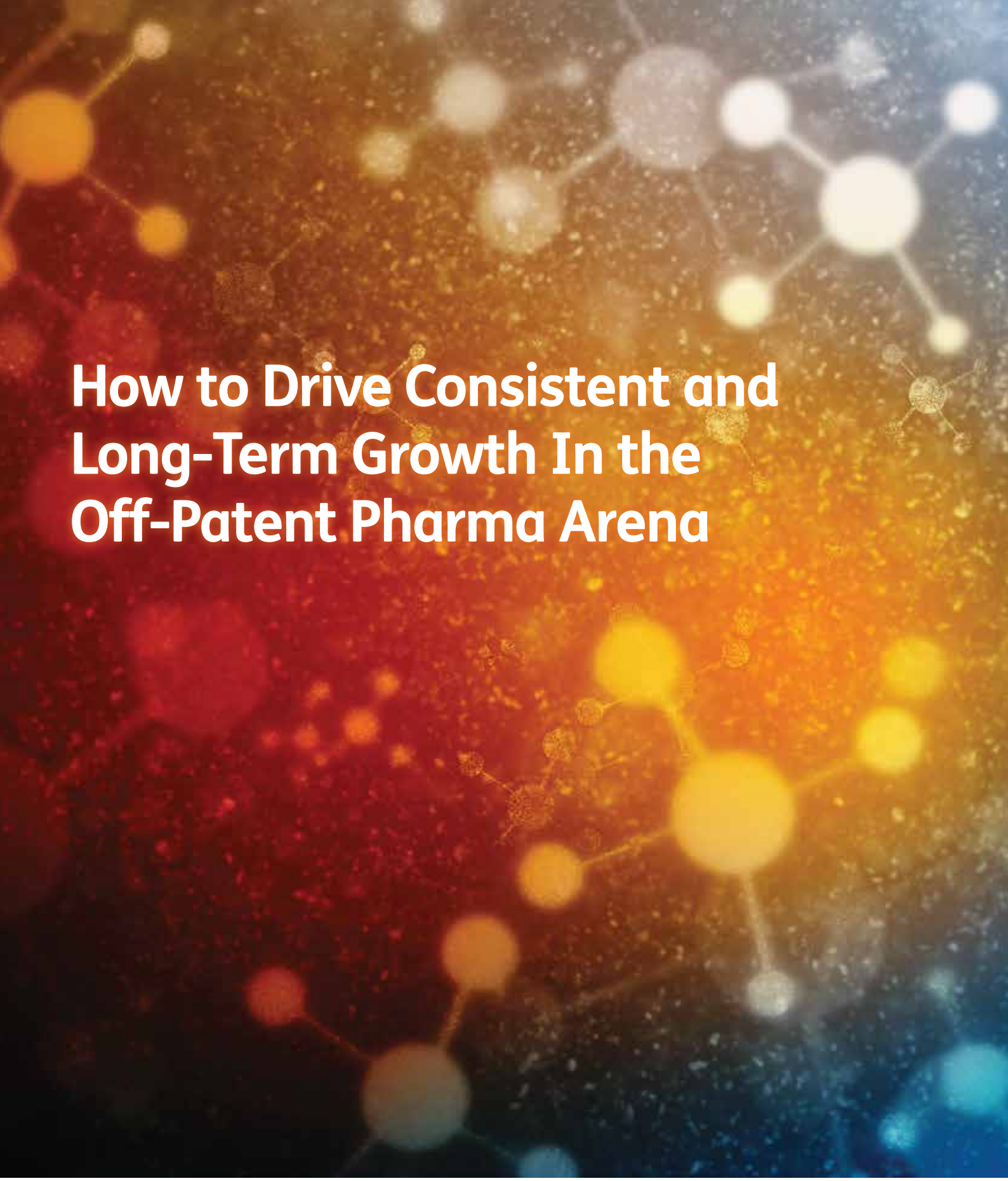

How to Drive Consistent and Long-Term Growth In the Off-Patent Pharma Arena

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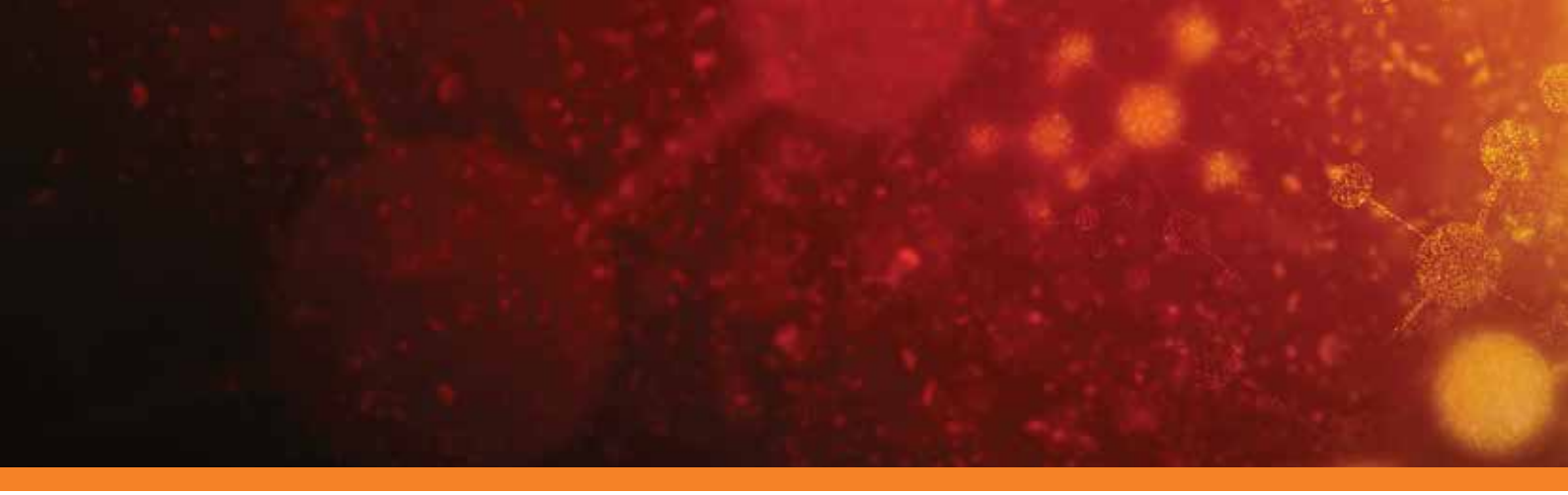

We knew that when we set-out with the Generics Bulletin to bring influential industry experts together to talk about how pharma companies should drive consistent and long-term growth that we were going to be in for a fascinating debate. This report provides highlights from some of the senior voices in the pharmaceutical and financial industry who participated in an intimate roundtable in November at the House of Lords.

For Accord, it provided a timely reflection on what is required to take the company forward and pivot towards more differentiated medicine. It is crucial, now more than ever, to add value both in thinking about the healthcare system and the patient. For me personally, this amplifies the strong belief that I know others share at Accord that we should never forget that patients should be at the centre of everything we do.

Generics are very important for making sure that healthcare is affordable, but medicine and science are developing rapidly, and we need to adapt to meet the growing needs of biologic medicines.

Biologics have provided incredible benefits for millions of patients but have caused a challenge for struggling healthcare budgets to afford them.

In the UK, the value of biosimilars is well-understood and prescribing is common, but this acceptance is not mirrored across Europe and the rest of the world. This is due to disparities in therapeutic interchangeability regulations, price and tendering negotiations, and the education of healthcare professionals.

Furthermore, manufacturers of biosimilars face an increasing challenge to differentiate products in the market place. Often faced with competing against a tried and trusted originator blockbuster, and the absence of typical generic price reductions of 50% to 70%, it is critical to offer a differentiated value proposition.

Whilst we all had very different experiences and perspectives that made for a lively debate, there were many important areas of consensus. It is clear that biosimilar manufacturers are navigating new and complex challenges, including changing value expectations, and this will require new approaches to strategic planning. To move forward, we will need to build upon the business models that have led to past success and evolve them to deliver differentiated value that will help us bring the medicines of tomorrow to the patients of today.

We invite you to be part of our discussion - through the insights that this report brings - and look forward to hearing your views.

