BioPharma Ambition 2020

An All-Island Event

Connect | Influence | Innovate | Inspire

Globally Networked Innovation

Perspectives on Ireland's Future in Medicines

#BioAmbition20

Presented by

biopharmachem Ireland Ibec

Irish Pharmaceutical Healthcare Association

nibrt

Preparing Now For The Future of Medicines Innovation and Investments

EXECUTIVE SUMMARY

The biopharmaceutical industry is among Ireland's most significant investors, creating some 45,000 jobs that are regionally distributed and account for 62% of the country's goods exports. We have a large biopharmaceutical manufacturing presence, relative to other big sectors and to other similar-sized countries.

None of this can be taken for granted. Product life cycles, industry consolidation patterns, the draw of emerging markets, skills readiness and slow speeds of adoption of new medicines in the health services are creating headwinds that could decelerate the pace at which the industry scales into the future in Ireland.

The response is to plan, together. Closer collaboration between industry and the State on the operating environment for medicines innovation and investments is the way forward. This happens in other countries in Europe and beyond.

In December 2019, the biopharmaceutical industry, in partnership with the government, organised the 'BioPharma Ambition Policy Forum'. The event was aimed at gathering expert perspectives on the future for medicines innovation and investments. It was supported by the Department of Business, Enterprise and Innovation under the banner of 'Future Jobs Ireland', the Government's enterprise agenda. The event drew about 60 leaders in industry, policymaking, research, academia, clinical care and patient advocacy.

"The response is to plan, together"

As part of our preparations for the Policy Forum, the partners behind BioPharma Ambition 2020, IPHA, BPCI and NIBRT, commissioned PwC, the consulting firm, to offer an independent analysis of the biopharmaceutical industry in Ireland — the strengths, weaknesses, opportunities and threats. In this document, we have included PwC's analysis, as well as a summary of the discussion at the Policy Forum. This work is designed to complement the government's evolving 'Future Jobs Ireland' enterprise agenda.

Some things are clear from PwC's analysis.

- The development of Advanced Therapy Medicinal Products (ATMPs) is likely to explode in the coming years. For many companies, the pipeline of complex biologic medicines is strong. The dividend of pursuing a strategy that plays to both strands will be distributed clinically, economically and socially.

Preparing Now For The Future of Medicines Innovation and Investments

- The future for Ireland's biopharmaceutical industry should not be a binary choice between continuous improvement in small and large-molecule medicines and the development of ATMPs.
- As sectors like technology, medical technology and biopharmaceuticals converge, similarly the gap between industry, policy, research and clinical leaders is narrowing. Connecting these players will enhance Ireland's life sciences proposition. It will help us to stay competitive for new investments in biopharmaceutical manufacturing and research.

Biopharmaceutical Innovation

BioPharma Ambition 2020, held at Dublin Castle on March 3rd and 4th, is about positioning Ireland at the heart of globally networked innovation. Biopharmaceutical innovators are bringing new therapies to patients that are transforming the trajectory of disease. It is clear that medicines innovation and development globally are intensifying. Digital technology and traditional medicine are combining in a way that is transforming health management. Digital therapeutics and diagnostics are reshaping our understanding of medical conditions and helping to personalise interventions.

"Ours is a global success story in biopharmaceutical manufacturing"

Data will play a much bigger role in the evolution of healthcare innovation, with outcomes tracked and measured so that improvements can be made in treatments and how we pay for them. Over time, the lines will blur between the major players in biopharmaceuticals, technology and medical technology.

Cell and Gene Therapy

Ours is a global success story in biopharmaceutical manufacturing. The number of biopharmaceutical manufacturing sites has grown from three in 2003 to 22 in 2019. But the success of our industry is no cause for complacency. In identifying new opportunities for Ireland, we must heed global industry trends. One of the most important of these is the sharp growth in cell and gene therapies (CGTs).

Cell therapies can treat potentially fatal blood cancers by reinfusing patients with their own engineered immune cells to tackle the illness. In the longer run, companies will likely target more challenging solid tumours. At the same time, scientists are making progress on gene therapy by replacing faulty DNA to cure genetic diseases.

Preparing Now For The Future of Medicines Innovation and Investments

Extraordinary clinical results in recent years have led to an explosion in the number of new companies developing CGTs. This has been driven, in part, by multi-billion dollar acquisitions by some significant industry players.

Major investments will be needed to create CGT manufacturing capacity and capability at sites in Ireland. We will need to meet training and skills needs linked to manufacturing this new wave of medical therapies. We will need to compete for investments against many other countries. If we move quickly, Ireland can build on our reputation as a global leader in biologics manufacturing to become a leading European destination for CGT production.

'BioPharma Ireland'

To future-fit the biopharmaceutical industry, the industry will need to work intensively in collaboration with the State and others. The upside for Ireland is clear - gains clinically, economically and socially by making the most of medicines innovation and investments. It will mean better health outcomes, higher levels of productivity and more jobs across the regions. At the Policy Forum, we listened closely to the experts, drawing on their insights to identify the opportunities for Ireland from a thriving biopharmaceutical industry. Together, we should take steps now to realise Ireland's potential.

The industry's goal should be to devise and implement a Strategy that supports the development, production and provision of 21st century

"We will need to compete for investments against many other countries"

medicines. The Strategy would guide how Ireland leverages the discovery, development, manufacture and adoption of new medicines for the betterment of human health.

'BioPharma Ireland: A Strategy for the Development, Production and Provision of 21st Century Medicines' should be clear about Ireland's potential in emerging areas like ATMPs, Industry 4.0, immunotherapies and genomics. It should ensure that we have the best operating environment for medicines innovation, including the availability of the right skills and talent, tax policies that catalyse research and development and draw new investments, a robust intellectual property (IP) regime, and a reformed approval and funding mechanism that makes us as fast as other western European countries in adopting new medicines in the health services.

The envisaged Strategy, proposed by the industry, would need to be developed in conjunction with the State. It could include the following action areas:

1. A focus on realising Ireland's potential in cell and gene therapy, including how the development of skills, new production sites, and

Preparing Now For The Future of Medicines Innovation and Investments

designated research and therapy areas could help foster innovation, create jobs and draw investments.

2. The development of a sophisticated data capture and analysis architecture in the HSE so that health outcomes can be tracked and measured, creating the foundation for more tailored treatments and precision medicine, improving patient outcomes using existing medicines, and establishing 'value' metrics for the pricing of new medicines.

3. The raising of Ireland's voice in Brussels and in Dublin so that it is an influential advocate for IP rights for medicines innovators, especially in the development of new drugs for rare diseases.

4. The tripling of the number of clinical trials conducted in Ireland, from 125 studies to 375, so that patients can benefit from better health outcomes. This would bring us to closer to Denmark through the standardisation of site contracts that shorten patient recruitment delays and save on legal fees for hospitals and companies.

5. The application of genomics for medicines discovery and development, guided by a White Paper that deals with issues around data privacy, ethics, regulation and research priorities.

6. The development of new higher education programmes, co-designed by industry, academic and clinical leaders, that deliver a new generation of medicines innovators with expertise in the intersection of areas like artificial intelligence, machine learning, CGT, genomics and digital therapeutics.

7. The resolution of Ireland's poor performance in the speed of access to new medicines through a new Agreement between industry and the State that funds innovation in a way that is sustainable and predictable.

8. A focus on sustaining the existing biopharmaceutical manufacturing base through the application of advanced manufacturing, including leveraging Industry 4.0 principles such as connecting information technology and operational technology systems.

"The industry's goal should be to devise and implement a Strategy that supports the development, production and provision of 21st century medicines"

Preparing Now For The Future of Medicines Innovation and Investments

This vision for the future of medicines innovation and investments has patients at its core. Each of the action areas outlined above will benefit patients and clinical care. Patient advocacy is increasingly geared towards engagement in health innovation. The growing personalisation of therapeutic interventions means patients will need to be more engaged in their development, as well as reporting the outcomes they generate. The patient's voice is critical.

Ireland needs a relentless focus on innovation at all stages of the medicines lifecycle if we are to retain the biopharmaceutical investments we have and win new ones. We must continue to pursue excellence in manufacturing and research, adapt public policy to the promise of science, and ensure standards of care are raised through the availability of new medicines to patients and their doctors.

All of this will require intense collaboration and a focus that is global-minded, ambitious, constructive and responsible. The beneficiaries of this collaboration will be people, communities and science.

This is a project for Ireland — one that can make us a medicines innovator of global consequence.

We look forward to helping to make it all happen.

Oliver O'Connor
CEO, Irish Pharmaceutical Healthcare Association

Matt Moran
Director, BioPharmaChem Ireland

Dominic Carolan
CEO, National Institute for Bioprocessing Research and Training

Overview of the BioPharma Policy Forum Discussions

On December 12th, 2019, some 60 experts from across government, industry, research, academia and patient advocacy gathered in the RHA Gallery, Dublin, for the BioPharma Policy Forum. We commissioned PwC to undertake an independent analysis of Ireland's biopharmaceutical industry — the strengths, weaknesses, opportunities and threats.

The goal of the BioPharma Policy Forum was to exchange expert views on the future for medicines innovation and investments as part of efforts to inform joint industry-government policymaking.

The group comprised senior representatives from three government departments, four government agencies, four universities, nine innovator biopharmaceutical companies, hospital specialisms and patient advocacy groups.

The half-day discussion was opened and closed by two Government Ministers. It was organised into four themes. These were handled by academic, clinical and industry thought-leaders. The themes were:

1. How industry-academic-Government partnerships can drive growth and create impact
2. What's in the pipeline for next-generation therapies
3. How industry creates impact and value regionally
4. How Ireland can stay competitive for future investments

The following is a summary of the main points made at the BioPharma Policy Forum.

Collaboration between industry, academia and government will drive growth and impact. Skills development is crucial.

