Article

Philadelphia And The Delaware Valley: A Geographically Distributed and Expanding Life Science Ecosystem

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Journal of Commercial Biotechnology (2021) 26(1), 43–47. doi: 10.5912/jcb968

Philadelphia has been considered by many to be the birthplace of the modern US pharmaceutical industry with Merck & Co. Inc.'s research division Merck Research Labs [originally called MSDRL] based in West Point and GSK's primary US labs [originally SKF] now based in Collegeville. The City of Philadelphia is also home to two of the oldest medical schools in the US: Perelman School of Medicine at the University of Pennsylvania founded in 1765 and the Sydney Kimmel Medical College [formerly Jefferson Medical College] founded in 1824. The conjunction of those two touch-points along with the other big pharma players, *e.g.*, Johnson & Johnson/Janssen and emerging biotech entities in the wider Delaware Valley region is significant. Also noteworthy is the presence of other research intensive universities such as Drexel University, Temple University, Jefferson University and research institutes such as the Wistar Institute, Fox Chase Cancer Center [associated with Temple University School of Medicine], Lankenau Institute, Monell Chemical Senses Center and the Coriell Institute in Southern New Jersey.

These anchor institutions have led JLL, a commercial real estate, property, and asset management services firm [1] to label Philadelphia as a "New World City". JLL did so as Philadelphia entered the global stage because of its ability to attract young talent and international investors due to its innovative ecosystem fostered by the mix of universities, medical schools, big pharma, and biotech spinouts from local universities. This emerging ecosystem is supported by its ever-expanding skilled talent pool and its increasingly supportive business infrastructure outside of the central business district and recently in the "collar counties" around Philadelphia *e.g.*, Bucks, Chester, Delaware, and Montgomery Counties. More importantly there is a depth of mature talent due to the downsizing of big pharma in the Delaware Valley. This downsizing has resulted in a significant number of recently retired or separated scientific and technical staff with extensive experiences especially in the areas of safety toxicology, regulatory affairs, process scale-up, and clinical sciences. Many of the mature members of these pools with deep biopharma knowledge have become the new entrepreneurs of the region in addition to reservoirs of talent start-ups seem more than willing to tap into as a pool of experienced staff and consultants.

JLL in their global map of major cities puts Philadelphia and the Delaware Valley in their Innovators Class with other cities such as Denver, Dublin, Seattle, San Diego, Tel Aviv, Austin, and the Silicon Valley. Cities such as these are usually ranked by their size and gross domestic product, but in the 21st Century such ranking are also influenced by other key metrics such as the talent pool, perceived innovation environment, and the real estate market momentum. One to two years ago, Colliers International felt that the burgeoning field of cell and gene therapy would become a major driver for growth in the region and that its expansion and development would be critical for Philadelphia to become a world class life science cluster (1). In fact, at one point, the marketing catch phrase "Cellicon Valley" was coined to try and capture the emerging spin-offs in the local cell and gene therapy space especially those from CHOP [Children's Hospital of Philadelphia] from where Spark Therapeutics emerged, and recently became part of the Roche "constellation".

A great benchmark to apply towards the success of any research-intensive university-centric ecosystem is their success in attracting National Institutes of Health research grants to support their scientific efforts. Metrics in other research-intensive ecosystems such as dual life science epicenters of Boston/Cambridge, San Francisco

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Table 1: Adapted from Colliers International (2).

Institution	2020 YTD	2019	2018	2017	% CHANGE '17->'20
Univ. of Penn	$1,237	$1,200	$1,145	$1,127	9.8%
CHOP	$290	$253	$236	$224	29.5%
Temple Univ.*	$261	$264	$271	$237	10.1%
Jefferson University	$197	$173	$165	$154	27.9%
Drexel University	$119	$99	$106	$102	16.7%
Wistar Institute	$54	$51	$49	$60	-10.0%
Univ. of the Sciences	$4	$2	$2	$2	100.0%
Lankenau Institute	$3	$4	$6	$7	-57.1%
SUM =	$2,165	$2,046	$1,980	$1,913	13.2%

** Includes Fox Chase Cancer Center*

and even San Diego show the relationship between levels of NIH funding at their universities and the continuum of funding that translates into early stage spin-offs and SBIR/STTR funded start-ups founded by university faculty and their students. The NIH has awarded, as noted in Table 1, $2.165 Billion [2020 YTD] in grant funding to the institutions highlighted in this table.

