Illustrating the declining attractiveness of Europe as an investment location through the lens of a small firm

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CRA Charles River Associates

June 2026

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Objectives and approach

Background

Policy Context

- While the European biotechnology industry has been growing, there are concerns about European competitiveness and whether Europe is lagging behind other global regions in terms of investment, manufacturing, and commercialization
- European pharmaceutical firms face structural barriers affecting investment decisions in clinical development, regulation, and manufacturing. For smaller firms, which play a vital role in innovation, these barriers may be exacerbated
- The European Biotech Act, proposed on December 16, 2025, contains provisions intended to address these barriers

Key Research Questions

- What are key decision points faced by biopharmaceutical companies (and particularly by smaller companies)?
- How does Europe's current policy environment compare to that of the US and China?
- What effect, if any, will the proposed Biotech Act have on the investment decisions these biopharmaceutical companies face?

VC: Venture Capital
R&D: Research and Development

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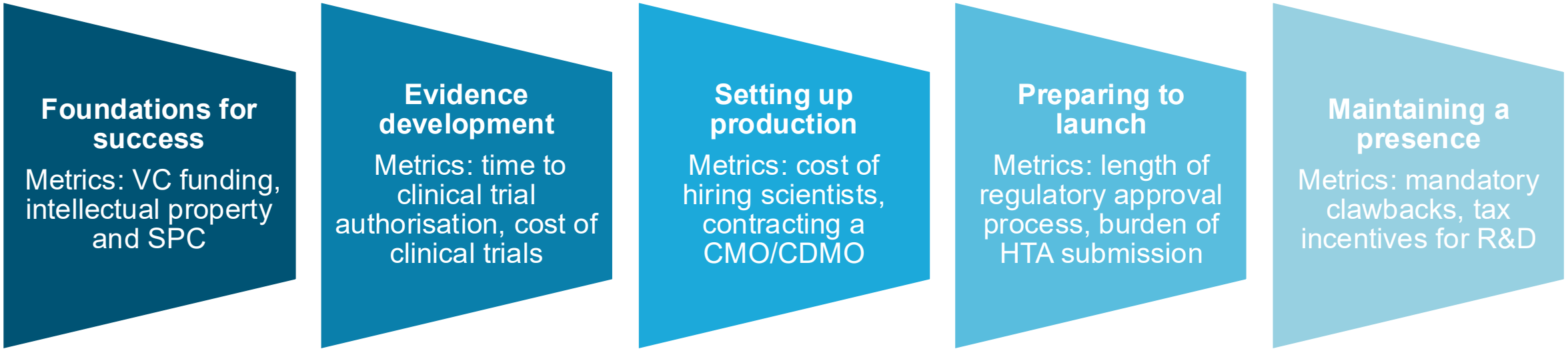
Five identified key investment decision points



This report presents an 'overall' visualisation aggregating metrics across the five categories.

To develop this visualisation, for each of these five categories, we:

1. Set out the policy context
2. Describe the perspective of large and small firms
3. Identify two easy-to-understand metrics
4. Assess the metrics across Europe, US, and China
5. Create global visualisations pre/post Biotech Act

Note: Large firms tend to be established, multinational enterprises. Small firms are not limited to the EU's legal definition of small and medium enterprises (under 250 employees); in this report, they are firms that tended to start as biotechs, focused on early-stage R&D that do not necessarily have an existing commercialized drug.

VC: Venture Capital; SPC: Supplementary Protection Certificate; CMO: Contract Manufacturing Organisation; CDMO: Contract Manufacturing and Development Organisation; HTA: Health Technology Assessment; R&D: Research and Development

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Metrics for evaluation

Investment Decision	Key Metrics	Broad Data Sources
Foundations for Success	• Availability of biotech VC funding • Strength and duration of IP protections and regulatory incentives	• US Government and IMF Publications • Pharmaceutical Industry Publications • Proposed EU Pharmaceutical Legislation
Evidence Development	• Wait time for regulatory authorisation for clinical trials • Cost of clinical trials	• EU, US, and China Regulatory Guidelines • Pharmaceutical Industry Publications • Health Economics Academic Journals
Setting Up Production	• Cost of hiring PhD scientists • Cost of contracting a CMO/CDMO	• Third-party and Government Data • Pharmaceutical Industry Publications • Proposed EU Pharmaceutical Legislation
Preparing to Launch	• Length of regulatory submission time • Burden of HTA submission	• EU, US, and China Regulatory Guidelines • Health Policy and Economics Academic Journals and White Papers
Maintaining a Presence	• Mandatory industry refunds • Tax incentives for R&D	• Pharmaceutical Industry Publications • OECD Databases and Publications • US and EU Government Publications

VC: Venture Capital; IP: Intellectual Property; CMO: Contract Manufacturing Organisation; CDMO: Contract Manufacturing and Development Organisation; HTA: Health Technology Assessment; R&D: Research and Development; IMF: International Monetary Fund; OECD: Organisation for Economic Cooperation and Development.

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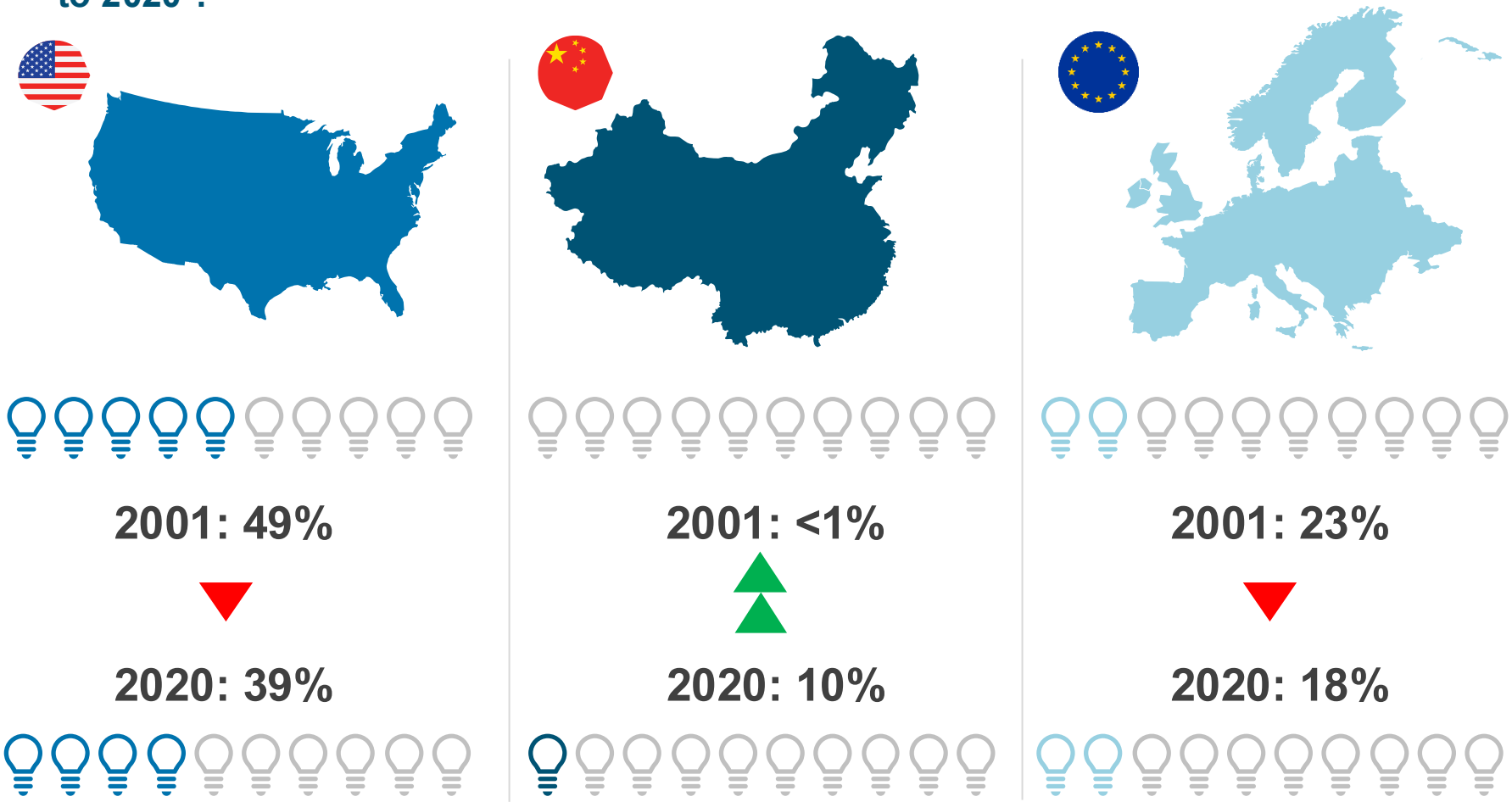
Foundations for success

Policy context: foundations for success

Foundations for Success

Change in share of biotechnology patent filings, 2001 to 2020[1]:



- Europe lags behind the US and is losing ground to China in the share of biotechnology patents filed globally[1]
- While Europe has a strong scientific research and publication base, it has difficulties in translating that research into commercially viable pharmaceutical products[2]
- Access to financial support for start-ups to scale up in Europe trails the US and China.[2]
- From 2020, 66 out of 67 EU biotech companies that went public did so by listing outside of the EU.[3]

Small decrease
Significant decrease
Significant increase

Note: Using EU flag but depicting Europe.

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Considerations by company size: foundations for success

Foundations for Success

Considerations Affecting All Companies

- European biotech companies report public R&D underinvestment, indicating poor alignment across policies and programs and a lack of public capital[1,2]
- Strong IP rights are foundational for continued pharmaceutical innovation[4]

Additional Burden for Smaller Companies

- Smaller companies rely on VC funding. The traditional VC investment cycle may not be suited to the long horizon of pharmaceutical R&D and commercialisation[2]
- Early-stage companies in particular face difficulties as investors prioritise later-stage companies with established data packages, de-risked development, and nearer-term catalysts that have clearer routes to commercialisation[3]

Total Consideration Affecting Smaller Companies

VC: Venture Capital
R&D: Research and Development

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Relevant metrics: foundations for success

Foundations for Success

Availability of biotech venture capital funding

- Venture capital funding plays a pivotal role in enabling biotech startups to pursue innovative and risky products where traditional loans are unavailable[1]
- In one study, approximately one-third of biotech companies reported that their current funding came from venture capital[2]
- Venture capitalists often provide not only funding but expertise, industry networks, and governance structure that can provide strategic advice to biotech startups[1]
- Venture capital funding is critical to new drug development, especially in the pre-clinical and early clinical research phase, before startups establish revenue streams[3]

Strength of intellectual property protections and related regulatory incentives

- Pharmaceutical R&D is risky and costly, and patent protections act as a mechanism to safeguard and incentivize innovation[4]
- Increased strength of patent rights strongly and positively affect R&D expenditure and foreign direct investment.[5] Regulatory incentives that extend patent life can have the same positive effects.
- The strength of intellectual property rights is closely correlated with the number of clinical trial starts in a country. Early-phase and innovative biologic clinical trials in particular are strongly correlated with the strength of the intellectual property system[6]

R&D: Research and Development

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Comparison across key markets: foundations for success

Foundations for Success

Country/ Region	Availability of Biotech VC Funding		Strength and Duration of Intellectual Property Protections and Related Regulatory Incentives		Aggregate Evaluation
	From 2015 to June 2025, US companies received **63 percent** of global health biotechnology venture capital investment[1]		Regulatory data protection lasts 5 years for small molecules and 12 years for biologics.[3,4] Patent term restoration of up to 5 years; total exclusive term for drug not to exceed 14 years.[5] The US is consistently ranked first for the strength of pharmaceutical IP protection.[6,7,8]		
	From 2015 to June 2025, Chinese companies received **14 percent** of global health biotechnology venture capital investment[1]		Recent legislation guarantees 6 years of regulatory data protection.[9] Patent term extension of up to 5 years only for drugs first approved in China; total drug exclusivity not to exceed 14 years. Due to concerns regarding patent enforcement and differential treatment of drugs first approved overseas, China continues to rank below the US and most European countries.[6]		
	From 2015 to June 2025, EU companies received **7 percent** of global health biotechnology venture capital investment[1] Capital markets are limited by national fragmentation and overall risk-aversion.[2]		Base level regulatory data protection lasts 8 years.[10] SPC extends patent rights for 5 years; total drug exclusivity term not to exceed 15 years. SPC applications are filed with national patent offices and decisions are often fragmented.[11] The GPL extends Bolar exemptions, weakening IP protections by extending the scope of pre-market activities generic manufacturers may participate in. Nevertheless, European countries remain ranked above China in overall IP indeces.[6,7]		
Post-Biotech Act 	The Biotech Act includes provisions to increase funding by an **unspecified amount** through the development of an investment pilot to support SMEs across their lifecycle by coordinating private funding and funding from Member States.[1]		The Biotech Act has no direct effect on the strength of IP protection, though it does extend SPC duration by 12 months if certain criteria (e.g. ATMP, "distinctly different" drugs) are met.[1]		

Lower VC funding; weaker IP protection
Medium VC funding; medium IP protection
Higher VC funding; stronger IP protection

Aggregate evaluation is the average of the evaluations for the availability of Biotech VC funding and the strength of IP protection.

