White Paper

2020’s top 20
Why the top 20 global pharmaceutical companies matter so much, where they are headed and what it means for the pharmaceutical industry

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Introduction

The Current Health of the World’s Top 20

The world’s top 20 pharmaceutical companies are important not just because they are a convenient number, but because they have, historically, been so dominant in the pharmaceutical market. In 2014, these top 20 players, accounting for 0.001% of all prescription medicines companies recorded on MIDAS, accounted for 81% of all global protected drug sales by value, and 57% of all global sales, protected and unprotected, in 2014. The world’s top 20 companies have been the owners (although not always the originators) of the largest selling blockbuster agents, the drivers of headlining megamergers, and the starting point for perspective on the current health and future direction of the pharmaceutical industry as a whole. However, there is strong evidence that the global top 20 will struggle to dominate the next decade of the pharmaceutical market as they have the most recent ones.

Analysis of the share that the global top 20 (in each case consisting of the companies that were or are expected to be in the top 20 at that time point) shows that the share that these companies have of the entire world pharmaceutical market value (protected and unprotected) has been falling for at least a decade as Graphic 1 shows, and could fall to a minority share by 2020, based on analyst consensus projections of the global top 20 combined with IMS projections of the global market (which of course cannot take into account any mergers and acquisitions which might happen). The global top 20 do, however, still dominate the value of the world’s protected market, but that share, too, has been in decline over the last decade. Partly this is a function of companies with a generic heritage (Teva, Mylan, Actavis) entering the global top 20. But it is also due to smaller, ex top 20 companies not simply developing innovative products, but marketing them too.

Membership of the global top 20 companies has, in many ways, been remarkably consistent. Despite many major mergers and acquisitions, and the patent driven imperative for portfolio renewal, truly new entrants to the global top 20 have been rare. M&A has largely served to re-arrange (often quite temporarily) the rankings for existing incumbents of the top 20. As the protected market shifts to greater specialty focus, with high value products for highly defined patient populations, this is much more likely to change.

As graphic 2 overleaf shows, the global top 20 has faced two key market shifts in the last decade, successfully riding the wave of one, but largely failing to ride the wave of the other, and is also shaped by two other key factors, the change in the pattern of revenue streams from blockbuster products, as small molecules are succeeded by biologics and in some cases highly compressed product lifecycles from novel antivirals, and the ever-present wild card of M&A.
INTRODUCTION

Graphic 1: The World’s Top 20 Hold a Reducing Share of Global Pharmaceutical Market Value, and also of protected Market Value

Graphic 2: The key shifts and trends which are impacting on the global top 20
The Impact of Mergers and Acquisitions

When top 20 companies are involved in major mergers and acquisitions, headlines are made, because of the sums of money involved, and because the landscape for the world’s largest companies is re-shaped. Over the last decade, top 20 companies swallowed by their peers include Wyeth, Schering-Plough and Schering AG. This is just the tip of the iceberg, as numerous smaller companies have been subsumed, with spending on acquisitions by the top 20 exceeding $700bn since 2005. More recently, while big pharma to big pharma mega-mergers continue to be attempted and in some cases consummated, there is also a move to more surgical uses of acquisition and asset swaps to re-shape companies’ strategic direction, an example being the swap that GSK and Novartis made which focused Novartis more on oncologicals and GSK on vaccines. While this massive spend has undoubtedly re-shaped individual companies, it has failed to grow or even maintain the collective share that the top 20 has of the global pharmaceutical market.

