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HEALTHCARE MARKET REVIEW AND OUTLOOK

In contrast to this year's prior quarters, healthcare underperformed the broad markets coming in almost three percentage points behind the world's quarterly return of 5.2% (MSCI AC World Index). The outperformers this quarter were biotechs (+9.5% for the quarter) and, in a reversal of recent standings, emerging-market healthcare (+3.3% for the quarter). The quarter's worst performers were services, down 0.3%, while medtechs and pharma tread water (+0.3% and +0.9%, respectively). Overall, this quarter's healthcare-sector performance was driven by innovative product approvals, M&A resurrection, and the seemingly endless (and futile!) attempts at Obamacare repeal and replace.

The world continued its synchronous developed- and emerging-market recoveries. There was relative quiet on the macro front; although politics (especially Obamacare, the German election, and North Korea) were a bit noisier than usual they had little impact on the markets. Accommodative monetary policy was generally reconfirmed, although rate repricing will likely not be an impetus for a future market correction, given the strong macro backdrop. We continue to see cyclicals performing well, and see the recent outperformance of small- and mid-caps continuing (thanks in part to ongoing US deregulation efforts by the Trump Administration), even without tax reform.

INDEX	CLOSE 9/30/2017	RETURN					ANNUALIZED VOLATILITY	
		1 MONTH	3 MONTH	6 MONTH	9 MONTH	12 MONTH	30 DAY	90 DAY
MSCI World Index (all country)	232.8	1.9%	5.2%	9.7%	17.3%	18.6%	5%	6%
MSC World Index	5619.2	2.2%	4.8%	9.1%	16.0%	18.2%	5%	6%
MSCI World Healthcare Index	299.0	1.3%	2.4%	9.5%	18.8%	12.4%	8%	8%
MSCI World Pharma	213.4	1.8%	0.9%	6.1%	13.8%	7.3%	7%	8%
MSCI World Biotech	1512.2	2.7%	9.5%	15.8%	26.1%	19.9%	14%	15%
MSCI World Equip and Supplies	439.3	0.9%	0.3%	10.1%	24.3%	13.4%	9%	9%
MSCI World Healthcare Prov & Serv	538.1	-1.0%	-0.3%	9.0%	15.6%	17.6%	11%	9%
MSCI Emerging Market Healthcare	553.9	3.0%	3.3%	7.9%	13.8%	2.9%	12%	11%
MSCI Emerging Markets	485.4	-0.4%	7.9%	14.7%	27.8%	22.5%	9%	9%

We also favour companies with significant ex-US exposure, given valuation differences and the likelihood of persisting USD softness.

Among pharmaceuticals, the most significant news concerned the dramatic weakness of generics in the face of continued pricing pressure and clinical developments in immune-oncology. The biggest pharma losers this quarter were generic companies, with Teva down almost 50%, and Mylan, Endo, Valeant, Mallinckrodt, and Hikma each falling about 20%. This weakness was related to continued pricing pressure on generics' base businesses. The drivers here were buyer consolidation and an acceleration of drug approvals in exiting generics markets, both of which pressure margins, along with a concomitant dearth of first-to-market generic approvals, which drive margins. While the FDA has expressed a desire to accelerate first-to-market generic-drug approvals and to target the creation of three-player markets as a drug price-control mechanism, the agency's approvals heretofore have been more of the latter variety, which are margin destructive, than the former, which are margin accretive. On the large-cap pharma front, the performance was much better, led by Bristol-Myers Squibb (up 15%) and trailed by GlaxoSmithKline (down 5%). The most significant clinical development was the announcement of results from AstraZeneca's failed MYSTIC clinical trial for their immune-oncology PD-L1 antibody Imfinzi in lung cancer. Roche announced a failed Phase III study with lampalizumab in geographic atrophy, an eye disease. A quite intriguing data set emerged from Novartis' monoclonal antibody canakinumab, which showed a mortality benefit in atherosclerotic patients through a heretofore unproven LDL-neutral anti-inflammatory process. Novartis also benefited from the first ever approval of a CAR-T (chimeric antigen-receptor T cell) drug approval and the promotion of Vasant Narasimhan, MD, to CEO from the position of Chief Medical Officer. Finally, this quarter marked the coming out party for GlaxoSmithKline's recently appointed CEO Emma Walmsley and her vision for the company, which got bogged down with dividend-stability questions. We continue to be selective among the large pharmas and will remain cautious with generics until evidence of an improvement in fundamentals is available. The industry is trading at 15.6x ntm P/E, a discount to the 16.5x ntm P/E of the MSCI World, with a dividend yield of 2.9%.

