

Longer Term Investments

Generics

CIO WM Research | 5 July 2017

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- Generic drugs are a vital pillar of affordable healthcare. Saving money on older, off-patent medicines frees up resources to pay for new treatments. Generics both save costs and broaden access.
- Demand is supported by the intersection of demographic trends and healthcare budget constraints. Aging and population growth drive greater healthcare utilization. Meanwhile, healthcare spending as a share of GDP is rising consistently in both developed and developing economies. Healthcare systems are focusing more on value for money, supporting generic drug demand.
- The flip-side is a challenging pricing environment in many markets, but we expect consolidation to reduce the pressure of oversupply in the medium term. Ultimately industry growth should stabilize in the low to mid-single digits range.
- The generics industry is truly global, with significant clusters of companies outside the usual US and European pharma hubs. We recommend investing in a diversified portfolio of companies to minimize company-specific risks.



Source: iStock

Jerome Brimeyer, Healthcare Equity Sector Strategist Americas, assisted in the analysis of the generics market.

Generic drugs are low-priced copies of off-patent medicines. They serve a critical purpose in healthcare provision: allowing cheap competition to older medicines frees up resources to pay for newer, innovative treatments. Generics both reduce the total cost of care, and broaden access to care.

Aging and population growth drive greater healthcare utilization, as the elderly population rises around the world. This has put both government and private health systems under enormous pressure. For example, the US spends over USD 3 trillion, or over 17% of GDP on healthcare, but similar trends are visible in all countries. Around the world, healthcare providers are under pressure to deliver more, for less cost, as payers and patients become more price sensitive. This focus on value will support generics demand.

Generic penetration now stands at nearly 90% of total prescriptions in the US, an enormous success story for the industry. But cut-throat price competition is being exacerbated by oversupply and other short-term factors. We expect consolidation of the generic drug industry to eventually return the industry to stability, although the timing is

unclear. The emerging biosimilar market could offer some relief from the negative pricing cycle.

We estimate the global generic drug market is currently worth around USD 185 billion. Growth is slowing, but we think a low to mid-single-digit rate globally is sustainable well into the next decade. The opportunity is best captured by investing in a geographically diversified portfolio of exposed companies.

The need for generic drugs – saving costs and broadening access

Generic drugs are low-priced copies of off-patent medicines. They serve a critical purpose in healthcare provision: allowing cheap competition to older, off-patent medicines frees up resources to pay for newer, innovative treatments. The benefit of generics is therefore twofold:

- **Reduce total cost of care.** Generics can be 90% or more cheaper than their branded counterparts.
- **Broaden access to care.** There is evidence that generics improve health outcomes at a population level by facilitating better access to drugs.

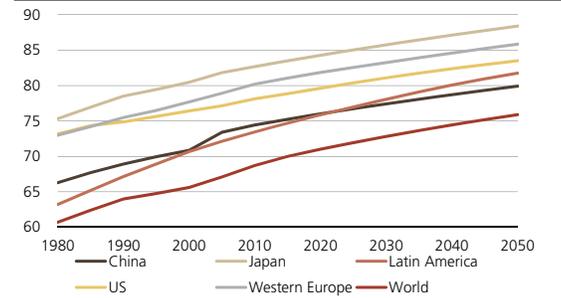
We see generic drugs as part of the provision of "affordable healthcare," contributing to the sustainability of healthcare provision. They contribute to significant savings for patients and healthcare systems and, according to a study*, generate a positive impact on population-based healthcare outcomes by increasing drug utilization. While recent trends in the market have proved a challenge for generics manufacturers, we believe the long-term drivers of the industry are supportive.

Long-term drivers of the generics market

Demand for generic drugs is supported by the intersection of demographic trends and healthcare system budget constraints:

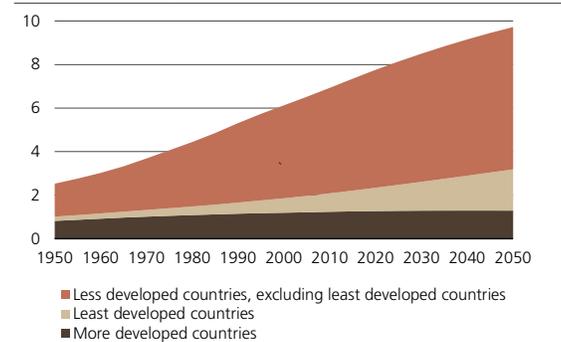
- **Supportive demographics:** aging and population growth drive greater healthcare utilization as the elderly population rises around the world (Fig. 1 & 2). The elderly often have chronic diseases, needing multiple drugs, so volumes can rise faster than population growth. This also puts greater pressure on costs.
- **Healthcare budgets under pressure:** healthcare costs have risen consistently as a share of GDP in all developed countries and are expected to keep rising (Fig. 3). In the US, healthcare expenditure rose to nearly USD 3 trillion in 2015 and is forecast to reach 20% of GDP by 2025 (source: CMS), but developed and developing countries alike are experiencing above-inflation rises in healthcare costs. As expenditure in developing countries catches up with the developed world, a greater share of these expenses is being borne by governments, further pressuring budgets. While a number of factors drive rising healthcare costs,

Fig. 1: Life expectancy rising globally
Life expectancy at birth, years



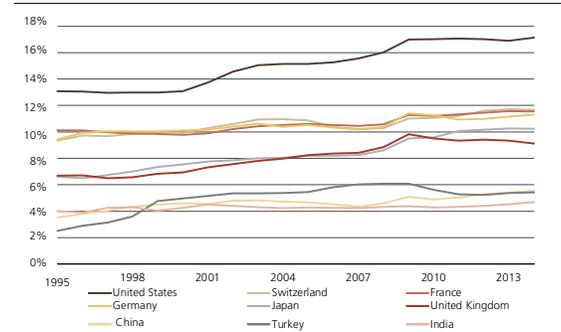
Source: UBS, UN. As of July 2015

Fig. 2: The world population is growing
Number of people, billions



Source: UBS, United Nations Population Division. As of July 2015

Fig. 3: Healthcare expenditure rising globally
Healthcare spend as a % of GDP



Source: UBS, World Bank. As of June 2017

*Source: Albrecht *et al*, "Value of Generic Medicines", 2015, published by the European Generic Medicines Association

and drugs account for only 10–15% of healthcare spending in most countries, pressure on healthcare budgets is unlikely to ease. The increasing focus on value in healthcare provision, and greater price sensitivity from patients, are both supportive of generics demand.

Significant savings for healthcare systems

In the US, generic drugs cost 75–90% less than their branded equivalents and now account for nearly 90% of prescriptions dispensed. The Association for Accessible Medicines (AAM) estimates that the use of generics saved the US healthcare system USD 253 billion in 2016, and cumulative savings of USD 1.67 trillion over the last decade. Substantial savings are not limited to the US: Medicines for Europe estimates the European healthcare system saved EUR 100bn in 2014 by using generics.

