

*Pharma's future has never looked more promising – or more ominous. Major scientific, technological and socioeconomic changes will revive the industry's fortunes in another decade, but capitalising on these trends will entail making crucial decisions first*

# ***From vision to decision***

## **Pharma 2020**



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*Many of the conditions that will determine what happens in 2020 are already in place. But does that mean pharma's fate is sealed? Far from it!*

## Introduction

Major scientific and technological advances, coupled with sociodemographic changes, increasing demand for medicines and trade liberalisation, will revive pharma's fortunes in another 10 years and deliver dramatic improvements in patient care. But if the industry is to prosper in the future, it must first make sure it *has* a future.

We've outlined our vision of what lies ahead in previous Pharma 2020 papers. The theme of our latest paper is decisions: the decisions pharma companies will need to make between now and the end of the decade to capitalise on the opportunities the next decade holds.

We believe the industry faces three fundamental challenges:

- **Rising customer expectations**

The commercial environment is getting harsher. Healthcare payers are imposing new cost constraints on providers and are scrutinising the value of medicines more carefully. They want new therapies that are clinically and economically better than the existing alternatives, together with hard, real-world outcomes data to back any claims about a medicine's superiority.

- **Poor scientific productivity**

Pharma's output has flatlined for the past decade. Yet the processes it uses to discover and develop new products remain much the same. So there's little reason to think its productivity will suddenly soar.

- **Cultural sclerosis**

The prevailing management culture, mental models and strategies on which the industry relies are the same ones it's traditionally relied on, even though they've been eclipsed by new ways of doing business.

Of course, many of the conditions that will determine what happens in 2020 are already in place. Most, if not all, of the products that will be launched by then are already in the pipeline. Similarly, many of the senior executives who will be at the helm have already been earmarked for high office or appointed. And changing the culture of a large organisation can take years.

But does that mean pharma's fate is sealed? Far from it!

We believe there are various things companies can do both to increase their chances of reaching 2020 and to ready themselves for more favourable conditions thereafter. In the following pages, we'll look at how to maximise the value of new and existing medicines, develop business models for the growth markets, improve scientific productivity and reinvigorate the corporate culture. We'll focus on the areas where the most important decisions must be made.

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# The best of times, the worst of times

*“It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity...”*

Charles Dickens

The opening words to Charles Dickens’s novel *A Tale of Two Cities* perfectly encapsulate the situation pharma finds itself in right now. The outlook has never seemed more promising – or more ominous.

## **The best of times**

Let’s start with the good news: a rapidly strengthening scientific base, growing demand for medicines and the removal of former impediments to free trade.

## **A strengthening scientific base**

The scientific foundation on which pharma rests is improving exponentially, thanks to massive increases in processing power; advances in genetics and genomics; and new data management tools. For the last half-century, computers have been doubling in performance and capacity every 18 months. This revolution has transformed biomedical research. In 2001, it cost US\$95 million to read an entire human genome.<sup>1</sup> Today, two leading manufacturers are developing machines that can do so for as little as \$1,000 – in a matter of hours.<sup>2</sup>

Inexpensive gene sequencing will let doctors diagnose and treat patients based on information about their individual genomes. And, by 2020, genetic testing will be part of mainstream medical practice in some countries.

Technological developments have also paved the way for electronic medical record (EMR) systems that capture vast quantities of outcomes data. Numerous healthcare providers in the mature and growth markets alike are building the necessary infrastructure. Meanwhile, with sophisticated data sharing, processing and mining techniques, scientists can easily collaborate and make better sense of what they see.

In effect, two changes are taking place concurrently. Our technologies for collecting biological data are improving by many orders of magnitude. Our technologies for synthesising and analysing that data are also becoming much cheaper and more efficient. Together, these advances will help pharma break through some of the barriers that have previously held it back (see box, **Big data’s big dividends**).<sup>3</sup>

The progress we’ve already made in understanding breast cancer is a quintessential example. For many years scientists thought breast cancer was a single disease. Then, in 1990, researchers discovered the first gene to be associated with hereditary breast cancer. Now they’ve succeeded in teasing apart differences in DNA to identify 10 subtypes, each with a unique genetic fingerprint (see **Figure 1**).<sup>4</sup>

## Big data's big dividends

One industry marketer recently remarked: "Every patient experience now generates rivers of data which, if pooled intelligently, can trace a detailed portrait of a patient's health and, when aggregated with other patient data streams, can coalesce into deep reservoirs of knowledge about entire disease states and patient populations."

That's the promise of 'big data', and the deluge is increasing all the time. We create about 2.5 million terabytes of data a day. Pervasive monitoring and 'anywhere interface' technologies that turn a rigid surface into an interface with an electronic device will make it easier still to collect huge quantities of data on how patients respond to different treatments. Combine that with ubiquitous gene sequencing and the *why* will begin to emerge.

Big data's potential in pharmaceutical R&D is enormous. Armed with vast amounts of biological data and the tools to process it – cutting-edge analytics, streaming, massively parallel processing and domain-specific access

and query technologies – the industry will be able to develop more effective, personalised medicines. It will also be able to shift the focus from reaction to prevention.

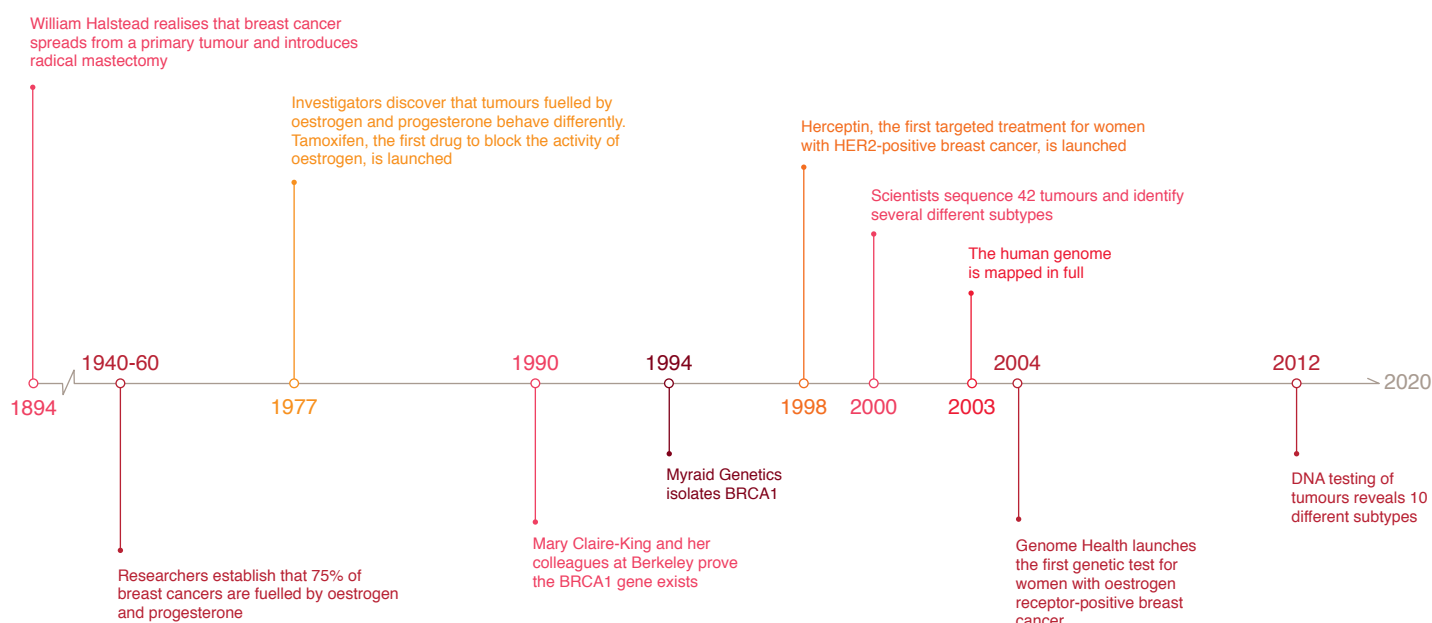
Several companies have already started exploiting this trend. Genomic research firm CardioDX analysed more than 100 million gene samples to identify the 23 primary predictive genes for coronary artery disease. It's now developed a test that can identify coronary artery disease in its earliest stages.

Meanwhile, US data and lab testing service company Medivo is mining laboratory records for patient and disease insights. It's consolidated data from more than 50 million patients in a simple, easy-to-use system that helps doctors see the patterns in a patient's disease, as well as the patient's response to a given treatment. And Sanofi recently tied up with pharmacy benefits manager Medco Health Solutions to get 'real-world' insights into how different therapies compare when used in a normal clinical setting.

This leap in our knowledge has transformed the prognosis for women with breast cancer. The five-year relative survival rate has soared from 63% in the early 1960s to 90%, and most of the improvement has taken place in the last two decades.<sup>5</sup>

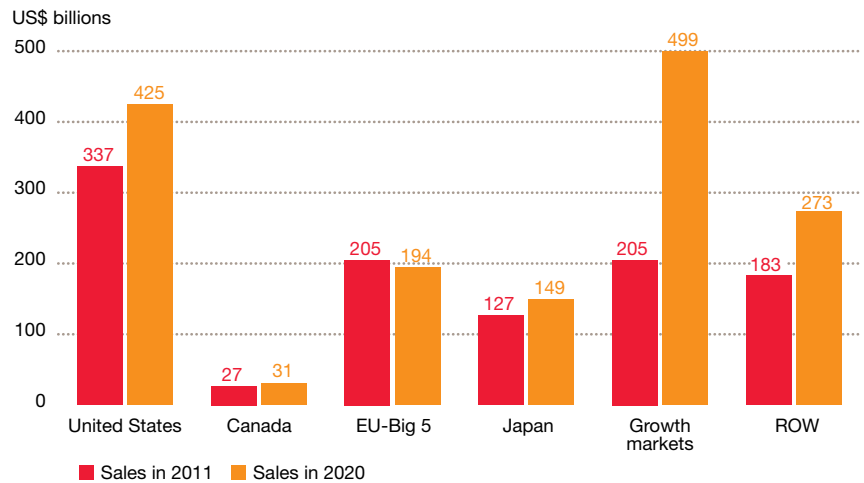
A better understanding of disease has produced new medicines, diagnostics and lines of research. Take Benlysta, one of the first treatments to come from mapping the human genome and the first new therapy for lupus in 50 years. The researchers who discovered Benlysta trawled through a library of human DNA hunting for genes whose function wasn't known, but whose characteristics suggested they were linked to lupus – ignoring the conventional wisdom that you couldn't use a gene to find a new medicine without understanding what the gene did.<sup>6</sup>

**Figure 1 Our understanding of breast cancer is being transformed**



Source: PwC

**Figure 2 The global pharmaceutical market could be worth nearly \$1.6 trillion by 2020**



Source: Business Monitor International

Notes: (1). All sales are expressed in US dollars at constant exchange rates; (2). The growth markets include, in descending order of size, China, Brazil, Russia, India, Mexico, Turkey, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan and Vietnam. (3) EU-Big 5 is France, Germany, Italy, Spain and United Kingdom.