M&A is therefore best seen as a driver of change in substance rather than size for the global top 20, one which has no clear overall strategic direction for the top 20 as a group. Looking at M&A activity in pharmaceuticals versus market capitalization changes for largely “pure” pharmaceutical players, it’s clear that some companies, Pfizer as an example, have recently spent considerable amounts on acquisitions, with little positive increase in market capitalization in the same period. Others, and Novo Nordisk is a key example, have spent little if anything on external acquisitions, but have seen the market reward their business model with strong growth in market capitalisation. Still others, and Actavis would be a prime example, have spent a great deal and also benefited from strong market cap growth. In short, there is no obvious pattern between pharmaceutical M&A spend and pharmaceutical market capitalization growth.
The Shift to Pharmerging

The other key shift in the global market has been the rise of the pharmerging markets – countries with low Gross Domestic Product per capita but significant prescription medicine market potential, defined as the potential to add on a minimum of $1bn of sales value in the next five years. IMS Health forecasts these markets will be half of the world’s top 20 global markets by value ranking by 2018, with China the world’s second most valuable medicine market (when traditional Chinese Medicine is included), after the US. Up until the start of 2014, there was a very clear gap between the strong, mostly double digit, growth of the world’s largest pharmerging markets and the much more modest, low single digit to negative growth of the developed markets of Europe, the US and Japan. In the five years post 2008’s financial crisis, pharmerging markets drove much of global growth, but the world’s top 20 pharmaceutical companies, despite all being very much international players, often with advanced pharmerging market strategies, were not the key players behind that growth. In fact, as Graphic 3 below shows, in the last decade, whilst the proportion of the global medicines market that is taken by pharmerging countries more than doubled, from 9% to 20% of world market value, the share those same countries took of the sales of the top 20 rose from only 6% to 10%. Whilst at the beginning of the decade the majority of pharmerging market value was in fact held by large, multi-national companies of developed world origin, by the end of the period, local pharmerging players held the majority of pharmerging market value.

Graphic 3: The Global Top 20 Have Fallen Behind the Market in Pharmerging

In the last decade, 21 pharmerging markets have driven 34% of all global value growth, and these pharmerging markets now account for 20% of world market but only 10% of Top 20 sales.

The global top 20 pharmaceutical companies largely failed to capitalise on the significant expansion of pharmerging market value in the last decade.

Pharmerging growth has been dominated by local, generic players—none of which touch the top 20.

Source: IMS MIDAS, Sept 2014 MAT US$
The global top 20 pharmaceutical companies, as a collective, largely failed to capitalize on the significant expansion of pharmerging market value in the last decade. This is unsurprising in many ways, because the growth of these markets has, at heart, been about low cost generics which are increasingly locally sourced. Governments focused on creating access to modern pharmaceuticals for the first time find high volume, low unit cost solutions which also drive the development of a local pharmaceutical manufacturing industry, highly attractive. The world’s largest pharmaceutical manufacturers, hailing from the developed world, still see only a relatively limited market opportunity in pharmerging markets for their core business of innovative, protected, and now most often specialist, pharmaceuticals. The contribution that the products at the core of most top 20 companies’ strategy are New Chemical Entities and protected biologics; but these agents derive only a minority of their early lifetime sales from pharmerging markets – in fact, regardless of whether new agents are specialty or primary care products, the percentage of their sales driven from all of the six largest pharmerging markets (Brazil, Russia, India, China, Turkey and Mexico) relative to the share driven by the major developed markets only climbs above 5% once. As discussed in greater depth in the IMS Health white paper “Pharmerging Markets Launch Excellence: from luxury to necessity”, this situation may not be a challenge for the world’s top 20 now, but will be in the future.

Currently when top 20 companies do well in pharmerging markets it is often driven by the sales of their older Original Brands. Products which dominated the world’s largest selling drugs lists a decade or more ago, but have mostly disappeared from the rankings in developed markets as patent protections have been lost. These products still generate substantial sales value in pharmerging countries, in many cases still growing in double digit value terms. In heavily out of pocket, brand driven countries, Original Brands dominate if patients can pay for them – and, in these growing economies, they increasingly can, sustaining the sales of Original Brands often long after exclusivity has been lost. However, because these sales are driven by brand rather than exclusivity their future is precarious, vulnerable to market changes which favour generics. If the market for older original brands came under substantial generic pressure – if, for example, government policies drove demand for generics, the global top 20 would face a substantial erosion of their core business unless they could improve the earlier sales of protected innovative products, or seek growth from other market segments, such as generics. While improving the early sales performance of newly launched innovative agents is possible, it is also tough in these markets, and profit margins from other businesses such as generics are challenging.