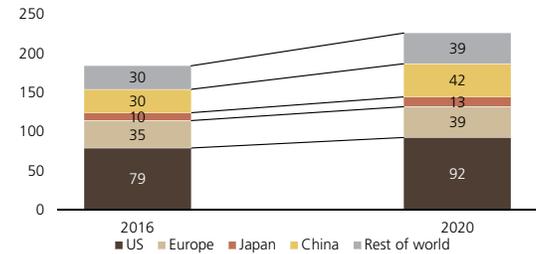
A global market worth nearly USD 200 billion

We estimate the global generics market at USD 185 billion, or 17% of the value of the global pharmaceuticals market (Fig. 4). The primary driver of volume growth over the past three decades has been rising generic penetration in developed markets, helped by a wave of patent expiries on mega-blockbuster primary care drugs in the US over the 2007–12 period. Generic penetration in the US is now 89% of prescriptions, while in Europe it averages 55% (Fig 5). Along with higher penetration, the US sees more aggressive generic pricing.

In emerging markets, the distinction between "brand" and "generic" drugs is less clear-cut, with many off-patent drugs available as "branded generics." While a counter-intuitive concept, consumers are often willing to pay a premium for drugs from brands they trust if quality is a concern. Most countries pursue policies aimed at increasing generic penetration, with key aims being to increase the quality and availability of generics. Unbranded, or commodity, generics have been outgrowing branded generics in most markets, notably China. Over time, we expect many developing markets to evolve in the direction of the Western commodity generics market (Fig. 6). While likely positive for industry volumes, this tends to have a negative pricing impact.

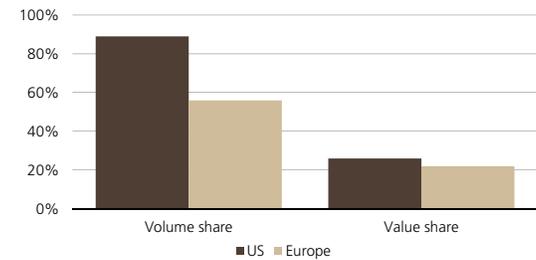
The biggest short-term question for the industry is the outlook for pricing in the US, which represents about 40% of the global generics market. Currently, US generic drugs are seeing significant price deflation: industry data suggest average like-for-like price declines of around 8% for the 12 months to end of 1Q17 for generics prescriptions. With FDA working down its approval backlog and increasingly sophisticated competition from Indian companies, we expect current levels of pricing pressure to persist in the US generics market for the remainder of this year and most of 2018. In the medium term, however, we expect the industry to enter another round of consolidation, which should reduce pressure on prices. Historically the industry has been able to manage with mid-single-digit price deflation in the US. The emerging biosimilar market, and opportunities in complex generics, could offer some relief from the negative pricing cycle.

Fig 4: Generics are a USD 185bn global market
Generic market size, USD billion, 2016 and 2020



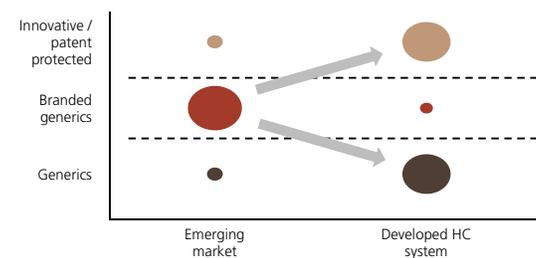
Source: UBS estimates. As of June 2017

Fig. 5: US discounts are higher than in Europe
US and European generics market share by volume and value, 2015



Source: AAM, Medicines for Europe, UBS. As of June 2017

Fig. 6: Markets to converge to Western model over time
Potential evolution of market structure



Source: Deutsche Bank

In the following pages we discuss key trends in the industry, with a focus on US pricing, and provide an overview of key generics markets globally. A more thorough technical and historical background on the industry can be found in the Appendix.

Current trends in the generics market

US pricing in a historical context

Deflationary pricing in the US generics industry is nothing new. Historically, prices for substitutable generics have fallen by low to mid-single-digits most years, and 73% of generic drugs in the US saw price declines over the decade to 2015, according to the AARP. But since 2016, a number of trends have coincided to create a "perfect storm" of challenges for the industry. Supply shortages have eased, and the FDA is working down its large backlog of applications, increasing supply just as the industry's customers have consolidated to increase their buying power. New volume opportunities are limited by already high penetration rates. To cap it all, the industry is under intense media and political scrutiny after a number of high-profile "price gouging" scandals in the last two years. As a result, like-for-like prices were declining around 8% on an annual basis at the end of 1Q17, according to industry data.

The US generics market saw an unusual period of rising average prices in 2013–15. But even during this time, most drugs actually continued to fall in price; the number of drugs seeing large price increases, while still relatively small, was larger than usual (Fig. 7). One driver of this was supply shortages, because greater FDA scrutiny of manufacturing, particularly outside the US, forced some products or companies off the market temporarily. These supply shortages have since begun to ease. Moreover, the FDA is reducing its backlog of pending generic drug approval applications, leading to increased competition in many products.

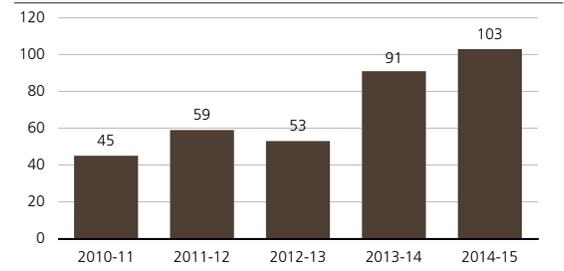
Supply does not look likely to tighten in the near-term

Supply is likely to rise over the next two years. Over the last decade, Indian companies have raised their volume share of the US market to around 30%. But their share of recently-approved generics is even higher at around 35% (Fig. 8), and they also hold a similar proportion of the current FDA backlog. Some of these companies were forced to withdraw products from the market in 2014–15, contributing to product shortages, due to manufacturing plants failing FDA quality inspections. However, since 2016 the rate of compliance failures in India has leveled off, and Chinese facilities are seeing closer regulatory scrutiny (Fig. 9). These companies supply less volume into the US market.

At the same time, FDA is making an effort to work down its approval backlog. As filings became more complex and new manufacturers entered the market, a large backlog of pending applications built up. Spurred on by new legislation and funding introduced in 2013, FDA is now trying to clear this backlog. The ANDA backlog has decreased from a peak of over 3,500 pending applications in 2014, but still

Fig. 7: Rising "average" prices driven by small number of extraordinary price rises

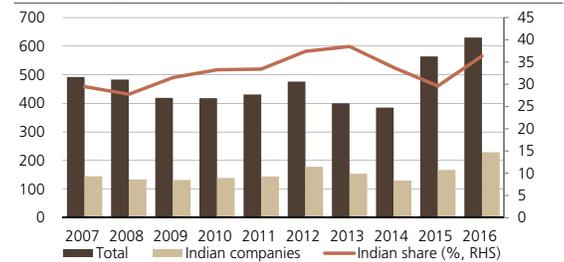
Number of drugs under Medicare Part D with price increases of 100% or more, 2010-15



Source: GAO analysis of Medicare Part D data. As of August 2016.

