Benchmarking Puerto Rico's Pharma Sector

An analysis of the Island's sector competitiveness and recommendations for driving economic transformation





Prepared by Invest Puerto Rico in collaboration with the Pharmaceutical Industry Association of Puerto Rico

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Current Landscape

For over sixty years Puerto Rico has stood as a global leader in biopharmaceutical manufacturing. The Island is home to 10 of the world's 20 top-grossing pharmaceutical companies, producing top-selling brands such as Humalog, Humira, Eliquis, Opdivo, Enbrel, Neulasta, Remicade, and Xarelto. In 2019, sector exports totaled more than \$44 billion. Of that, \$30.89 billion was exported to the U.S. market, while \$13.2 billion went to more than 130 countries, significantly more than any U.S. state. Pharma represents 30% of the Island's GDP, 30% of all manufacturing jobs, and employs over 78,000 people.

While Puerto Rico continues to lead all U.S. states in pharmaceutical production, sector growth and innovation has stagnated, opening the door to competition from other domestic and global jurisdictions. Growth in U.S. and global biopharma hubs is the result of longterm planning and strategic implementation to improve foundational factors of competitiveness. Despite a strong pharma ecosystem, Puerto Rico, once an economic development model emulated by several jurisdictions around the world, has fallen behind in terms of global competitiveness.

This report seeks to

- Explore why other jurisdictions have surpassed Puerto Rico in the sector
- Analyze and compare the sectors of those jurisdictions to Puerto Rico's
- Grade Puerto Rico's performance in key areas
- Recommend what the Island can do to reinvigorate pharma growth and strengthen global competitiveness

To accomplish this, the report focuses on the pharma sectors of four U.S. jurisdictions (Indiana, California, North Carolina, and Pennsylvania) and four countries (Ireland, Singapore, Switzerland, and Costa Rica). For each of these jurisdictions, the report will examine strategies for attracting capital investments, establishing R&D ecosystems, creating regional networks, digitization, and workforce development. These investment destinations were chosen based on size, relative regional comparative advantages, and pharmaceutical prowess.



Puerto Rico

Strengths

Puerto Rico has the legacy of being one of the most productive pharmaceutical manufacturing hubs in the world, let alone in the United States. Puerto Rico is a unique place that competes with both U.S. and global economies. Domestically, Puerto Rico leads all states in pharmaceutical production, more than doubling the next states of Indiana, California, and North Carolina. Internationally, Puerto Rico is also recognized as one of the key pharma destinations, along with Ireland, Singapore, and Switzerland. In fact, local engineers helped develop the capacities in other hubs around the world. Here are some of the strengths Puerto Rico offers:

- 60-year experience in biopharmaceutical manufacturing and ancillary biomedical services
- Logistics expertise in handling and shipping time- and temperature- sensitive materials
- Favorable regulatory environment governed by the FDA
- Regional leadership in biopharmaceutical production with easy access to the world's largest market
- Knowledge of global regulations facilitates product supply to international markets
- Given Puerto Rico's tropical geographical location, the local biopharmaceutical industry has developed unique resiliency capabilities and business continuity plans that have been proven in the preparation for and recovery from atmospheric events.
- World class STEM education and a qualified, cost-effective workforce
- Logical jumping off point for companies to expand into Latin American markets
- Competitive incentives for R&D, manufacturing, and exporting pharmaceutical

goods matched with an already favorable tax landscape

Also, current initiatives on the Island will significantly improve the landscape, including

- Transshipment: A waiver granted by the U.S. Department of Transportation in April 2020 allows the Island's three international airports to serve as global transshipment hubs for passengers and cargo. This designation increases Puerto Rico's logistics capabilities while also expanding the global market reach that on-island companies have.
- Digital Technologies: Puerto Rico is home to two 5G and IoT labs, test beds for industrial applications for the next generations of telecommunication and digital technology. With regards to the pharmaceutical industry, these technologies enable confidential sharing of clinical trial data, end-to-end tracking of sensitive materials, reduced time and costs for transshipment, and greater transparency in patient data and healthcare provision in general.
- Energy: Fueled by billions of dollars of federal recovery aid, the Island's energy system is on track to becoming one of the most modern and sophisticated grids in the world. Improvements will support the resiliency and cost-effectiveness of industry operations, greatly improving Puerto Rico's capability to attract high-demand industrial partners like pharmaceutical companies.
- Incentives: Puerto Rico has a competitive incentives structure. However, though incentives are an important part of attracting and retaining biopharma companies to any jurisdiction, this research emphasizes the importance of complementary factors of a pharmaceutical ecosystem that must exist for long-term, sustainable growth.



Jurisdiction	Local Corporate Income Tax Rate	Federal Corporate Income Tax Rate
Puerto Rico	4%	0%
Indiana	8.5%	10%-37%
North Carolina	6.9%	10%-37%
Pennsylvania	9.99%	10%-37%
Massachusetts	8%	10%-37%
New Jersey	9%	10%-37%
Maryland	8.25%	10%-37%

Jurisdiction	Corporate Income Tax Rate	R&D Incentives	Manufacturing	Free Trade Zones
Puerto Rico	4%	50% tax credit on R&D	50% tax credit on manufacturing	Yes
Ireland	12.5%	25% tax credit for R&D (option to combine with corporate income tax rate for 37.5% credit on R&D)	Project-specific grants available	Yes
Switzerland	8.5%	R&D super deduction at cantonal level of up to 150%	N/A	Yes
Singapore	17%	Enhanced deductionsConcessionary rate of between 5% and 15%Yefor R&D of 250%for manufacturing		Yes
Costa Rica	30%	N/A	N/A	Yes



United States Jurisdictions

Indiana

Strong cluster model with Eli Lilly as anchor

Indiana is home to a large, diverse, and specialized life science cluster, anchored by companies such as Eli Lilly and Co., Cook Medical, DuPont AgroSciences, Elanco Animal Health, and Roche Diagnostics. Rather than compete against one another, a spirit of collaboration ensures that local life science companies remain cutting edge. Indiana is also home to the world's biggest orthopedic medical device cluster based in Warsaw, with companies like DePuy, Medtronic, and Zimmer Biomet.

