Factors affecting the location of biopharmaceutical investments and implications for European policy priorities

Summary of report findings

3 October 2022

efpia – CRA Charles River Associates

Objectives of the report

OBJECTIVES

- To provide an up-to-date assessment of the drivers of investment location by look at:
  - Trends in R&D hubs, clinical trial location and types of manufacturing and key drivers
  - The impact on different types of technology (digital technology/artificial intelligence, gene/cell therapy and regenerative biology)
  - Recent economic and geopolitical events
  - Relating theory to real-life major investment decisions
- To provide recommendations on European policies to attract greater research, clinical trial, and manufacturing investments in the future

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Methodology

LIT REVIEW

- We assessed literature on **factors affecting location of investments** focusing on studies published over the last five years
- The range of literature reviewed include (# of articles):
  - Academic articles (52)
  - Consultancies' annual reports on investment trends and drivers (23)
  - Country specific innovation plans and country analysis of location factors (25)
  - Industry-led research and insights (15)
  - Grey literature (43)

DATA ANALYSIS

- We examined **quantitative historical data** to understand patterns of investment and relate these to the drivers of location choice identified in the literature review
- The range of data reviewed include:
  - Investment in R&D and manufacturing
  - Clinical trial locations
  - Location of ATMPs manufacturing
  - Level of employment in R&D and manufacturing
  - Foreign direct investment and exports

INTERVIEWS

- We selected **actual major investment decisions** and tried to un-tease the company specific and environmental factors through a series of interviews
- Interviews include (# of case studies):
  - Roche (2)
  - Merck (1)
  - MSD (1)
  - Moderna (1)
  - Eli Lilly (1)
  - Sanofi (2)
  - Menarini (1)
  - UCB (1)
  - Bayer (1)
  - Pfizer (1)
  - WuXi (1)
  - Takeda (1)
  - Biogen (1)
  - PTC Therapeutics (1)

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Summary of policy recommendations

Europe's relative decline in attractiveness as a centre for biopharmaceutical investment	1	Incentivise the development of truly world class innovation hubs in EU
	2	Enhance end-to-end capabilities and funding of disruptive pharma innovation
The impact of new technologies on dynamics and location of investment	3	Rethink policies along the supply chain to attract ATMP investment in Europe
	4	Support innovation by implementing early access mechanisms, including generation and use of real-world evidence
	5	Boost EU digital transformation and support development of digital capabilities
Learning from COVID-19 and managing risk and the external environment	6	Foster adoption of sustainable procurement and pricing policies for innovation
	7	Develop a longer-term, collaborative method for encouraging growth in Europe's attractiveness for biopharmaceutical investments

