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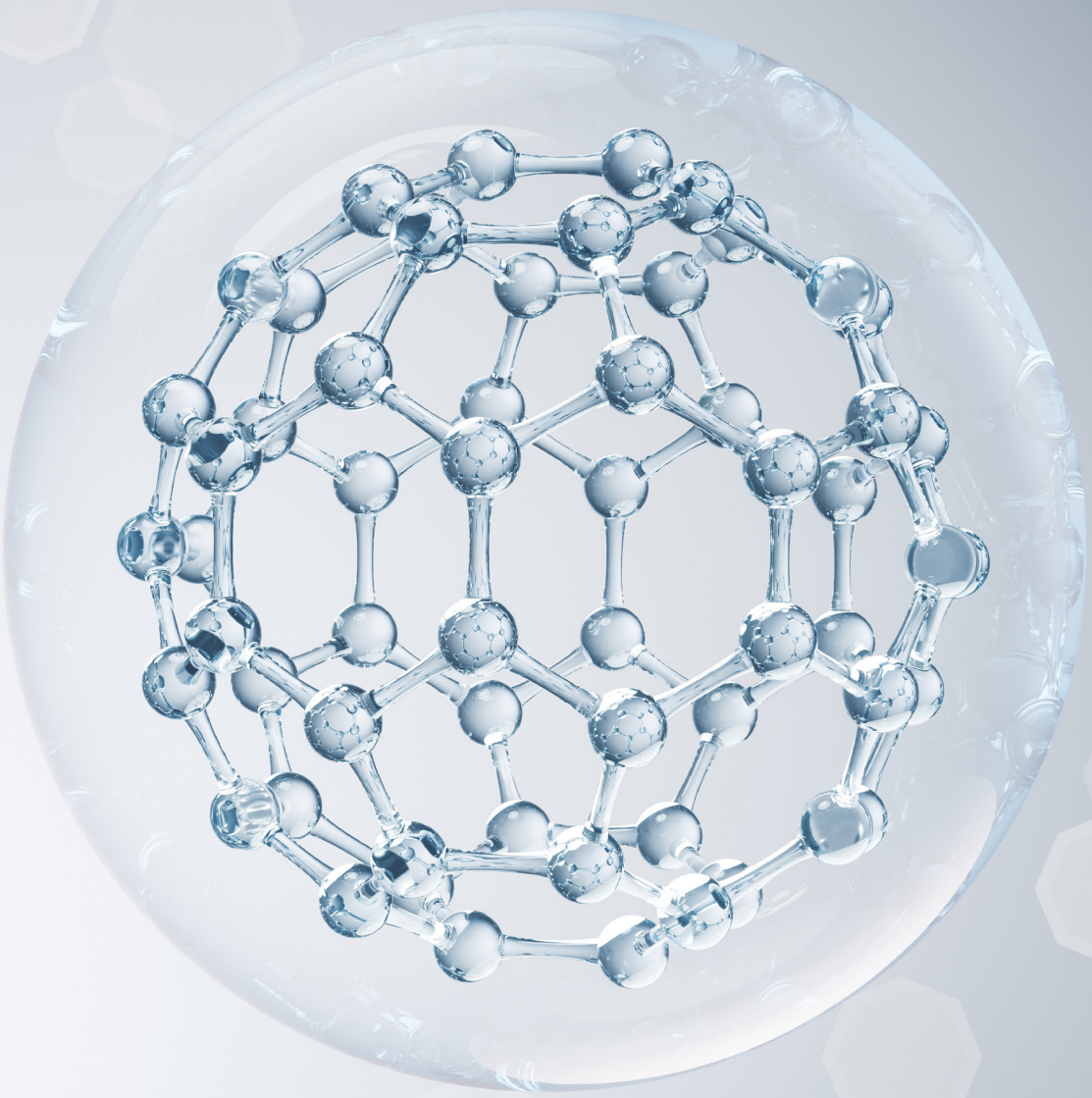

European expansion

How emerging biotechs are exploring the opportunities of out-licencing

July 2023

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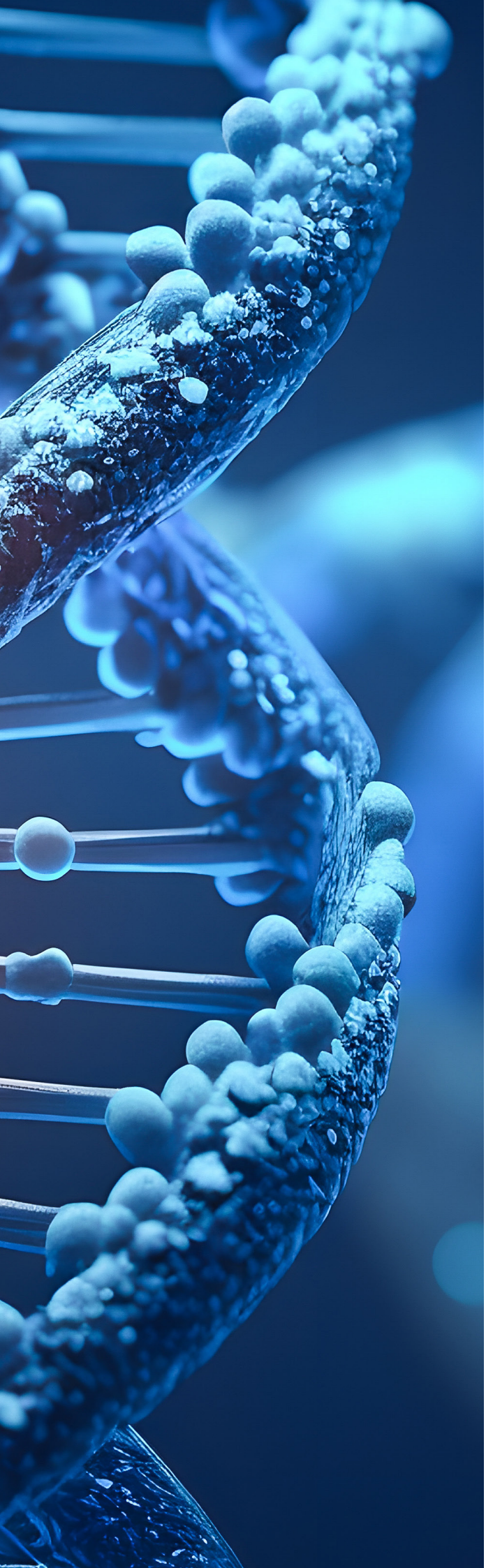