Fig. 8: Indian manufacturers' share of US generic approvals recovered in 2016

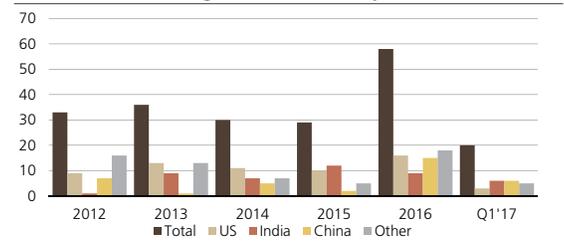
ANDA's approved (number and percent)



Source: FDA, UBS. As of June 2017. Note: ANDA = Abbreviated New Drug Application

Fig. 9: FDA enforcement actions rising

Number of warning letters issued by FDA



Source: FDA, UBS. As of June 2017

exceeded 3,000 applications at the end of March 2017, including filings returned to the industry for further work. Approval rates increased in 2015 and 2016, and are annualizing at nearly 700 so far in 2017 (Fig. 10). Separately, the new FDA commissioner, Scott Gottlieb, has signaled a desire to streamline generic drug approvals to promote competition. Much of the backlog consists of additional competitors to existing generic drugs, rather than first generic approvals. This suggests a higher rate of approvals will continue pressuring prices.

Distributor consolidation shifts power to drug buyers

The US drug wholesale and pharmacy industries are highly consolidated. Thanks to both consolidation and the formation of buying groups among wholesalers, retail pharmacies and pharmacy benefits managers (PBMs), three groups now account for more than 80% of generics purchasing (Fig 11). These groups are able to secure significant volume discounts in exchange for access to formularies. While we do not expect this trend to reverse, we think the major impact has occurred, since there is little room for further consolidation in the distribution chain.

High penetration means fewer new volume opportunities

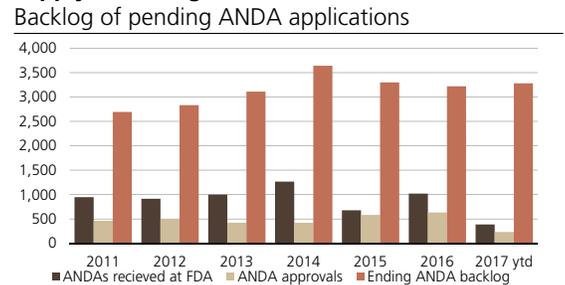
Rising generic penetration rates have been a steady driver of market growth since the 1980s. For example, in the US, generics now account for 89% of prescriptions, or 3.9 billion prescriptions annually, according to the AAM. Prior to the creation of the modern generics industry, with the passage of the Hatch-Waxman act in 1984, generics represented 12% of US prescriptions. Penetration in Europe is lower, around 55% on average in 2014 according to Medicines for Europe, although rates vary by country (Fig. 12).

In the US, most primary care therapies are now dominated by generics, with penetration rates in the 90%-plus range (Fig 13). For example, the typical first-line treatment for Type 2 diabetes (T2DM) is metformin, a drug initially developed in the 1950s and available in a variety of generic formulations. As patients' disease progresses (T2DM worsens over time, even with treatment), newer drugs are added. Similarly, for many patients, high cholesterol can be adequately controlled with generic statins, allowing insurance companies to hold back treatment with high-cost, newer medicines such as PCSK-9 inhibitors for more severe patients. While newer drugs may offer slightly better efficacy in hard-to-treat cases, a generic version of an older drug is often perfectly adequate to treat the majority of patients.

Fewer new generic opportunities; biosimilar market emerging

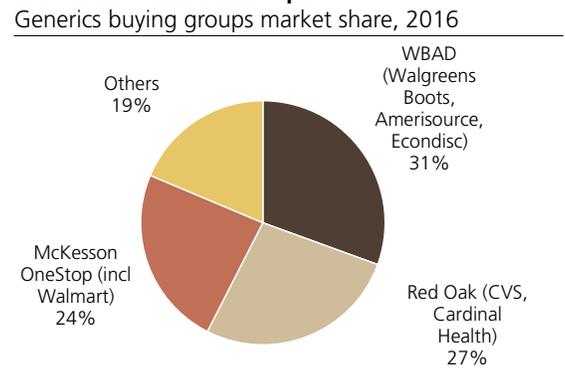
The period from 2007–12 saw large volume gains for generics as many of the primary care blockbusters launched in the late 1990s lost patent protection. We expect a smaller set of opportunities in traditional commodity generics over the next five years (Fig. 14): we estimate USD 90 billion of non-biologic drugs will face first-time generic competition in the US during the 2016–20 period; this compares to over USD 100bn between 2011–15. On the positive side, a growing share of the new volume opportunities are so-called "complex generics" that may have less competitive intensity, with

Fig. 10: FDA clearing its backlog but plenty of supply overhang remains



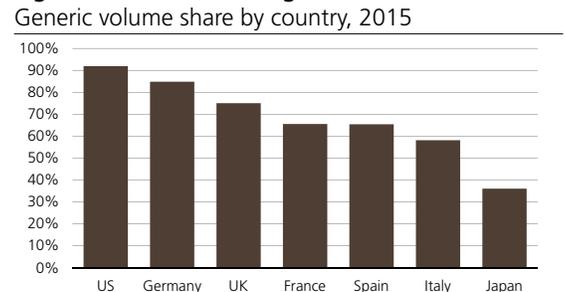
Source: FDA data, BAML. As of June 2017. Note: data for calendar years (FDA's fiscal year ends in September); 2017 year-to-April

Fig. 11: Buying groups have led to highly consolidated customer landscape



Source: UBS estimates, company data. Note: Econdisc/Express Scripts included in WBAD share following co-operation announced in May 2017

Fig. 12: Generic use is highest in the US



Source: MHLW, Citi Research, UBS. As of December 2016.

more pricing power for companies able to develop and manufacture them.

A significant unanswered question is how large a market will emerge for "biosimilars," or generic versions of biologic drugs (derived from living cells). Biologics now represent 25% of the global drug market, and are beginning to see significant patent expiries. Unlike traditional chemical drugs, it is not possible to create directly substitutable copies of biologics (see Appendix). The main impact of this distinction will be that biosimilars are sold at a less substantial discount relative to their brand equivalents than traditional generics. So far, the European biosimilar market is the most advanced. We estimate the global biosimilar market could reach USD 15bn by 2020, with the potential to be significantly larger over time. However, there is substantial uncertainty around this point estimate due to outstanding questions over price, launch timing and other legal uncertainties. For comparison, Sandoz estimates the global biosimilars market is currently worth around USD 2bn.