- Economic impact of its life sciences industry: \$77 billion (2019)
- Capital expenditure investments (2019): +\$800 million
- Home to 2,185 companies and 59,096 employees in the sector
- Ranks 5th in most concentrated life sciences states in the country
- 2nd highest exporter of life sciences products, behind Puerto Rico, with +\$10.5 billion in exports*
- Average wage for the life sciences sector: \$102,370 per worker

The strong cluster requires engagement and commitmentfrom the local academic community. Indiana University, Purdue University, and the University of Notre Dame are joined by one of the top NIH funded Clinical and Translational Sciences Institutes (CTSI). The Indiana CTSI is based near the administrative offices of the IU School of Medicine – the largest research medical school in the U.S. Building upon this research strength is the Indiana Bioscience Research Institute – a public-private partnership focused on the development of therapies for all aspects of metabolic disease.

Population

6.76 million (2020 est)

Population Growth Rate +0.5% (2020 est)

GDP Per Capita \$49,321

Average Annual Growth

+1.1% (5 yr. annualized GDP growth rate through 2020) Unemployment: 3.2% (Dec 2019), 5.5% (Oct 2020)

Total Manufacturing Output \$102.09 billion (2018)

Total Exported (outside of U.S.) \$39.3 billion (2018)

Biopharma Production \$22.5 billion

Bioscience Industry Employment 59,096

Bioscience Industry Establishments 2,185

Total Bioscience Industry, Average Annual Wage \$101,226

NIH Funding, FY2019 \$324,182,168

Bioscience Venture Capital Investments, 2016-19 \$289,490,000

Academic Bioscience R&D Expenditures, FY2018 Comparative Data \$683,436,000

*According to data provided to BioCrossroads by the Indiana Business Research Center (IBRC) at the Indiana University Kelley School of Business



INVEST

Strengths of Indiana

Supporting Increased Cluster Activity

The Indiana Biosciences Research Institute was launched in 2013 to accelerate collaboration across and among Indiana's academic and commercial research assets. The State of Indiana provided the initial seed money of \$25 million to create the Institute. This initial investment was matched with funding totaling another \$25 million from Eli Lilly & Company, Dow AgroSciences, Roche Diagnostics, Indiana University Health and the Indiana University School of Medicine. In 2017, the Indiana General Assembly included an additional \$20 million in the state's two-year budget to accelerate buildout and continued growth of the Indiana Biosciences Research Institute (IBRI). With the state's additional investment, the IBRI is on track to deliver an economic impact of roughly \$400 million over the next ten years.

Supporting Increased Access to Capital

Indiana BioCrossroads, a public-private partnership supporting Indiana's life sciences industry, announced a \$9 million seed fund in October 2018. The Indiana Seed Fund III is BioCrossroads' third fund since it formed in 2002. The fund invested in early-stage life science startups, including in health IT and agricultural biosciences.

Supporting Increased University-Industry Partnership

In July 2017, Eli Lilly and Purdue University announced a five-year research collaboration initially focused on developing predictive models for clinical success and on improving the delivery of injectable pain medicines. This \$52 million agreement is much larger than past Lilly-Purdue projects and is Purdue's largest collaboration with a single company.





California

Strong R&D and Access to Venture Capital

California companies excel at translating science into products that help patients, farmers, consumers, and many others. Therefore, the state is a magnet for investment.

- \$7.6 billion received in venture capital funding for biotechnology and medical device companies (2018)
- \$3.9 billion in VC investment for digital health
- 130 mergers and acquisitions in 2018 and 13 initial public offerings

With more than 4,000 Orange County employees, Edwards is a major anchor company for the medical device industry, along with Allergan, Medtronic and Abbott. As often happens, these companies have attracted small startups to the area, providing a supportive ecosystem and a pool of talented industry professionals.

Orange County benefits from academic resources in and near the county, including UC Irvine, USC, UC San Diego and many others. These schools graduate more engineers and computer scientists than anywhere else in the state. The results have been impressive. Orange County life sciences companies employed nearly 45,000 people in 2017, an 11 percent increase from the previous year. Of these, more than 23,000 were employed by device, instrument, or diagnostic companies.

The region has also attracted tremendous investment. In 2016, LA and Orange County drew \$269 million, for 2018 the number increased to \$348 million. While much of the capital comes from the venture capital community centered on Silicon Valley, around 24 percent of the capital came from either New York or Boston. Orange County's supportive environment for small and emerging companies boasts many success stories.

INNOVATION THAT CARES

Population

39.51 million (2019)

Population Growth Rate +0.05% (2019 est)

GDP Per Capita \$70,662 (2019)

Average Annual Growth

+3% (5 yr. annualized GDP growth rate through 2020) Unemployment: 3.9% (Dec 2019), 14.9% (Oct 2020)

Total Manufacturing Output

\$316.76 billion (2018)

Total Exported (outside of U.S.) \$149.56 billion (2018)

Biopharma Production \$57.0 billion

Bioscience Industry Employment 290,296

Bioscience Industry Establishments 11,705

Total Bioscience Industry, Average Annual Wage \$133,642

NIH Funding, FY2019 \$4,591,581,664



Strengths of California

Supporting Increased Access to Venture Capital

California Bioscience Los Angeles County (BioLA) was launched in late 2018 with support from Los Angeles County and eleven founding corporate sponsors. Each partner will be contributing \$750,000 over a three-year period. The public-

private agency's mission is to strengthen the life sciences ecosystem by convening key players in the industry, accelerating startup activity, stimulating job growth, and attracting investment to the area. The collaboration's first measure is the Bioscience Investment Fund, with an initial \$15 million provided by the county for seed investments in startups. The fund ultimately aims to raise \$40-\$60 million.