The go-to-market strategies deployed by emerging biotechs to launch their first products into Europe have changed in the last two years. Instead of building their own infrastructure, emerging biotechs are primarily commercialising their products through out-licencing agreements.

The European market offers a lucrative option to global biopharma and emerging biotech companies. In 2021, Europe accounted for over 20 per cent of the global pharmaceutical market, making it the second largest market behind North America.[1] The European market regulatory process is governed by the European Medicines Agency (EMA). Since its inception in 1995, the EMA has operated as the agency which approves drugs for use by Member States of the European Union and the European Economic Area (EEA) – approval is the first crucial step in gaining access to over 400 million patients.

However, entering the European market is challenging for emerging biotechs. The healthcare systems are fragmented with different regulatory requirements, country specific health technology assessment (HTA) processes, and health system funding policies which require deep understanding and resources to address.

1 The Pharmaceutical Industry in Figures 2022, EFPIA, 2022. See also: https://www.efpia.eu/media/637143/the-pharmaceutical-industry-in-figures-2022.pdf

The European market is large and complex – strategic choices are crucial for successful commercialisation

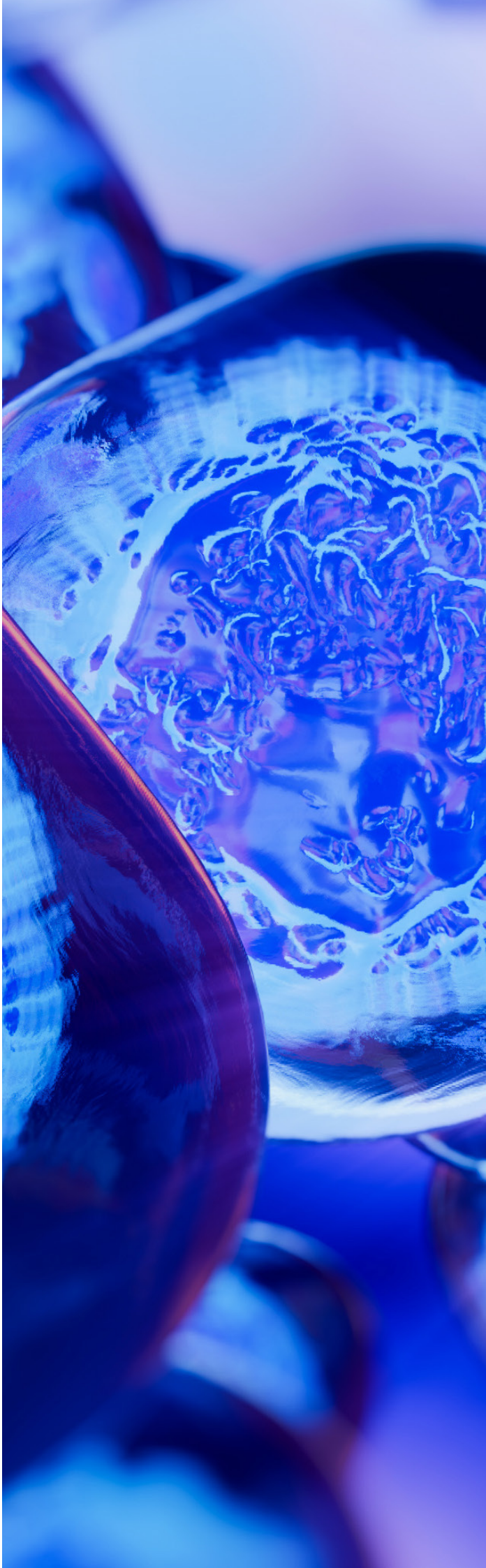
There is significant cost associated with launching a drug, from research and development (R&D) all the way through to product launch. In 2022, average cycle times – the time it takes for a new drug to progress from starting clinical trials to approval – were more than seven years for the 20 leading global biopharma companies. The average cost of bringing an asset to market was $2.3 billion last year.[2]

Following regulatory approval, commercialising the drug requires management of emerging biotechs to make many new types of decisions. Going-alone involves setting up infrastructure to manufacture, distribute, market, and sell the product. These all come with significant costs. Another choice many companies make is instead to partner with a global biopharma company, through joint ventures or out-licencing agreements. In some cases, emerging biotechs are acquired instead of pursuing these decisions.