Industry response – consolidation and evolving business models

In our view, the generic industry is likely to react to the current challenging landscape in two ways. First, we expect companies to move "up the value chain" to more complex generics. In fact, this is already visible even among the Indian manufacturers who traditionally competed as low-cost manufacturers. Second, we expect to see more consolidation, consistent with historical patterns in the industry.

As a commodity industry, generics manufacturers gain most from scale in manufacturing. However, additional benefits come from stronger negotiating position with customers (who themselves have consolidated, see above), and a better ability to manage increasingly complex regulatory and compliance procedures.

Earnings growth outlook

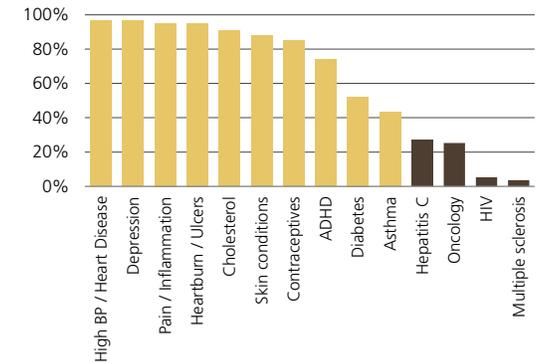
We estimate that historically, global generics volumes have grown in the low double digits, with value growth in the mid to high single-digit range due to generally deflationary average pricing in several markets. We expect growth to slow over the 2016–2020 period, to around 5% in US dollar terms. Our outlook assumes continued pricing pressure in the US market for another 12–18 months, offset by new opportunities in complex generics and biosimilars. Our forecast is consistent with recent estimates for the total pharma market over the same period (4–6%).

Link to Sustainable Investing

To identify whether a Longer Term Investment (LTI) theme qualifies as a Sustainable Investment (SI) theme, we follow a two-step process. The first works top-down. LTIs are assessed according to whether they match one or more of the sustainability topics within the environmental, social or governance categories (Fig. 17). In general, these

Fig. 13: Primary care treatment now dominated by generics in US

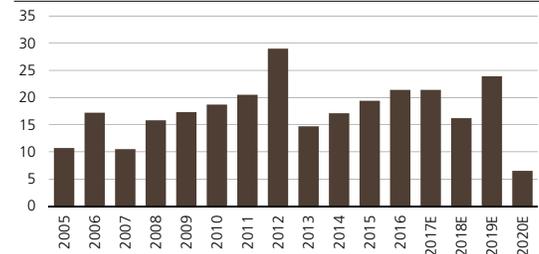
US generic fill rates by disease area, % of prescriptions



Source: Express Scripts Drug Trend Report data, UBS analysis. As of February 2017. Note: yellow-colored categories are predominantly or initially treated by primary care physicians

Fig. 14: Fewer new generic opportunities expected in next five years

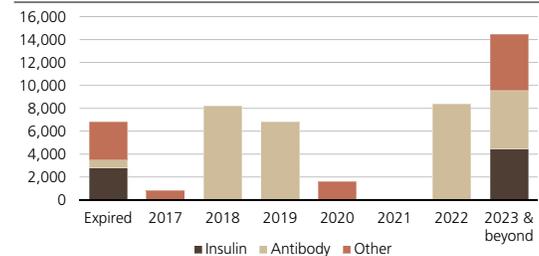
Value of branded drugs at risk of first generic competition in US, USD bn, 2005-20E



Source: UBS estimates. As of February 2017

Fig. 15: US biologic sales of at least USD 47 billion lose patent protection by 2030

Current US sales of selected major US biologics, by year of key patent expiry (USDm)



Source: Company data, UBS estimates. Note: drugs with known biosimilars in development. As of June 2017

themes must contribute to environmental sustainability (e.g. a low-carbon economy), resource-efficiency (e.g. energy, water), sustainable society (e.g. health, education, poverty reduction, equality and social inclusion, etc.) or sustainable corporate governance. The second, bottom-up step, consists in considering a thematically aligned representative universe of companies. A large majority of included companies (80% or more) must align with one or more of the ESG categories. For each individual company, a minimum business involvement threshold is applied, e.g. 25% of revenues must be derived from the thematic activity under consideration.

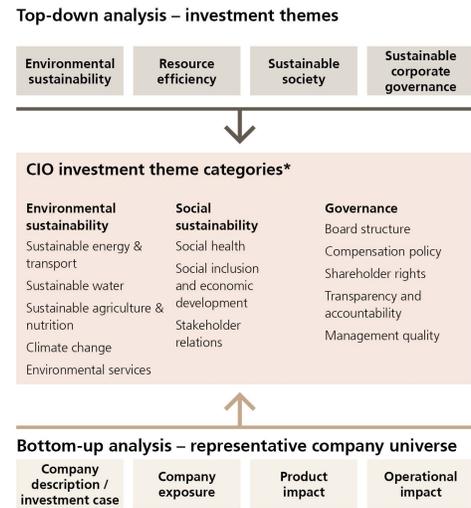
In our view, investing in generics fits our SI framework. Generics contribute to the sustainability of healthcare provision in two ways:

- **Reduce total cost of care**, enabling budgets to go further. Shorter development pathways allow generics to be sold at significant discounts to innovative drugs: in mature generics markets like the US, prices can be 90% or more below the branded price, leading to significant total savings. The AAM estimates that the cumulative savings from generic drugs over the last decade have been USD 1.67 trillion in the US alone; Medicines for Europe estimates the European healthcare system saved EUR 100bn in 2014 by using generics.
- **Broaden access to care**. As well as stretching total budgets, generics can make drugs more affordable at an individual level. Patients struggling to afford co-pays may skip prescriptions, reducing the benefit of preventative treatment. According to the AAM, over 20% of branded drug prescriptions are "abandoned" (i.e. never collected from the pharmacy), compared to only 8% for generics. This difference is largely attributable to lower cash co-pays for generic prescriptions. One study (Albrecht et al, "Value of Generic Medicines," 2015, published by the European Generics Medicines Association) has shown that where generic use leads to a higher treatment adherence rate, it can generate a positive impact on population-based health outcomes.

Along with the question of whether generics constitute an SI theme, investors can consider whether the companies with high exposure to this topic have a solid environmental, social and governance (ESG) profile. This analysis is based on MSCI ESG Research ratings that rank companies between AAA (best) and CCC (worst), focusing on the most important ESG issues in each industry. In the case of the pharma and biotech industry, key ESG issues are product safety, access to healthcare, corruption safeguards, human capital development, toxic emissions and corporate governance.