IP: Intellectual Property
SME: Small and Medium Enterprise
SPC: Supplementary Protection Certificate
GPL: General Pharmaceutical Legislation

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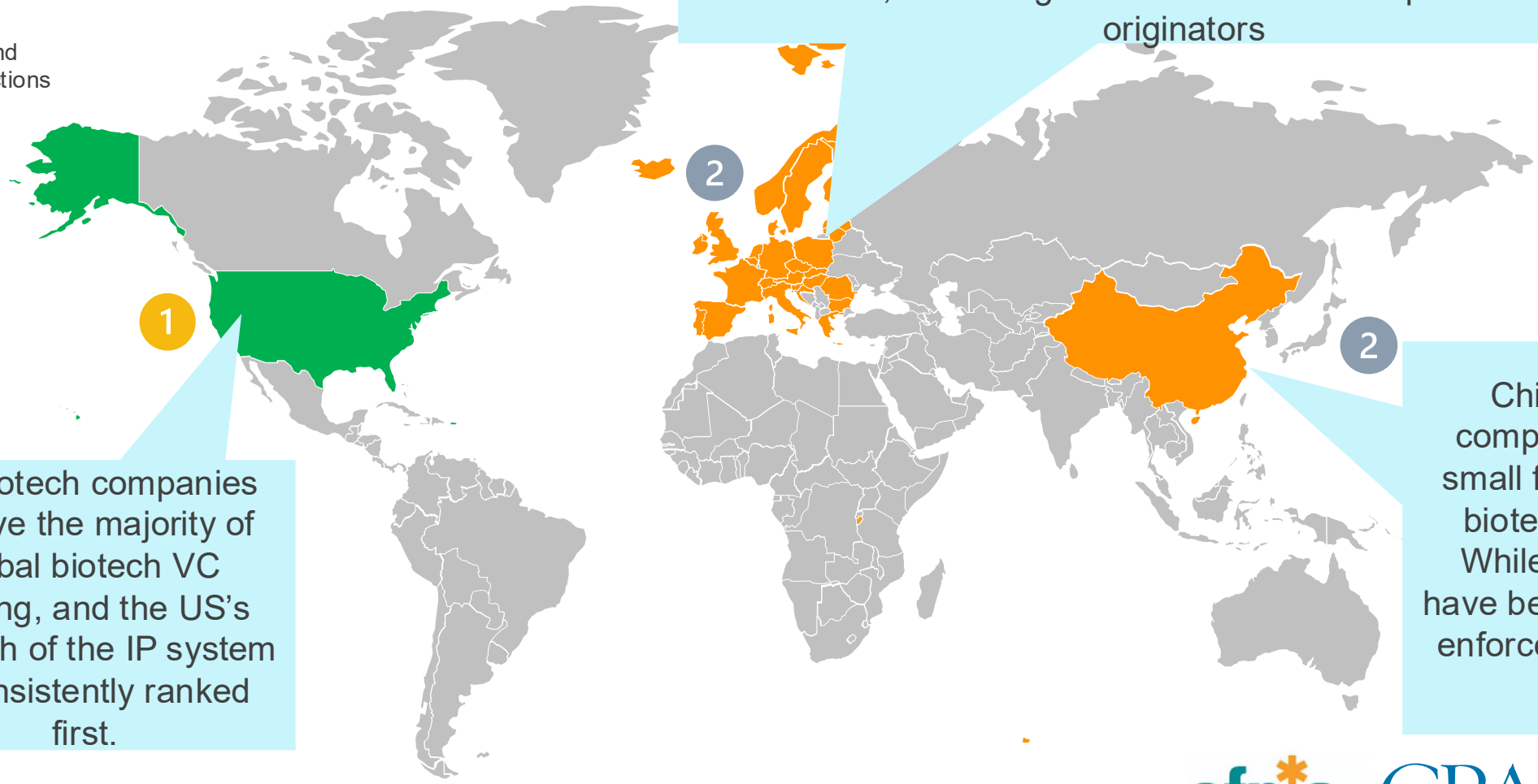
Availability of biotech VC funding and strength of IP system, Europe pre-Biotech Act

Foundations for Success

Higher funding and stronger IP protections

Lower funding and weaker IP protections



European biotech companies receive a small fraction of global biotech VC funding. While IP protections are historically well-reviewed, recent legislation has weakened protections for originators

US biotech companies receive the majority of global biotech VC funding, and the US's strength of the IP system is consistently ranked first.

Chinese biotech companies receive a small fraction of global biotech VC funding. While IP protections have been strengthened, enforcement remains a concern.

* Europe includes the EU27, EFTA, and the UK

VC: Venture Capital
IP: Intellectual Property

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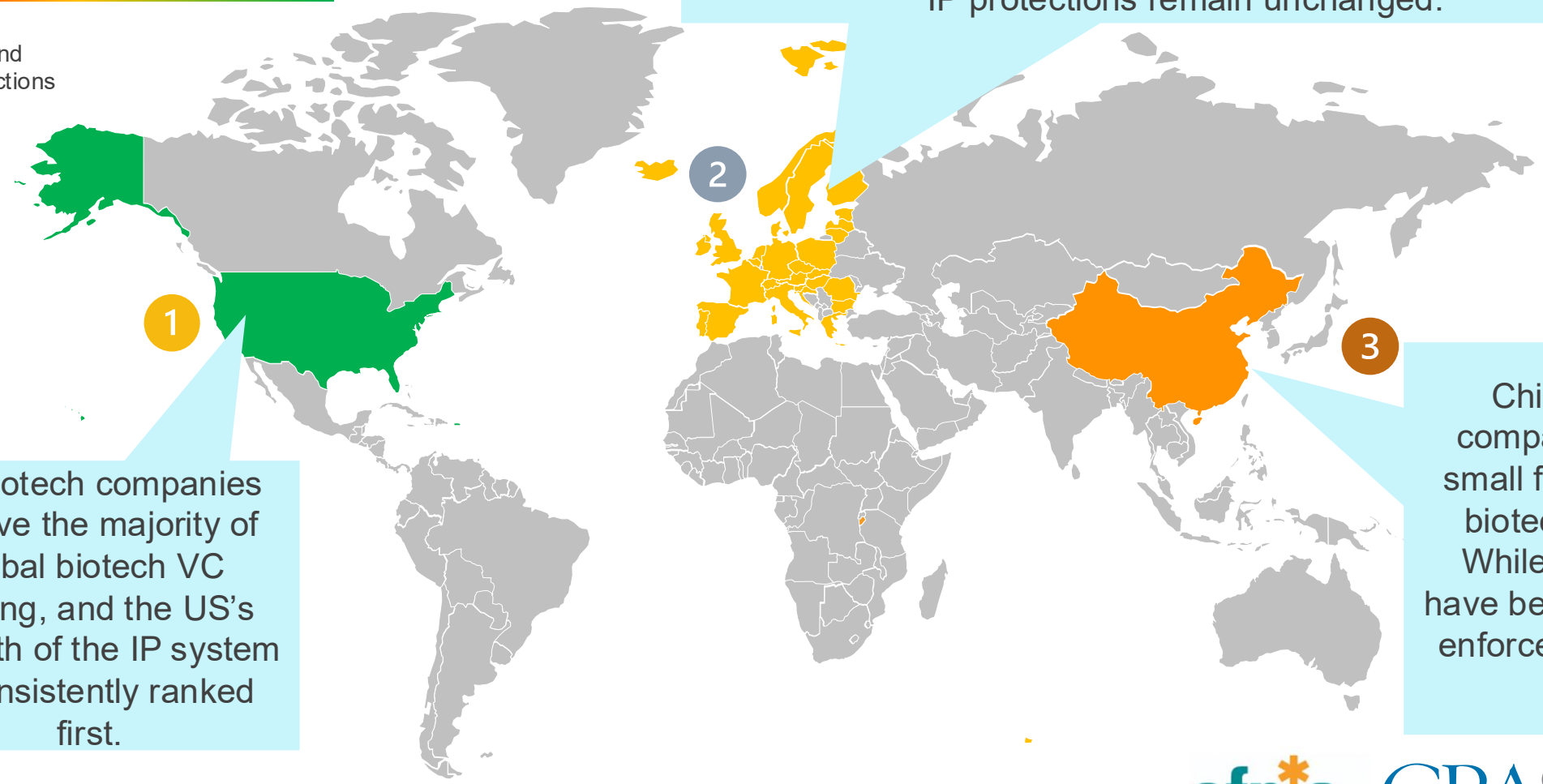
Availability of biotech VC funding and strength of IP system, Europe post-Biotech Act

Foundations for Success

Higher funding and stronger IP protections

Lower funding and weaker IP protections

The Biotech Act increases private and public funding, but the amount will vary depending on the success of implementation. IP protections remain unchanged.



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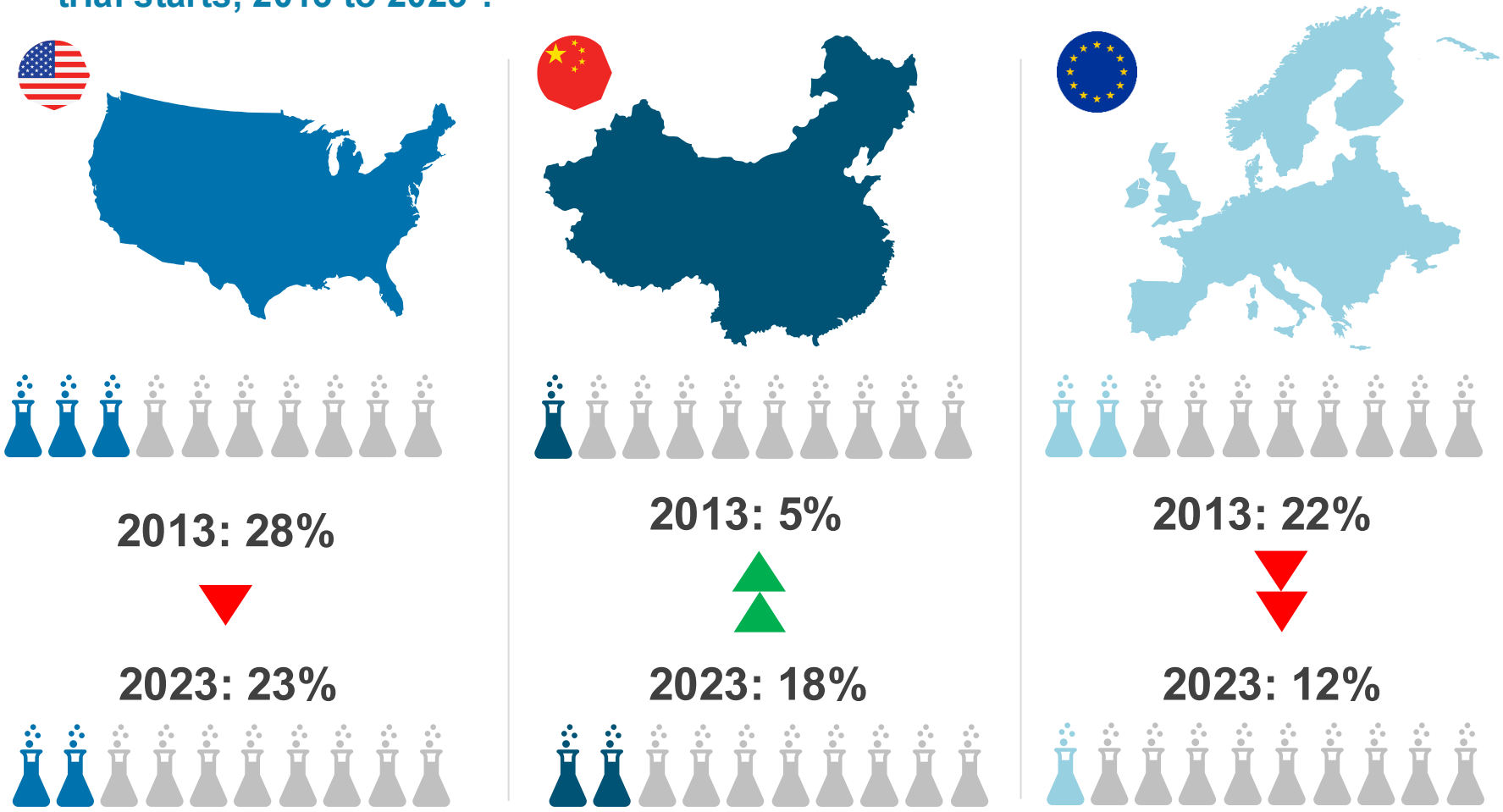
Investment in evidence development

