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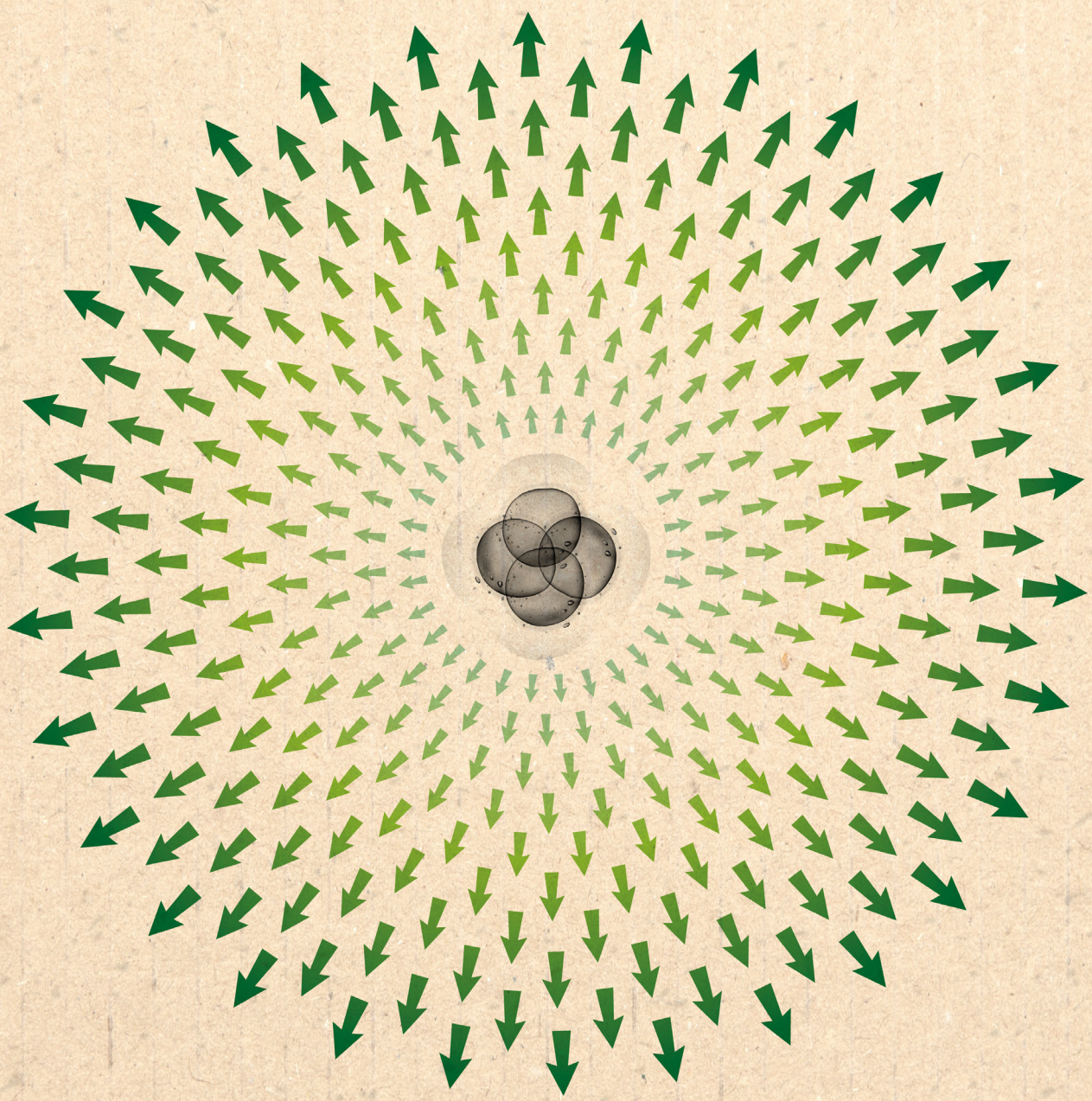

