THE NOVASECTA EUROPEAN MIDPHARMA REPORT 2022

Novasecta

STRATEGIC PARTNERS FOR PHARMACEUTICAL LEADERS

Europe is home to 97 'MidPharmas': companies that develop and commercialise pharmaceutical products, with €100m-€6bn annual revenue. In our seventh annual report into this sector, we examine how its companies thrive, and conclude with imperatives for the entire pharmaceutical and biotech ecosystem.

EXECUTIVE SUMMARY

Europe's MidPharmas are **resilient**. This is a result of their ownership: three-quarters are privately controlled by families, foundations or more recently Private Equity funds. By contrast the more mature capital market environment in the United States has resulted in many fewer privately-held companies. Indeed there is a more global bi-modal pharma industry ecosystem of listed Big Pharmas acquiring or collaborating with venture-funded or listed pre-revenue biotech companies.

European MidPharmas are also **changing**: business models that relied on selling Big Pharmas' products in local markets are not profitable any more; Research and Development (R&D) has become more difficult and expensive; incremental innovation cannot command the price that it used to. Sustainability is no longer guaranteed.

In this report we analyse the performance of European MidPharmas, examining public domain data across multiple metrics. We structure our analysis according to the four fundamental **strategic imperatives** in such companies:

1 – Sharpen the strategic focus

2 – Reimagine R&D

3 – Seize external opportunities

4 – Prioritise profitability growth

MidPharmas that have changed themselves based on these imperatives continue to thrive. They are an inspiration for both Big Pharma and the pre-revenue biotech companies that aspire to more than being acquired by a Big Pharma.

Novasecta analysed public domain data for European-headquartered companies that develop and commercialise pharmaceutical products and generate €100m-€6bn annual revenue. This definition excludes service companies, distributors, and US companies that domicile in Ireland or the UK. It also excludes biotechs that do not have a commercial footprint but happen to have license revenue exceeding €100m in a single year, such as Argenx, Basilea, Curevac and UniQure. Companies are also excluded from relevant sample sets where there are insufficient public domain data available. We analysed data for the years 2016 – 2021 (calendar years or nearest published business year) sourced from GlobalData, company websites, and other public domain sources. Data analysed includes annual revenue, R&D spend, profits (using operating income as a proxy for Earnings Before Interest and Tax), market capitalisation and number of Mergers & Acquisitions and Strategic Alliances deals. All data reported in local currencies has been converted to Euros at the average exchange rate for the calendar year analysed. For R&D investment as a percentage of revenue, data was used from 2020 or 2019 where more recent data was not published. For EBIT as a percentage of revenue, 2020 data was used where 2021 data was not published. For market capitalisation vs revenue, 2022 market capitalisation and 2021 annual revenue was used. For R&D investment as a percentage of revenue, of the 97 MidPharmas identified, 54 have sufficient recent public domain data on both revenue and R&D spend. Of those 54, MorphoSys (125%) and Galapagos (101%) are not displayed in our graphic as they are outliers. Other companies are included in the remainder of the report where some data (such as revenue trends) are available. Compound Annual Growth Rates (CAGRs) are based on 2017 – 2021 data, or 2016-2020 where 2021 data are unavailable (four-year revenue R&D spend CAGR is used for Bial, and four-year Annual Revenue CAGRs are used for Uriach, Aguettant, Bial, Kern, Galderma, Olainfarm and Insud). For EBIT trend, companies where EBIT margin (EBIT divided by revenue) for all 5 years (2017-2021) was not available were excluded. Deal analyses examine data on Mergers & Acquisitions and Strategic Alliances, collected from the GlobalData deal database for years 2017 – 2021. For the performance ranking, 51 ranked companies were assigned to 5 equal groups with integer scores from 0 to 4 representing the number of quadrants of the Harvey balls. Total rank is based on the sum of all three sub-rankings (Revenue CAGR, Absolute Revenue and EBIT margin), and the lowest sum is the highest total rank. Companies that have changed ownership structure in 2022 are shown with the ownership at 2021 year end to correspond with the performance for 2021, for example Clinigen was public in 2021 and was acquired by international private equity company Triton in 2022.

SHARPEN THE STRATEGIC FOCUS

1

Focus is widely considered to be a worthwhile aspiration for a successful business. The alternative unfocused approach suggests diffuse, sub-optimal, sub-scale. While many MidPharmas have adopted focus in their businesses, some still seem to find it hard to either sustain or align on a strategic focus for their companies, preferring a diverse or hedged business model that keeps top-line revenue stable or growing.

1

SHARPEN THE STRATEGIC FOCUS

THE CORPORATE STRATEGIC FOCUS IS DRIVEN BY THE NATURE OF COMPANY OWNERSHIP

Each MidPharma's degree of focus appears to be correlated with the ownership structure of the company. Three quarters of European MidPharmas are privately held or controlled, with 67% being fully private, and 10% with both a dominant private shareholder (>50%) and a public listing. Some families and foundations prefer keeping business units that employ staff and generate at least some modest marginal income. Employees are indeed often seen as part of a big family. Listed companies and Private Equity owned companies have financial analysts and activist investors who do not tolerate such an approach. The families and foundations that have opened up to external investors tend to lean towards more focus, such as Almirall focusing on dermatology by divesting its respiratory franchise to AstraZeneca in 2014 and Ipsen selling its consumer business to Mayoly Spindler in 2022.

As a result of their ownership structure, MidPharmas often have diversified businesses including multiple interests such as consumer healthcare, nutritionals, primary care, specialty care, generics, contract development and manufacturing (CDMO) operations, and/or many therapeutic areas (TAs). While Big Pharma has been relentlessly focusing by divesting non-core businesses (e.g. most recently GSK with consumer, Novartis with generics).