Source: https://www.bio.org/value-bioscience-innovation-growing-jobs-and-improving-quality-life





North Carolina

Strong University Industry-Partnerships and Ability to Attract NIH funding

North Carolina's biosciences industry is welldeveloped, ranging from pharmaceutical manufacturing and health informatics to crop genetic engineering. Comprised of 600+ companies and over 80,000 employees, the cluster has grown 36% since 2001.

Research Triangle Park (RTP), the largest research park in the U.S., is notable for:

- 200+ companies and 50,000+ employees with industry expertise in biotechnology and pharmaceuticals
- The North Carolina Biotechnology Center and the First Flight Venture Center
- Driving the state's economic transformation, from tobacco, textiles, and furniture manufacturing in the 1950s, to current biotech leadership

Major research universities and top medical schools, like Duke University, the University of North Carolina at Chapel Hill, North Carolina State University, East Carolina University and Wake Forest University contribute to an established workforce pipeline, active industry partnerships and an innovative business environment. This is coupled with lowest corporate income tax rate in the U.S.

All of this adds up to a solid and growing biosciences sector, and some of the highest per capita NIH funding and academic bioscience research & development spending in the country. Population

10.49 million (2019)

Population Growth Rate

+1.0% (2019 est)

GDP Per Capita \$48,496

Average Annual Growth

+1.6% (5 yr. annualized GDP growth rate through 2020) Unemployment: 3.6% (Dec 2019), 6.2% (Oct 2020)

Total Manufacturing Output \$103.59 billion (2018)

Total Exported (outside of U.S.): \$31.06 billion (2018)

Biopharma Production \$25.6 billion

Bioscience Industry Employment 83,245

Bioscience Industry Establishments 4,210

Total Bioscience Industry, Average Annual Wage \$97,553

Total Private Sector, Average Annual Wage

NIH Funding, FY2019 \$1,589,742,045

Bioscience Venture Capital Investments, 2016-19 \$1,513,190,000

Academic Bioscience R&D Expenditures, FY2018 Comparative Data \$2,352,469,000





Strengths of North Carolina

Supporting Increased University-Industry Partnership

In October 2018, Minnetronix Neuro announced that it had cofounded The Neurapheresis Consortium with Duke University. The consortium was created to bring together researchers and clinicians to advance Minnetronix's Neurapheresis Therapy through pre-clinical research and into the clinic to treat patients suffering from diseases involving infectious, inflammatory and neurodegenerative agents in the central nervous system.

In October 2018, Deerfield Management announced a \$65 million partnership with UNC-Chapel Hill to create Pinnacle Hill LLC to support the development of novel therapeutics at the University. The goal of the collaboration is to accelerate the translation of research in UNC-Chapel Hill faculty laboratories into clinical therapeutics. Profits from successful projects, if any, will be shared by Deerfield and UNC-Chapel Hill.





Source: https://www.bio.org/value-bioscience-innovation-growing-jobs-and-improving-quality-life







Pennsylvania

Small Businesses as an Engine to Grow the Bioscience Sector

Pennsylvania's bioscience sector is small business oriented, with more than half of industry establishments comprised of fewer than 10 employees.

The state also had the highest National Science Foundation (NSF) funding rate in comparison to peer states and was awarded the second highest NSF & National Institute of Health (NIH) funding per capita in comparison to peer states, and was a top contributor to innovation, boasting recipients of over 4,000 patents over the previous five years, among the top five states nationally.

Pennsylvania is home to 7 of the top 100 universities ranked in 2016 according to the Shanghai Index, including two universities in the top 100 Biological Sciences Program. Pennsylvania universities were also leaders in offering doctorate degrees in life sciences, ranking 4th highest in the nation during 2015.

Biosciences directly employed 87,000 people in 2018 and were responsible indirectly for an additional 230,000 jobs through business and household expenditures. purchases The Pennsylvania government offers several supportive incentive programs across various industries which are often utilized by companies in the biosciences.

Strengths of Pennsylvania

Supporting Increased Cluster Activity

In January 2018, Johnson & Johnson Innovation LLC and Janssen Pharmaceuticals Inc. (JPI) announced an exclusive research collaboration with the University of Pennsylvania's Gene by the University of Pennsylvania and antibodies Therapy Program.

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Population 12.8 million (2019)

Population Growth Rate +0.8% (2019 est)

GDP Per Capita \$56,868 (2019)

Average Annual Growth

+1.3% (5 yr. annualized GDP growth rate through 2020) Unemployment: 4.5% (Dec 2019), 13% (Oct 2020)

Total Manufacturing Output \$93.75 billion (2018)

Total Exported (outside of U.S.) \$35.9 billion (2018)

Biopharma Production \$17.7 billion

Bioscience Industry Employment 86.753

Bioscience Industry Establishments 2,622

Total Bioscience Industry, Average Annual Wage \$112,516

Total Private Sector, Average Annual Wage

NIH Funding, FY2019 \$1,944,017,304

Bioscience Venture Capital Investments, 2016-19 \$3,476,070,000

Academic Bioscience R&D Expenditures, **FY2018** \$2,766,568,000

partnership utilizes Adeno-associated The virus (AAV) vectors developed targeting Alzheimer's disease developed by JPI. JPI will have exclusive global rights to commercialize products developed under this agreement. In October 2018, Amicus Therapeutics announced a research collaboration with the University of Pennsylvania to develop novel gene therapies. Then, in February 2019, Amicus Therapeutics announced plans to open a Global Research and Gene Therapy Center in Philadelphia. The company said that the proximity to researchers at the University of Pennsylvania was a major draw.