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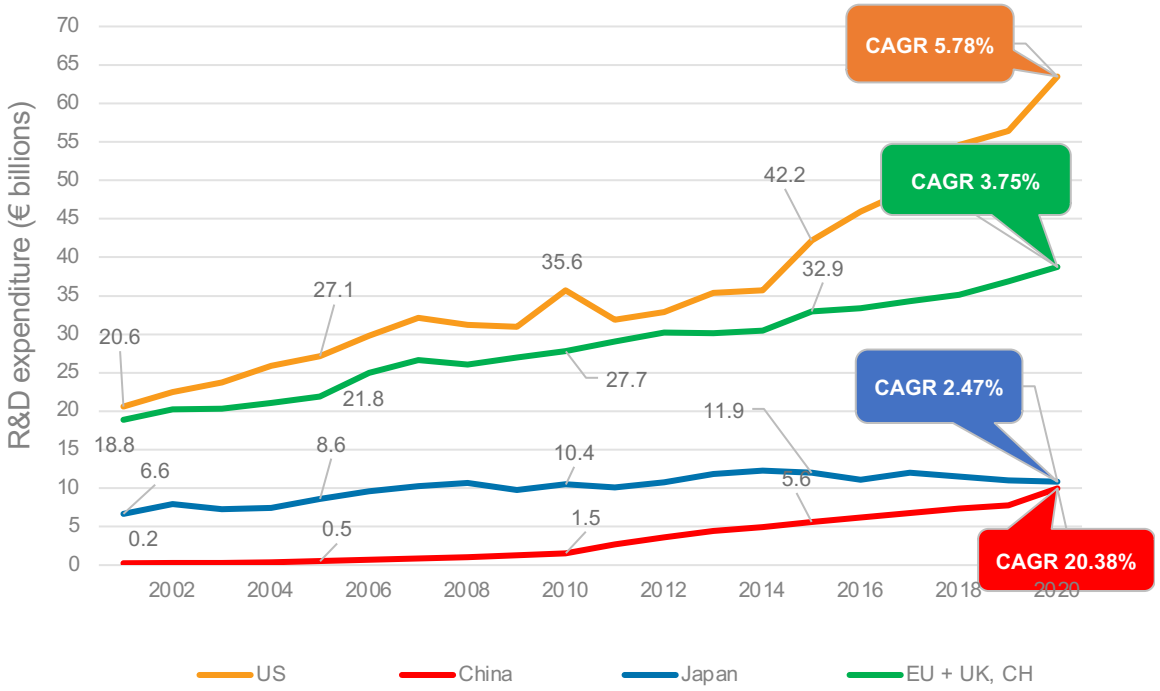
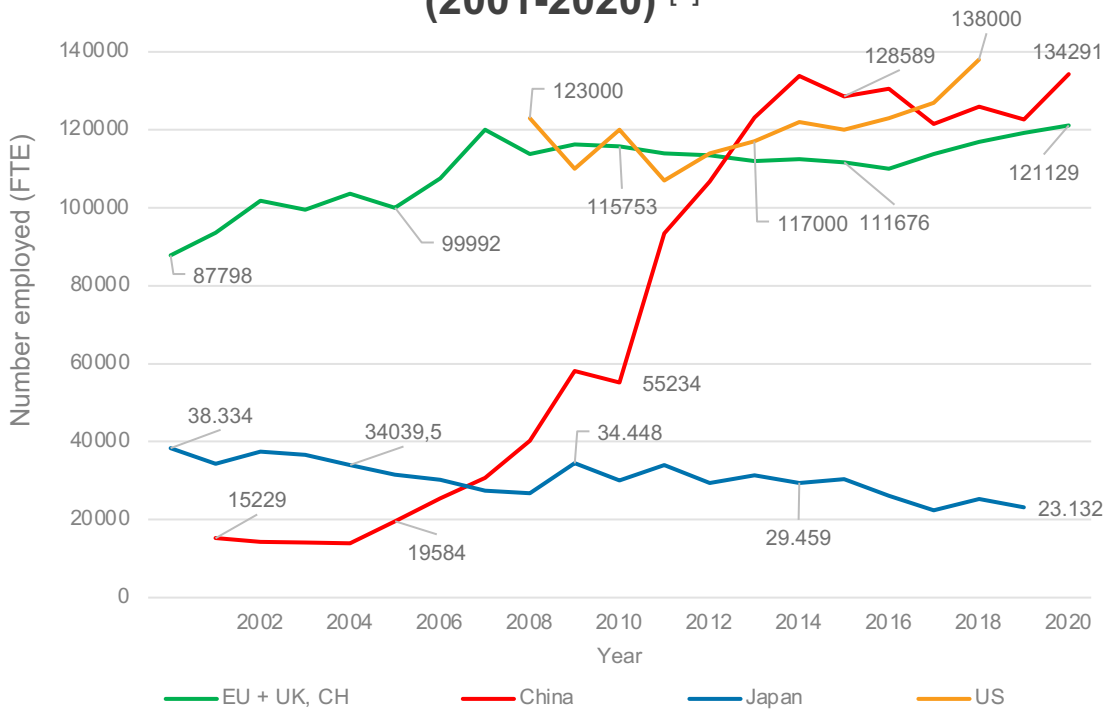
(1) Pharmaceutical R&D expenditure is growing at a faster rate in the US and China

Pharmaceutical R&D expenditure in major markets (2001-2020) [1]



