and the region, we won't continue to have a strong cluster. We need to deliver the same, consistent BHCR message when we are at conferences and traveling around the country and the globe."

Bendis added that the region has largely adopted the BHCR as its overall brand identity, moving away from the 270 Corridor or DMV names of the past, which were too limited in scope. Bendis stated, "Having forums like the BioHealth Capital Region Forum, which had 1,200 registrants in 2019, our new investor conferences, or a program like BHI's International Soft Landing is an opportunity to sell the BHCR cluster nationally and internationally."

Bendis also feels strongly that BHCR brand promotion needs to happen more frequently and in a more coordinated fashion.

A unified effort at brand promotion is even more critical for the BHCR due to its large geographic area and a lack of geographic density found in other clusters like Cambridge, Massachusetts. Elevating the region's brand awareness and promotional initiatives will help raise the cluster's profile and generate greater connectivity across the diverse and highly dispersed players that call the BHCR home.

The BHCR is making progress across Bendis' 6 key elements that build successful biohealth clusters. The region has remarkable strengths and significant untapped potential that could propel it into the top 3 by 2023. Bendis strongly believes in a thoughtful, measured, and strategic approach to cluster building where a rising tide lifts all boats. "The key is that the GEN bio cluster annual report is based on five indicators, and the region has made progress in 3 out of 5. It's not one thing but rather a combination of things that are coming together; we are not yet #1 in any one indicator, but we've progressed from 6 to 5 to 3 or 4 in some categories," stated Bendis.

"I look at this through the recognition of people outside the region that this is a great place to start or have a business, and it's a good place to seek investments. We have outstanding leadership, a deep and diverse life science talent pool, remarkable assets, and tremendous opportunities for local, regional and international collaboration," stated Bendis.

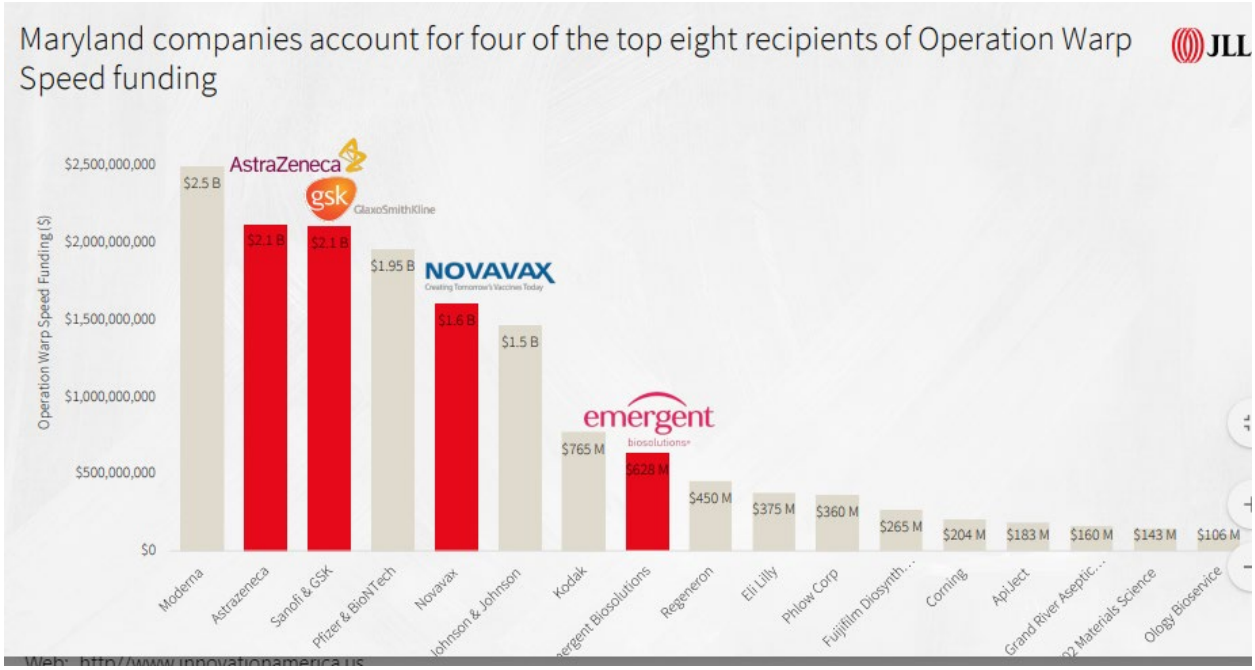
"People and companies are increasingly recognizing the BHCR as a go-to biohealth cluster rather than a drive-through or fly over destination," added Bendis.

THE COVID-19 PANDEMIC IMPACT ON THE BIOHEALTH CAPITAL REGION

While the Pandemic has been devasting to the U.S. and the world, it has had some positive benefits to the BHCR.

The BHCR has been recognized for its unique assets that no other region in the world has, namely the Food and Drug Administration (accelerated approvals), National Institute for Health (research, world-class scientists and funding), NIST, DARPA, BARDA (and its $20 Billion Operation Warp Speed) and the presence of the Director of NIH Institute for Allergies and Infectious Diseases, Dr. Anthony Fauci, who lives in the region.

Astra Zeneca, GSK, Novavax, Emergent BioSolutions, and several other companies have received over $8 billion in funding within the last six months to focus their resources on vaccine, therapeutic and



Source: JLL, Life Sciences in the Mid-Atlantic Region, 2020

diagnostic development as well as vaccine manufacturing. More importantly, several BHCR companies that may have been competitors are now collaborating to fight this dreaded Pandemic. Lastly, the BHCR has become more visible globally due to its importance in addressing this global crisis, as the graph below demonstrates.

CONCLUSION:

The growth of biotech clusters in the United States has been supported by new developments in research and technology supported by scientists working in the private sector, university, and federal labs accompanied by supportive federal, state, and local policies. The COVID-19 Pandemic has shown the incredible speed by which scientists can collaborate with industry and the federal government to create new technologies supporting human health.

Regions can support their bio clusters' growth by taking advantage of existing institutions, aligning talent, technology, leadership, financing options, and creating neutral intermediaries that can bring together regions, regardless of institutional and political jurisdictions. The lessons learned from the BioHealth Capital Region demonstrate that new bio clusters can receive national attention through strategic alignment of existing institutions and creative branding.

With the anticipated successful deployment of a COVID-19 vaccine to the general population in 2021, an 'era of good feelings' for the bioscience industry should result. Without question, new funding for bioscience will likely be available from federal, state, community, foundation, and other resources.

Jurisdictions that take advantage of the biotech revolution through the right leadership and institutional alignment –as the BioHealth Capital Region has done— will be the regions that thrive in the future.

AURP is a global non-profit representing research parks and innovation districts sponsored by universities, federal labs, hospitals, and communities celebrating its 35th anniversary in 2021. The AURP Bio Health Caucus focuses on the unique challenges and opportunities of life science communities of innovation. www.aurp. net
BioHealth Innovation is a public-private partnership serving as an innovation intermediary in the BioHealth Capital Region to advance local technologies, assets, and resources, accelerate innovation and globally connect sectors, industries, communities, and markets. http://www.biohealthinnovation.org/