Deciding on the right path

How biotechs should expand in(to) Europe

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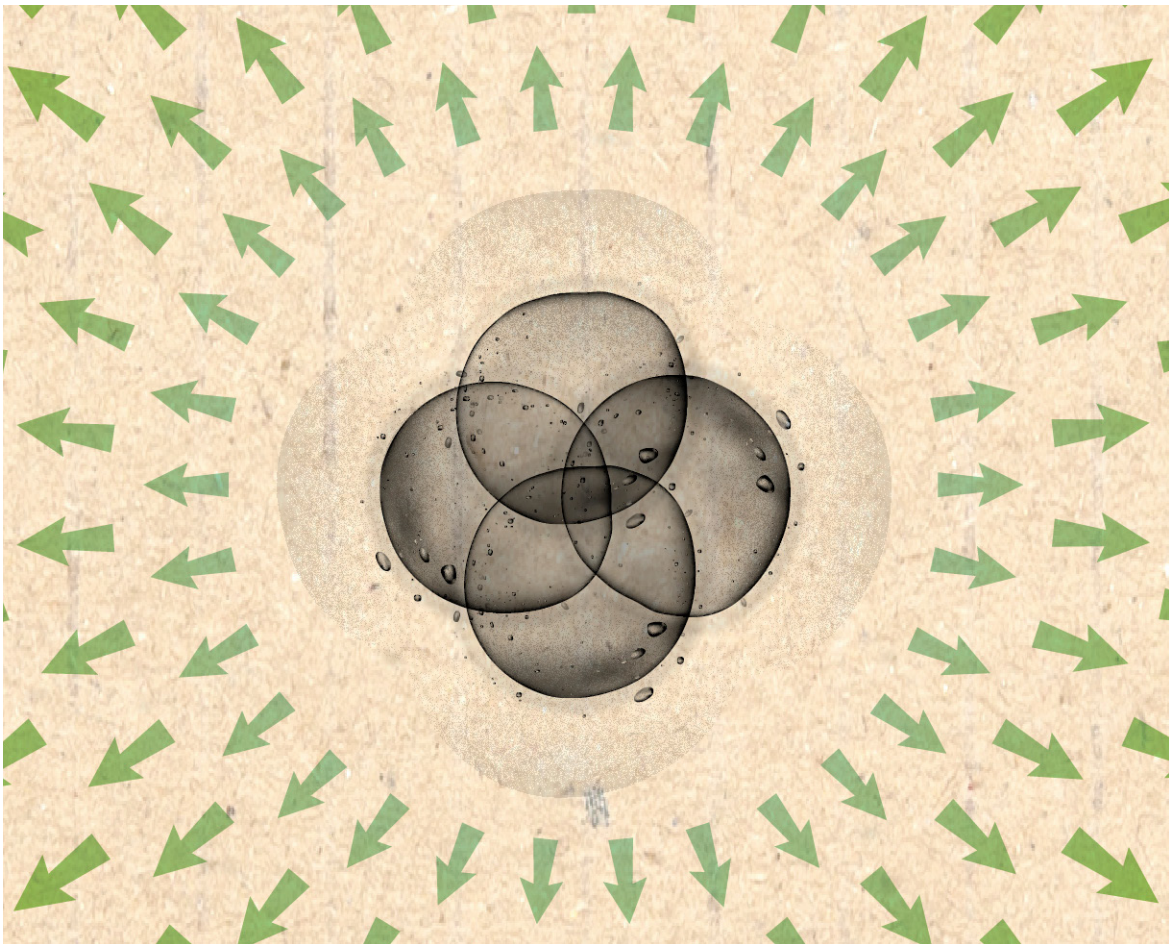
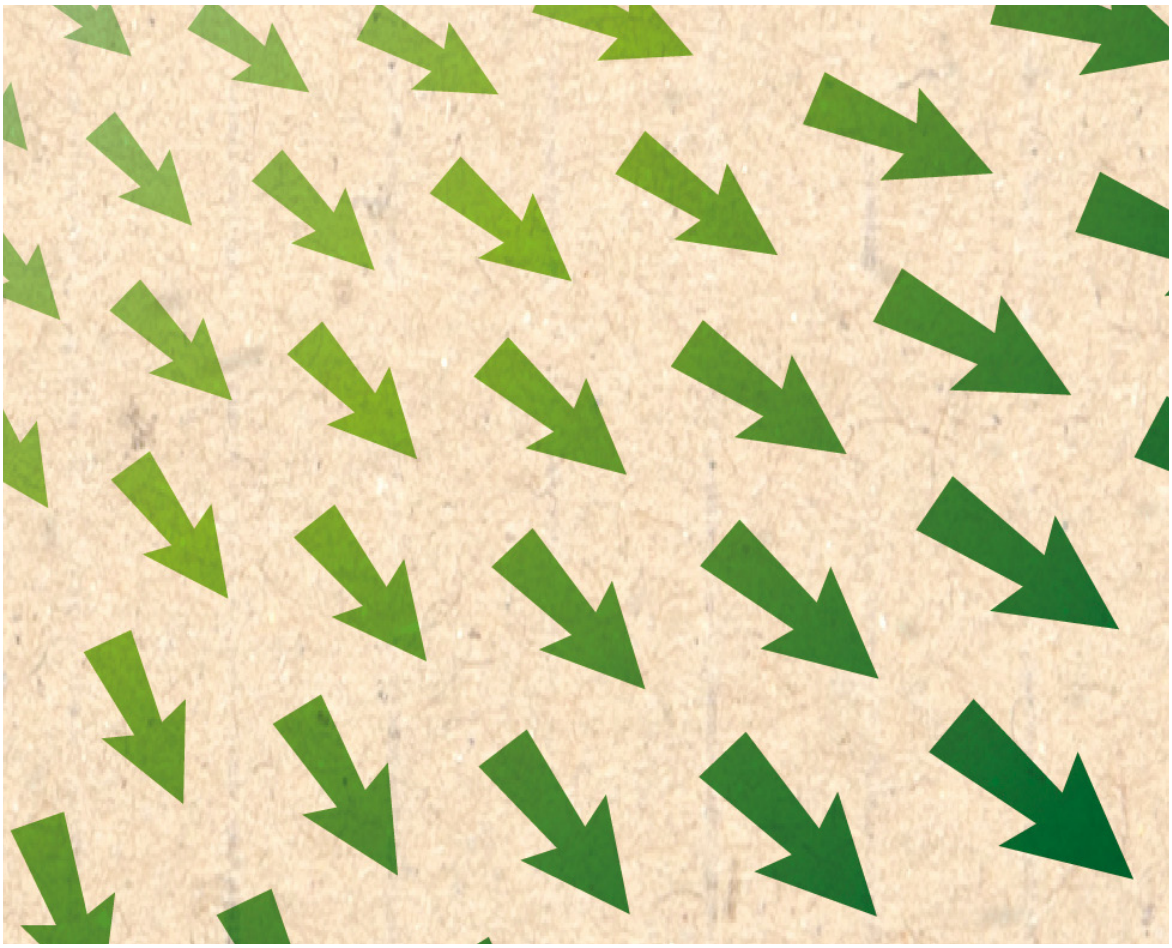