Growth of pharmaceutical R&D expenditure in Europe has slowed relative to US and China

Pharmaceutical R&D employment in major markets (2001-2020) [2]

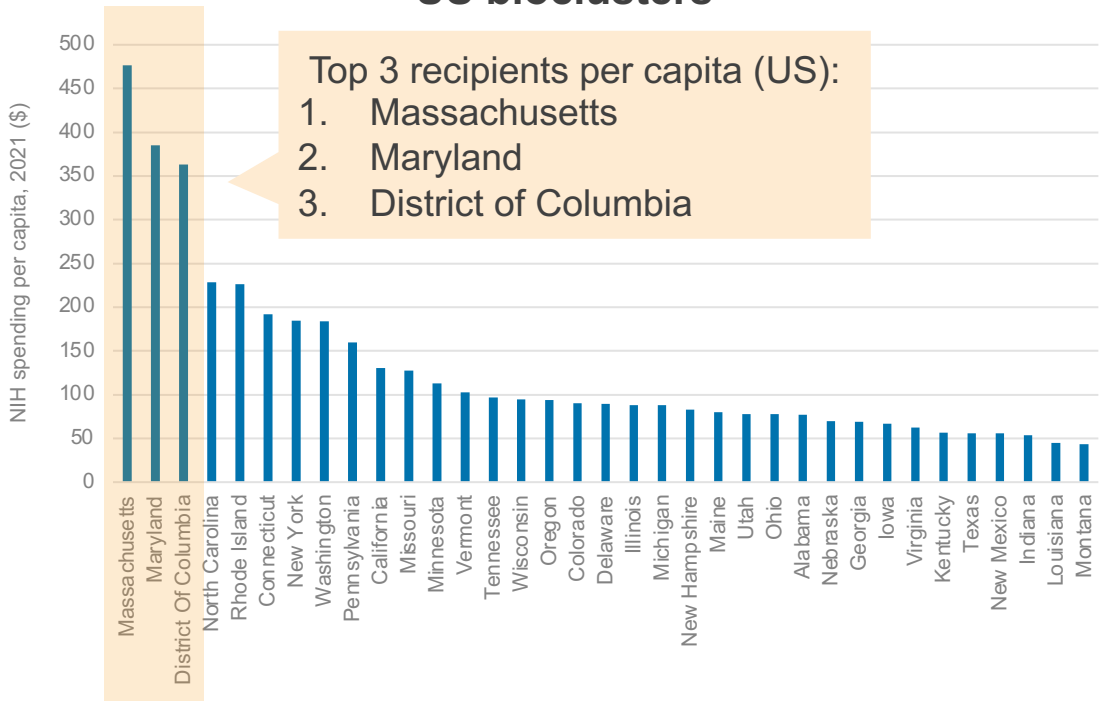


Pharmaceutical R&D employment has largely stalled relative to US and China in recent years

Sources in notes section

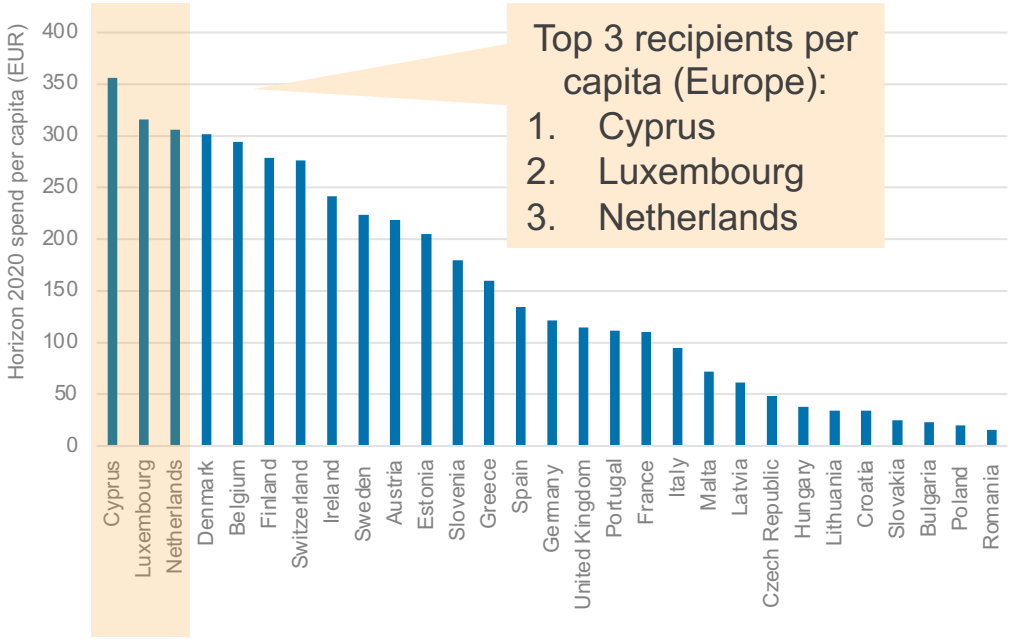
(1) Whilst the US invests heavily in its leading clusters, the EU appears to focus on evening out spending across Member States