Lord Jitesh Gadhia

ROUNDTABLE PARTICIPANTS

Hosted by:

Lord Jitesh Gadhia

Moderated by:

Aidan Fry
Executive Editor, Generics Bulletin

Panellists

James Burt
Executive Vice-President EMENA,
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Tim de Gavre
UK Country Head - Sandoz

Rupert Hill
Managing Director,
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Chris Watt
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DIFFERENTIATING TO MAKE A DIFFERENCE

As global competition and customer consolidation make margins in the commodity generics sector increasingly slim, moving towards a differentiated offering is vital for the industry's leading players. But delivering added value to patients and healthcare systems whilst securing a return on investment is challenging, participants at a recent high-level round table contended.

For James Burt, Accord Healthcare's head for the Europe, Middle East and North Africa (EMENA) region, the strategic imperative to develop and offer a portfolio of products with added-value features is clear. "Our five-year growth plan is very much around pivoting into differentiated products," he stated during a recent round table organised by Accord Healthcare and Generics Bulletin. "We are really trying to add value, both thinking about the healthcare system and the patient being at the centre of what we do" he explained.

Burt's colleague, Badri Wadawadigi – who oversees Accord's EMENA acquisitions and strategic growth initiatives – acknowledged that many other companies were seeking to diversify beyond "constantly declining generic price points" by identifying niches and products that had barriers to entry. "The challenge is to find a way to execute on opportunities that many other people are chasing," he outlined.

Citing an example of how his company had identified just such an opportunity to bring added value through innovation around known molecules, Federico Seghi Recli – chief executive officer of Italian family-owned producer Molteni Farmaceutici – explained how the firm was using patented technologies to deliver controlled substances in novel ways, such as offering the analgesic fentanyl as a nasal spray.

Other innovations such as a six-month buprenorphine implant that Molteni had recently licensed could, Seghi Recli argued, bring considerable benefits not only for patients, but also for health systems in moving away from daily dosing of the opioid-dependence treatment. The question for companies rooted in the traditional generics sector, he maintained, was whether they were prepared to invest in communicating such product benefits, not only through salesforces but also via pharmacoeconomic studies. Molteni's experience in convincing national systems and payers of the additional value of such innovations had generally been positive, he revealed.

Burt suggested that adding value to known molecules represented a spectrum that required tailored promotional approaches, rather than binary choices on whether to operate large salesforces. "It is also about segmentation, because markets are not homogenous," he insisted, contrasting the "effective monopsony" of the UK's National Health Service (NHS) with less monolithic health systems elsewhere in Europe.

Wadawadigi believed the key was not just finding the right innovation, but also convincing other stakeholders of the value of such innovation. "Maybe originators have been better at making that case and convincing the payers than generics companies have been," he conceded. "This is almost a new skill that the generics companies are learning," he said, noting that originators were practised in lifecycle management "as an instinctive defence mechanism".

Sandoz' UK country head Tim de Gavre agreed that generics companies needed to take an approach of differentiating effectively and how to convince clinicians and payers to favour one product over another, rather than relying on a substitution model.

Highlighting Sandoz' commitment to value-added medicines, de Gavre observed that the retail market was not always receptive to differentiation, such as when switching patients to an improved inhaler device required investment in training patients. "There are a series of questions around sustainability, value and what is best for the patient versus driving down cost," he summarised.

And for generics companies' management teams that were used to relatively rapid returns on investment, a mental switch would be required, de Gavre contended. "It is a very different business case that requires a clinical sell," he pointed out. "Because of the slower ramp up in the market, you may not get pay-back until year four or five, if at all."

Chris Watt, chief executive officer of UK-based compounding and homecare specialist Bath ASU/Qualasept Pharmaxo, stressed the central role that patient needs should play in any differentiation strategy. Given their proximity to the patient, he proposed that producers should consider compounders and homecare providers as "late-stage differentiation partners" for features such as extended shelf lives or exploring alternative delivery channels.

Particularly in the biologics arena, Watt argued, there were several opportunities to redevelop molecules to add value for patients, such as by minimising immunogenicity issues. As an example of how novel approaches to drug delivery could bring benefits, he cited work that was being conducted on formulating bevacizumab as eye drops rather than in an injectable format.