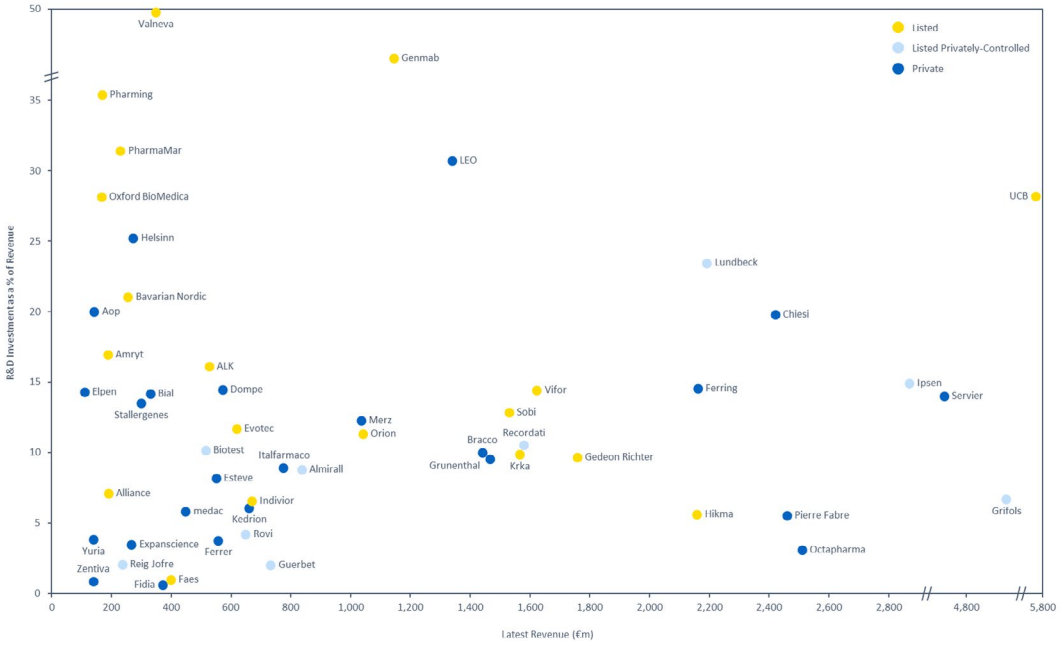
It is notable that the top six best-performing MidPharmas in our ranking this year are those that have a sharp strategic focus – whether that be on a technology platform (Genmab in antibodies, Octapharma in plasma-derived medicines) or one or two specialty TAs (Ipsen in oncology and neuroscience, Sobi in rare diseases, Chiesi in respiratory and rare diseases, Dermapharm in dermatology), all without the distractions of consumer, generics or CDMO businesses. Similarly those MidPharmas that have chosen to focus on generics or branded generics have performed well. Focus is particularly important for MidPharmas that lack the scale or access to capital markets that enables growth across many fronts.

The argument for a narrow strategic focus is clear: A company that wants to attract the best global talent and strategic partners that will enable it to grow sustainably has to stand for something and be world class at it. One or two priorities is fine; more than that starts to confuse matters.

RISK APPETITE IS A FUNDAMENTAL DETERMINANT OF STRATEGIC FOCUS FOR EACH MIDPHARMA

MidPharmas that have already strategically focused in terms of the businesses they operate in – for example innovative specialty care for 1-2 TAs, rare diseases, or branded generics – are distinguished from each other by the degree to which they accept innovation risk. Those that believe in the value (and risk) of product innovation tend to spend more as a proportion of revenue on R&D than those that believe in the value of commercialising a wide range of products in a profitable and flexible way. And risk appetite is ultimately a matter for ownership: some shareholders are comfortable with innovation risk, others less so.

THE PROPORTION OF REVENUE INVESTED IN R&D SIGNALS EACH MIDPHARMA'S APPETITE FOR RISK



Ownership therefore plays an important part in both strategic focus and the appetite for innovation risk. Private Equity funds favour stable commercial businesses without (or with a small amount of) the risks associated with discovery and clinical development of new molecular entities, for example with Acino, Clinigen, Galderma, Nordic Group, Pharmanovia, Recordati, and Theramex.

MidPharmas that are listed on public markets have two archetypes.
The first listed archetype is to invest in innovation and risk for shareholders that value the upside of R&D pipeline risk, for example with ALK, Galapagos,

Genmab, MorphoSys, UCB and Valneva. The second listed archetype is for shareholders that prefer profitable stable growth that can be made from generics, branded generics, or consumer businesses such as Alliance Pharma, Gedeon Richter, Hikma, and Krka, and Private Equity owned companies.

It is the foundation-held and family-controlled businesses that are the most diverse in terms of strategic focus, reflecting the fact that foundations and families do not conform to stereotypes. Some are seriously committed to early-stage R&D innovation and the risks associated with it, for example Chiesi, Dompé, Ferring, Ipsen, LEO Pharma, and Lundbeck. Others prefer a less R&D-intensive and often more diversified model, for example Esteve, Ferrer, Grünenthal, Italfarmaco, medac, Merz, and Pierre Fabre. Some choose to embrace both R&D risk and the more stable commercialisation of branded generics or primary care portfolios, for example Menarini and Servier.

In conclusion, strategic focus must reflect the ownership of the company. The listed markets and Private Equity funds tend to demand that their companies strategically focus. By contrast, MidPharmas that are foundation or family controlled either embrace a strategic focus or choose to remain diversified. So far the most focused companies have performed better than those that have not.

THE IMPERATIVE TO SHARPEN THE STRATEGIC FOCUS

Sharpening the strategic focus of a company is easier said than done. It requires an honest **assessment** of the competitive realities for each part of the corporate business model, and an **evidence-based belief** in how the company can differentiate itself in the future. Difficult decisions must be taken, legacies must be confronted. Those that have seen the value of focus in the realities of executive team agendas and discussions have not looked back. Their businesses are easier to explain, easier to manage, and attractive to the top talent that will help them evolve and grow.

REIMAGINE R&D

2

In most MidPharmas, R&D has a dual role – to sustain the regulatory compliance and availability of the on-market portfolio, and to create new medicines for commercial launch and/or out-licensing for selected regions. These require different skills and mindsets: R&D leaders who manage both must find ways to value and drive excellence in both.

SUPPORTING THE ON-MARKET PORTFOLIO IS AN ESSENTIAL ROLE OF R&D

For the MidPharmas that have large legacy on-market portfolios, the headcount and investment required to keep multiple products on the market and register them in new countries can be significant. Furthermore R&D organisations often include the Medical Affairs function (and associated budget) that is more aligned with on-market products than new product innovation. Once life cycle management (LCM) of on-market products is added into the mix – whether through registration of new geographies, new formulations, new indications or all three – the important responsibility of R&D for the existing portfolio can limit the resources that are available to put into new product innovation when caps are set on R&D budget (absolutely or as a % of top-line revenue).

For the MidPharmas that have chosen to rely on on-market portfolio expansion with Business Development efforts to acquire registration stage or on-market products the role of R&D is clear: ensure the portfolio is registered and expanded into new countries, and invest in late-stage LCM as required to drive top-line growth of the portfolio. This is now the favoured model for Private Equity funded MidPharmas that do not require the company to invest in the risky creation and development of new molecular entities.