Biotech performance was driven by large-caps this quarter, with the big five (Gilead, Amgen, Celgene, Biogen, and Vertex, all of which were up more than the NBI's 6.8% performance) contributing about 70% of the Nasdaq Biotech Index's quarterly performance. By far the most significant development was Gilead (finally!) activating its business development with the USD12bn purchase of CAR-T technology pure-play Kite Pharmaceuticals. This move propelled Gilead and drew attention to the other large-caps. In small- and mid-caps, clinical results were aplenty, with notable successes reported by Insmed (with their novel antibiotic), Fibrogen (in idiopathic pulmonary fibrosis), and Zogenix (for Dravet syndrome). At the same time, significant misses were reported by Versartis (with their growth hormone) and Axovant (with an in-licensed Glaxo reject for Alzheimer's disease). Finally, we note the FDA has approved 34 drugs so far this year, versus 22 in 2016 and 45 in 2015. This record lays the foundation for a rather productive year and sales-and-earnings acceleration for the industry. Early launch dynamics appeared solid for several companies with new products, including Neurocrine's Ingrezza, Acadia's Nuplazid, and Biogen's Spinraza. Valuations here are still undemanding. Profitable biotechs are trading at 16.2x ntm P/E, which compares favourably to their slower-growth pharma relatives at 15.6x. The Nasdaq Biotech Index trades at a 6.2x Price/Sales multiple, relative to its historic range of 4x to 10x.

Medtechs, healthcare's darling for many of the last few quarters, paused their ascent this quarter. The leveling was driven by three factors: investor caution prompted by historically high valuations; the lack of convincing proof that growth acceleration in some areas, such as orthopaedics, will continue; and uncertainties stemming from hurricane-related manufacturing disruptions. Strong performances were reported by dental innovator Align (+24%) and supplies company Teleflex (+16%), while Hologic (-19%) and Medtronic (-11%) under-performed. Although volume and pricing

trends continued to be decent in most segments, orthopaedic players such as ZimmerBiomet, Integra, Nuvasive and, to a lesser extent, Stryker, struggled because of earnings, hurricane-related disruptions, and volume concerns. Significant news flow included announcements of Fresenius Medical's acquisition of home-hemodialysis player NxStage Medical for USD2bn, Abbott's obtaining FDA approval for the FreeStyle Libre Flash Glucose Monitor, and MRI-safe ICD approvals from Boston Scientific and Abbott. Valuations, at 21.1x ntm P/E, have contracted marginally but remain quite close to all-time highs, a reflection of generally good fundamentals. We remain cautious given valuations.

For much of the quarter, the services industry traded largely in-line with healthcare. Then, Senators Graham and Cassidy made one more last-minute Obamacare repeal and replace Hail Mary pass. (This one followed August's penultimate play, of course.) The pass fell incomplete thanks to the repetitive "No!" votes from Senator McCain and a handful of other Republicans, who argued for a fairer legislative process and a bipartisan effort. Earnings for managed care players were largely in-line, with the exception of Medicaid-focussed Molina, while providers continued to struggle with disappointing results driven by decelerating volume trends. We have not changed our preference for payers over providers and continue to focus most of our attention on small- and mid-cap service companies with innovative healthcare service and delivery-of-care offerings. Valuations here are reasonable at 15.3x ntm P/E.

Emerging-market healthcare equities outperformed their developed-market peers, while continuing to underperform emerging markets overall. As in previous quarters this year, this scenario is largely attributable to an investor preference for reflationary and cyclical exposures. Most Indian generics players had a difficult time stemming from weaknesses in US generic markets, some continuing manufacturing-quality issues, and disruptions from the country's GST implementation. In China, drug manufacturers were strong, thanks to solid quarterly results and bright volume forecasts, even as distributors came under some pressure because of concerns surrounding the implementation of the two-invoice system. In South East Asia, medical tourism continued to be sluggish affected by a number of Gulf countries cutting civil service compensation and benefits. Thai hospital services were also weak for the same reason, while domestic spending continues to be weak from low retail confidence and (still) mourning for the late King. In Indonesia, the implementation of the social security scheme BPJS continues to crowd out private healthcare expenditure. Korean giants Celltrion and Samsung continued their ascent, despite the announcement of tax reforms by President Moon. At 15x forward EV/EBITDA, emerging market healthcare companies are attractively valued, given their superior growth prospects.

Valuations in healthcare are attractive. Healthcare continues to trade largely in-line with the broad markets at 16.6x ntm P/E vs MSCI World 16.5x ntm P/E, a figure below its historically typical premium of a couple of points. The only industry pulling up healthcare's valuation is medtech (21.1x ntm P/E), while biotechs (16.2x ntm P/E), pharmaceuticals (15.6x ntm P/E) and services (15.3x ntm P/E) all trade at a discount to the world. Many of the headwinds from 2016 – drug-pricing concerns and healthcare reform – are continuing to dissipate. Repeated repeal and replace efforts have failed, and attention in Washington seems to be shifting to tax and foreign-profit overhaul and away from wholesale healthcare reform, although minor tweaks remain likely. FDA

GROWTH P.A. 2017-2019E					
	SALES	EPS	PE17E	EV/SALES17E	COGS
MSCI World Pharma	3%	7%	16x	4.0x	27%
MSCI World Biotech	5%	10%	17x	6.2x	17%
MSCI World Equip and Supplies	6%	11%	23x	4.1x	39%
MSCI World Healthcare Providers	11%	10%	17x	0.6x	83%

Commissioner Gottleib has made accelerating generic-drug approvals and smoothing the regulatory pathway for biosimilars his preferred price-control solutions. Thus, biopharma drug developers are increasingly trading on their own merits rather than on political machinations. We are most excited about the prospects for biotechs and emerging-market healthcare equities. Biotechs should continue their outperformance, driven by attractive valuations, good fundamentals, and news flow. Emerging-market healthcare equities continue to be quite attractive over the medium and long-term, driven by rapid growth in healthcare spending, although they might still face cyclical performance headwinds in the near-term relative to their emerging market peers.