- While there are several successful industry-academic collaborations, these can be broadened and deepened to focus on delivering a workforce required by the biopharmaceutical industry in the future. This type of collaboration in workforce development is common in the professional services, technology and medical technology sectors. The approach used by these sectors could be exemplars for the development of programmes in biopharmaceutical innovation. We will need new skills in areas like data science, machine learning and artificial intelligence. The convergence of biopharmaceuticals, medical technology and technology demands that skills be mobile and adaptable.

- Academia and industry should partner to advance basic research for new ideas and therapies. The challenge is to align the understanding of disease biology and drug-discovery science with patients' needs. New tools and technologies will provide novel ways of looking at diseases which could lead to a pipeline of new products. We need a new generation of problem-solvers to enhance Ireland's innovation and discovery credentials.

- We must catalyse new investment opportunities, working as one team for Ireland. Some companies and universities work in silos. Instead, we should work together to maintain Ireland's current advantage in small and large-molecule manufacturing, and exploit the new opportunity in next-generation therapies.

Overview of the BioPharma Policy Forum Discussions

- Ireland should look to Cambridge, Massachusetts as an example of skills nurturing and industry-academic collaboration. The proximity of world-class universities and industry leaders means the talent and ideas pipeline is strong. This promotes excellence in academic research, cross-functional collaboration and better innovation. It draws venture capital and government funding, as well as new industry investments.

The discussion cited several examples of excellent collaboration in Ireland. These include:

- AMBER at Trinity - an SFI -funded centre that provides a partnership between leading researchers in materials science (Physics, Chemistry, Bioengineering and Medicine) and industry. It has a 100-square metre bioprinting centre of excellence.
- The strategic partnership between UCD and Icon Plc for Data Analytics. Icon has funded several academic positions. It is helping to produce a pool of Masters students each year.
- AbbVie partners with IT Sligo, and with local schools, on skills development for the next generation of leaders in biopharmaceuticals.
- NIBRT emerged from a collaboration between UCD, Trinity, DCU and IT Sligo. It is a successful exercise in collaboration and shared goal-setting, backed by the Government.
- FutureNeuro - an SFI-funded research centre connecting national and multinational industry with academics and clinicians based in leading hospitals to provide diagnostic, therapeutic and eHealth solutions.
- SFI research centres connect industry, science and academia in solving specific industry problems.

Ireland should target focus areas in biopharmaceutical innovation and back them with a coherent policy framework.

- Ireland has been successful over the past 30 years in small molecule and biologics manufacturing. The growth of the industry was facilitated by a favourable and stable enterprise policy environment sustained over decades. Ireland should plan now for the next decade and more of biopharmaceutical innovation.

- Digital technology and traditional medicine are combining in a way that is transforming health management. Digital therapeutics and diagnostics are reshaping our understanding of medical conditions and helping to personalise interventions. Data will play a much bigger role in the evolution of healthcare innovation, with outcomes tracked and measured so that improvements can be made in treatments and how we pay for them. The lines between the major players in biopharmaceuticals, technology and medical technology will, over time, blur.

- As well as advanced therapy medicinal products (ATMPs), cancer immunotherapies, genomics, Industry 4.0 and continuous-flow manufacturing can be strong drivers of future investment. Ireland is among the largest manufacturers of immunotherapies globally. In the first nine months of last year, biopharmaceuticals accounted for 62% of the goods sold abroad. Our industry has dominated growth in exports over the past 18 months.

Overview of the BioPharma Policy Forum Discussions

- Ireland will need a Strategy, co-created by industry and the State, that seeks to make the most of Ireland's potential in emerging areas like ATMPs, Industry 4.0, immunotherapies and genomics. This Strategy must aim to create the best operating environment for medicines innovation. That includes a focus on skills and talent, tax, research, intellectual property rights and faster access to new medicines for patients.

- The industry should take the lead in calibrating how best to invest in Industry 4.0 and work with the government on identifying the right focus areas, as well as the regions that could become centres of excellence for manufacturing. Ireland should maintain the industry's deep regional footprint.

- Innovation districts or hubs should be developed near universities or health research centres. These are possible in Dublin and in other locations. Policies to support the development of districts or hubs could borrowed or adapted from other countries like Belgium.

ATMPs should be a key focus area.

- ATMPs are forecasted for exponential growth over the next five years and more. Most new biopharmaceutical companies are in the cell and gene therapy (CGT) space with a significant focus on oncology and rare diseases.

- CGTs are expensive, ranging from US$200,000 to US$2 million per treatment, and they typically treat small patient populations. CGTs deliver significant downstream savings to the health service over the longer term. CGTs are here to stay and these novel therapies should be integrated into current health service strategies.

- The increase in marketed CGT products is leading to competitive pricing models. Value-based pricing and shared-risk models are needed for effective reimbursement of these one-time, often curative treatments.

- Ireland needs to establish a team, led by the State but with participation from industry and others, to set out and implement a roadmap for developing CGT capability. The UK created the Catapult Programme some 10 years ago. It has delivered more than 4,000 industry collaborations and over 1,100 academic collaborations.

- Ireland will compete to manufacture ATMPs. It could compete to treat patients, too. Initially, ATMPs will focus on rarer, hard-to-treat disorders that will require skilled delivery. Patients may have to travel to centres of excellence outside Ireland for treatment if the skills and infrastructure are not available here.

Overview of the BioPharma Policy Forum Discussions

- CGT treatment centres are needed in Ireland. We will need to upgrade our infrastructure including:
    - The creation of registries supported by electronic health records and access to diagnostics.
    - A reimbursement system capable of accommodating one-time, curative treatments.
    - Accredited staff in hospitals to treat patients.
    - A talent pool experienced in the manufacture of ATMPs.

Ireland should invest in health data and clinical trials infrastructure.

- Clinical trials are used to evaluate the safety and effectiveness of a medicine. Clinical trials can save lives and improve patient care. A strong clinical research infrastructure gives patients access to sometimes life-saving trials.

- Patients have been shown to have significantly better health outcomes by taking part in clinical trials. As well as the positive human health impact, clinical trials enhance the value proposition for innovation on which Ireland needs to keep working to secure future global investment in manufacturing and discovery activity.

- Site contracts (the Clinical Trial Agreement) should be standardised. This would shorten delays and save on legal fees for both hospitals and companies. There should be protected research time for clinicians and hospital staff. We should set realistic targets for clinical trials. This means meeting a lower target is better than partially meeting a higher target.

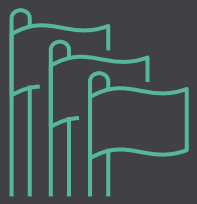
- The absence of a proper health data infrastructure makes it hard to attract clinical trials for new medicines. In the future, patients will likely have access to their own genomic data and medicines will be more personally tailored. Ireland must build a system for electronic medical records that is secure and available. This will likely be an important requirement for companies choosing to invest in Ireland.

Attendance

The following organisations attended the BioPharma Policy Forum: PwC; UCD; Our Lady's Children's Hospital, Crumlin, Dublin; Astellas; AbbVie; Orbimed; Department of Business, Enterprise and Innovation; GSK; Janssen; Eli Lilly & Company; BPCI; IPHA; NIBRT; Innopharma; American Chamber of Ireland; Cancer Trials Ireland; CF Ireland; Chambers Ireland; Health Products Regulatory Authority; Health Research Board; HRB-CRCI; IDA Ireland; Enterprise Ireland; Pfizer; Health Innovation Hub Ireland; UCC; UL; DCU; Takeda; MSD; United Drug; Novartis; Department of the Taoiseach; Department of Public Expenditure and Reform; IPPOSI; Trinity; and the Department of Health.

We asked PwC to set the scene for the BioPharma Policy Forum with a SWOT analysis of Ireland's biopharmaceutical industry.

Context



The partners behind BioPharma Ambition, IPHA, BPCI and NIBRT, want to deepen stakeholder understanding about the future for medicines innovation, so that Ireland's biopharmaceutical industry continues to scale, attract investment and support jobs across the regions.

To do this, the partners are inviting leaders across industry, government, research, academia and patient advocacy to a Policy Forum to share perspectives and start to shape a vision for Ireland's future in biopharmaceuticals across the lifecycle.

PwC aims to set the scene for the Policy Forum with an analysis of Ireland's biopharmaceutical industry - its strengths, weaknesses, opportunities and threats. This work is designed to complement the Government's evolving 'Future Jobs' enterprise agenda.

High-level Messages

Biopharmaceuticals will play an important role in the future of Ireland from both a domestic health policy and economic development point of view.

Economic development:

- Ireland has an outsized biopharmaceutical manufacturing presence, relative to other big sectors and to other similar-sized countries.
- This should not be taken for granted, especially when we look at product life cycles, industry consolidation patterns and the draw of emerging markets.
- The development of Advanced Therapy Medicinal Products (ATMPs) is likely to explode in the coming years. For many companies, the pipeline of complex biologic medicines is strong. The dividend of pursuing a strategy that plays to both strands will be distributed clinically and economically.
- However, the future of the biopharmaceutical industry in Ireland should not be a binary choice between continuous improvement in new medicines and the development of ATMPs.
- If sectors like technology, medical technology and biopharmaceuticals are converging, similarly the gap between industry, policy, research and clinical leaders is narrowing.
- Unless we find a way to connect us all together into a broad life sciences strategy, Ireland could lose competitiveness for new investments in manufacturing and research.

Health policy:

- By 2040, an extra million people will live in Ireland. An additional two-thirds of a million people will be working. By 2030, one in six people will be over 65 and there will be twice as many people aged 85 and over.
- This change will challenge our health system like never before to deliver care to more people than ever and to treat more complicated diseases associated with an ageing population.
- Medicines innovation will have a major role in maintaining population health and tackling unmet clinical need in the coming decades.

Biopharmaceutical companies have created a thriving industry that makes an economic and societal contribution to the EU

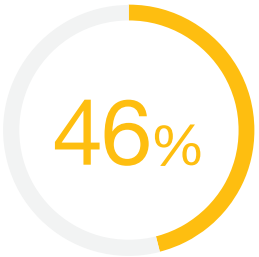
We have shown that the whole of the biopharmaceutical industry across the EU in 2016 contributed to...

