



CPHI Pharma Survey and Industry Rankings 2024

BIOSECURE; bio innovation and processes; VC funding return; the pharma league tables and the quiet rise of Lombardy

Produced by **defacto**



Methodology

This is the eighth CPHI Annual Survey and explores the insights of nearly 280 industry executives from every region of the globe – survey completed in September 2024. The rankings evaluate all major pharmaceutical markets across key indicators including ‘growth potential’, ‘quality of API manufacturing’, ‘competitiveness’, and ‘quality of finished product manufacturing’ among many other survey questions – culminating in overall scores for each country. In addition, this year we have launched the European Manufacturing Hub index for both solid dose and biologics.

Respondent Breakdown: Europe 25%, Latin America 3.5%, North America 14%, India 25%, Africa 3%, Middle East 4%, Southeast Asia 7.5%, China 8%, Rest of the World 10%

Top Firms Involved: Pharma Company Innovator 49%, Biotech 5%, CROs & CDMOs 10%, Government Academia 3%, Distributors 9%, Ingredients Manufacturer 4%, Consultancy 9%, Wholesale 3%, Financial Institutions 1%, Other 7%

When we reviewed industry prospects and looked at the primary issues de jour at this time last year we saw four major uncertainty’s affecting prospects, namely: funding, inflation, war and reshoring. The first question was when will funding return to biotech and how quickly this would transfer through to CDMOs. The answer to this first question appears to have been slower than expected and Brian Scanlan will give his full funding predictions latter in this report. The second issue of inflation last year’s analysis correctly identified as ‘falling back in 2024’, yet at the time of writing, the nadir of a slowing US economy has wobbled stock markets. The war in Ukraine, while not resolved, and certainly still having the potential for global disruption, has become a known uncertain, and as such, has dissipated from pharma media narratives. Which leaves finally the elephant in the room that has unsettled drug discovery and development paradigm – reshoring, near shoring and stability in supply chains – and in particular the continuing tensions between the United States and China. Few will have failed to notice the BIOSECURE Act and along with a change of President in the White House – if not necessarily party – what is the direction of travel for US-Sino relations. The pharma industry is, of course, incredibly global and starting materials are primarily sourced from Asia markets – mainly China. As we will discuss later in this piece, the industry is ambivalent on what comes next, with even the most clairvoyant of analysts scrambling to anticipate how this debate will resolve, and what the short-, medium- and long-term implications are.

The positives however are also again accelerating, and we saw a continued glut of FDA approvals, with rates equivalent to the record levels seen pre-pandemic. In 2023, there were 55 drug approvals, which is just four shy of the all-time high reported in 2018, and significantly 28 (54%) were for Rare Disease indications and 17 for biologics^{1,23}. So far in 2024 the rate of innovation has remained strong, the FDA has approved a further 29⁴ drugs including notable breakthroughs like Donanemab – a drug to treat the underlying biology of Alzheimer’s – and Casgevy the first approval of

CRISPR/Cas9 gene editing technology (which famously won its inventors the 2020 Nobel prize)^{5,6,7}. The latter two potentially herald the emergence of new era of drugs. For Alzheimer’s we have long sought for any effective treatment options that could address the underlying disease progression and so we it marks the begging of a new era in which we can begin preventing and potentially one day reverse decline. For Casgevy the effects are no less impressive as the beginning of the next 30-years of gene editing. Already new variations of CRISPR are being developed, such as base editing, which allows changes to be made to individual letters inside DNA, and prime editing – which replaces the CRISPR 1.0 ‘molecular scissors’ with enzymes and genetic instructions to insert, delete or rewrite short segments of DNA⁸.

GLP-1 (Ozempic, Wegovy, Trulicity, and Mounjaro) and PD-1 (e.g. Keytruda and Opdivo) drugs have also continued their meteoric rise and Globaldata predicts they will be worth a staggering \$156bn in annual sales by just 2029 – with GLP-1s growing at nearly 20% (CAGR) and reaching \$105 billion and PD1s returning figures of 5% and \$51 billion. The question is therefore do contract services firms have the right mixture of capabilities and capacities for the developments to emerge in the pipeline over the next 2-3 years.

Pharma investments in the supply chain are typically reactionary and especially those in the contract services sector, which relies upon commercial contracts to fund investments, so the implications of large numbers of molecules in the development pipeline could potentially mean slowing timelines. Two of the largest five CDMOs – WuXi AppTec and Catalent – have obvious questions about the availability of resources moving forward, particularly in the medium term. WuXi has no issues regarding available capacity, however, the implications of some of its massive volume of customers attempting to move to other outsourcing resources will most certainly have an indirect impact on the wider market. While Catalent’s acquisition by Novo Nordisk also creates some

1. <https://pharmaboardroom.com/articles/2023-fda-drug-approvals-second-highest-count-in-30-years/>
2. <https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2023-biological-license-application-approvals>
3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10856271/>
#:~:text=The%2055%20drugs%20approved%20this,so%2Dcalled%20small%20molecules%2C%20in
4. <https://www.fda.gov/drugs/novel-drug-approvals-fda/novel-drug-approvals-2024>

5. <https://www.nature.com/articles/d41587-023-00016-6>
6. <https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease>
7. <https://www.gov.uk/government/news/mhra-authorises-world-first-gene-therapy-that-aims-to-cure-sickle-cell-disease-and-transfusion-dependent-thalassemia>
8. <https://www.statnews.com/2023/11/16/crispr-vertex-sickle-cell-beta-thalassemia-casgevy-approval/>

uncertainly as we await the outcome of the Federal Trade Commission's view on the potential takeover. Namely, whether it sees the ability of Novo to boost capacity at the potential expense of its rivals as fair. So the medium-term implications of this acquisition on the contract services space and likely supply side economics remain opaque⁹.

Another new area of research for the Report in 2024 is to explore in detail the pharma manufacturing hubs across Europe in addition to the biotech centres added to our analysis last year. In particular with CPHI hosted in Milan – Lombardy being a major pharma hub – we rank the largest areas of production in Europe for best regions to undertake small molecule, device and/or biologicals manufacturing.

Additionally, the survey will deliver its usual global manufacturing rankings, while also exploring how many novel drugs the industry expects to be approved in 2025. As well as the ongoing implications of AI technologies on drug discovery/clinical trials and global efforts to reduce the costs of biologics production, notably through titre improvements and/or continuous manufacturing. The latter trend our report predicts will become increasingly intertwined with pharma's ongoing sustainability efforts, which increasingly include scope 3 emissions.

The other big trend from 2023 was the predicted revolutionary impact of Psychedelic drugs and, despite their strong efficacy potential, the last year has in fact been disappointing for its advocates. The potential we have seen and continue to see in trials has not yet been matched by a clear regulatory pathway with many companies failing to prove efficacy to the FDA. The two primary intractable issues remain 'how to blind studies effectively and show efficacy', but also, the added complexity of 'approving a drug/psychotherapy combination within existing rules'. Lykos Therapeutics failure in August – the FDA rejected its use of MDMA to treat post-traumatic stress disorder (PTSD) – is the indication's biggest setback to date but with other psychedelic innovators now hoping to learn the lessons with decisions pending on two further phase 3 trials for psilocybin use in combatting depression^{10,11}.

Where does all of this leave the industry looking forward to 2025 and beyond?

This is perhaps the million, billion or even trillion-dollar question, the short answer is in a very good place to build from in 2025 through to 2030. Innovation has continued apace despite lagging VC funding, while the stock market has – despite a few wobbles remained impressively strong. So with both capital expected to be imminently deployed by Private Equity in 2025 for acquisitions and the almost certain surge in VC funding ahead (it cannot stay parked indefinitely) we are potentially on the brink of one of pharma's best ever years in 2025 with the medium term for both biotech and contract services firms looking incredibly robust. This report's long-term projection is therefore that both

CRO and CDMOs will need to evolve more quickly than in the past to meet the next generation medicines now in early development, but also, will become more profitable and grow faster as a consequence.

The BIOSECURE Act

The Act had inauspicious beginnings late last December (2023) when a cross-party group put forward the legislation, with the Senate version passing to congress in January 2024. The original goal of which was a direct response to concerns about access to American patients' genomic data and allegations of involvement from the China Communist Party potentially accessing American innovation^{12,13}. However, these explosive origins have evolved over the year into a form that seeks to broadly allay concerns in the United States around pharma supply side security. An update to the bill in May 2024¹⁴ named 'companies of concern' – genomics companies BGI, MGI, and Complete Genomics and, perhaps most significantly, global CRDMO WuXi AppTec – and set a notional deadline of 2032 for US companies to remove or not renew contracts with the companies¹⁵. Until just before the time of publication the bill had reached a, at least temporary, impasse as it was not included in the National Defence Authorization Act for the fiscal year 2025. However, that was most likely a result of parliamentary procedures rather than a distinct change of legislative direction, and it may simply mean a new bill is needed to take this forward¹⁶.

Update: At the time of writing, we have just seen a major move forward as the Bill was passed on September 9th in the House of Representatives [the House] by 306 to 81 [i.e. greater than the two thirds majority needed to advance]. However, most analysts still predict the Bill will "need to hitch a ride" with another legislative vehicle to advance, especially as we enter the dead season between administrations¹⁷. The true litmus test of the way forward however will come on Senate review where individual law makers have much greater powers. It is likely the Bill will be modified in some form after further Senate scrutiny and could yet see Lawmakers set aside the legislation in light of recent opposition from prominent democrats [e.g. Rep. Jim McGovern (D-Mass.) and Rep. Jake Auchincloss (D-Mass.)]¹⁸. Ultimately, if it does advance further the most likely route to become Law would be via a larger legislative bill such as the annual defence bill or government funding legislation. Putting aside the implications for the named companies, it still leaves both the innovators and wider outsourcing sector with significant uncertainty. For example, assuming it goes ahead in some form, are there opportunities for other global CRO/CDMOs, and/or do preclinical biotechs now need to be mapping and changing their journey to commercialisation much earlier – with competition for places rising if China's considerable discovery and development resources are likely removed from the equation.

13. <https://www.reuters.com/technology/chinas-wuxi-apptec-shared-us-clients-data-with-beijing-us-intelligence-officials-2024-03-28/>

14. <https://cen.acs.org/business/outsourcing/Amended-BIOSECURE-Act-sets-new/102/i15>

15. <https://www.fiercepharma.com/manufacturing/wuxi-apptec-wuxi-biologics-shares-jump-after-BIOSECURE-acts-unexpected-exclusion>

16. https://identity.biocentury.com/?redirect_uri=https%3F%2Fwww.biocentury.com%2Farticle%2F652699%2FBIOSECURE-act-may-have-less-impact-positive-and-negative-than-anticipated

17. <https://www.statnews.com/2024/09/09/house-passes-biosecure-act-targeting-china-biotechs/>

18. <https://www.biocentury.com/article/653505/biosecure-passes-house-but-senate-fate-uncertain>

9. <https://www.statnews.com/pharmalot/2024/08/19/novo-nordisk-catalent-ftc/>

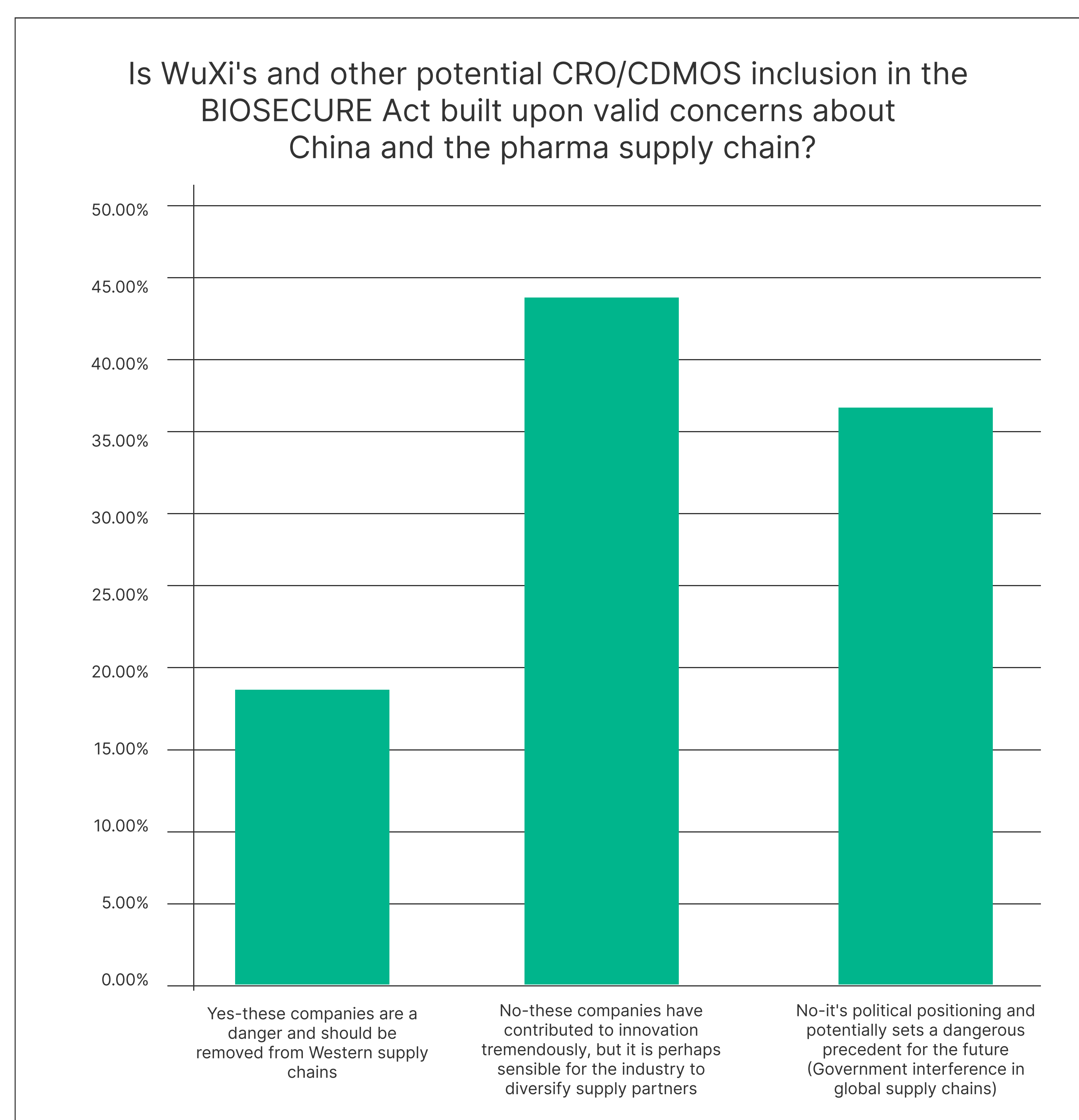
10. <https://www.nature.com/articles/d41586-024-02597-x>

11. <https://www.science.org/content/article/fda-rejected-mdma-assisted-ptsd-therapy-other-psychedelics-firms-intend-avoid-fate>

12. <https://cen.acs.org/business/outsourcing/House-bill-targets-Chinese-outsourcing/102/i4>

So with these great variables and winds of legislative change as our backdrop we asked global pharma what they felt was behind the BIOSECURE Act and their perspectives on potential outcomes in 2025. Not surprisingly, the industry has responded with tremendous ambivalence: yet only 19% have taken a very hard-line perspective that China based-CDMOs 'are a threat and should be removed from Western Supply chains'. Diametrically opposed to this position are 38% of respondent who argue that BIOSECURE is entirely a 'politically motivated issue that sets a dangerous precedent for the industry'. For example, while Indian CDMOs have chiefly reported a beneficial impact thus far, some analysts are postulating whether this might be the beginning of a much larger US protectionism and move toward near and or home shored options. These concerns are of course being monitored by the larger global players and it will be unsurprisingly to see further acquisitions of US sites by foreign owned outsourcing providers in 2025 – as they will then have the flexibility to offer a US based resource to customers.