The time immediately following EMA approval is critical. Marketing authorisation is invalidated if a product is not launched within three years of EMA approval. Other interim/lean models – like outsourcing to wholesalers/distributers – can be used to buy time to negotiate partnership agreements with global biopharma companies.

The focus of this paper will be on how the go-to-market (GTM) strategy for emerging biotechs launching into Europe has changed from a pre-pandemic environment (specifically, during 2021 and 2022). The following definitions will be used for an emerging biotech and global biopharma company throughout this article:

- **Emerging biotech:** a company with a market capitalisation of less than $10 billion at the time of EMA approval.
- **Global biopharma:** a company with a market capitalisation of more than $10 billion at the time of EMA approval.



2 Measuring the return from pharmaceutical innovation 2022, Deloitte, January 2023. See also: https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-seize-digital-momentum-rd-roi-2022.pdf

The analysis for this paper only considers drugs which are defined by two criteria. Please note, a drug must adhere to both criteria to be considered – this will be referred to as 'gaining approval' in the rest of this article. The two criteria are:

01) The drug must be defined as a new active substance (NAS) by the EMA. The EMA defines an NAS as a substance not previously authorised as a medicinal product in the EU.

02) The drug must have received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) from 2015 to 2022. The CHMP is the EMA committee responsible for human medicines.

When analysing an expansion model, we have used the following definitions for different commercialisation options:

- **Go-alone:** The emerging biotech commercialised the drug on their own (i.e. they set up means to manufacture, distribute, sell, and market the drug). Please note, if the manufacturing and/or distribution associated with the drug is outsourced this still qualifies as a go-alone strategy.
- **Partnership:** Different commercial models, including out-licensing (the emerging biotech sells the European rights or licence for royalties to a global biopharma company) and co-promotion (where an emerging biotech co-commercialises the product with a partner, sharing returns, risks, and costs).
- **Acquired:** This classification includes emerging biotechs which were acquired post-EMA approval but prior to product launch in Europe.
- **Undefined:** Products which have not yet been commercialised in Europe or their GTM strategy has not been publicly announced.

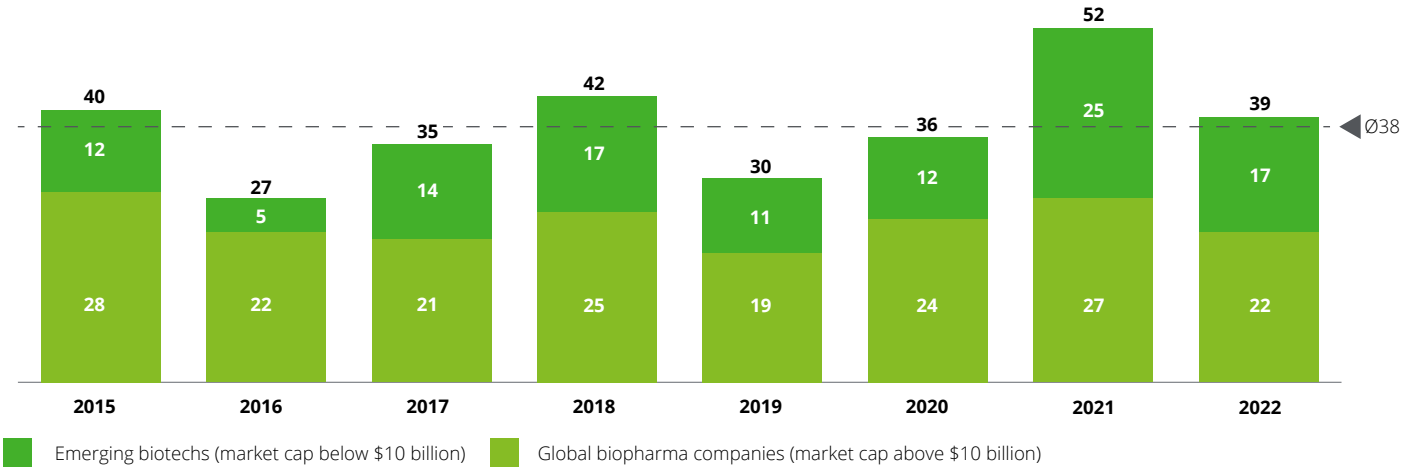
The spike in drug approvals caused by the pandemic has now normalised to a pre-COVID value

The number of drugs gaining EMA approval fluctuates each year with an average of 38 drugs gaining approval annually. However, the number of drugs launched in Europe by global biopharma companies has stayed relatively constant over the eight-year period with an average of 24. This suggests that emerging biotechs have driven the level of fluctuation. The standard deviations of the two data sets reinforce this point. The standard deviation for emerging biotech and global biopharma drug approvals is 5.8 and 3.1, respectively.

2021 saw 52 new active substances receive approval from the EMA – the highest number of approvals from the eight years that were analysed. This was driven by the conditional marketing authorisation of seven COVID-19 related medicines. COVID-19 reached Europe in early 2020 - with the first officially detected clusters originating from Northern Italy in February 2020.[3] Many companies rushed to bring new vaccines and treatments to market. The World Health Organisation (WHO) declared COVID-19 a global pandemic in March 2020 and the EMA declared it a public health emergency. This allowed the use of rolling reviews which provided accelerated assessments for COVID-19 vaccines and treatments.[4]

Figure 1

Breakdown of drugs gaining approval from emerging biotechs and global biopharma companies (2015 – 2022)



Source(s): Deloitte analysis, EMA, GlobalData.