Policy context: investment in evidence development

Evidence Development

Change in share of commercially sponsored clinical trial starts, 2013 to 2023[1]:



- Europe faces barriers in clinical development and regulation[2]
- These include conflicting application requirements, bureaucratic and technical issues with submissions, and overall increased burden on clinical trial applicants[3]
- Despite proposed legislation, regulatory fragmentation within the EU remains and poses barriers to clinical trial efficiency. There are also issues related to clinical trial costs and wait times for authorisation[2]

▼ Small decrease
▼▼ Significant decrease
▲▲ Significant increase

Note: Using EU flag but depicting Europe.

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Considerations by company size: evidence development

Evidence Development

Considerations Affecting All Companies

- Slow and complex regulatory frameworks lead to long and uncertain authorisation processes, hindering innovation[1]
- Regulatory fragmentation results in high regulatory costs in both time and money[1]

Additional Burden for Smaller Companies

- Smaller companies report longer clinical trial timelines, which often correspond to increased monetary costs, than large companies[2]
- Smaller companies often lack internal experience in clinical development and limited infrastructure, compounding time and money costs[3]
- Biotech firms and smaller pharmaceutical companies face more pronounced funding constraints, especially during pre-clinical and early clinical trials, due to the high level of uncertainty and risk[3]

Total Consideration Affecting Smaller Companies

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Relevant metrics: evidence development

Evidence Development

Wait Time for Regulatory Authorisation

- Streamlined clinical trials authorisations are necessary for both the effectiveness of the other measures in the Biotech Act and all strategic health biotechnology projects [1]
- Defined timelines for clinical trial approval would enhance the speed of the authorisation process, allow for quicker starts, and increase transparency and predictability[2]
- Disparate regulations are cited as a key driver contributing to regulatory delays[3]
- Delays in clinical trial start-up time are associated with lower project success[4]

Cost of Clinical Trials

- Across all company sizes, the rising cost of clinical trials has been reported as one of the largest challenges faced in drug development[5]
- Clinical trials are increasing in complexity, requiring greater funding and time[6]
- Longer trial timelines delay the launch of new therapies[6]
- Increasing clinical trial costs are a cause of reduced R&D productivity per approved medicine[7]
- High clinical trial costs may impact research integrity and capacity[2]

R&D: Research and Development

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Comparison across key markets: evidence development

Evidence Development

Country/ Region	Statutory Time to Regulatory Authorisation for Clinical Trial Initiation	Cost of Clinical Trials (without failure or capitalisation costs)	Aggregate Evaluation
	Up to 30 days from filing with the FDA, barring further information requests and contingent on ethical approval. There is no statutory timeline for ethical review, and ethical approval may be received prior to scientific review. A "no objection" system is in place.[1]	Clinical trial costs are among the highest in the world. Phase II trial costs estimated at €51,000 per patient.[2] Clinical trial costs have increased over time due to geopolitical unrest, regulatory uncertainty, and increasing trial complexity.[10]	
	Filing of up to 5 working days, authorisation takes up to 30 days for fast-track drugs, 60 days for others. Scientific and ethical review may run in parallel. A "no objection" system is in place.[3]	Offers comparatively low clinical trial costs, up to 60% less than the US.[4] Despite becoming a larger contributor to global clinical trials, costs have not increased.[9] Phase II trial costs estimated to be as low as €20,000 per patient.[4]	
	Up to 60 days without further requests for information; 110 days if the product is an Advanced Therapy Medicinal Product. Ethical review is conducted after scientific review.[5] SMEs are eligible for regulatory, procedural, and administrative support and fee waivers.[8]	Costs vary widely depending on the country, ranging from as low as €25,500 per patient in Central and Eastern Europe to being comparable with costs in the US in Western Europe.[6] Clinical trials costs have been increasing.[11]	
Post-Biotech Act 	After the passage of the Biotech Act, regulatory authorisation time falls to up to 47 days, and scientific and ethical review occur in parallel.[7]	No direct effect. Costs vary widely depending on the country.[6]	

Slower authorisation time; higher cost

Medium authorisation time; medium cost

Faster authorisation time; lower cost

Stripes indicate geographic variation within Europe

Aggregate evaluation is the average of the evaluations for the time to regulatory authorisation and the cost of clinical trials.

FDA: Food and Drug Administration
SME: Small and Medium Enterprise

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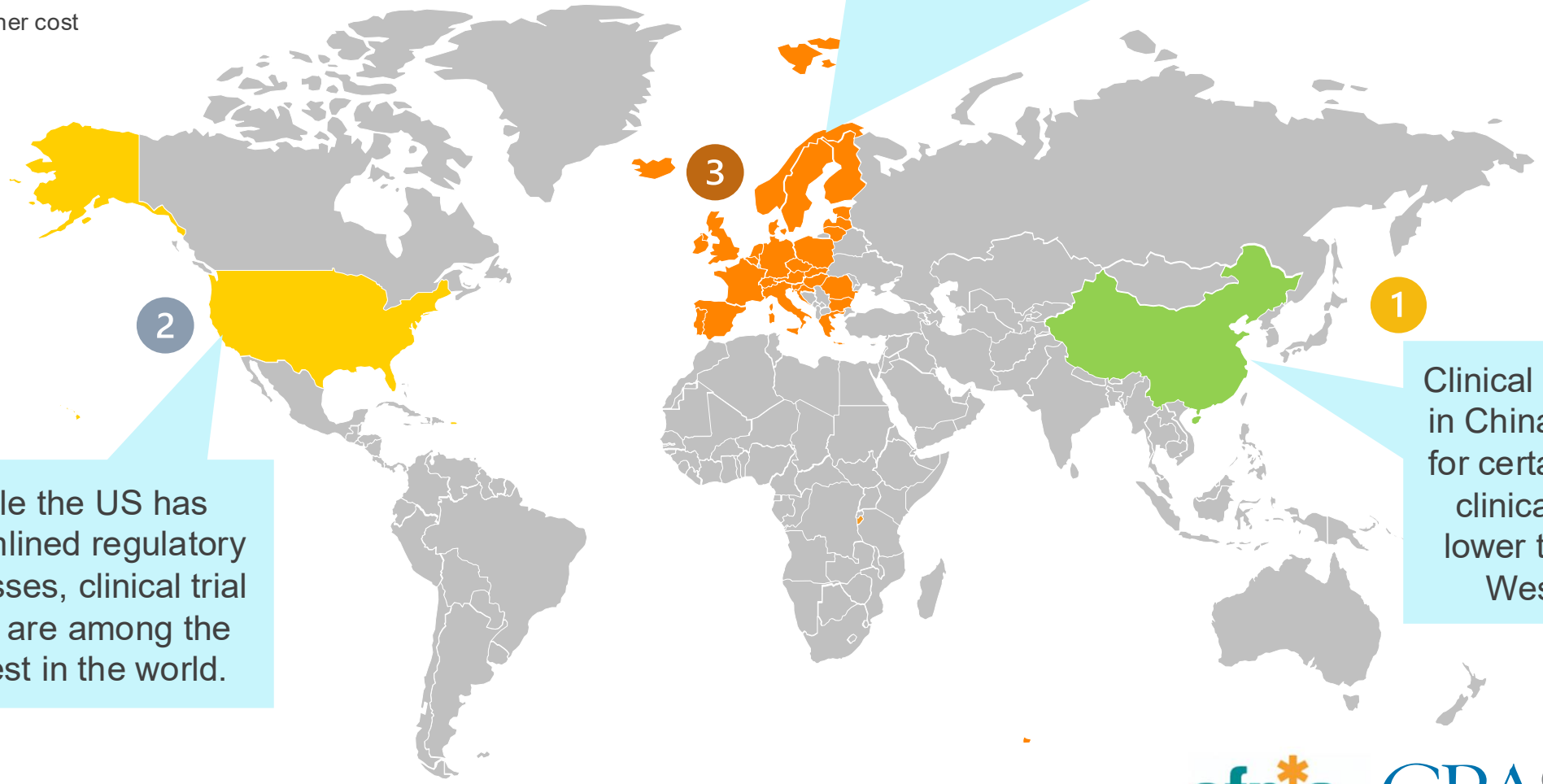
Regulatory authorisation speed and cost of clinical trials, Europe pre-Biotech Act

Evidence Development

Faster and lower cost

Slower and higher cost

In Europe, clinical trial authorisation is lengthy and fragmented, and costs vary widely depending on site and personnel costs.



While the US has streamlined regulatory processes, clinical trial costs are among the highest in the world.

Clinical trial authorisation in China has a fast-track for certain products, and clinical trial costs are lower than the US and Western Europe.