Pharmerging markets are also on a growth downswing at present, driven by increasingly fragile economic prospects for some of the major countries: Russia sees economic challenge because of sanctions and the decline in oil prices, and China and Brazil also seeing a moderating of GDP growth prospects. These economic challenges combine with maturation and other changes in the pharmaceutical markets which reduce growth prospects in pharmerging, just as certain parts of the developed world are seeing a pharmaceutical market growth recovery. Accordingly, the value growth gap between pharmerging and developed markets is at its lowest for over a decade. Whilst developed markets still grow slower than most pharmerging, their improved growth is coupled with their ability to support new innovation at a significantly higher level than pharmerging countries. On the other hand, once pharmerging markets no longer have super-high growth, the challenges these markets have for building significant sales for innovative new agents, especially if they are specialty, is thrown into sharp relief.

1. Pharmerging Markets Launch Excellence: from luxury to necessity, published 2014
IMS Health believes that the top 20 companies are moving to a much more nuanced perspective on pharmerging markets, where there’ll be much less uniformity either in terms of expectations or actions for these countries. There’ll be a split:

• Some top 20 companies will continue to have a broad investment across pharmerging markets, from the most nascent through to the more highly developed. For these companies pharmerging will be about a mix of businesses to reflect demands and growth opportunities. Innovative, protected brands will play a part and will likely include products which meet specific pharmerging needs: Sanofi may shortly launch the world’s first Dengue vaccine, for example, and Novo Nordisk has seen strong pharmerging performance for its new insulin, Tresiba. In addition, top 20 companies with a pharmerging focus will often also have a diversified offering including consumer health and generics.

• Other top 20 companies will make highly selective investments in pharmerging markets, with a focus on the largest and most advanced. For companies that are already have, or are moving towards, a speciality innovative product model, the relative value of pharmerging markets to their global sales potential is low and slow. They will prioritise their presence in the very largest pharmerging markets, the markets of the BRIC, and outsource or de-prioritise the rest. The strategic decision of Gilead to out-licence their flagship hepatitis agent Sovaldi to seven companies to market the product in pharmerging markets at a fraction of the developed world price is one new model for some of the global top 20.
The Shift to Specialty

From an innovative perspective, protected market value made a significant shift away from primary care, largely small molecule products, to specialty care, often biologic agents, driven by the small molecule genericisation in primary care of 2011/12 and an innovative explosion in oncology and other highly specialist areas. The prime drivers of this move were the global top 20 companies, largely in the developed markets, although now we are seeing companies that have only recently joined the top 20 or are even outside it with major specialist products – Biogen, for example, with its stable of multiple sclerosis products. As Graphic 4 below shows, the value shift to specialty has disproportionately affected the global top 20, as analysis of specialty share for the top 20 versus the global markets’ change in a ten year period shows; while the global value share for specialty rose from 16% to 26%, in the top 20 the rise was from 18% to 33%. An analysis of the pipeline, dominated by the top 20, shows this trend will undoubtedly continue to 2020: at all stages of clinical development research projects with a specialty indication dominate, and biologics, most often specialty, are a significant (one third share) of the pipeline at each stage.