Stephan Patten, CFA
Managing Director & Deputy Chief Investment Officer

THE GLOBAL DEMAND FOR HEALTHCARE AND THE THORNY MATTER OF DRUG PRICING

INTRODUCTION

Fueled by aging, the prevalence of chronic diseases, rising incomes, and innovation, global health expenditures will rise from USD7.6tn in 2014 to nearly USD9tn by 2020. Health systems around the world are already struggling to provide sustainable care. Global prescription-drug sales are forecast to grow by 6.5% annually from 2016 to 2022, surpassing the trillion USD mark. It is not a surprise that drug pricing continues to garner considerable attention and scrutiny, especially in the US, where drug prices are often more expensive than in other developed markets. This spotlight on drug pricing was amplified in 2016, thanks to the US presidential election. In most developed markets, health expenditures as a percentage of GDP have doubled in the last 40 years, increasing from about 5% of GDP to well over 10%. In the US, health expenditures account for more than 17% of GDP. This rate makes the US the healthcare market with the highest spending globally, both in relative and absolute terms, eclipsing the Organisation for Economic Co-operation and Development (OECD) 2016 estimated average of 9% of GDP. The global growth in health spending is projected to continue rising faster than GDP, leading to even higher shares of GDP spent on healthcare and higher health expenditures per capita. This finding is especially true for emerging markets, where current per-capita health expenditures remain a small fraction of those in developed markets (see Figure 1). India, for example, spends only 4.7% of GDP on healthcare, or about USD75 per capita. China, at 5.5% of GDP and USD420 per capita, is clearly higher but will require significant increases in spending over the coming years to meet rising demand. Emerging markets are seeing significant growth in affluence and the middle class. This modernization is leading to higher levels of urbanization and increasingly more sedentary lifestyles, which in turn are driving higher the incidence of obesity and chronic diseases, such as cardiovascular and metabolic diseases.

As we move forward, the rapidly rising demand for healthcare will amplify pressures on already-strained public-health systems and budgets. Between 1995 and 2014, the average percentage of government budgets allocated to healthcare rose from 14.2% to 19.1% in the US, Canada, Germany, France, the UK, and Switzerland (see Figure 2). The burden of satisfying this demand, while simultaneously ensuring sustainability, controlling costs, and maintaining access and quality, will require further investment in R&D and increased collaboration between the public and private sectors. The demand for innovative medicines and technology that better treat or even cure diseases will increase.

Of course, innovative treatments usually come with a hefty price tag. Payers struggling to keep up with rising costs are understandably hesitant about paying more. As a consequence, we are likely to see further discussions about drug pricing, especially in the US. A recent confluence of factors, including newly released high-priced drugs, a lack of pricing transparency, substantial price hikes for older drugs, a focus on nominal pricing (as opposed to net pricing), and politics during the last election (drug pricing is a convenient punching bag for politicians) were largely responsible for the latest round of scrutiny. Despite the fact that the growth in drug and total health expenditures has been comparable across most developed markets, representing only 10-15% of all health expenditures, pricing scrutiny is unlikely to fade in the medium term, even though drugs are not the dominant driver behind the rise in healthcare spending. Recognizing that self-generated solutions are preferable to those imposed by governmental or regulatory bodies, pharma manufacturers are increasingly turning to alternative payment models that better demonstrate the true value of their drugs over time. Equally encouraging, in several instances payers and pharma manufacturers are already working together to optimize value-based models and have realized these are not zero-sum games. The emerging cooperation between payers and pharma manufacturers in seeking mutually beneficial solutions is an important positive for the healthcare sector and a significant catalyst for even greater innovation.

What follows in this article is a review of the outlook for global healthcare demand and the drivers behind it; a discussion of the outlook for global drug spending and an exploration of the increasing use and benefits of alternative payment models.

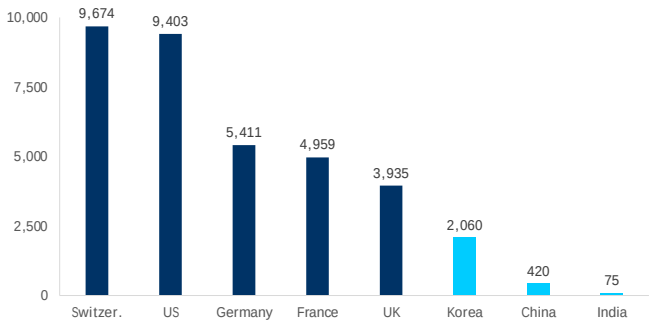

Figure 1: Health expenditures per capita (in nominal USD). Source: WHO Global Health Expenditure Database 2017 (2014 values).