€206 billion

in Gross Value Added and...

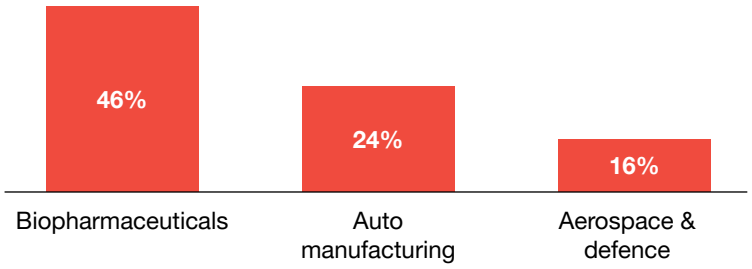
2.5 million

jobs



of people employed directly by the industry are women

Share of female employees



Medicines benefit millions of people on a daily basis. In just a subset of medicines within HIV (HAART) and breast cancer (HER2+, HR+) we saw that...

Over 650,000

people in the EU were treated with these medicines between 2007–2017, who are estimated to have gained around...

€27 billion

In productivity gains for EU economies, and approximately...

2 million

healthy life years, leading to around...

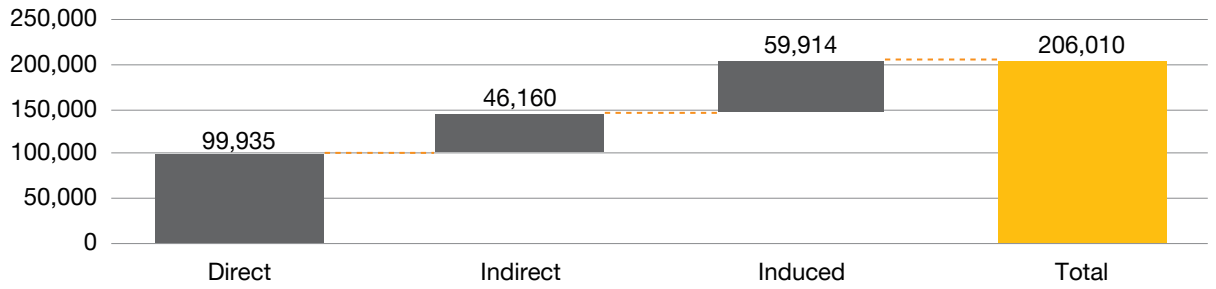
€13 billion

in healthcare cost savings due to avoided complications

The biopharmaceutical industry drives economic growth in the EU both in terms of GDP and jobs contribution

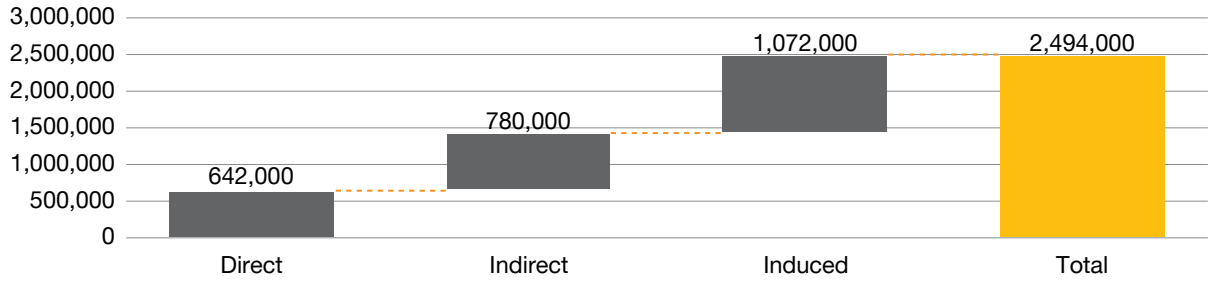
The biopharmaceutical industry supports a total of 1.4% of the EU's GDP

GVA impact of the biopharmaceutical industry on the EU (€, millions)



The biopharmaceutical industry supported nearly 2.5 million jobs across the EU

Employment impact of the biopharmaceutical industry on the EU



We have conducted a SWOT analysis of the biopharmaceutical industry in Ireland with a focus on 12 analyses

Strengths

1. Significant presence established in Ireland
2. Broad regional distribution with multiple centres of gravity
3. Quality and experience of Irish workforce

- Strong research capability in place
- Presence of a deep manufacturing, supply chain, finance and services base

Weaknesses

6. Potential benefits from next generation therapeutics will be difficult to capture without significant investment
7. Lack of a guiding strategy in developing next generation skills and platforms innovation
8. Significant risk of offshoring production of generic drugs
9. Late adopter of new medicines

Opportunities

4. ICT convergence for smart manufacturing
5. Next generation therapeutics driving future industrial and financial growth

- Leverage Medtech capability to drive next generation biopharmaceuticals

Threats

10. M&A activity in biopharmaceutical resulting in dominance of a small number of players
11. Competitiveness or loss of competitiveness
12. Potential underinvestment in creating the “workforce of the future”

- Nationalist-driven trade policies potentially harming FDI
- Significant potential competition from emerging markets
- IP Incentives framework erosion

Ireland's biopharmaceutical sector is a success story...

Manufacturing

15 of the top 20 biopharmaceutical companies have manufacturing sites in Ireland

Employment

30,000 people directly employed

Regionally distributed

High quality biopharmaceutical jobs are very well distributed throughout the country

Exports

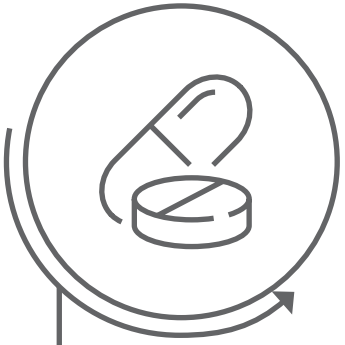
Over €73 Bn worth of goods exported in 2018

Leading FDI position

Current FDI position for the sector far exceeds that of competitor nations

Home of top products

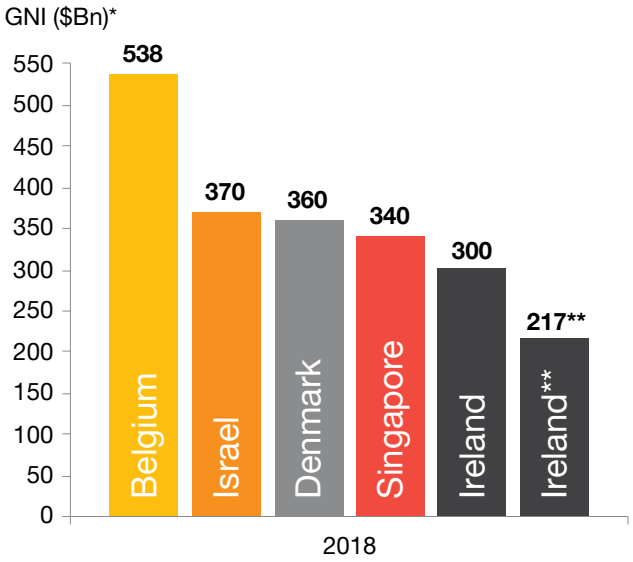
50% of the top 20 selling products in 2018 were made in Ireland*



*By revenue. Irish involvement at some point in value chain

When Ireland's economy is compared to those of competitor nations, it is clear that Ireland punches above its weight regarding biopharmaceutical exports

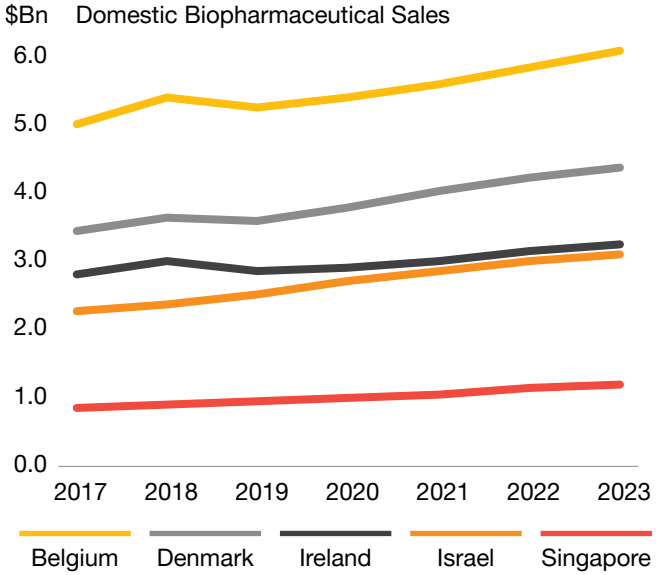
Whilst Ireland's economy is smaller than those of the benchmark countries…



*Current US$
**Modified GNI (GNI*)

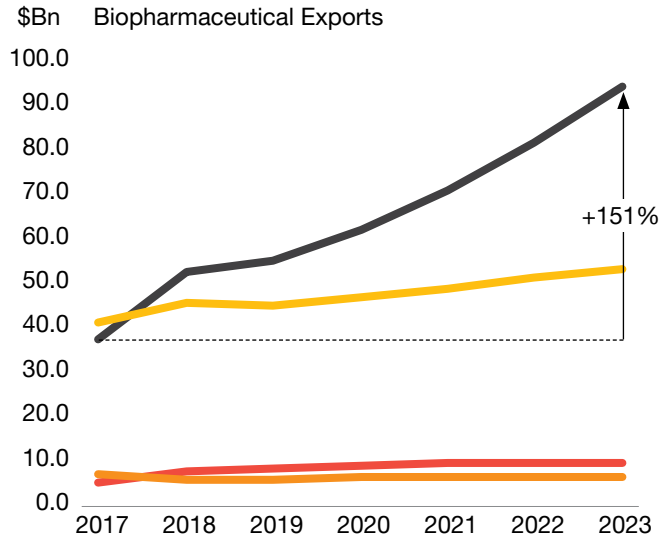
Sources: World Bank, CSO

…and domestic biopharmaceutical sales reflect this…



Source: FitchSolutions

…its biopharmaceutical exports are expected to grow at a far higher rate in the near term