Graphic 4: Specialty and Particularly Biologic Medicines Drive Much of the Top 20’S Growth

(*) IMS definition: Specialty products defined as medicines that treat specific, complex chronic diseases with four or more of the following attributes: Initiated only by a specialist, require special handling and administration; unique distribution; High cost; warrants intensive patient care; might require reimbursement assistance

Source: IMS Health, MIDAS, MAT Sept 2014, Non Rx Bound
The Shift of Innovation

Ownership of this innovation is also changing. As graphic 5 shows, companies ranking below the top 20 have always been a significant source of innovation, in terms of being the patent originators for new chemical entities and biologics. However, over the last decade their share of all innovation origin has risen significantly, from 50% to 73%, at a time when the global top 20 companies share of innovation origin has dropped from one third to 23%. It’s still the case that the global top 20 companies hold the lion’s share of commercialisation; by the time products are approved by the FDA 56% are owned by the global top 20. With an increasingly specialist pipeline this may change. Highly specialist products, especially if orphan drugs, require smaller scale in terms of sales and marketing investment and will realise the vast majority of their sales from a very small number of countries – the US, Europe, and Japan. In these circumstances it becomes perfectly possible for smaller companies to commercialise themselves, when in the past they would have partnered with a top 20 company to provide the commercial infrastructure and the global reach. A case in point is Vertex. This company launched Incivek/Incivo, one of the first of the new Hepatitis C antivirals on their own in the US but partnered with Janssen/Johnson&Johnson outside the US. However, for their next launch, the orphan drug Kalydeco which treats a genetically defined subset of cystic fibrosis sufferers, Vertex launched the product themselves across the US, Canada, UK, and other countries.

Graphic 5: The Top 20’S Origination of Innovation Declines

The dominance of innovation ownership by smaller companies, combined with a movement to products which those companies can more easily commercialise themselves poses a threat to the dominance of protected Rx products of global top 20 companies. Whilst it’s still the case that the vast majority (more than 80%) of all protected value is in the hands of the global top 20, that figure has been in decline for a decade, and we expect that this decline will continue.
Companies that wish to remain in the global top 20 must be on top of their game in business development, as the battle for innovation moves faster and is more expensive than ever before. IMS analysed the change in FDA new drugs approved between 2004 and 2014 in terms of the average number of years from patent filing to first licensing/acquisition and the number of times that innovation changed hands between filing and approval. As Graphic 6 shows, the average number of years in the patent filer’s hands before the product was sold or licensed-on declined from 8.4 to 5.9 years in this decade: promising IP (Intellectual Property) is sold earlier than ever before. IP also changes hands more frequently between patent filing and approval: the percentage of approvals which changed hands three times in development has trebled to 17% in the last decade. With this increase in churn, the price tag associated with IP inevitably rises. Faced with rising costs, companies will seek to acquire or option promising platforms still earlier, requiring their assessment of opportunity and risk ever to be more sophisticated and rapid.

Simultaneously, however, companies should think about how they can better leverage late stage opportunities. Despite the shift to specialty and the renewed focus on developed markets for innovation driven companies because of this, not all smaller companies will be successful launching their own products, or want to take on the risk of doing so. Top 20 companies which demonstrate their commercial/market access strength, are flexible and easy partners to work with will benefit most. These will include:

- Companies such as Johnson & Johnson which have a track record of partnership and making partners launches a success. This opportunity may also extend to smaller regional specialists, although they generally have less of a track record in highly successful launches.
- Companies which continue to have the broadest geographic reach across pharmerging, such as GSK, Sanofi or Bayer, as they may be best positioned to roll out smaller companies’ NCEs across pharmerging, as and when that is appropriate.

**Graphic 6: The War for Innovation is Hotting Up**

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<tr>
<th>Year of approval</th>
<th>Average years from patent filing to first licensing or firm’s acquisition</th>
<th>Innovation – changing hands</th>
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<td>Only once</td>
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<td>8.4</td>
<td>69%</td>
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<tr>
<td>2014</td>
<td>5.9</td>
<td>44%</td>
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Source: IMS Health MIDAS MAT Sept 2014. Market Segmentation + LIC countries, *Rx and Non Generics only. Methodology – Highest movement in rankings in 10 years to be part of Sept 2014 top 50 companies by revenue
The Shift of Product Lifecycles