De Gavre cautioned that creating 'biobetters' by altering known biologic molecules presented many of the marketing challenges associated with small-molecule added-value medicines while also potentially requiring an expensive, full clinical program. "You are talking about a new drug with massive investment and high risk," he commented.

Burt felt that the level of training and patient interventions required made adding value in the mass-market and retail settings quite challenging, but saw opportunities to generate returns in the acute hospital sector, much as originators did through lifecycle-management and evergreening strategies. "We may need to move away from the dichotomy of a tender-driven race to the bottom on biosimilars on one hand, and salesforce detailing of novel biologics on the other," he suggested. "Industry tends to focus on the pure biosimilar play, but there may be another way of doing it."

INDUSTRY INVESTS IN MOVING UP CHAIN

Amid fierce competition and severe pricing pressure in the commodity generics arena, leading companies are increasingly looking to move up the value chain into value-added medicines and biosimilars. But that brings its own challenges, not least in having to invest large sums years ahead of any return, industry thought leaders outlined during a recent round table.

Industry leaders gathered at the UK's House of Lords for a high-level round table organised by Accord Healthcare and Generics Bulletin were united on issue at least – making an acceptable return in the commodity generics space is extremely difficult. With fierce competition and price erosion showing little signs of abating, the off-patent industry's leading players are all seeking refuge in differentiated products, such as value-added medicines and biosimilars (see opposite).

"If you are just a commodity generics player, you are going to struggle. You are going to need to find other areas," contended Tim de Gavre, country head for Sandoz in the UK. Much as many Indian suppliers had moved up the value chain from active pharmaceutical ingredients (APIs) into marketing their own finished dosage forms, he foresaw Chinese companies following a similar path in highly developed markets, potentially unleashing a further wave of competition in the commodity generics sector. "That could change the entire generics landscape," he predicted.

And while biosimilars and small-molecule value-added medicines both offered considerable potential, they did so in different ways, de Gavre believed. The biosimilars market was, he observed, evolving towards a tender-driven, substitution model similar to commodity generics in which originators may be unable or unwilling to compete. "If you get fast uptake through switching, you can get a strong return," he remarked, contrasting this with the clinical detailing and gradual market gains that characterised the value-added sector.

But just as the sustainability of the small-molecule generics sector was being threatened by payers focusing almost exclusively on price – pressure that was forcing players out of the market, concentrating supply and exacerbating shortages – 80%-plus discounts were also squeezing margins on biosimilars. "As competition builds on biosimilars, there is not necessarily going to be the sustainability that many companies have been hoping for," de Gavre forecasted. He questioned whether, at 80% discounts to the reference-biologic price, vital homecare services could be maintained.

Chief executive of homecare and compounding specialist Bath ASU/Qualasept Pharmaxo, Chris Watt, said there was "a growing recognition that some patients are better treated in their home than in a hospital", not least in terms of improved adherence and freeing up resources. "While there may always be patients that need a homecare provider to support them," he suggested, "many biologics could be dispensed from a retail pharmacy."

Sagar Patel, commercial head of Hikma's Injectables business in Europe, asserted that, in many European markets, "it is still about the lowest price", creating an environment in which the race to the bottom was resulting in supply disruptions and shortages. "As an industry, we need to educate payers, insurers and others that unsustainably low prices will invariably see fewer competitors and, ultimately, more shortages," he insisted. Patel appealed to payers to follow best practice in considering aspects such as label benefits such as stability as well as reliability of supply when awarding tenders and contracts. Working with payers to develop a sustainable biosimilars markets would be crucial, the round table participants felt, given that payers were driving uptake. "It is not the physicians making the decisions; it is the pharmacists," de Gavre observed.

Highlighting the major role played by regional bodies in many countries, James Burt – head of Accord Healthcare in the Europe, Middle East and North Africa (EMENA) region – noted that "prescribers in the UK are told what to prescribe". Whereas the UK once been at the vanguard of recognising value-added features through the Most Economically Advantageous Tender (MEAT) model, that had been eroded, in part through the pharma industry launching legal challenges over contracting decisions.

"As an industry, we should get behind the European MEAT Directive," Burt advised. He praised Scandinavian authorities for conducting tenders in which the various assessment criteria, such as packaging quality and duration of shelf life, were transparent. "We have to convince the buyers they are getting a better product and should not just focus on price," he recommended.