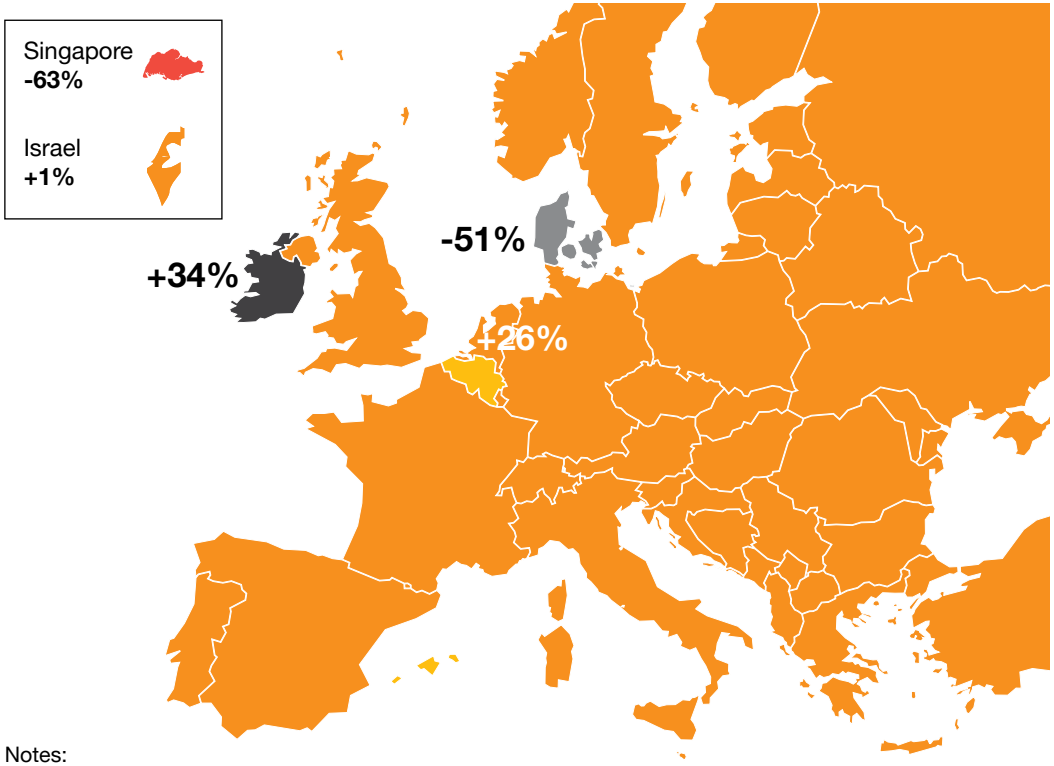


*Denmark projections unavailable

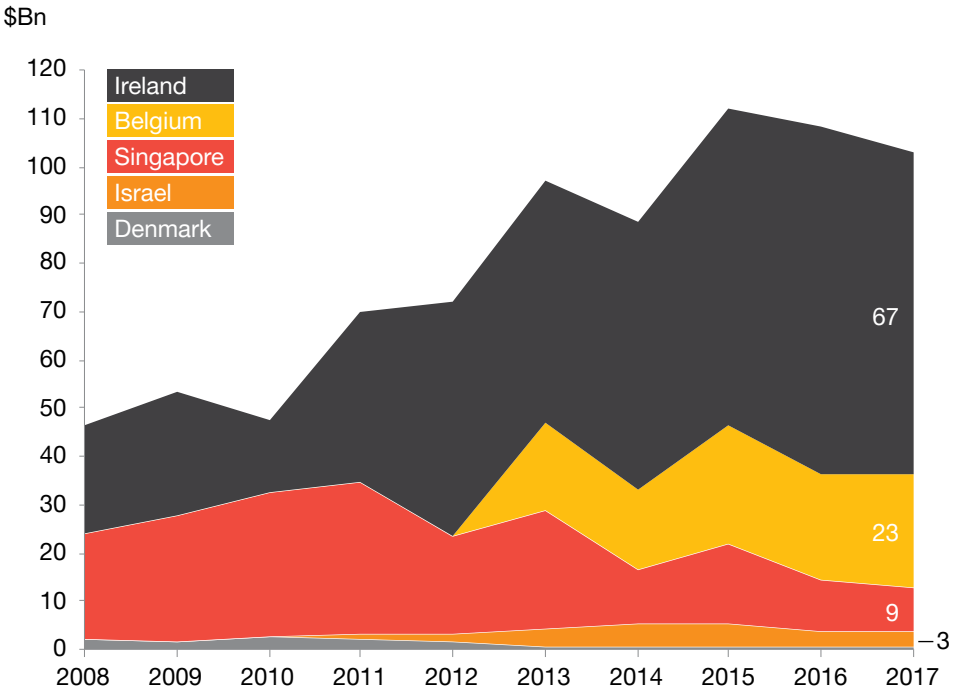
Source: FitchSolutions

Ireland has a clear strength in attracting and retaining FDI compared to peer countries

Net Inward FDI Biopharmaceutical Position growth 2013 - 2017



Net Inward FDI Position due to Biopharmaceutical Industry



Notes:

1. FDI positions represent the value of the stock of direct investments held at the end of the reference period (typically year or quarter). The change in direct investment positions from one period to the next is equal to the value of financial transactions recorded during the period plus other changes in prices, exchange rates, and volume.
2. FDI positions include equity capital, reinvested earnings, and other capital (e.g. intercompany debt)
3. OECD data refers to C21: Manufacture of basic biopharmaceutical products and biopharmaceutical preparations
4. SingStat data refers to biopharmaceutical products
5. Singapore data converted to USD using average closing price

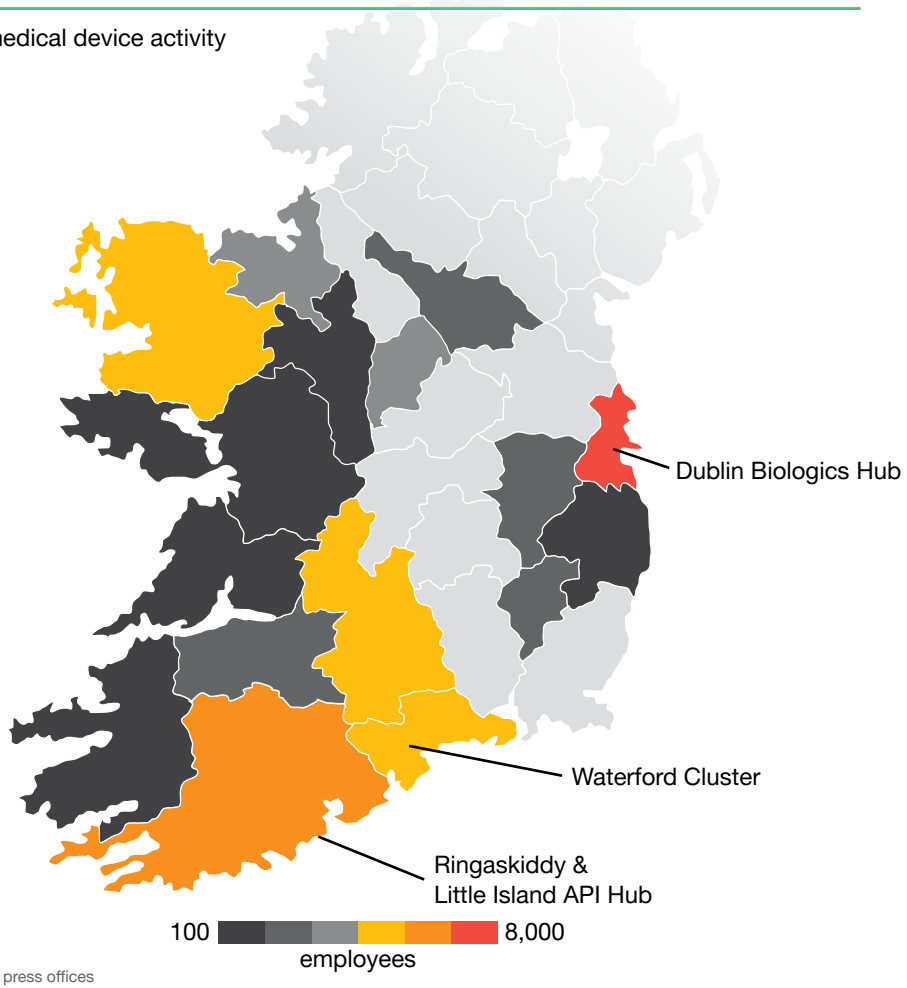
*Whilst both the OECD and the Singapore Department of Statistics produce FDI data in accordance with the IMF's Balance of Payments Manual, some variations in methodology may exist.