Based upon 2019 full year data, Philadelphia ranks 6th nationally in such funding only behind the Raleigh-Durham area and ahead of the Los Angeles area. The Penn School of Medicine at the University of Pennsylvania, Penn Medicine, Children's Hospital of Philadelphia and the Wistar Institute, part of what Colliers International terms the Philadelphia Institutional Core, alone received over 73% of the NIH grants awarded in 2020 in the Philadelphia cluster. While a trite phrase, Colliers noted that these institutions are the engine that in 2020 stimulates an emerging future pipeline of new cutting-edge start-ups in cell and gene therapy, medtech and novel small molecules design and development. Spin-off start-ups such as Spark from CHOP, doctoral student conceived start-up like Invisible Sentinel [recently acquired by BIoMerieux] or well established CDMOs such as WuXi Biologics represent the future direction for the urban-based life science ecosystem.

Recently, new purpose-built lab facilities are being developed near the Science Center on Market Street by University Place Associates with the Wistar Institute and the Benjamin Franklin Technology Partners as anchor tenants speaks to the importance of "place" in the continuing growth of this urban life science ecosystem though neighborhoods are scattered. Recognizing the possibilities of this urban life science cluster, a new 1.5 million square foot life sciences development will be emerging in the years ahead just east of the University Science Center at the doorstep of Drexel University and marketed as Schuylkill Yards. This will further validate the decision of Roche/Spark to further develop their presence in this new neighborhood in downtown Philadelphia near the institutional research core of the city and its deep pool of talent.

Indeed, Philadelphia has an interesting history in the development of big biopharma and the beginnings of an ever-expanding life science's presence in downtown Philadelphia west of the central business district. One critical area that needs expansion is in funding for start-ups. Significant funding is needed to go beyond what has been termed the 5 F's of funding:

- Founders – Equity stakes
- Family – Loans, Equity, or both
- Friends – Loans, Equity, or both
- Feds – RO1 Grants, SBIR/STTR awards
- Fools – Probably Angels for equity

It is that the final source of funding as represented by Fools which many consider to be represented by Angel funding organizations that is still a bit lacking in the Delaware Valley, especially in Philadelphia proper. There are some firms based in Philadelphia such as Broad Street Angels, Gabriel Investments, Keiretsu Forum Mid-Atlantic Angel Group and Robin Hood Ventures. One local educational institution, the University of Pennsylvania, also started their own angel fund for faculty just a few years ago with an initial $50 million investment. In addition, the University of Pennsylvania renovated the former DuPont Labs near Gray's Ferry south of the city's institutional core and created a 62,000-square foot incubator space called Pennovation and used by faculty and non-university associated entrepreneurs but managed by an outside organization. They have plans in the works to expand the footprint of the existing site.

But the real money in that continuum of funding comes from venture capital or VCs. While they expect a greater ROI and a higher multiple on their return than Angels, plus having a longer horizon than angels for that payback, they too are not that well represented in the immediate Philadelphia ecosystem. One funding opportunity not frequently thought about is corporate venture capital. It was represented in the Delaware Valley by SR-One which was associated with GSK. However, recently GSK has spun them off as separate entity with offices now, not just Philadelphia but London and San Francisco. They have completed their first fund with $500 million and while GSK still is engaged, SR-One is a standalone VC at this stage. Other big pharma firms have VC groups such as the J and J Foundation and the Merck Foundation, but they are not domiciled locally. Closer to home however are the VCs that have grown up in the region either as privately funded operations from partnerships or from Commonwealth-backed funds. The major player in Philadelphia is the Benjamin Franklin Technology Partners [BFTP] with Commonwealth-back seed funds. They have invested in over 350 companies between 2010 and 2019. The next most active VC investor in the region is BioAdvance followed by Robin Hood Ventures and Osage Venture Partners. Funding for BioAdvance was allocated from the Pennsylvania's tobacco industry settlement.