The final 43% of the industry – and therefore the largest grouping – take a balanced view, which is both in support of 'WuXi's tremendous contribution to the industry', but also suggesting that it is perhaps sensible for the industry to 'diversify supply partners'. This position reflects the long-term debate – running as far back as the middle part of the last decade – on how much of the industry should be outsourced and to where for optimal discovery and commercialised supply chains.



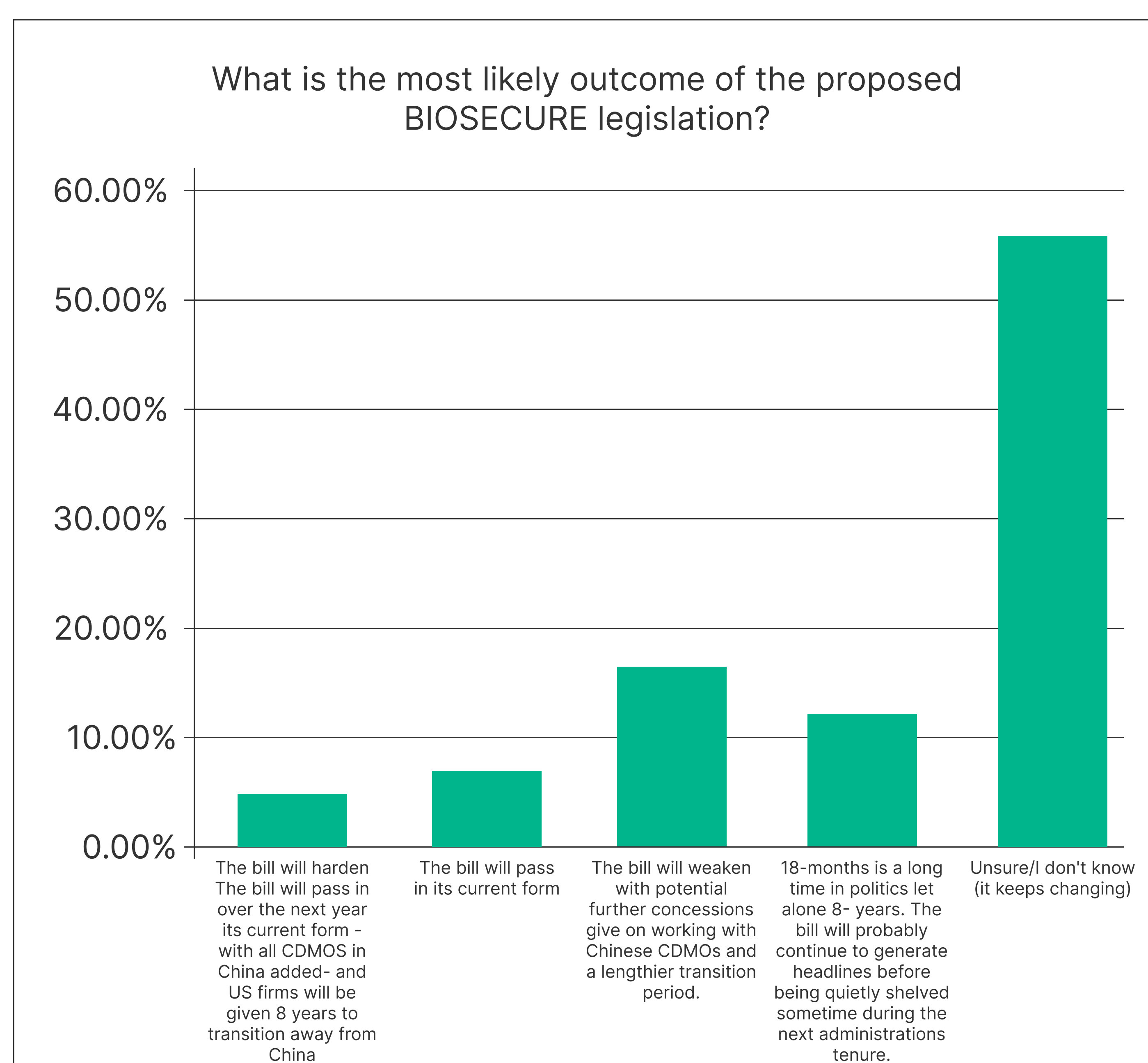
Where does the legislation go next.... Report update: as of September 9th - the Senate

Perhaps the bigger and more interesting question is, of course, what comes next and here the industry is at the mercy of both political winds of change as well as what form of legislation lawmakers in the Senate take, and how it potentially moves forward either as a standalone Bill or as part as another act.

For example, the prescriptive details of the Act have changed a few times already and many experts suggest it will change further as more legislators are made aware how disruptive a full or even partial decoupling will be [putting aside any thoughts of fairness and due process – which have been terms frequently used by the accused companies]

The ongoing debate has shone a special light on WuXi AppTec and taking just its small molecule [Chemistry] unit – excluding both its biologics and advance therapy companies – it was recently reported to be involved in a staggering circa 62 FDA approved drugs²⁰ during DCAT Week²¹. That means the company is responsible for manufacturing either the API, intermediate or finished dose of these drugs and, in many cases, all aspects the drug manufacturing. In fact, the CDMO supported 27% of all FDA small molecule drug approvals from 2023 – so its impact on commercial drugs is enormous, not even accounting for the thousands of molecules it supports in various phases of development²². To put these figures into context, India's contract services industry at present is believed to support around a dozen [novel] commercial FDA approved drugs from the country.

Emphasising the ongoing uncertainty over half (52%) of the industry said they simply did not know how it might unfold as the situation 'keeps changing' – however, it should be noted the survey question was asked prior to the September 9th House vote decision. Of those that did proffer potential outcomes the consensus is that the bill will likely be weakened or shelved at some point in the future (34%). In fact, just 8% of the industry believe the bill 'will pass in its present form' with even fewer just (6%) believing the legislation will be hardened before becoming law. So as we head into a new administration next year, the analyst consensus is that with so much of American drug development and innovation riding upon a global supply chain it may well be a self-inflicted wound to aggressively pursue the removal of China based CDMOs that contribute so much to therapeutic development. Especially, when so much of the industry's starting materials originate in China meaning that BIOSECURE will slow novel development hindering USA-based biotech, but without really tackling the biggest area of supply chain insecurity in chemical precursors and starting materials. What it has done however, is created a renewed optimism among Indian CRDMOs – who excel in the discovery to development paradigm thanks to large scientific workforces – but also CDMOs and CMOs in the West that are now potentially more attractive commercial supply options. Investors are already reportedly looking at opportunities in other Asian markets – mainly India and Korea – and in the West with leading CDMOs [e.g. Lonza, Recipharm and Thermo fisher et al]²³



One of the speculated ‘side-effects’ of the BIOSECURE uncertainty is whether this is slowing development decisions in the United States, as biotechs – the most likely effected group in a ‘disorderly decoupling’ – are re-evaluating partners and therefore taking longer selecting CRO and CDMO partners. In a surprising result earlier this, WuXi has reported only a 1% fall in US revenues [effects of Covid contracts removed], having gained a 5% uptick in revenues from Europe – with 500 new customers added in the last year²⁴.

“One of the unintended consequences of this turbulence, is that biotechs in Europe should look at the instability of BIOSECURE as opportunity to advance more quickly than their US based rivals – with notably few places to outsource projects that transitions the CRO to CDMO pathway. Another potential unidentified issue is US-based VCs backers withholding investment decisions and slowing advancement while they wait and see where the chips fall. Better to go slow now, if your project team is working with China so that its less disruptive if a switch is need. These companies are the engine of innovation but under the radar in the legislative debate so remain unheard. No one wants to make a big 3-year decision they might regret in 6-months’ time. So for the sake of US innovation, we must reach a consensus soon. It’s a particularly acute issues for those of us used to working with CROs in China – it’s difficult to get what we need elsewhere” commented a top twenty VC director on condition of anonymity.

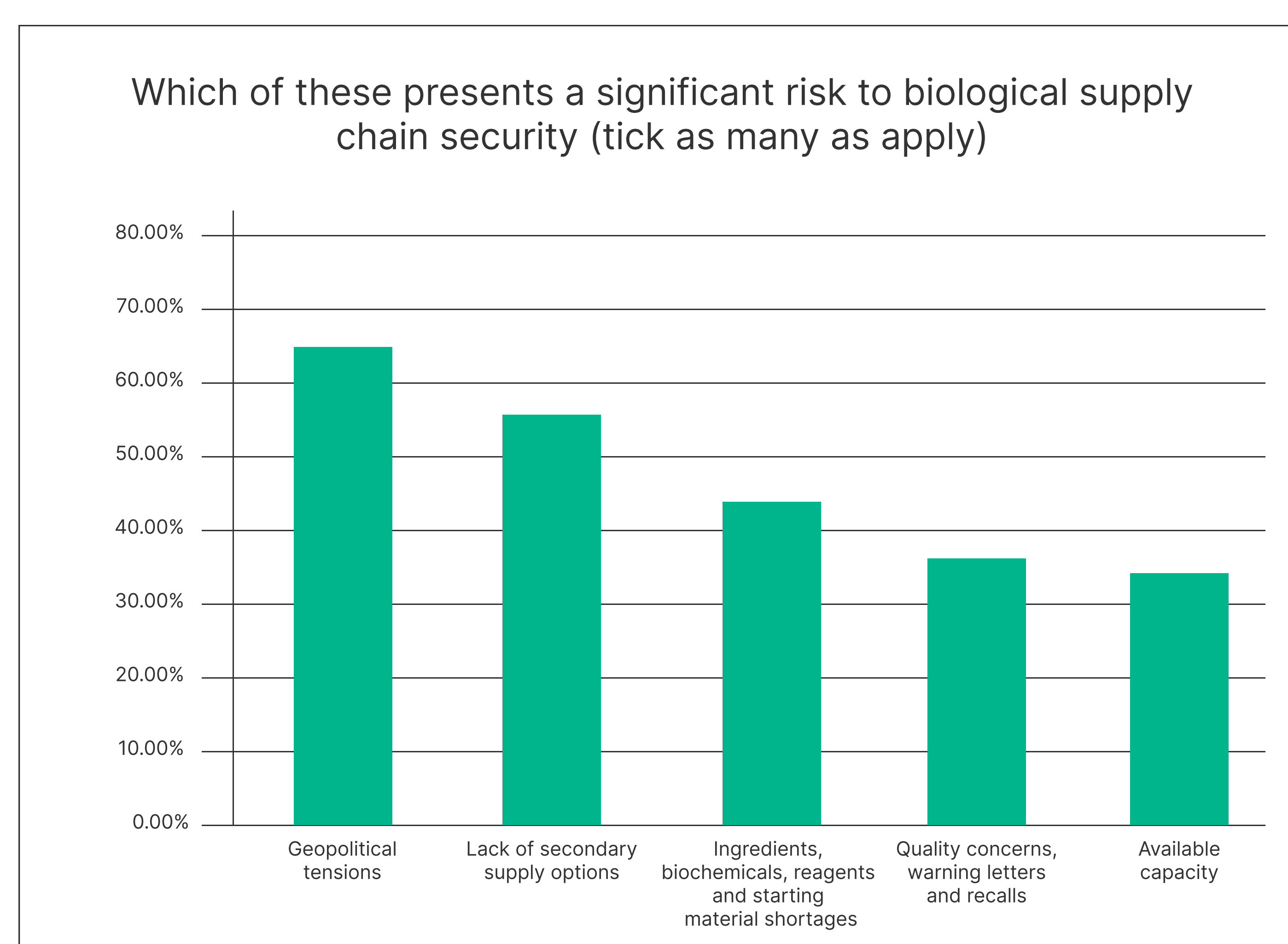
In a further complication for early stage biotechs, Gil Roth, President of the PBOA notes within his article [in this report] that the funding recovery is not being felt evenly and it is indeed the early-stage projects – the “lifeblood of CDMOs” as he coined it – where investment dollars remain scarce, while for late-stage assets investment is now again flowing in.

So what are the biggest threats to supply chains?

Predictably [see paragraphs above], in a year of increased ‘geopolitical tensions’, this theme was

identified by nearly 70% of the industry as presenting the biggest threat to biological supply chain security followed by a ‘lack of secondary supply chain’ options – the latter, of course, becoming a much more complex issue should geopolitical tensions arise within your primary partner. This is an existential threat faced by many biotechs currently advancing their clinical products in China – do they slow development and/or risk failure by attempting to move or mitigates with secondary supply options or stay the course and continue development in China and hope the political winds of change have shifted come approval in a few years’ time.

Encouragingly for all of the industry, ‘quality concerns and warning letters’ were seen as a far less likely cause of supply chain disruption – with around only one third believing this presents a risk to security. What’s unclear, is if this result represents improved confidence in quality standards across the industry or that simply other concerns are now more pressing.