Sources: OECD: FDI by country and economic activity BMD4 and historical BMD3 series, SingStat:M084831 - Foreign Direct Investment In Singapore By Industry (Stock As At Year-End), Annual

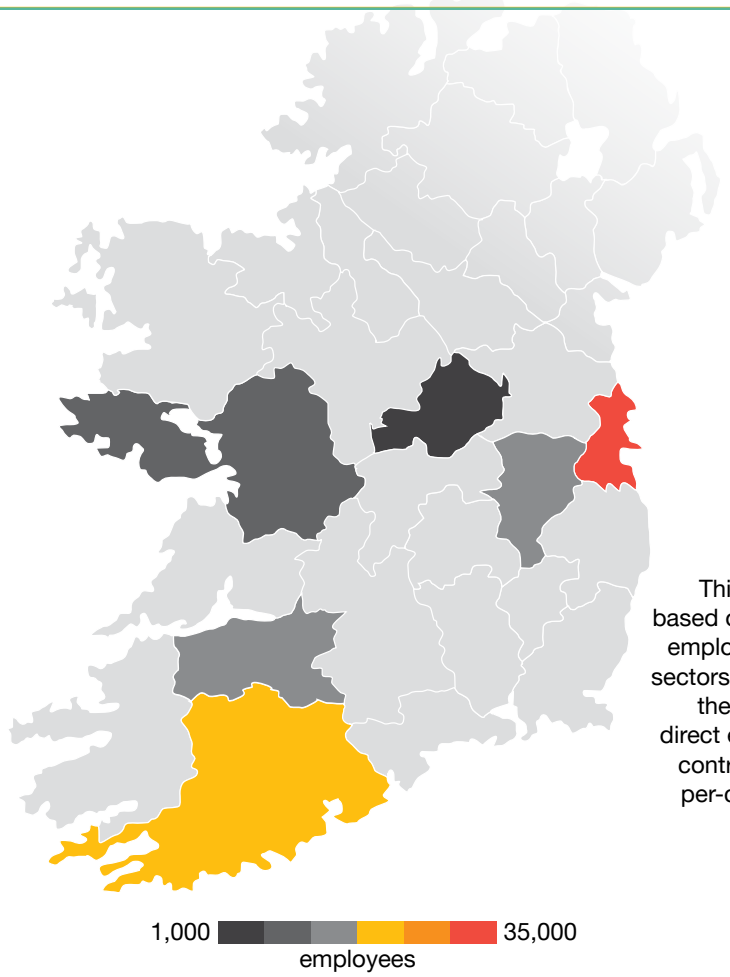
The biopharmaceutical industry in Ireland is broadly distributed across the regions compared to technology with hubs in Dublin and Cork

Direct employment – top 20 Biopharmaceutical companies*

*Excludes medical device activity



Direct employment – top 20 Technology companies



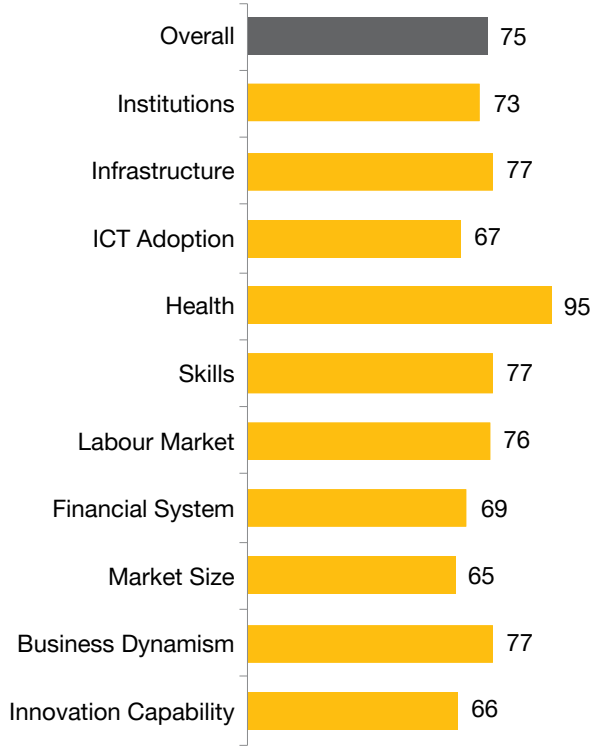
This analysis is based on the major employers in both sectors, and shows the aggregated direct employment contribution on a per-county basis

Source: Company press offices

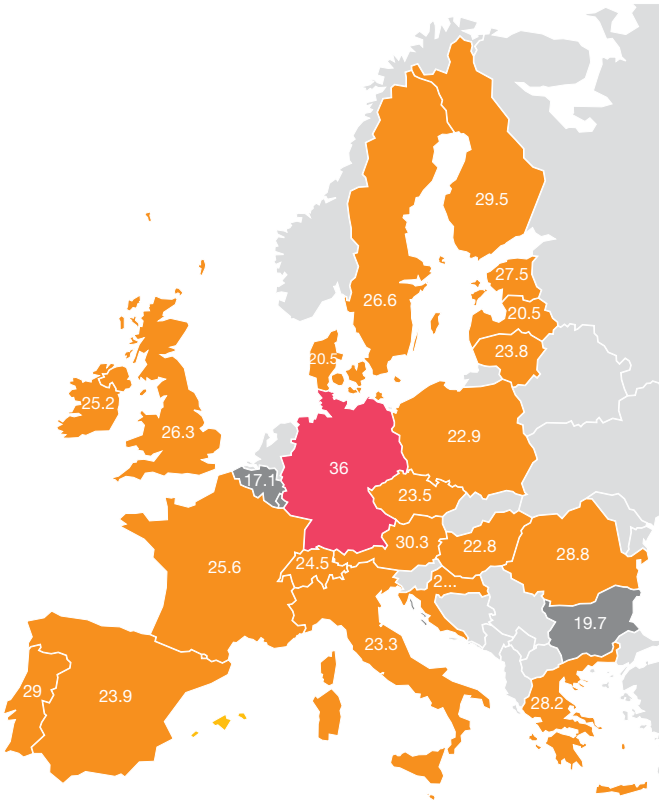
Ireland rates highly in general competitiveness, STEM graduates and biopharmaceutical patents

Ireland in the World Economic Forum's Global Competitiveness Index 2019

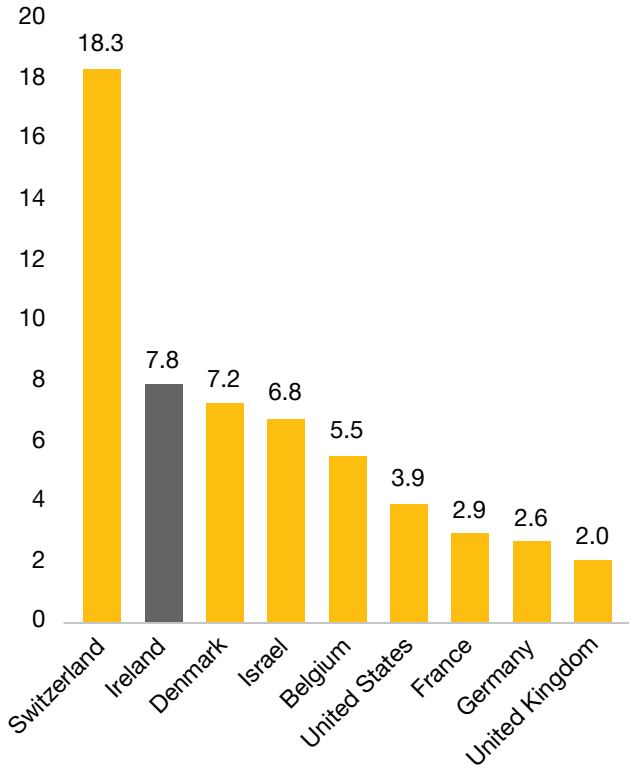
Comparison of 141 economies accounting for 99% of global GDP; maximum score 100



Percentage of Graduates in Science, Technology, Engineering and Mathematics (2016)



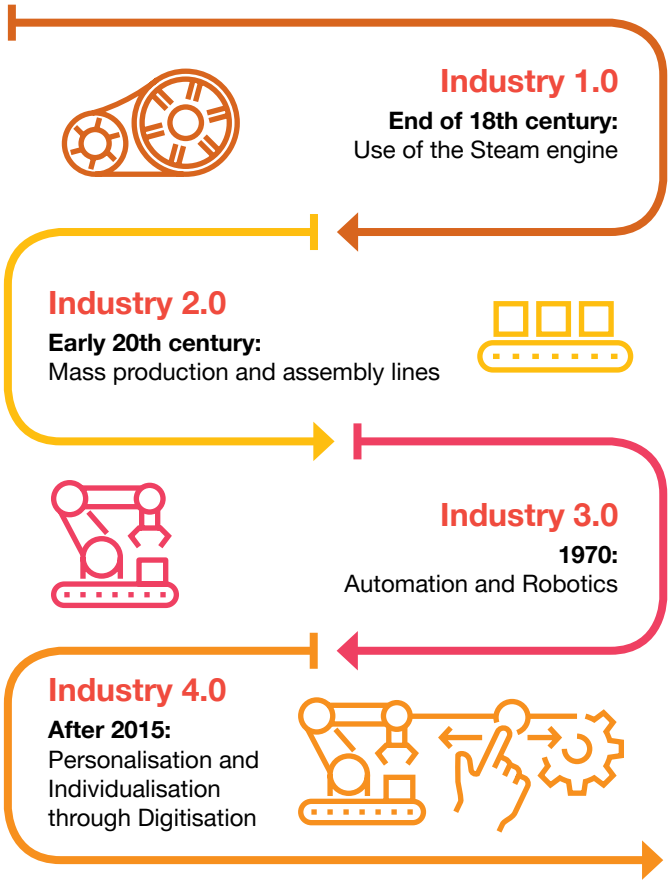
Biopharmaceutical Patents Granted in 2018 per Million of Population



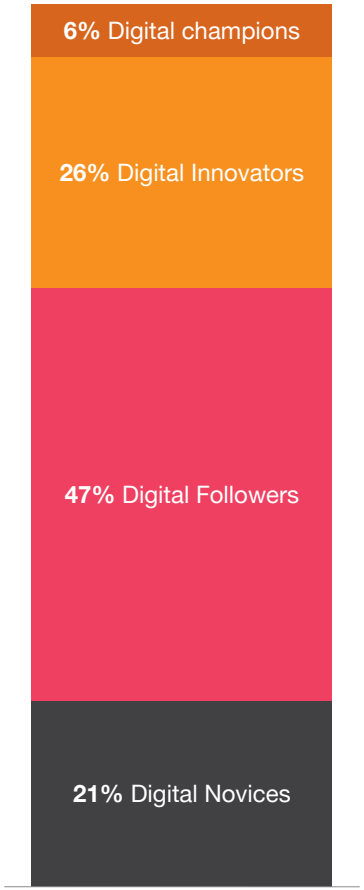
Sources: UNESCO/UIS, European Patents Office, World Bank, World Economic Forum

ICT improvements are driving a 4th industrial revolution and this will drive significant change in biopharmaceutical manufacturing and operations