Introduction: A compelling market, despite everything

For biotech companies, Europe has been a tough market to conquer. Nonetheless, it remains a too important and large playing field to omit.

WHETHER BASED IN the US or in a European country, biotech and pharma companies have continued to look to expand in(to) Europe (including the UK), as their top priority. However, some have struggled to make a success of their attempts at European geographical expansion. The most relevant and recent example of this is US-based Bluebird Bio. Following unsuccessful negotiations with national agencies (e.g. in Germany) to try and launch their first drug in Europe, Zynteglo executives made the decision to wind down their operations and focus their business on the US.[1]

Nonetheless, Europe remains an important market for biotech companies (biotechs) launching their new drugs, as it accounts for over 20 per cent of the total global pharma market.[2] In this piece, we explore how best to expand into Europe.

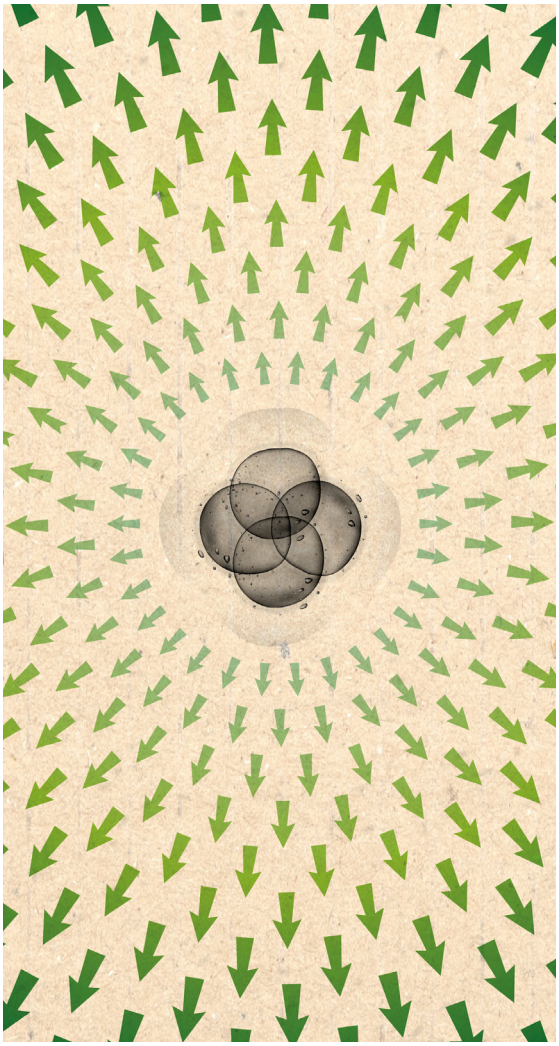


A complex and fragmented market

THE EUROPEAN MARKET is complex and fragmented. It comprises 31 markets across Europe, including the UK and Switzerland. Biopharma products require regulatory approval from the European Medicines Agency (EMA) and/or the Medicines and Healthcare products Regulatory Agency (MHRA) for the UK. In addition, some nations (e.g. Italy) require approval from their own local/regional regulatory authorities.[3] There are also distinct healthcare systems, separate health technology assessments (HTA) and reimbursement processes for each market. Additionally, recent changes to EU regulations (for example, the Clinical Trial Regulation and new Medical Device/IVD Regulation)[4] and other market uncertainties, such as cross-border collaborations and their potential impact on market access, are making it increasingly difficult for biotechs to forge ahead.[5] Given all these changing dimensions, determining how best to expand effectively has never been more crucial.