Compared to the global universe (Fig. 19), the generics theme has an unfavorable distribution of ESG ratings. This can be explained by two important factors: first, generics companies usually have a lower disclosure level than large pharmaceutical companies regarding ESG issues, yet they are in the same peer group. Further, exposure to corruption and to potential operational disruptions, for example, is

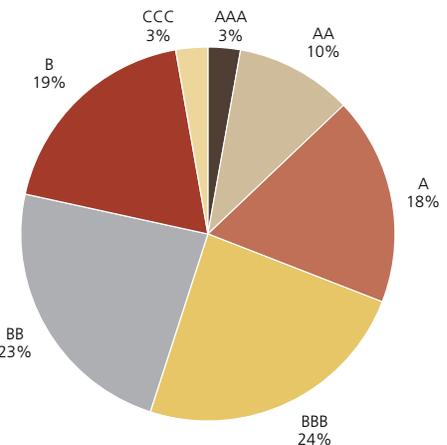
Fig. 17 Overview of longer-term investment topic clusters



* For simplicity, all topic clusters include several subcategories not included in the graph. For example: sustainable water includes water utilities, treatment, desalination, infrastructure & technology, water efficiency and ballast-water treatment. Within each subcategory are further specifications; e.g. water treatment includes filtration, purification and waste treatment. In total, we have more than 100 categories (potential SI investment themes) in our thematic database.

Source: UBS

Fig. 19: MSCI ESG research corporate coverage
Rating distribution in %, 5,720 companies



Note: AAA = best possible ESG rating; CCC = worst.

Source: MSCI ESG Research, UBS, as of Feb 2017

higher in emerging markets, where many of the generics companies are located. This does not necessarily mean that these companies have serious issues in these areas. In fact, they are currently less involved in controversies than some of the developed markets healthcare companies. However, they are viewed as having higher ESG risks because their policies and programs may not be adequate considering their exposure.

Corporate governance is another area where many companies score below average. This is partly due to local factors such as ownership structures of many Indian companies, where "promoters" have major shareholdings. It should also be mentioned that some of the generics companies, while their sustainable investment case is based on the fact that they facilitate access to healthcare by providing cheap drugs, have been involved in high-profile controversies related to overpricing and price fixing.

Conclusion

Underlying trends support long-term market growth, despite short-term challenges

Government policy and demographics are important structural drivers of increased generic drug sales. Most countries encourage the use of generic drugs through a variety of "carrot" and "stick" measures such as mandatory substitution at the pharmacy and elsewhere in the distribution channel. Increasingly, countries such as Japan are adding financial incentives for doctors to prescribe generics. All of these measures should support generic volumes in the coming years.

The *quid pro quo* will be more challenging pricing, currently most obvious in the US. But despite these short-term challenges, we expect the industry to consolidate and pursue new higher-value opportunities in complex generics and biosimilars. We think this can support market growth in the low to mid-single digits over the medium to long term, with low sensitivity to the economic cycle.

This should provide a lasting opportunity for companies exposed to the theme. We recommend a diversified exposure to minimize stock-specific risks associated with drug development. In a portfolio context, generics exposure can offset patent-related risks in branded pharma companies.

Risks

- **Pricing outlook.** As discussed extensively above, the primary risk to the near-term outlook for the generics industry is the pricing environment in the US. While we see pressure continuing, in the long term, we believe that stability will be established by a process of consolidation.
- **New competition from emerging markets.** Chinese companies already supply a large part of the world's active pharmaceutical ingredients (API) and, over time, some are likely to emerge as big players in the generic finished drug business.

- **Price-fixing allegations.** In 2015 and 2016, the US Department of Justice (DoJ) subpoenaed several generics companies, investigating alleged collusion in the marketing and pricing of certain generic drugs. Similar actions are ongoing led by various States' attorneys general. While these investigations carry a risk of fines against specific companies, we view the long-term impact on the industry as likely to be minimal relative to other sources of pricing pressure discussed elsewhere in this report.
- **Macro / market factors.** Healthcare stocks are sensitive to changes in interest rates, typically falling in value when bond yields rise.
- **ESG risks.** From an ESG perspective, several of the stocks have low ratings. This primarily reflects weak governance, particularly family or founder control, and low disclosure relative to innovative pharma companies in the peer group. We think the best mitigation is to be selective where ESG risks are a concern.

Appendix 1: Overview of the global generics market

We estimate the global generics market at around USD 185 billion in 2016 (Fig. 20). We estimate that historically global generics volumes have grown in the low double digits, as penetration rates rose in developed markets. But pricing tends to be deflationary, and value growth was lower, in the mid to high single-digit range, we believe. We expect growth to slow over the 2016–2020 period, to around 5% in US dollar terms, as pricing toughens and high levels of generic penetration limit volume growth opportunities in key markets like the US. Offsetting this are new opportunities, particularly in complex generics and biosimilars, where less competitive pressure may support stronger pricing power, and pockets of higher growth.

Over the medium to long term, total generic industry growth should average low to mid-single digits, broadly in line with the global drug market. While the pharma industry is not economically sensitive, generics growth may exhibit some year-to-year volatility due to the ebb and flow of patent expiries that drive new business opportunities. This is especially true in the US market, where these opportunities allow stronger pricing power than older drugs with multiple competitors.

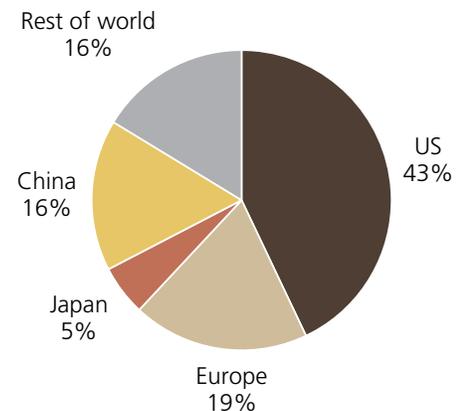
Below we provide brief overviews of key generic markets around the world.

US

We estimate the US generics market was worth around USD 80bn in 2016. Currently, the outlook for the industry is subject to intense debate given heightened pricing pressure, fewer new market opportunities from patent expiries than in the past, and significant uncertainty over the size of the biosimilars opportunity. Our best estimate of market growth over the period to 2020 is around a 4% CAGR.

Fig. 20: Regional split of the global generics market

Key regions share of the global generics market, 2016 (total market USD185 billion)



Source: UBS estimates, as of June 2017. Note: estimates of market sizes vary widely, and many markets feature off-invoice discounts and rebates of 30% or more. We have tried to capture these rebates in our estimates where possible.

This figure is lower than estimates published by many companies and consultants.

The US generics market is mature, with high generic penetration and intensely competitive pricing. The modern market was created by the Hatch-Waxman Act of 1984, designed to foster early and aggressive generic challenges against branded drugs' intellectual property. Near-universal substitution of generics for brands at the pharmacy, as well as financial incentives in the distribution channel, ensure high rates of generic use. Generics accounted for 89% of US prescriptions in 2015, compared to 12% in 1984. For large-volume primary care drugs, generic prices can undercut brands by 90% or more: for example, Pfizer's cholesterol-reducing drug Lipitor (*atorvastatin*) cost USD 3.29 per pill in 2011, prior to generic entry. Today, generic atorvastatin costs as little as USD 0.11 per pill, a 97% saving, according to the AAM. Overall, generics represent just 26% of US drug spending.