The question of how much to invest in R&D for the on-market portfolio can be partly answered by examining the R&D intensity of the companies that are more oriented to this as the core role of R&D. An annual R&D investment of 4-7% of top-line revenue is a reasonable benchmark for this approach. Companies that spend slightly more can both support on-market products and sustain a limited commitment to innovative R&D. Krka, Gedeon Richter, Grünenthal, Italfarmaco, Almirall and Esteve all invest 8-10% of revenue in R&D.

FOR COMPANIES THAT ACCEPT THE RISK, R&D MUST ALSO CREATE NEW MEDICINES

Many MidPharmas still believe in a vertically integrated business model, incorporating the discovery, development, marketing, and sales of new pharmaceutical assets. The strategic focus of such companies is often based on deep scientific and clinical competencies in one or two TAs, or a multi-use technology platform. The intention being to create new products to replace those that no longer have patent protection or have been superseded by competition.

The MidPharmas with the largest investment in R&D as a proportion of revenue are those that clearly believe in the power of innovation to drive revenue growth. This includes the newer MidPharmas that have grown into the space by forward-integrating to add commercial capability as a result of successful R&D such as Galpagos, Genmab, MorphoSys, Pharming and PharmaMar. It also includes the companies that have valued R&D and invested in it year on year at a high percentage of revenue. For example, seven MidPharmas invest 20%+ of corporate revenue in R&D: LEO Pharma, UCB, Helsinn, Lundbeck, Bavarian Nordic, AOP Health, and Chiesi. Notably, the majority of these companies are either private or have a significant long-term family shareholding.

The role of R&D in such innovator companies is clear: primarily creating innovative products while maintaining the on-market portfolio. This can be challenging, as on-market support often has short deadlines that ties up resources and results in delays to innovative projects. The organisational model for such work needs to be carefully balanced, as the nature of work is quite different and can be spread across several functions.

The key imperative for innovator R&D heads is to be totally transparent about R&D's double role (existing and new products) and to organise the function accordingly, ensuring close cross-functional links when required and managing the expectations of commercial colleagues.

With R&D budgets measured in tens or hundreds of millions of Euros per year (vs Big Pharma billions) and high attrition rates, the reality is that new product launches can be rare. Although five to ten years might seem a long time to wait between genuinely new products, it is quite normal at this scale. The implication for R&D organisations is to embrace external innovation and business development to enrich the pipeline further – and to be clear that top quality scientific expertise is required to do this well.

SUSTAINING COMMITMENT TO R&D YEAR ON YEAR

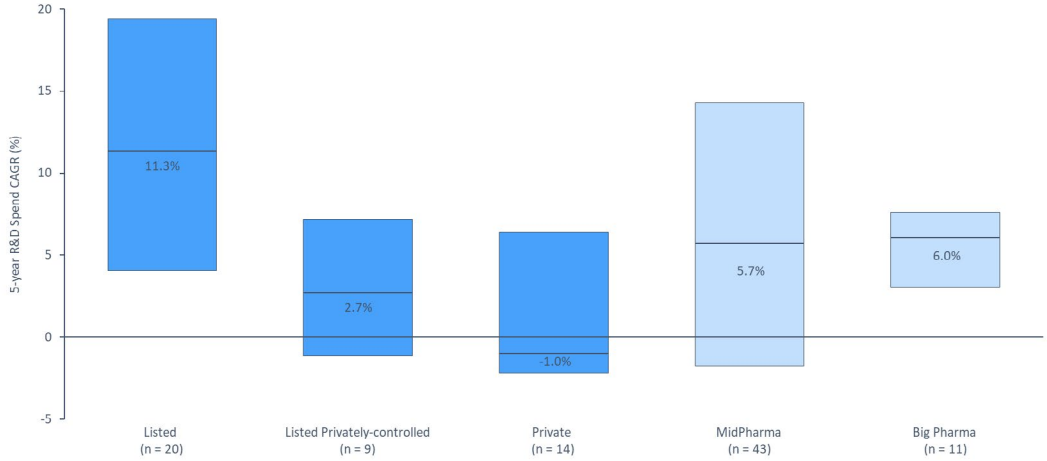
There is no question that over the past five years many MidPharmas have questioned both the level of commitment they should make to R&D and the

nature of such investment. Particularly in light of how many new products it has delivered to the organisation. However measuring the worth of R&D by how many new products it has delivered to the sales reps' bags does not reflect the more complex reality. A single R&D success can (and has in the past) completely transform the fortunes of a MidPharma company. But every time the next big thing fails (as it often does), confidence in R&D drops.

In this context there are numerous ways to measure pipeline value and the return that pharma companies make on R&D – all of which require assumptions. Unfortunately many of those are neither soundly based nor unbiased. Yet, most can agree that if a corporate leadership team commits more funds to R&D year on year, and is supported by its shareholders, it's engaging in productive R&D. Increased R&D investment suggests that either projects are advancing to the more expensive stages of development, or that there is more belief in the value that R&D will bring to shareholders. Or better still, both.

By the measure of increasing R&D investment year on year, MidPharmas and Big Pharmas are similarly productive in R&D. Looking at MidPharmas alone, the listed MidPharmas are much more productive than their fully private or listed privately controlled counterparts:

PUBLICLY CONTROLLED MIDPHARMAS INVEST MORE IN R&D THAN PRIVATE MIDPHARMAS AND BIG PHARMA



The median 11.3% annual increase in R&D investment for listed MidPharmas over the past five years is impressive. Clearly, public ownership drives management discipline through the need to constantly prove to shareholders and stock market analysts that value is being created. Ownership also influences corporate behaviour – with the listed MidPharmas that are growing, analysts and boards are focused on rewarding increased pipeline value, which requires more R&D investment. Interestingly, Big Pharmas' annual R&D investment median increase of 6.0% also demonstrates that capital is being increasingly deployed into R&D organisations.

The stark contrast of the median -1.0% decline in R&D investment in private MidPharmas partly highlights a change in the R&D approach of many of these companies. In some cases, this represents an ongoing long-term

commitment despite setbacks. In others, it's because of a strategic shift of the business model to drive short-term EBITDA increases by reducing the commitment to R&D that cannot deliver a visible EBITDA return for several years. This is ultimately a matter for the shareholders to choose between one to five year EBITDA or pipeline value creation. Neither is right or wrong, but clarity in the organisation about the trade off is essential.