Digitisation is driving a fourth revolution in production…



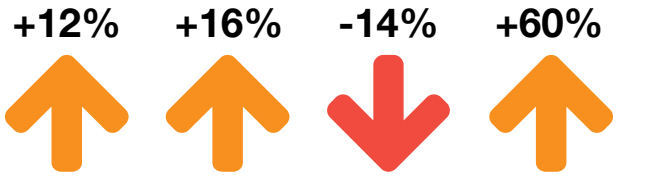
…with biopharmaceutical companies being primarily digital followers…



Source: PwC Strategy & Digital Operations Survey 2018

…However they still expect to realise significant gains

Average expected impact of Industry 4.0 on the biopharmaceutical industry



$30bn increase in revenue

$50bn reduction in cost

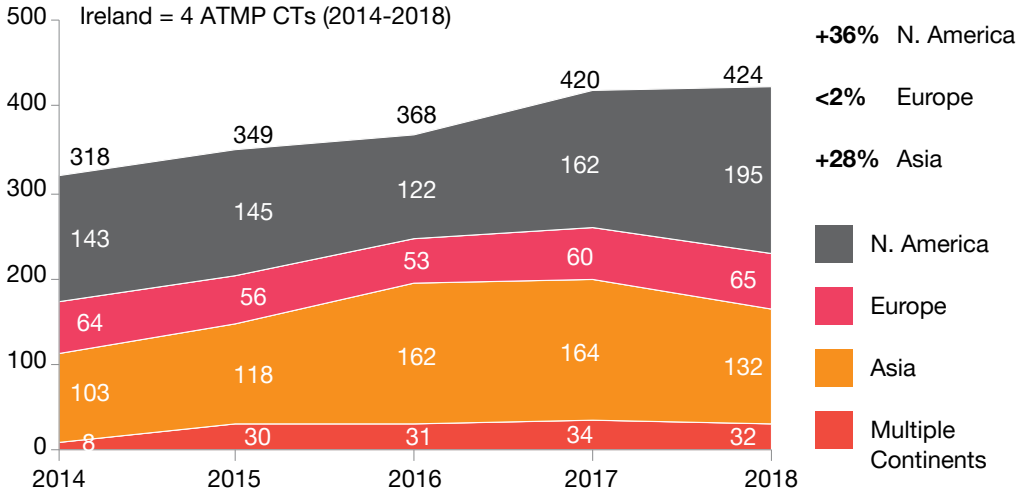
Source: PwC Strategy & Digital Operations Survey 2018

Advanced Therapeutic Medicinal Products (ATMPs) will be a high growth area over the next 6 years

Single shot Cell and Gene Therapies are transforming lives

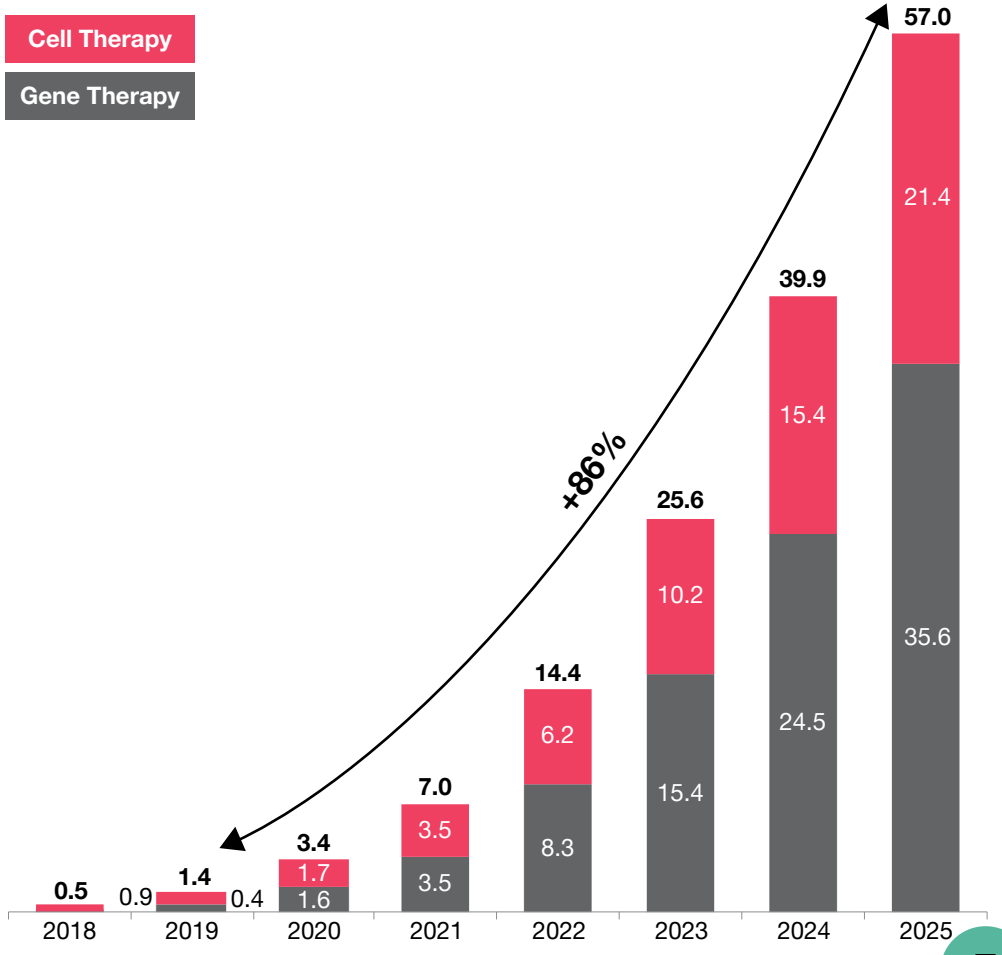
	Disease	Without Cell & Gene Therapy	Impact
Therapy A	Acute Lymphocytic Leukaemia	Likely Death	82% remission rate
Therapy B	Retinitis pigmentosa	Blindness	Sight Returned
Therapy C	Spinal Muscular Atrophy	Childhood death	After 24 mnts: 100% survivability

Clinical trials for ATMPs are growing to match



Note: ATMP CTs initiated only in South America, Africa, Oceania were excluded
Figures above represent the number of clinical trials initiated in a continent per year
Source: Alliance for Regenerative Medicine – Clinical Trials in Europe: Recent Trends in ATMP Development

The Global Cell and Gene Therapy Market will grow significantly



All figures are in $Bn
Source: GlobalData: Drug Sales and Consensus Forecast (2015-2025)

Ireland lags other key European competitors in putting in place enablers to succeed in advanced therapeutic medicinal products (ATMPs)

	Ireland	Belgium	United Kingdom	Ireland's Position
1 **Supportive Clinical Trial Environment**	• 4 ATMP CTs initiated 2014-2018 • 60 day assessment timeline for CTs	• 56 ATMP CTs initiated 2014-2018 • 15 day approval time for Phase 1 CTs • 2nd in EU for CTs per inhabitant	• 112 ATMP CTs initiated 2014-2018 • 40 day approval time, 21 days for "first-in" CTs	↓ Lagging
2 **Favourable Tax Environment & R&D Incentives**	• 12.5% corporate tax rate • 25% R&D tax credit • Knowledge development box	• 29.5% corporate tax rate (20% for SMEs) • Innovation Income Deduction for R&D / IP • Tax exemptions for employing people with advanced STEM degrees	• 19% corporate tax rate (2020) • R&D tax credits • Patent Box	↑ Leading
3 **Excellence in Academic / Clinical Research**	• NIBRT • REMEDI at NUIG • Centre for Cell Manufacturing Ireland	• Large network of universities / hospitals • Wallonia has 5 universities and >30 labs active in gene therapy	• CGT Catapult Programme • World class universities / hospitals	↓ Lagging
4 **Strong Funding for Entrepreneurs & Startups**	• Small individual funding opportunities	• >€400m public & private funding in ATMP research from 2006 – 2015 • Several BioTech Incubators	• £775m raised in 2018 for ATMPs • Innovate UK have strategic focus on ATMPs	↓ Lagging
5 **High Quality Manufacturing Facilities**	• Takeda ATMP facility • Existing biopharmaceutical facilities could be converted for ATMP production	• MaSTherCell – 600m2 ATMP CDMO • Cell & Gene Therapy Lab – 220m^2 ATMP CDMO	• Cell and Gene Catapult Manufacturing Centre • 25 Manufacturing Facilities • ~20,000m^2 footprint	↓ Lagging
6 **Dynamic Innovation Ecosystem**	• 5 ATMP companies • 10 of Global Top 10 biopharmaceutical producers	• 11 ATMPs companies • Wallonia Health Cluster (BioWin)	• 70 ATMP companies (56 headquarters) • Advanced Therapy Treatment Centre Network	↓ Lagging

In addition, ATMP manufacturing plants will not bring the same investment and job numbers that traditional biopharmaceutical plants have

Cell and Gene Therapy Manufacturing Plants

Plant	Location	Size	Approximate No. of Employees
Lonza	Houston, Texas	300,000 ft²	200+
Paragon	Maryland	151,000 ft²	100
Pfizer	Durham, North Carolina	60,000 ft²	120
Lovance*	Philadelphia	136,000 ft²	300-400
MaSTherCell* (owned by Orgenesis)	Belgium	61,000 ft²	300-400
CellVec	Singapore	5,382 ft²	10
AveXis	Durham, North Carolina	85, 749 ft²	200
WuXi	Pennsylvania	150,000 ft²	200
Anemocyte	Italy	26,910 ft²	30
ElevateBio	Massachusetts	100,000 ft²	50
	Median	**93,000 ft²**	**160**