* Europe includes the EU27, EFTA, and the UK

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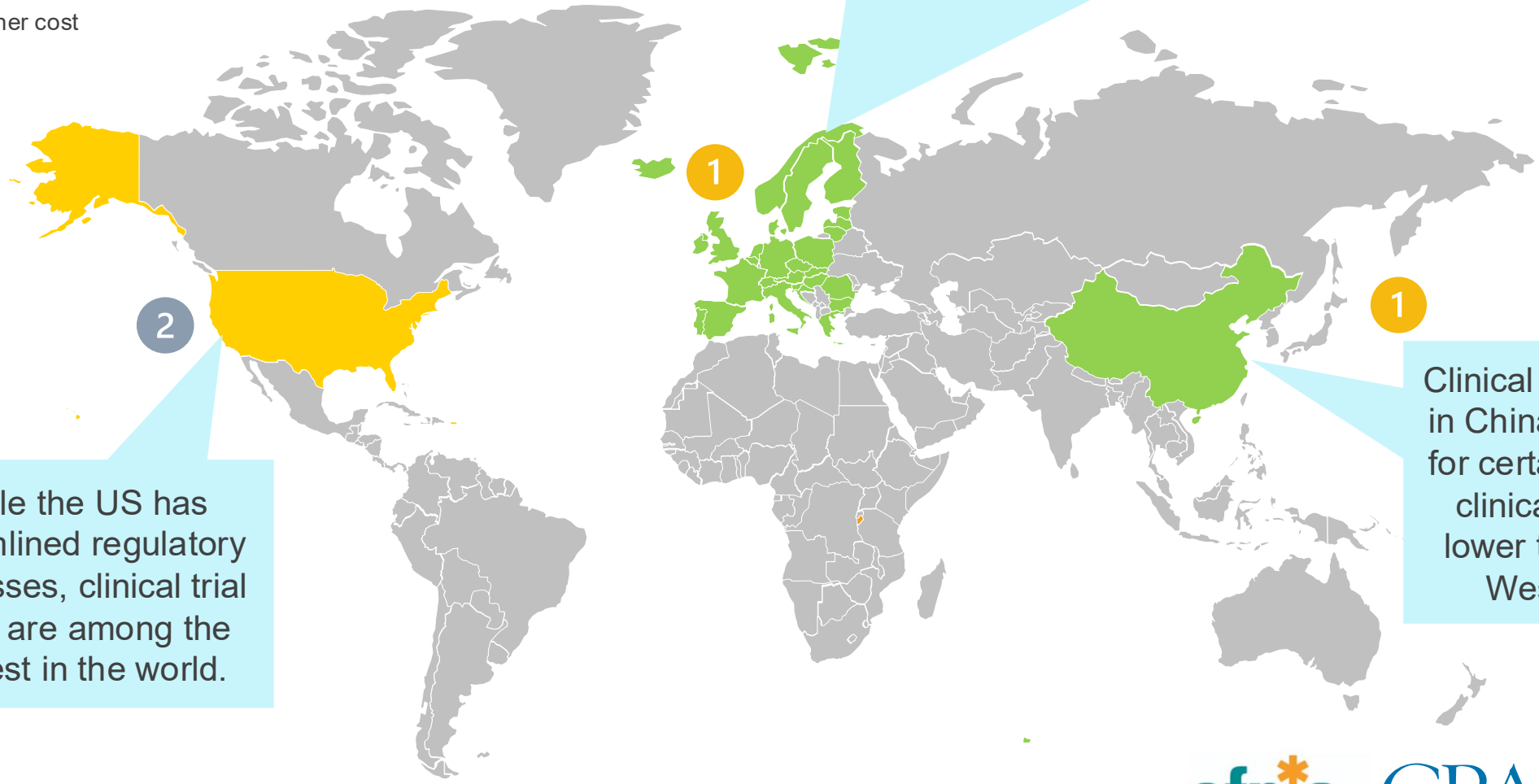
Regulatory authorisation speed and cost of clinical trials, Europe post-Biotech Act

Evidence Development

Faster and lower cost

Slower and higher cost

In Europe, clinical trial authorisation is shorter than before the Biotech Act, but clinical trial costs remain varied.



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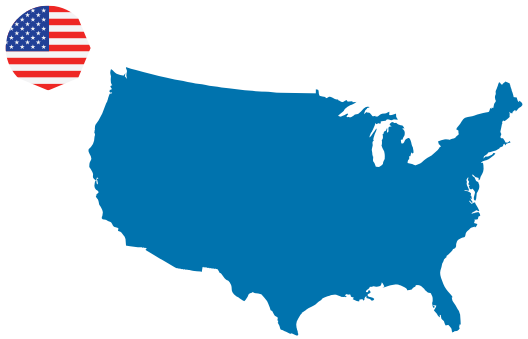
Setting up production

Policy context: setting up production

Compound annual growth rate of pharmaceutical R&D employment, 2014-2024:

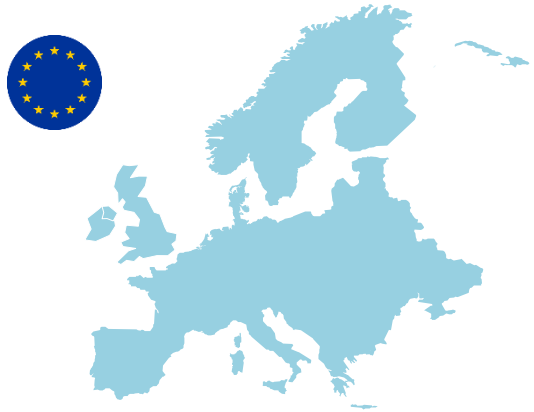


3.3%

10-year compound annual growth rate for life scientists engaged in manufacturing and professional, scientific, and technical services[1,2]

4.2%

10-year compound annual growth rate of R&D employment[3]



0.7%

10-year compound annual growth rate of R&D employment[3]

- Europe faces skilled biotech labour shortages in R&D, regulatory affairs, AI, and data analytics, partially caused by an insufficient number of STEM graduates and inadequate funding for continued education (e.g. digital and AI competencies)[4]
- Stakeholders have expressed concerns regarding brain drain and global competition, which are exacerbated by barriers that hamper cross-border and cross-sector mobility[4]
- Stakeholders have similarly expressed concerns over the limited manufacturing capabilities in Europe, in addition to supply chain vulnerabilities, high costs, and fragmented regulations[4]

R&D: Research and Development
AI: Artificial Intelligence
STEM: Science, Technology, Engineering, and Mathematics

Note: Using EU flag but depicting Europe.

Considerations by company size: setting up production

Considerations Affecting All Companies

- In one survey, the majority of European pharmaceutical and biotech companies stated they felt the supply of skilled professionals was insufficient[1]
- Despite labour shortages, employers often lack understanding and trust in skills gained in third countries, leading to "brain waste"[2]

Additional Burden for Smaller Companies

- Smaller companies report most frequently facing shortages for technically trained staff, sometimes leading to reduced profitability and growth[3]
- A greater proportion of smaller companies report hiring as "very difficult" than do large companies[3]
- Smaller companies may lack the funds to contract with pricier, domestic CMOs/CDMOs, requiring them to invest additional time working with overseas suppliers[4]

Total Consideration Affecting Smaller Companies

CMO: Contract Manufacturing Organisation
CDMO: Contract Development and Manufacturing Organisation

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Relevant metrics: setting up production

Cost of Hiring PhD Scientists

- In one survey, approximately one-fifth of pharmaceutical companies reported that talent and staffing shortages were among their top 5 challenges[1]
- In particular, a lack of talent was identified as the top challenge for advanced therapy firms when scaling up manufacturing[2]
- One study in Europe found that there are often over 20 candidates per advertised role, but firms continue to report staffing difficulties, suggesting that there is a skill mismatch[3]

Cost of Contracting an CMO

- The percentage of global pharmaceutical production outsourced to contract development and manufacturing organizations has risen from 34% in 2014 to 49% in 2023, with the potential to exceed 55% by 2030[4]
- In-demand CDMOs are highly utilised and may be contracted years in advance for their capacity, increasingly requiring companies to maintain and pay for a secondary supplier[5]
- While offshore contract organisations may reduce costs, additional regulatory site inspections, internal management, and shipment transportation costs require consideration[5]

CDMO: Contract Development and Manufacturing Organisation

Comparison across key markets: setting up production

Country/ Region	Cost of Hiring a PhD Scientist (ex. Biomedical Research Scientist)	Cost of Hiring a Contract Manufacturing Organisation	Aggregate Evaluation
	Average salary for a biomedical research scientist is €103,000[1]	Hiring a contract manufacturing organization for a single early-stage clinical trial for an oncology project may cost up to €427,000, depending on complexity. Late-stage clinical trials incur greater costs.[5]	
	Average salary for a biomedical research scientist is €40,000[2]	Due to lower labour costs, government-subsidized facility construction, and domestic API supply integration, rates may be 30 to 50% below Western companies[6]. Manufacturing for early-stage clinical trials can be as low as ~€213,500.	
	Salaries vary by country, but range from €34,800 (Slovakia) to €129,600 (Switzerland)[3,4]	Varies by country. CMOs/CDMOs in Germany, Switzerland, and the UK command prices comparable to the US, while organizations in countries with lower labor rates offer lower prices[7,8]	
Post-Biotech Act 	No direct effect from Biotech Act	The Biotech Act includes provisions offering regulatory and administrative support and financial assistance to initiatives improving manufacturing, but the effect will depend on implementation[9]	

Higher cost
Medium cost
Lower cost

Stripes indicate geographic variation within Europe

Aggregate evaluation is the average of the evaluations of the costs of hiring a PhD Scientist and a Contract Manufacturing Organisation.

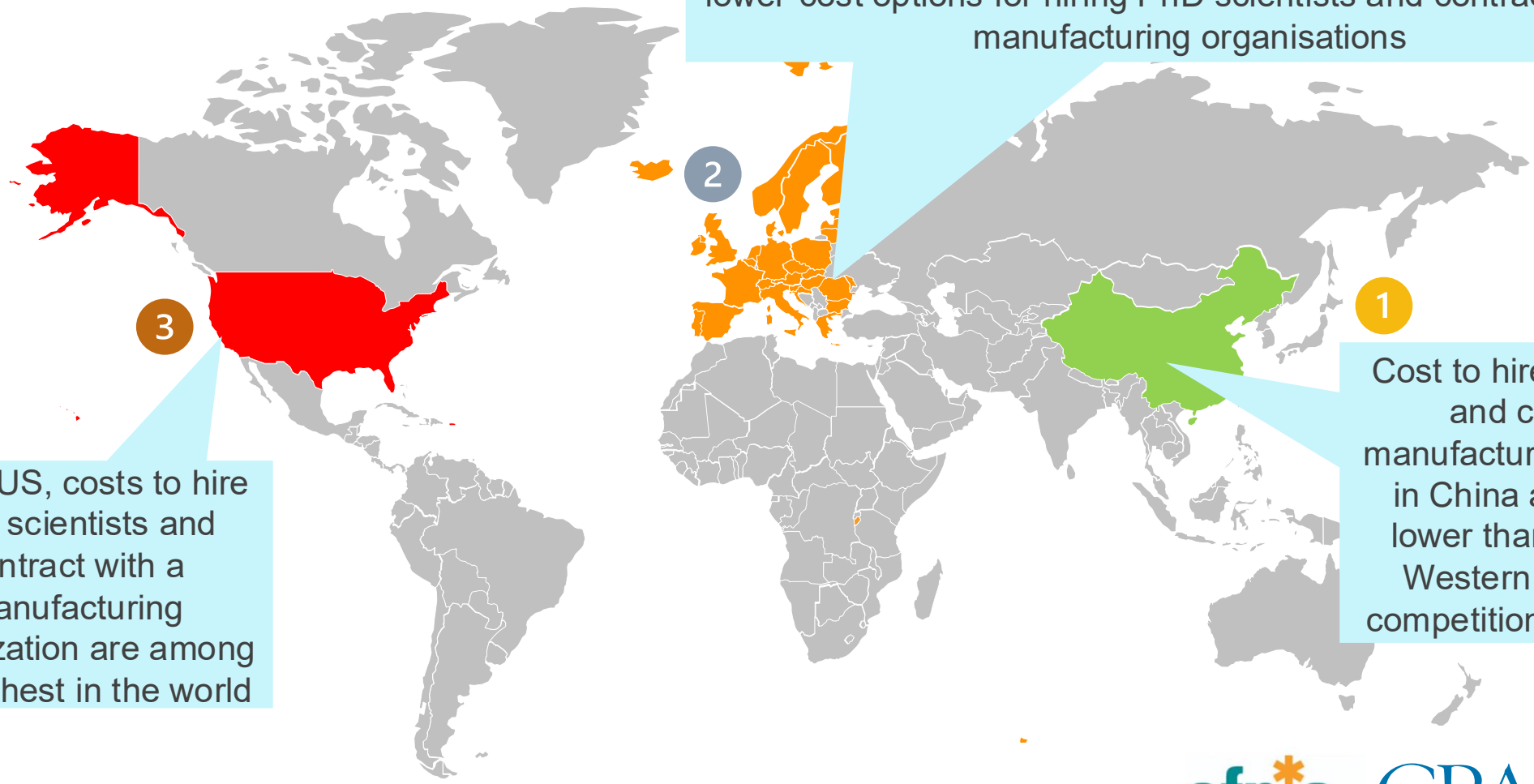
CMO: Contract Manufacturing Organisation
CDMO: Contract Development and Manufacturing Organisation

Cost of hiring PhD scientists and contracting CMOs/CDMOs, Europe pre-Biotech Act

Lower cost

Higher cost

Costs vary widely by country. Western Europe countries have comparable prices to the US, while Eastern Europe offers lower-cost options for hiring PhD scientists and contracting with manufacturing organisations