In the biosimilars sphere, Burt believed that capitalising on modern technologies to improve yields and minimise cost of goods would become increasingly important. Given the inherent complexity of biologic production and need to demonstrate efficacy through trials and detailed characterisation, controlling costs by switching raw-material source – as in the small-molecule generics world – was usually not a simple option. And on the regulatory front, real-world evidence would increasingly come to the fore.

Burt's Accord colleague Badri Wadawadigi, who oversees acquisitions and strategic growth initiatives in the EMENA region, agreed that changing manufacturing processes or sites for biosimilars in a bid to cut costs was challenging. "There is often a tension between rushing to be first to market and having the cost base to be last man standing after prices drop," he observed, pointing out that biosimilar programs typically required significant investment several years before the competitive landscape became clear. "It is much more difficult to adapt your cost base after launch in biosimilars compared to generics. This means that those who don't plan for competition while in their early development phase, will find themselves quickly competed out of the market after product launch".

Comparing biosimilars to the Klondike gold rush, Burt forecasted that some players would drop out as the commercial realties hit home. Particularly for originators, he felt, it would be difficult to square having a broad biosimilars portfolio with targeting operating margins of 40% to 50%.

BREXIT MAY BRING WOE OR BENEFITS

Even with a proposed deal on the UK's 'Brexit' withdrawal from the European Union (EU) on the table, the implications for the pharma industry and supply chain remain uncertain. But participants in a high-level round table held at the UK's House of Lords were clear on one issue – companies need to be preparing for Brexit now.

Gathered within the hallowed halls of the UK's Houses of Parliament, participants in an inaugural round table on growth prospects for the pharma and off-patent medicines industries organised by Accord Healthcare and Generics Bulletin shared many of the concerns and questions of the general public in the UK and continental Europe. Meeting as UK Prime Minister Theresa May presented a proposed Brexit deal to her cabinet, the round table contributors saw both potential upsides and downsides for industry from whatever deal, if any, emerged from the UK's exit negotiations with the EU.

Sagar Patel – who recently joined London-listed Hikma Pharmaceuticals as commercial head of the group's Injectables business in Europe – described the UK as "an important market for us" as the company looked to expand both its pipeline and its geographic presence, including through licensing and partnerships. "At the moment, it is difficult to speculate on the future of the UK with Brexit looming large," he conceded. "We, like every business, are looking for greater certainty about what the Brexit deal will mean."

For Rupert Hill, managing director and head of global pharmaceuticals and European healthcare at investment bank Greenhill, long-term potential benefits of being an independent economic actor were difficult to compare with more easily quantifiable short-term costs and financial impacts of Brexit.

The ability to strike free trade agreements with trading blocs around the world was a potential longer-term upside for the UK, provided it was not fettered by membership of the EU customs union, highlighted Chris Watt, chief executive officer of UK-based compounding and homecare specialist Bath ASU/Qualasept Pharmaxo. Of more immediate concern, he warned, was a potential shortage in the UK of healthcare consumables such as intravenous tubing sets that were typically imported from overseas but were essential to the UK's healthcare system continuing to function effectively.

Sandoz' UK country head Tim de Gavre warned, however, that free trade agreements might have adverse impacts for the off-patent industry in both the UK and Europe. De Gavre – who became chair of the British Generic Manufacturers Association (BGMA) in May 2018 – suggested that a trade deal with the US could see the UK implement the US' 'Orange Book' patent-linkage model that could delay generic and biosimilar launches pending resolution of intellectual-property disputes. Any future deals needed to ensure the right incentives for competition, he insisted.

"If the UK does not maintain regulatory alignment with Europe, I see that as a risk for patients," de Gavre stated, pointing out that the UK was typically one of the lead markets for biosimilar launches in Europe. Regulatory divergence would, he believed, delay UK biosimilar launches by years, depriving the National Health Service (NHS) of savings and patients of improved access to cutting-edge treatments. Greater UK regulatory convergence with the US would, he noted, align the UK with a country in which biosimilars were struggling to get a foothold.