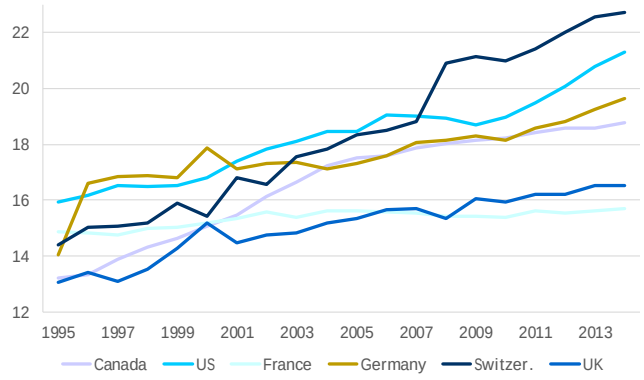

Figure 2: Government health expenditures as a percentage of total government expenditures. Source: WHO Global Health Expenditure Database 2017.

GLOBAL HEALTHCARE DEMAND AND DRIVERS

The primary drivers of healthcare demand are the aging population, the high prevalence of chronic diseases, rising incomes, and ongoing innovation. As these factors intensify further, health expenditures will grow, resulting in an even greater share of GDP for healthcare. In 2014, health expenditures amounted to USD7.6tn and consumed 9.9% of global GDP (see Figure 3). Experts expect to see the fastest growth rates in Asia-Pacific where a confluence of factors (highlighted below) are coming together to increase demand and spending. China alone is expected to approach USD900bn in health expenditures annually by 2020-21. Moreover, across most developing and emerging markets, the trend towards universal healthcare and increased coverage will continue, as governments aim to reduce out-of-pocket spending for individuals and expand access. Such efforts likely will encourage further cooperation with the private sector, while increasing public/private investment. For example, in recent years China has been increasingly promoting the use of public-private partnerships (PPPs) to help improve healthcare delivery. As a result, PPPs in China have become more commonplace in the domestic healthcare industry, especially in the case of hospitals. In coming years, this approach will solidify, given the Chinese government's 13th Five-Year Plan, which promotes building domestic medtech capacity, further increasing access, and using digital health to reduce the cost of, and increase the efficiency of, care.

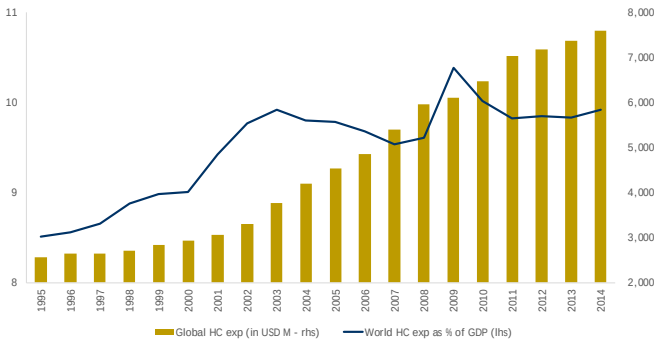

Figure 3: Global health expenses. Source: WHO Global Health Expenditure Database 2017.

According to the United Nations (UN), the number of people >60 years of age in the world has increased substantially in recent years and is projected to accelerate over the next several decades. A combination of increased longevity and shifting demographics (ie, larger cohorts of older people) means increasingly greater numbers of older people are living even longer. As a consequence, the number of individuals globally aged 60 or over is projected to grow by 56% (from 901m to 1.4bn) between 2015 and 2030 (see Figure 4). Compared with 2000, the over-60 category grew by 48% through 2015. About two-thirds of these individuals live in emerging/developing markets, and these groups are growing even faster than their peers in developed markets. The 2015 revision of the UN's World Population Prospects reports that by 2030, the over-60 group in developed markets will grow by 26% to reach 375m, while in emerging/developing markets the older population will reach 1bn, a growth rate of 71% (see Figure 5). As these groups increase, healthcare demand will mushroom, as older individuals consume on average three-to-four times more healthcare (including prescription drugs) than younger people. In the US, patients aged ≥65 received 39% of all prescriptions and accounted for 41% of the increase since 2011.

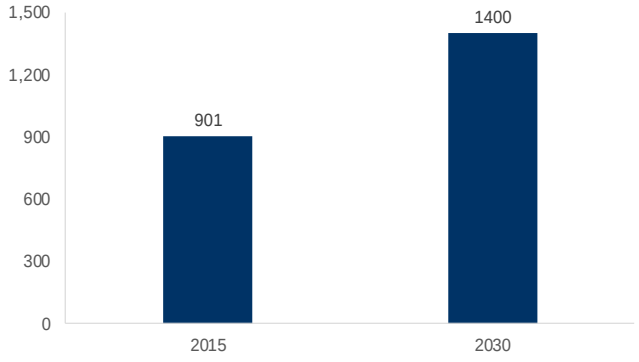

Figure 4: Global number of people over 60. Source: UN World Population Prospects: the 2015 Revision.