US generic pricing is generally deflationary, presently more than usual, and we expect this to remain the case for another 12–18 months. Growth is therefore driven by low single-digit volume growth and the beneficial effect (mix and volume) of new launches. Incremental shift from brands to generics is a minimal driver. In an attempt to improve pricing and margins, US companies (and increasingly the Indian companies who are challenging them for market share) are moving "up the value chain" into complex generics such as injectables, inhaled respiratory drugs and biosimilars.

Despite multiple rounds of consolidation over the years, the US market remains fragmented. While the top five companies account for around 40% of the market in value terms, the "tail" of companies with a small number of approved drugs is long. In 2016, over 170 different companies filed an ANDA (generic drug approval application) in the US. This suggests a competitive pricing environment as those applications are approved, but it also suggests scope for consolidation.

Europe

We estimate the European generics market was worth about USD 35bn in 2016. We expect the market to grow by around 3% CAGR to 2020.

Generic market share in Europe as a whole is lower than in the US (56% of volume according to Medicines for Europe) and ranges from 50–70% in the major countries. Generic penetration has risen over the last decade in every European market and we expect this to continue. Average discounts vs. branded equivalents are less than in the US, but since European markets tend to be dominated by government-sponsored single-payer healthcare systems, generic drug manufacturers have very little, if any, pricing power. Prices or reimbursement levels for pharmacy drugs are usually tightly controlled, and the growing use of tenders is pressuring prices in many countries.

Pharmaceutical markets are regulated at the national level in Europe. Therefore "Europe" is actually a patchwork of independent markets with different regulations covering generic substitution, market

access and pricing. Pro-generic policies such as encouraging prescribing by generic name and reference pricing vary by country: for example, the Netherlands, Spain and the UK all have lower patient co-pays on generic drugs, while France also provides financial incentives to doctors to prescribe them. Most European countries recommend pharmacists substitute generics for prescribed brands; the UK, which requires explicit permission from the physician, is a significant exception. One clear trend is the increasing use of tender-based pricing, particularly in Eastern European markets that have traditionally been dominated by promotion-sensitive branded generics. This is likely to drive a further shift from branded toward commodity generics, at the expense of price.

Japan

While Japan is the third-largest drug market globally, historically the country has had an under-developed generics market (Fig. 21) due to a perception of generics as lower quality products, as well as a lack of financial incentives to use generics. Both are now changing. We estimate the market size at around USD 10bn in 2016. As a result of historic concerns about product quality, the market is dominated by domestic manufacturers.

Japanese generic use has come a long way, but still lags Europe and the US: generics accounted for 36% of total Japanese prescriptions in 2016. In order to raise usage further, the government is pursuing a "carrot and stick" approach, implementing a series of financial incentives to doctors and pharmacists. For example, in 2008 a reimbursement premium was introduced that allows pharmacists to claim higher service fees for dispensing more generic drugs. Moreover, financial penalties are now levied if minimum levels of generic dispensing are not met. The government currently targets 80% generic penetration of drugs with expired patents (so-called "long-listed" drugs) in the 2018–20 time frame, although this goal may be refined in the coming months. In 2015, around 55% of these eligible prescriptions were filled with generics, up from just 10% in 2001.

The *quid pro quo* for incentives to use generics is a deeply negative pricing environment. A number of new price control mechanisms have been put in place since 2014, including annual price cuts and defined price bands for generics. Pricing is likely to remain negative. We expect the market to grow around 11% in volume terms to 2020, but only 6% in value given negative pricing.

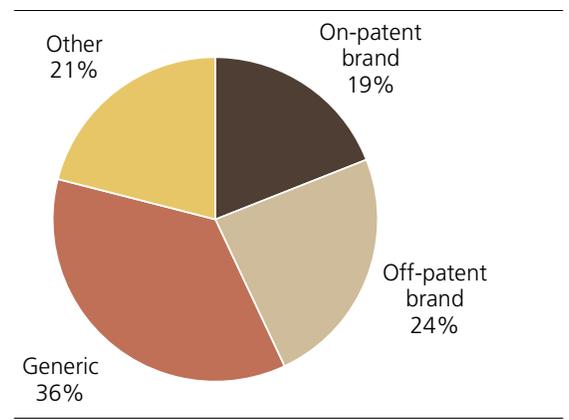
China

We estimate the Chinese generic market was worth around USD 30 billion in 2016, but add the caveat that estimates of the size of the market vary widely. Chinese drug sales are dominated by "branded generics," or off-patent drugs sold as brands. There is also a significant market for traditional Chinese medicine (TCM), although we exclude this from our analysis of the market.

In recent years, the Chinese government has made significant efforts to modernize the country's healthcare system, broadening access to care by introducing near-universal health insurance coverage and

Fig. 21: Long-listed drugs maintain a high share of the Japanese market

Japanese drug market by volume, year ending March 2016



Source: MHLW, Citi Research. As of December 2016. Note: long-listed drugs refers to off-patent brands for which generics are available.

reforming the hospital system to rein in costs. Given the lack of primary care provision in China, most drugs are dispensed in hospitals (Fig. 22). Selling drugs for a mark-up was a substantial revenue source for these hospitals, running counter to the government's aim of controlling drug spend. Now, a new reimbursement model has turned drugs from a revenue source to a cost center. Other changes include a new system of tendering to set drug prices that encourages hospitals to seek even greater discounts, and reform of the drug distribution system. Notably, the Chinese FDA is working to improve the quality of drugs available in the market, with a program to tighten enforcement of bioequivalence standards in drug applications. We expect these changes to benefit the larger companies in the market and lead to some consolidation. However, drug prices may remain under pressure given hospitals' new focus on drug cost management, and the rising use of tenders for sourcing.

In the long-run, leading Chinese companies may seek to internationalize their business. China is already a significant supplier of active pharmaceutical ingredients (API) to the global generics industry, but few Chinese companies sell finished drugs directly into Western markets. This could change over time as higher domestic quality requirements raise compliance costs, driving smaller companies out of the market, and raising overall quality to Western levels. As a result more of the larger, more sophisticated Chinese manufacturers may seek to launch their drugs in the US and other developed markets during the next decade. However, there is little sign of this so far (Fig. 23).

India

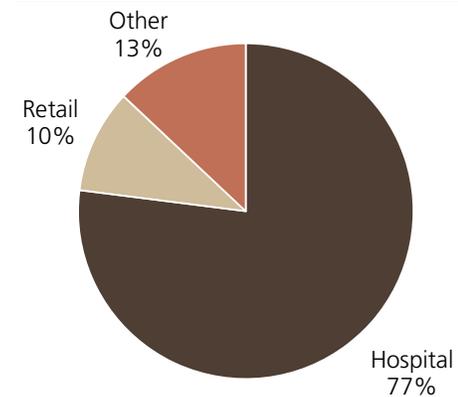
We estimate the total Indian domestic pharma market at around USD 15bn in 2016, mostly supplied by domestic companies. More than 80% of the market is branded generics, with patent-protected brands and true commodity generics making up the remainder.