Like its venture funding-base, due to its geography and infrastructure, the urban Philadelphia and the Delaware Valley have been and is still to some extent a decentralized real estate development market for start-ups and established life science entities looking to expand or establish a new base of operations. Basically, it is a region of submarkets and even fractionation of those submarkets [Ranked by size] (1):

- Philadelphia
  - Upper Market Street [University Place]
  - Lower Market Street [University Science Center, Century Therapeutics, Roche/Spark]
  - Lower Schuylkill [Pennovation Works]
  - Institutional Core [Wistar Institute, Penn Medicine, CHOP, Penn School of Medicine]
  - Navy Yard [WuXi, AdaptImmune, Iovance]

- Interstate-476 NE Corridor
- Route 202 Corridor
  - Merck & Co, Inc. [MSD, MRL, MMD]
  - Pennsylvania Biotech Center in Doylestown
  - The Spring House Innovation Center [Former Dow Chemical/Rohm & Haas site]
  - The Discovery Labs in Upper Merion [Former GSK West Campus]
  - Pfizer
  - WuXi Biologics

- PA Turnpike Corridor
  - Johnson & Johnson

- Route 422 Corridor
- Interstate-95 South
- Lehigh Valley [OraSure Technologies]
- Southern New Jersey
  - Coriell Institute

The above list of scattered "neighborhoods", all supporting life science enterprises to one degree or another is both a strength and weakness of the region and is a follow-on to JLL's concept of satellite real estate markets developing. These satellite markets develop as urban epicenters become too expensive and too crowded for early stage firms and even more established entities to partake of the urban ecosystems. The University Science Center and facilities being developed by University Place Associates as noted previously speaks to the importance of place in the continuing growth of this urban though scattered Philadelphia neighborhoods: Neighborhoods chosen for expansion and *de novo* development. However, as with any new establishment focused on entrepreneurs, it will take a while to firmly create the "buzz" that entrepreneurs desire in any new ecosystem and convince them that life and operations in a major city have the advantages they seek. Those senses of buzz are hard to create however, when the ecosystem resides in high rise multitenant or even mid-rise buildings separated by concrete and major roads.

While indeed Philadelphia has tried and succeeded in many instances to attract capital investment by suspending taxes using Keystone Opportunity Zones to attract other commercial ventures. We noted above a move to downtown Philadelphia such as FMC, and there are still issues. More than 20 years ago, far sighted Philadelphia officials looked at the 7.5 million square feet of space occupied by the US Navy at the foot of Broad Street and had visions of a business center that would house mixed use retail, private firms and with the aid of far-sighted firms such as Liberty Property Trust, be developed into a life science neighborhood. Indeed, one of the first tenants as WuXi Biologics in 2003: A firm that has expanded with the addition of three additional labs and buildings for a significant CDMO manufacturing site that now employees over 600 scientists and technicians in their four buildings in

the Navy Yard. Fast forward to the present and other firms planted their flags there such as GSK with their US corporate headquarters, AdaptImmune, Benjamin Franklin Technology Partners, RevZilla and Azalta. The site is now about 95% fully leased and has grown so much that the Navy wants 23 acres back to add to the 200 acres they currently use.

One observation though of recent tenants that have left the Navy Yard is that it is so large that some of the corporate employers may actually be crowding out the start-ups and life science firms that they originally hoped to attract to the site. One former tenant felt that because the site had become so crowded it had really lost its sense of buzz and place that start-ups thrive on [3][4] That tenant's decision was to move from the city to an expanding site in Montgomery County. The site, the Spring House Innovation Park [SHIP], is a repurposing by MRA Group of an abandoned Dow/Rohm & Haas site occupied now by some start-ups, established firms and a bio manufacturing training facility operated by Thomas Jefferson University as part of their academic programs.