Our original report explored How to 'ACE' geographical expansion in Europe. This follow-up piece aims to serve as an empirical analysis of the different choices biotech companies have made when expanding in Europe. It includes an analysis of 60 biotech companies seeking EMA approval over the past six years (2015–20), the types of drugs they have launched into the European market and the paths they have chosen to do so.

What is an emerging biotech?



WE DEFINE AN emerging biotech as a company with a market capitalisation of less than $10 billion at the time of EMA approval. The analysis for this paper considers:

- drugs registered as new active substances in 2015–20 (as opposed to generics or biosimilars), which received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) – the EMA committee responsible for human medicines (this is referred to as gaining EMA approval in the rest of this research)
- the Marketing Authorisation Holder (MAH) registered to have the licensing rights; this would not include biotechs who may have out-licensed the product rights to large pharma before the product gained EMA approval (where the large pharma would be the MAH instead of the biotech).

When analysing an emerging biotech's expansion model, the following definitions have been applied for the different options:

- **Go-alone** - The biotech builds commercial operations and supporting capabilities, such as logistics distribution, in at least five major EU markets.
- **Partnership** - Different commercial models, including out-licensing (the biotech sells the European rights or licence for royalties to a large pharma); co-promotion, where a biotech co-commercialises the product with a partner, sharing returns, risks and costs; and outsourcing some commercial capabilities (a partnership with specialty distributors such as contract sales organisations or regional/local distributors).
- **Acquired before commercialisation** - This classification includes biotechs which were acquired post-EMA approval but prior to the product launch in Europe.
- **Pending launch** - Products which have not been commercialised yet in Europe.

An emerging biotech's choice of corporate headquarters (HQ) is defined as the location of the majority of its management and/or research teams. The location of tax, supply chain and other functions, as well as the MAH location, could be different.

Emerging biotechs continue to drive new drug EMA approvals

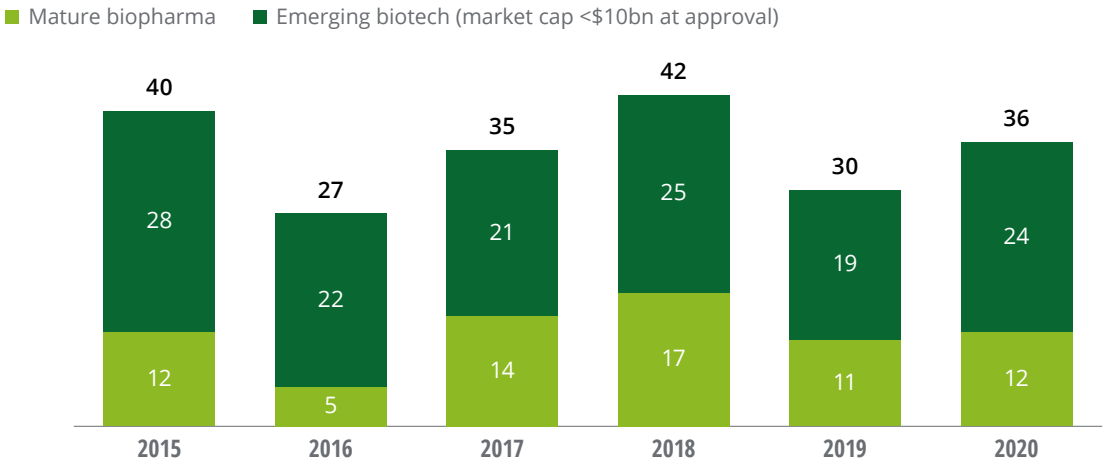
OVER THE PAST six years, while the absolute number of companies (both emerging biotech and mature biopharma) seeking EMA approval has fluctuated, emerging biotechs have consistently made up a significant proportion of these approvals (figure 1), accounting for an average of 33 per cent of all EMA drug approvals every year.

Of the emerging biotechs that have expanded into Europe, about 52 per cent are of US origin, followed by those of Japanese or Canadian origin. Europe remains a logical next step, especially for US biotechs, for a number of reasons:

- Europe's large overall commercial potential
- strong hotspots of research and industry expertise to support innovation
- an abundance of high-calibre talent
- a focus on advanced therapy medicinal products (ATMPs)
- European patients are more open to innovative drugs and technology than US patients.[6]

FIGURE 1

Breakdown of total emerging biotechs and mature biopharmas seeking EMA approval (2015–20)



Note: Of the emerging biotechs that have expanded into Europe, 52 per cent are of US origin, leading EMA approvals, followed by those of European origin or other (e.g. Japanese or Canadian origin).