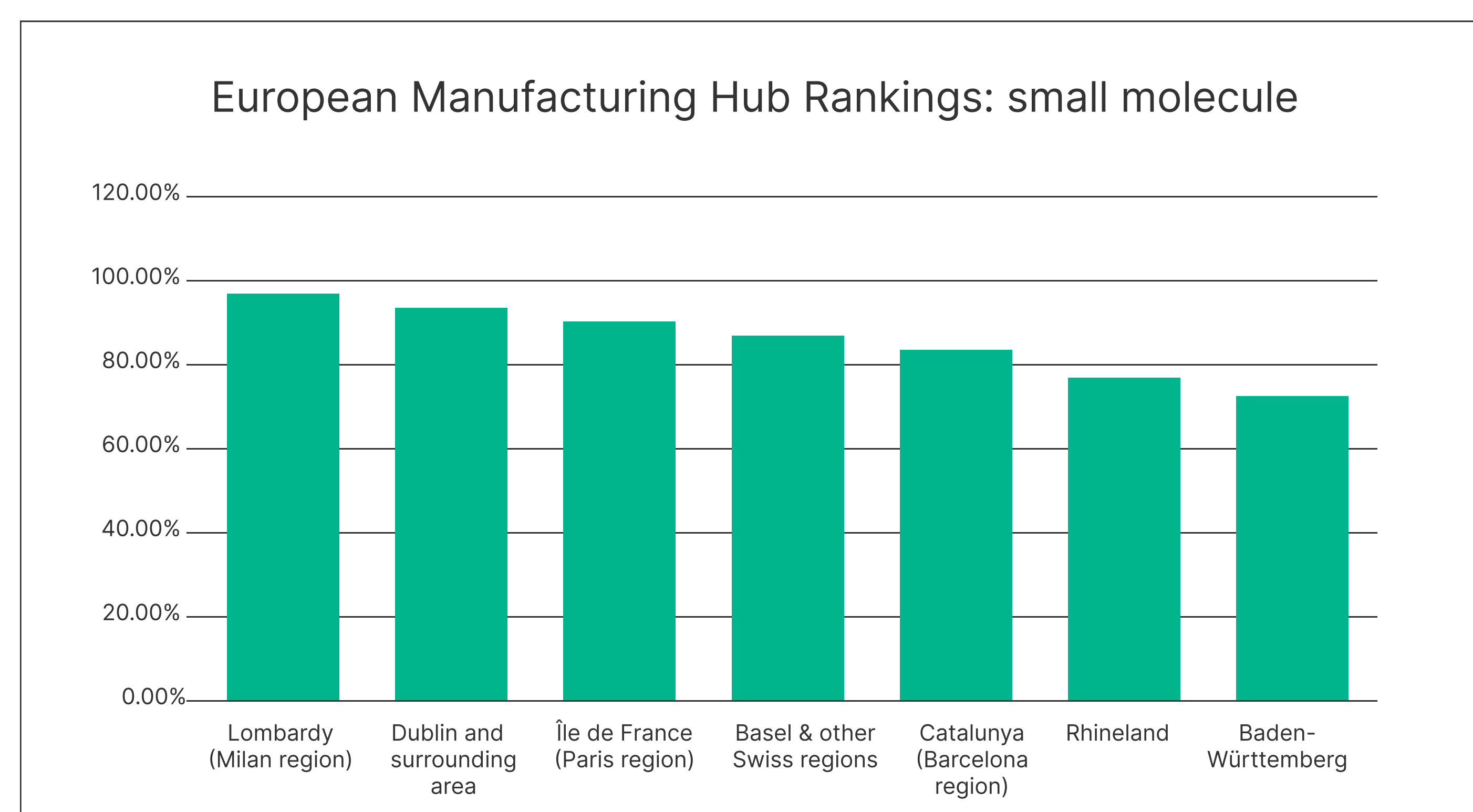
Lombardy and European Manufacturing Rankings

Last year we introduced a new index to the report which ranked the top biotechnology hubs – i.e. the most productive regions to launch a biotech – and following this success we have launched the inaugural **European Manufacturing Index [EMI]**. The EMI rankings will evaluate all the major manufacturing centres across Europe with three separate categories for small molecules, biologics and medical devices.

The small molecule ranking is designed to evaluate the most attractive destination to build a new manufacturing facility factoring- in ‘the cost of plants, access to qualified personnel, and cost of on-going operations’. This category is particularly significant for the host region of this year’s CPHI Milan, as Lombardy has historically vied with Germany (both Rhineland and Baden-Württemberg) as the continent’s largest production centre by volume. Significantly, while Lombardy did emerge as the key winner, several other regions in Europe finished ahead of the major German hubs, with the Dublin region and Île de France

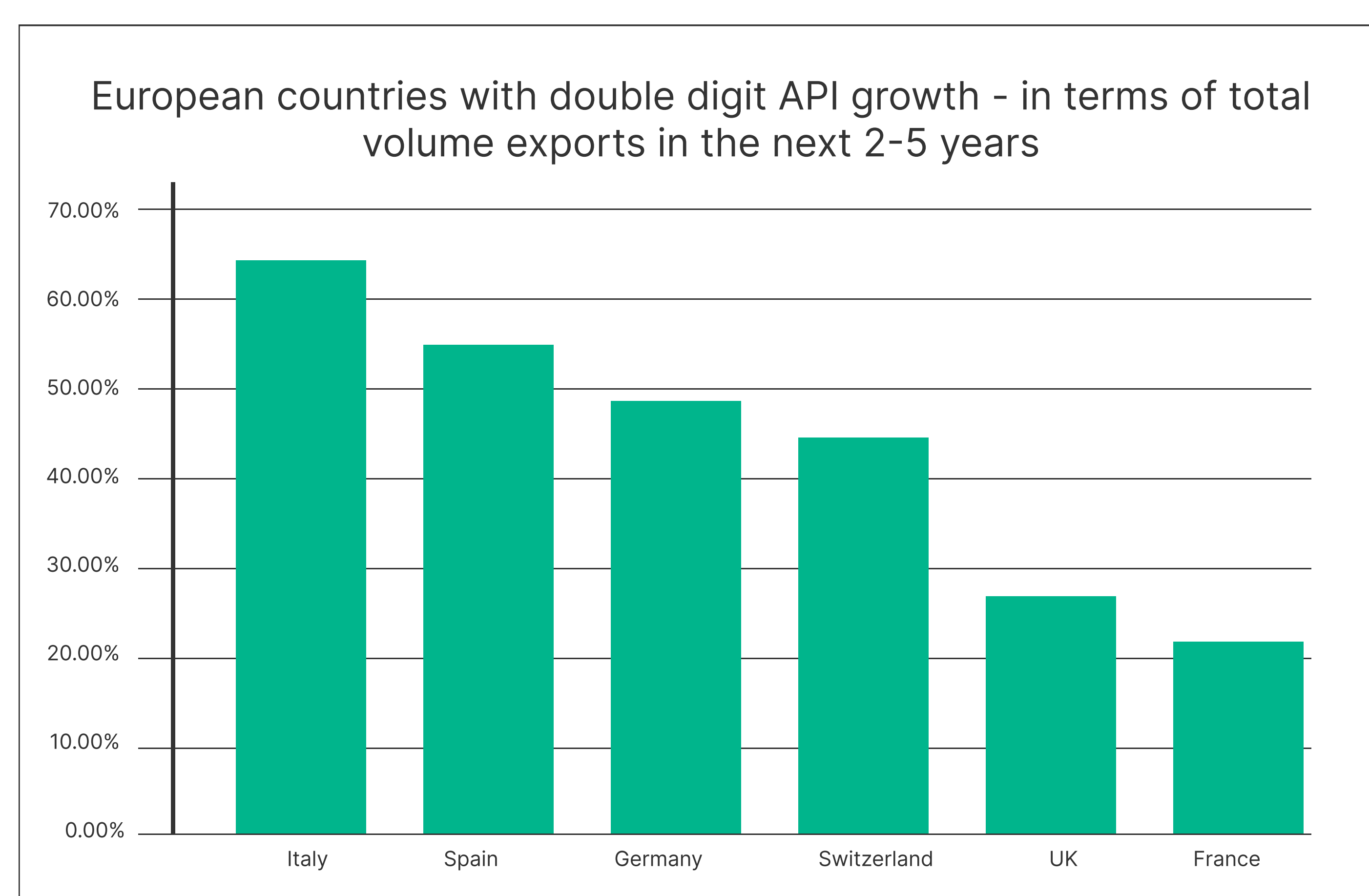
24. <https://www.fiercepharma.com/manufacturing/bioseecure-act-looming-wuxi-apptec-shows-declining-revenue>

(Paris region) scoring very strongly among respondents to the survey. Switzerland with its long-established innovative pharma industry and major international pharma companies unsurprisingly scored highly, but so did the newer Catalunya region, which has grown impressively in recent years²⁵. For example, earlier this summer Esteve announced plans to invest over €100m in building a new API production plant in Girona²⁶, while Siegfried opened a global Development Center for Drug Products in Barcelona last year²⁷.



When we asked the same questions for biological manufacturing two locations ranked clear above all others in Europe. Namely, 'Basel & Swiss regions', perhaps unsurprisingly considering its long pedigree in advanced manufacturing, however, the 'Dublin region' also scored nearly identically. Ireland has become a major player in biologicals – perhaps originally driven by favourable tax rates – but increasingly by the ecosystem of companies and employees in the country. In just the last few years Ireland has seen large biological investments, hundreds of millions each from BMS, Eli Lilly, and MSD, while Pfizer famously committed €1.2bn²⁸ to its biological drug substance manufacturing site in Dublin.

In a further boon to the prospects for Lombardy in the next 5-years, Italy was selected as the top European nation in terms of API growth potential. In fact, 63% of pharma professionals expect the country will report 'double digit growth in terms of total volume of exports over the next 2-5 years'. Spain, a country that has seen fast improvements in its reputation for API manufacturing, finished second (56%), ahead of Germany (49%) and Switzerland (47%). Both the United Kingdom and France scored relatively poorly with just 24% and 21% respectively anticipating double digit growth over the same timeframe.



Lowering the cost of biologics production

The cost of biologics production has long been an industry issue but in recent years we have seen an acceleration of cost reduction technologies, and not just at lab scale as many manufacturers, biosimilar producers and even contract providers looking to break the symbolic \$100/gram level, with several companies on record as aiming for sub \$50/gram. For example, while the technology is still in its infancy with only a few manufacturers using it, continuous biologics processing was identified by the industry as the most likely (62%) technology to have the biggest impact over the next years.

Significantly, outside of big pharma only two CDMOs are currently operating continuous biologics set-ups, namely, Just Evotec and Enzene Biosciences. Continuous biomanufacturing means fresh cell culture media is continuously added with less accumulated by-product, which means a higher degree of intensification and much greater yields. Just Evotec is on record as stating its J.POD® can hit the \$50/gram²⁹ mark and Enzene are on record as aiming for below \$40/gram with their next generation continuous systems EnzeneX™ 2.0/3.0.³⁰ Interestingly, traditional cell line improvements – the technology that has made the greatest contribution to lowering costs over the last five years – is only the third favoured option looking ahead five years. Perhaps signally the relative maturity in this area and that the next major step-changes breakthroughs in cost reductions will require newer technologies.

In a surprisingly result, 'AI and automation' finished only narrowly behind continuous bioproduction as the industry increasingly embraces its potential for process improvements, real-time monitoring and analysis.

The ability to run bioproduction facilities more efficiently and with lower energy usage should not be underestimated and signals a new era in which we look holistically at the problem from all sides – so cost is no longer solely a yield-based issue, but rather, one of resources and achieving overall efficiencies. For example, 'digital twins' are now being routinely used to simulate production scenarios and optimise process before real world testing begins – however, with the addition of AI technology this can potentially be optimised in days or seconds rather than months.

Taking this a step further, AI can take forward the theoretical (digital twin) data and compare this in real time as live batches are produced – ensuring that any out of spec issue is identified, mitigated and or even improved during production³¹. In advanced therapies automation is also predicted to produce step change improvements in costs, as they empower greater scaling, integration of automated quality-control monitoring, and again, the potential to modify manufacturing conditions in real-time³².

25. https://www.biocat.cat/sites/default/files/content/file/2024/02/08/2022_catalonia_bioregion_report_en.pdf

26. <https://catalonia.com/w-invests-100-million-euros-to-strengthen-its-manufacturing-presence-in-catalonia>

27. <https://www.siegfried.ch/news-archive/?y=2023&tag=38>

28. <https://www.pfizer.ie/media/pfizer-announces-12-billion-investment-and-hundreds-of-jobs-at-grange-castle-site>

29. <https://sciencepool.evotec.com/j-pod-toulouse-revolutionizing-biologics-manufacturing-in-europe/>

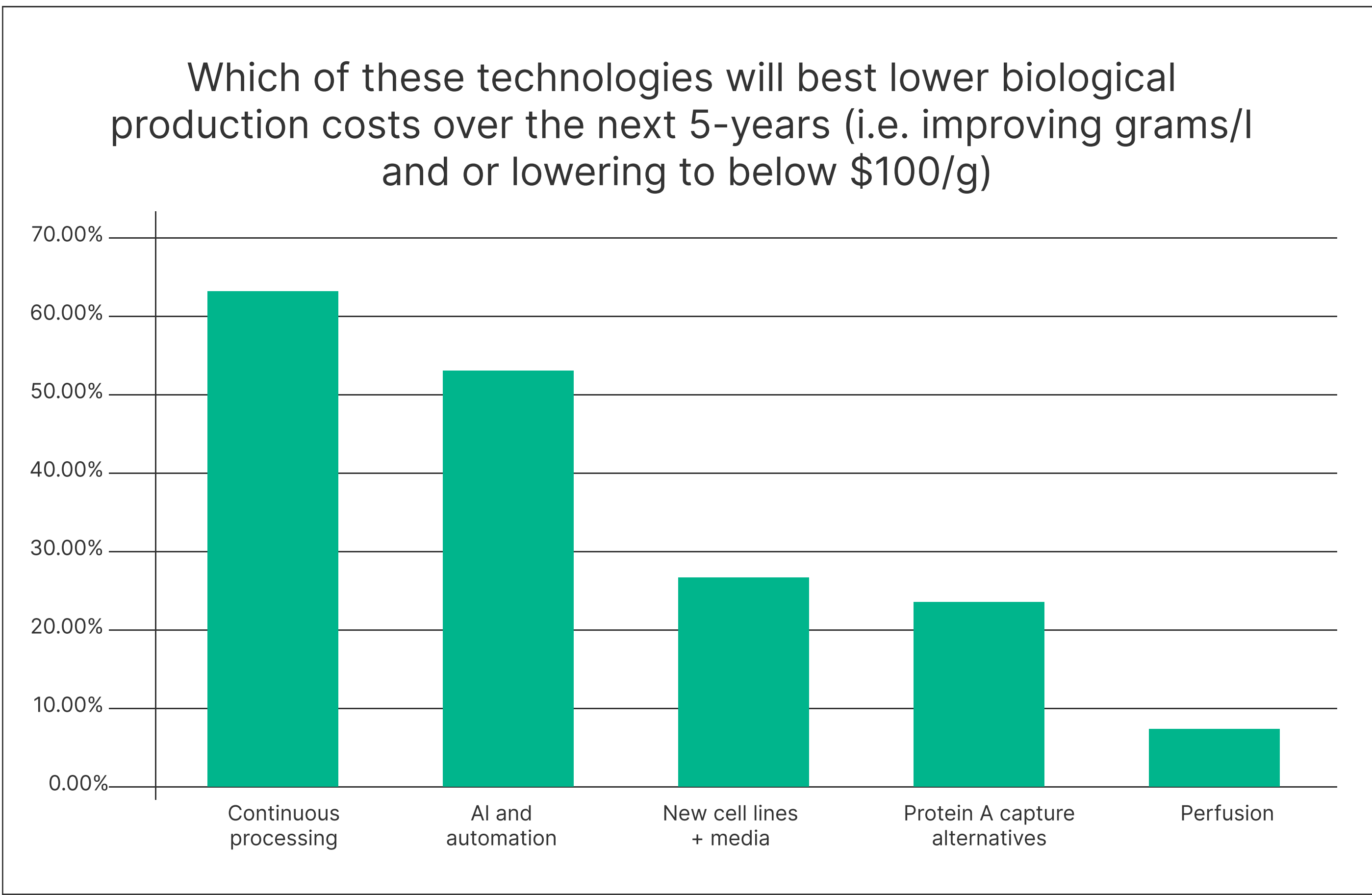
30. <https://x.com/enzenebio/status/1805245009207103989>

31. <https://www.bioprocessintl.com/sponsored-content/ai-enabled-digital-twins-in-biopharmaceutical-manufacturing>