* Plant is under construction

Source: Company press releases and associated collateral

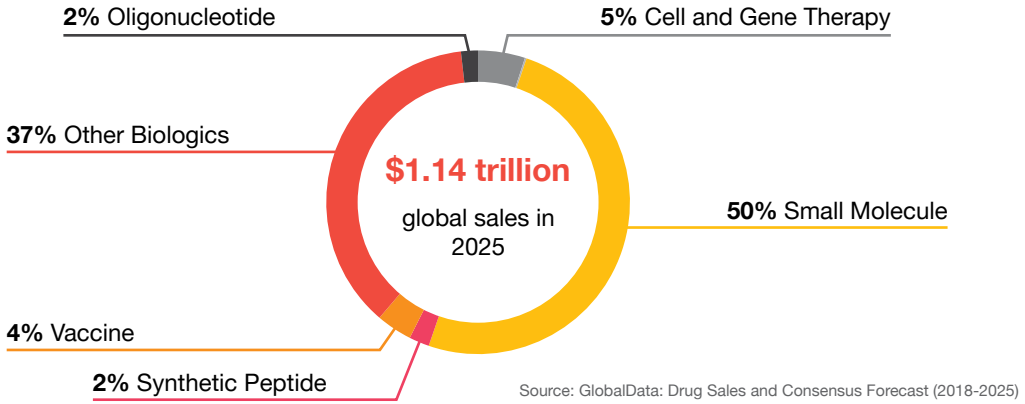
Biopharmaceutical Manufacturing Plants Ireland

Plant	Location	Size	Approximate No. of Employees
Pfizer	Grange Castle Dublin	>1 million ft²	1,539
Pfizer	Newbridge, Kildare	>1 million ft²	800
Pfizer	Ringaskiddy, Cork	Site >200 acres	600+
Novartis	Ringaskiddy, Cork	914,932 ft²	375
Eli Lilly	Kinsale, Cork	240,000 ft²	700
MSD	Swords, Dublin	610,000 ft²	350
BMS	Dublin	322,917 ft²	130
Takeda	Meath	120 acre site	400
Abbvie	Sligo	110,000 ft²	200+
Takeda	Dublin	140,070 ft²	120
Amgen	Dublin	536,043 ft²	300
MSD	Carlow	200,000 ft²	670
	Median	**430,000 ft²**	**700**

Note: Pfizer Ringaskiddy and Takeda plants excluded from median calculations as exact plant sizes unavailable

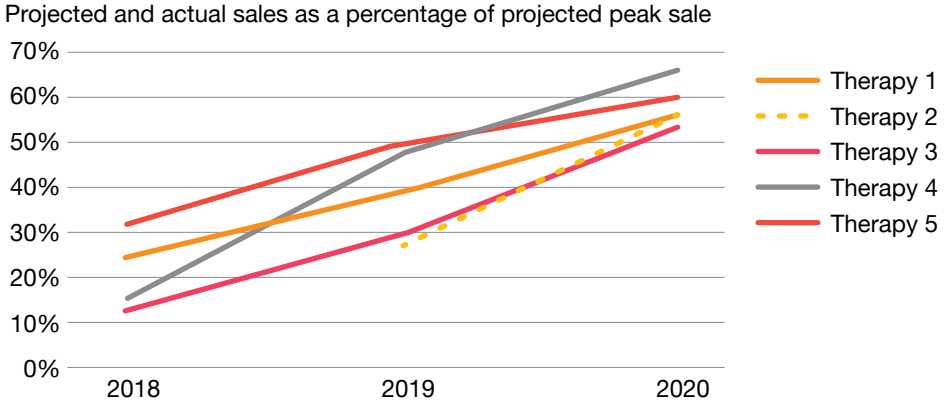
There are a number of challenges ATMPs must overcome to deliver on its early promise

Cell and Gene Therapy sales will be equivalent to 5% of Global Prescription Drug Sales in 2025



Source: GlobalData: Drug Sales and Consensus Forecast (2018-2025)

Cell and Gene Therapies have seen slow growth in sales after launch



Source: PwC Health Research Institute analysis of Evaluate Pharma historical sales data and consensus sales estimates. As of August 1, 2019.

Therapies will target small numbers of patients

Product Name	Disease	Est. US Patient Population
Therapy A	Relapsed or refractory Diffuse Large B-Cell Lymphoma (DBCL)	24,000 patients per year
	Acute Lymphocytic Leukemia(<25 yrs old)	600 patients per year
Therapy B	Inherited retinal disease	1,000 – 2,500 patients in total
Therapy C	Spinal muscular atrophy (Child < 2yrs)	300 - 450 patients per year
Therapy D	Relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy.	24,000 patients per year
Therapy E	Melanoma	7,200 patients per year

*Source: PwC Health Institute Analysis (cost per treatment sourced via company websites and press releases)

WEAKNESS

Ireland lacks a guiding approach for Industry 4.0 initiatives

Country	Core approach	Strategic direction set by	Primary funding	Impact
Ireland	**Strategy under development – due 2020**	Public Led / Mixed / Industry Led	Public Led / Mixed / Industry Led	• €45m invested in 2 core research centres • Focus on industry/academic partnerships
Denmark	**Industry led** initiative to ensure Denmark's readiness for I4.0	Public Led / Mixed / Industry Led	Public Led / Mixed / Industry Led	• €50m budget for 2014-19 • 143 initiative members • 70 industrial projects supported
Belgium	**Industry led** initiative focused on transforming manufacturing into the "factory of the future"	Public Led / Mixed / Industry Led	Public Led / Mixed / Industry Led	• 265 companies currently involved in the programme
Singapore	**Public led** initiative focusing on support for upgrading facilities	Public Led / Mixed / Industry Led	Public Led / Mixed / Industry Led	• Developed Smart Industry Readiness Index and provides upgrade planning support
United Kingdom	**End to end support** of advanced manufacturing through the creation of the High Value Manufacturing Catapult	Public Led / Mixed / Industry Led	Public Led / Mixed / Industry Led	• €164 million invested by UK Government over 2012 – 2018 period • 2015/16: €79.7m commercial revenue achieved

Ireland manufactures a significant proportion of the leading biopharmaceutical products but will need to combat LOE in the medium term

	2018	2024	% Change	Trend
Revenue from top 20 selling products worldwide	$143 Bn	$180 Bn	+26%	
Number of top 20 selling products manufactured in Ireland	10	9	-10%	
Revenue from top 20 selling products manufactured in Ireland	41% ($59 Bn)	45% ($82 Bn)	+4% (+39%)	
Irish manufactured top 20 drugs with LOE in 5 years time	60%	90%	+50%	

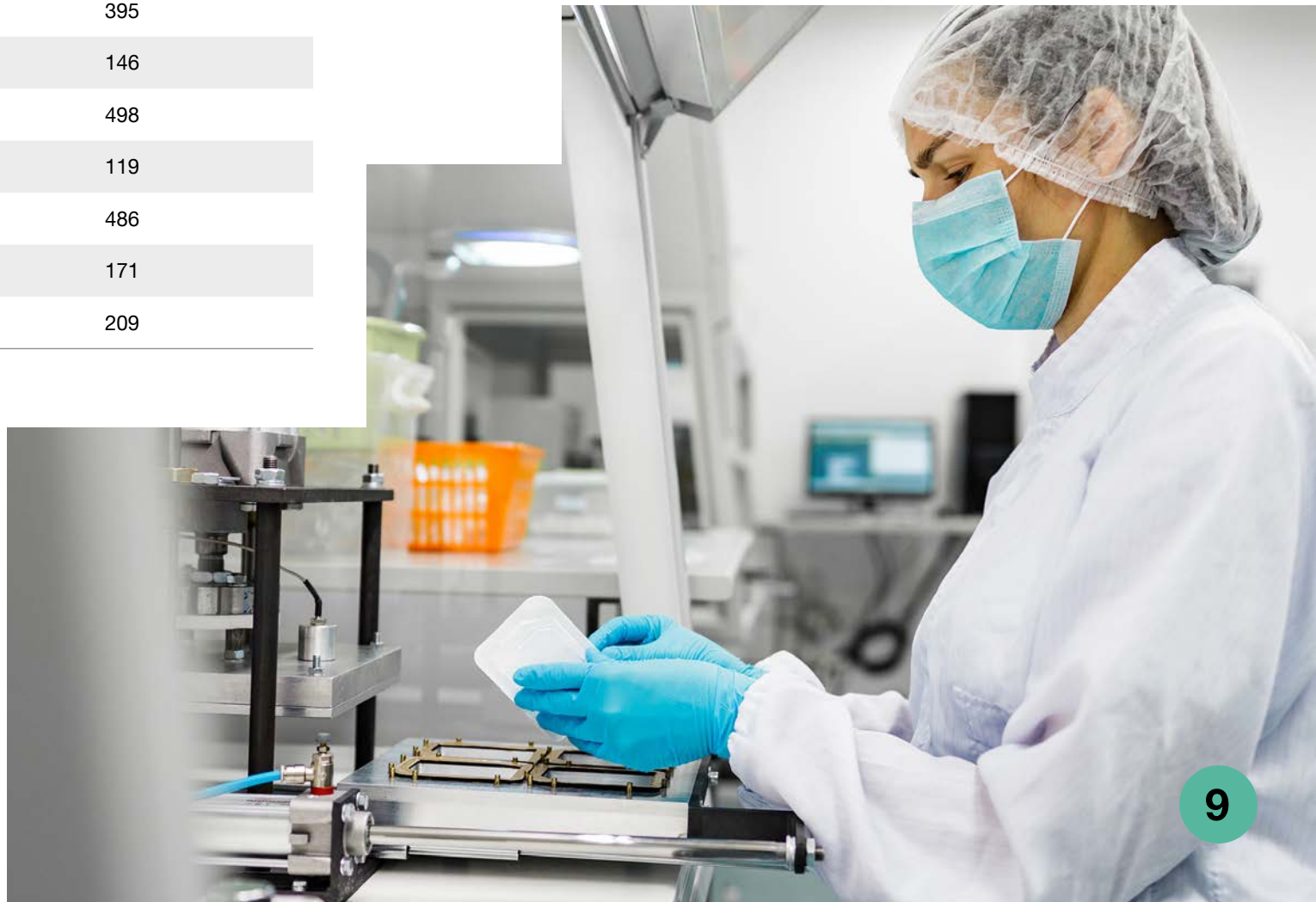
Immediate impact likely to be mitigated by high number of biologics