Top twenty companies are also experiencing a shift in product lifecycles which will potentially lead to further churn and M&A activity. Companies have worked through the upheaval of peak small molecule genericisation for primary care blockbusters, where the typical product lifecycle was one of ten to fifteen years of protected commercial life, followed by a precipitous decline of sales immediately post patent expiry, as shown in Graphic 5. Pfizer’s Lipitor is, of course, the classic example of this type of product’s lifecycle for global top 20 players: launched in 1996, at its peak generating $13bn a year, the product disappeared from top global rankings of best selling products within two years of its US patent expiry in late 2011. Lipitor’s lifetime revenues in the 16 years between 1996 and 2012 are estimated at $141bn, or an average of $8.8bn a year.

Around the time of Lipitor’s launch, the first of a new generation of biologics also started to launch: the monoclonal antibodies for autoimmune diseases and for the treatment of certain cancers. The first, rituximab, with indications in both oncology and autoimmune disease, also launched in 1997. Infliximab, or Remicade, the first of the MAbS to experience biosimilar competition in the European markets, launched in 1998. The first infliximab biosimilars launched in Europe in 2014, providing 16 years of absolute exclusivity, and, since the erosion of the brand by biosimilars will be a slow process, there is expectation for several more years of multi-billion dollar sales. As the Biosimilar market for MAbS gains momentum in Europe, and the crucially important US biologic market also sees biosimilars enter, major MAb biologics can expect to see progressive erosion. In the future, biologics may have lifecycle expectations that are little longer than those for small molecules, and a post patent expiry “soft landing” might, quite rapidly, change to a hard one.

The most intriguing development of recent years, as shown in Graphic 5, has been the way in which the new Hepatitis C therapeutics have serially smashed records for the fastest launches ever, risen to multi-billion dollar blockbuster status in the shortest times ever, and then shown every indication that their commercially viable lives will also be unusually short, ending well in advance of patent expiry. Incivo/Incivek, one of a pair that constituted the first of the new era of Hepatitis C agents, was first launched in October 2011, then the fastest launch in history and by August 2014 Vertex announced that production was to be discontinued because of dramatically falling sales. The cause of this decline, Sovaldi, launched in December 2013, also had the fastest launch in pharmaceutical history, but within a year was declining as Gilead moved attention onto the combination product, Harvoni. It’s therefore possible that the commercially viable lifetime of Sovaldi could be no longer than three years, meaning that even though its first year sales were $9.3bn, its lifetime sales will be a fraction of those of a Lipitor or a Remicade.
While the extreme lifecycles of Hepatitis C agents are unusual, it’s clear that future products can expect lifecycles that are shorter, and that the global top 20 will struggle to achieve individual product lifetime returns seen by Lipitor and its peers. Compressed product lifecycles and smaller lifetime returns imply the need to launch more products, more rapidly, to a consistent standard of excellence, something which previous Launch Excellence IMS Health studies have demonstrated that top 20 companies historically are not good at.
Being a “Launch Excellent” Company

We expect that the companies which will continue to thrive in the global top 20 will, therefore, be those that are consistently excellent across new launches, and can handle highly challenging multiple launch schedules. Top 20 companies have “Launch Excellence” programs in place, but with varying degrees of effectiveness and consistency. The most effective, in IMS Health’s experience, have three core characteristics:

- **Common and consistent expectations**

  What this means in practice is a small group of key performance indicators (KPIs) which are used consistently across products, therapy areas and countries. Whilst most companies pay lip service to this ideal, in practice KPIs get adapted and altered by launch and country. **Launch Excellent** companies don’t let this happen; by keeping a core set of common KPIs they enable their launches to be rigorously, transparently and consistently compared to allow the highs and lows of performance to be identified objectively and used as learning opportunities.

  While this approach is vulnerable to the criticism that it is a blunt instrument, its advantages are that it eliminates time wasting discussion of different performance metrics and so frees up time to ask more useful questions about what is driving outstanding or poor performance and what can be learned.