32. <https://www.genengnews.com/topics/bioprocessing/automation-and-standardization-will-cut-cell-and-gene-therapy-production-costs/>

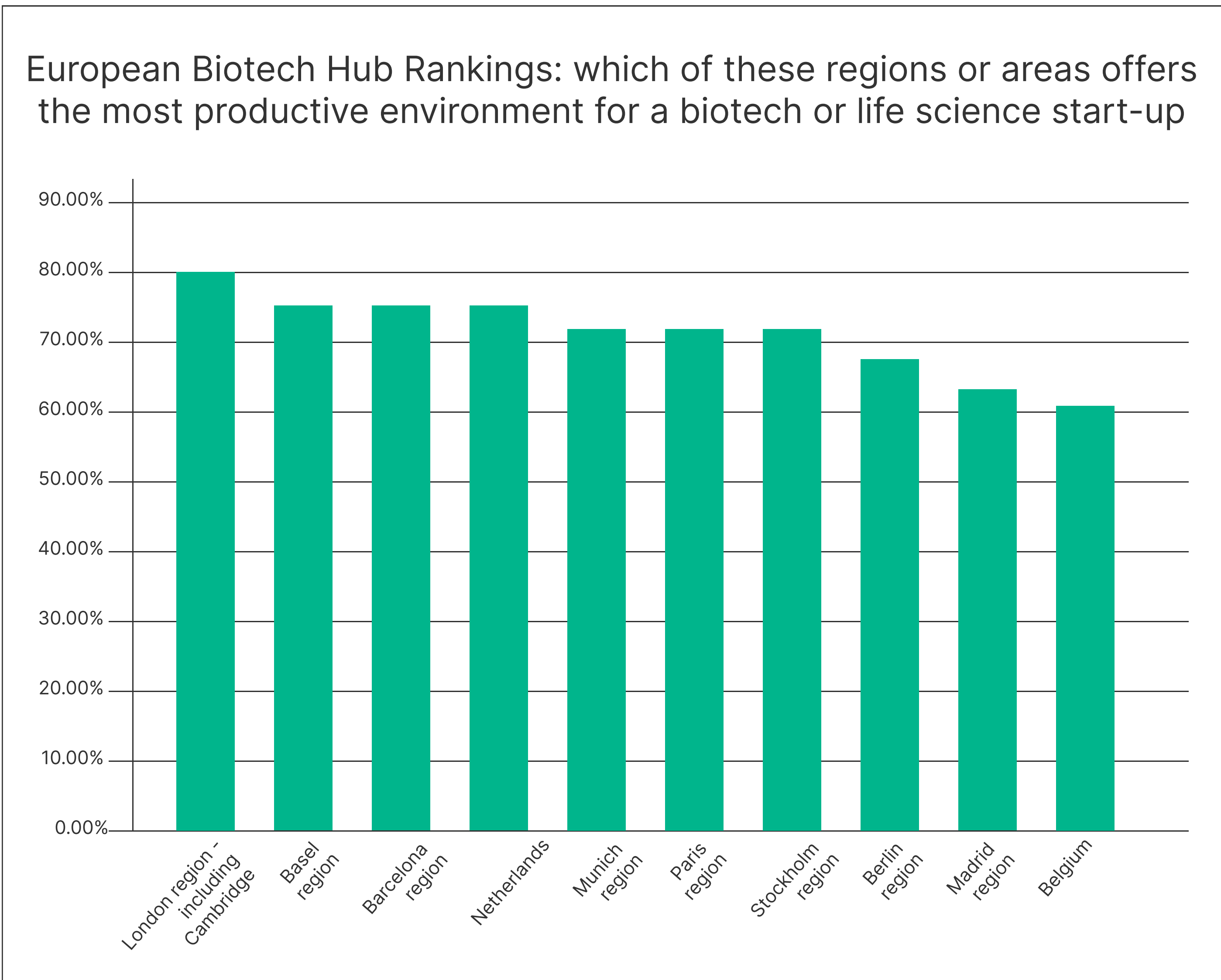
Additionally, there is now great interest in developing more standardized platforms for delivering gene therapies, to reduce both the cost and the regulatory burden. AAV-based therapies have advanced the furthest with common vector ‘backbones’ for multiple indications, into which a specific gene [depending upon the disease targeted] could be inserted³³.

In contrast, alternatives to the Protein A capture step – at present the most expensive element of production – and perfusion, which has greatly intensified processes in batch production were seen as less likely alone to drive change in the next five years. Perfusions very low score in particular, is quite surprising, especially at a time when so many biosimilars producers and CDMOs investing in this to lower costs. Our speculation here then is that the market believes the big gains have already been had using these technologies that are widely used.



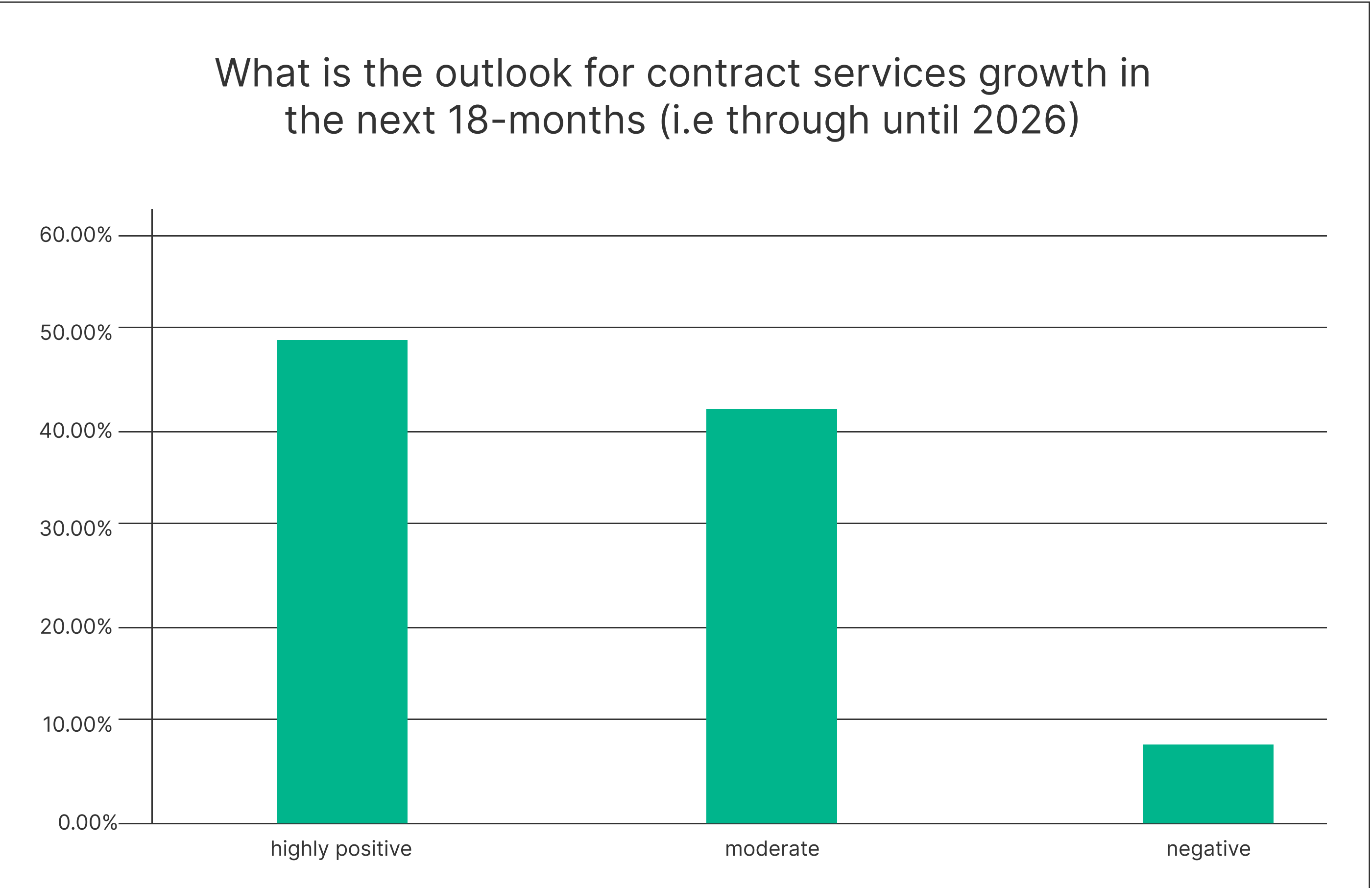
Biotech rankings

The European Biotech Hub Ranking returns for its second year, with largely consistent results as the best locations to launch a new biotech. London and the wider golden triangle has retained its top spot ranking for a second year, but Barcelona has fallen back narrowly behind Basel and level with the Netherlands. The overall trend here is for slightly lower year-on-year scores, but also, a much smaller spread between regions – suggesting that the European biotech landscape has become more competitive with smaller centres increasingly attractive.



Contract Services

Last year’s report documented the shifting narrative, with the latter half of 2024 expected to see more rapid growth after a cooling in the first half of 2024, most analysts (see Gil Roth’s piece) observe a recovery to growth has been slower than expected. However, this new analysis suggests this is now underway, as just 7% of the industry had a negative outlook for contract services companies over the next 18-months, with 49% ‘highly positive’ and 44% ‘neutral’. With the staggering demand for PD-1 drugs and both WuXi and Catalent’s capacity uncertain, it would appear certain this will raise demand for other providers. In a further data point of this trend underway, CDMO and non-clinical CROs saw surging support as the most appealing investment options, moving well ahead of last year’s one and two: AI companies and late-stage biotech’s respectively.

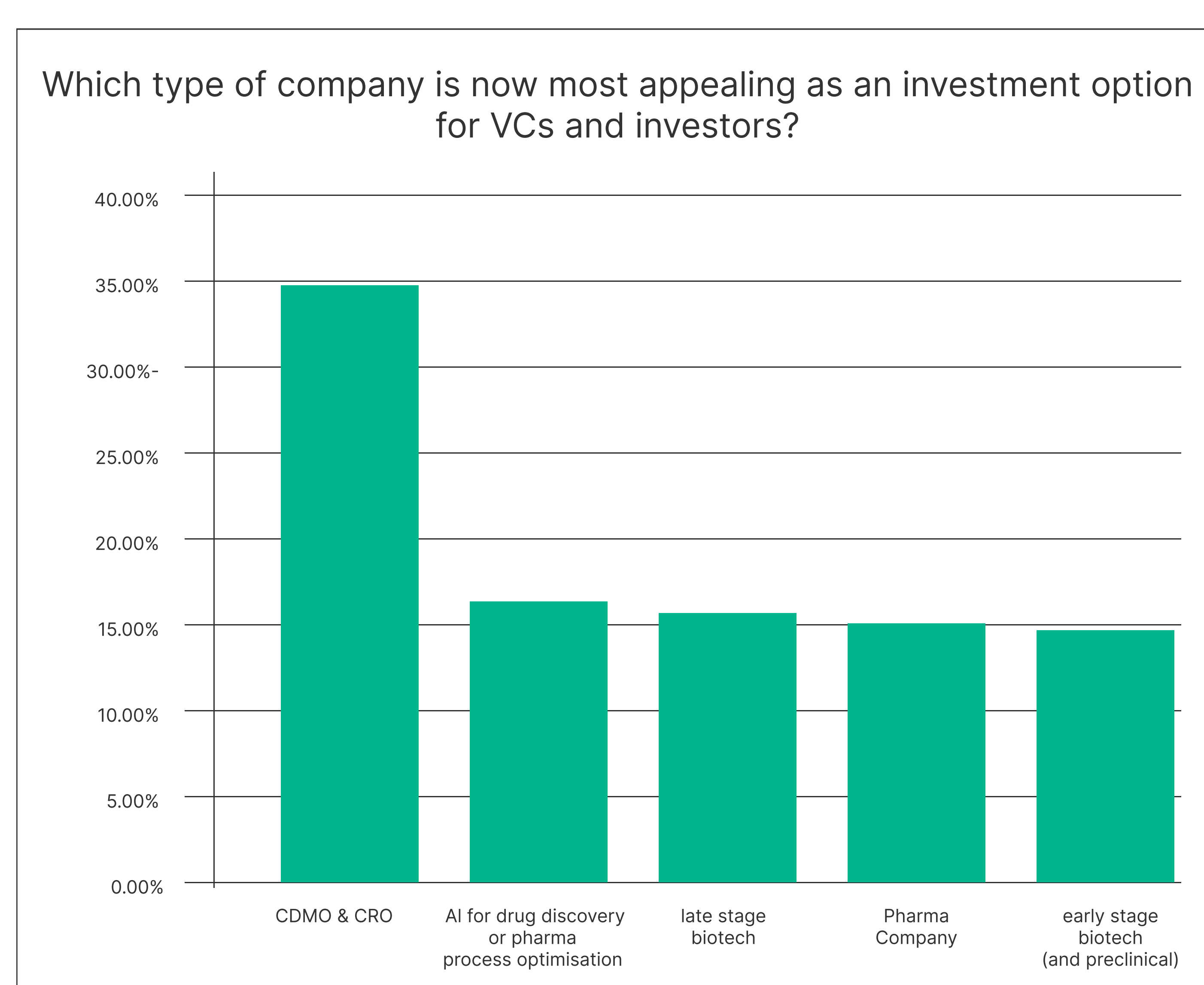
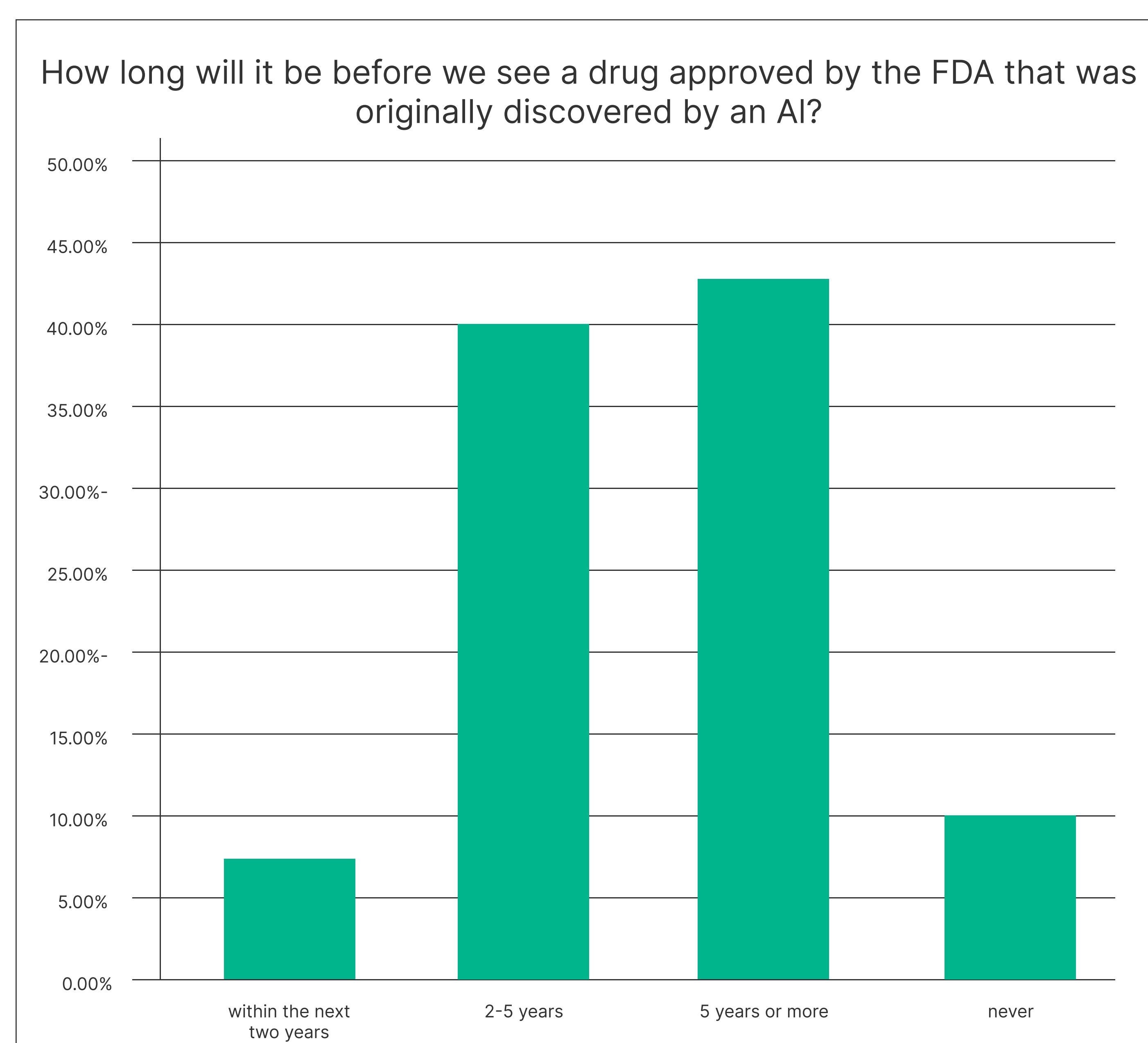


The fall of AI from being the golden child of pharma in 2023 perhaps reflects a more muted environment after the well-publicised failures of several lead candidates from Exscientia, BenevolentAI, and Sumitomo Pharma³⁴.