R&D MUST FOCUS AND STAND FOR SOMETHING

The MidPharmas focusing on product innovation are almost always focused on either one or two TAs or a technology platform. This is no accident – building differentiated capability is tough and, at this scale, MidPharmas must stand for something to attract talent.

The larger MidPharmas with a long heritage of specialising in product innovation will usually focus on a TA, and usually it's a single area – though sometimes with (or building) an additional complementary one. Examples of globally renowned TA-focused MidPharmas are: Lundbeck in CNS, Chiesi in Respiratory, Ferring in Women's Health, and both LEO Pharma and Almirall in Dermatology. As with Big Pharma, this has often been founded and built from a single great product, one that forms the basis of physician relationships and disease understanding that mark out the most successful TA-focused players. Such in-depth pharmacological and medical disease understanding increases the likelihood of identifying and progressing successful assets. It can also act as a magnet for the world's most innovative clinical and scientific talent, to either join or collaborate with the company.

By contrast, the newer MidPharmas that prioritise product innovation often have a technology platform focus. A frequent characteristic of pre-revenue biotechs, this kind of focus creates a deep scientific understanding of a technology that can create multiple products. The challenge is to create multiple products that span either a single or several disease areas, which can make end-to-end therapeutic focus harder to achieve. As is often the case, the exception is oncology, where a platform focus – for example, in antibodies like Genmab and MorphoSys – can be leveraged into multiple indications in a single TA.

A further area that has become popular with some MidPharmas is Rare Diseases. In reality, this is neither therapeutically nor platform focused. Rare Diseases cover thousands of diverse indications and lend themselves to multiple technology modalities, including Cell and Gene Therapy as well as small molecules and biologics. The appeal of potentially shorter development timelines, higher prices, and fewer patients all suggest promising profit margins for MidPharmas. The niche patient populations and small, centralised treatment networks of rare disease indications also lend themselves to smaller and more focused commercial organisations – though these are very different to traditional primary or specialty commercial capabilities, so are not an easy bolt on. As such, some MidPharmas are

creating special integrated units to focus on this area – notably Chiesi and Recordati, who have both pursued this path alongside their core businesses.

R&D LEADERS MUST CREATE AND SUSTAIN A FIT-FOR-PURPOSE INTERNAL OPERATING MODEL

Success in R&D comes from people. Great science and medicines are created by great people working together, standing on the shoulders of giants that came before, and inspiring investors to back them. Attracting and motivating the right people from multiple disciplines (both inside and outside the organisation) to work together effectively is the central R&D challenge for the entire industry. It's this operating model that distinguishes the winners from the losers in R&D. Winners are agile, flexible, motivated and above all fast in both decision-making and execution. Capital is always available for organisations with amazing operating models.

European MidPharmas are typically committed to retaining people, particularly in family firms, which ensures they maintain the right level of knowledge through the long process of idea to product. However, such commitment becomes a risk in terms of losing scientific edge and sustaining an inward focus that doesn't accept new ideas and capabilities from external sources. Managing this balance is tough. And unsurprisingly, top management teams who are disappointed with their R&D organisations are naturally attracted to the allure of external innovation and acquiring successful biotechs. Yet they need great internal capabilities to decide what is good externally. And without a healthy internal R&D organisation and a pipeline that attracts great people, they are stuck.

THE IMPERATIVE TO REIMAGINE R&D

R&D is an activity that both secures access to on-market products and determines the future for pharmaceutical companies. MidPharma R&D organisations work at a scale and budget where the statistics are not favourable for launching new medicines. The imperative for all MidPharmas is therefore to reimagine R&D as a value-creating activity that sustains the on-market portfolio and may or may not deliver new products for the commercial organisation to launch.

Reimagining R&D also means sustaining a long-term commitment to it that suits the corporate appetite for risk. A clearly articulated, value-based and commercial **focus** for R&D is the essential foundation. A genuinely **cross-functional approach to governance** breaks siloes and enables high quality decision-making by adding perspectives from marketing, value and access, manufacturing and BD to the classic scientific/medical R&D functional perspectives. A **flexible and dynamic** approach to innovation drives speed in product development. And a highly developed process and mindset for **external innovation** ensures R&D adds value to science wherever it comes from.

SEIZE EXTERNAL OPPORTUNITIES

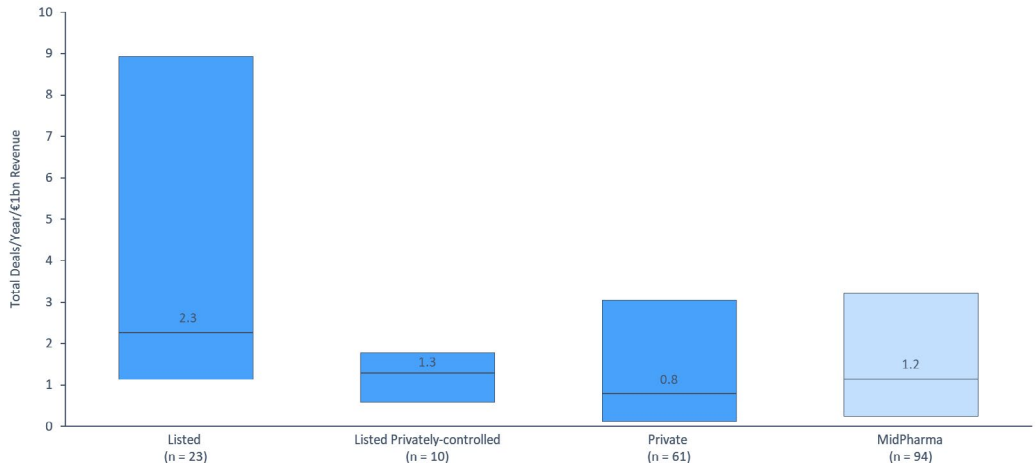
3

Most Big Pharmas realised many years ago that even at their scale they cannot go alone and need the external pharma/biotech ecosystem to evolve and grow. This has led to deals with other companies, either M&A or in-licensing or some other form of partnership. Many MidPharmas have reached the same conclusion.

3

SEIZE EXTERNAL OPPORTUNITIES

LISTED MIDPHARMAS EXECUTE MORE EXTERNAL DEALS FOR THEIR SCALE THAN PEERS



Listed MidPharmas lead the way in terms of deal execution, with a median of 2.3 deals/year/€1bn revenue. This is most likely down to having greater funds to participate in mergers, acquisitions and collaborations, and added motivation to create news flow which may impact valuations. Regardless of ownership, however, MidPharmas have been conducting a median of 1.2 deals/year per €1bn of revenue from 2017-2021, demonstrating a universal understanding that they can't go it alone to be successful.