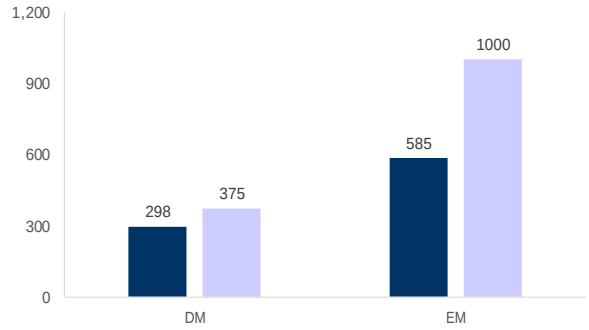

Figure 5: Geographically - number of people over 60. Source: UN World Population Prospects: the 2015 Revision.

At the same time, the global middle class is burgeoning. The Brooking's Institute estimates that about two-thirds of the world's population will be middle class by 2030. The increase will be especially pronounced in Asia-Pacific, which is forecasted to account for 88% of the growth (see Figure 6). This dramatic rise of the middle class in the emerging markets will have marked effects on healthcare demand. As incomes rise, especially from low levels (as is the case in most emerging markets), healthcare demand typically expands at a much faster pace than it does at higher income levels. The reason is that healthcare is a "superior good," which, in economic terms, is one that comprises a larger share of consumption as income rises. Applied to emerging markets, the concept means that for every additional dollar increase in income, an individual will spend relatively larger amounts on healthcare than they did before the increase. In other words, healthcare spending is a priority.

In addition, along with a growing middle class, evidence of increasing urbanisation and sedentary lifestyles is apparent. These features of modern life, in turn, are contributing to the rising incidence of obesity and chronic diseases such as heart disease and diabetes. The World Health Organization calculated that in 2001, chronic diseases represented 46% of the global disease burden – by 2020 this is projected to rise to 57%. In fact, the growth is occurring faster in emerging/developing markets today than it did in developed markets 50 years ago. For example,

cardiovascular disease today affects more people in India and China than in all developed markets combined. The number of people with diabetes worldwide is estimated to spike from 387m in 2016 to 592m by 2035, according to the International Diabetes Federation. China and India account for over 160m patients today.

Finally, and especially in developed markets, innovative treatments and medical progress will almost always drive up the cost of healthcare. Keep in mind, though, innovative treatments typically also provide indirect benefits that have substantial positive economic implications. Unfortunately, these indirect

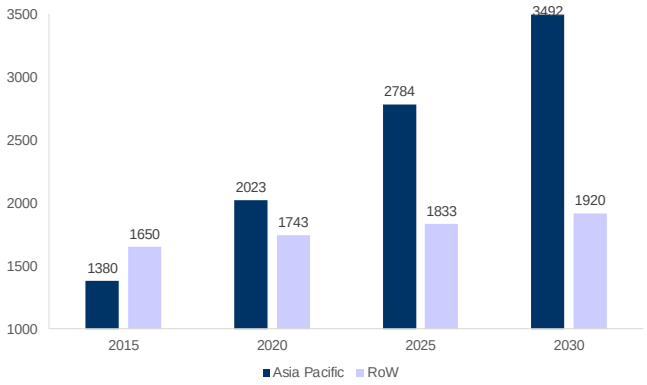

Figure 6: Number of global middle class (m). Source: Brookings Institute Global Economy & Development Working Paper 100 – February 2017.

benefits are not always immediately obvious, especially when considering the high upfront cost of treatment. Therefore, when evaluating new treatments, their costs should not be assessed in isolation. In other words, one must account for both direct and indirect costs. (Direct costs are typically the cost of treatment, whereas indirect costs can include such things as the loss of work for the patient, the fall in productivity, sick days, and the time friends and family spend taking care of the patient.) A 2013 study reported in Lancet Oncology estimated that the, direct and indirect costs of cancer in Europe in 2009 were EUR126bn, of which the direct costs of treatment were EUR51bn, while the indirect costs due to productivity losses amounted to EUR42.6bn, costs for lost working days were EUR9.4bn, and informal care costs were EUR23.2bn.

The increase in life expectancy from innovative treatments and its associated effects on economic growth must be considered as well in determining value. In the US, life-expectancy gains between 1970 and 2000 were estimated to be worth USD95tn. Consider, too, a 10% reduction in mortality due to cardiovascular diseases and diabetes is estimated to be worth a total of USD10tn in the US. Furthermore, a 2008 report from the UK found that public investments in cardiovascular research from 1975 to 1992 yielded returns of about 39%. In economic terms, this means that for each GBP invested in public cardiovascular research, the UK earned GBP 0.39 annually in perpetuity in economic benefits. Somewhat paradoxically, part of the solution to rising healthcare demand (and expenditures) is further (expensive) innovation, which will spur even further (expensive) innovation. This approach will help ensure that the potentially enormous indirect economic costs of disease are minimized.