Following this downturn in AI both Recursion and Exscientia have lost much of their value since going public and merged in August 2024³⁵. With even Insilico founder, Alex Zhavoronkov warning, that after billions in industry write-downs and consolidations we must be more careful as an industry to sperate ‘real progress in AI’ from ‘dangerous financial hype’³⁶³⁷. What we have seen as a result is that the industry is much more reticent on a likely FDA approval, with just 7% of those surveyed believing this could come within two years. In fact, 43% believe its timescale of 2-5 years is most likely with another 40% believing it will be 5-years or longer – and 10% suggest we will ‘never see an AI discovered drug approved.’

So confidence in the technology to power a new age of drug targeting and discovery has fallen back in particular among those predicting approvals within the next two years – falling from 20% in 2023 to just 7% this year [a notable shift as we are obviously also one year into that two-year survey and no approval has been forthcoming]

33. <https://www.genengnews.com/topics/bioprocessing/automation-and-standardization-will-cut-cell-and-gene-therapy-production-costs>
34. <https://endpts.com/first-ai-designed-drugs-fall-short-in-the-clinic-following-years-of-hype/>
35. <https://www.biopharmadive.com/news/recursion-exscientia-merger-deal-artificial-intelligence-drug-discovery/723714/>
36. <https://www.genengnews.com/topics/artificial-intelligence/is-generative-ai-in-drug-discovery-overhyped/>
37. <https://www.unite.ai/beyond-the-hype-unveiling-the-real-impact-of-generative-ai-in-drug-discovery/>



In terms of which types of contract services provider is expected to see the greatest growth in the next five years, we see another major trend underway – as biologics are identified as the modality most likely to be the most lucrative. We have seen a steady and continued rise in the number of new biological agents approved by the FDA with 10 in 2019, 13 in 2020, 14 in 2021, 15 in 2022, and a record 17 in 2023 – with a total of 22 BLA [Biologics License Application] approved by Center for Biologics Evaluation and Research (CBER) i.e. when accounting for therapies approved for multiple indications. Monoclonal antibodies unsurprisingly have led the charge with 12 new molecules and a further 5 enzymes and/or proteins based biological agent approvals.

Improved linker technologies and broadening payload options³⁸ have marked a coming of age for ADCs, which garnered much media coverage and interest during the last few years – with the 2023³⁹ CPHI Annual Report noting the large investments made by CDMOs. However, in 2023³⁹ for the first time since 2016, the FDA approved no new ADCs (antibody drug conjugates). It should be noted that three new approvals are expected in the 2024/25 – for Datopotamab Deruxtecan, Patritumab Deruxtecan, and Telisotuzumab vedotin⁴⁰. The significance of this

becomes apparent when we switch to look at Tides drug approvals – which although are classified as small molecules show many structural complexities similar to that of biologics – during 2023 where there has been a sudden glut of approvals, with nine approvals in 2023 (five peptides and four oligonucleotides) and a further three so far in 2024 at the time of writing.

So looking ahead while small molecules [34%] & cell and gene therapies (37%) – which are hard to scale – are still performing strongly, the industry now expects easily scalable advanced therapies either peptides [43%] or biologics [53%] to be the best performing modalities for CDMOs [i.e. delivering the best marginal and overall returns]. As an aside to this, much of the attention of GLP-1 drugs has focussed on the fill finish process – since the Catalent acquisition – but there are far fewer CDMOs currently specialised in the development and commercial production of peptide actives. So while, as previously discussed the role of WuXi AppTec is pervasive in commercial supply, what has also gone under the radar during the last few months of BIOSECURE turbulence is that they are also perhaps the largest CDMO in Tide's active production – for example, supplying the active for Eli Lilly's blockbuster Zepbound/Mounjaro⁴¹. Taken collectively, if Tides are to remain a key modality moving forwards does this present a massive opportunity for CDMOs with cash to spare to invest – our CPHI analysts think yes.

Looking further ahead to the next generation of PROTAC (PROteolysis TARgeting Chimera) drugs – an emerging class of drugs that use a bifunctional molecule to target and degrade specific disease-causing proteins via the ubiquitin-proteasome system – while to date we are yet to see an FDA approval this is likely to be another 'growth modality' to watch closely in the years ahead. Analysts expects a first approval by the earliest in 2025 or latest 2027, with GlobalData predicting annual sales of \$3.7billion by just 2030⁴².

The CROs with current PROTAC teams included Charles River and WuXi AppTec along with Indian pair Syngene and Aurigene, and we anticipate greater investment and the building of PROTAC teams at CDMOs over the next 2-5 years as more targets progress to late-stage development.

Prestigious rate of novel drug innovative to be maintained in 2025

The majority of the industry also expects the recent rates of innovation to continue in 2025, with a majority [67%] expecting that FDA approvals will again surpass 30 – of which 15% are expecting more than 50 approvals, 14% predicting 41-49, and the largest group expecting somewhere between 31 and 40 approvals [39%]. What we did not ask and might have proved enlightening, is by when the industry expects biological and advanced therapy approvals to overtake those of

38. <https://www.nature.com/articles/s41587-024-02168-5#:~:text=Many%20development%2Dstage%20ADCs%20chase,patients%20with%20advanced%20urothelial%20cancer>

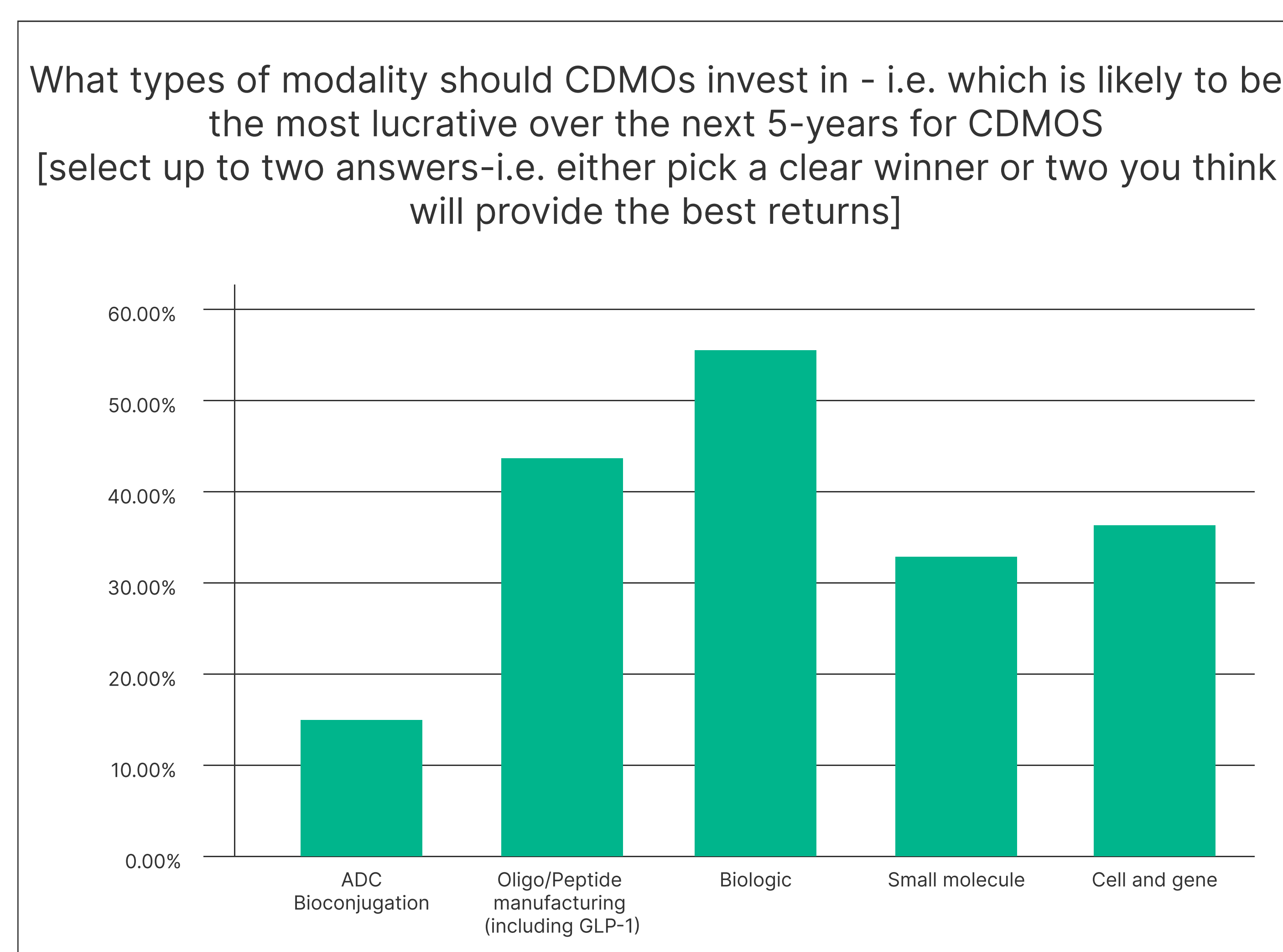
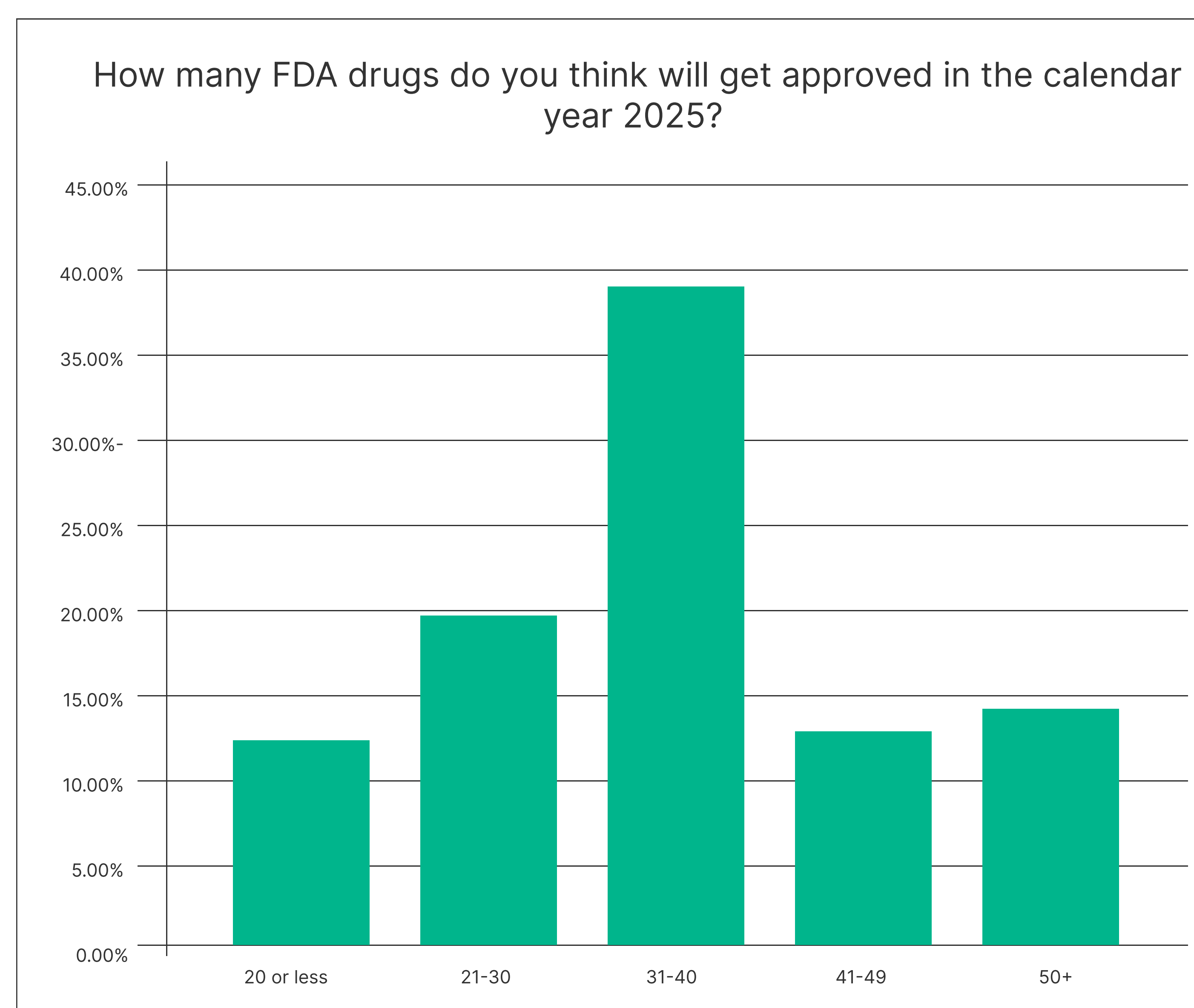
39. <https://broadpharm.com/blog/ADC-Approval-up-to-2023>

40. [https://www.biochempeg.com/article/397.html#:~:text=In%202024%20or%202025%2C%20three,vedotin%20\(ABBV%2D399\)](https://www.biochempeg.com/article/397.html#:~:text=In%202024%20or%202025%2C%20three,vedotin%20(ABBV%2D399))

41. <https://www.bloomberg.com/news/articles/2024-03-06/weight-loss-drugs-threatened-by-us-effort-to-contain-china?embedded-checkout=true>

42. <https://health.economictimes.indiatimes.com/news/pharma/pharma-industry/protacs-oncology-market-to-reach-3-7-bn-by-2030-despite-regulatory-challenges-globaldata/110698322>

conventional small molecules. For context, while there were 17 approvals – of 59 – last year for pure play biologics, there were also however, a further nine Tides approved perhaps showing that for the first time complex molecules are now extremely close to parity. In fact, looking more closely at the approvals year-on-year small molecules have remained consistent over time and it is the growing rate of complex drug approvals that is driving the steady growth in numbers. So our report's experts now predict that within the next three years we will see the combined number of Tides, biological and cell and gene therapy approvals approved in a year surpass small molecules for the first time.