As attractive as Philadelphia might be as an urban life sciences hub as noted above, Philadelphia has its weaknesses that have impacted the site choices of some start-ups and expansion plans for established firms. With rapid expansion of sites such as the Navy Yard, a lack of supportive infrastructure as become an issue. Components such as public transportation, quality of life issues, affordable housing and the state of the public schools are key factors. They have impacted siting and desirability of place as decisions many potential hires approach as barriers to entry before making the decision of moving to distributed urban life science clusters in a big city. Competing against Boston casts Philadelphia as not quite serious about being that world class city as projected by JLL. As noted by Joseph Distefano in a recent article in the Philadelphia Inquirer, the city is more interested in a progressive image rather than being a place where firms wish to set-up shop or employ talent that might otherwise go to the life science competition in Boston/Cambridge, San Francisco Bay area or even San Diego [4].

One important consideration for a start-up or even the expansion of an existing enterprise is in that comparison to Boston. It has been noted that Boston has no wage tax. Philadelphia has a wage tax that is levied not only on urban employees who live in the city but at a slightly reduced rate on suburban employees that commute and work in the city. The City also has a business-receipt tax. That makes for an interesting calculus, since for now not only does a start-up have to factor in rent, but differential insurance rates (urban *vs.* suburban), available parking, staff commuting costs and where their potential workforce live but the burden of operational taxes on their firms and their employees. One also must never forget that every recruit is a spousal recruit and that must be considered in a firm's recruiting strategy.

If one looks at that calculus problem, it appears to be addressed recently by firms trying to balance the advantages of being near that intellectual core of the City with the financial advantages of more space and lower operating costs. Even Roche/Spark Therapeutics with their significant ties to CHOP made the interesting decision recently to buy a lab campus for their R&D Center in Glenolden in Delaware County. From an historical standpoint Glenolden, PA is also geographically interesting as the place where Sharp & Dohme had their original labs prior to their merger with Merck & Co. and their move to West Point, PA. More importantly, WuXi Biologics, as successful as they have been in expanding their manufacturing and employee base since 2003 in the Navy Yard complex, has made the strategic decision to expand not in the city but at the repurposed GSK West Campus site now rebranded as the Discovery Labs: 1,000,000 square feet of space gradually being renovated and redeveloped for small and big companies especially in the cell and gene therapy CDMO space. A major selling point for the site is accessibility to major highways, affordable housing, and quality of life issues.

In this era of Covid-19 with is impact on safety, health, and social distancing, established firms and start-up entities are reassessing the proposition of place in their decision-making process. Cities such as Philadelphia are and will remain epicenters for business and especially innovation due to the proximity of the central business district to the intellectual core of the city. Philadelphia however needs to realize its distributed urban life science clusters must experience a transformation for the 21st Century. This transformation is necessary for it to continue to be relevant as a life science epicenter and realize as noted by JLL [1] there is no reversal of the urbanization process: Only new cycles the city can take advantage of will encourage transformation, innovation on all levels and firmly establish a degree of resilience the city and its surrounding counties in the Delaware Valley can take advantage of to improve their competitive advantage and status. It cannot however ignore the revitalization being experienced by its surrounding collar suburbs and their desire to make themselves even more attractive as a place for the expansion of established firms and as a place for start-ups to find their niche and establish themselves in satellite ecosystems. Places that also hope to replicate that vibe and buzz once only reserved for civic centers. What the area cannot forget is that it is not just the City but the entire Delaware Valley region that will now and, in the future, be the

attractant for its growth as a world-class life science hub. The City must figure out a way to balance that growth and attractiveness while at the same time being the engine that drives life science innovation from its enviable intellectual base [5][6].

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