3 When did coronavirus arrive in Europe, Springer Link, 20 May 2021. See also: https://link.springer.com/article/10.1007/s10260-021-00568-4

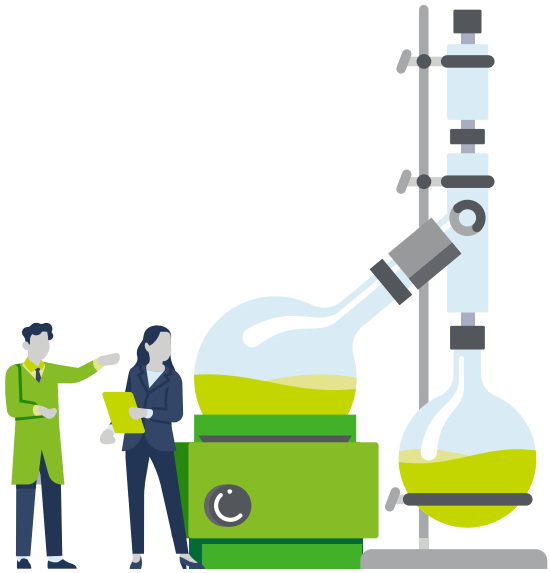
4 EMA initiatives for acceleration of development support and evaluation procedures for COVID-19 treatments and vaccines, EMA, May 2020. See also: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/guidance-developers-companies/covid-19-guidance-evaluation-marketing-authorisation

Even when COVID-19 related vaccines and treatments are excluded, 2021 was still an above average year for drug approvals.

In the past two years, emerging biotechs have launched 42 drugs into the European market. More than two-thirds of these emerging biotechs originated from the USA. Europe has historically been and continues to be a popular next step for American biotechs. From 2007 through to 2017, 75 per cent of new drugs that gained FDA approval also gained EMA approval.[5] Europe has remained a popular next step due to the large commercial potential of the pharmaceutical market.

5 Association between FDA and EMA expedited approval programs and therapeutic value of new medicines: retrospective cohort study, BMJ, 24 August 2020. See also: https://www.bmj.com/content/371/bmj.m3434

Emerging biotechs are opting for partnership and out-licencing agreements which offer lower risk, less cost, and increased speed to market

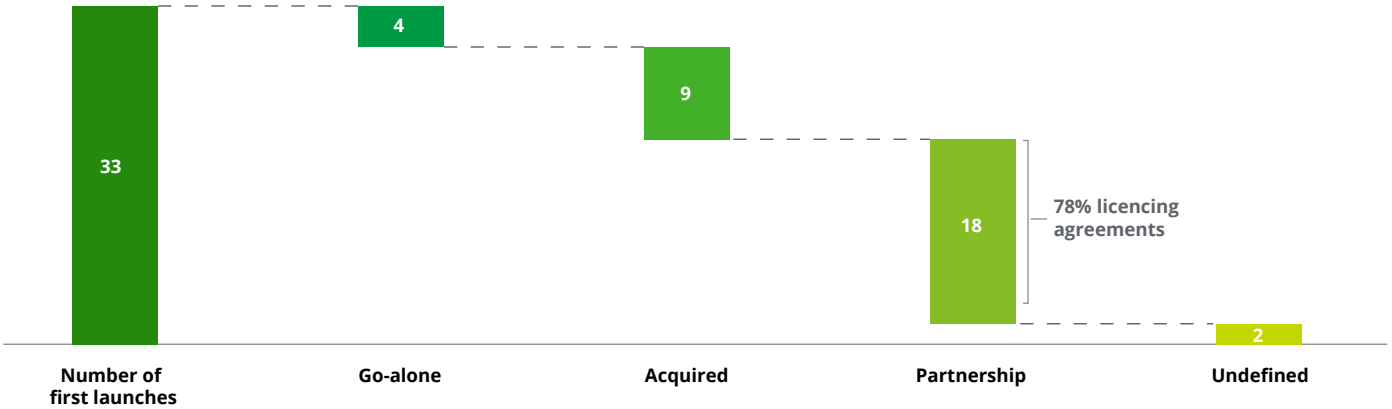


When assessing how emerging biotechs commercialised a total of 42 drugs in 2021 (25 drugs) and 2022 (17 drugs), three GTM approaches were considered: go-alone, partnership (which includes out-licencing), and acquisition. From the 42 emerging biotechs which gained approval for a drug in 2021 and 2022 only nine companies had previously launched a drug in Europe. This resulted in 33 emerging biotechs launching their first drug into Europe – this is the dataset which will be analysed in this article. Most launches were through partnership deals (18 new drugs), which primarily consisted of out-licensing agreements (14 new drugs).

Out-licencing a drug provides a low cost, lower risk launch option for emerging biotechs. The agreement removes many costs for an emerging biotech. They do not have to cover manufacturing, sales, marketing, or distribution costs – just to name a few. The emerging biotech company (the licensor) sells the rights to their product, for a given geographical area, to a third party (the licensee).[6] Out-licencing agreements often involve an upfront payment and royalty payments to the licensor from the licensee company.