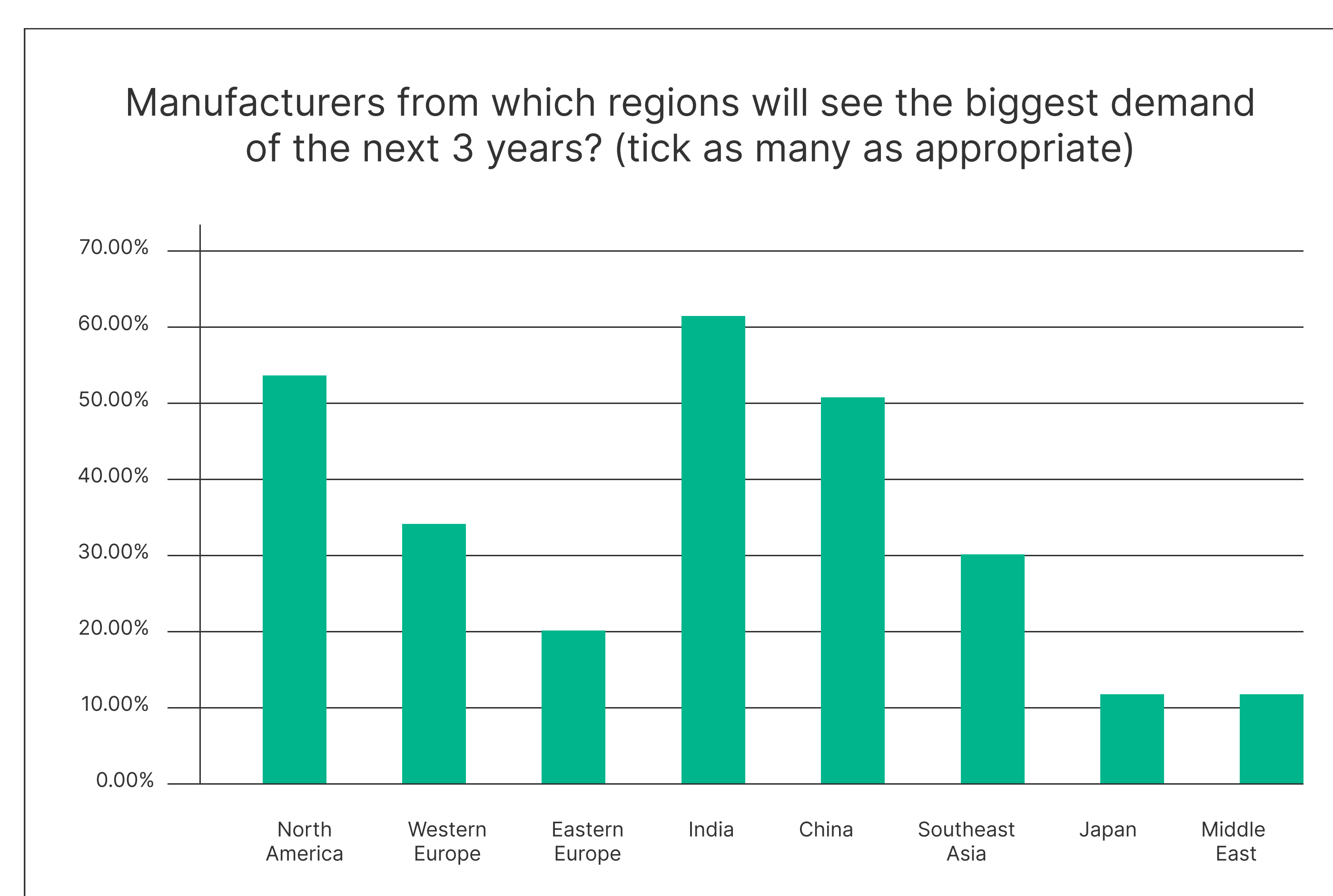
Geographical location of CDMOs?

The general trend globally, especially post pandemic, is to have manufacturing options in at least two continents for greater supply chain security. However, mirroring the industry debate running in a myriad of stories⁴³ throughout 2024, India is predicted to be the biggest medium-term beneficiary for CDMOs services. Yet beyond India, the industry remains ambivalent on prospects between the United States, China and India – in a perhaps surprising finding Europe remained a little adrift of these regions, with much fewer professionals predicting as good prospects over the next three years. A conclusion we can infer from this: is that while Indian and China remain unrivalled for

chemistry and biology services – as the world's CRO powerhouses, where cost and access to scientific personal makes their leads unassailable – the United States is potentially the biggest beneficiary of drive for domestic production [as the biggest home market]. However, we temper this prediction with the reality this topic – 'made in the USA' – has been long muted now, and unless facilities are built and invested in, the rhetoric will remain just that⁴⁴.

In fact, US Government Analysis is underway to try and map the complete API and starting materials supply chains and perceived vulnerabilities to China – including across more than 2800 generic molecules⁴⁵.

The other aspect we did not explore and is covered in greater depth by Gil Roth in his piece, is the potential role of 'friend shoring' and 'near shoring' – so might we see more significant growth in Canada as well as the USA.



In terms of capacity challenges, perhaps unsurprising considering the shift – albeit gradual – we now see in approval numbers is that once again biologics CDMOs were seen by the industry as the ones with the most likely [54%] to see capacity shortfalls in the next year. Significantly and, perhaps a reference to the slow return of funding, all other CDMO types were seen as unlikely by most respondents to have industry-wide capacity issues.

Longer term (3-4 years hence) however, Dawn Ecker of BDO suggests – later in this report – that increased CMO capacity will help power a new age of MAb approvals from smaller companies that previously might have seen development slowed (due to a lack of available capacity).

Novel excipient creation

This is a question we have asked for three consecutive years. In the 2022 – around the time the FDA Novel Excipient Review Pilot⁴⁶ Program was first introduced and encouraged by the recent Covid successes the industry was much more confident of an approval within a year or two. Yet this year, like in 2023, the majority of industry respondents now believe 2027-2030 is the most likely timeframe for the introduction of an approved novel excipient.

43. <https://cen.acs.org/business/outsourcing/India-seeks-seat-drug-services/102/i25>

44. <https://www.atlanticcouncil.org/blogs/econographics/the-us-is-relying-more-on-china-for-pharmaceuticals-and-vice-versa/>

45. <https://www.pharmamanufacturing.com/production/unit-operations/article/55042959/mining-the-reshoring-rush-targeting-government-spending>

46. <https://www.fda.gov/drugs/cder-conversations/cder-conversation-novel-excipient-review-pilot-program#:~:text=With%20this%20pilot%20program%2C%20FDA,and%20the%20facilitation%20of%20new>

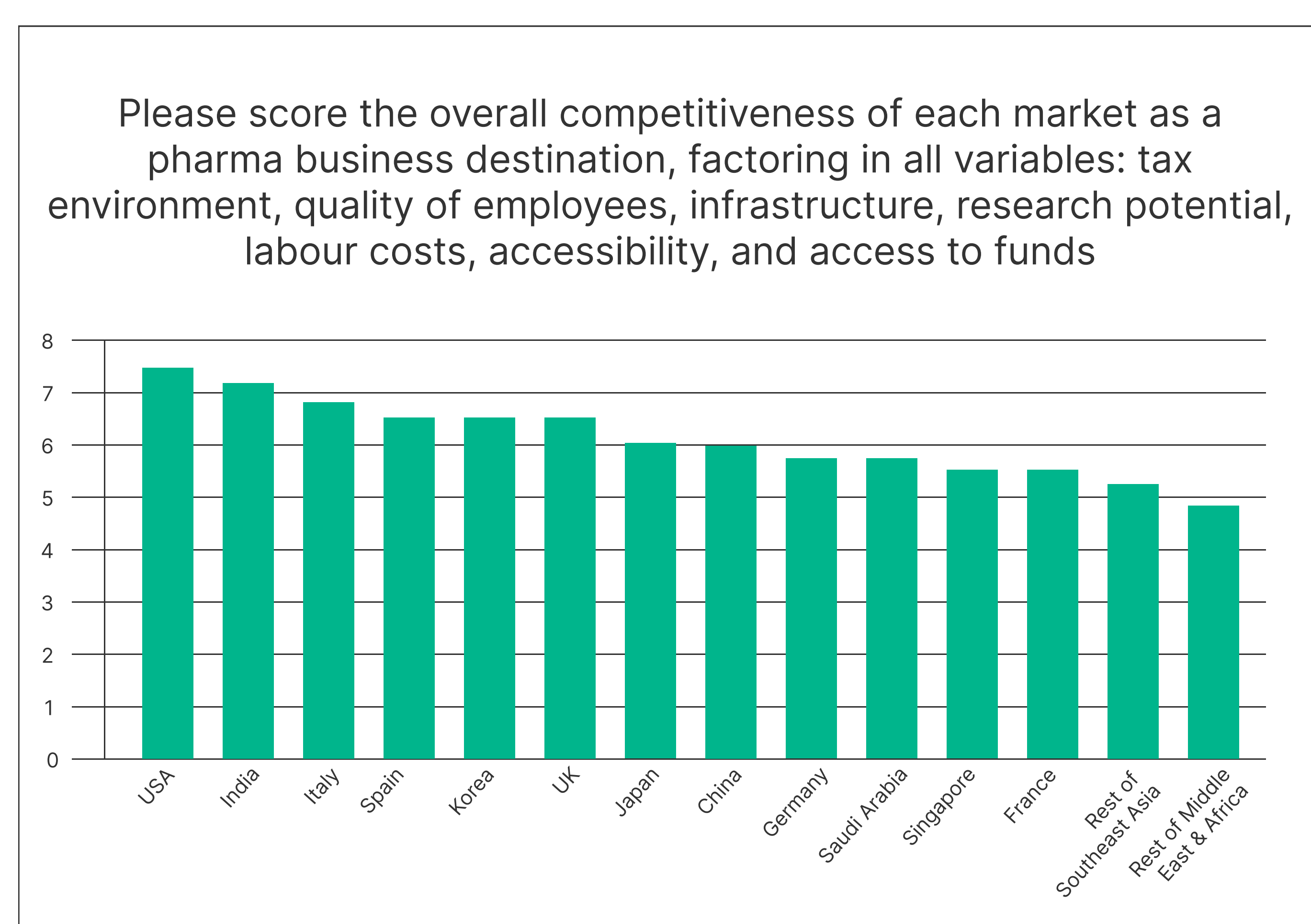
Encouraging Dr. Iain Moore – a senior advisor at EXCiPACT [and former Croda Global QA] – is however, a little more positive suggesting the rise of mRNA will necessitate newer excipients. He added, *“I think this is a conservative view, and there will be a burst of mRNA and related therapies, and these will require customised nanoparticle lipids. So it’s here we could well see more novel excipients and the existing ones adjusted to the new products. Especially as there are now very exciting developments in curing what has been incurable in the past, and this will create a pull on the market to overcome any hurdles in the approval of novel excipients.”*

Overall competitiveness by region

This category is typically the best overall reputational gauge – i.e. how a country’s pharma market is perceived and the strength of its pharma industry – has been topped by the United States every year since the survey inception [around 7 years now]. So it is of little surprise to the USA [7.3] again lead the way. However, mirroring last year’s results, it remains only narrowly ahead of India [7.1].

In fact, since the first ever survey we have seen notable shift and the USA’s overall dominance is gradually reducing and the European nations are aligning with similar scores. In 2024, scores have remained consistent with just a few big year-on-year moves. Notably Spain has backed up its strong performance in 2023 to rise to 4th place in the tables, and Italy has emerged as the European winners for the first time. Both France and Germany have displayed weakening reputation – finishing 10th and 13th respectively – with Korea [6.3] again scoring strongly.

The obvious trend reversal is that the post-covid gains China saw last year – when it had nearly achieved its pre-pandemic highs – have fallen away, with the Country’s business reputation falling a full 20% fall, moving it from third to ninth. Notably, this still leaves it ahead of European heavyweights Germany and France. Germany was the worst performing major economy during the last year, but after yearlong weak manufacturing data⁴⁷, output may now be rising again – possibly marking the beginning of a turn in fortunes⁴⁸. However, with continuing capital investment concerns and expensive energy we may see more modest growth in the next few years verses recent historical averages⁴⁹.