NIH spending per capita is greater in the strongest US bioclusters [1]



Public research funding in the US (NIH) is relatively concentrated in Massachusetts

Horizon 2020 research spending in Europe is not concentrated in Member States with high R&D activity [2]



Conversely, public research funding in the EU is more evenly distributed among Member States

Sources in notes section

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(1) A policy that focuses on developing truly world class innovation hubs would serve Europe well

RECOMMENDATION #1:

Incentivise the development of truly world class innovation hubs in the EU

- The **leading research centres** (Boston and San Francisco in the US), in addition to having proximity to world-class academic institutions, also receive considerable policy and funding focus. California, New York and Massachusetts rank as the states **receiving the most funding from the National Institutes of Health**
- Research spending in Europe is significantly more uniform and the **countries with the highest spending per population are not the centres of innovation**
- The European Commission should consider **more strategic allocation** of resources to foster growth of world-leading research centres

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(2) Factors influencing the location of both small and large pharmaceutical companies needs consideration

Share of European-headquartered emerging biopharma is declining relative to US and China

Most emerging biopharma companies can be found in the US [1]

- The share of European-headquartered emerging biopharma companies has been declining over the last ten years
- The US dominates in terms of number of companies and their contribution to the global pipeline
- Contribution of emerging Chinese biopharma companies to the global pipeline has grown rapidly at a rate of 456% between 2016 and 2021

Large pharmaceutical companies generally continue to invest in R&D at their headquarter location

Global pharmaceutical companies typically conduct R&D across a range of markets, including their HQ location [2]

Company	Headquarter location	R&D hub at headquarter?
J&J	New Brunswick, NJ, US	Same country
Pfizer	New York, NY, US	Same country
Roche	Basel, Switzerland	Same city
AbbVie	Chicago, IL, US	Same country
Novartis	Basel, Switzerland	Same city
MSD	Kenilworth, NJ, US	Same city
BMS	New York, NY, US	Same country
GlaxoSmithKline	Brentford, UK	Same country
Sanofi	Paris, France	Same city
AstraZeneca	Cambridge, UK	Same city

Sources in notes section

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(2) Europe's comparative weakness in attracting and growing emerging biopharma companies is damaging its competitiveness

RECOMMENDATION #2:

Enhance end-to-end capabilities and funding of disruptive pharma innovation

- Europe's comparative weakness in growing small companies has **a spillover effect:** a critical driver of most new investments from large companies is the location and performance of existing R&D or manufacturing footprints, which tend to be **in proximity to their headquarters**
- As emerging US- and China-headquartered companies continue to grow into medium- and large-sized enterprises, it is likely that they will invest in Europe, but their investments will be **more heavily directed towards the US and China than to Europe** (i.e. **close to their home base**)
- Although positive trends can be observed in some Member States in supporting the growth of companies, there could be benefit from adopting a more **pan-EU policy and funding strategy** to accelerate these efforts