India's importance in the global generics supply chain has grown enormously in the last decade: Indian companies had a 7% volume share of the US generic market in 2006, which grew to 30% in 2016. However, this equates to less than 18% of the value of the market, as Indian companies have historically focused on the more commoditized end of the market. While the reputation of Indian companies' manufacturing plants suffered as FDA enforcement actions against them rose in the 2014–15 period, they appear to have improved their compliance processes and we expect share gains to continue. This will likely add further pressure to US pricing, particularly as these companies seek to produce more complex generics.

Traditionally, India's advantage was its lower cost manufacturing base for API and finished drugs. However, as the industry has globalized and many US companies are now manufacturing in India, Indian companies have been forced to shift their pipelines toward more complex products such as injectables, hormonal products and even inhaled respiratory drugs and biosimilars. This is likely to provide another source of pricing pressure in the US market as these categories become more competitive. So far, few of these drugs have been approved in the US.

Fig. 22: Most Chinese drugs are sold through hospitals

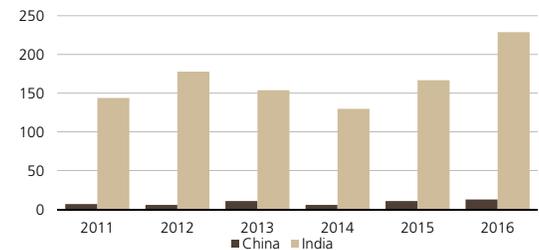
Share of prescription volume by channel



Source: UBS estimates. As of January 2017

Fig. 23: Chinese companies far behind India in US generic approvals

Number of ANDA's approved in US



Source: FDA, UBS. As of June 2017

Appendix 2: Understanding the generics industry

The generic drug market is highly complex, with many technical, regulatory and commercial challenges. Below, we present a brief historical overview of the development of the industry over the last 30 years, intended to familiarize the reader with important elements of the market structure. We focus on the US market, as it was the birthplace of the modern generics industry in the 1980s, and remains the paradigmatic "commodity generics" market today. However, a full description of the technical and legal complexities of the US and European generic markets is beyond the scope of this report.

Background

The US Congress essentially created the modern generics industry in 1984 with the passage of the *Drug Price Competition and Patent Term Restoration Act*, better known as the "Hatch-Waxman Act." At the heart of Hatch-Waxman is a compromise between the need to promote innovation while saving money for the healthcare system: branded drug manufacturers are given a long enough period of marketing exclusivity to recoup their R&D investment, after which the law encourages aggressive entry of generics to bring down prices.

In practical terms, Hatch-Waxman introduced an efficient framework for generic drug approval, taking account of both technical and legal factors. The legal framework enables generic manufacturers to proactively challenge brand manufacturers' patents in certain cases. As defined in Hatch-Waxman, generics are interchangeable with brand drugs, leaving price as the only means to compete. The result is an intensely competitive generics market.

The generics approval process

The most important technical concept in the generic drug market is *bioequivalence* (see Box 1), which ensures that a generic is an acceptable substitute for the branded drug it is based on. In fact, two generic drugs shown to be bioequivalent to a brand name drug are considered to be interchangeable, both with the branded drug and with each other. This means that either can be substituted for the branded drug at the pharmacy, potentially without the knowledge or consent of the prescribing doctor.

Using bioequivalence as the measure of approvability also lowers development costs, as no clinical trials are required. Instead, a generic manufacturer is allowed to rely on the original drug sponsor's clinical data. One widely-quoted study* estimated the average out-of-pocket cost to develop a branded drug at USD 1.4bn; a generic can be brought to the market for as little as a few tens of millions. Moreover, the cost of failed trials is almost completely avoided, since generics are only developed for products that are already medically and commercially successful. (The cost of failed trials is a significant part of branded pharma companies' R&D costs.)

From a legal perspective, generic companies must normally demonstrate that they do not infringe a branded manufacturer's intellectual property (IP) in order to be granted FDA approval. This is trivial after patent expiry of a drug, but in the US can also be achieved by

Box 1: Generic concepts (1) – what exactly is "bioequivalence"?

According to FDA*, in order to be approved in the US, a generic drug must:

- contain the same active ingredient
- be the same strength, dosage form and route of administration
- be *bioequivalent* to a branded drug

FDA's website states: "*bioequivalent drug products are those that show no significant difference in the rate and extent of absorption of the therapeutic ingredient.*" In practice, this means that two drugs have the same therapeutic effect (within statistical limits), by delivering the *same amount of drug* to the body *over the same period of time*. Note that "bioequivalent" does not necessarily mean "identical": non-active components of the drug may differ, and generics may differ visually from the original brand they copy.

* Source: www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm144456.htm

pro-actively challenging the validity of innovator companies' IP (a process known as a "Paragraph IV filing"). Successful Paragraph IV challenges can bring generics to market years before the branded drug's patents would have otherwise expired, with commensurate financial rewards for the generic manufacturer.

The legal details are complex but can be illustrated simply: Hatch-Waxman legislation grants a 180-day period of generic marketing exclusivity to the first company to successfully challenge a branded drug's IP. For a blockbuster drug (i.e. one with annual revenues of USD 1 billion or more) this represents a USD 3 million market *per day* at the branded drug's price. A classic example of this process in action was Barr Labs' overturning Eli Lilly's patent on Prozac (*fluoxetine*) in August 2001, allowing Barr to sell generic fluoxetine three years before the drug's patent was originally set to expire.

As noted above, in addition to their patents, innovative drugs in the US benefit from periods of exclusivity granted under Hatch-Waxman rules, all of which must have expired prior to the launch of generics. In Europe, generics can usually only be launched once the originator's patents have expired.

Generics distribution and marketing

Many countries' drug markets are structured to promote the use of generics. In markets with mandatory generic substitution a pharmacist must dispense a generic drug where one is available, unless the prescribing physician explicitly rules it out. In the US, for example, near-universal pharmacy substitution has led to extremely high rates of generic penetration: nearly 90% of prescriptions, according to the Association for Accessible Medicines (AAM). For the same reason, genericization is rapid: a brand can lose half its market share within just months of generics' availability.

Away from the pharmacy, other financial incentives are built into the US drug distribution system to encourage generic use. For drugs dispensed in pharmacies, most companies in the supply chain, including pharmacy benefit managers (PBMs) and wholesalers, earn higher margins on generics than branded drugs. As a result, these companies use a variety of tools to steer doctors and patients toward drugs for which generics are available. For example, PBMs (who negotiate drug prices on behalf of large employers and insurance companies) place generics on a "preferred tier" versus brands, which reduces the out-of-pocket costs (co-pay) by the patient. Patients are therefore given an incentive to accept generics over drugs that are still patented. This so-called *therapeutic substitution* can lead to a branded drug losing market share when a competing product goes generic.

Other markets, including Japan and most European countries, include similar financial incentives for doctors and pharmacists to prescribe generics. In China, recent changes to drug reimbursement rules have turned drugs from a revenue source to a cost center for hospitals, which should increase incentives for generic prescription.