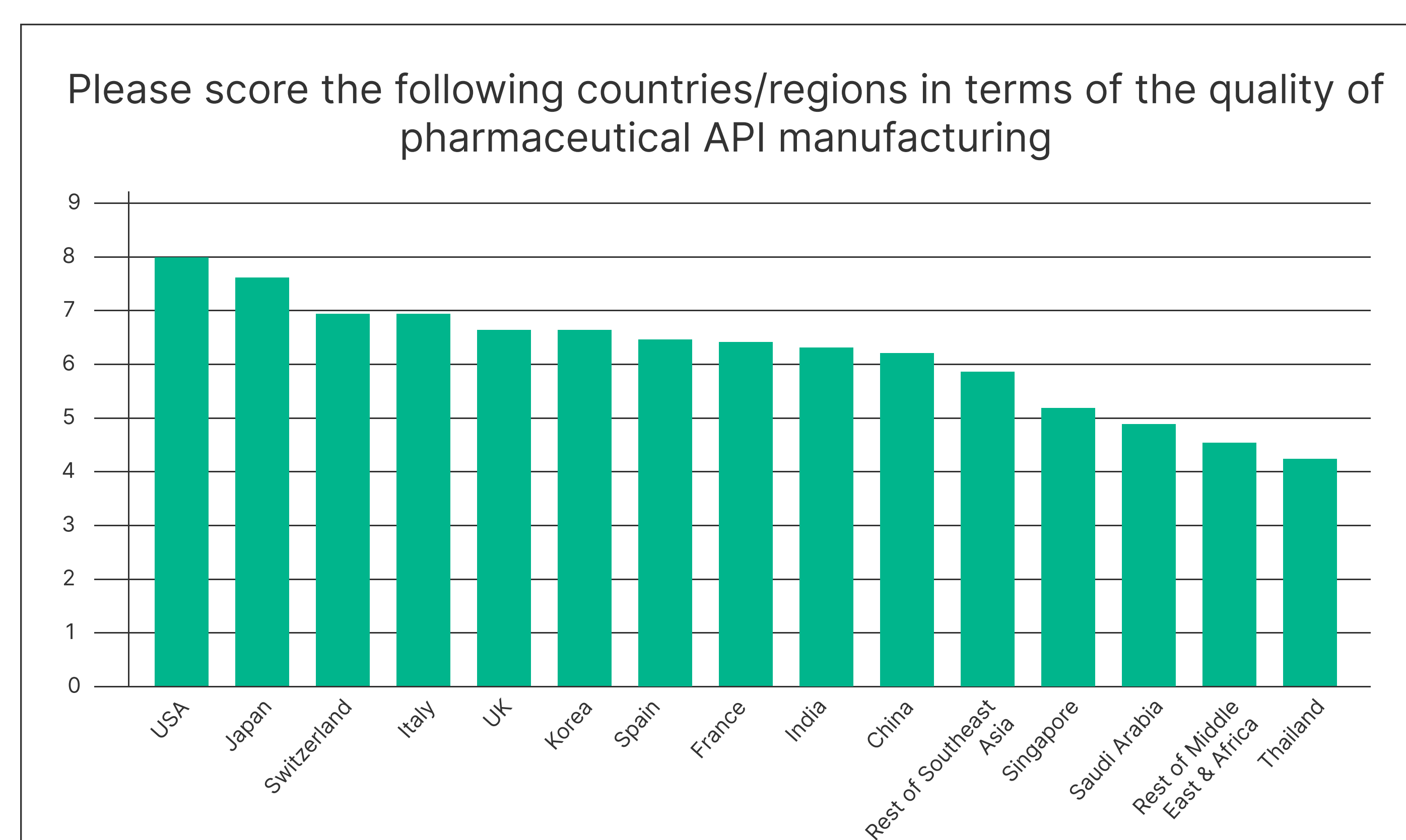
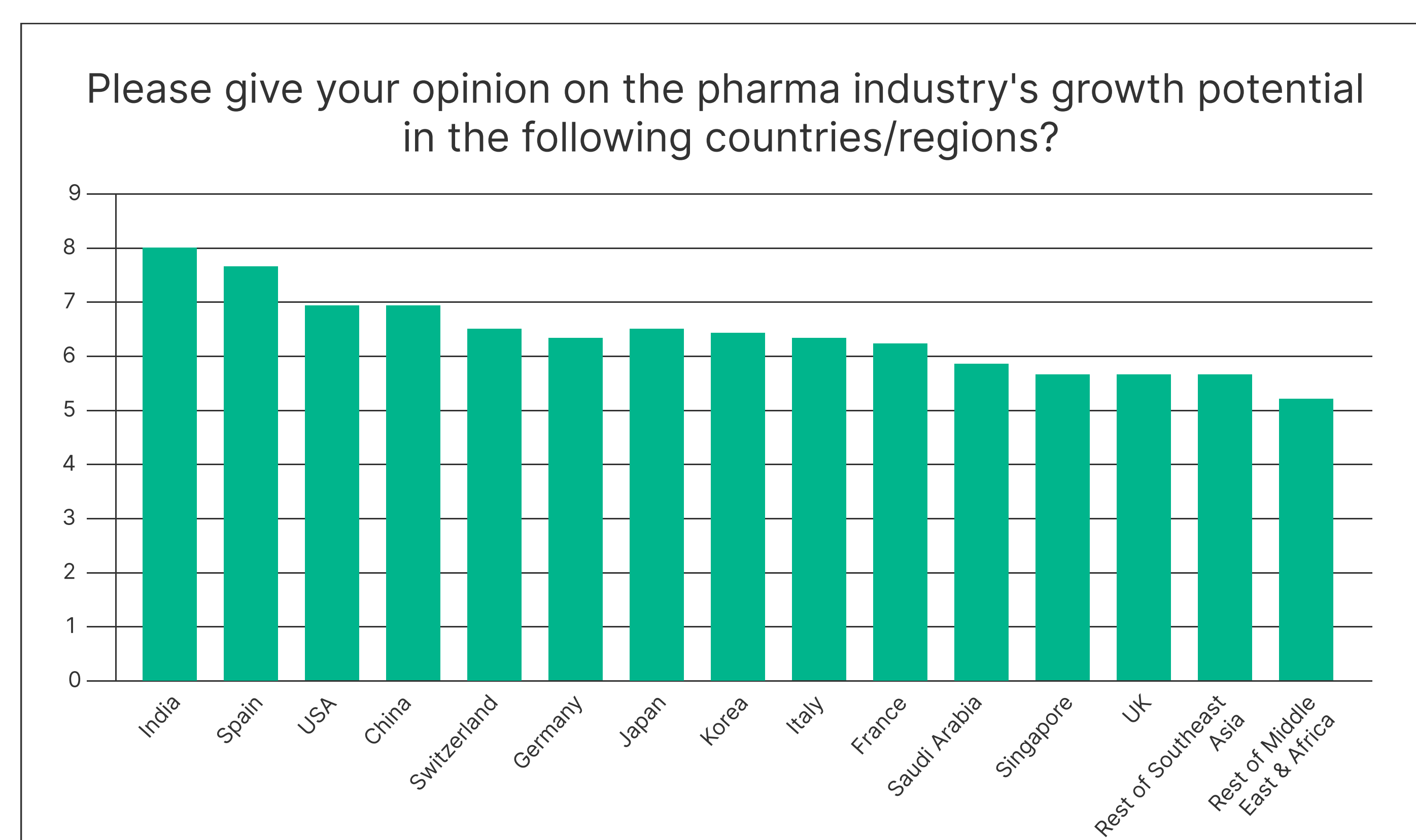


Growth Potential

In one of the more surprising findings of this year’s survey, Spain has continued its surge up the rankings – last year it went from 12th to 6th – and has overtaken the United States in second place. The reasons for this are not completely clear, however, Spain has been on the rise for over 18-months with its burdening biotech sector now helping stimulate growth in adjacent parts of the industry. For example, recent data shows the country is now the leading nation for clinical research, with 40%⁵⁰ of clinical trials authorised by the EU via the Clinical Trials Information System conducted in centres across the country⁵¹. Further adding to the positive conditions, in a depressed investment year [2023] Spanish biotech R&D hit record levels – according to Farmaindustria reaching 1.5bn – with this now increasingly passing through to a growing manufacturing base⁵².

India has retained its position at the head of the table and unsurprisingly has further improved its score [8.1] in a year of positive sentiments. The country, buoyed by a wave of positive stories, growth in the CDMO sector, and an expected medium-term surge of CRO services – accelerated by BIOSECURE

France having plummeted down the rankings last year has clawed back some ground – improving to 11th from last place – but is still performing weakly compared with its historical averages. China despite the ongoing uncertainty with macro tensions with the United States is performing steadily – largely retaining its year-on-year score [at circa 7].



47. <https://www.ft.com/content/46ab3c55-21c1-4941-ad0d-0cd27a7c593c>

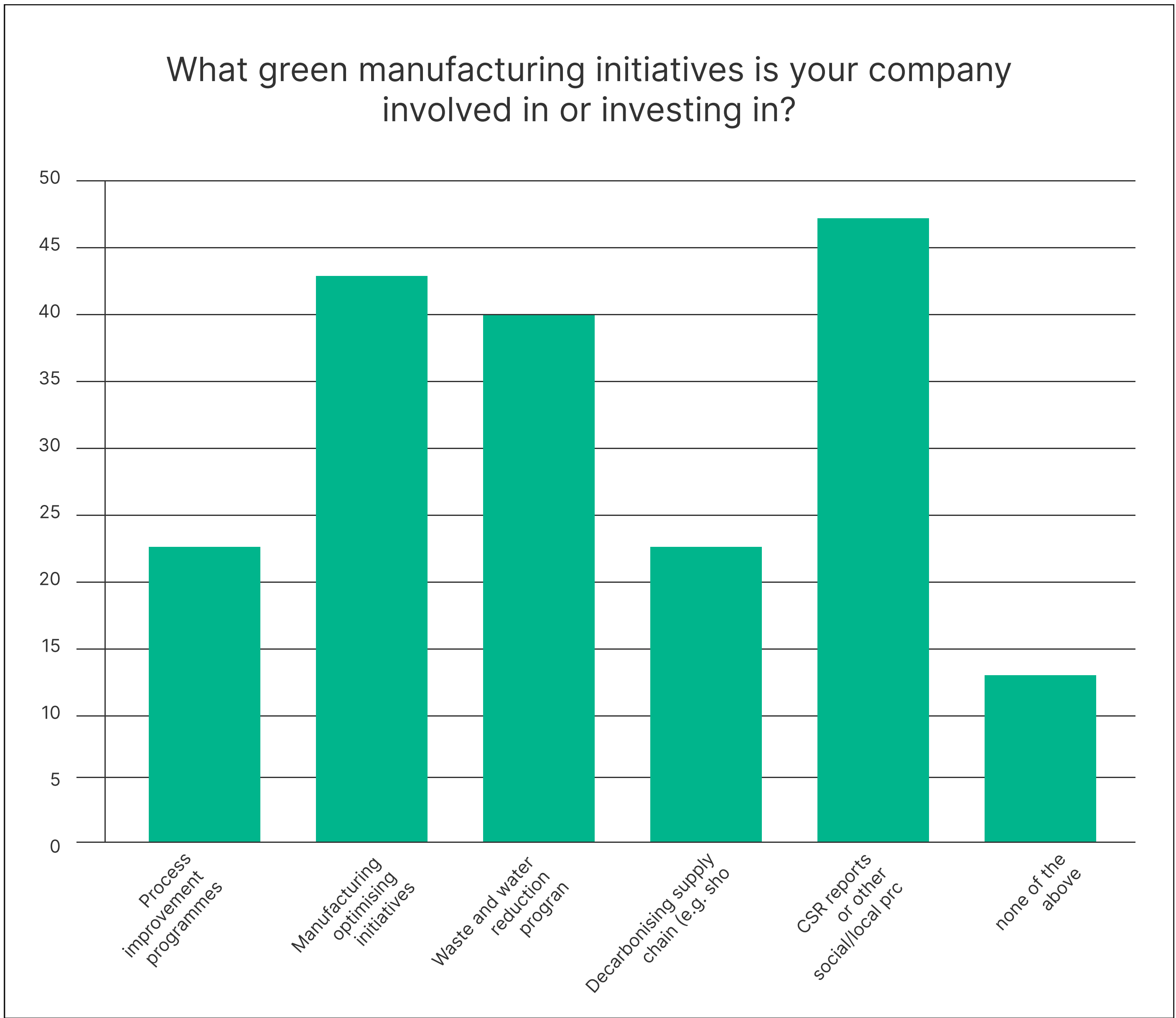
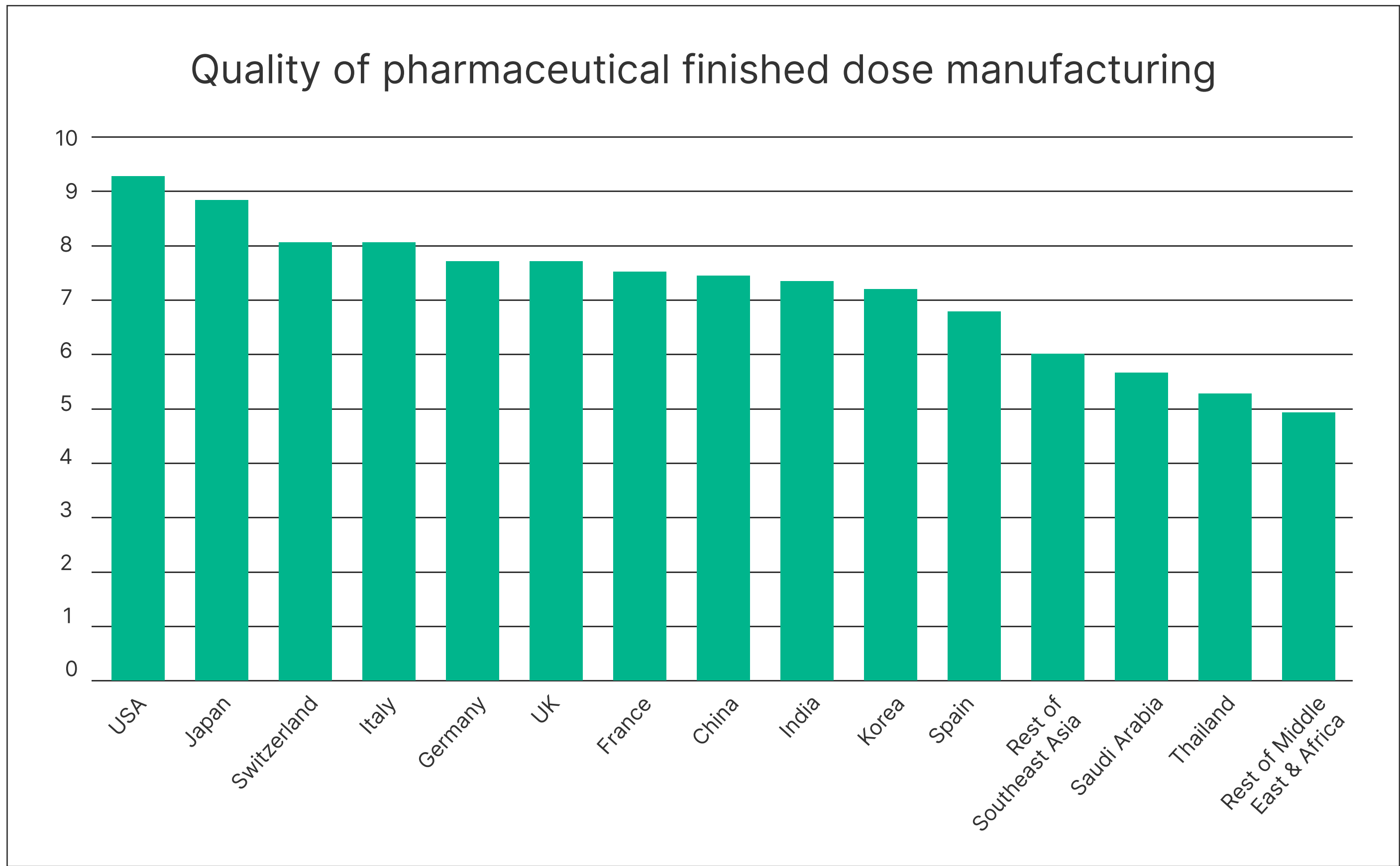
48. <https://www.reuters.com/markets/europe/german-industrial-orders-rise-39-june-2024-08-06/>

49. <https://www.telegraph.co.uk/business/2024/08/25/germanys-economic-woes-much-more-deeply-rooted-britain/>

50. <https://www.farmaindustria.es/web/otra-noticia/espana-es-el-pais-de-europa-con-una-mayor-participacion-en-ensayos-clinicos-de-nuevos-medicamentos/>

51. <https://ionanalytics.com/insights/mergermarket/coming-to-the-boil-spanish-pharma-ma-simmers-as-country-tops-clinical-trials-leaderboard-dealspeak-emea/>