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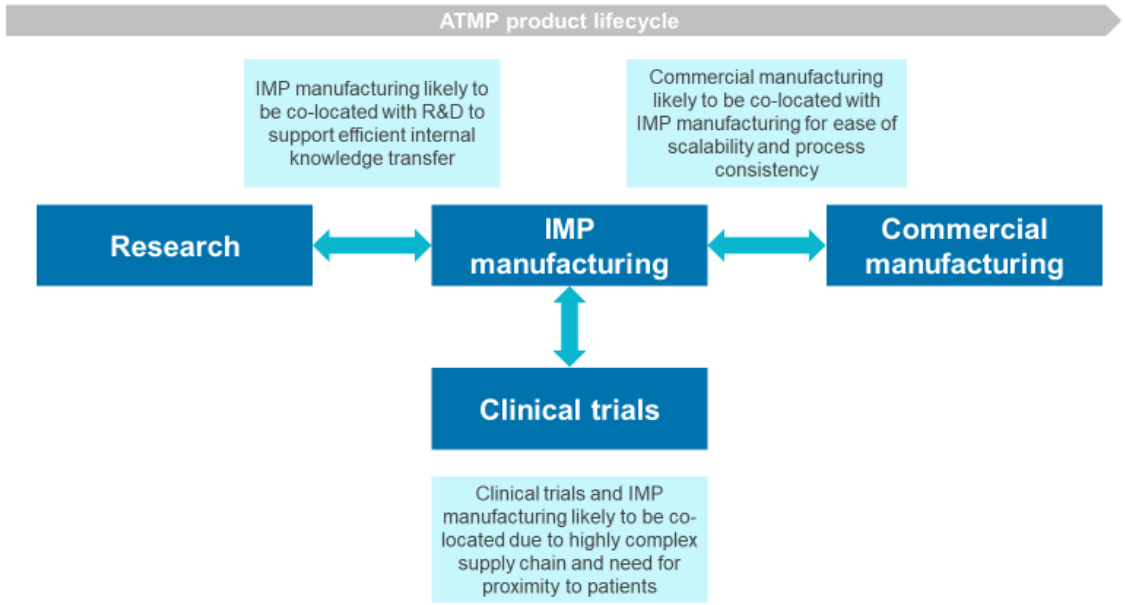
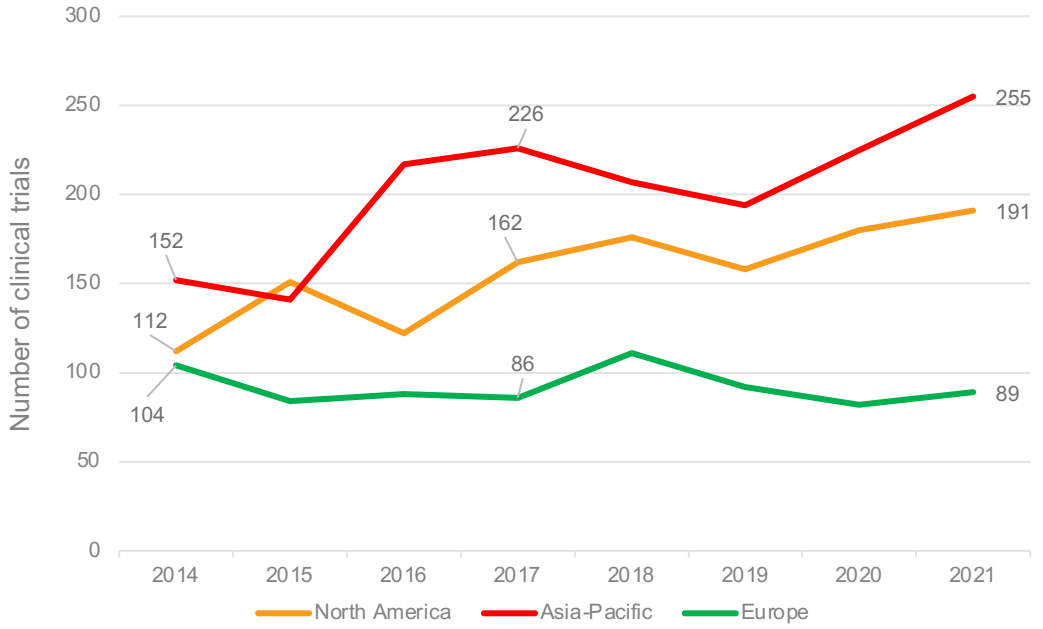
(3) Asia has been the most competitive region in attracting ATMP research and development activity; Europe lags behind