Supporting Increased University-Industry Partnership

The University of Pittsburgh and the University of Pittsburgh Medical Center (UPMC) announced in February 2018 that they are transforming a warehouse into a \$200 million immunotherapy research center. The UPMC Immune Transplant and Therapy Center is intended to serve as the anchor of a new life science-based innovation district to attract R&D companies to Pittsburgh.

Number of Projects from Top 10 Pharma & Top 10 Biotech Firms by State

Number of Projects from Top 10 Pharma & Top 10 Biotech Firms by Metro Area

North Carolina	14
Munster, Ireland	12
Texas	10
California	8
New York	7
Singapore	7
England	6
Massachusetts	6
Pennsylvania	4
New Jersey	4

New York-Newark, NY	8
Cork, Ireland	7
Singapore	7
Durham-Chapel Hill, NC	6
Raleigh, NC	5
Boston-Cambridge, MA	5
Dallas-Ft. Worth-Arlington, TX	5
San Francisco-Oakland-Hayward, CA	5

Source: https://siteselection.com/issues/2020/mar/biopharma-market-cap-meet-capital-investment.cfm





Recommendations

State governments and regional economic development organizations continue to target the bioscience industry because it is an economic engine that provides high wage, high-skilled jobs across a broad range of occupations.

Puerto Rico has followed suit with some incentive programs, including preferential industry tax rates, Small Business Innovation Research (SBIR) Matching Grants through the Puerto Rico Science, Technology and Research Trust (PRSTRT) Program, tax credits to investors in early-stage venture funds, R&D tax credits, and some sales tax exemptions.

There are some best practices from other states that could be replicated to increase investment into the pharmaceutical sector, including:

- Tax credits to bioscience-specific angel investors and public investment in "funds of funds" to increase the availability of venture capital for bioscience companies.
- Increased support for University-Industry partnerships, either through grant activity, public-private partnerships, or direct advocacy by government actors. This could bring in more academic bioscience research & development expenditures and attract additional NIH funding.
- Advocating for the establishment of a permanent NIH facility on the Island to contribute to federal spending in bioscience innovation in Puerto Rico.



International Jurisdictions

Ireland

Irish economic growth kicked off a new era with the integration of Europe. Protectionism, which had served to support Irish agricultural development, gave way to free trade. Ireland was included in the European Communities in 1973 and the nation benefited greatly from the partnership. From 1973 to 2018, Ireland was a net beneficiary of EU funds, including European Social Fund training programs that supported a million Irish people. Similar partnerships and funds exist for R&D. Participating in an open, single-market significantly supported Irish economic growth in areas like pharmaceuticals and financial services, high-value exports.

The history of pharmaceutical production in Ireland began in the 1960s with key investments in small molecule productions by Leo Laboratories and Bristol Myers Squibb. Other key early players included Pfizer, Novartis, GlaxoSmithKline, Merck Sharp & Dohme, Janssen, and Lilly. For the next decade, pharmaceutical production focused on API development. Only in the 1990s did a shift take place towards higher value secondary manufacturing, mainly in oral solid dosage and vaccines.

In 2005 Ireland became home to the largest biopharmaceutical facility in the world after a \$2 billion investment by Wyeth (now Pfizer). This was early in the global industry shift towards biopharmaceutical development. Today, Ireland is one of the world's most prolific pharmaceutical exporters, with 50% of all manufacturing exports consisting of pharmaceutical products.

Ireland benefits from a highly flexible and diverse economy, readily available finance skills, international culture and EU access, freedom for foreign investors to acquire control in domestic companies, and attractive investment incentives. Low corporate income tax rates and international, mostly U.S., investors acquiring Warner Chilcott (2013), Elan (2013), and Vidara (2014) supported Ireland's growth. **Population** 4.9 million (2019)

Population Growth Rate +1.4%

GDP Per Capita \$88,240 (2019)

Average Annual Growth +10.37% (since 2010)

Unemployment 4.93% (2019)

Total Goods Exports \$175 billion (2018)

According to Collins McNicholas

Biopharma Exports €39 billion

According to the OEC

Pharmaceutical products (35.5%): \$62.1 billion

Organic Chemicals

(16.3%): \$28.6 billion

Chemical Products Exports \$106 billion

> **Blood, antisera, vaccines, toxins and cultures** (18.8%): \$32.9 billion

Packaged medicaments (16%): \$28.1 billion

Nitrogen heterocyclic compounds (10%): \$17.6 billion

Largest Export Partner

USA (\$49.3 billion or 28.2% of all product exports)





R&D Spending

\$2.78 trillion (\$967 billion in domestic expenditures; and \$1.8 trillion in foreign investment)

Pharma Employment

60,000 (direct and indirect, 2020)

Previously, Ireland served mostly as an overseas outpost, but with the favorable conditions just mentioned, it began to grow around 2012. Interestingly, the country has not been named in GEN's annual top 10 European biopharma clusters since 2014. Nevertheless, the influx of foreign pharma companies into the Irish economy was important in raising the standard of quality expected across the country's industry, boosting quality and productivity in indigenous companies, including the service-oriented bioscience companies.