Box 2: Generic concepts (2) – what's in a name?

Most drugs are known by at least two names:

- **Brand name:** often used to market the drug to doctors and, in some countries, directly to patients. Brand names may vary around the world due to local considerations.
- **Generic name or INN** (international non-proprietary name): used to identify the drug in scientific literature.

A drug's INN may give physicians a better indication of its class and intended use than its brand name. For example, the INN for Pfizer's Lipitor is *atorvastatin*. This name identifies the drug as a member of the statin class of cholesterol-reducers. It also facilitates generic substitution at the pharmacy as *all* generic versions of the drug will be labeled atorvastatin.

For biologics, this convention has been modified slightly as biosimilar products are not considered bioequivalent to the original innovator brand. Thus the biosimilar version of Amgen's Neupogen (*filgrastim*) produced by Sandoz has the INN *filgrastim-sndz*, and is marketed by Sandoz using its own brand name (Zarxio). Zarxio and Neupogen are *not* substitutable and the physician, rather than the pharmacist or insurance company, must decide which drug to prescribe.

*Source: DiMasi *et al*, "Innovation in the Pharmaceutical Industry: New estimates of R&D costs", 2016, *Journal of Health Economics*

In markets where generics are interchangeable and can be substituted at the pharmacy, such as the US, competition is primarily based on price. The first generic to launch may undercut a brand's price by only 30–40%, but pricing typically erodes rapidly once multiple-source generics are available, with volume-driven discounts or tenders often used to set prices. Prices typically fall by 80% or more within two years of generic competition, with some larger and more competitive products seeing erosion of over 95%. In Europe, some countries set generic prices at mandated discount levels.

In these regions, quality is by definition consistent across companies. Scale, and low-cost manufacturing, is therefore a significant advantage in developed generics markets. Further, more marginal ways companies can differentiate themselves include product range, security of supply and service. In less developed regional markets there has historically been more differentiation on the basis of product quality. This leads to the odd-sounding concept of "branded generics," where companies are able to leverage their brand names to denote quality in the eyes of doctors and patients. However, we expect more markets (e.g. CEE, China) to move to the commodity model over time, as product quality is harmonized and tender-based pricing becomes more widespread.

The generics supply chain is global, with important clusters of companies found in India, China and Korea. Indian companies have approx. 30% share of the US generic market by volume. Chinese companies are major suppliers of active pharmaceutical ingredients (API), but have yet to internationalize their finished drug sales. Korean companies have been among the pioneers of biosimilars.

Biosimilars

Biologics are drugs derived from living cells. Broadly speaking, biosimilars are equivalent to generic versions of biologic drugs, but, due to the technicalities of biologic manufacturing, it is not possible to create an exact copy of a biologic. Instead, regulators have settled on a definition of "highly similar" products with no clinically meaningful differences in terms of safety, purity or potency. This subtlety is recognized by the use of the term "*biosimilar*." Generic companies must conduct a limited set of clinical studies to demonstrate this similarity to an approved drug.

In principle, US regulations allow a biosimilar to be substituted with its brand equivalent at the pharmacy, just like a traditional generic, but only as long as additional standards are met to demonstrate interchangeability. In practice, these standards have not yet been defined. The latest FDA guidance suggests additional clinical studies would be required to show there is no impact of switching between the biosimilar drug and its originator reference product. We do not expect any interchangeable biosimilars to be approved in the US in the foreseeable future. In Europe, substitution is not generally permitted (although some countries such as Finland allow it in limited circumstances).

Unusually, Europe and Asia have led the development of the biosimilars market. Around 30 biosimilars have been approved in Europe since 2006, while in the US the first approval was not until 2015. There are now five US biosimilars approved, although only two have been launched commercially due to IP constraints (Fig. 24).

Biologics now represent 25% of the global drug market, suggesting a large market opportunity. However, uncertainties over pricing and reimbursement, as well as substitutability, make it a challenge to forecast the eventual size of the biosimilars market, even with the benefit of 10 years' early experience in Europe.

Given the need for clinical trials and lack of substitution, biosimilar companies' R&D and marketing expenses significantly exceed traditional generics manufacturers' costs. This suggests prices are unlikely to fall to the highly-discounted levels seen with commodity generics. Evidence from Europe is broadly consistent with this hypothesis, with most biosimilars being priced at a 35–50% discount. However, intensely competitive tendering in some Scandinavian countries has seen prices occasionally fall by up to 80%, a level that some companies suggest is unsustainable. Interestingly, in some Asian markets, biosimilars can be bought at discounts comparable to Western small-molecule generics: for example, biosimilar Enbrel is available in China at an 85% discount to the originator brand.

Early evidence in the US suggests penetration can be meaningful, but significantly slower than traditional generic erosion rates. Sandoz's Zarxio captured about 20% market share of the US short-acting G-CSF market in its first year of availability, initially priced at a 15% discount to branded Neupogen. However, due to the complexity of the distribution system for biologics in the US, it is not clear whether biosimilars in other therapeutic areas would see similar penetration rates, or prices.

Emerging markets could offer an additional, but hard to quantify, opportunity for biosimilar developers. An observation from Europe is that as biologics' prices fall with competition, volumes increase. This suggests that in emerging economies where biologics' use has been limited by budget constraints, biosimilars could open up new markets by entirely leapfrogging more expensive branded originators to market. However, there are several barriers to this happening, including questions over local manufacturing capacity, and as-yet-unclarified regulatory pathways.

While the jury is still out on the ultimate winners in the biosimilar market, scale, manufacturing quality and marketing ability are likely to be key differentiators. We expect price to be less of a factor than with traditional generics.

Fig. 24: Only two biosimilars have yet launched in the US

FDA-approved biosimilar drugs

Approval date	Biosimilar	INN	Reference brand
Mar-15	Zarxio	filgrastim-sndz	Neupogen
Apr-16	Inflectra	infliximab-dyyb	Remicade
Aug-16 *	Erelzi	etanercept-szsz	Enbrel
Sep-16 *	Amjevita	adalimumab-atto	Humira
Apr-17 *	RenFlexis	infliximab-abda	Remicade

Source: AAM, UBS. As of June 2017. Note: 351(k) approvals only. Between approval of Zarxio and Inflectra, FDA changed its naming guidance to use a random four letter suffix with no obvious link to a manufacturer. Drugs marked * are pending commercial launch.

Appendix

Terms and Abbreviations

Term / Abbreviation	Description / Definition	Term / Abbreviation	Description / Definition
1Q, 2Q, etc. or 1Q11, 2Q11, etc.	First quarter, second quarter, etc. or first quarter 2011, second quarter 2011, etc.	A	actual i.e. 2010A
bn	Billion	CAGR	Compound annual growth rate
COM	Common shares	E	expected i.e. 2011E
GDP	Gross domestic product	K	One thousand
Shares o/s	Shares outstanding	UP	Underperform: The stock is expected to underperform the sector benchmark
CIO	UBS WM Chief Investment Office		

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