There is a degree of interconnectivity in the value chain for ATMPs, between research, clinical development and manufacturing [1]



The ATMP value-chain differs from traditional therapies in that it is more interconnected

The location of ATMP clinical trials differ from the overall geographic pattern of biopharma clinical trial activity [2]



Europe consistently hosts the lowest number of ATMP clinical trials

Sources in notes section

(3) Attracting ATMP investment into Europe requires a rethink of policies affecting the pharmaceutical value chain

RECOMMENDATION #3:

Rethink policies along supply chain to attract ATMP investment in Europe

- Given the complexity of the technology and the precision involved, the ATMP value chain is **more interconnected than for small molecules and biologics**
- Attracting early research that is then translated into therapies that can reach patients requires an **innovation-oriented access environment**, not just an academic ecosystem with strong centres of excellence
- For ATMPs, this access environment, in which companies can be sure to achieve an **appropriate return on investment**, then also **acts as a magnet for attracting manufacturing activities**, because for ATMPs "the process is the product"

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(4) Regulatory, value assessment and price and reimbursement systems are important factors for ATMP innovation

Summary of factors driving the location of biopharmaceutical investments [1]

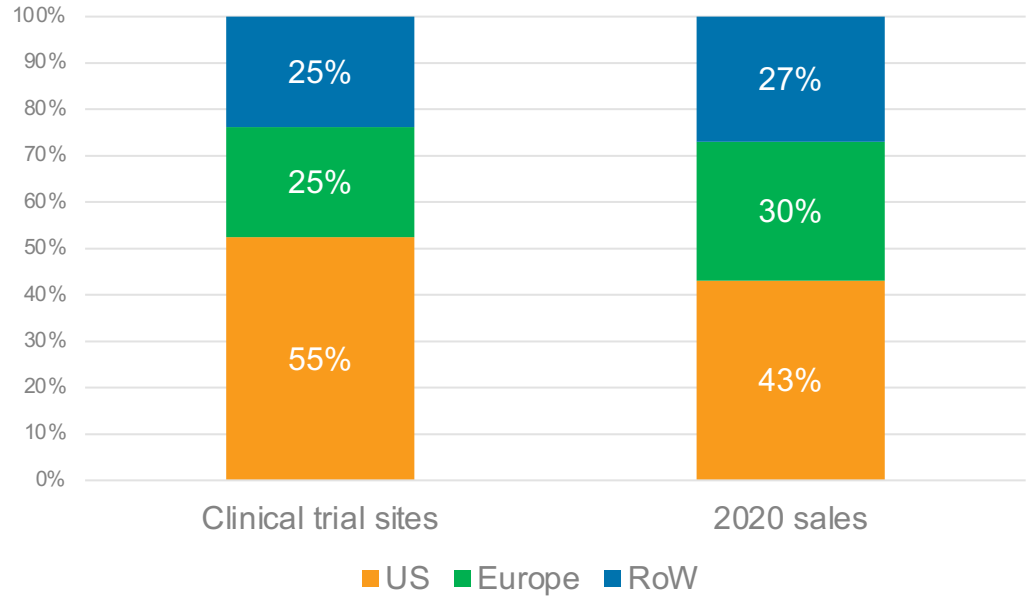
Do the most important drivers differ for new therapeutic solutions (example ATMPs)?