The growth and development of local skills in biopharma manufacturing and adjacent activities has helped Ireland broaden its pitch from beyond just being a low-tax destination to one with real home-grown talent. Ireland's GDP has been increasing every year since 2012 and unemployment has fallen every year since 2012. The nation's tax incentives have supported this trend by attracting businesses and encouraging growth:

- 12.5% corporate tax rate (this is second in the EU behind Hungary at 9%)
- 25% tax credit on R&D expenditures
- Relief on investment in intangible assets (ie, intellectual property)

When Ireland closed the tax loophole, known as Double Irish between 2015-2020, it was replaced with a Single Malt and the Capital Allowances for Intangible Assets (CAIA). With the U.S. Tax Cuts and Jobs Act, companies pay between 0-3% on profits that can be fully repatriated to the US without any additional US taxation. This is expected to cause a boom in the use of Ireland's new tax structure as companies closed their Double Irish schemes in 2020.

Strengths of Ireland

Supporting Increased University-Industry Partnership

Ireland is home to phenomenal universities that are routinely included in global rankings. Trinity College Dublin, RCSI University of Medicine and Health Sciences, and University College Dublin. All three are research universities with specialties in the humanities, science and healthcare related programs, and clinical and health fields, respectively. They are all in the top 300 global universities and together educate around 53,770 students.

In 2006, Ireland's economic development organization, IDA Ireland, funded and created the National Institute for Bioprocessing Research and Training (NIBRT) in a response to expected pharma job losses from patent expirations and consolidation. The NIBRT is the collaborative effort of Ireland's top universities, the government, and industry leaders to best align current and upcoming talent with the evolving biopharma industry. The NIBRT, which brands itself as the "'one stop shop' for the bioprocessing industry's training requirements", uses its state-of-the-art bioprocessing plant to train professional, teach undergraduates and post grad students, and help companies adapt to changing realities.

The NIBRT was a successful development, as biopharma firms injected at least \$10 billion into Irish biopharma from 2009-2019. In 2018, the NIBRT continued in support industry by forming the Biopharma 4.0 Alliance for Digital Innovation in Operations.





The Alliance and its digital test bed will focus on developing cell and gene therapy skills to encourage such cutting-edge investment and production in Ireland.

Supporting Cluster-based Growth

Ireland's biopharma success stems from clear, strategic prioritization of the pharmaceutical sector from multiple angles. Recognizing the precariousness of leaning too heavily on tax rates and incentives, Ireland initiated the training and R&D programs details above, along with strengthening logistics infrastructure encouraging industrial digitization. and This combination is attracting companies, like Novartis and Eli Lilly (who already have significant experience with Ireland) to use their Irish facilities as 'lighthouse projects' to test out new platforms, data analytics operations, digital clinical trials, and other experimental methods. According to IDA Ireland, the emphasis on digitization has also encouraged several clinical research companies and contract research organizations, building out core and ancillary pharmaceutical activities on the Island.*

The NIBRT also performs research and is available for contract research. Its activities in this area span four key areas of the biopharmaceutical industry: cell biology engineering, bioanalytics, advanced and manufacturing, and bioinformatics and data analytics. This range encourages companies of diverse activities and capabilities to participate in Irish biopharma, as they can be confident of the support they will find.

These activities, the EDO claims, will be supported by logistics infrastructure that is

regularly being updated. Ireland has three international airports (Dublin, Cork, and Shannon) with 200 destinations across 43 countries; and seaport infrastructure saw 53 million tons of goods in throughput in 2017. Multimillion dollar investments are currently underway to expand the facilities at Dublin, Cork, and Limerick (Tier 1 ports) and some Tier 2 ports to expand interconnectivity with Europe. These infrastructure assets are connected by an urban motorway that was built between 2000 and 2010; there are plans to further expand the network by 2027 with a 6.6-billion-euro national investment. Road networks are complemented by an extensive rail network that provides connections between Ireland's five major urban areas.

Supporting Regional Access

With the expansion of free trade regimes throughout the 70s and 80s, Ireland was a "lowwage, low-cost platform for multinationals to enter the huge EU market" (Splinter News). Tax favorability, skilled labor, and free trade with one of the largest markets in the world, the EU, all made Ireland an attractive place to manufacturing high-value exports.

This landscape is further supported by 'enterprise zones', free-trade zones, which specifically add value to industrial firms with expensive imports and high-value exports. There are over 10 around Ireland and are conveniently co-located with logistics infrastructure. Each zone was coupled with a new institution for advanced training and education (Splinter News). Not only did this support business attraction efforts for the pharmaceutical industry, but it encouraged companies in Ireland to stay, grow, and explore new areas of the industry.



INVEST

^{*}Microsoft, GECAS, Apple, Intel, Google all have a large presence in Ireland, further supporting the infusion of technology and a cluster mindset in the pharmaceutical industry.

+ Switzerland

With a relatively small domestic market, Swiss companies were always focused on exportdriven growth, particularly with high-value exports, like clocks, medical devices, and other heavy manufacturing. Further contributing to the strength of these sectors is the geographic centrality of Switzerland compared to the largest European markets. The longevity and convenience of Switzerland's industrial landscape contributed to the strong pharmaceutical cluster that currently exists, though the central European undertaken Confederation has significant measures to support its economic success and biomedical sciences industry

Switzerland's 250-member pharma community, with global names like Roche, Novartis, Abbot and Bayer, constitutes around 40% of total Swiss exports. The Swiss Federal Council in 2013 approved a plan to strengthen and promote the country's biomedical research and technology fields. Emphasis was placed on education, continued education, and training; publicly funded research; and digitalization to improve the availability and the quality of health data.

The high costs associated with new R&D or manufacturing departments has led to local strengths in CRO and CMO offerings. In addition to an export-focused economy, the availability of research or manufacturing for-hire means that small- and medium-sized companies can excel without needing a budget to compete with large multinational corporations. This contributes to the cluster development of Switzerland's pharmaceutical sector.