OUTLOOK FOR GLOBAL DRUG SPENDING

From 2011 to 2016, global prescription-drug sales remained relatively flat, increasing from USD732bn to USD768bn (see Figure 7). In real terms, sales declined, particularly in developed markets. According to the OECD, between 2009 and 2014, member countries experienced sales reductions of 1.1% annually in real terms. This decline was due largely to a combination of patent expirations, pro-generic policies, and greater price concessions offered by manufacturers. However, over the past 18 months, these factors have started to abate. The result has been increased pharmaceutical sales. Global prescription drug sales are forecast to grow 6.5% annually between 2017 to 2022, surpassing the trillion USD mark and outpacing overall global health spending. The acceleration will be driven by a slowdown in patent expiries and further development of innovative therapies, particularly in the oncology and orphan-drugs categories, with a modest impact from biosimilars.

A biosimilar regulatory pathway in the US was created in 2010, but the uptake of these generics has been relatively lukewarm thus far. There are two main reasons for this. The first is cost: unlike a traditional chemical generic, which typically sells for 40-50% less than the original, biosimilar discounts have been much less generous at 15-30% because of their higher development costs. The second is that biosimilars are often not viewed as equivalent to their branded counterparts. Traditional chemical generics are exact copies of the original drug. In contrast, biosimilars are complex molecules made in living organisms such as cells, and therefore are highly "similar" but never exact duplicates of the original drug. Payers and physicians will need to become more confident that biosimilars yield efficacy and safety effects that are close enough to the original branded versions before more broadly embracing them. This process is expected to be slow and gradual, but over time, biosimilars will capture a significant share of the biologics market outside the patent-protection corral. In Europe, for example, where a biosimilar pathway was created much earlier, the uptake of biosimilars has been far more robust. In this respect, it is encouraging to note that global R&D will continue growing steadily, reaching USD181bn by 2022, up from USD157bn in 2017.

In the near term, orphan-disease drugs are expected to add about a third of the growth in sales (USD95bn) through 2022, while oncology will continue as the therapeutic category with the highest total sales (USD192bn in 2022). During this time frame, nearly half of all drug spending in the US will be for specialty medicines. Furthermore, a favorable regulatory environment in the US and the appointment of Scott Gottlieb, MD, a proponent of reduced regulation, as the new FDA commissioner, should speed the approval of new therapies and contribute to higher spending. Dr. Gottlieb is also a proponent of increased competition for generic drugs and wants the FDA to focus on bringing more low-cost generic drugs to the market more rapidly.

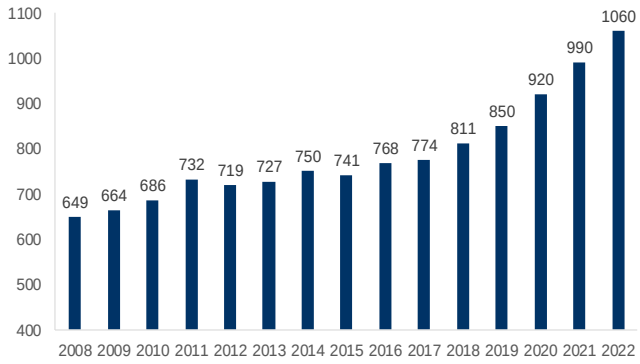

Figure 7: Worldwide total prescription drug sales (USD bn). Source: EvaluatePharma World Preview 2017 Outlook to 2022.

OUTLOOK FOR DRUG PRICING AND USE OF ALTERNATIVE PAYMENT MODELS

Having largely cleared the patent cliff for now, pharma's most significant headwind through the medium term is pricing scrutiny and regulation. Drug pricing, especially in the US where pharmacotherapies often cost more than in other developed markets, is garnering considerable attention. The spotlight on pricing was sparked in 2015 by the media-grabbing headlines generated from a 5,000% price hike for daraprim, a drug approved in 1953; the following year, the scandal became a hot topic during the US presidential election. Approvals of innovative, life-saving, but often-expensive therapies also have caused a public backlash. Examples include Gilead's hepatitis C drug sofosbuvir (Solvadi), approved late in 2013, which launched at an initial gross price of USD90k per treatment (net price about half of that). More recently, Regeneron and Sanofi launched Dupixent for the treatment of atopic dermatitis, an inflammatory skin condition with a significant impact on quality of life. Although Dupixent's initial gross price is about USD37k, this and other innovative drugs that bring clear value to patients continue to benefit from robust pricing and adoption. The strong uptake of Dupixent has been a surprise, with payers providing access for appropriate patients. Consensus estimates are now

approaching USD1bn in revenues in 2018, the drug's first full year on the market.