Source: EMA, Deloitte analysis.

New launches continue to focus on oncology

LOOKING CLOSER AT the type of products gaining EMA approval, emerging biotechs play a bigger role than mature biopharma in the orphan diseases space: products designed to treat relatively rare conditions, with a patient prevalence equal to or below 5 in 10,000, according to the EMA. Fifty-five per cent of the products developed by emerging biotechs are orphan drugs (figure 2), compared to 29 per cent for mature biopharma companies.

Oncology is the leading therapeutic area for emerging biotech products gaining EMA approval – as Deloitte's R&D ROI report[7] also shows – followed by haematology, metabolic and neurology (figure 3), indicating the magnitude of funding entering the area and the large clinical unmet need in cancer.

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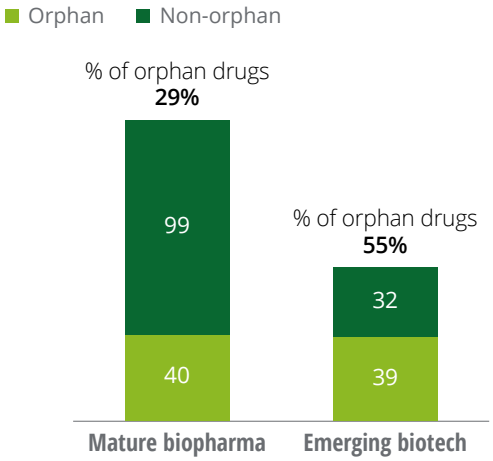
FIGURE 2

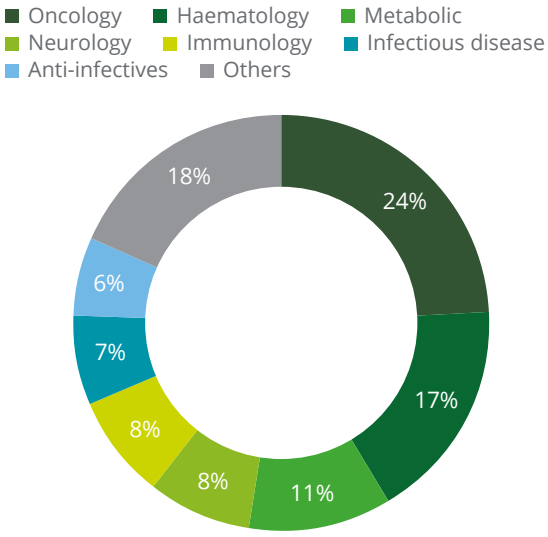
Proportion of orphan products gaining EMA approval (2015–20)



Source: EMA, Deloitte analysis.

FIGURE 3

Therapeutic areas of products by emerging biotechs gaining EMA approval (2015–20)



Note: Due to rounding, percentages do not sum up to 100.

Source: EMA, Deloitte analysis.

How emerging biotechs have expanded into Europe

EMERGING BIOTECH COMPANIES expanding in Europe have several go-to-market options – go-alone, partnership and, acquisition prior to commercialisation.

In the past five years emerging biotechs launching their first therapy in Europe have used a go-alone expansion model most often, while the partnership model is the least popular choice (figure 4).

Of the emerging biotechs expanding on their own, over half launched an orphan drug into European markets. Launching an orphan drug has a number of advantages, which include:

- a more compelling value proposition, addressing a serious unmet clinical need
- a leaner, less resource-intensive commercial operating model, driven by a smaller target patient population and set of prescribers
- the opportunity to take advantage of early-access schemes and innovative contracting which can help reduce the time to patient access.

Many of the go-alone manufacturers who did not receive orphan designation from EMA for their drug nevertheless launched 'innovative' therapies.

FIGURE 4

Go-to-market approach by emerging biotechs launching their first product in Europe (2015–20)

Note: Across five years, emerging biotechs launching their first therapy in Europe most often utilised a go-alone expansion model, while the partnership model is the least popular choice. Of the emerging biotechs, over half launched an orphan drug into European markets.

Source: EMA, Deloitte analysis.

A likely reason why these emerging biotechs pursued a go-alone model is that the therapies were either an efficacious first-in-class drug (e.g. in its mechanism of action), an ATMP or both. Indeed, 80 per cent of these go-alone non-orphan biotechs were later acquired (one to two years after their launch) by another biopharma player, further demonstrating the innovative nature of the therapy and the commercial opportunity it offered.