In the US, costs to hire PhD scientists and contract with a manufacturing organization are among the highest in the world

Cost to hire a PhD scientist and contract with manufacturing organisations in China are significantly lower than in the US and Western Europe due to competition and high supply

CMO: Contract Manufacturing Organisation
CDMO: Contract Development and Manufacturing Organisation

* Europe includes the EU27, EFTA, and the UK

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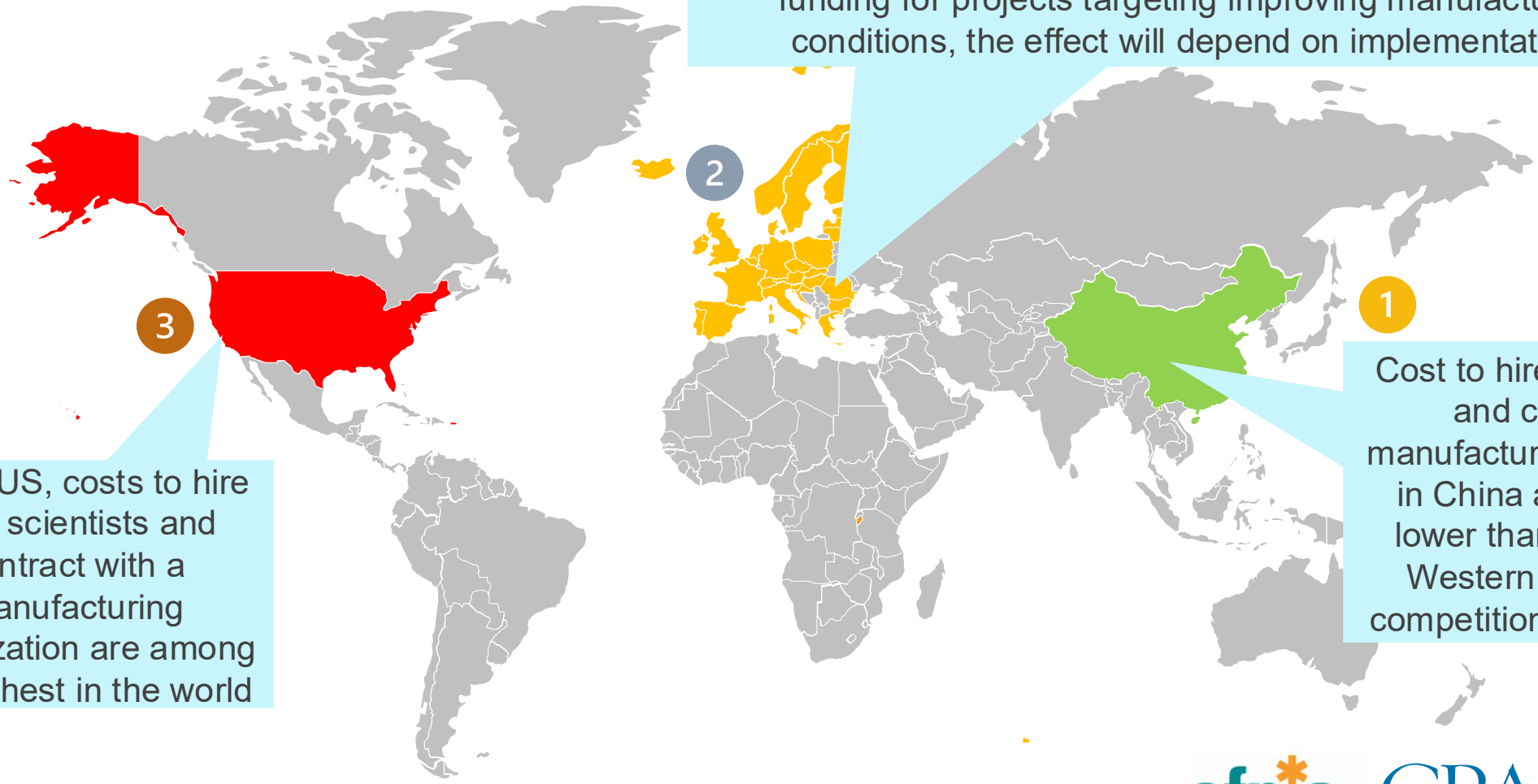
Cost of hiring PhD scientists and contracting CMOs/CDMOs, Europe post-Biotech Act

Setting Up Production

Lower cost

Higher cost

The Biotech Act has little impact on the cost of hiring PhD scientists. While the Biotech Act may result in increasing funding for projects targeting improving manufacturing conditions, the effect will depend on implementation.



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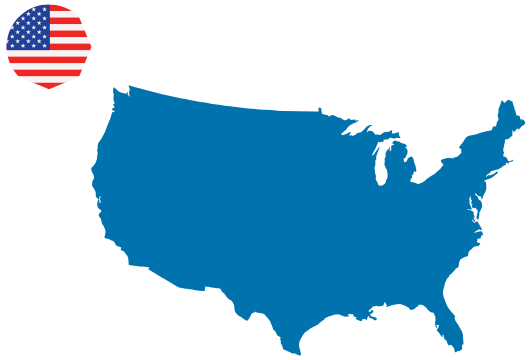
Preparing to launch

Policy context: preparing to launch

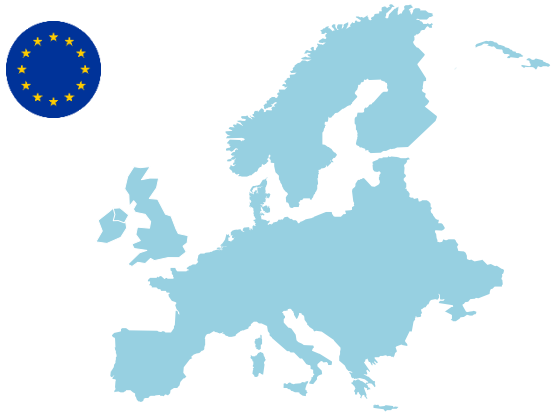


78%

The proportion of new drugs globally sold in the US within 1 year[1]

3%

The proportion of new drugs globally sold in China within 1 year[1]



15%

The average proportion of new drugs globally sold in Europe within 1 year[1]

- Launch preparations in the EU require marketing authorisation from EMA and country-specific HTA[2,3]
- The JCA moves the EU towards a standardised HTA dossier for clinical effectiveness and safety, but economic analyses remain at the country-level[4]
- While the EU targets a 90 active day initial review of HTA dossiers, real review times often exceed this[5,6]
- Reimbursement and access are decided by HTA bodies, which differ by country[7]
- Delayed access to innovative oncology drugs due to regulatory approval and HTA timelines has led to 3000 life-years lost per drug per country in Europe[8]

EMA: European Medicines Agency
HTA: Health Technology Assessment
JCA: Joint Clinical Assessment

Note: Using EU flag but depicting Europe.

Considerations by company size: preparing for launch

Considerations Affecting all Companies

- Slow, complex, and fragmented regulatory frameworks lead to long, costly, and uncertain authorisation processes, hindering innovation[1]
- HTA filing requirements may ask for data beyond clinical endpoints required for marketing authorisation, creating an additional evidence gap that manufacturers must fill[2]

Additional Burden for Smaller Companies

- Smaller companies are less likely to have dedicated staff with regulatory expertise, which may exacerbate difficulties in responding to agency questions[3]
- Smaller companies have significantly longer submission delays than larger companies, typically due to clock stop time[3]
- HTA fees in some countries may be particularly burdensome for smaller companies focused on developing orphan diseases with reduced funding[4]

Total Consideration Affecting Smaller Companies

HTA: Health Technology Assessment

Relevant metrics: preparing to launch

Preparing to Launch

Length of Regulatory Submission Process

- Increases in regulatory review times are associated with reduced R&D in the corresponding therapeutic area[1]
- Extended regulatory submission processes delay patient access to drugs and exacerbate inequities in medicine availability within Europe[2]
- One study found that, even among therapies first filed with the EMA, the majority receive approval from other regulatory agencies first due to differences in review time[2]

Cost of HTA Submission

- Countries with public health systems are increasingly using HTAs to assess pricing and reimbursement of new treatments[3]
- High HTA fees may be burdensome, especially for companies focused on orphan/rare diseases or other diseases with low expected reimbursement prices[3]
- Differences in speed and cost of HTA review introduces patient access inequalities across different countries[4]

R&D: Research and Development
EMA: European Medicines Agency
HTA: Health Technology Assessment

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Comparison across key markets: preparing to launch metrics

Country/ Region	Length of Regulatory Submission Process		Cost and Time-to-Decision of HTA Submission		Aggregate Evaluation
	From filing (which is up to two months), up to 10 months (around 200 working days) for standard review; up to 6 months for priority review.[1]		The US lacks a centralised healthcare system that requires HTA filing, so there is no cost or time involved.[6]		
	Up to 200 working days; 130 for priority review; 70 for rare disease drugs marketed overseas. This does not include time provided for the applicant to submit a supplemental dossier at Day 80.[2]		Required by the NHSA as part of NRDL inclusion negotiations, but cost to file is unknown.[7] Median time to NRDL listing is 12 months.[8]		
	Up to 180 “active days”; 150 for accelerated assessment. This time does not include the up-to 4 months for “clock-stops” during which the applicant prepares answers to questions raised by the CHMP.[3,4] In one study, all applications receive at least 1 clock-stop, and 99% received at least 2.[5]		Under the JCA, the HTA dossier for a single treatment may require compliance with dozens of PICO schemes for different countries.[9, 10] Dossiers must be submitted within 100 days of PICO scope confirmation and can be 30,000 pages.[11] The median time from HTA dossier submission to reimbursement recommendation varies widely for countries, from 53 to 264 days.[12]		
Post-Biotech Act 	No direct effect from Biotech Act		No direct effect from Biotech Act. Costs and time vary by country.		

 Slower authorisation time; higher cost

 Medium authorisation time; medium cost

 Faster authorisation time; lower cost

 Stripes indicate geographic variation within Europe

Aggregate evaluation is the average of the evaluations of the length of the regulatory review process and the cost of and time-to-decision for HTA submissions.

CHMP: Committee for Medicinal Products for Human Use
HTA: Health Technology Assessment
NHSA: National Healthcare Security Administration
NRDL: National Reimbursement Drug List
PICO: Population, Intervention, Comparator, Outcomes