*While there's still a lot more to learn about the human body, medical researchers have made huge strides in the past few years – and even better things lie ahead*

Genomics isn't the only field in which we've made great headway. Several stem cell therapies have already reached the market and Canadian regulators recently approved the first stem cell medicine manufactured for off-the-shelf use. Developed by Osiris Therapeutics, Prochymal is a treatment for acute graft-versus-host disease, using mesenchymal stem cells derived from the bone marrow of healthy adult donors.<sup>7</sup>

With disciplines like epigenetics, we're also beginning to understand the impact of heritable biological elements that aren't directly encoded in our DNA. And with concepts like network medicine, we're developing the means to understand the molecular relationships between apparently distinct 'pathophenotypes' (see box, **Working out our wiring**).<sup>8</sup>

So, while there's still a lot more to learn about the human body, medical researchers have made huge strides in the past few years – and even better things lie ahead. By 2020, the financial and intellectual investment of the last 10 years should be starting to yield big rewards.

## Working out our wiring

Most diseases stem from disturbances in the way the molecular components in a human cell interact, rather than a single genetic abnormality. This intracellular network is immensely complex. It has more than 100,000 different components – including about 25,000 protein-encoding genes, 1,000 metabolites and an as yet unknown number of distinct proteins and functional RNA molecules – all of which function interdependently.

With network medicine, researchers aim to create 'wiring diagrams' of the cells whose breakdown causes a particular disease – much as vehicle manufacturers create wiring diagrams of a car's electronics, so that a mechanic can fix any faults. Such diagrams will ultimately help pharma develop treatments that can 'fix' the underlying components of disease, as distinct from its symptoms.



## Escalating demand for medicines

That's not all. The global pharmaceutical market is growing steadily, with sales reaching \$1.08 trillion in 2011 – a year-on-year increase of 7.8%. The mature economies proved very sluggish, but the growth economies were another matter. Sales in the BRIC countries (Brazil, China, India and Russia) rose by 22.6%, while sales in the other 13 growth countries (the 'fast followers', as we call them) rose by 7.2%.<sup>9</sup>

If this pattern continues, the market for medicines could be worth nearly \$1.6 trillion by 2020 (see Figure 2).<sup>10</sup> Indeed, it could be worth even more. Demand for pharma's products is rising dramatically, as the global population increases, ages and becomes more sedentary. In 2010, there were an estimated 6.9 billion people. By 2020, there will be more than 7.6 billion.<sup>11</sup> And, if present trends are any guide, many of them will have health problems.

More than 30% of the population won't get enough physical exercise;<sup>12</sup> more than 20% will be overweight or obese;<sup>13</sup> and more than 13% will be 60 or older.<sup>14</sup> These are all factors that increase the risk of developing heart disease, diabetes and cancer. The number of people reaching really old age is also mounting, and the prevalence of dementia doubles every five years after the age of 65.<sup>15</sup> Hence the World Health Organisation's prediction that, by 2020, non-communicable diseases will account for 44 million deaths a year, 15% more than in 2010.<sup>16</sup>

The global incidence of infectious diseases is increasing as well. That's partly because some diseases have become drug-resistant. But over the past few decades new pathogens such as HIV and MRSA have emerged. And old scourges like pertussis have reared their heads again. In fact, the number of cases of pertussis in the US is now higher than at any time since the early 1970s.<sup>17</sup>

Meanwhile, many of the growth economies are improving access to healthcare. Brazil's introducing mobile clinics for rural communities.<sup>18</sup> China's on track with a US\$125 billion programme to extend health insurance cover to more than 90% of the population by the end of 2012. Mexico has just completed an

eight-year drive to provide universal coverage.<sup>19</sup> And India's National Rural Health Mission has achieved considerable progress in the 6½ years since it was launched, although much still remains to be done.<sup>20</sup>

In short, there are more people – and more sick or elderly people – in the world today than ever before. More people have access to affordable healthcare than ever before. And, by 2020, access to healthcare may well be regarded everywhere as a basic human right.

## Trade liberalisation

Many of the historical barriers to free trade have also been removed, bringing a period of unprecedented growth in global trade. Between 2001 and 2011, the total value of merchandise export flows (excluding services) soared from \$6.2 trillion to \$18.2 trillion in current US dollars.<sup>21</sup>

In some respects, then, pharma's never had it so good. The tools to develop remarkable new medicines are materialising, demand for its products is escalating and trade is getting easier.

## The worst of times

Yet pharma also faces some enormous obstacles. Innovation has declined, the regulations are becoming more onerous and market conditions are getting harsher, as healthcare costs everywhere keep rising.

## Poor scientific productivity

Take the vexed issue of the industry's scientific productivity. Although the number of new medicines reaching the market picked up in 2011, pharma's annual output has effectively flatlined for the past 10 years (see Figure 3).

Developing new medicines is becoming an increasingly expensive business, too, although precisely how expensive is the subject of fierce debate. In 2006, the Tufts Center for the Study of Drug Development put average costs per molecule at \$1.24-1.32 billion.<sup>22</sup> Various commentators have since challenged these figures, claiming that the real cost is anything from \$75 million to \$4 billion, although most people lean towards the higher end of the range.<sup>23</sup>

## Tighter regulation

The regulatory environment is simultaneously getting more rigorous. The European Medicines Agency (EMA) recently introduced a new, three-pronged approach to the management of adverse reactions.<sup>24</sup> And the Food and Drug Administration (FDA) is building an active surveillance system called Sentinel to oversee the safety of all medicines on the US market.<sup>25</sup>

**Figure 3 Pharma's scientific productivity has flatlined for a full decade**



Source: EvaluatePharma, 'World Preview 2018' (June 2012)

*The market's getting much tougher, with tighter regulation, harsher price controls and greater government scrutiny, all trends that will grow*

Regulators around the globe are also collaborating more closely, so a product that's rejected in one region is more likely to be rejected in others. In late 2010, for example, the EMA pulled diabetes drug Avandia, while the FDA imposed strict restrictions on its use, and the two agencies swapped notes before reaching a decision.<sup>26</sup>

#### **More difficult market conditions**

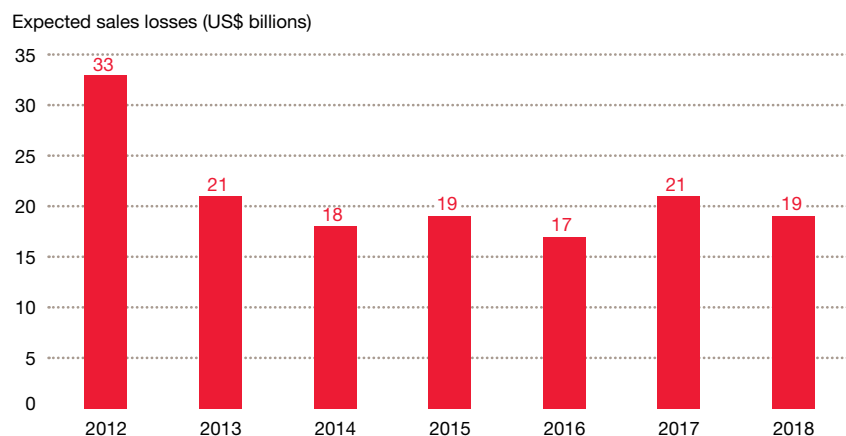
Things are even tougher on the marketing and sales front. The 'patent cliff' is one major factor; between 2012 and 2018, generic erosion will wipe about \$148 billion off pharma's revenues (see Figure 4). Harsher price controls are another. Most of the mature economies already use direct and indirect price controls, as we noted in 'Pharma 2020: Taxing times ahead'.<sup>27</sup> But conditions are getting more difficult in the growth economies as well.

Some instances? Russia started enforcing mark-up limits on imported medicines in April 2010.<sup>28</sup> India announced plans to control the prices of 400 essential products in November 2011.<sup>29</sup> And Turkey has upped the discount on treatments reimbursed through its social security system.<sup>30</sup>

Many governments are also clamping down on dubious promotional practices. The US authorities have been particularly active. Between 2000 and mid-2012, the industry paid more than \$30 billion to settle 226 violations, including off-label marketing and overcharging of taxpayer-funded health programmes like Medicaid – and the penalties have been steadily escalating (see Figure 5).<sup>31</sup>

The US is by no means alone, though; 24 countries have now introduced laws or codes of conduct requiring that pharma companies disclose any interactions with healthcare professionals who are also customers.<sup>32</sup> And a recent analysis of the Securities and Exchange filings made by the top companies shows that eight face charges of corruption in foreign markets.<sup>33</sup>

**Figure 4 Big Pharma's earnings are tumbling over the patent cliff**



Sources: EvaluatePharma, 'World Preview 2018' (June 2012)

Note: Estimate of losses based on top 500 pharmaceutical and biotech companies.



As the governments of the growth economies invest more public funds in healthcare, the regulators become more proactive and patients become more demanding, pharma will come under even closer scrutiny. The way it conducts clinical trials, the partnerships it forms with payers and providers, its tendering and contracting strategies, pricing agreements and digital marketing, how it handles patient safety – all will attract more attention.

### Soaring healthcare costs

Yet, serious as these issues are, there's arguably an even bigger hurdle facing pharma: namely, the rising healthcare bill. Healthcare expenditure as a percentage of gross domestic product (GDP) is climbing in countries in every income bracket, and it's climbing most steeply in the mature markets where the industry has historically made most of its money (see Figure 6).