Figure 2

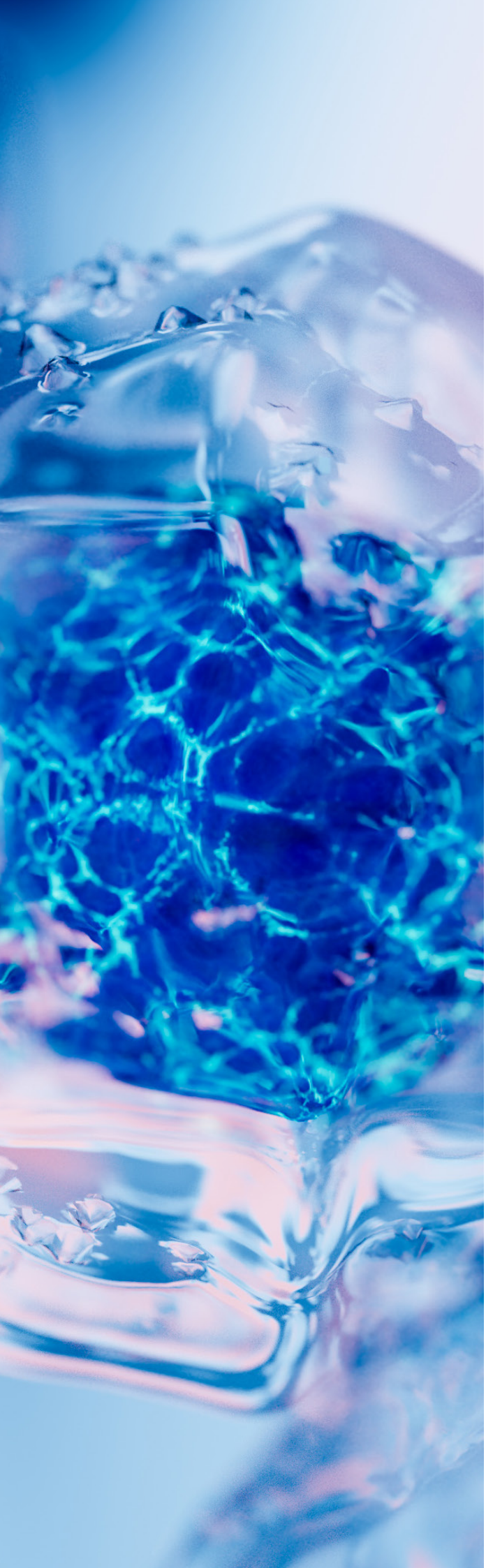
The go-to-market approach of emerging biotechs launching their first drug into Europe (2021 – 2022)



Note(s): (1) The number of emerging biotechs gaining approval is equal to the number of drugs gaining approval (i.e., every drug which gained approval is from a different emerging biotech). (2) The total number of emerging biotech drugs which gained approval was 42. From this, 33 biotechs were launching their first drug in Europe.

Source(s): Deloitte analysis, EMA, GlobalData.

6 Pharma Licensing, Deloitte, January 2022. See also: https://www2.deloitte.com/content/dam/Deloitte/uk/Documents/life-sciences-health-care/deloitte-uk-pharma-licensing.pdf



The risk comes from which third party the emerging biotech chooses to sell the rights to, as they are responsible for the successful commercialisation of the drug. The licensor has limited control over the product after the deal is agreed. This risk is often mitigated by choosing a global biopharma company as the third party. Often, these companies already have the required capabilities in place. If they do not, they have the capital that is required to set them up. The main drawback from out-licencing is that it limits the revenue the emerging biotech can make from the drug.

Acquisition is the second most popular GTM strategy. This is when an emerging biotech either sells their whole company or the asset to a global biopharma company. This often occurs during late-stage clinical trials when the drug is in phase II or phase III development. This offers a similar cost and risk profile to out-licencing but at an earlier development stage – resulting in less cost and less risk. This is a popular option for emerging biotechs as it alleviates the risk of the drug failing a clinical trial and not gaining approval. As with an out-licencing agreement, the emerging biotech will receive an upfront payment. However, it would be unusual for them to also receive royalty payments. Due to the emerging biotech selling the whole product to the buyer, and not just the rights to it, acquisition deals often include a more financially lucrative upfront payment than out-licencing agreements. The drawback is that, especially in 'one product companies', the whole company is sold.

The least popular option in 2021 and 2022 was to self-commercialise a drug. A go-alone strategy offers a higher risk, high reward outcome. Directly commercialising the product offers complete control over its development, the commercialisation options, and consequently all the revenues. However, building the commercialisation infrastructure requires spend on license to operate infrastructure (office addresses, distribution licenses, quality assurance, reimbursement approvals, etc.) as well as commercial differentiators (e.g. GTM investments around digital, sales and key account management). Often this is done in different time zones to the headquarters (HQ) and with nuances of different countries.

To reduce or manage these additional costs some emerging biotechs choose to commercialise their product but outsource their manufacturing and/or distribution to a third party. This allows the emerging biotech to focus their limited budget on what is most important – commercialising the product – rather than spending time and money on the lengthy processes involved in building and maintaining facilities to manufacture and distribute drugs.

The cost to set up manufacturing and distribution capabilities vary depending on scale and can range anywhere from $10 million to $500 million.[7] The use of a contract manufacturing organisation (CMO) or a contract development and manufacturing organisation (CDMO) can greatly reduce this cost by providing an outsourcing strategy. In addition, using a CMO/CDMO reduces time to market as they already have the required infrastructure in place. The drawback of using these organisations is that they reduce profits by receiving commission based or fixed fee payments.