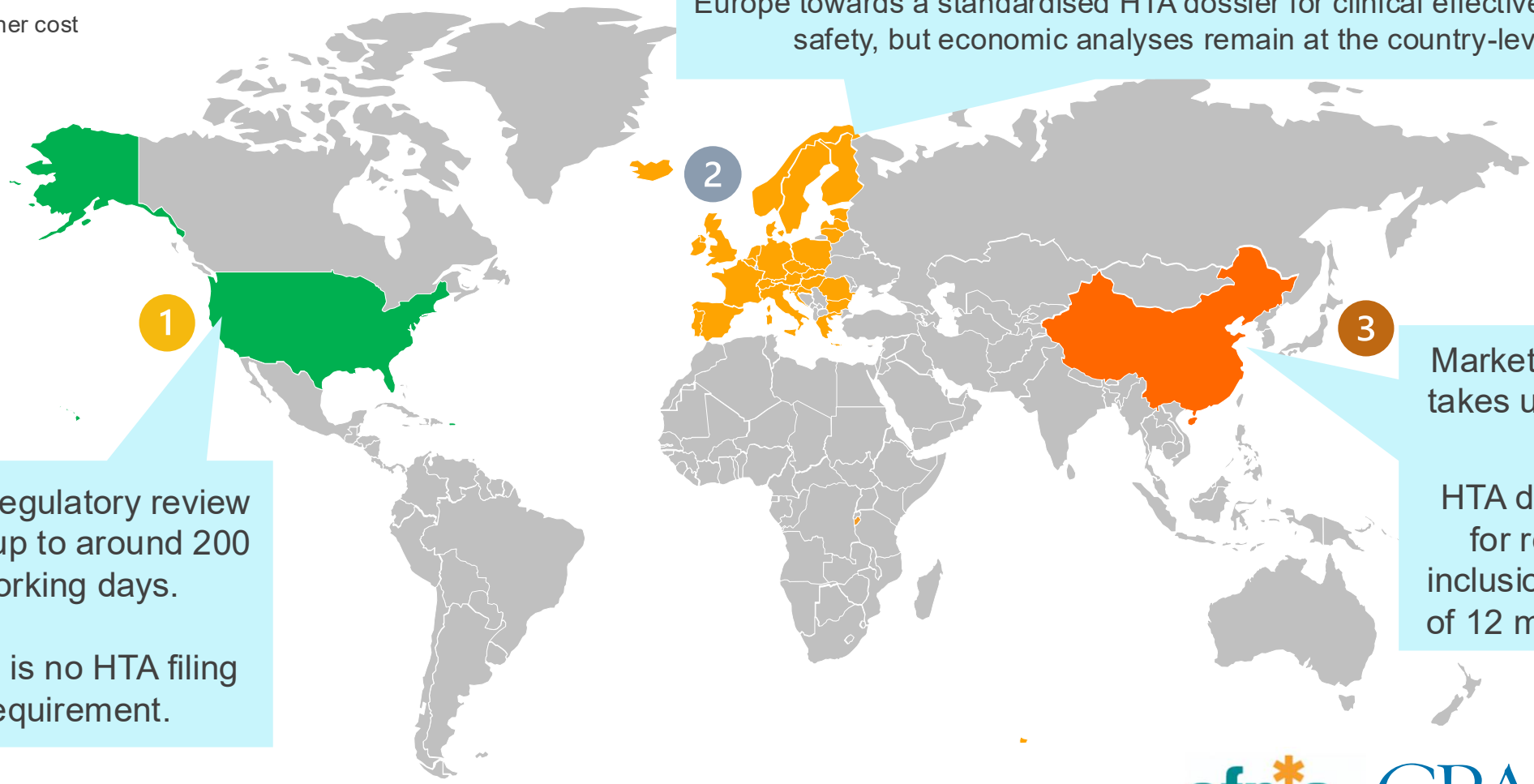
Marketing authorisation speed and cost of HTA submission, Europe pre-Biotech Act

Preparing to Launch

Faster and lower cost

Slower and higher cost

Marketing authorisation takes up to 180 active days. HTA requirements vary across countries in both cost and length of time. The JCA moves Europe towards a standardised HTA dossier for clinical effectiveness and safety, but economic analyses remain at the country-level.



Initial regulatory review takes up to around 200 working days.

There is no HTA filing requirement.

Marketing authorisation takes up to 200 working days.

HTA dossiers required for reimbursement inclusion, with a median of 12 months for review.

HTA: Health Technology Assessment
JCA: Joint Clinical Assessment

* Timelines given for standard review; expedited review timelines differ

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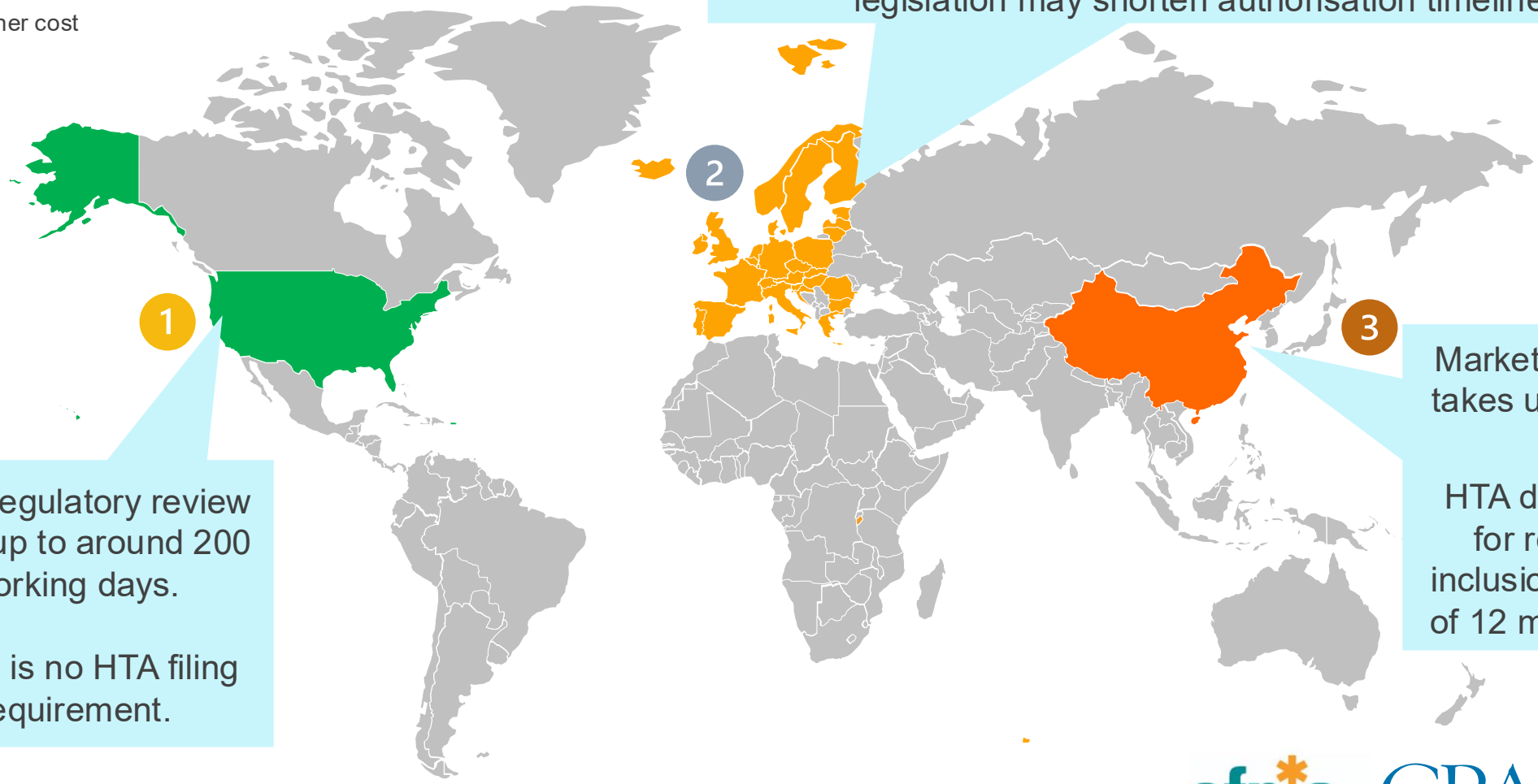
Marketing authorisation speed and cost of HTA submission, Europe pre-Biotech Act

Preparing to Launch

Faster and lower cost

Slower and higher cost

Marketing authorisation time is unaffected by the Biotech Act, and HTA requirements remain fragmented by country. Other legislation may shorten authorisation timelines.



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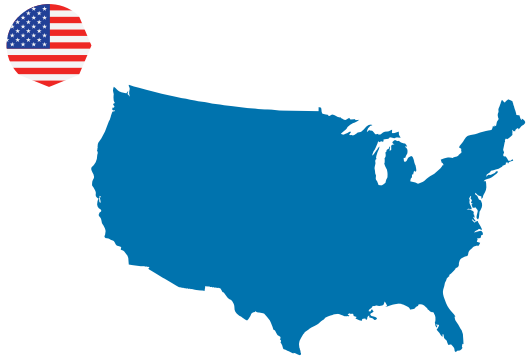
Maintaining a presence

Policy context: maintaining a presence

Maintaining a Presence

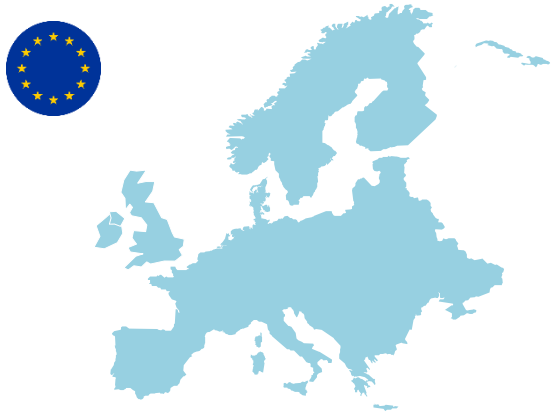


~5,700

Small pharmaceutical and medicine manufacturing firms and small R&D biotechnology firms[1]*

~8,300

Small enterprises engaged in manufacture of medicines[2]*



~1,900

SMEs engaged in developing and marketing medicines[3]*

- To act as a marketing authorisation holder in Europe, pharmaceutical companies must hold a European address or appoint a representative to handle compliance obligations[4]
- Some European countries require separate local authorisations to sell drug products, adding physical presence requirements[5]
- The EU lags behind the US and China in the number of small enterprises engaged in pharmaceutical R&D and manufacturing[1,2,3]

* Captures small pharmaceutical enterprises with fewer than 250 employees in the US and Europe, but unknown employee size for "small enterprises" in China.

R&D: Research and Development
SME: Small and Medium Enterprise

Note: Using EU flag but depicting Europe.

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Considerations by company size: maintaining a presence

Considerations Affecting All Companies

- R&D tax incentives vary by country, and there are transaction costs associated with changing geographies for more favourable regions[1]
- Increasing clawback rates require manufacturers to ensure an annual sales growth rate at least as high as that of the clawback rate, in some instances incentivising health expenditure inflation[2]
- Cost-containment measures are increasingly popular for innovative drugs in some countries[3]

Additional Burden Affecting Smaller Companies

- Even in countries with tax policies promoting R&D investment, smaller companies often fail to claim available support due to tax system complexity[4]
- Cost-containment efforts impact the commercial potential of both current and future assets, which may place additional burden on smaller companies operating with limited capital[5]

Total Consideration Affecting Smaller Companies

R&D: Research and Development

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Relevant metrics: maintaining a presence

Tax Incentives for R&D

- The majority of government support for business R&D comes from tax incentives, rather than direct funding[1]
- In one statistical model, increased governmental R&D tax incentives resulted in a greater number of pharmaceutical companies choosing to innovate, which has a knock-on effect on further innovation[2]
- R&D tax incentives have a significantly larger effect for smaller companies than larger firms across both research and experimental development[3]

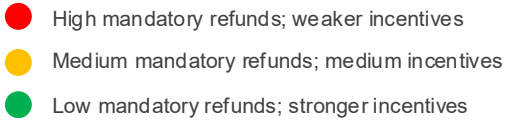
Mandatory Industry refunds

- Continued pressure from clawbacks threaten the uninterrupted supply of medicine to hospitals, especially in less-affluent countries[4]
- High clawback rates create unpredictability and both lead to reduced future investment and jeopardise existing investment presence[5]
- Cost-containment measures that lower manufacturer profitability have a direct negative impact on corporate R&D investment decisions, resulting in long-run reduced patient access to novel medicines.[6,7]

R&D: Research and Development

Comparison across key metrics: maintaining a presence

Country/ Region	Presence of Mandatory Industry Refunds		Generosity of Tax Incentives for R&D		Aggregate Evaluation
	No mandatory industry refunds. Manufacturers engage in rebating discussions with pharmacy benefit managers and payors in exchange for formulary placement.[1,2]		The US ranks far below the EU and China in expected tax relief per additional unit of R&D investment. This remains true across the entirety of profitable and loss-making large firms and SMEs.[5]		
	No mandatory industry refunds. Manufacturers instead enter into volume-for-price negotiations in order to be included on the National Reimbursement Drug List.[3]		China is ranked in the top 10 countries for expected tax relief per additional unit of R&D investment, which remains true across both profitable and loss-making large firms and SMEs.[5]		
	As of 2024, mandatory industry refunds, including mandatory rebates, mandatory sales tax, clawbacks, and refunds under managed entry agreements, have risen to 24% of European public pharmaceutical revenue.[4]		With 4 EU Member States in the top 5 countries for expected tax relief, European countries provide some of the strongest R&D tax incentives. On average, however, European countries lag behind China, suggesting variation in R&D tax incentives.[5] In some countries, SMEs benefit from higher tax subsidy rate.[6]		
Post-Biotech Act 	The Biotech Act has no direct effect		The Biotech Act has no direct effect		