Sources: GlobalData, EvaluatePharma

Ireland is a late adopter of innovative medicines

Patients' waiting time to access innovative therapies across Europe (2018)

Country	Rate of Availability (%)	Length of Market Access Delays (average number of days)
Belgium	56	395
Denmark	83	146
France	60	498
Germany	86	119
Ireland	42	486
Switzerland	74	171
United Kingdom	88	209



The top 10 biopharmaceutical companies have increasingly used M&A to maintain their position and this is likely to continue in the future

Top 20 biopharmaceutical companies by 2018 revenue, and select deal activity since 2009

Rank (Vs 2008)		Organisation		No. Deals > $ 2 Bn
1	—	Johnson & Johnson	☘	2
2	↑ 3	Roche		2
3	↓ 1	Pfizer	☘	6
4	↑ 2	Novartis	☘	3
5	↓ 2	Bayer		1
6	↑ 4	Merck & Co.	☘	4
7	↓ 3	GlaxoSmithKline	☘	3
8	↓ 1	Sanofi	☘	4
9	→	AbbVie	☘	3
10	↓ 1	Abbott Laboratories	☘	-
11	↑ 2	Eli Lilly & Co.	☘	1
12	→	Amgen	☘	2
13	↓ 1	Bristol-Myers Squibb	☘	5
14	→	Gilead Sciences	☘	2
15	↓ 7	AstraZeneca		2
16	↓ 1	Boehringer Ingelheim		-
17	→	Teva Pharma.	☘	5
18	↓ 2	Takeda Pharma.	☘	2
19	→	Novo Nordisk		-
20	→	Allergan	☘	5

— No Change

↑ Upward move

↓ Downward move

→ New entrant

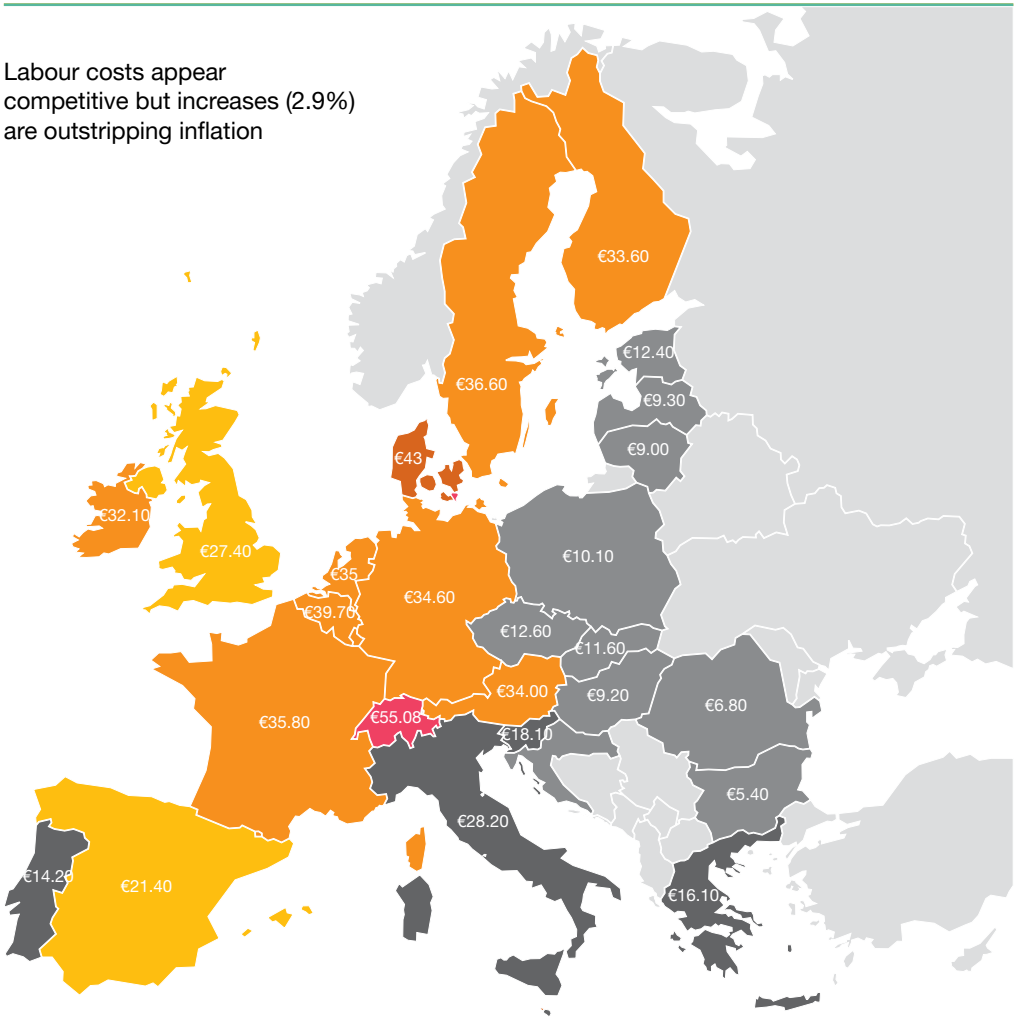
☘ Irish manufacturing

Sources: Annual reports, Capital IQ

Ireland's competitiveness is under pressure from rises in labour, services and construction costs

Average Hourly Labour Costs (2018)

Labour costs appear competitive but increases (2.9%) are outstripping inflation



Service Cost Increase (2018)

Service	Cost Increase
Air transport	2.30%
Employment and HR Activities	4.70%
Industrial and Building Cleaning	2.30%
Architecture and Engineering	2.10%
Warehousing and Storage	6.80%

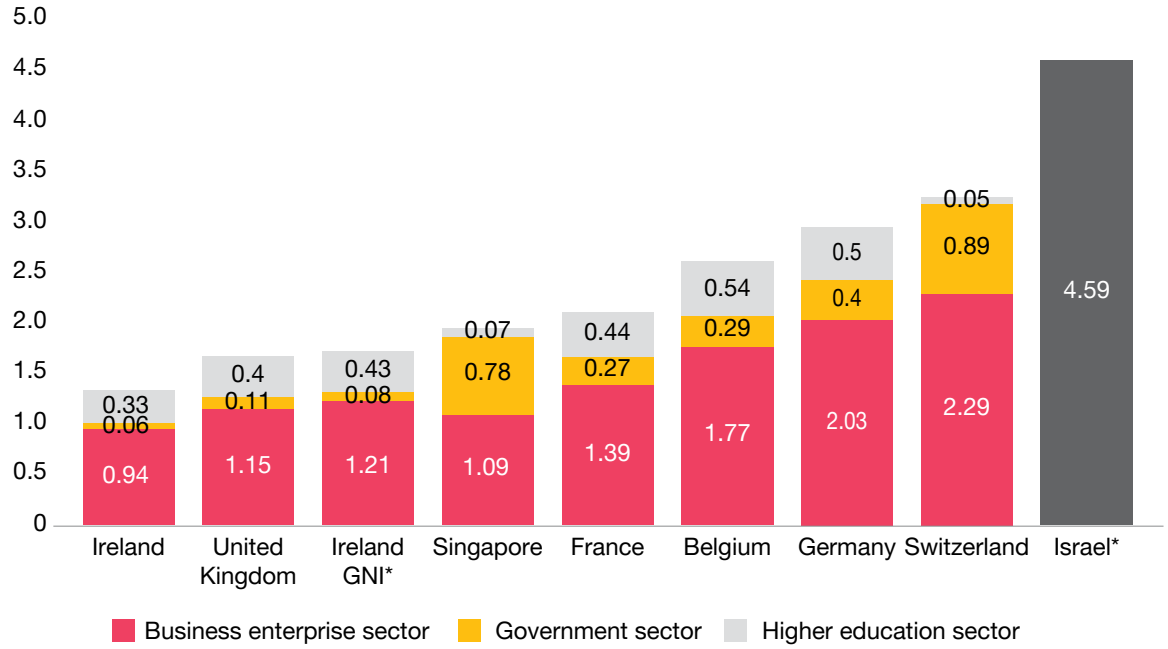
Construction Costs (2018)

City	Building cost per m² of internal area – USD
Zurich	$3,380
London	$2,895
Dublin	$2,824
Munich	$2,705
Amsterdam	$2,459
Singapore	$2,339
Paris	$2,232

Sources: Eurostat, Includes Wages, Salaries and Non-Wage Costs; please note that Switzerland value is from 2016 and is from the Swiss Federal Statistical Office, Turner & Townsend, International Construction Market Survey 2019, CSO

Ireland risks underinvesting in the key areas required to provide the biopharmaceutical workforce of the future

Research and Development Spending as a Percentage of GNI (2017)



Government Expenditure on Education as a Percentage of GNI (2017)

Country	Total Education Spending (% of GNI)	Tertiary Education Spending (% of GNI)
Denmark	6.3	1.6
Belgium	6.3	0.9
Switzerland	5.7	1.3
Ireland GNI*	5.3	0.8
France	5.3	0.6
United Kingdom	4.7	0.3
Ireland	4.1	0.7
Germany	4.0	0.8

*Modified GNI *Israel data from 2016 (2017 not available); source of funds not stated due to differences in calculation methodology

Sources: Eurostat & OECD; EFPIA Patient W.A.I.T. Indicator 2018 Survey

Some key questions to consider

- What should Ireland do to become a **global hub for the discovery, development and manufacture of innovative medicines,** whether complex biologics or ATMPs?
- **What level of investment** and commitment is appropriate for Ireland to **compete in advanced therapeutics** and on how broad a front do we want to compete (e.g. manufacturing vs general innovation hub)?
- Where should Ireland invest to **improve its innovation potential** and be recognised as such?
- Does the late adoption of **innovative medicines** impact our reputation as a leading hub for biopharmaceuticals?
- How can we continue to ensure a strong regional focus in biopharmaceutical investment?

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