- **Cross functional teams**

  While many functions are inevitably involved in the development of a launch, **Launch Excellent** companies are far more effective at creating a true cross-functional team. Structures that promote this include mirroring the cross-functional make-up of the global launch team with local country teams. Incentives that promote it include a very clear measurement of performance as contribution to launch, rather than function, success.

- **Specialised Launch Excellence training and skills development**

  A crucial way of building teams with common and consistent expectations is provision of specialised Launch Excellence training at the start of the launch process. **Launch Excellent** companies make time for global and local teams to undertake common training courses, building teams and starting all members on the same foot in the process.
Thriving in Tomorrow’s Global Top 20

Entering the top 20 may be relatively easy for certain companies with extremely strong launches, or a highly aggressive acquisition program. What might be much, much harder, both for new entrants and some struggling incumbents, is staying in it. IMS Health believes that a best in class specialty commercial model and highly effective strategic choices will underpin the companies that thrive in the global top 20 to 2020.

A best in class specialty commercial model becomes an absolute necessity because being a specialist powerhouse will be the rule, rather than the exception, for the global top 20. IMS Health estimates that by 2020 three quarters of the global top 20 will either be driven primarily by specialist sales or they will be well on the way to being so. It will therefore not be enough to simply have a specialty commercial model; to thrive the model will have to be exceptional. Selling specialist products requires multi-skilled individuals operating in a multi-functional team. Increasingly, a successful team must also operate in a mature multi-channel marketing environment; these have yet to develop.

The right strategic choices recognise that the broad model of a top 20 pharmaceutical company with interests across specialist and primary care therapeutic areas, spread across developed and pharmerging markets will be increasingly difficult to maintain – and, more importantly, not necessary for all top 20 companies to maintain. In the future, being a successful major company will more often be about choosing to focus on specialty products in developed markets, or (less frequently) choosing a broader geographic spread with an appropriate (ie largely primary care focused) portfolio. Between these two stools there’ll also be a more opportunistic breed of player – the deal-driven fast mover with both innovative and less innovative portfolio segments, but a focus on opportunity within the developed markets.
A New Approach to Development, Access and Marketing

The future of innovative products will be one of increasingly defined patient populations for new products, regardless of whether they are specialist or primary care agents. The reasons are multiple. At one extreme of the specialist spectrum, the enabling legislation of the early 2000s in the US and Europe now yields fruit in the form of significantly increased numbers of orphan drugs. To October 2014, there were 31 NMEs approved globally and 26 launched, six of which were classified as orphans in either the U.S. or EU. This trend is likely to continue, not least because whilst expensive, these agents can present a strong case to payers if they present a breakthrough or unique treatment for an otherwise untreatable disease with a small and highly defined group of sufferers. In addition, new regulatory legislation on breakthrough drugs, such as the FDA’s Breakthrough Therapy Designation or the NHS’s Early Access to Medicines Scheme, supports the access environment.

Patient segments will be increasingly defined by a number of mechanisms, some technological, some payer or clinical practice driven as Graphic 8 illustrates.

Graphic 8: Defined Patient Population, Defined Outcome

Across both specialty and primary (traditional) therapy areas, the trend will be to increasing sub-division and definition of patient populations. This is likely to be welcomed by payers, as it provides greater certainty on their commitment and risk in terms of patient volumes (if of course payers and pharmaceutical companies agree on the appropriate patient group). It can also, potentially, provide benefit to pharmaceutical companies if a segment of patients can be defined for which there is a differentiated benefit for their innovative agent, making that segment protectable. The challenge will, however, be in defining the patient segment and then in identifying patients that meet that definition.
Even genotypically or biomarker defined patient segments are challenging to identify

We would perhaps expect genotypically defined orphan diseases to be definable and identifiable, but in practice this is not the case. Rare diseases often have generalised and non specific symptoms, and because they are rare, few healthcare professionals will have the experience or knowledge to make a correct diagnosis rapidly. Patients therefore can suffer years of mis–diagnosis and lack of treatment. Pharmacotherapies addressing specific rare diseases help raise awareness of a disease and increase motivation to identify potential sufferers and make diagnoses but the process is still inefficient, and patients may not be identified early enough to realise the full benefit of disease modifying treatments.