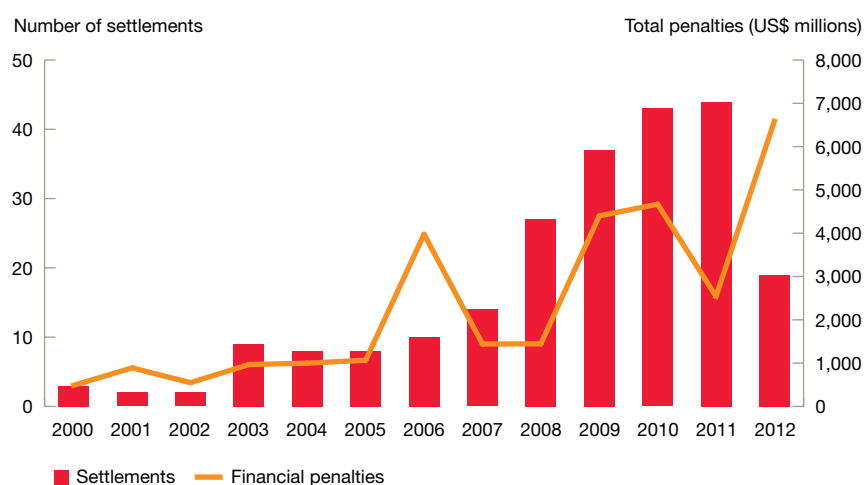
This trend is unsustainable, but the only way to reverse it is by altering our concept of healthcare itself. Instead of focusing on the treatment of disease, we need to focus on curing – or, better still, preventing – it. And pharma has a crucial role to play in making the transition.

### Two key challenges

So where does the industry now stand? It's proved remarkably resilient, given the many problems it's dealing with. But, in essence, it faces two overarching challenges. Tomorrow's challenge is to develop new medicines that can prevent or cure currently incurable diseases. Today's challenge is to get to tomorrow – and that's a tall order in itself.

Fortunately, there are a number of steps senior executives can take to help their companies reach 2020 and ready them for the opportunities the next decade brings. But some of these steps will entail making very difficult decisions.

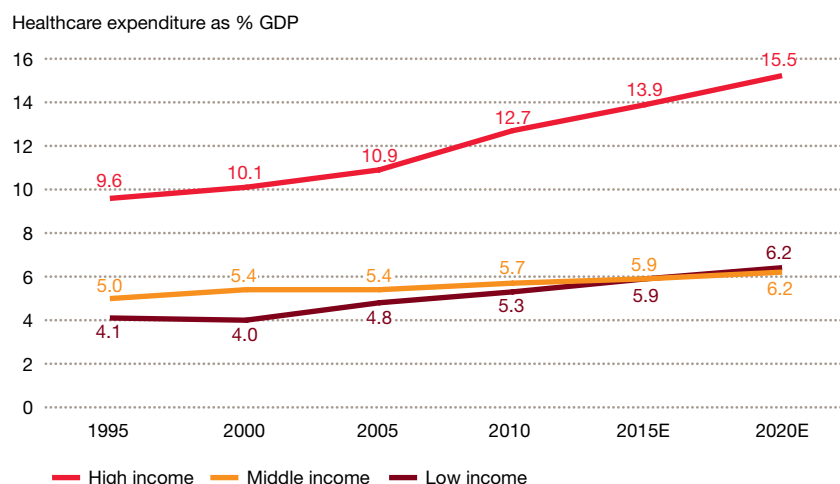
**Figure 5 Pharma's incurring bigger and more frequent financial penalties in the US**



Source: Public Citizen

Note: Figures for 2012 cover period up to 18 July 2012.

**Figure 6 Healthcare's consuming a larger share of GDP in rich and poor countries alike**



Source: World Bank and PwC analysis

# The mature markets: Maximising the molecule

*“A thing is worth only as much as it can be sold for.”*

Publilius Syrus

There are big differences within the mature markets and over the past few years the differences have been growing. In this chapter we'll focus on pharma's prospects in Canada, France, Germany, Japan, the UK and US, and the decisions involved in maximising returns in these markets. We'll also touch on the situation in Greece, Ireland, Italy, Portugal and Spain (the GIIPS economies), where the issue is not so much how to increase sales as how to reconcile conflicting ethical and commercial responsibilities.

Collectively, Canada, France, Germany, Japan, the UK and US still generate 59% of the industry's total revenues (see **Figure 1**). But they're becoming more difficult places in which to prosper for one key reason. They're all demanding better outcomes as a precondition for paying for new medicines – a change we expect to result in new regulatory requirements by 2020.

## Crushing burdens

Financial pressures have played a part in hardening healthcare payers' policies. The mature markets have experienced enormous turmoil in the past five years – and though fiscal stimuli have produced a fragile recovery in the strongest economies, the situation is still dire in the GIIPS countries (see **Pharmageddon? on page 16**).

Crushing demographic and epidemiological factors have compounded these economic woes. More than three-quarters of all Americans are overweight or obese. Obesity is also a big problem in the rest of the mature markets, with the exception of Japan. But Japan has other troubles; by 2020, 34% of the population will be 60 or older. (See **our list of key national indicators on page 48**.)

Age and obesity are both associated with more illness and, sure enough, the prevalence of diseases like diabetes has soared.<sup>34</sup> The US has been hit especially hard. Some 11.3% of adults – rising to 26.9% of those aged 65-plus – have diabetes. Another 35% – rising to 50% of those aged 65-plus – have prediabetes.<sup>35</sup> In fact, diabetes now accounts for about one in every 10 healthcare dollars.<sup>36</sup> But the US isn't alone. The prevalence of diabetes has been creeping up in Europe, too.<sup>37</sup>

Consumer power is increasing the challenge. Patients in the mature economies have higher expectations than ever before. They want medicines for conditions previous generations simply endured. They want medicines that work for them. And they only have to turn to the Internet to find out what's available – or, indeed, to broadcast their opinions: 16% of US adults in one recent survey said they post reviews of the treatments they take on social media sites.<sup>38</sup>

These financial, demographic and social pressures are driving up healthcare expenditure dramatically. So it's easy to see why healthcare payers and providers in the mature countries are doing all they can to curb the bill. Their resources are finite – and they're particularly keen to address the so-called HONDAs (Hypertensive, Obese, Non-compliant, Diabetic Asthmatics) who account for an estimated 70% of healthcare costs.<sup>39</sup>

## Affordable care and its implications

Consider the recent healthcare reforms in the US. The Affordable Care Act aims to improve access to healthcare by bringing another 30 million citizens within the insurance net.<sup>40</sup> It also aims, among other things, to reduce out-of-pocket expenses on pharmaceuticals, which should enhance patient compliance.

The act includes various provisions intended to offset the cost of the changes, some of which will fall on pharma's shoulders. We estimate that these provisions will reduce the industry's revenues from branded medicines by \$112 billion over the next decade (excluding the effect of introducing a biosimilars pathway). Assuming a modest increase in sales from expanded insurance coverage, the net loss will be about \$97 billion.<sup>41</sup>

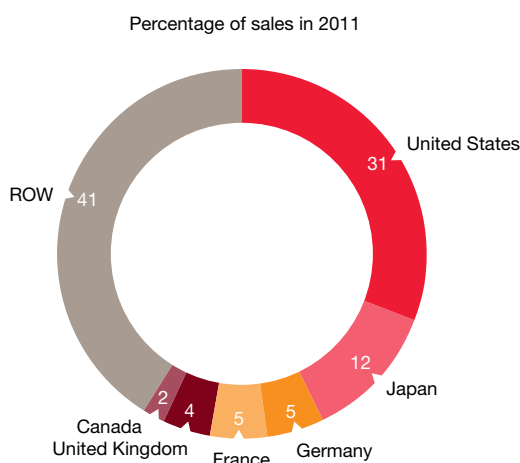
But the new law has far wider ramifications – and the biggest of all, perhaps, is value-based purchasing. From 2013, all hospitals serving Medicare patients with the most common conditions will be paid for the quality of the care, rather than the quantity of services, they supply. The same concept will be extended to other healthcare providers over the next few years.

The law also encourages healthcare professionals to band together in accountable care organisations (ACOs) to deliver better, more coordinated care, help prevent disease and reduce unnecessary hospital admissions. Those that offer a superior service and cut costs will be allowed to keep some of the money they've saved – an incentive that's generated considerable interest. To date, 65 ACOs have been set up and the number's expected to double over the coming 12 months.<sup>42</sup>

These changes will inevitably expose medicines to much greater scrutiny. When healthcare providers are paid for the value they create, they'll apply the same criterion to the therapies they prescribe. In fact, they're already starting to do so. Four-fifths of the US health insurers we polled in a recent survey now require evidence of cost savings or a clear clinical benefit to include new products in their formularies. 16% have also entered into outcomes-based contracts with pharma companies, while another 33% expect to do so within three years.<sup>43</sup>

So the Affordable Care Act will have a huge impact on pharma. Historically, drugmakers have sold their products by the unit at prices they themselves have set, with discounts for volume buyers. But with the shift from unit pricing to value-based purchasing, it's what customers think – not what the manufacturer thinks – that matters most. New products will be priced on the basis of the value buyers accord them. And the pharma company's relationship with the healthcare community won't stop when the deal's signed; it will continue for the duration of the patient's treatment.

**Figure 1 Six markets generate three-fifths of pharma's revenues from prescription products**



Source: Business Monitor International

## Tough talk in the EU, Canada and Japan

The other mature economies have also been reforming their healthcare systems, as we predicted in ‘Pharma 2020: The vision’. And, like the US, they’re taking a much harder stance.

In 2010, the German Bundestag passed the AMNOG health bill, under which all new therapies must be independently assessed against a comparator within 12 months of reaching the market and priced in line with the improvement they offer.<sup>44</sup> The UK will also introduce compulsory, value-based pricing of all new drugs in 2014.<sup>45</sup> Both these systems mark a major departure from previous practice; in the past, economic evaluation of medicines in the EU has been used to determine whether to reimburse them – not to set prices.

Meanwhile, health researchers in Canada are investigating the idea of a pan-national body to negotiate drug prices, thereby reducing the inequities between provinces with more and less buying power. They’re also examining the feasibility of performing real-time evaluations of medicines.<sup>46</sup>

Japan is exploring yet other options, including the expansion of its scheme for re-pricing medicines whose sales are much higher than expected.<sup>47</sup> It also imposed a 1.26% cut in prices (using total healthcare expenditure as its base) in April 2012.<sup>48</sup> And the Ministry of Health, Labour and Welfare is considering whether to introduce health technology assessments.<sup>49</sup>

Further changes are afoot. Several countries have introduced fixed, all-inclusive hospital tariffs for the treatment of specific diseases, with penalties for emergency re-admissions. And many healthcare payers are looking for opportunities to reduce costs by moving the point of care from the hospital to the doctor’s office or patient’s home.