7 Manufacturing Generic Drugs, The Washington State Department of Health, December 2019. See also: https://app.leg.wa.gov/ReportsToTheLegislature/Home/GetPDF?fileName=Manufacturing%20Generic%20Drug%20Report_899c9be4-ed5b-41b7-96c2-4f8a9a7cc3ef.pdf

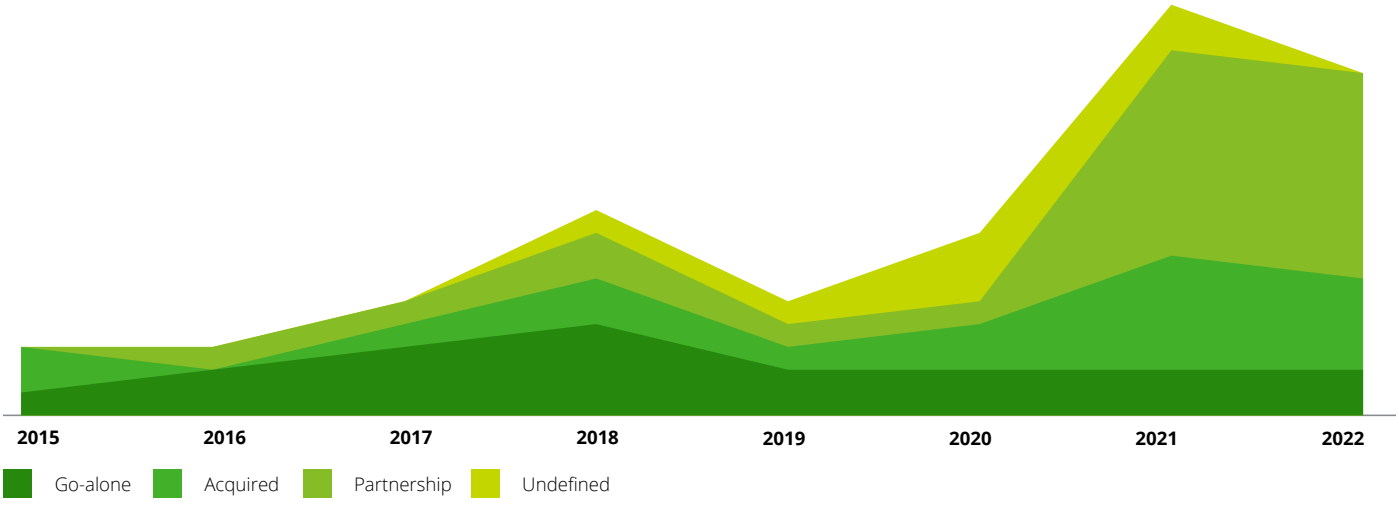
Over the past two years, partnership (including out-licencing) and acquisition strategies have gained popularity

The most common GTM strategy has changed over the years. The frequency of partnership and acquisition agreement have grown by 550 per cent since 2019. In contrast to this, go-alone has stayed relatively constant at a low baseline, particularly since 2019, with an average of two drugs gaining approval through this strategy each year.

The impact of COVID-19 will have influenced the decision making of many emerging biotechs. The pandemic disrupted borders, workforces, and supply chains. During this period, it became difficult to source bioreactors and other types of production equipment due to the factories responsible for production being closed. Additionally, the attention of CMOs and CDMOs was, understandably, focused on vaccine and therapeutic manufacturing. This limited the capacity available to emerging biotechs. As a result, many chose to partner with established global biopharma companies due to the pandemic-related complications.

Figure 3

The go-to-market approach of emerging biotechs launching their first drug into Europe (2015 – 2022)



Source(s): Deloitte analysis, EMA, GlobalData.

Previous launches generate revenue and may provide pre-existing infrastructure – both make a go-alone strategy more favourable

It is interesting to look at the GTM splits between emerging biotechs launching their first drug in Europe and emerging biotechs which have previously launched in Europe. The approach taken by emerging biotechs launching their first drug into Europe is dominated by partnership and acquisition deals. In contrast, if an emerging biotech has already launched in Europe, they are most likely to launch the drug through a go-alone strategy.

This is not surprising. If an emerging biotech has previously launched a drug successfully, they benefit from several factors which may make their next drug launch easier. Firstly, they have revenue from previous drug sales. This will provide the company with an increased number of resources to invest in future drug launches. Additionally, they may have some pre-existing capabilities in place (e.g. commercial workforce, infrastructure, etc.). When launching another drug, these pre-existing capabilities can be leveraged to make a go-alone strategy more effective and efficient.

Figure 4

Breakdown of the go-to-market strategy used by emerging biotechs for their initial or noninitial European launch (2021 – 2022)

	Go-alone	Acquired	Partnership	Undefined
Initial launch in Europe	4 *(12%)*	9 *(27%)*	18 *(55%)*	2 *(6%)*
Noninitial launch in Europe	4 *(44%)*	2 *(22%)*	3 *(33%)*	0 *(0%)*
All emerging biotechs	**8 *(17%)***	**11 *(29%)***	**21 *(50%)***	**2 *(5%)***

Note(s): Due to rounding, some percentages do not sum up to 100.