The experience of identifying rare patients via biomarkers also throws up inefficiencies: Xolair is currently the only biologic used in asthma to treat patients who are severely allergic and manifest high levels of Immunoglobulin E (IgE) – serum levels of which are measurable using a diagnostic test. Even with recognition of the role of IgE and the value of an anti–IgE monoclonal antibody in treatment of this expensive segment of extremely allergic patients, Xolair’s uptake has been slow and steady rather than spectacular and Novartis/Genentech have had to work hard to support better identification of candidate patients.

Failing on first line/payer identified unmet need also poses identification challenges

Patients who are treated with common chronic medications but are failing to reach treatment goals undoubtedly represent a prime target for innovation in therapy areas with effective generic agents for first line use. These patients are also inefficiently identified: many patients will continue on medication with no testing as to whether they are achieving treatment goals or not. These are often the patients that will end up in the final segment consisting of those patients which healthcare payers/providers identify as particularly costly and problematic. Healthcare providers may clearly identify these patients, but have less clarity on how to treat them or prevent patients becoming members of this group– even though the root cause may be failing to use pharmacotherapy early enough or effectively enough.

The logical implication of these observations is clear: companies with innovative medications for patient segments that are increasingly defined must be very effective at defining and identifying those patients if they are to achieve optimal uptake of these products. To use an analogy, much of commercial effectiveness in the past has been about the effective segmentation and targeting of prescribers of medications. This model evolved with the addition of payers as a key decision maker. With the rise of specialty, it will evolve again, with the effective segmentation and identification of patients as a key differentiator of commercial effectiveness.
Who Are the Candidates for New Entry into the Global Top 20 by 2020?

Excluding the wild card of M&A, fast moving members of the global top 50 are the most obvious candidates for entry into the global top 20 in the next five years. Of the companies which are the fastest movers in global top 50 in the past decade, three moved to become top 20 players already: Novo Nordisk, Gilead, and Otsuka. In each case, innovative product growth has been the driver, although acquisition of the originator company (Pharmasset) was behind Gilead’s most recent innovative product growth drivers, the Sovaldi/Harvoni family. Rapid movement up the rankings of the top 50 via innovative product sales is, therefore, a reasonable predictor of top 20 membership: who’s next? Of the remaining seven fastest movers, two, Lupin and EMS are major pharmerging companies, Lupin originating in India and EMS in Brazil. Both of these companies have generic/non-original origins but increasingly innovative aspirations. Two companies, Endo and CSL, have a developed markets focus across a range of specialist and other products. However, the three companies which most closely resemble those that have broken into the global top 20 before are the trio of Celgene, Shire, and Biogen, based on fast movement on a small group of new innovative products. Of these, Biogen, currently 24th in the world, is within touching distance. Each of these three companies have in common a focus on specialty and highly defined patient segments:

- Shire evolved from an ADHD driven company into an orphan drugs specialist via acquisition
- Celgene focused on oncology and has the leading product (Revlimid) for multiple myeloma as well as building a wider oncology portfolio
- Biogen has specialised in multiple sclerosis, moving from older interferons into newer oral agents and with a strong track record in identifying areas of unmet need and finding drugs to address them

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<td>10 Endo Health Solutions</td>
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Source: IMS Health MIDAS MAT Sept 2014. Market Segmentation + LIC countries, *Rx and Non Generics only. Methodology – Highest movement in rankings in 10 years to be part of Sept 2014 top 50 companies by revenue
2020’s Top 20: Some Predictions

Specific forecasts of the exact membership of the global top 20 in the next five years have extremely limited shelf lives and are inevitable hostages to fortune, and we do not propose providing one in this Thought Leadership white paper. We think that it’s more fruitful instead to discuss the types of companies we believe will dominate the global top 20, in 2020 and indeed in the decade of the 2020s.