DOUBLE DOWN ON EXTERNAL INNOVATION

Effective external innovation – accessing great people and science from around the world – is one of the hallmarks of the successful MidPharmas that are looking to R&D for innovative products. Science moves too fast to keep it all internally.

Product innovation in pharmaceuticals is notoriously expensive and risky, so it demands a certain amount of fortitude and resilience. It's testament to the owner-entrepreneurs and families who have undertaken such innovation that they've often used mostly their own money for an uncertain return, and continue to do so. Yet, the reality of product innovation now is that no single

organisation can control and own all of the capabilities required to create a rich pipeline of potential products.

Accepting and sharing risk with outside parties, such as other companies or new investors, is an essential element of any MidPharma (or indeed Big Pharma) business model, particularly in R&D.

SELECTIVELY ACQUIRE COMPANIES AND ON-MARKET PRODUCTS

For MidPharmas without any source of new products from internal R&D, growth requires the acquisition of products from external sources – which usually means the company acquisitions, product/portfolio acquisitions, and roll-ups that are typically favoured by cash-rich Private Equity funds. Correspondingly, Big Pharmas wanting to divest portions of their established portfolios can create bidding wars to secure a significant premium for their assets. While capital is plentiful, Private Equity funded MidPharmas can afford this. And as a result, family-owned and listed companies with less appetite for leveraging up their balance sheets can find it hard to compete.

For some privately held and long-established MidPharmas, acquiring to build has been a legacy strength. Over decades, the entrepreneurial (and often acquisitive geographical) expansion of companies such as Recordati and Menarini has transformed them from local pharmacies to successful global pharmaceutical companies. The challenge now lies in the limited supply of small companies to acquire at reasonable prices. Those that wish to play in the established brand space now find many competitors for products, and companies that are already generating EBITDA. This has resulted in the price to acquire or license them going up significantly.

In-licensing of on-market products presents an alternative to M&A, but there are many more buyers than sellers of such products. In our experience many business development functions of MidPharmas are searching for the same thing – an on-market or at least registration stage asset that has potential for growth and can be more or less immediately EBTIDA generating. And the pitch is usually that the MidPharma is specialist, Europe-knowledgeable and happy to take a regional rather than global licence. Needless to say there are not many such assets available. The simple reason being that most of the companies that have them have no desire to give others rights to generate profit from them. The exception can be US biotechs that want to self-commercialise in the US and can out-license European rights, but again such companies have other options, and their shareholders may prefer that they are acquired outright rather than complicate an exit.

MidPharmas therefore need to be creative with M&A and in-licensing, for example not requiring immediate EBITDA, accepting products that do not

have many prospects for growth in them. And always asking the question: is it helping with the strategic focus of the company or a simple financial arbitrage?

When it comes to sourcing expertise, bolt-on acquisitions and strategic partnerships, successful MidPharmas need to be very externally wired. This mindset shift manifests itself in companies actively building relationships with high quality expert scientists and physicians. Again, it's about people – the right experts can often provide access to wider expert networks that ultimately guide portfolio and project decision making. MidPharmas, therefore, need to develop and leverage a network of innovators in numerous areas – academia, biotech, pharma companies, venture funds, tech transfer offices – to access expertise, new project ideas and asset opportunities.

THE IMPERATIVE TO SEIZE EXTERNAL OPPORTUNITIES

Whether the MidPharma strategic focus is founded on innovative R&D or adding value to generic medicines or both, MidPharmas cannot grow without embracing external opportunities that complement internal capabilities. **Partnerships** offer a cost-effective way to do this, and leading MidPharmas ensure they have transparent and well articulated criteria and decision-making processes for both engaging in these and importantly managing the alliances after deal signing. Partnerships should be as broad-based as required to fit the criteria, including other pharma/biotech companies, academic institutions, venture funds, patient organisations and other stakeholders.

For on-market products or strategic entry into a new technology area (for example biologics) and/or TA, **bolt on acquisitions** can be favoured over partnerships to ensure a full set of cross-functional capabilities are brought to the acquirer. Again clear criteria and rapid decision-making are the keys to success.

PRIORITISE PROFITABILITY GROWTH

4

Profitability is arguably the only essential for a sustainable business. This is particularly the case with MidPharmas, since those that are private have no other way of accessing capital to invest and grow other than debt. And many choose to avoid debt, to be resilient in the case of potential corporate or geopolitical shocks. For those MidPharmas that have a market listing, European capital markets are less easy to tap than US capital markets, leading to many biotechs seeking NASDAQ listings.

4

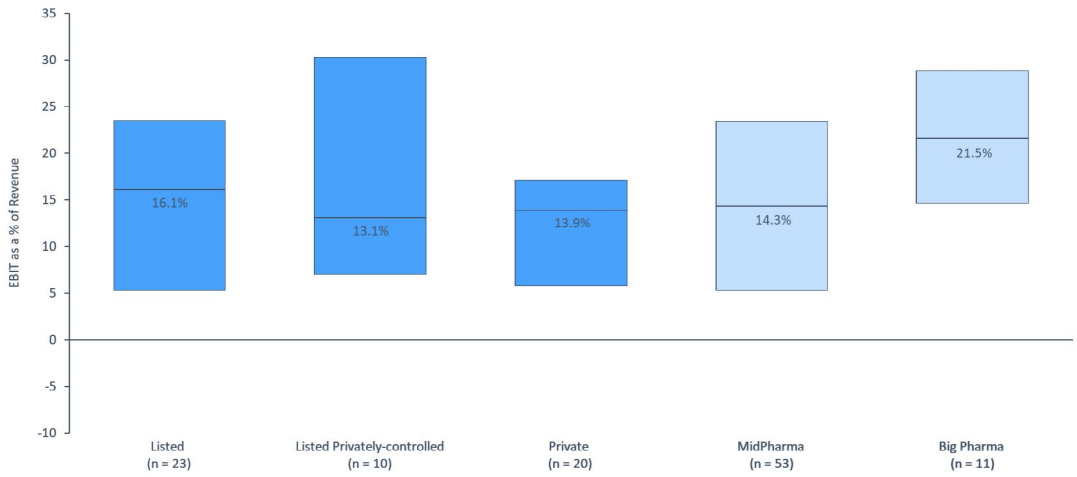
PRIORITISE PROFITABILITY GROWTH

Paradoxically the mindset of many MidPharmas has traditionally been one of scale, with the simple measure of top-line group revenue as the marker of success. This has led to companies seeking top-line growth without sufficient regard for profitability. The more recent manifestation of this desire for scale is found in M&A-focused MidPharmas that apply the measure of Earnings before interest, tax, depreciation and amortisation (EBITDA) to justify spending precious reserves on the balance sheet on expensive acquisitions that deliver top-line revenue while the amortisation of such costs is not counted in EBITDA.