"The power of being part of the EU and the European Medicines Agency (EMA) is that it is all aligned, and everything is done with one approach," de Gavre maintained. Recognising the key role that the UK's Medicines and Healthcare products Regulatory Agency (MHRA) had played as a rapporteur within the EU medicines regulatory system, he feared that a national licensing procedure in the UK could prove less efficient and transparent for companies. And while the MHRA had adopted a pragmatic approach to batch testing and release, de Gavre said EU member states were having to prepare 0066 or a 'no deal' Brexit scenario in which the UK was considered a third country for medicine supplies.

Accord Healthcare's head for the Europe, Middle East and North Africa (EMENA) region, James Burt, revealed that his company had already been preparing for having to perform batch release and quality control within the remaining EU member states. Suggesting that MHRA assessors who had previously worked as rapporteurs for decentralised and mutual-recognition applications might post Brexit be able to accelerate national reviews in the UK, he observed that there was an "increasing degree of convergence at supranational level" between regulatory agencies. For example, the US Food and Drug Administration (FDA) was increasingly recognising facility inspections conducted by EU agencies, while Australia's Therapeutic Goods Administration (TGA) customarily referenced EMA biosimilars guidelines. The recognition between Switzerland's Swissmedic agency and the FDA was also a potential model for the MHRA, he proposed.

While the 'no deal' Brexit outcome of reverting to World Trade Organization (WTO) rules would not bring tariffs on pharmaceuticals, Burt acknowledged that much of the regulatory work caused by Brexit, such as carving out national authorisations from centralised and decentralised dossiers, was a bureaucratic headache that was not adding any value.

"But when I look at Brexit, I do not see massive upside or downside risk for pharmaceuticals" he concluded. "despite the current hyperbole its worth remembering over the past thousand years, from the Norman Conquest to separating from the Church of Rome, the UK has joined and separated from Europe many times."

MARKETS RATHER THAN MULTIPLES SHIFT

Recent mergers and acquisitions activity in the off-patent pharmaceuticals arena has led to a series of write-downs and impairment charges. But the problem may not be the cost of those deals so much as how the market has since shifted, a high-level round table panel has suggested.

In operating in the healthcare space for around 20 years, Rupert Hill – managing director and head of global pharmaceuticals and European healthcare at investment bank Greenhill – has seen several waves of generics mergers and acquisitions activity, often reflecting whether the 'big pharma' multinationals saw their strategic priorities at the time as building a broad medicines portfolio or as narrowing their focus onto innovation.

"I have seen various cycles of major pharma divesting generics because they did not think they could run generics businesses as they had a completely different mentality," Hill commented during a round table on growth prospects in the off-patent pharma arena hosted by Accord Healthcare and Generics Bulletin and held in the UK's House of Lords. At other times, major pharma players had looked to the off-patent sector as a means to broaden their offering and find a way into new territories, especially in emerging markets.

One of the key changes over those 20 years, Hill observed, had been that generics were no longer being vilified as cheap copies. "Health systems are now recognising that generics are part of the solution," he said, adding that as biosimilars and hybrid value-added medicines took hold, it would become more appropriate to look at a broader class of low-cost, affordable medicines.

Looking at current trends in off-patent mergers and acquisitions activity, Hill pointed out that the multiples and valuations paid in recent transactions – even if they were not reflected in the purchasers' current market capitalisations – were not generally out of line with the historical trends. "Our charts showing deal multiples and trading models going back about 20 years demonstrate there is no real anomaly now compared to where they have been over time," he remarked.

But while multiples of 15 to 20-times earnings before interest, tax, depreciation and amortisation (EBITDA) for attractive assets had been commonplace throughout this period, what had changed in recent times had been a sharp downturn in the US generics market. "There has been a pricing collapse and it has been almost a perfect storm for a lot of US companies," Hill observed. Several major players that were significantly exposed to the US market had been highly active in mergers and acquisitions, and were consequently highly levered with debt, he noted. These difficulties had been exacerbated by continuing buyer consolidation and the US Food and Drug Administration (FDA) stepping up its pace of generic approvals, thereby intensifying competition.

By contrast, Hill pointed out, Europe had largely been spared similar pressures, with any market changes over the past five years having been relatively minor in nature. "That is part of the answer as to why the European companies' transaction multiples are still relatively high."