Protected innovation focused

Generic-lead or generic heritage players exist in the global top 20: Teva, Actavis and Mylan all fit that description. However, we believe that the proportion of the global top 20 that are traditionally generics focused to 2020 won’t increase, despite the increasingly payer driven environments of the developed world and generically driven pharmerging market growth. This is because the environment for the core of oral solid formulation generics is progressively squeezed on margin, as in the developed world payers use rebates, discounts and tenders to drive down price, and in pharmerging markets local players increasingly dominate the traditional generics market. Top 20 members with a generics heritage are moving in a more innovative direction, whether by acquisition, such as Actavis’s acquisition of Allergan, or organically, with the launch of Biosimilars and the development of third sector products.

Specialty dominated

The first, most obvious characteristic of 2020’s top 20 is that it will be dominated by companies that are either wholly or largely driven by specialty product sales. Three quarters of all top 20 companies could fit this description by 2020. This does not mean that the products will necessarily be in the therapy areas currently seen as specialty, although oncology will continue to be overwhelmingly the most valuable therapy area for the foreseeable future. The period to 2020 will see significant expansion of specialty, biologic agents into therapy areas that are currently characterised by primary care, mostly generic treatments.

This specialty dominance will have some important consequences. As discussed earlier, the playing field is much more level between smaller and larger pharmaceutical companies when driving the success of a specialty product, for two key reasons. The first is geographic scope: highly sophisticated products for small patient populations are likely to realise the vast majority of their value in the US, a select group of European countries, and Japan, as those are the countries with the resources and health infrastructure to support the use of these products. The second is commercial scale: the level of resource to launch small patient population specialist products is lower than major primary care or even mainstream specialist launches.

Developed markets focus

This specialty focus is, however, likely to lead to even greater divergence between the companies that are driving the developed world market growth and those driving the growth of pharmerging markets (already, often, the local pharmerging players). There will be (likely a minority) of top twenty players, those with the right portfolio which have already built appropriate pharmerging experience and scale, which will continue to have a broad spectrum commitment to the global pharmaceutical market.

Diabetes, vaccines, generics and consumer health businesses will feature for the top 20 “true global scope” players. The other top 20 players will take a much more selective view of the pharmerging markets, playing in those which are closer to developed maturity and/or significant in size and deprioritising other markets or licensing their agents out. This may in turn create opportunities for the more sophisticated pharmerging players or those top 20 companies which retain true global scope.
In summary, members of the global top 20 will be most likely to be innovative specialist focused players with an emphasis on developed markets. There will, of course, be exceptions to this rule, and the swing back to developed markets focus may be just that – a swing, with reversal likely if some pharmerging markets develop the ability to support an increasingly large protected launch market segment.

The hegemony of the global top 20 companies in the pharmaceutical market is under threat now as never before. The share these companies have of global market value slips below 50% some time before 2020, and from then on global top 20 dominance will retrench to the innovative sector of developed markets. Could this mean the pharmaceutical market becomes less global than it has been? Will it in fact allow the rise of new major players in a more diverse pharmaceutical market where the traditional distinctions between generic and innovative companies become increasingly blurred? These questions are not yet clear, but one thing is: the global top 20 are on an irreversible route to significant change.

### Graphic 10: 2020’s top 20: some predictions

<table>
<thead>
<tr>
<th>2020’s top 20</th>
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<tbody>
<tr>
<td>1</td>
<td>Novartis</td>
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<td>2</td>
<td>Pfizer</td>
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<td>Sanofi</td>
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<td>Merck &amp; Co</td>
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<td>Johnson &amp; Johnson</td>
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<td>Allergan/Actavis</td>
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<td>20</td>
<td>Mylan</td>
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