Above all, the mature economies are encouraging generic prescribing – and some have been doing so for many years. Indeed, as of 2009, the French social health insurance system even offers doctors individual guidance on rational prescribing.<sup>50</sup> Such initiatives have had a pronounced effect on prescribing patterns. Generic spending in the mature markets is forecast to rise by \$35-40 billion over the next five years, with 60% of the increase coming from greater utilisation of existing generics.<sup>51</sup>

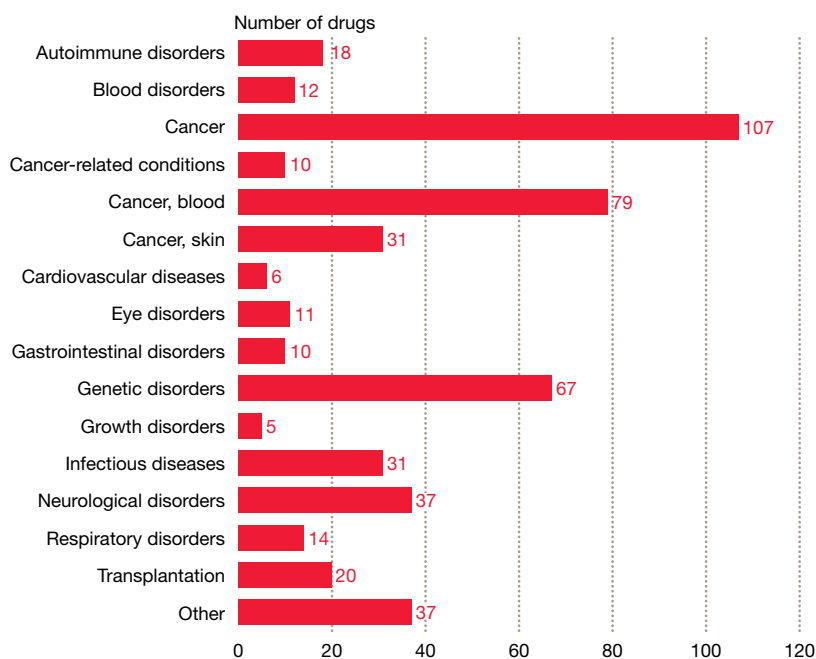
So the message healthcare payers in the mature markets are sending out is loud and clear: give us new medicines that are clinically and economically better than what’s already available – medicines that decrease mortality or morbidity, make the care pathway more efficient or reduce the total resources a patient consumes. And give us hard, real-world data to back up your claims.

## Pharma’s biologics bet

But what’s pharma been doing? It’s been concentrating on biologics for cancer and rare diseases. Nearly 30% of the 7,891 molecules currently in clinical testing cover cancer and autoimmune conditions.<sup>52</sup> An estimated 460 medicines for rare disorders are also in trials, although there’s some overlap between the two areas (see Figure 2).<sup>53</sup>

Most such treatments cost far more than chemical molecules. In the UK, for example, the average price of a biologic is about £9,500 (\$14,750) per patient per year, compared with £450 (\$700) for a conventional therapy.<sup>54</sup> Prices are even higher in the US and some products for rare diseases cost hundreds of thousands of dollars.

**Figure 2 There are 460 therapies for rare diseases in the pipeline**



Source: PhRMA

## The value dilemma

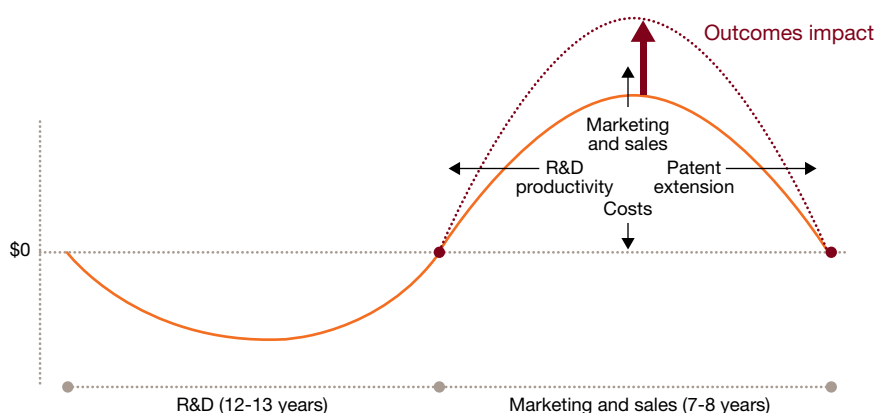
In short, the mature markets have been evolving economically, demographically and structurally, but pharma hasn't kept abreast of the changes. It's continued to pursue its old 'get more, pay more' approach, even though the mature markets are running out of money and some of the medicines it's developed arguably provide little extra value.

What healthcare payers want, by contrast, is more value for the same money or the same value for less. And they can afford to play a waiting game. As a growing number of treatments come off patent, they'll soon be able to buy the same medicines at lower prices anyway.

So pharma's contributed to the position in which it finds itself. And any company that wants to reach 2020 will either have to offer more value without charging more or prove unequivocally that it can remove costs from another part of the healthcare system to make room for the higher prices it's charging.

Moreover, since many of the medicines in the industry's pipeline went into development before these market forces were so strong, some products may be incapable of meeting healthcare payers' expectations. It takes at least a decade to develop a new drug and only six months to change a clinical pathway. A lot of companies may thus have to slash their portfolios at very short notice.

Figure 3 Pharma has an additional lever in the form of outcomes data



Source: PwC

## The outcomes lever

There are other implications, too. In the past, pharma had four 'profit' levers: R&D productivity, cost cutting, marketing and extension of the period of market exclusivity. Most businesses relied mainly on marketing, but this lever has become much less effective now that payers and providers scrutinise outcomes so carefully. No matter how many sales reps a company fields or how many samples it hands out, if a new treatment doesn't offer more value than competing therapies, healthcare payers in the mature markets simply won't buy it.

That said, the industry now has another lever in the form of outcomes data. Instead of 'creating awareness', it can demonstrate the worth of its products with real-world evidence of lower mortality and morbidity rates or savings in total healthcare costs (see Figure 3).

But pulling the 'outcomes lever' will require major changes, and three functions will be particularly deeply affected: R&D, health economics and

marketing and sales. Rather than focusing on commercial potential, for example, the R&D function will have to focus on creating value for customers when it decides which medicines to progress through the pipeline. It will also have to collect proof of that value, using real-world outcomes data.

Similarly, rather than using unit prices and sales volumes to produce budgets and forecasts, the health economics function will have to use outcomes-based modelling and make sure that investors understand the approach it's adopting. It will also have to set up systems capable of managing an intricate network of contingency payments and rebates.

The marketing and sales function will have to make even bigger adjustments. It will have to grapple with rigorous scientific data and complex economic studies, as well as developing the skills to negotiate with healthcare payers equipped to perform their own sophisticated analyses.

## Maximising the molecule

So what, more specifically, can pharma companies do to ‘maximise the molecule’? We’ll look at four ways to create more value for customers: plugging ‘leaks’ in the healthcare system; collecting real-world evidence of a medicine’s effectiveness; measuring how patients feel; and developing companion diagnostics for specialist therapies.

## Plug leaks in the healthcare system

Since healthcare payers want better clinical and economic outcomes, one logical place to start is by analysing the care pathway to identify where the outcomes from existing treatments are impaired. Our research shows that, in the US alone, roughly \$210 billion a year is wasted on overuse or misuse of medicines and procedures. Care for conditions that could be corrected through lifestyle changes costs another \$303-493 billion a year.<sup>55</sup>

The first step is to map out the different stages in the pathway for a given disease – from the stage at which the patient is at risk to the stage at which the disease is no longer controllable through medication. The next step is to find the places in the care pathway where value is lost, because of the patient’s behaviour or failings in the healthcare system. Many of these leaks occur at transition points in the care pathway, where there’s unnecessary duplication and waste.

Once a company has pinpointed the leaks, it can identify the sort of interventions that might help and where they’re required. This might include screening for a disease while it’s still in the asymptomatic stage, offering dietary advice, reducing a drug’s dosing frequency, providing reminders or, indeed, many other things (see box, **Reinforcing the power of the pill**).<sup>56</sup>

## Reinforcing the power of the pill

With ingestible microchips embedded in drugs, doctors will soon be able to tell whether patients are taking their medicines as prescribed. Proteus Digital Health’s chips are one of several new technologies that aim to improve compliance. Other devices in the pipeline include implants that wirelessly inject drugs at pre-specified times and sensors that send a patient’s electrocardiogram to a smart phone.

Mobile health applications also hold huge promise. mHealth apps store Haptique has, for example, launched a pilot programme that lets doctors prescribe apps as part of an overall healthcare package. mHealth will revolutionise healthcare in at least two respects. It will encourage patients to take responsibility for their own health and provide a means of measuring key health parameters in a comprehensive, continuous fashion.

Remote monitoring devices and mHealth will eliminate some of the obstacles to non-compliance. The ‘gamification’ of healthcare has a different end: encouraging people to lead a healthier lifestyle by making it fun. Nintendo’s Wii Fit video game is probably the best-known example of this approach. Several hospitals have

now incorporated the game into physiotherapy programmes.

But other companies have used the same idea. HopeLab has launched a video game designed to foster a positive attitude in young cancer sufferers. Players can use a variety of ‘weapons’ to zap malignant cells, with 20 levels each providing information about different treatments and the importance of adhering to them. Bayer has also created a blood glucose monitoring system that can be plugged into a Nintendo. Didget aims to teach children with diabetes how to manage their disease by rewarding them for testing themselves regularly with new scenarios and characters.

Health video games merge the worlds of healthcare and entertainment. More sophisticated biomonitoring devices and mHealth apps will produce further convergence. Fast-forward and biosensors will eventually be able to record everything we eat and drink, as well as the amount of exercise we take. They’ll track the number of calories we consume, remind us to go to the gym and warn us when we open the refrigerator for that diet-blowing snack.



A number of medical technology firms are already exploring new ways of creating added value, as we noted in ‘Owning the disease’.<sup>57</sup> A few pharma companies have started doing likewise. In June 2010, for example, Pfizer launched a vascular health check service in British pharmacies.<sup>58</sup> Similarly, GlaxoSmithKline (GSK) has linked up with specialist technology provider MedTrust Online to offer an iPhone app that lets US oncologists search for clinical trials by cancer type and automatically identifies the trial centres nearest their patients.<sup>59</sup>

Meanwhile, Boehringer Ingelheim is piloting a digital health management service for patients with diabetes. It combines a personalised action plan and digital coaching with wireless monitoring to measure the impact of behavioural changes.<sup>60</sup> But many more opportunities for stopping the leaks and enhancing outcomes exist.