52. <https://www.investinspain.org/en/news/2024/farmaindustria>

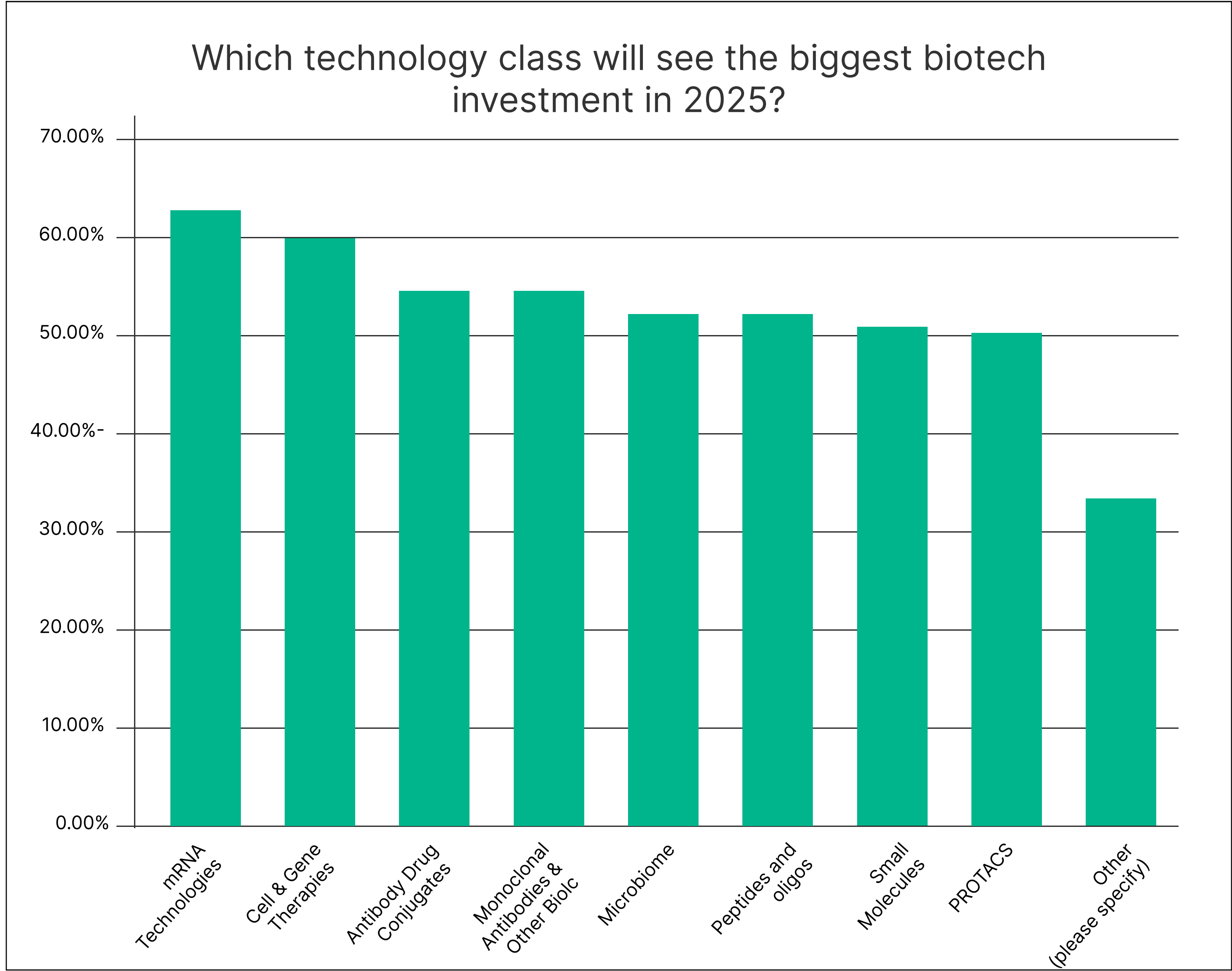
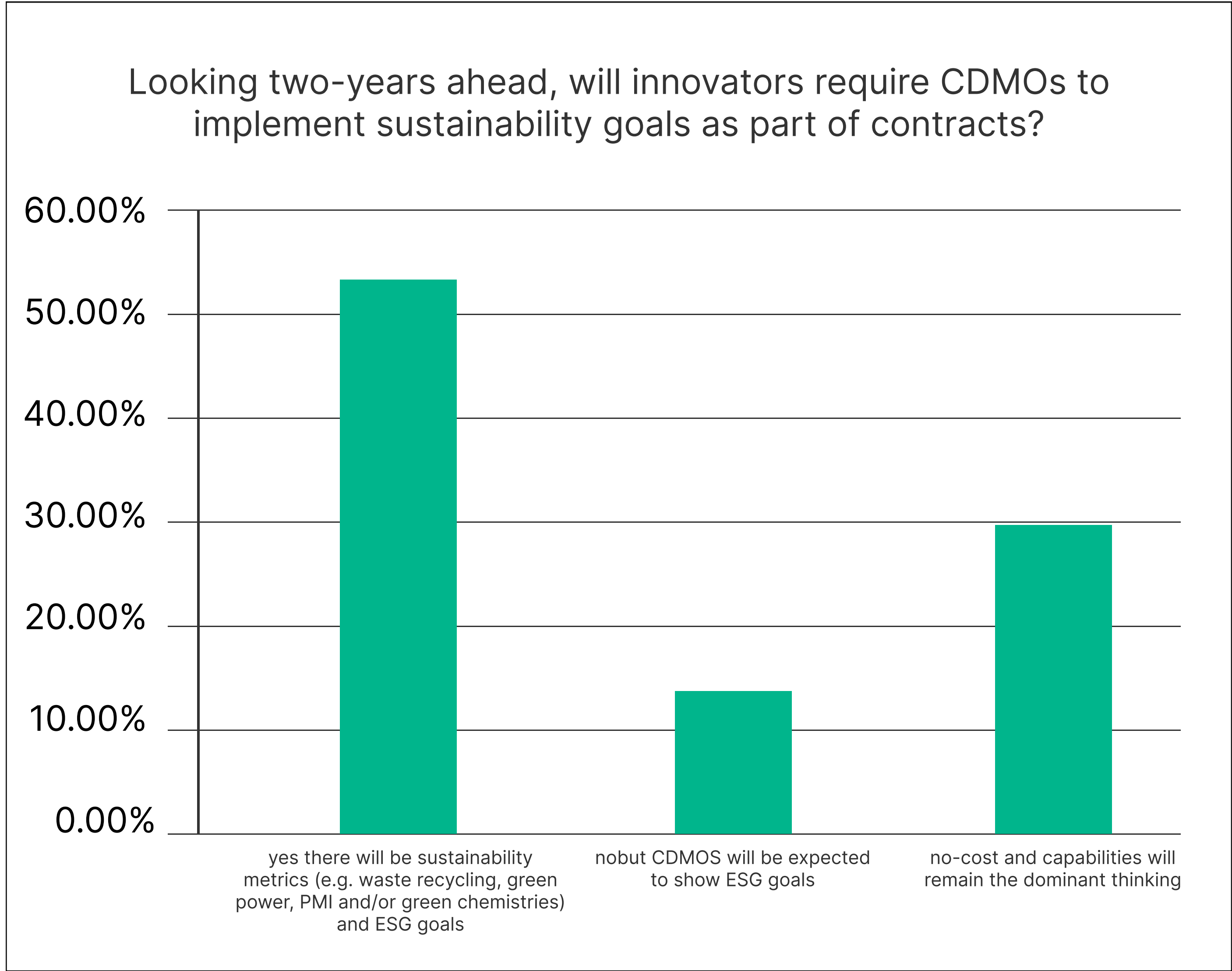


change improvements in manufacturing costs and timelines ahead, so medium term prospects through to 2030 look robust.

The stock market – AI hype and September crash aside⁵⁵ – has also shown impressive resilience, signalling strong investor confidence in the sector's long-term potential. In fact, most biotech and leading CDMO stocks have recovered from a difficult 2023 and are now once again above pre-pandemic valuations.

A key factor driving this optimism is the anticipated surge in capital deployment. Private equity (PE) firms are expected to make significant acquisitions in 2025, while VC funding, which has been on hold, is almost certain to flow again soon. It should be noted this report anticipated a faster return of funding last year, but this does not negate this prediction being accurate today and moving into 2025.

In fact, this capital influx means, once deployed, that 2025-27 will likely be some of pharma's best ever years for growth and therapy approval rates – with CDMO capacity once again potentially strained. The other advantage for accelerating innovation is that CMO capacity is growing and will reach 60% of total capacity available in largest [top ten] companies by 2028 [or 52% of all available capacity when grouped together with hybrid companies – see Dawn Ecker's article in this report for more details]. Why is this significant? Because in the United States there are currently over 1,800 biopharmaceutical products in some stage of clinical development and the majority (~88%), are produced in mammalian cell culture systems. These biotech companies in most cases do not have commercial facilities, so this improved access will help supercharge the next era of MAb approvals – as even smaller biotechs will be able to access appropriate capacity quickly.



Report conclusions

The 2024 CPHI Annual Report paints, despite some short-term concerns, a compelling growth narrative for the medium term of the pharma, biotech and associated outsourcing sectors. For example, while investment (both VC and PE) has been slow to recover and filter through into outsourcing, over two thirds of novel therapies – particular complex drugs – are now discovered by biotechs, which are much more reliant on CDMO services meaning a faster growth as capital is released⁵³. Significantly, there are also now more targets than at any point in history [20,000+]⁵⁴ and attrition rates are improving with potentially step-

53. <https://www.norstella.com/small-biopharma-end-to-end-cdmo-partnerships-accelerate-development/>
 54. <https://www.statista.com/statistics/791288/r-and-d-pipeline-drugs-worldwide-by-phase-development/>
 55. <https://www.ft.com/content/eb21baea-6050-42b2-a17a-c1122e9ae8b4>

In small molecule manufacturing, our first ever European Manufacturing [hub] index identified Lombardy as Europe's preeminent region for API and small molecule production. However, the area is also now building a stellar reputation as location for the switch to advanced manufacturing and biologics. Similarly, the European Biotech [Hub] Ranking reflects a landscape that is becoming increasingly competitive. London and the Golden Triangle remain dominant, but regions like Basel are catching up, while Barcelona has slipped slightly on last year's impressive second place. Despite this, the overall trend suggests a narrowing gap between major biotech hubs, indicating that regional centres are becoming more attractive for biotech innovation and investment is becoming more dynamic – with Europe as a collective beginning to rival the output of the nine major US centres⁵⁶. This increased competitiveness, combined with innovation happening across the continent, sets a strong foundation for the future.

In terms of contract services, the outlook is similarly positive. The cooling seen in early 2024 has given way to renewed growth, with only 7% of the industry reporting a negative outlook for the next 18-months. The demand for contract development and manufacturing organizations (CDMOs) and contract research organizations (CROs) is likely to grow, and with uncertainty at both WuXi and Catalent – demand could outstrip supply for the most qualified CDMOs. In fact, this shift in prospects has seen CDMOs and CROs surpass biotech and AI companies [which dominated the investment landscape last year] as the most appealing investment options.

However, this report also emphasizes the need for evolution within these sectors. The long-term projection is that both CROs and CDMOs will need to evolve more quickly than in the past to meet the demands of next-generation medicines. Biologics, peptides, and advanced therapies are expected to increasingly dominate growth in the coming years, requiring CDMOs to adapt their capabilities to handle these complex modalities. For instance, biologics have seen a steady rise in FDA approvals, with 17 new approvals in 2023, and this trend is expected to continue. Additionally, the rapid rise of Tides drugs, which blur the line between small molecules and biologics, presents both a challenge and an opportunity for CDMOs. Focus has mostly centred on the 'fill finish' component for injectables, with big pharma investing billions in plants, yet very few CDMOs specialise in peptide actives – and even fewer have the capabilities to take these from discovery through to commercial supply. If R&D rates and consumer demand are sustained, both types of CDMO facilities will need to be expanded.

Similarly, the innovation happening in next generation biologics and advanced therapies is not only driving demand, but also creating new opportunities for profitability. With improved linker technologies and broader payload options, antibody-drug conjugates (ADCs), after a quiet 2024, will likely see at least three approvals in 2025. MABs will potentially see approvals in the teens, while in 2023 the industry saw a record five cell and gene therapy approvals – suggesting we

will now see consistent and rising approvals numbers [after many years of promise yet slow approval rates]⁵⁹.

Meanwhile, PROTAC drugs are a significant medium- and long-term opportunity, and it's very possible that once we gain a first approval, we will see a similar cascade in activity not dissimilar to peptides – albeit without the 'supercharged' demand of weight loss drugs. What is interesting is that very few CRDMOs are active in this area and, those that invest now, will likely see tremendous demand in 2-3 years' time assuming the technology further matures. Put this together and we forecast that a new approval record will be secured in the next few years, with FDA approvals rates routinely above 40 and possibly 50 in most years.

Geographically, India is expected to be the biggest medium-term beneficiary for CRDMO services, driven by its strength in chemistry and biology. However, the United States also stands to gain, particularly as domestic production [CMO] becomes a priority for supply chain security. But much further investment is needed if the big goals are to be achieved, with rhetoric alone not sufficient to transform a multi trillion-dollar industrial base. However, the creation of US domestic starting materials – if it ever happens – is at least a decade or more away. The other nagging uncertainty that will likely reach a crescendo by the end of 2024 is BIOSECURE and the likelihood is a version will pass [70%⁶⁰] – probably encased within a bigger act and the National Defense Authorization Act [NDAA] has been muted as one option – but what the specifics of this are, and its timelines, are well beyond this report's powers of prediction.

The conclusion is that despite a more difficult 18-months – with smaller CDMOs known to be struggling – the industry is in a strong position to build from 2025 through to 2030, with the promise of significant growth and profitability on the horizon. The capital is there, the innovation is there, and the market demand is there. So the industry's key players need to react to the future growth, rather than base the next 18-months on what happened in the preceding 18 – to seize the moment and shape the future of pharma, with regions like Lombardy at the forefront of the ongoing manufacturing transformation in Europe. If investment can be made and commitments sustained beyond the next election, the US is also poised further grow its manufacturing base – particularly for innovative medicine – while India increasingly, if gradually, is replacing China as the world's research powerhouse, bridging the translational gap in discovery and commercial supply with CRDMO services. These two trends are likely to sustain over the medium term and will profoundly shape discovery and supply networks built in the next 5-years. What we will see in five years, is greater CRO research options, but also, a more competitive manufacturing space – where decisions about clinical and commercial supply are made based on security, robustness and access to technology [gone are the days where outsourcing is a simple cost/gram, API or tablet unit measure].

56. <https://www.biospace.com/hotbeds>

57. <https://www.reuters.com/business/healthcare-pharmaceuticals/weight-loss-drugs-fuel-boom-firms-that-fill-syringes-2023-10-09/>

58. <https://www.bioprocessintl.com/facilities-capacity/eli-lilly-novo-nordisk-expand-operations-amid-glp-1-drug-boom>

59. <https://www.nature.com/articles/s41587-024-02166-7>

60. <https://www.bloomberg.com/news/articles/2024-09-09/after-tiktok-china-biotech-next-to-face-wrath-of-us-congress>