THE DISCIPLINE OF EBIT

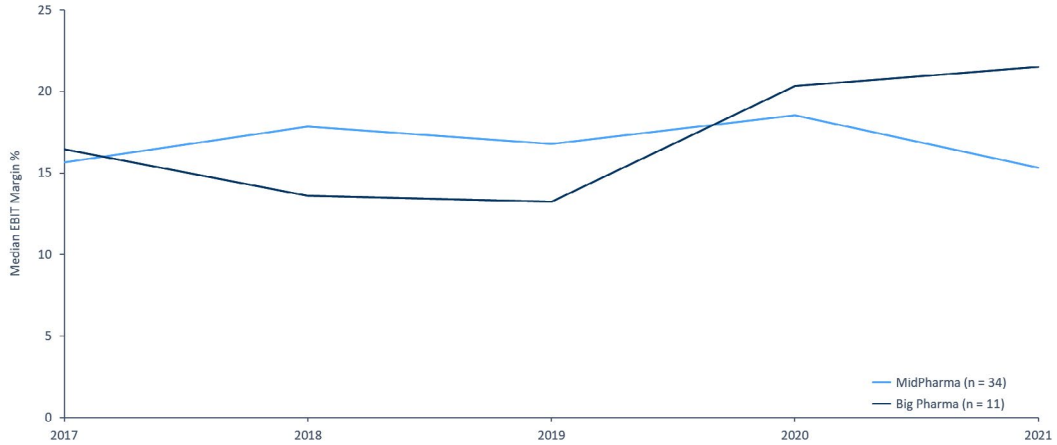
In our analysis of MidPharmas we focus on Earnings Before Interest and Tax (EBIT), or Operating Income, as a key metric of success. Unfortunately, many private MidPharmas do not disclose their EBIT. However, it is notable that disclosure signals strength and an openness to new sources of capital, as well as an internal discipline that profitability is important for the business. For those that do disclose EBIT, we suspect that either EBIT performance is not something to be proud of, or (for example in the case of Private Equity funded companies) that EBIT is none of the business of external stakeholders.

MIDPHARMAS HAVE SIGNIFICANTLY LOWER EBIT MARGINS THAN BIG PHARMA



The median MidPharma's EBIT margin of 14.3% is a full seven percentage points below the corresponding 21.5% for European-headquartered Big Pharmas. In some cases this reflects the reality that EBIT may not be as important to the shareholders as other matters such as scale and employment. Alternatively some may argue that there are scale economies in Big Pharma, but this does not explain the impressive EBIT margins of MidPharmas like Ipsen (35%), Recordati (31%), Indivior (27%), Sobi (24%), and Faes (24%). The discipline of having a full or part listing of the shareholdings in these five top performing MidPharmas on the measure of EBIT margin is no accident.

EBIT MARGINS FOR MIDPHARMAS HAVE RECENTLY DETERIORATED COMPARED TO BIG PHARMA



Over the past five years Big Pharmas have increased their EBIT margins and thereby diverged from MidPharmas that have remained relatively flat. Again this is a matter of concern for MidPharmas. EBITs in the region of 20% are feasible for both Big Pharma (median 21.5% EBIT) and MidPharmas (18 companies that disclose have EBIT margins above 20%). The MidPharmas that achieve lower EBIT margins are either suffering from intensive M&A or are comfortable with keeping lower margin business, for example contract sales arrangements to keep salesforce employment in countries with products that are no longer profitable. This is ultimately both a drag on profitability and a burden when trying to simplify and focus top management attention.

MidPharmas that prioritise EBIT rather than top-line growth find that great products can still generate revenue and margin after their patents have expired. Some companies that favour a less R&D intensive model based on incremental innovation and branded generics have achieved impressive EBIT margins (Dermapharm 32%, Hikma 23%, Krka 23%). Some of these companies own or acquire brands that require very little promotional spend, some find patient journey niches where reliable drug supply is limited, and others create new business models to drive margin growth. With Big Pharmas often wishing to divest established products to fund innovation or cut costs, there are opportunities for MidPharmas to buy assets and find more profitable paths for non-innovative medicines. This can include investing in lower risk R&D activities, including reformulating

and enhancing off-patent medicines, to expand and find underserved markets for established products. The market opportunity for older medicines with potential for margin improvement has not gone unnoticed by Private Equity funds that favour companies with strong EBIT performance and lean cost structures.

MidPharmas that continue to believe in innovative R&D as a source of value growth and long-term sustainability have also been amply rewarded in EBIT performance. Innovation focused MidPharmas with discovery and development capabilities that have achieved impressive EBIT margins include Orion (23%), UCB (22%), and Chiesi (18%). Others that have a more external innovation approach for early-stage assets have also out-performed, for example Ipsen (35%), Recordati (31%) and Sobi (24%).

The leading MidPharmas demonstrate that good EBIT margins are both possible and a sign of strength and resilience. They prioritise driving EBIT upwards more than the pursuit of top-line growth.