### **Collect real-world evidence of value**

We’ve talked about maximising molecules that are already on the market. What about those that are still in the pipeline? With value-based purchasing, it’s imperative to collect the sort of information healthcare payers want – and traditional randomised controlled trials don’t capture that data. They’re designed to measure the safety and efficacy of a new medicine in carefully managed conditions, not how well it works in the real world.

We’ll discuss the sort of trials that provide evidence of a medicine’s economic value in more detail in chapter 4. But, among other things, they entail setting up a real-world data infrastructure. Most companies will have to collaborate with other organisations to do this, since much of the information that’s needed to develop medicines with a better clinical and economic profile lies outside

pharma’s walls. EMRs, electronic prescribing data, patient compliance data and the like are important pieces of the jigsaw puzzle.

The industry will also have to convince healthcare payers of the reliability of its data and that could be an uphill struggle. Only 5% of the US health insurers we recently surveyed are very confident of the quality of the economic data pharma companies provide, and only 7% are very confident of the quality of the information they receive on a drug’s comparative effectiveness.<sup>61</sup>

There are several things the industry can do to foster trust. For instance, it can sponsor independent research on the cost-effectiveness of its products or get independent verification of its data. It can also agree on a set of common measures for assessing clinical and economic value to reduce the administrative burden on its customers.

### **Measure the feel factor**

It’s not just clinical and economic outcomes that count, though. Nearly a third of the quality measures initially used for value-based purchasing of healthcare services in the US rest on patient satisfaction.<sup>62</sup> So healthcare providers will have to take account of how patients feel.

The number of pharma companies that measure the patient experience is still very small. But Incyte’s recent use of patient-reported outcomes with myelofibrosis drug Jakafi shows just how valuable a tool it can be. The FDA stated that it was a vital element in the decision to approve Jakafi and, unusually, let the company include information about symptom relief on the packaging. Incyte’s efforts have been recognised in the marketplace, too. Jakafi sells for \$84,000 a year in the US – compared with the \$40,000-60,000 it was originally expected to fetch.<sup>63</sup>

But capturing patient-reported outcomes in clinical trials requires a lot of upfront planning, particularly when new measurement tools must be developed and validated first. So it’s essential to start early in the process. It’s also important to capture the patient perspective from as many sources as possible. Social media can be a rich source of information here – and the number of people using such outlets will only increase. In the US, for example, 83% of Internet users aged 18-29 use social networking sites, compared with just 33% of those aged 65-plus.<sup>64</sup>

Online patient groups and blogs provide an opportunity to listen to patients talking openly about their experiences. Several firms have already set up disease-specific communities and sell the insights they collect. With new technologies for processing natural language and analysing unstructured data, it’s also getting easier for pharma companies to monitor the digital grapevine themselves.

That said, it’s imperative the industry secure proper patient consent and treat all such data responsibly. Privacy and security violations can cause serious reputational damage, in addition to other problems like the loss of vital clinical data. Yet our research shows that nearly three-quarters of US healthcare organisations (including pharma companies) use health data for secondary purposes other than those for which it was collected, and less than half have put robust safeguards in place.<sup>65</sup>

## Creating companion diagnostics for medicines that target a specific disease subtype lets doctors maximise the value of those medicines themselves

### Develop companion diagnostics for specialist medicines

Another way companies can maximise the molecules they're developing is to create companion diagnostics that let doctors maximise the value of those molecules themselves. There's no point in prescribing therapies that target one disease subtype for patients who suffer from another, as healthcare payers recognise. And they're prepared to reward innovations that help them direct precious resources more effectively. (see Table 1).

The FDA has also signalled that it would like to see more specialist medicines paired with companion diagnostics and sometimes accelerates the review process for such products. But when the 'carrot' doesn't work, it's ready to wield the stick. In 2010, the agency refused to approve leukaemia treatment Omapro without a diagnostic to identify the target patient base.<sup>66</sup>

NICE rejected melanoma therapy Yervoy for reimbursement on the same grounds in 2011.<sup>67</sup> So failing to develop a diagnostic test for a costly treatment that's aimed at a tiny patient population may damage its prospects of commercial success. Indeed, we think that, by 2020, companion diagnostics will be mandatory for approval of all such medicines.

**Table 1 Targeted medicines with companion diagnostics generate high revenues because they work so well for specific patient segments**

Product	Indication	Annualised cost per patient in US	Biomarker	Population testing positive for biomarker (%)	Projected sales (2012-2018)
<b>Erbix</b>	Colorectal, head and neck cancer	\$84,000	EGFR+ KRAS-wt	37.5	\$13.42 billion
<b>Herceptin + Perjeta</b>	Breast cancer	\$124,800	HER-2+	25	\$49.96 billion
<b>Tarceva</b>	Non-small cell lung cancer	\$52,800	EGFR+	10-15	\$10.8 billion
<b>Xalkori</b>	Non-small cell lung cancer	\$115,200	ALK+	4-7	\$4.76 billion
<b>Zelboraf</b>	Melanoma	\$112,800	BRAF+	13.5	\$4.25 billion

Sources: EvaluatePharma and The Pink Sheet

Note: Projected sales are cumulative and global.

*Healthcare payers in the mature markets want more value for their money and they're measuring the value they get much more carefully*

### **What's it worth?**

To sum up, the message healthcare payers in the mature markets are sending is clear: they want more value for their money, they're measuring the value they get more carefully and they're not prepared to pay thousands of dollars for medicines that offer only incremental improvements in outcomes. Their pockets aren't deep enough.

But what healthcare payers mean by 'value' is also becoming clearer, as the pricing and reimbursement processes they use become more transparent. And the scope for helping them make savings is huge. Thus far, pharma's focused on the roughly 15% of the health budget that goes on medicines.<sup>68</sup> That leaves another 85% from which it can generate revenues by reducing consumption of more costly medical services. If it succeeds in doing this – and in surmounting sociopolitical opposition to the rebalancing of the mix – we think its share of healthcare expenditure in the mature economies could rise to 20% by 2020.

Maximising the molecule will involve major decisions about which diseases to concentrate on, which medicines to pursue, what data to collect and how best to plug leaks in the healthcare system. The vast majority of companies will also need to revise their budgeting and forecasting processes, billing and payment systems and the way they go to market.

Most importantly of all, they'll need to keep the big picture in mind at all times. Treatments that prevent disease, cure otherwise incurable diseases, reduce the overall use of resources and let patients stay as productive as possible for as long as possible: these are the sort of medicines governments and health insurers in the mature markets will buy.

And, in the end, as the Roman writer Publilius Syrus once noted, "A thing is worth only as much as it can be sold for." So it's what payers, providers and patients value that will determine the value pharma creates for its shareholders.

## Pharmageddon?

The financial problems in the GIIPS economies have already had a significant impact on pharma. The European Federation of Pharmaceutical Industries and Associations (EFPIA) estimates that price cuts and discounts in all five markets reduced the industry's revenues by more than €7 billion (\$8.8 billion) in 2010 and 2011. But, with other countries demanding similar discounts, the indirect cost was much higher.<sup>69</sup>

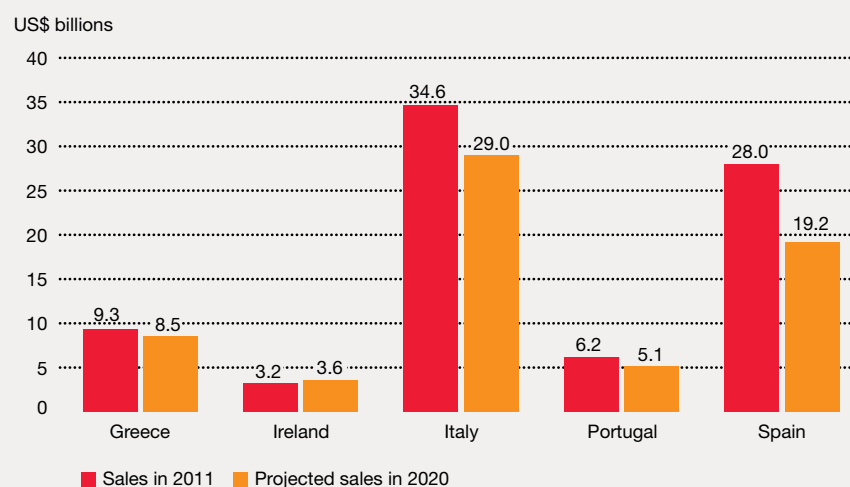
The next few years also look bleak. The governments of the GIIPS states are tightening their budgets, and expenditure on healthcare – including prescription medicines – is a prime target. Opposition from the voting public, industry advocates and subnational governments in some countries may temper these efforts. Even so, pharmaceutical sales in the five GIIPS economies are expected to fall to \$65.4 billion by 2020, down from \$81.3 billion in 2011 (see Figure 1).

## Tighter economic governance

Under EU law, national governments are responsible for setting health policy and organising and financing healthcare, so the EU's health initiatives are generally confined to promoting cross-border cooperation and setting health and safety standards. But, with strict fiscal rules enshrined in the EU treaties and European Fiscal Compact, as well as stringent bailout terms for the member states that have accepted help from the EU and International Monetary Fund (IMF), EU economic governance poses an increasingly important constraint on healthcare.

Portugal, for example, is currently implementing the terms of an EU/IMF rescue package under which the government is required to enact legislation to rationalise the use of health services and reduce overall public spending on medicines. So it's likely to issue new cost-saving provisions. One option is to halve the prices of drugs whose patents expire.<sup>70</sup> The next annual review of drug prices, due in early 2013, may well bring additional cuts.

**Figure 1 By 2020, pharma's revenues will be lower in four of the five GIIPS markets**



Source: Business Monitor International

Note: All sales are expressed in US dollars at constant exchange rates.