The two remaining alternative approaches to go-alone have approximately equal popularity for the remainder of our emerging biotech pack (both orphan and non-orphan). Slightly more popular over the past few years is acquisition of emerging biotechs after receiving EMA approval but prior to any European launch. This can be viewed as a 'golden window' or an inflection point for value realisation for shareholders, a point at which an appealing balance is struck between high optimism for the recently approved product and low relative risk of going to market.

Trailing slightly behind this approach is commercialisation via partnership(s). The majority (75 per cent) of those acquired (typically by pharma companies) had an orphan drug, while almost all of those who leveraged partnerships to launch in Europe did so with a non-orphan drug. It should also be noted that the average-dollar market capitalisation for partnering biotechs was much lower than those utilising go-alone/acquisition models ($1.8 billion vs $4.2 billion). This suggests that biotechs using partnerships as a driver for expansion are smaller and have less ample funds available to them.

A go-alone strategy, by contrast, offers greater commercial opportunity. And that is a central reason why emerging biotechs choose to retain their European rights and go-alone. When the opportunity outweighs the costs and operational/financial risks and aligns with the company's ambition, executives have made the decision to pursue Europe on their own.

FIGURE 5

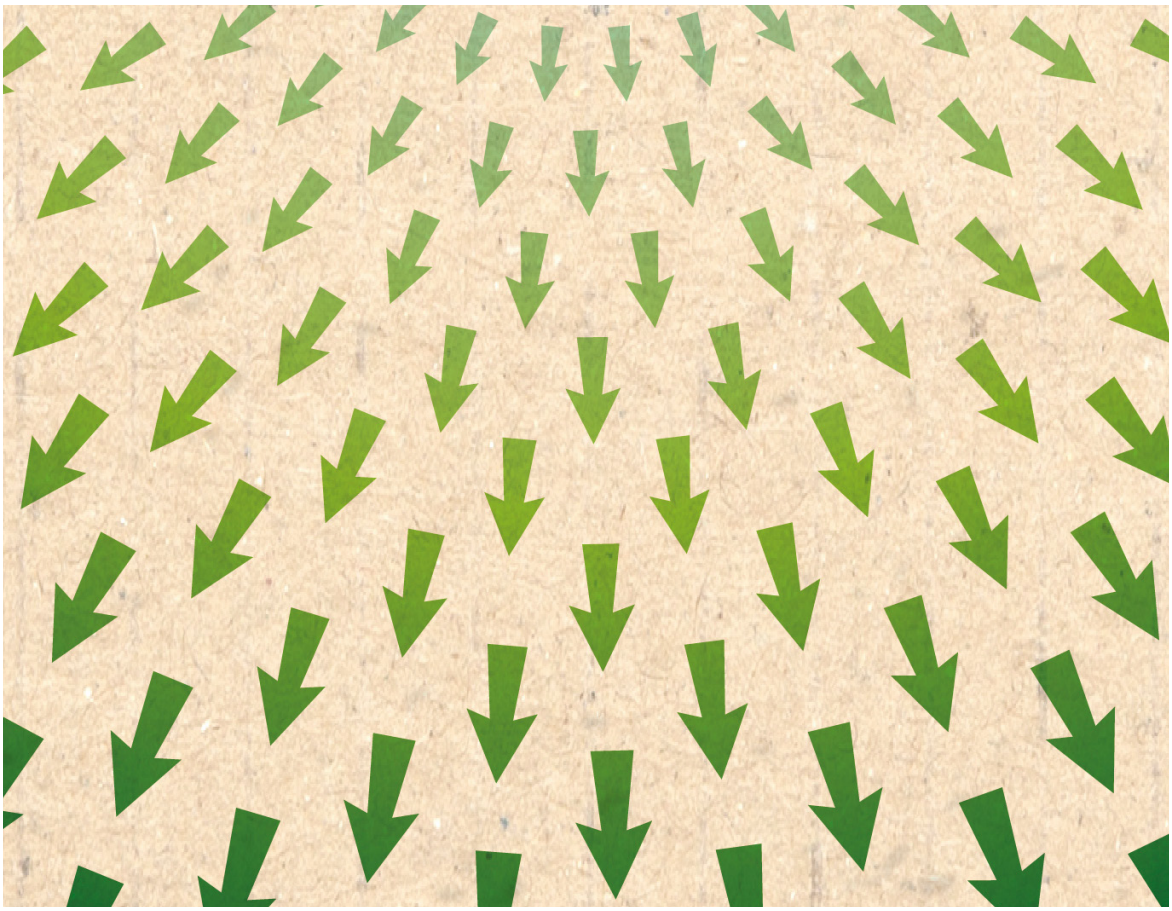
Go-to-market approach for all emerging biotechs with EU launches (2015–20)

	Go-alone	Acquired before commercialisation	Partnership	Pending launch
Orphan	56%	24%	11%	8%
Non-orphan	35%	16%	26%	23%
All emerging biotech	**48%**	**20%**	**17%**	**15%**

Due to rounding, percentages do not sum up to 100.