Research	Clinical trials	IMP manufacturing	Commercial manufacturing
1. Interconnected innovation ecosystem ▲	1. Location of leading hospitals and specialists	1. Co-location with late-stage research ▲	1. Co-location with rest of value chain ▲
2. Access to highly qualified research staff	2. Flexibility of regulatory environment	2. Access to highly qualified staff	2. Access to highly qualified staff ▲
3. Existing R&D footprint ▼	3. Pricing and access environment ▲	3. Proximity to major markets/ ease of transport ▲	3. Proximity to major markets/ ease of transport ▲

Key: ▲ = increase in importance relative to historically important drivers ▼ = decrease in importance relative to historically important drivers

Favourable market access and conditions are mentioned as top factors for ATMP-focused investments

The location of clinical trial sites and commercial sales of first cell therapies are similar [2]



Commercial sales of first cell therapies closely follow location of clinical trials

Sources in notes section

(4) Robust market access mechanisms in Europe could play a role in supporting innovation as well as patient access

RECOMMENDATION #4:

Support innovation by implementing early access mechanisms, including generation and use of real-world evidence

- Given the challenges with evidence development, ATMPs for instance are more likely to launch with **limited Phase II/III data** and subsequently **generate real-world evidence (RWE)**
- Europe needs to create an environment that is more conducive to ATMP development, by supporting **generation and use of RWE and acceptance of RWE** by payers and health technology assessment (HTA) bodies through **appropriate pricing and market access routes**

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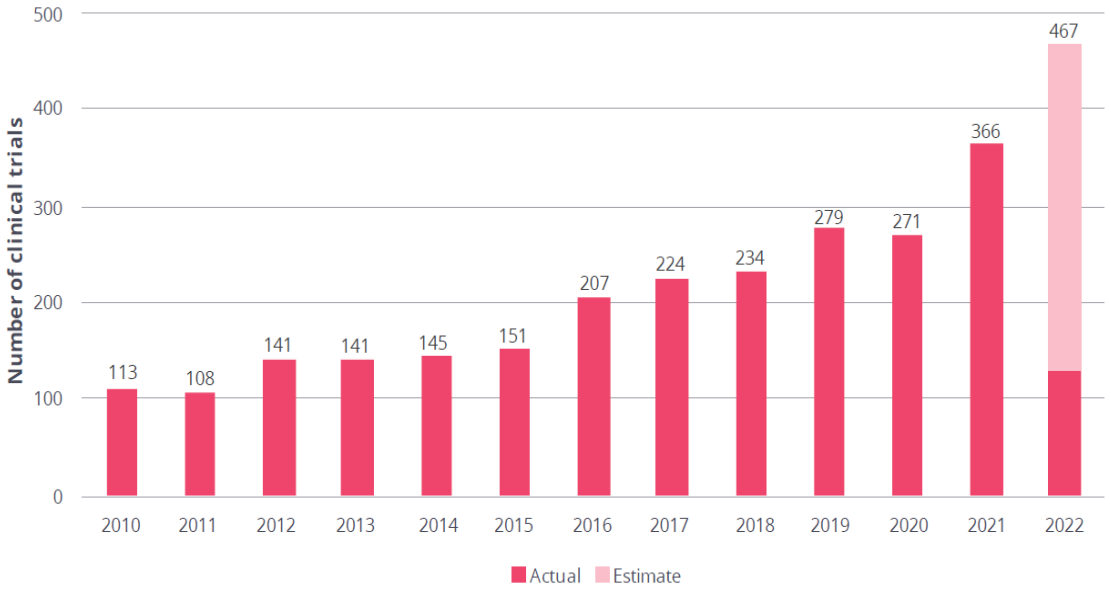
(5) Digital transformation in life sciences is impacting all aspects of the value chain, including R&D and manufacturing

There has been strong growth in the number of clinical trials employing digital technologies or virtual interactions [1]



Clinical trials employing digital technologies and virtual interactions are on the rise

Digital competitiveness of countries versus pharmaceutical R&D investment [2]

IMD World Competitiveness Center (WCC) World Digital Competitiveness Rankings 2022		Countries ranked on 2021 pharmaceutical R&D expenditure	
1	Denmark	1	United States
2	United States	2	Japan
3	Sweden	3	China
4	Singapore	4	Germany
5	Switzerland	5	Switzerland
6	Netherlands	6	United Kingdom
7	Finland	7	Belgium
8	Republic of Korea	8	France
9	Hong Kong	9	Italy
10	Canada	10	Denmark
Lower ranking or no data		*Lower ranking or no data*	