The Greek government has also initiated various healthcare reforms, including a restrictive reimbursement list, under its two EU/IMF Memorandums of Understanding.<sup>71</sup> Other cost-saving measures may involve the promotion of generics. In March 2012, for example, the Italian government passed a 'liberalisation' law strengthening the rules on the use of generic alternatives.<sup>72</sup> And, in July 2012, the Irish Minister for Health introduced a draft bill permitting automatic generic substitution which, if passed, could cut the country's expenditure on medicines by €50 billion a year.<sup>73</sup>

### **Mounting debts**

Price cuts and generic erosion aren't the industry's only grounds for concern, though. Ireland apart, all the GIIPS countries have deferred payment of their medicines bills, with an estimated €12-15 billion owing by the end of 2011.<sup>74</sup>

The problem started in Greece, where the hospitals racked up debts of about €7 billion in the latter part of the last decade. Many of those bills remain unpaid, and the Greek government recently passed a law stipulating that if the country exceeded its annual medicines budget, the industry would be required to pay for any overspending.<sup>75</sup>

The contagion subsequently spread to Italy, Portugal and Spain. Macroeconomics research group Prometeia reports that Italy's local health authorities took an average 262 days to pay their medicines bills in 2011, while payment delays in Portugal rose from 375 days to 453 days.<sup>76</sup> The Spanish health system was in an even worse position until June 2012, when the government set aside €17 billion to cover rising debts in the autonomous regions.<sup>77</sup>

The Italian and Spanish governments are both at loggerheads with the regional administrations, which manage most public healthcare spending. In Italy, this is partly because the Cabinet hopes to conclude a health pact with the country's regional governments in mid-November that will probably reduce the amount of money transferred to them.<sup>78</sup> The Cabinet will also set new standard cost measurements to allow for more efficient healthcare budgeting and lay out a timeline for adoption by the end of 2012.<sup>79</sup> Its recent spending review includes other measures to limit public spending on medicines and medical devices, force suppliers to return part of their compensation when hospitals run over budget and impose deeper discounts on pharmaceuticals.<sup>80</sup>

Patients will be expected to pick up a bigger share of their medical expenses in the coming years, too. Italy and Spain are both trying to reduce costs by shifting more of the burden of pharmaceutical expenditure to private payers. For example, the Spanish Health Ministry recently eliminated over 400 drugs from its reimbursement lists.<sup>81</sup> And, in April 2012, it introduced co-payments on medicines for pensioners, as well as raising co-payments for everyone in the workforce, with increases tied to income levels.<sup>82</sup>

### **Grey trading**

The financial plight of the GIIPS economies has had one last change of particular significance for pharma: the increase in re-exportation of medicines from lower-priced to higher-priced countries. In 2009, the 'grey' market for prescription drugs in Europe was worth about €5.2 billion a year (at ex-factory prices).<sup>83</sup> But EFPIA reports that there's been a marked rise in parallel trading in recent months.<sup>84</sup>

Pharma's efforts to curb the practice have been repeatedly stymied, even though most studies show that it's the middlemen – not healthcare payers – who benefit most. But resistance may finally be softening. In May 2012, the European Commission launched an investigation into the parallel trade of pharmaceuticals. It's reported to be considering whether the industry is justified in arguing for differential pricing of drugs bought for re-exportation.<sup>85</sup>

### **A tightrope to walk**

The key issue pharma companies trading in the GIIPS economies face, then, is how best to balance the needs of patients with their own commercial imperatives. That entails making some hard decisions about whether to impose more rigorous payment terms, whether to restrict the products they supply and whether to serve patients via different channels, thereby giving patients access to the treatments they require without going through bankrupt public hospitals.

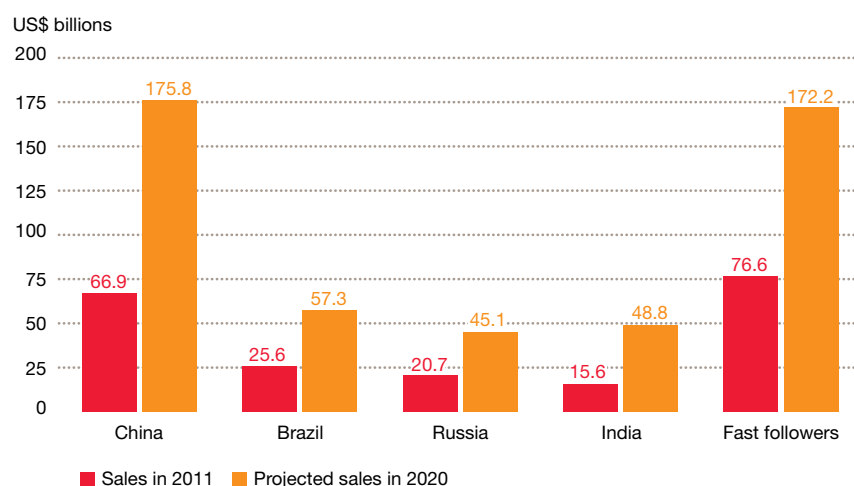
It also entails coping with considerable uncertainty. As the Eurozone crisis unfolds, prolonged austerity and market pressure may contribute to public discontent and political instability. Changes in government in the GIIPS countries and elsewhere haven't generally resulted in the reversal of austerity measures and structural reform policies thus far. But it remains to be seen whether voters will continue to tolerate austerity in the longer term.

# The growth markets: Hot, cold, hard to get right

*“If a man has one foot in a bucket of ice and the other in a bucket of boiling water, he is, on the average, very comfortable.”*

Mark Twain

**Figure 1 Demand for medicines is rising rapidly in the growth markets**



Source: Business Monitor International

Notes: (1) All sales are expressed in US dollars at constant exchange rates; (2) The fast followers include Argentina, Egypt, Indonesia, Mexico, Pakistan, Poland, Romania, South Africa, Thailand, Turkey, Ukraine, Venezuela and Vietnam.

## Hot and cold at the same time

The growth markets are as hot as boiling water, but they can also be as cold as ice. On the one hand, they're expanding rapidly. By 2020, the BRIC economies alone will account for 33% of the world's GDP, measured in terms of purchasing power parity (PPP) – up from 25% in 2009.<sup>86</sup>

On the other hand, the growth markets come with some enormous challenges, including their geographic size, cultural diversity, underdeveloped infrastructure, fragmented distribution systems and weak regulations that are often ineffectively enforced. Average incomes are also much lower than they are in the developed world.

So the growth markets have great commercial potential, but they could take as long as 20 years to catch up with the mature markets. And, in the meantime, doing business in these countries carries a lot of risks for the inexperienced or unwary.

## A foot in each bucket

Pharma's prospects reflect this dichotomy. On the upside, expenditure on medicines is rising far faster in the growth economies than it is elsewhere. In aggregate, it could reach \$499 billion a year by 2020 – up from \$205 billion in 2011 – as economic expansion and better access to healthcare drive up demand (see Figure 1).

On the downside, serving the growth markets is very difficult, both because of their intrinsic problems and because they vary so much. They differ politically, geographically, religiously,



socially and structurally. They differ in terms of the treatments they need, since ethnic origin, diet and environment play a huge part in determining the particular disease subtypes from which people suffer. And they differ in their ability and willingness to pay for new medicines.

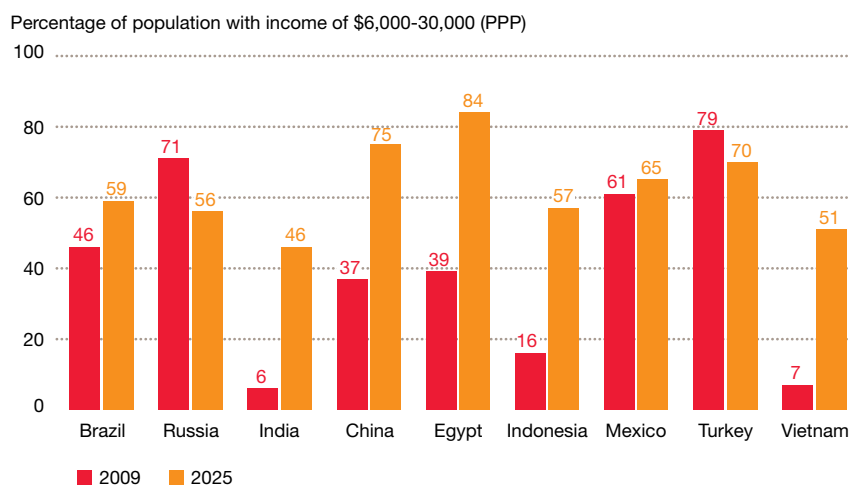
There are pockets of great wealth, and the overall level of affluence is increasing. The number of ‘middle-class’ consumers – defined as those with annual incomes of between \$6,000 and \$30,000 (PPP) – is forecast to rise from 1.7 billion to 3.6 billion by 2025 (see Figure 2).<sup>87</sup>

But patients in the growth economies typically have to fund a larger share of their own healthcare costs than patients in the mature economies. And even in the BRIC countries, where the rate of expansion is fastest, per capita expenditure on healthcare is far too low to support biologics priced at many thousands of dollars (see Table 1).

In fact, reconciling the healthcare needs of the rich and poor is one of the biggest challenges the governments of the growth economies face. They must juggle rising demand for higher-value medicines from wealthy citizens with calls for better access to essential medicines from those in the lower socioeconomic strata – a delicate political balancing act that will probably prove a mixed blessing for pharma.

For instance, the Brazilian government recently acted on concerns about slowing economic growth by exempting a number of industries, including pharma, from payroll tax.<sup>88</sup> But it simultaneously imposed tariff hikes on 100 products, some of which will affect pharmaceutical inputs, to protect domestic industries from cheaper imports. So pharma companies operating in Brazil will benefit from significantly lower labour costs while incurring higher import fees.<sup>89</sup>

**Figure 2 The middle class is expanding**



Source: Goldman Sachs

Note: In Russia and Turkey, the percentage of the population falling within these parameters is declining as more people move into higher-income groups.

**Table 1 Patients in the growth markets can't afford costly biologics**

	Private share of healthcare expenditure (%)	Per capita health spending, 2010, US\$	Population with net assets of US\$10,000 or less (%)
<b>Brazil</b>	53.0	990	62.1
<b>China</b>	46.4	221	66.4
<b>India</b>	70.8	54	92.8
<b>Russia</b>	37.9	525	75.4

Sources: World Bank Indicators and Credit Suisse, Global Wealth Databook (October 2010)

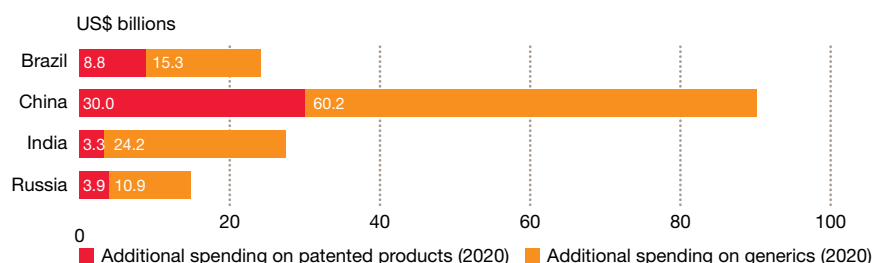
Similarly, Mexico's President Enrique Peña Nieto is expected to push through fiscal reforms that could involve reworking various tax exemptions, including the current exemption from value added tax on food and medicines.<sup>90</sup> But he may well make the move more politically palatable by routing some of the revenue it generates into the national health insurance programme.