Stripes indicate geographic variation within Europe

Aggregate evaluation is the average of the evaluations for XX and the generosity of R&D tax incentives

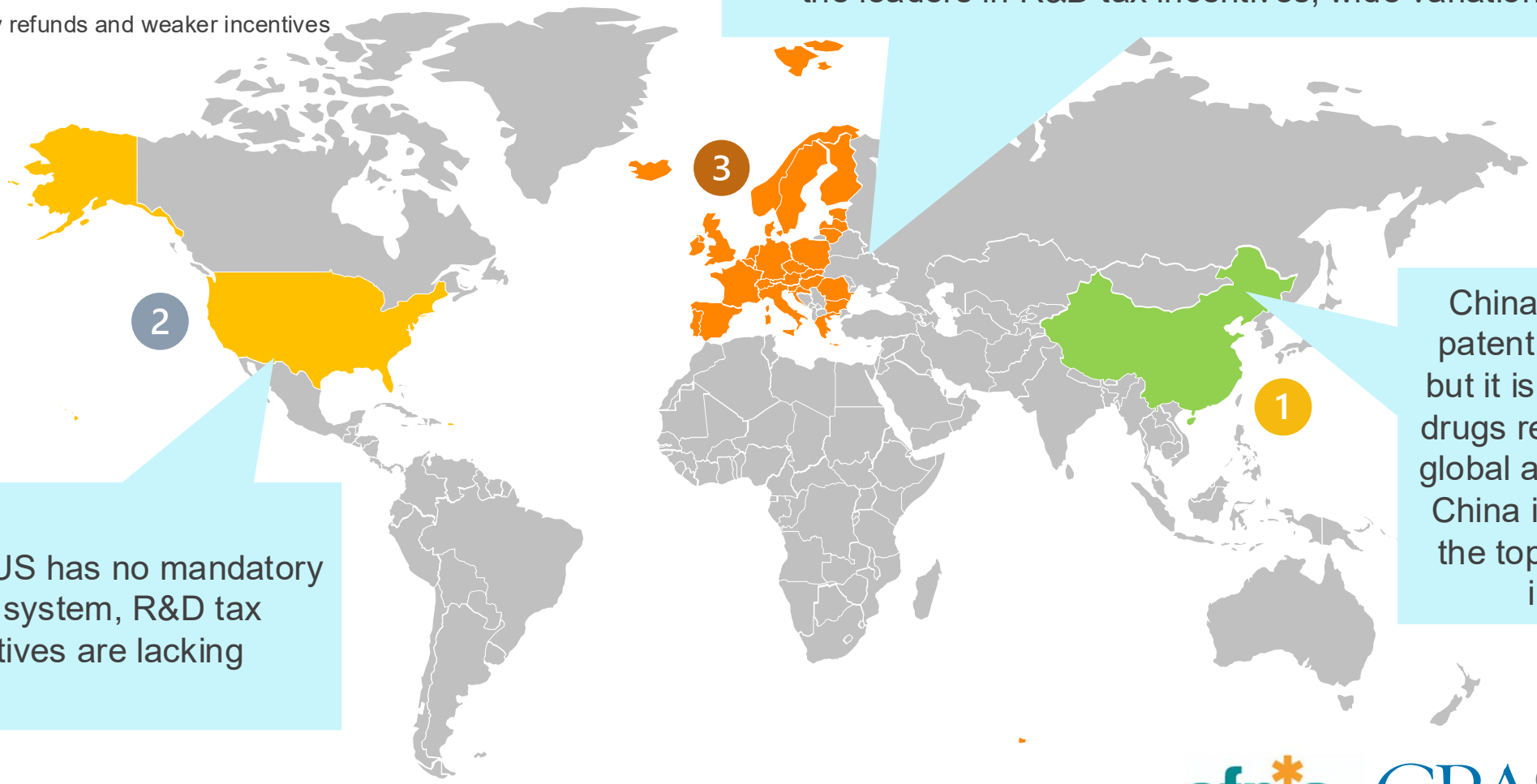
R&D: Research and Development
SME: Small and Medium Enterprise
SPC: Supplementary Protection Certificate
ATMP: Advanced Therapy Medicinal Products

Mandatory industry refunds and R&D tax incentives, pre-Biotech Act

Low mandatory refunds and stronger incentives

High mandatory refunds and weaker incentives

In 2024, the mandatory industry refunds reached 24% of public pharmaceutical revenue. While EU Member States are among the leaders in R&D tax incentives, wide variation exists.



While the US has no mandatory refund system, R&D tax incentives are lacking

China offers a 5 year patent term extension, but it is only available to drugs receiving their first global approval in China. China is ranked among the top 10 for R&D tax incentives.

R&D: Research and Development

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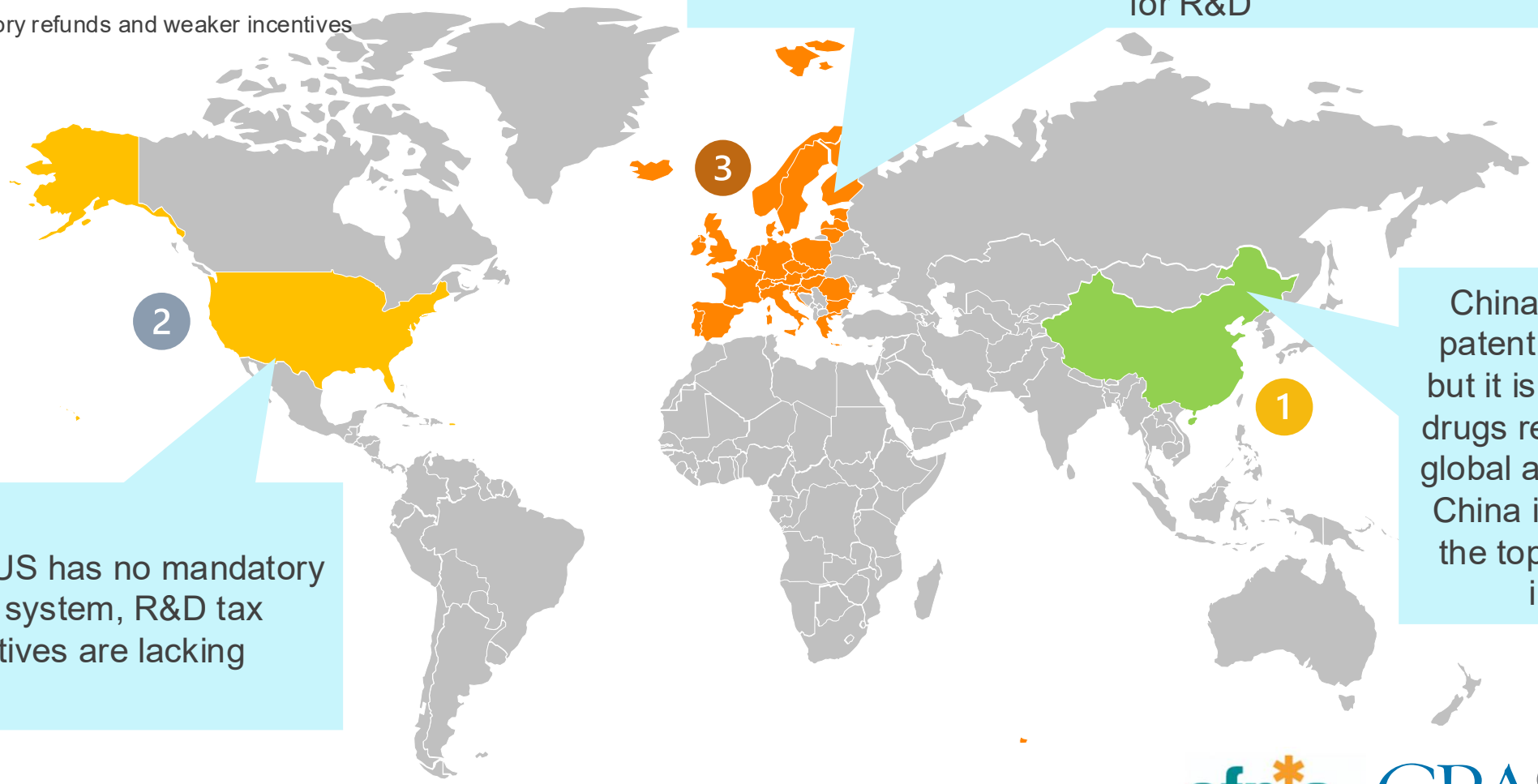
Mandatory industry refunds and R&D tax incentives, post-Biotech Act

Maintaining a Presence

Lower mandatory refunds and stronger incentives

Higher mandatory refunds and weaker incentives

With the passage of the Biotech Act, there are no changes to either the mandatory industry refund system or tax incentives for R&D



While the US has no mandatory refund system, R&D tax incentives are lacking

China offers a 5 year patent term extension, but it is only available to drugs receiving their first global approval in China. China is ranked among the top 10 for R&D tax incentives.

R&D: Research and Development

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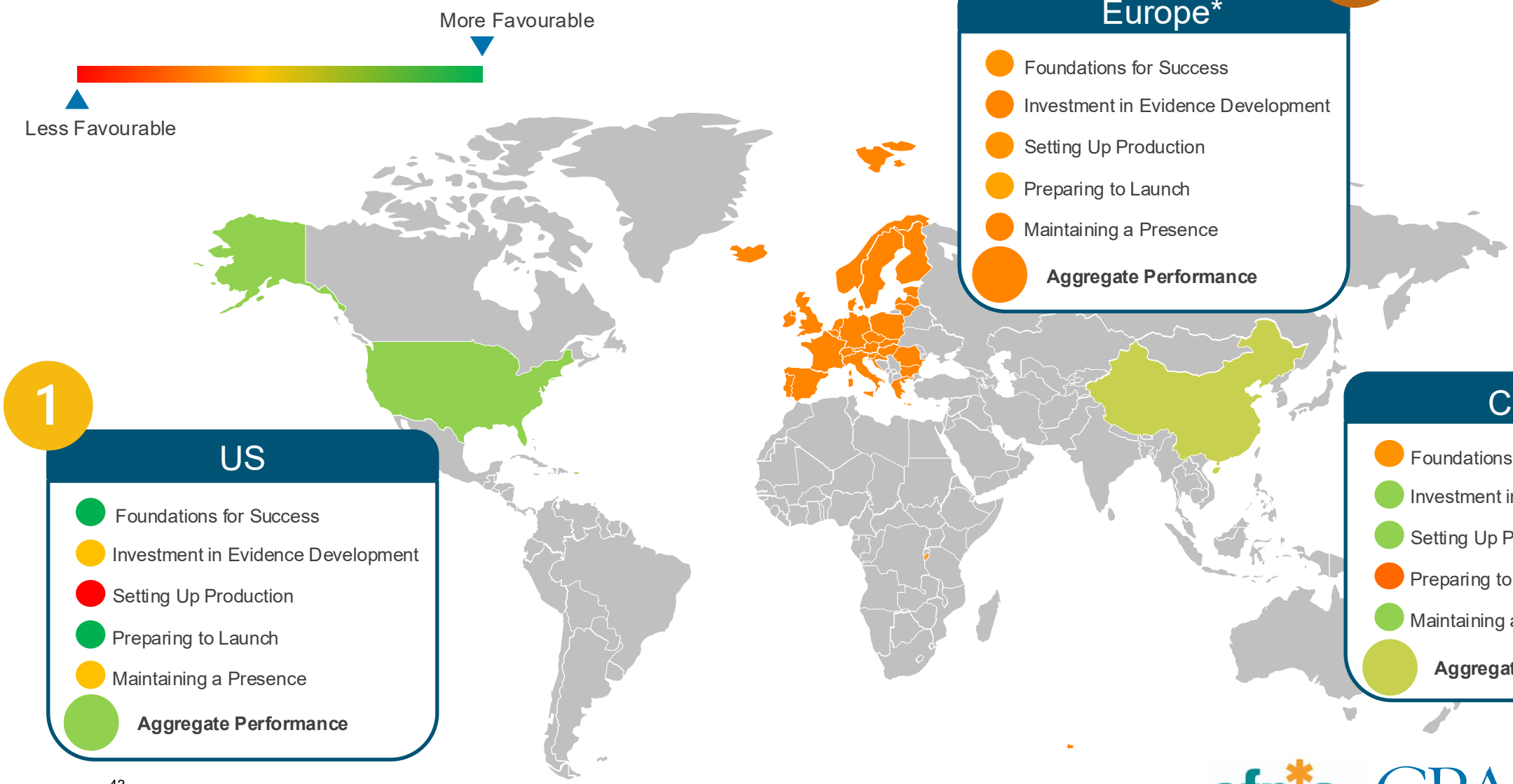
Summary