Additionally, the geographic proximity of Switzerland and the global recognition of the regulatory agency Swissmedic mean that companies that choose Switzerland as their home have immediate access to a regional and global marketplace for their products and services. **Population** 8.55 million (2018)

Population Growth Rate +0.8%

GDP Per Capita \$70,989 (2019)

Average Annual Growth +3.37% (since 2010)

Unemployment 4.58% (2019)

Total Goods Exports \$310 billion (2018)

Biopharma Exports \$108.5 billion (35%, 2019)

According to the OEC

Pharmaceutical products \$73.4 billion (23.7%)

Organic Chemicals \$20.7 billion (6.7%)

Chemical Products Exports \$103 billion (33.2%)

> Blood, antisera, vaccines, toixins and cultures \$62.2 billion (20.1%)

Packaged medicaments \$28 billion (9%)

Nitrogen heterocyclic compounds \$9.6 billion (3.1%)

Largest Export Partner Germany (\$47.9 billion or 15.5% of all product exports)

R&D Spending \$25 billion (private); 3.37% of GDP (2017)

Pharma Employment 135,000 (direct and indirect, 2020) This supports smaller and mid-sized companies who otherwise would not be able to afford the costs associated with doing business in Switzerland, but in doing so supports a cluster approach where companies of all size and complementary specialties are attracted and thrive.

Strengths of Switzerland

Supporting the Continued Emphasis on Education and Training

Switzerland boasts the highest quality of life in Europe, with three cities represented on the global index in 2020. The country benefits from top notch universities and high wages, both attractive to geographically flexible pharmaceutical talent. In Switzerland's 2013 Master Plan, the government placed emphasis on education, continuous training, and publicly funded research opportunities to complement the sector.

Supporting Cluster-focused Development

Switzerland has notoriously high wages, but the Swiss pharmaceutical industry overcomes this potential barrier by ensuring high quality at the source and strong contract research and manufacturing organizations. This corporate diversity contributes to the clustered nature of the landscape, which attracts large multinational companies and small enterprises, alike.

According to the World Economic Forum's Global Competitiveness Report, Switzerland has ranked #1 on the global innovation index since 2013. Results of this innovative nature are evident in new pharmaceutical technology that emerges out of Switzerland and Swiss companies: Novartis Oncology; OMPTA antibiotics; Car-T therapies; and stem cell therapies.

Supporting Digitization with High Premium on Privacy and Data Management

Switzerland has put a high premium on privacy and proper data management. This is evident in the centuries-old Swiss banking industry. It is also clear in the more recent push for digitization. As with other digitization campaigns, Switzerland is exploring how digital technology can improve industrial processes, protect and share patient data securely, and improving the types of medicines being developed.



Singapore

Singapore's pharmaceutical prowess is only about 20 years old but is based on decades of expertise in high-value manufacturing. Singapore's number one export category is machinery, with integrated circuits making up \$61 billion or 18.9% of their total exports. The citystate's excellence in manufacturing is reflected in their pharmaceutical production as well. There are over 50 pharmaceutical plants and medicine exports valued \$8.1 billion in 2019.

Starting in 2000, Singaporean leaders made biotech and pharmaceutical research and production strategic focal points in the citystate's future economic development plan. That same year, the city government implemented the three-phase Biomedical Sciences Initiative with the vision of adding biosciences to complement the strong pillars of Singapore's economy: electronics, engineering, and petrochemicals. Singapore began to shift resources to build core research capabilities, and, later, more specific biomedical research capabilities.

In the first five-year plan, Singapore created two research councils built out of the previously existing National Science and Technology Board, the Agency for Science, Technology, and Research (A*STAR) was founded in 2002 to support strategic research and development. The Biomedical Research Council (BMRC) at Biopolis and the Science and Engineering Research Council (SERC) at Fusionopolis were created with hundreds of millions of public funds.

The purpose of these councils was to lay the groundwork for core research capabilities and create a space to develop future human and industrial capital. By 2005, ten thousand high-value jobs had been added; and production soared from \$\$6 billion in 2000 to over \$\$23 billion in 2007.

Population 5.7 million (2019)

Population Growth Rate +1.2%

GDP Per Capita \$101,649 (2019)

Average Annual Growth +3.5% (since 2010)

Unemployment 2.3% (2019)

Total Goods Exports \$323 billion (2018)

Biopharma Exports (35%): \$108.5 billion (2019)

According to the OEC

Pharmaceutical Products \$13.3 billion (4.1%)

Organic Chemicals \$21.3 billion (6.6%)

Chemical Products Exports \$49 billion (15.2% of total)

Packaged medicaments \$8.26 billion (2.6%)

Oxygen amino compounds \$6.57 (2%)

Blood, antisera, vaccines, toxins and cultures \$3.63 billion (1.1%)

Largest Export Partner China (\$44.3 billion or 19.1% of all product exports)

R&D Spending

\$9.28 billion (\$5.6 billion in private + \$3.6 billion in public)

Pharma Employment

24,000 (direct and indirect, 2020):

In phase two of the Biomedical Sciences Initiative, Singapore more than doubled the available R&D funding. Between 2006-2010, Singapore's government committed \$8.3 billion to R&D; just over 25% was specifically for the biomedical sector. This funding supported diverse research areas within the recently minted Councils and contributed to the clustered reality of Singapore's biopharma industry.

The BMRC houses seven research institutes and five research consortia that advance Singapore in six key areas: biomedical engineering, cancer genetics, infectious disease and immunology, metabolic diseases, molecular cell and development biology, and stem cells and regenerative medicine. These focus areas position Singapore as a supportive jurisdiction for companies at any stage of development. This strategy explicitly supports Singapore as a biomedical cluster.