Despite some of these high list prices (net prices are usually much lower), drug costs are not the main driver of total health expenditures. Over the past two decades, drug expenditures have closely tracked with total health expenditures across many developed markets and today comprise only 10-15% of the whole (see Figure 8). In the US in 2015, for example, according to the OECD, expenditures on drugs made up only 12.2% of total health expenditures[1]. In addition, the growth of net pricing for branded drugs grew only 3.5% in 2016 (see Figure 9). Although this figure is higher than the 2.8% in 2015, it is considerably lower than the increases from 2011 to 2014. Looking forward, the QuitilesIMS Institute is forecasting modest growth of 2-5% for net drug pricing in the US through 2021. However, even with these relatively benign figures, drug pricing continues to garner increased scrutiny. This is understandable. In a world of rising healthcare demand and increasingly-strained healthcare budgets, it would be naïve for pharma companies and investors to imagine pressure for pricing reform will recede going forward, even when price increases for drug therapies are small. In the face of these pressures, pharma companies are under increasing pressure to justify the price of their products. Fortunately, the industry realizes it must adapt to new realities and is already taking steps to shift the discussion accordingly. One such step is a focus on alternative payment models, discussed below.

The current pricing model for drugs (ie, high list prices followed by undisclosed negotiated discounts based on the payer, geography, and technological assessment) is under pressure. Clearly, transparency must improve. However, in a market in which scrutiny is increasing and budgets are tighter, pharmas must also better demonstrate the value of their products. They can do so by shifting the focus to alternative payment models, especially for high-priced specialty drugs. One such model is value-based pricing (VBP), which is generally

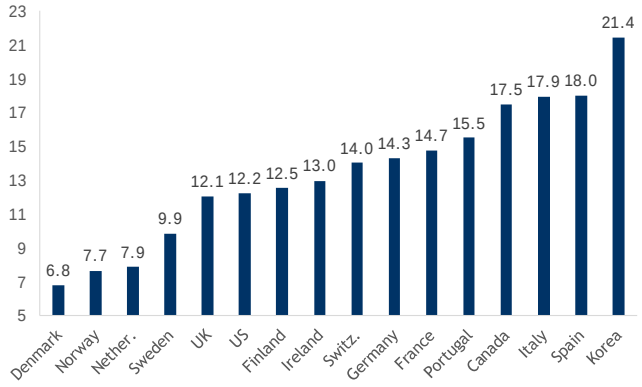

Figure 8: Pharma expenditures (% of total health expenditures). Source: OECD Health at a Glance 2015.

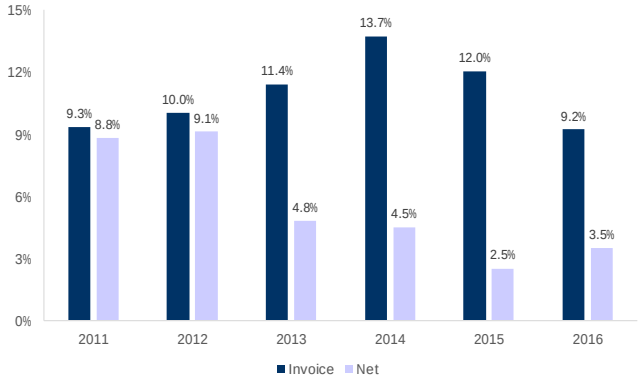

Figure 9: Growth in invoice and net pricing for branded drugs. Source: QuintilesIMS Medicines Use and Spending in the US, May 2017.

defined as "determining drug price by its measured benefits, during and after clinical trials." Value-based approaches can include concepts such as "pay-for-performance" or "outcomes-based" pricing. Methods used to determine VBP should be transparent, reproducible, and data driven. To capture the complete set of benefits, pharma companies need to collect data outside the clinical-trial setting to demonstrate value in the real world. For example, Novartis plans to use outcomes-based pricing for its very recently approved novel anticancer CAR-T therapy Kymriah, charging the Centers for Medicare & Medicaid Services (CMS), public payer, only for those patients

[1] Drugs administered in hospitals and other health care settings are excluded

that respond to the drug within the first month of treatment.

In essence, VBP helps better align the interests of manufacturers and payers. It does so by recognising the holistic set of drug benefits (or lack thereof), thus allowing a more accurate pricing for different and complex treatments. In so doing, VBP allows for a more equitable sharing of risk between manufacturers and payers, and helps ensure that innovative life-saving treatments will continue receiving premium pricing. Although we are still in its initial stages, VBP is already gaining traction, as several pharma companies are experimenting with different approaches.

Similar to the Novartis/CMS example above, drug companies are also working with private payers. In October 2016, Merck and Aetna announced a value-based contract, in which rebates provided by Merck to Aetna on the type-2 diabetes drugs Januvia and Janumet will depend in part on those products' ability to help Aetna patients achieve or maintain treatment objectives. Merck will also collaborate with Optum (the health-services business of United Health) to develop and simulate the performance of reimbursement models in which drug payment is aligned more closely with health outcomes. A third example is Amgen's contract with Harvard Pilgrim. Terms of the agreement require Amgen to provide pay-for-performance rebates for its cholesterol lowering drug Repatha if the reduction in LDL levels for Harvard Pilgrim members is less than what was observed during clinical trials. As the number of high-priced specialty drugs coming to market in the coming years is expected to rise, the pressure on pharma to differentiate new drugs from old ones will increase. Value-based pricing allows pharma to better demonstrate this differentiation. From a structural perspective, VBP is positive for the industry, as more accurate and transparent pricing will boost the long-term sustainability of the industry.