Major European hubs of biopharma R&D and manufacturing investment are lagging in digital competitiveness

Sources in notes section

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(5) Europe needs to catch-up with the digital transformation to compete for pharmaceutical investments

RECOMMENDATION #5:

Boost EU digital transformation and support development of digital capabilities

- To enable digitalisation, for example through automation of value chains or virtual clinical trials, pharmaceutical companies are being drawn towards locations with a workforce that is well-versed in digital technology and **where the broader ecosystem is digital-ready**
- The EU's top-ranking biopharma clusters, however, rank poorly on digital competitiveness
- Europe could take a more proactive role in **upskilling the scientific workforce** in digital technologies and **accelerating the digitalisation of health systems**

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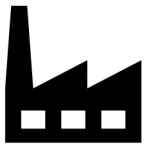
(6) There is a danger that policy focuses on the most innovative medicines and off-patent medicines leaving a gap in the middle

[Gap]

Policy focused on production of off-patent medicines

The EU Pharma Strategy prioritises security of supply of critical medicines and may result in re-location of manufacturing focusing on off-patent medicines[1]



Policy focused on sustainability of conventional therapies

There has been a lack of focus on sustainable procurement and pricing policies to support ongoing investments for conventional therapies [2]

Policy support for advanced therapies

The importance of creating an ecosystem in Europe that support early access, leans into the digital transformation and supports the use of RWE, is clear for newer technologies such as ATMPs

Sources in notes section

(6) Market sustainability affects investment in innovation and investigational and commercial manufacturing

RECOMMENDATION #6:

Foster adoption of sustainable procurement and pricing policies for innovation

- There is a danger that industrial policy becomes focused on the most novel technologies and relocating manufacturing of off-patent medicines, and **the need for a sustainable market is overlooked**
- Ongoing investment in manufacturing and the development of medicines **needs to be supported by policymakers and governments**, for example through sustainable pricing policies and a **robust and stable intellectual property** environment
- This has implications for types of innovation receiving public support, procurement, and the trade-off between investing in mature and future technologies

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(7) The global geopolitical environment creates potential risks which can have large impact on investment decisions

COVID-19 pandemic

Russia-Ukraine war

Global trade tensions

Climate emergency

Impact

Summary of factors driving the location of biopharmaceutical investments [1]

What are the most important drivers of investment location?

Research	Clinical trials	IMP manufacturing	Commercial manufacturing
1. Existing R&D footprint	1. Location of leading hospitals and specialists	1. Existing IMP manufacturing footprint	1. Existing manufacturing footprint
2. Access to highly qualified research staff	2. Regulatory environment	2. Access to highly qualified staff	2. Cost (labour, production, tax)
3. Overall innovation ecosystem	3. Strategic commercial considerations	3. Co-location with late-stage research	3. Access to highly qualified staff

What has changed as a result of recent global and geopolitical trends?

New driver:
4. Strength of digital infrastructure

More important:
5. Political stability and risk
6. Proximity to major markets

Political stability and risk has emerged as an increasingly important driver for investment location

Sources in notes section

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(7) European policy needs a long-term outlook to create long-term stability for attracting investments

RECOMMENDATION #7:

Develop a longer-term, collaborative method for encouraging growth in Europe's attractiveness for biopharmaceutical investments

- The **increase or perceived increase in risk in the global environment** resulting from recent geopolitical challenges has implications for where companies are placing their investments
- This could affect the attractiveness of Europe, **both positively and negatively**
- Europe needs to **establish an effective process for implementation of the Pharmaceutical Strategy** (its first in over 50 years since the first pharmaceutical legislation was implemented in the EU) with **ongoing dialogue regarding how the environment** will change over 5-, 10- and 20-year timescales, and the expected and actual impact of policy changes, and ensuring a focus and impact on innovation as well as production

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