Furthering this strategy, in 2009, Singapore created the A*STAR Joint Council to coordinate efforts between the two Research Councils. The two councils are housed only 600 meters apart and each contain corporate labs and private-sector companies to align public and private sector development. In June 2019, the Experimental Drug Development Centre (EDDC) was established to coordinate public-private partnerships in the local drug development ecosystem. It will combine the efforts of the Experimental Therapeutics Centre, the Drug, Discovery, and Development, and the Experimental Biotherapeutics Centre.

Singapore also benefits from having one of the most liberal economies in the world and an efficient and pro-business public bureaucracies. According to the World Bank, Singapore is at or near the top in ease of doing business. Nearly every public service is digitized; it has the best IP protection in Asia Pacific and second in the world; the freest economy in the world; on average, opening a business takes 3 days. The pro-business nature of the Singaporean government has inspired a liberal use of publicprivate partnerships to grow R&D and labs, talent, and industry capabilities.in ease of doing business. Nearly every public service is digitized; it has the best IP protection in Asia Pacific and second in the world; the freest economy in the world; on average, opening a business takes 3 days. The pro-business nature of the Singaporean government has inspired a liberal use of publicprivate partnerships to grow R&D and labs, talent, and industry capabilities.

Industry leaders across the biosciences formed the Asia Pacific Medical Technology Association (APACMed) in 2014. It was created to coordinate efforts across the entire region beyond the scope of national industry associations.

Strengths of Singapore

Lessons for Puerto Rico

Singapore has a well-coordinated public sector that supports research with billions of dollars. The government, as well as the publicly funded and run research councils, have long-term strategies for developing biomedical capabilities, in particular research. They specifically target research silos as to improve interdisciplinary development. In doing so, Singapore has taken it upon itself to serve as the regional leader in biopharmaceutical development.

Supporting Efficient Government Administration

Singapore created an attractive place to do business, with digitized public services, expedited permitting processes, and world-class intellectual property protections. Ranking at the top of economic freedom indices, Singapore outperforms regional and global competitors in attracting business activity.



Supporting Clear and Coordinated Economic Development Strategy

Singapore's Economic Development Board, with offices around the globe, engages in strategic economic planning and execution. With almost 60 years of experience, Singapore EDB coordinates private sector priorities within public agencies and initiatives to maximize the business-friendliness of the broader economy. By using P3s as feedback mechanisms, Singapore EDB ensures that both sectors are aligned for future growth.

Supporting Regional Leadership

Singapore is the regional leader in biomedical research, development, and manufacturing, leveraging this position to coordinate amongst regional neighbors to support access, innovation, and collaboration of biomedical advancements through the APACMed. This provides companies in Singapore with access to a broader market, with larger, more diverse demographics and disease profiles. Singapore maximizes itself as a cluster, drive advancement in its logistics infrastructure, and attract companies looking to grow.



📕 Costa Rica

Costa Rica has emerged as a stable, uppermiddle income country that has experienced regular economic growth over the past 25 years. Economic crisis in the 80s and 90s inspired government officials to design an export-oriented economy, as opposed to the import substitution model that had led to inflation and poverty. By undervaluing its currency, Costa Rica was able to make its export sector more competitive, while boosting tourism. To support exports, Costa Rica established extensive privately-owned free trade zones. In 1997, Intel was one of the first major global companies to play a role in diversifying Costa Rica's economy.

In the 90s, state-owned enterprises were mostly privatized, free trade agreements were signed with regional and global markets, and tariffs dropped from around 55% in 1985 to 5.4% in 2000. Additionally, multinational companies benefit from tax and regulatory incentives. Today, there are about 200 multinational companies in Costa Rica and 90% of exported goods go through FTZs. Since the 80s, Costa Rica transitioned from a mostly agricultural economy to one where 40% of the GDP is high-tech manufacturing related.

Essential to this economic transition is a qualified workforce. When Costa Rica abolished its army in 1948, it directed its focus to support education and human capital development. Constitutionally, at least 6% of the budget must be directed toward education. Nationally, there are 95 technical schools and 60 universities. The quality education and health metrics, paired with comparatively low wages, are driving success in knowledge sectors. Microsoft and Intel both plan to expand their R&D facilities in Costa Rica. Pfizer has opened an Institute for Science and Research; Costa Rica biotech company Speratum is dedicated to R&D for pancreatic cancer therapies; Microtechnologies, Roche, **Population** 5.05 million (2019)

Population Growth Rate +.96%

GDP Per Capita \$19,642 (2019)

Average Annual Growth +2.5% (since 2010)

Unemployment 11.49% (2019)

Total Goods Exports \$12.9 billion (2018)

Total Medtech Exports \$3.7 billion (2019)

According to the OEC

Pharmaceutical products \$327 million (2.5%)

Chemical Products Exports \$726 million (5.6% of total)

> **Packaged medicaments** \$185 million (1.4%)

Blood, antisera, vaccines, toxins and cultures \$130 million (1%)

Largest Export Partner United States (\$4.7 billion or 36.4%)

R&D Spending \$247.4 million or .423% of GDP (2017)

Pharma Employment 3,500 (direct, 2020)



INVEST

Proquinal, and AstraZeneca all announced expansion projects in Costa Rica in 2020; there is a growing contract manufacturing scene, with ADMEDES as an anchor.

While Costa Rica's pharmaceutical production numbers are significantly lower than the rest of the peer group analyzed in this paper, and Costa Rica was the largest importer of pharmaceutical products in Central America during the first half of 2020, these above expansion and attraction announcements provide clear evidence that Costa Rica's bioscience industry is growing and may compete openly with Puerto Rico, broadly, as an access point for the Americas.