Source(s): Deloitte analysis, EMA, GlobalData.

Switzerland and The Republic of Ireland are the most popular locations for a European HQ

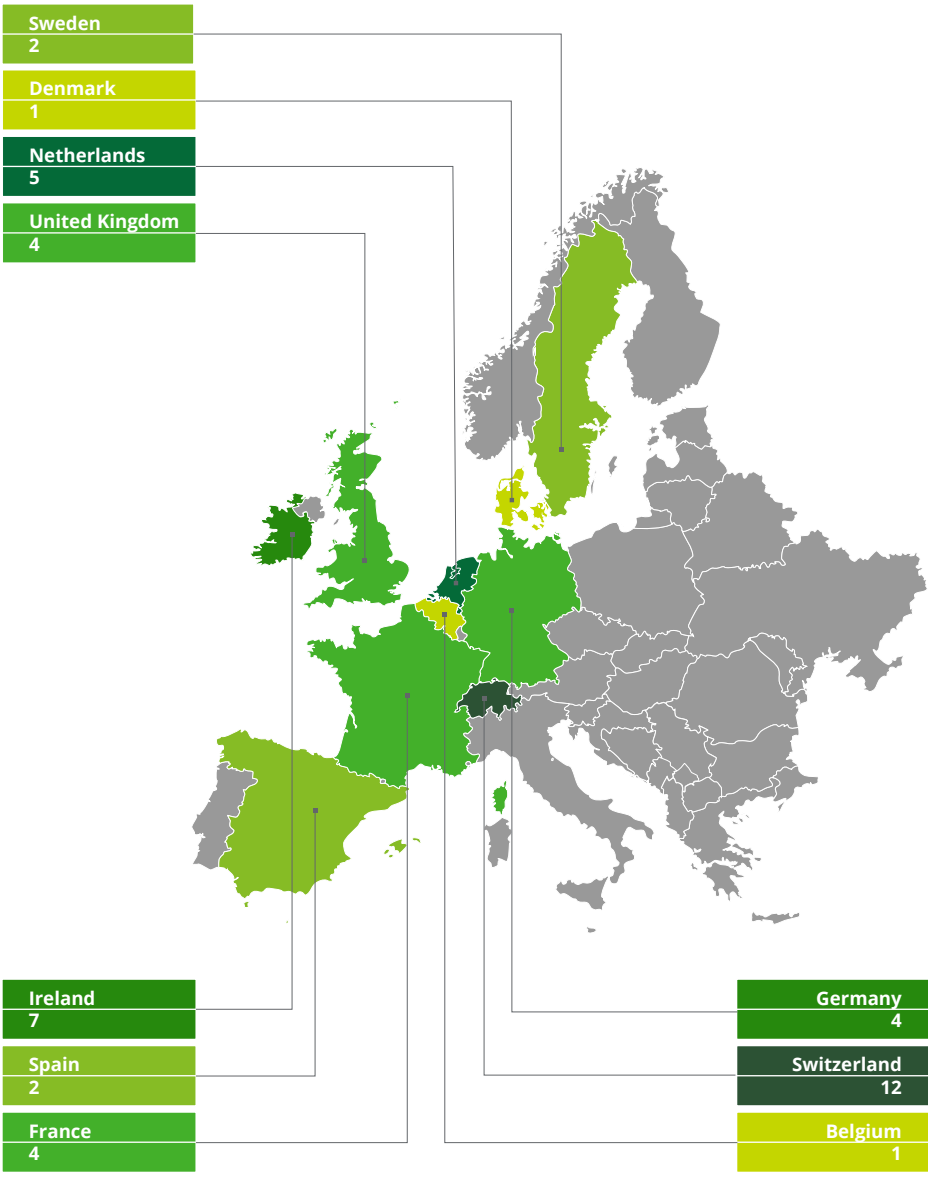
The location of a European HQ will be a significant decision for an emerging biotech company. This may be determined by a range of factors such as the business's existing footprint, location of target market, tax environment and available tax incentives, IP protection regimes, and market practice.

Historically, Switzerland has been a popular location due to a combination of factors listed above. This remained true in 2021 and 2022, as over a quarter of the 42 emerging biotechs which gained approval for a drug set up their HQ in Switzerland – resulting in the country being the most popular choice.

The Republic of Ireland is the only country to be English speaking and an EU and Eurozone member. Along with its low 12.5 per cent tax rate, Ireland's unique position is allowing the country to emerge as a popular European HQ for biotech companies.

Figure 5

European HQ locations for all emerging biotechs gaining approval (2021 – 2022)



Note(s): The number of emerging biotechs gaining approval is equal to the number of drugs gaining approval (i.e., every drug which gained approval is from a different emerging biotech).

Source(s): Deloitte analysis, EMA, GlobalData.

The trends towards partnership (including out-licencing) and acquisition deals are expected to continue

COVID-19 has led to a dramatic shift in the way emerging biotechs are launching their first drug into Europe by focusing on out-licensing/ partnerships and acquisitions. While some of the pandemic challenges are resolving themselves, other uncertainties have emerged in Europe and globally, including increased inflation, the Russian military invasion of Ukraine, and the reduced availability of biotech financing due to the higher cost of capital. In addition, several European countries have driven austerity measures (e.g. France, UK, Germany), focusing on drug spend and drug pricing.