Meanwhile, in China, where the one-child policy has accelerated the aging curve, healthcare reform has become a pillar of the central government's 12th Five-Year Plan. And Beijing's recent efforts to improve the regulatory environment for

privately run hospitals, including the removal of certain barriers to foreign investment, suggest that it's willing to increase the overall presence of the private sector in the healthcare space.<sup>91</sup>

This could bode well for foreign companies in related industries, including pharma. But implementing the changes at local level will be very difficult. And, as in Brazil, there are concerns about declining growth. If China's economy continues to slow down, some of the more ambitious and expensive components of Beijing's healthcare reform could be derailed.

**Figure 3 Patented medicines will play a small role in driving up pharmaceutical sales in the growth markets**



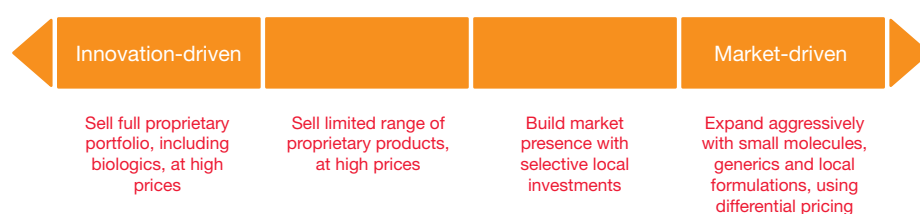
Source: Business Monitor International

Note: All sales are expressed in US dollars at constant exchange rates.

So the growth countries currently lack the financial power to reward innovation. Near-term economic uncertainties are also likely to render progress in reforming their healthcare systems uneven. Hence the fact that most of the projected increase in pharmaceutical sales over the next decade is expected to come from generics rather than patented products (see Figure 3).

That, in turn, means pharma can't rely on its usual methods for making a profit in mature countries. It needs to adopt a totally different strategy – or, rather, different strategies for each market, since they vary so greatly.

**Figure 4 Big pharma's using four strategies in the growth markets**



Source: PwC

### Value or volume?

How, then, have the industry majors responded to date? Our analysis indicates that they've adopted one of four policies (see Figure 4). Those at the innovation-driven end of the spectrum have focused on quality rather than quantity. Roche is a case in point. In 2010, Pascal Soriot, former chief operating officer of Roche's pharma division, stated that it aimed 'to sell innovative, higher priced products' to the growth markets – a strategy it believed would eventually pay off, 'as China and other countries...close the gap [with] the West'.<sup>92</sup>

The companies at the opposite end of the spectrum have focused on volume sales and market share, mainly by selling primary-care products, using differential pricing and building generics divisions with acquisitions in key territories. GSK exemplifies this approach; chief executive Sir Andrew Witty is a self-professed 'extreme bull' on the growth economies.<sup>93</sup>

The other leading players sit somewhere between these two poles (see Figure 5). Eli Lilly has been quite selective in its growth-markets forays, for example. It's concentrated on selling branded medicines.<sup>94</sup> Sanofi, by contrast, has invested heavily in building a generics arm.<sup>95</sup> And Merck & Co. (known as MSD outside the US) lies in the middle. It's linked up with Indian generics manufacturer Sun Pharma, but the aim is not only to sell existing treatments. The two companies have also set up a joint venture to develop more convenient formulations of branded generics.<sup>96</sup>

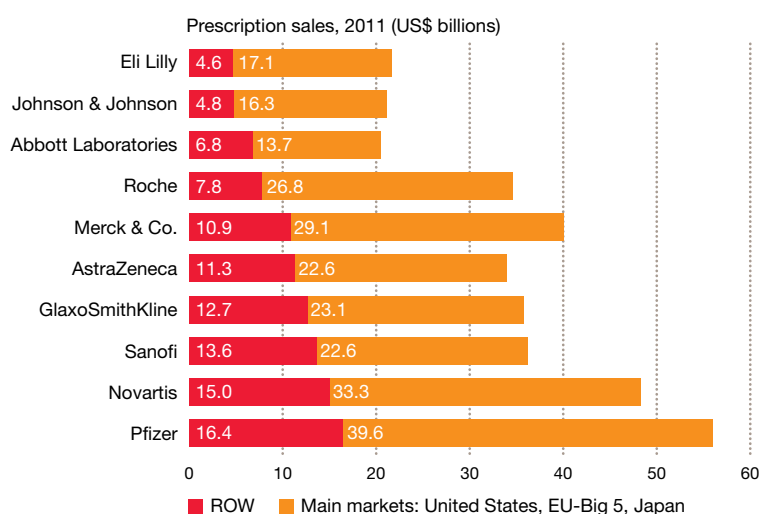
Yet few, if any, of these strategies have gone without a hitch. In March 2012, for example, the Indian government authorised a local producer to make and sell a generic version of Bayer's cancer treatment Nexavar, even though it's still under patent.<sup>97</sup> Novartis is also battling with the Indian patent office over its refusal to grant a patent for Gleevec.<sup>98</sup>

These two cases are probably what prompted Roche to reverse its longstanding policy of charging the same prices for the same products, regardless of where they're sold. The company recently announced that it would offer 'significantly' cheaper versions of its two cancer therapies Herceptin and MabThera in India by 2013.<sup>99</sup>

Now China has also revised its intellectual property laws to permit compulsory licences for the production of generic versions of patented drugs during state emergencies, unusual circumstances or 'in the interests of the public'. And industry insiders report that it has Gilead Sciences' *tenofovir*, part of a first-line treatment for AIDS, in its sights.<sup>100</sup>

It seems likely, then, that patent challenges will continue to pose a problem for those companies operating at the high end of the market. But the volume plays have encountered their share of troubles, too. Political instability in the Middle East, price cuts in Russia and Turkey and intense generic competition in Brazil have dented their performance.<sup>101</sup> And though several multinationals have prospered by muscling out indigenous rivals with branded generics, that's at best a short-term measure. Some patients may be willing to pay extra for the reassurance that comes with big brands, but the numbers will diminish as governments cut back on reimbursement charges and promote local champions.

**Figure 5 Four companies now earn a third of their revenues outside the main markets**



Source: Datamonitor

Note: EU-Big 5 is France, Germany, Italy, Spain and United Kingdom.

### **Throwing out the rulebook**

So focusing on the masses isn't proving any easier than focusing on the affluent elite who can pay for costly new medicines. But that doesn't mean it's impossible to make a profit in the growth markets. On the contrary, there's much pharma can learn from the most innovative organisations. Consider the following examples.

### **Designing products for people in the lower part of the income pyramid**

When Ratan Tata decided to develop a car for India's urban masses, he started with a question: how to produce an affordable – and better – mode of transport for people who normally used motorbikes. The result was the \$2,500 Nano, a fuel-efficient vehicle that seats four passengers but comes without expensive frills.<sup>102</sup> GE Healthcare has applied the same approach to the medical equipment sector. Among other things, it's launched two stripped-down MRI machines that sell for \$700,000 to \$900,000, compared with a normal price of about \$1.6 million.<sup>103</sup>

### **Using mass-market techniques to deliver complex services**

Dr Devi Shetty has perfected the science of high-volume heart surgery. At Narayana Hrudayalaya Hospital, in Bangalore, 42 surgeons – each specialising in a single procedure – perform some 600 operations a week. Dr Shetty charges about \$1,500 per operation. Yet his profit margins are higher than those of the typical US hospital, and his quality as good.<sup>104</sup>

Eye-hospital chain Aravind has also used assembly-line techniques to deliver healthcare. It performs about 350,000 operations a year and its operating rooms have at least two beds, so that surgeons can swivel from one patient to the next.<sup>105</sup>

### **Pooling resources for different purposes**

When Simon Berry, founder of British charity Colalife, wanted to distribute anti-diarrhoea products in the developing world, he had a brainwave: Coke gets everywhere aid doesn't, so why not pack the crates with medicines? Colalife designed a wedge-shaped container that fits between rows of Coke bottles and is now piggybacking on Coca-Cola's distribution network.<sup>106</sup>

The same concept can be used with other products and markets. Indeed, we anticipate that, by 2020, the biggest pharma companies will be pooling resources with health insurers and community care providers in the growth markets to stimulate demand for their products. They'll also be participating in cross-industry transportation networks to reduce their distribution costs.

*There's much pharma can learn from organisations that have mastered the art of serving the lower part of the income pyramid profitably*

### **Making old tools do new tricks**

In 1973, a Motorola employee made the first public call from a personal mobile phone.<sup>107</sup> Today, some 4.2 billion people have one or more mobile phones.<sup>108</sup> And they're using them to do things Motorola could never even have imagined (**see box, Mobile care for the masses**).<sup>109</sup>

Almost 14 million Kenyans use mobile-banking system M-Pesa.<sup>110</sup> The Bangladeshi government uses text messages to publicise nationwide health campaigns and provide prenatal advice to pregnant women. Ghana's Medical Association relies on SMS to send doctors information about national emergencies. And the Cambodian Ministry of Health operates an SMS-based disease-surveillance programme.<sup>111</sup>

Smartphones and video streaming facilities will open the doors to other health services. By 2020, patients will be able to consult a doctor remotely and send information about their symptoms to the doctor during the consultation itself. Hospitals in major cities will also be outfitted with interactive holograms that can answer basic health questions, eliminating the need to talk to a doctor at all in some cases.

The possibilities don't stop there. The same technologies could be used to improve patient compliance, which is even lower in the growth markets than the mature ones. They could also be used to sell certain medicines in very small units, with daily or weekly payment via a service like M-Pesa.

### **Realism required**

These examples demonstrate how some organisations have tackled the challenge of serving the lower part of the pyramid profitably. They've created new business models, not just new products or services. Yet even if pharma becomes more pioneering – and succeeds in

## **Mobile care for the masses**

Patients in many emerging countries have to travel long distances to see a doctor. But take-up of mobile technologies is much faster than it is in industrialised economies with a strong infrastructure. That's paving the way for 'care anywhere'.