Strengths of Costa Rica

Like Costa Rica, Puerto Rico will need to continue to emphasize education and human capital metrics, competitive wage rates, easy access to broader geographic markets, and specialized knowledge-based capacity, be it in R&D, process improvement, tech manufacturing, 5G, etc. As some of the weaker points of the economy get addressed, like public governance, infrastructure, and bureaucratic regulation, it will be important that Puerto Rico not be priced out by less expensive destinations like Costa Rica.

Supporting Cluster Development

Costa Rica's BioTech & Medical Device Cluster is in "excellent health" a Costa Rican news publication declares. The sector represents over a third of all export value, with 70% of the products going to the United States. The export value has also increased, going up 19% from 2018 to 2019. At the end of 2018, the cluster represented 92 companies, many of whom are globally known producers like Medtronic, Boston Scientific, and Thermo Fisher Scientific.

Based on the expansion news announced in 2020 and the diversity of the operations, from R&D to CROs and CMOs, local startups and large multinationals, Costa Rica is developing an attractive landscape to build, grow, and export biomedical products.

Supporting a Qualified Workforce

Costa Rica's emphasis on literacy, health, and education have created a talented, often bilingual, and adaptable labor force that support large tech companies like Microsoft and Intel. Seeing these global giants put their faith in Costa Rica's economy and high-value sectors will inspire additional companies looking to employ highly technical workers at competitive wages.



Conclusions & Next Steps for Puerto Rico

Opportunities / Competitiveness Scorecard

Puerto Rico's pharma sector can and should take cues from other jurisdictions and undertake efforts to support:

Cross-Sector Bioscience Partnerships

While Puerto Rico has strong industry associations and the Puerto Rico Science Technology and Research Trust, the Island can do better in establishing successful private-public and academic partnerships to create additional economic opportunities. North Carolina has the advantage in this area.



Cluster-Based Development

Puerto Rico's pharmaceutical cluster is well established, but in other jurisdictions clusters have been more successful in working together to grow the industry. Ireland has the advantage in this area.



Workforce development and talent attraction

Puerto Rico is a leader in producing top-notch engineering talent but can learn from other jurisdictions in how to attract, develop, and retain a bioscience productive workforce. Singapore has the advantage in this area.



Regional Leadership

Puerto Rico is a regional leader in pharmaceutical manufacturing in the U.S., Caribbean, and Latin America. It can learn from other jurisdictions to leverage and market this distinction to even greater expand its influence and economic force in the sector. Singapore has the advantage in this area.



Supporting Efficient Government Administration

Puerto Rico needs to develop an efficient process to deal with the needs of the companies that are or plan to invest in the Island. Puerto Rico can learn from other jurisdictions, like Singapore, that have been able to create an attractive place to do business, with digitized public services, expedited permitting process, and other aspects.

Supporting Clear and Coordinated Economic Development Strategy

Puerto Rico's lack of coordinated strategy planning across government, academia, and the private sector to develop and maintain the pharmaceutical sector on the Island has hindered its performance. Singapore's Economic Development Board, with offices around the globe, engages in strategic economic planning and execution. With almost 60 years of experience, Singapore EDB coordinates private sector priorities within public agencies and initiatives to maximize the business-friendliness of the broader economy. By using P3s as feedback mechanisms, Singapore EDB ensures that both sectors are aligned for future growth.

2019 World Bank - Ease of Doing Business Rankings

- 1. Singapore
- 24. Ireland
- 36. Switzerland
- 65. Puerto Rico
- 74. Costa Rica

Supporting Increased University-Industry Partnership

Universities are positioned to play a significant role in encouraging entrepreneurship as part of their organizational models. This would plant the seed for proliferating startups and attract venture capital, including for startup development programs at universities and the intellectual property developed therein. The Puerto Rican universities, the UPR in particular, should play a major role in promoting R&D and entrepreneurship in this field.

Access to Capital

Puerto Rico's bioscience entrepreneurship ecosystem has struggled compared with other states, attracting \$5,460,000 in venture capital investments, 2016-19. California has the advantage in this area.





Recommendations

Pharmaceutical manufacturing is a critical component of Puerto Rico's economic development strategy and the Island has what it takes to succeed as a global bioscience hub. Based on this benchmarking exercise, Puerto Rico should strongly consider the following to achieve the sector's full potential on the Island:

Engage in comprehensive long-term planning to	Support entrepreneurship in the sector to
 Garner support from key stakeholders Develop cross-sector partnerships 	 Gain greater access to capital Accelerate cluster development Create strategic partnerships
Develop pharma industry corridors that foster the creation of	Enable bioscience research across the Caribbean to
 Partnerships Clusters Workforce development initiatives Funding procurement efforts 	 Develop strategy with neighboring Island-nations Strengthen regional leadership Create LAC-facing research and collaboration Establish regional logistics links
Improve Government Efficiency	Industry Academia Partnerships
 Digitize public services Expedite permitting process 	 Seed for capital ventures Encourage entrepreneurship Develop intellectual property

A Final Thought

Puerto Rico's business ecosystem is ready to support growth in the biopharmaceutical sector. Working in alliance, the local government, InvestPR, PIA and other stakeholders are actively leveraging the power of collaboration to accelerate growth and drive new investments in pharma manufacturing. This means accelerating economic development efforts on par with that of other world leaders.

The Puerto Rican government and the private sector should collaborative develop and implement a long-term strategy to maintain and increase the bio-pharmaceutical investment and activity on the Island. Cross-sector stakeholders should develop governance structure and processes to assure the continuity in executing the plan and evaluating outcomes.

This analysis may serve as a blueprint to developing those strategies, ultimately to improve Puerto Rico's biopharmaceutical prospects by strengthening key components of the Island's competitiveness. These components are purposefully apolitical, long-term, and stabilizing, regardless of public tax incentives, for instance. Fundamentally, then, the recommendations here are private-sector led, but public-sector supported.





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