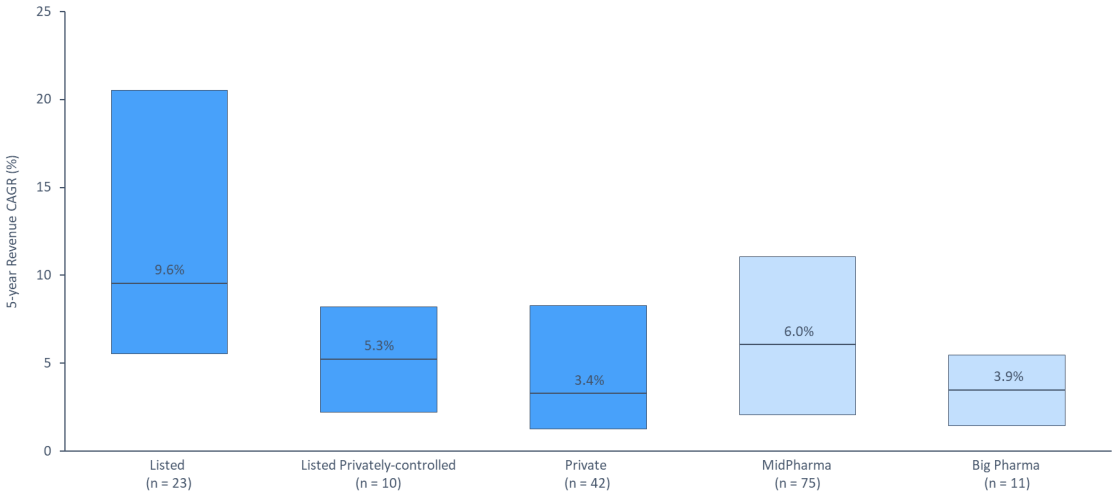
TOP-LINE GROWTH IS AN ENABLER FOR PROFITABILITY GROWTH

Long-term growth in a company's top-line (measured as **revenue** or **turnover**) is both evidence of entrepreneurial success and a requirement for long-term EBIT growth. So it is an important metric for MidPharmas to track, and aspire to achieve, albeit not without attention to the EBIT that is generated by it.

When measured as a Compound Annual Growth Rate (CAGR) over a five-year period, it is the relative newcomers to the MidPharma sector that have been performing the best. Formerly pre-revenue biotechs that have started to forward integrate and add commercial capabilities are being rewarded both by increasing royalty revenue streams from out-licensing fantastic assets and the top-line (and margin) benefits of own-commercialisation.

While accepting that high CAGRs are easier for companies starting from a small base, the performance of the new cohort of innovation-focused MidPharmas has been impressive, for example with five-year revenue CAGRs of 25%+ including Galapagos (31%), Genmab (29%) and Valneva (26%). We await the entry of other biotechs into the MidPharma sector that are building their own commercial capabilities such as Argenx and Idorsia. With a very different business model, a new cohort of commercially-focused MidPharmas have been able to grow revenue through acquisition, such as Swixx Biopharma (45%) and Cheplapharm (37%).

MIDPHARMAS CONTINUE TO GROW TOP-LINE AT A FASTER RATE THAN BIG PHARMA



As a cohort, the listed MidPharmas' impressive median five-year revenue CAGR of 9.6% contrasts with the 3.9% CAGR achieved by Big Pharma. While it's admittedly easier to post such growth rates when a company is smaller, the median CAGR of the entire MidPharma sector has also been 50% higher than Big Pharma (6.0% vs 3.9%).

This performance hasn't gone unnoticed by Private Equity funds seeking opportunities to invest capital for medium-term growth – as illustrated by controlling investments or acquisitions in multiple MidPharmas that are less R&D-intensive than the emerging biotechs, including companies such as Acino, Advanz, DOC Generici, Ethypharm, Galderma, Neuraxpharm, Nordic Pharma Group, Pharmanovia, Stallergenes Greer, Theramex, and Zentiva. While the revenue growth rates of these companies are typically not disclosed, history suggests that they will mostly be strong.

PAY ATTENTION TO EBIT GROWTH THROUGH FOCUS AND SIMPLICITY

MidPharmas that have scaled up top-line without evolving the operating model to suit new competitive realities have been struggling to sustain profitability and manage multiple complex business interests. M&A might offer a temporary respite and drive up EBITDA short term, but the EBIT issue often remains. While no company builds its future on cost cutting alone there is a reality of efficiency that often needs to be addressed. There are big gains to be had from considering the complete business operating model strategically. Is each piece of the business still required, and generating sustainable margin? Can others do the tasks we do more efficiently? Are we really focused on the things we are best at? The MidPharmas that have chosen to focus are the ones with the best EBIT performance, and scaling a focused business drives profitability growth much better than keeping and adding diverse business units.

THE IMPERATIVE TO PRIORITISE PROFITABILITY GROWTH

Too many MidPharmas have traditionally focused on driving top-line revenue growth at the expense of profitability. This is not sustainable, as EBIT is required to invest in future growth, particularly for privately-held companies that choose not to dilute their equity holdings or leverage the business through debt. Seeking EBIT growth is therefore a discipline that MidPharmas must apply to every part of their businesses.

Applying the proxy measure of profitability, EBITDA, is a good start, however the risk is that it encourages top line growth through acquisition of on market products that do not have underlying profitability potential or synergy with the existing business. With too many acquisitions, MidPharmas' balance sheets that have been carefully built through past profitability run dry, leaving companies vulnerable to market shocks. Companies therefore need to deeply **understand** which parts of their businesses are generating EBIT and which are not, then use the understanding to make difficult **decisions** to sell or partner the pieces that are better in others' hands.