Aggregate attractiveness for investment, pre-Biotech Act



* Europe includes the EU27, EFTA, and the UK

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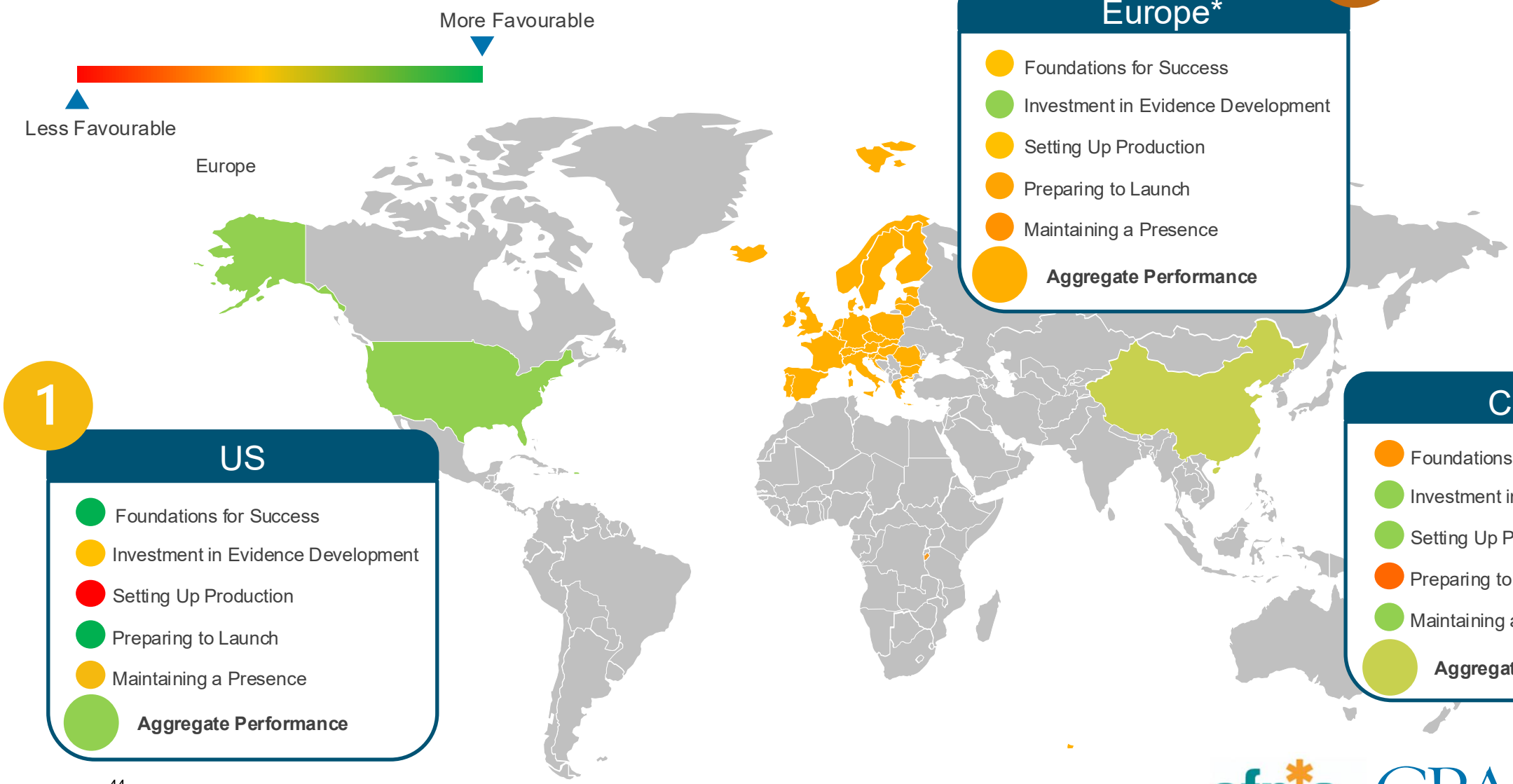
Aggregate attractiveness for investment, post-Biotech Act



3

Europe*

- Foundations for Success
- Investment in Evidence Development
- Setting Up Production
- Preparing to Launch
- Maintaining a Presence
- **Aggregate Performance**

1

US

- Foundations for Success
- Investment in Evidence Development
- Setting Up Production
- Preparing to Launch
- Maintaining a Presence
- **Aggregate Performance**

2

China

- Foundations for Success
- Investment in Evidence Development
- Setting Up Production
- Preparing to Launch
- Maintaining a Presence
- **Aggregate Performance**

* Europe includes the EU27, EFTA, and the UK

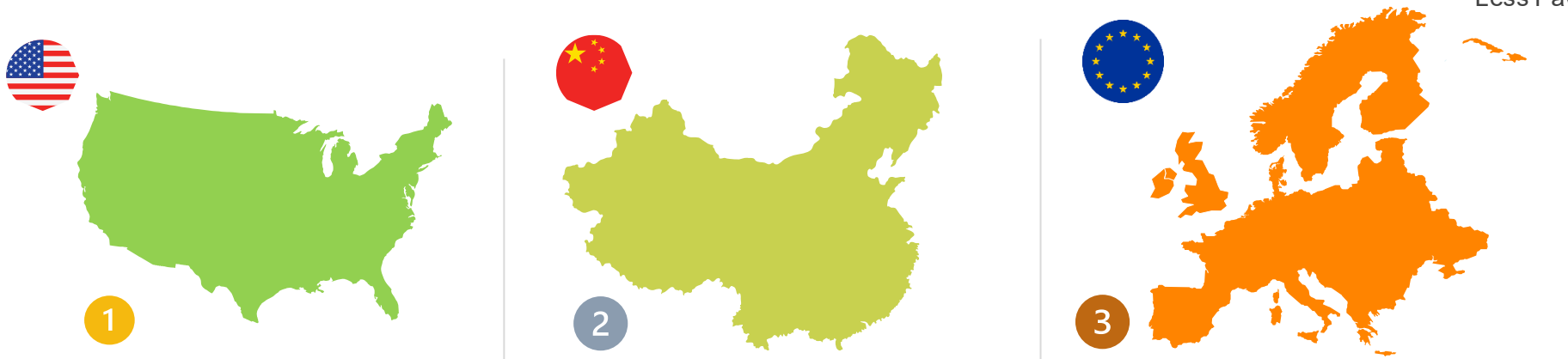
44

Aggregate attractiveness for investment, pre- and post-Biotech Act

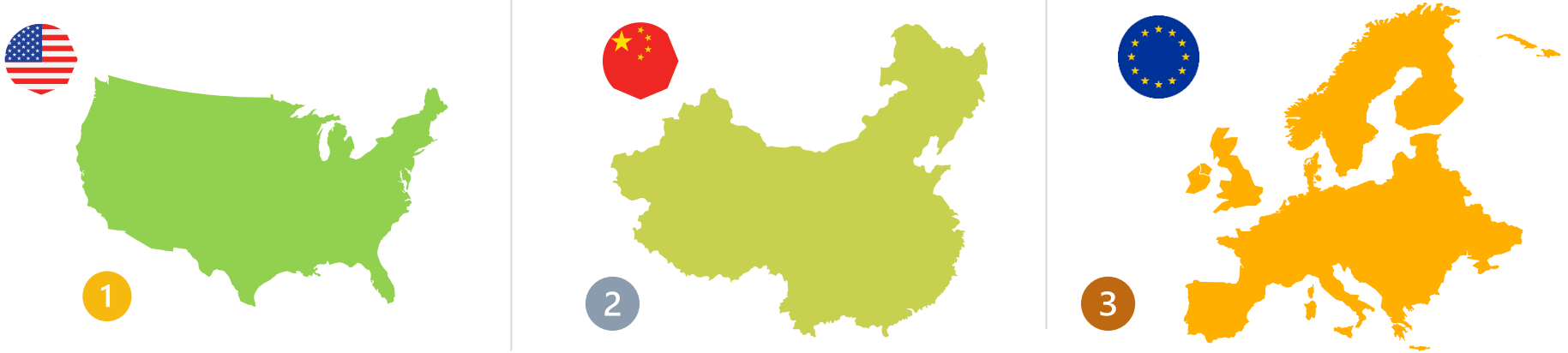
More Favourable

Less Favourable

Pre-Biotech Act:



Post-Biotech Act:



While certain provisions in the Biotech Act help to narrow the gap between Europe and the US and China, it is insufficient to fully close the gap, and Europe remains in third place.

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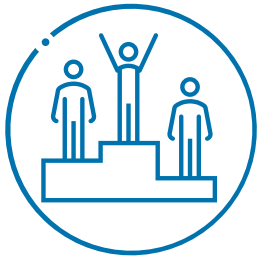
Key takeaways

Looking at Europe‘s competitiveness as a location for Life Science investment from a smaller company perspective brings the challenges into focus



Out of the 5 identified key investment decision points Europe is not leading the other regions on any category.

The proposed European Union Biotech Act has some positive impact on European attractiveness but is not a panacea.

Further actions beyond those set out in Biotech Act are necessary to elevate Europe’s competitiveness as a destination for pharmaceutical investment.

Regional takeaways

- Although the US is a costly environment for clinical development and setting up production, this is **more than made up by access to funding, speed to market and market size**.
- China offers a **low-cost, flexible environment**, with a competitive regulatory regime.
- Europe is **losing ground** in terms of competitiveness and has a **challenging access environment**.

Appendix

Appendix

Methodology and additional considerations

Evidence

- Key investment decision points for life sciences companies were selected based on desk research and validated with discussion with small firm experts (with additional interviews on-going).
- The underlying references are reported in the notes pages of this report. This is based, where possible, on recent academic studies. However, in other cases, it is based on estimates from the grey literature. Although not as robust, these sources are often the only ones with comparable data or data on the small company perspective.

Aggregation

- Europe (EU27 + EFTA + UK), the US, and China are evaluated using a traffic light system for each investment decision on the basis of two key metrics. In reality, many other considerations could be taken into account in an evaluation of each of the investment decision points.
- For simplicity, we have assumed that the two key metrics in each investment decision point are equally weighted. An aggregate evaluation was determined for each investment decision and country. This is a key limitation of the study.
- The aggregate evaluations for each of the investment decisions were combined into a composite evaluation for each of Europe, the US, and China, and corresponding rankings were assigned.

Forward looking approach

- The text of the Biotech Act was reviewed for provisions that could directly impact the key investment decisions.
- US and China policies both pre- and post-Biotech Act reflect the current state of the policy ecosystem and do not predict future policy actions. It is possible that current proposed legislation, such as MFN pricing in the US, will change the policy landscape and the decisions that biotech firms make. Equally, regions could respond to changes in the Biotech Act.

Interaction between the decision points and regional focus

- In reality, the decision to invest in a country or region will depend on the interaction between the decision points. For example, the increased cost of investment can be overcome by the strength of the commercial environment.
- The focus is on regionally relevant policy issues affected, so we have chosen primarily not to focus on pricing and reimbursement issues (a national competence) issues.