Source: EMA, Deloitte analysis.

A likely reason why these emerging biotechs pursued a go-alone model is that the therapies were either an efficacious first-in-class drug (e.g. in its mechanism of action), an ATMP or both.



Sequencing the launch

FOR US BIOTECH companies (80 per cent of the go-alone cohort), a driver that weighs on the risk profile of EU expansion is the launch sequence. Successful Food and Drug Administration (FDA) approval in the US and a prior launch there help to support and reduce the risk when expanding into Europe. This is the approach taken by 50 per cent of US biotechs, and especially by those with limited or no international and/or commercial experience, as it helps to provide cash flow to fund the new European operations.

Companies expanding from the US into Europe face a number of complex operational and financial challenges, including:

- the ability to provide sufficient executive oversight and presence in Europe to steer operations
- acquiring the right competencies and talent, overcoming complexities in the different countries, such as access, legal, cultural and linguistic differences
- acquiring the ability to recoup investments while disbursing significant capital over a relatively short time frame to fund European operations.

These challenges can typically be addressed by having a strong governance framework in place, balancing autonomy and oversight of the new European branch of the organisation. It is crucial to recruit successfully, positioning the company in the strongest European biotech talent markets.

Favoured EU HQ locations and operating models

EMERGING BIOTECHS THAT have expanded into Europe using a go-alone strategy have also had to determine which operating model they will use to ensure success. Ten US biotechs have taken this course, and among them the leading model has been to establish a central EU headquarters (HQ) and local affiliate offices in some or all of the largest EU commercial countries (Spain, Italy, France and Germany), the UK and a Nordic country. Decision-making to determine where a direct local country presence is required has typically been driven by a country's strategic importance (e.g. the size of the target population, commercial opportunity and the optimal pricing for that market[8]). The speed at which a biotech company puts in place its operating model will depend on its expected cash flow and reimbursement timeline in each market.

In European countries that do not warrant a direct local presence, launch activities can be managed centrally by the EU HQ or by regional offices. Alternatively, less strategically attractive countries can be managed via partnerships. For our cohort of emerging biotechs, this has been in the form of commercialisation or distributor partnerships.

Regardless of which EU operational model is used, for all biotech companies (excluding those acquired or wholly relying on a partner for EU expansion), the choice of location for a European hub is a critical part of their EU expansion.

The UK and Switzerland, though both are now outside the EU, remain the top choices for headquarters (figure 6). For biotechs of non-European origin, the UK is by far the top choice (reinforced by the scale of biotech and innovation support available), followed by Switzerland, Ireland and Germany. The choice of EU HQ is driven by a number of factors, such as the available talent, tax environment, existing pharma ecosystem and network, and strength of the infrastructure, with good transport connections to the rest of Europe and the US highly desirable.

The choice of location will also affect how efficiently an organisation can serve customers in different markets from one location. For example, a Netherlands hub could serve customers in Belgium.

Out-licensing a therapy's rights to an established European commercial partner may help to skirt the operational, regulatory and commercial pitfalls of go-alone. But, as demonstrated by the majority of our emerging biotechs, the go-alone expansion model remains their preferred one.