To be sure, legitimate questions surround drug pricing, especially concerning transparency and price increases for older drugs. However, using drugs, even new expensive ones, to treat or modify a disease is one of the most effective solutions in healthcare. For example, prior to Gilead's cure for hepatis C, the typical treatment cost USD50k and required injections for up to 1 year. Tolerability issues were common, and the treatment worked in only one of three people. Today, nearly all patients can be cured, with a much more tolerable regimen, and an effective cost per patient of about USD50k. In other words, the cost-per-cure used to be nearly three times as high. Similar points can be made for the introduction of protease inhibitors more than 20 years ago, which turned HIV into a manageable chronic condition, or statins, which have markedly reduced the rate of heart attacks and hospitalizations. Drugs hold significant potential to slow or reduce future indirect costs from chronic diseases and aging. Unfortunately, this message sometimes gets lost in the noise and controversy of drug pricing. Used effectively, VBP can clarify the true benefit of pharmaceutical products, while acting as a catalyst for further innovative therapies that generate even greater value from healthcare spending.

Value-based-pricing is not without its challenges. Accurately demonstrating the long-term value of a drug in the present is easier said than done, as many of the benefits will occur only in the future. For example, taking a prescribed drug today can prevent a lengthy hospitalization years later. Kenneth Frazier, the CEO of Merck, described this problem best at a forum sponsored by the Department of Health and Human Services in November 2015, when he said, "the value of a drug is like an annuity – the issue for the health system is that the return on investment needs to be made up front." Moreover, in cases with private payers, even if the future value of a benefit can be accurately measured right now, it is still unclear who should pay for the treatment today, as the future benefit may accrue to an entirely different payer if the patient changes insurers. (Of course, this is not an issue with centralized reimbursement, such as with Medicare or Medicaid.)

Furthermore, the length of time in which the benefits accrue is also a key factor in defining value, and the period of activity varies from drug to drug and

indication to indication. Despite these issues, pricing by value is a step in the right direction. Value-based pricing can help pharma companies better demonstrate the long-term benefits of their drugs, while at the same time promoting and supporting innovation. The pressures facing pharma companies and payers are not likely to dissipate; to the extent that these two entities can cooperate and identify mutually beneficial arrangements, all stakeholders, including investors, will benefit.

CONCLUSION

Looking forward, our outlook for the healthcare sector remains quite encouraging. Although the sector is not immune from the ups and downs of cyclical volatility and macro headwinds, the underlying secular demand-drivers ensure healthcare will continue its current expansion while outpacing global growth over the near and medium term. However, the strains imposed on health systems and budgets from rapidly rising incidences of chronic disease and demographics will increase scrutiny on drug prices, especially in the US. This is particularly true as the number of high-priced specialty drugs coming to market in the coming years is expected to rise. Given this, biosimilars will capture a significant share of the biologics market without patent protection, but only gradually over time.

At the same time, pharma companies recognize the challenges ahead and are adapting quickly. The price of an innovative treatment cannot be evaluated in isolation. There are direct costs that are known today but there are also indirect economic costs related to a disease (including poor or ineffective treatment), some of which are not always obvious. Alternative payment models allow pharma manufacturers to better capture the holistic set of benefits of a treatment while linking payers' drug costs to performance. Many pharma manufacturers are already cooperating with payers to identify mutually beneficial arrangements. Such partnerships will further benefit innovative drugs that bring clear value to patients, as these drugs will continue to benefit from robust pricing and adoption.

In contrast, products with generic or even branded alternatives, such as hepatitis C drugs or insulins, which are viewed as equal or close enough by doctors and payers will be under increasing price pressure. For investors with medium- to long-term horizons, the safest haven remains innovation. Only truly innovative products, backed up by alternative pricing models and pharmacoeconomic data, will be able to sustain an elevated level of pricing.

Finally, although much of our discussion here has dealt with the effect of drugs on healthcare spending, we should not ignore other healthcare cost-bending issues. Although these initiatives fall outside the scope of this article, they range from the modification of the organization of care from acute-focused to chronic-care management, the need for preventive-care initiatives that draw on the experiences of the successful anti-smoking campaigns, the reduction of defensive litigation-driven medicine, ethical issues including the final-year-of-life care, and the treatment of the terminally ill.

Vasilios Tsimiklis, CFA
Economist

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SECTORAL ASSET MANAGEMENT

NEWSLETTER

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Contact Information
Phone: +1 514 849 8777 ext. 223 **Fax:** +1 514 849 6777
1010 Sherbrooke St. West, Suite 1610, Montreal QC H3A 2R7, Canada
www.sectoral.com