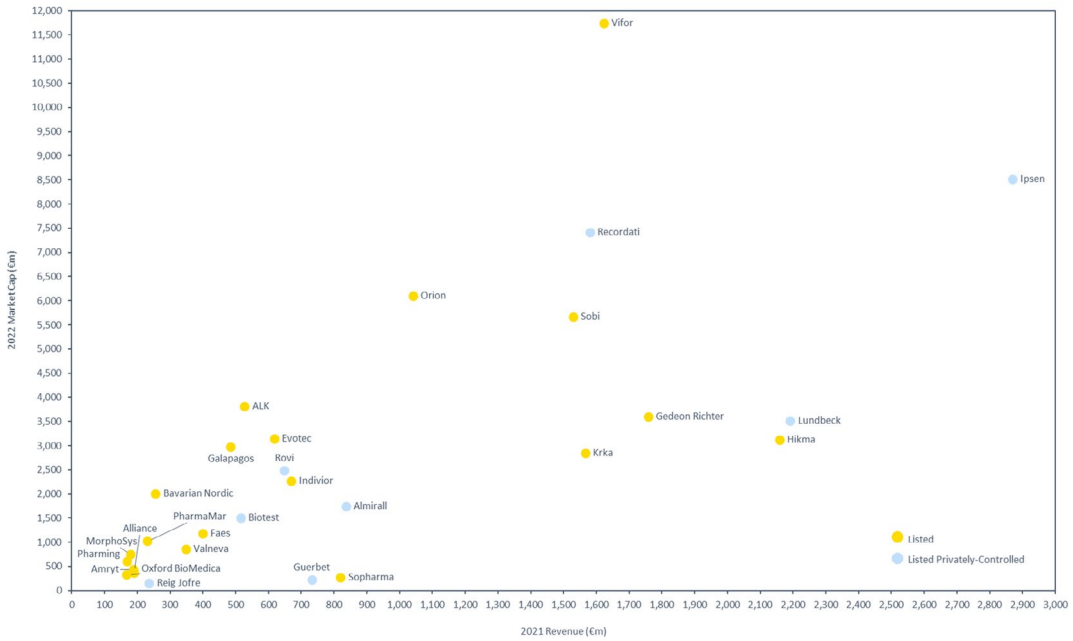
OUR MIDPHARMA PERFORMANCE RANKING

Novasecta

For listed companies, market capitalisation is a good but not perfect measure of a company's underlying strength and capability to generate future returns. For the 31 (out of 97) MidPharmas that have a public listing, market capitalisation broadly correlates with scale. Two-thirds of MidPharmas have market capitalisation between 2x and 8x revenue. The notable outlier is Genmab, with a €25bn market capitalisation, 22x sales in 2021, largely because it has created outstanding products from its antibody platform. The two largest-by-revenue MidPharmas have market capitalisations (UCB €14bn, 2.4x; Grifols €5bn, 1x) that show scale in itself is no guarantee of performance. The other 28 MidPharmas illustrated below further demonstrate the wide variation in performance and business models of the individual MidPharmas.

OUR MIDPHARMA PERFORMANCE RANKING

LISTED MIDPHARMAS HAVE HIGHLY VARIABLE MARKET CAPITALISATIONS



Since 67% of MidPharmas are not listed, we created a proxy ranking of performance to identify those that have been doing well, and those that are still on the journey. As with last year, we have ranked the MidPharmas in terms of both top-line and bottom-line using three metrics: five-year revenue CAGR, absolute revenue, and EBIT margin. These three allow a comprehensive view of growth, current size, and profitability. We have taken public domain data on each of these three attributes for the companies that disclose such data (51 out of 97) and have ranked the companies based on the combination of the three.

OUR MIDPHARMA PERFORMANCE RANKING

KEY

- Listed
- Listed Privately-Controlled
- Private

NOVASECTA'S EUROPEAN MIDPHARMA PERFORMANCE RANKING 2022

Rank	Company	Revenue CAGR	Absolute Revenue	EBIT margin
1	Ipsen	◕	●	●
2	Genmab	●	◕	●
3	Sobi	●	◕	◕
4	Dermapharm	●	◑	●
=5	Chiesi	◕	●	◕
=5	Octapharma	◕	●	◕
7	Rovi	●	◑	●
8	UCB	◑	●	◕
=9	Hikma	◑	●	◕
=9	Recordati	◔	◕	●
11	Vifor	◕	◕	◑
=12	Gedeon Richter	◔	●	◕
=12	Krka	◑	◕	◕
14	Alliance	◕	○	●
15	Grifols	◔	●	◑
15	Faes	◕	◔	◕
=17	Ferring	◔	●	◑
=17	Orifarm	◕	◕	○
=17	PharmaMar	◑	○	●
20	Evotec	●	◑	◔
21	Oxford BioMedica	●	○	◑
22	Clinigen	◕	◑	◔
23	Servier	◔	●	◔
24	Orion	○	◕	◕
25	Sopharma	◕	◑	◔
26	Bial	◑	◔	◑
=27	Abiogen	◔	○	●
=27	Lundbeck	○	●	◑
29	Grunenthal	◔	◕	◔
30	Indivior	○	◑	●
31	Galapagos	●	◔	○
32	Almirall	◔	◑	◑
33	Valneva	●	◔	○
34	Zentiva	◑	○	◕
=35	ALK	◑	◔	◔
=35	Amryt	●	○	○
=35	Pharming	◕	○	◔
38	Angelini	○	◕	○
39	Kedrion	◔	◑	◔
40	MorphoSys	●	○	○
41	Biotest	◑	◔	○
=42	Merz	○	◑	○
=42	Reig Jofre	◑	◔	○
44	Bavarian Nordic	◑	◔	○
=45	Elpen	○	○	●
=45	Genesis	◔	○	◑
47	Guerbet	○	◑	◔
=48	Fidia	○	◔	◑
=48	LEO	○	◕	○
50	Esteve	○	◔	◔
51	Olainfarm	○	○	◑

OUR MIDPHARMA PERFORMANCE RANKING

The top six in our ranking perfectly demonstrate the strength and diversity of the MidPharma space. Four of these have a controlling private shareholding, demonstrating that this is far from an obstacle to great performance.

The top company this year, listed and privately controlled Ipsen, has delivered impressive profitable growth from entering and succeeding in the US market with great clinical data for one of its long-established products. Private control (> 50% shareholding) with a stock market listing has served other companies well, such as other top ten companies Dermapharm (family), Rovi (family), and Recordati (Private Equity, previously family).

Fully family held Chiesi and Octapharma demonstrate that stable family ownership can deliver. But it is not necessary. For the two pure listed companies in our top six this year, both Genmab's antibody products and Sobi's profitable growth in rare diseases have served both companies and their investors well over the past five years.

CONCLUSION

MidPharmas are both a microcosm and exemplar of what it takes to be successful in the pharmaceutical industry – a sharp strategic focus, a fit-for-purpose operating model, and an appetite for external collaboration. Change is the norm, as without the scale of Big Pharmas which are able to absorb setbacks, MidPharmas must both consistently choose the right path for their companies and adjust rapidly to competitive and market developments. This keeps management on its toes.

MidPharmas are increasingly choosing between a business model based on innovative products from R&D, and one that is based on R&D to sustain and deliver commercial growth from more mature products. In most cases we see MidPharmas inexorably choosing one or the other, with important implications for the R&D budget and mindset. Some companies feel they can do both, keeping the commercial focus to drive EBITDA, while limiting new product R&D investment to a level where it is affordable, even if it doesn't deliver new products. With the right operating model this is feasible, but by no means easy. Boards and management teams can find it hard to invest in scientific risk if the dominant part of the business lies in commercial growth. Time will tell – either way management teams must ask themselves the question strategically.

Novasecta has supported many MidPharma leaders with empowering their functions and organisations to deliver improved performance through strategic and operational excellence. Our work with biotechs and Big Pharmas also draws on this experience of operating under constraints; after all, necessity is the mother of invention. Successful MidPharmas have demonstrated the value of creating and cascading an unambiguous strategic focus, while evolving to a fit-for-purpose operating model that is both internally and externally effective. We will continue to help them to both create and provide access to medicines for patients that need them.

PLEASE GET IN TOUCH TO FIND OUT MORE

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