This uncertainty is compounded by the EU discussing the passing of new pharma legislation. The European network for Health Technology Assessment (EUnetHTA) aims to establish a new framework for HTA processes in member states.[8] The impact this legislation is currently not understood, causing uncertainty around the location and capabilities needed for launch and the time to revenue.

For these reasons we believe the trend towards licensing/partnership, or even acquisition, is unlikely to materially change in the next two to three years.

8 European collaboration between regulators and health technology assessment bodies, EMA, April 2022. See also: https://www.ema.europa.eu/en/documents/work-programme/european-collaboration-between-regulators-health-technology-assessment-bodies-joint-work-plan-2021_en.pdf

Deloitte can offer a ‘one stop shop’ to assist small to mid-cap companies in commercialising their drugs

There are many complex questions that must be answered to ensure a drug is commercialised in the most effective way. Each GTM strategy discussed has its own unique sets of advantages and disadvantages. It is important to know which strategy best suits a drug launched by a specific emerging biotech and when and how this strategy can be activated.

Deloitte’s Life Sciences Catalyst and Biotech-in-a-box™ offerings can assist emerging biotechs to make the best choices in these challenging, company defining decisions. The Catalyst is a ‘one-stop shop’ to support the growth of small to mid-cap life sciences companies along their journey to market by providing easy access to Deloitte’s whole portfolio of capabilities: Strategy, R&D, Commercialisation, Tax, Finance, Legal, IP, Supply Chain, Regulatory, Technology, and Human Resource. Our team provides end-to-end support for the lifecycle of an emerging biotech company (i.e. pre-revenue, commercialisation, and scaling).

The ACE framework is a three-step game plan designed by Deloitte to assist emerging biotechs in their decision making. It is based on our experience of helping emerging biotech companies navigate geographical expansion.

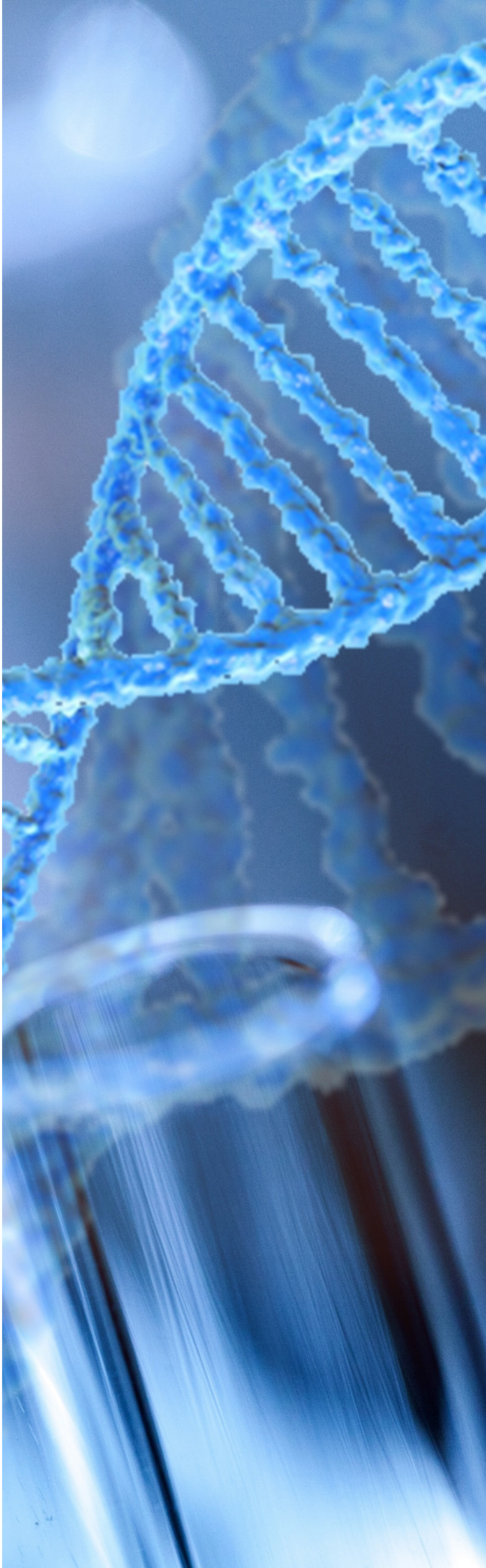
We have defined three steps to:

Firstly assess potential - where management agrees on the guiding principles for the European business, and assesses the commercial opportunity, route-to-market options, and associated costs across the European markets.

Secondly consider alternative options - select the most appropriate GTM options using a set of strategic criteria (e.g. investment required, time to value, complexity to manage, resources required), align on the priority factor(s) for decision-making and define the cut-off points for a go/no-go decision.

Thirdly establish a presence - choose the best route to successfully establish presence in Europe, which could either be via a partnership or out-licensing route, or the company choosing to go-alone. Alternatively, the best route could be to allow the company to be acquired by a global biopharma.

- **Partnership or out-licensing route:** Important to understand the value of the assets, potential tax implications, different partnering models, and aligning incentives.
- **Go-alone:** Necessary to map out the commercial and launch strategy, as well as identify the capabilities required to manage the successful build-up and implementation in Europe (incl. medical, commercial, regulatory, supply chain, legal and compliance, finance/Tax, HR, IT, etc.).
- **Acquired:** Important to assess the value of the asset, gather an in-depth understanding of potential buyers, and determine how being acquired will affect the company moving forward.



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