James Burt, who heads Accord's operations in the Europe, Middle East and North Africa (EMENA) region, suggested that "multiples in generic pharma, particularly in Europe" were rising to levels that made realising a return on investment increasingly difficult. A driving force for such high valuations, he believed, was the unprecedented level of cash that private-equity investors were looking to pour into a healthcare arena that offered favourable demographic trends.

Burt's Accord colleague Badri Wadawadigi, felt that private-equity investors often tabled relatively attractive offers for off-patent companies as a means to enter the space. "Private equity is paying a premium for access to a platform to go and do more deals," he asserted.

Hill agreed that private-equity funds were "paying to play" in pharmaceuticals, having experienced mixed fortunes in other healthcare fields such as medical devices, nursing homes and homecare services. In some cases, he said, investors had identified opportunities to generate value through greater operating efficiencies, while in others they were likely to seek synergies between a series of acquired assets. Due to these considerations, private investors were sometimes prepared to pay when industry buyers chose to walk away from deals.

And at the same time, several large generics players were pruning portfolios, closing plants and divesting parts of their businesses. Hill maintained that there was merit in streamlining operations, such as by exiting commodity generics in favour of specialty drugs and biosimilars, especially where a generics division might be divested or spun out via an initial public offering (IPO). "It is not a perfect science, you need to generate excitement through an attractive story," he argued.

Hill's call for a clear narrative appealed to Burt. "As you get to scale, there is a danger that you end up doing everything badly, rather than focusing on a few things very well," he cautioned. He compared the difficulties of remaining nimble while achieving critical mass to the challenges of right-sizing manufacturing plants. "You get economies of scale, but then you get diseconomies of complexity," he pointed out. And with any merger or large transaction, he insisted, considering potential clashes of corporate and regional cultures was crucial.

Sandoz' UK country head, Tim de Gavre, observed that generics price erosion was a major challenge. "Even if you can grow volumes, you are trying to fill a leaky bucket," he said.

Federico Seghi Recli, chief executive officer of family-owned Italian controlled substances specialist Molteni Farmaceutici, highlighted the benefits of independence in being able to act quickly and flexibly. For Molteni, he added, partnerships would be key to expanding the firm's geographic reach.

Chris Watt, chief executive officer of UK-based compounding and homecare specialist Bath ASU/Qualasept Pharmaxo, observed that "the bigger you get, the further the decision-making gets from the patient or the clinician that is making decisions about which products to use."

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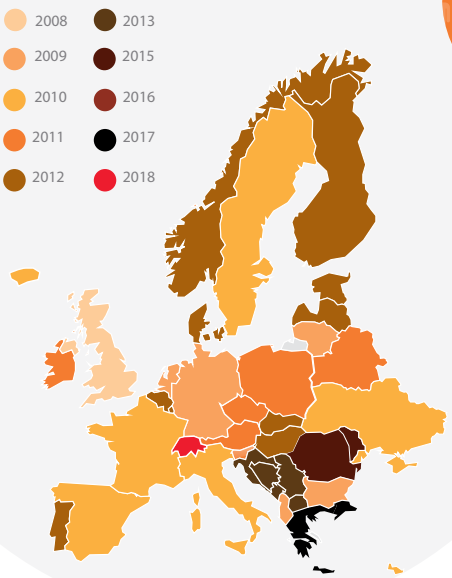
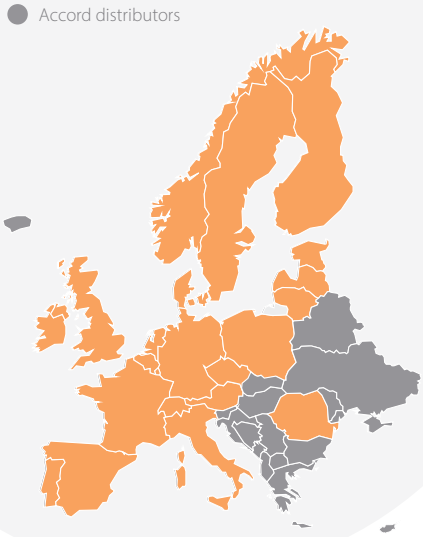


Business Model



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