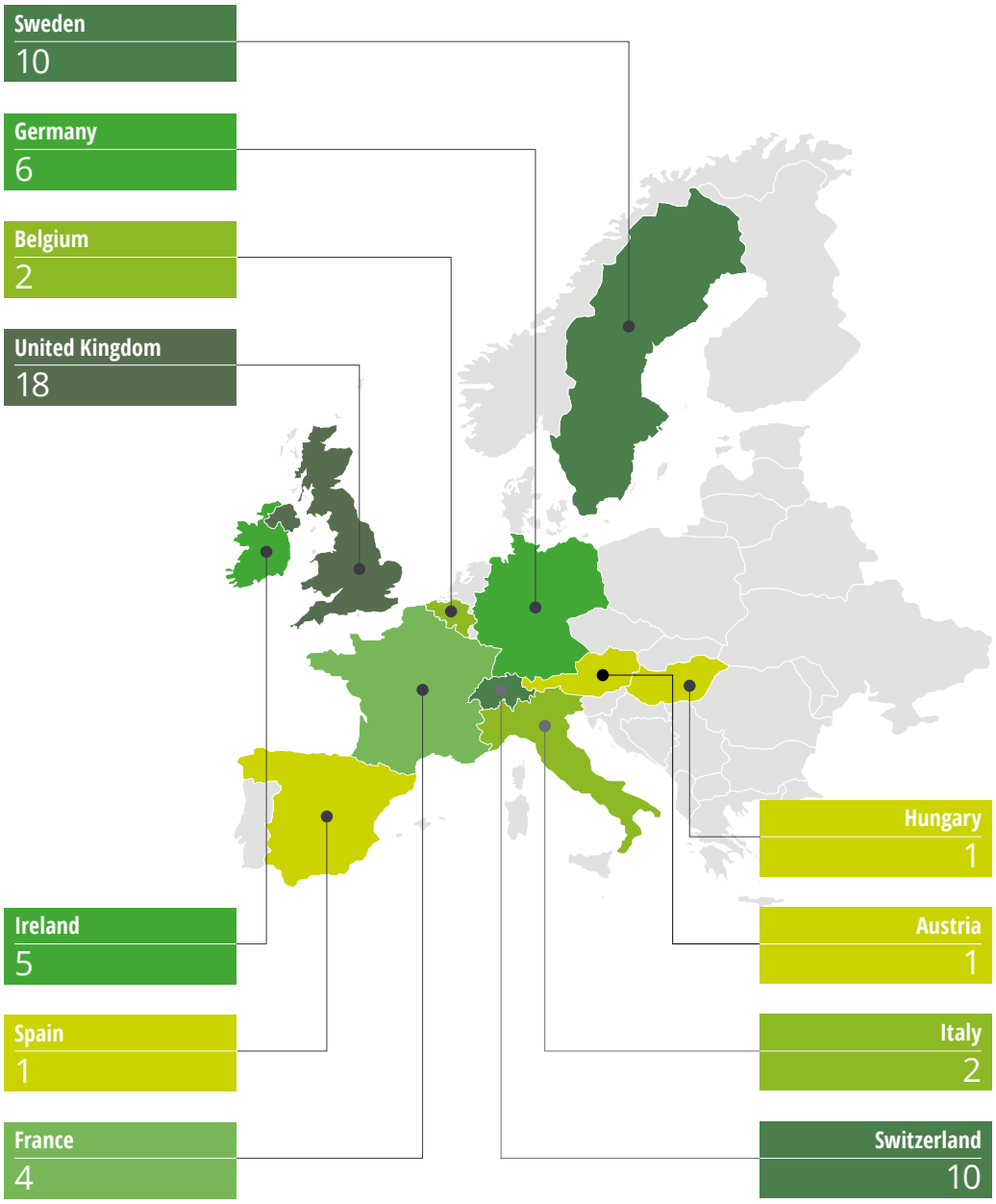
However, while previous successful expansions can provide a reference point for others, a deep understanding of European markets, realistic expectations and a clear strategic vision are essential.

The task of launching and commercialising a first drug in Europe is challenging. It demands that biotech executives consider a number of critical factors, such as the commercial potential (including market access), overall cost (the typical investment required to build a European operation from scratch over the first few years ranges from €60 million to €150 million), profit sharing, management complexity, tax and risk.

In our original report we outlined what it would take to 'ace' geographical expansion in Europe, and this analysis of drug launches by biotechs over the past six years furthers the relevance of that framework.

FIGURE 6

European HQ locations for all emerging biotechs seeking EMA approval (2015–20)



Source: EMA, Deloitte analysis.

Regardless of which EU operational model is used, for all biotech companies (excluding those acquired or wholly relying on a partner for EU expansion), the choice of location for a European hub is a critical part of their EU expansion.

How do expanding biotech companies get it right?

Despite the complexities and challenges of the European market, we consider that Europe (including the UK) offers an opportunity to capture significant commercial potential while also providing a platform for biotech companies to deliver improvements in patient outcomes through the provision of new therapies.

DRAWING ON OUR experience helping biotech companies navigate geographical expansion, we would recommend that executives planning expansion into Europe work through a three-step game plan:

ASSESS POTENTIAL

A critical first step before starting market exploration (and one that is often missed) is to agree on the vision and principles for the European business. Senior executives must decide:

- What is our vision and aspiration?
- What is the opportunity?
- What are the options?

CONSIDER OPTIONS

After assessing all possible go-to-market options, the next step is to start eliminating those that are less relevant for the product/portfolio and the company. A set of strategic criteria and the priority factor(s) for decision-making must be agreed upon:

- What are the cost implications of possible go-to-market options?
- In what time frame will we realise product/portfolio value?
- What risks are associated with launch options?

ESTABLISH PRESENCE

The best route to establish a presence successfully in Europe must be chosen. It could either be via a partnership or licensing route, or by choosing to go it alone. Separate decisions can be made for each market or market segment in Europe.

- How to partner?
- How to build?

To see how to 'ACE' your biotech's geographical expansion in Europe, read our three-step game plan to help biotechs take small steps to achieve a greater goal.

Endnotes

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Our insights can help you take advantage of change. If you're looking for fresh ideas to address your challenges, we should talk.

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