US software firm Dimagi has developed a mobile phone-based programme called CommCare that allows community workers to gather information and refer patients for treatment by following an electronic questionnaire. More advanced systems will eventually be used to warn patients about nearby outbreaks of disease or environmental hazards like pollution.

India's Apollo Hospitals Group has already gone much further. It runs a remote triage advice and health monitoring service, using an IT platform with a structured query database. The service has handled more than 700,000 calls since it was set up. Apollo's now trialling a remote analytics service. Patients with diabetes can, for instance, measure

their blood sugar count and upload the data to a clinician via SMS. They get an SMS text back explaining the readings and advising them on whether they need to do anything more.

In the long term, it may even be possible to perform operations remotely, without human input. The da Vinci Surgical System is currently the most advanced commercially available surgical robotic system, and it's used only in operations where a doctor's present. But Italian surgeon Carlo Pappone supervised the first unmanned operation in 2006, using a robot based in Boston to perform heart surgery on a patient in Milan.

University of Washington surgeon Dr Richard Satava predicts that surgery will be fully automated in the next 40 to 50 years. "The future of technology, and medicine in general, is not in blood and guts, but in bits and bytes," he says. That would make complicated operations much more widely and economically available, even to patients in regions with few proper medical facilities.

capturing more custom from the roughly 80% of consumers who live outside the developed world – it would be wrong to suggest that all its problems will be solved. There are impressive gains to be made in the growth markets, but they *won't* be enough to offset price erosion and patent expiries in the mature markets.

The crucial issue, then, is how to capitalise on the opportunities the growth markets offer without risking too much or having unrealistic expectations: how to balance boiling water with ice. That involves making a number of key decisions, including which countries to

concentrate on; which business models to use; how much to invest; and how to allocate the funds.

And those decisions will have to be made fast. We predict that, by 2020, the biggest domestic players in the BRIC economies will otherwise dominate the local generics scene. And we fully expect several of these companies to break out of generics with innovative medicines developed in their own labs. By the end of 2010 Chinese drugmakers had 39 compounds with US or European patents in clinical trials – a sure sign of what's to come.<sup>112</sup>

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## ***R&D: Beautiful hypotheses, ugly facts***

*“The great tragedy of science – the slaying of a beautiful hypothesis by an ugly fact.”*

Thomas Huxley

### ***The productivity crisis***

We touched on pharma’s flagging productivity earlier. The situation is now so serious that we believe only a few fully integrated organisations will remain by 2020. Some companies will be acquired and stripped of their assets. Others will separate their R&D from their revenue-generating activities to reduce risk and unlock shareholder value.

We think there are two aspects to the productivity problem: one scientific, the other managerial. We’ll discuss the scientific issues – and the decisions they entail – here. We’ll cover the managerial issues in our next chapter.

### ***Some ugly facts***

Between 2002 and 2011, the pharma and biotech sectors spent nearly \$1.1 trillion on R&D.<sup>113</sup> What has this investment produced? Clearly, new medicines originate in many countries, but most of them are eventually launched in the US. FDA approvals are thus a reasonable proxy for the industry’s overall output over time.

In the 10 years to 2011, the FDA approved 308 new molecular entities (NMEs) and biologics. Given how much the industry invested in R&D each year during the same period, that means the annual average cost per approved molecule ranged from \$2.3 billion to \$4.9 billion. And there’s no sign of it coming down. On the contrary, costs are still rising relentlessly. In the second half of the decade, the average cost per molecule was \$4.2 billion – 50% more than in the first half (see **Figure 1**).<sup>114</sup>

### ***More with less***

This trend isn’t sustainable, as the industry majors realise. Several companies have recently reined in their R&D spending. In February 2011, for example, Pfizer announced plans to cut its R&D budget by a third.<sup>115</sup> Sanofi has also been slashing its R&D costs.<sup>116</sup> And AstraZeneca’s making 2,200 scientists redundant.<sup>117</sup>

Many of the big players have simultaneously been experimenting with new R&D structures. GSK set up several Centres of Excellence for Drug Discovery and split them into even smaller units in 2008, hoping this would inject a more entrepreneurial spirit. Sanofi subsequently reorganised its research departments by underlying causes rather than disease areas.<sup>118</sup>



Meanwhile, Eli Lilly has acquired ImClone but left it as a standalone business, as Roche did with Genentech.<sup>119</sup> Abbott's hiving off its research arm as a separate public company.<sup>120</sup> Pfizer's concentrating its resources, with the sale of its nutrition and animal health operations.<sup>121</sup> And AstraZeneca's converting its neuroscience unit into a virtual research enterprise.<sup>122</sup>

In effect, the industry leaders are all trying to do 'more with less', but there's no sign of a big surge in productivity. Between January and September 2012, the FDA's Center for Drug Evaluation and Research approved 27 NMEs and biologics.<sup>123</sup> That's an improvement on 2011, when the agency approved a total of 30 new drugs in the course of the entire year.<sup>124</sup> Yet research from KMR Group shows that the number of NMEs

required to achieve one new drug approval is increasing in every stage of development. In 2007-2011, it took an average 30.4 NMEs in preclinical development to secure one approval, compared with just 12.4 NMEs in 2003-2007.<sup>125</sup>

### Frontloading the R&D process

So what accounts for pharma's poor performance in R&D? One of the many arguments put forward to explain it is that the industry's now focusing on more complex diseases involving novel targets. That's true but it's by no means the whole story.

The most important – and arguably hardest – decision a pharma company makes during the R&D process is which

target or mechanism to focus on. It usually starts by collating numerous sources of evidence, drawn largely from the public domain, to create a hypothesis about the role of a mechanism in a given disease.

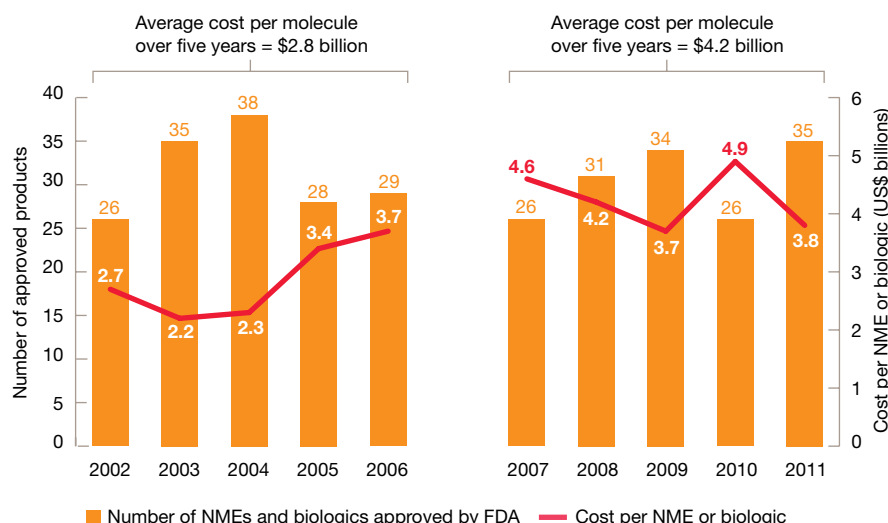
But there's rarely a single, compelling piece of data validating the mechanism's role in the underlying pathophysiology of the disease. And even if there is, the data may be incorrect. When one industry researcher tried to replicate 53 'landmark' cancer studies, he found that 47 couldn't be reproduced.<sup>126</sup> Moreover, very little is known about the feasibility of intervening pharmacologically or demonstrating the desired clinical effect at this stage.

In other words, the company has to decide on a course of action before it has much information to go on – and the stakes are very high. If it makes the wrong choice, it could end up eight or nine years later with a failure that's cost \$1 billion dollars or more.

It's therefore essential to focus on understanding a mechanism's role in disease as much as possible before embarking on an expensive development programme. That means investing more in translational medicine for the validation of targets and small, speedy clinical studies designed using sensitive endpoint biomarkers.

Animal models should, by contrast, be used much less frequently because they're a very inaccurate means of predicting efficacy in humans, as experience with the chemokine receptor CCR5 shows. Studies of rhesus monkeys with collagen-induced arthritis suggested that CCR5 played a part in rheumatoid arthritis (as it does in HIV).<sup>127</sup> But when Pfizer launched the first CCR5 inhibitor for the treatment of HIV in 2007, it also tested the drug on patients with rheumatoid arthritis – and found no evidence of efficacy whatever.<sup>128</sup>

**Figure 1 Costs per approved molecule are unsustainably high**



Sources: EvaluatePharma and PwC analysis

Notes: (1). R&D expenditure on newly approved medicines is clearly historic, but comparing annual investment with annual output over a 10-year period provides an accurate picture of the direction in which costs are moving. (2). We have not taken account of expenditure on line extensions, which varies significantly from one company to another.

In short, investing more money early on in understanding the molecular basis of a disease and the role a particular mechanism plays reduces the risk of losing a lot more money further down the line. And that research should be rooted in studies of human beings, not other species. Yet, on average, pharma companies spend only 7% of their R&D budgets on target/mechanism selection and validation – a fraction of the sum they spend on clinical trials (see Figure 2).

### Lighting the way

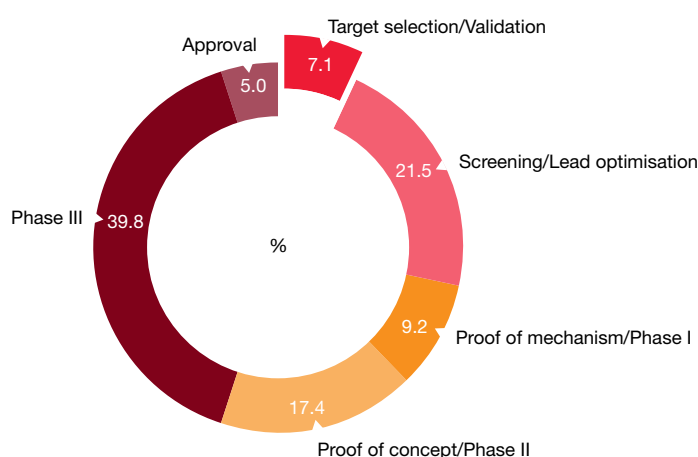
Fortunately, there are now grounds for hope, as genetics and genomics finally come into their own. With whole-genome sequencing, we can put diseases under the spotlight as never before.

By the end of 2011, there were 1,068 published genome-wide association studies.<sup>129</sup> Such studies normally compare the DNA of patients suffering from a specific disease with a control group to identify the alleles associated with that disease. They can't, alone, determine which genes are causal. But, by covering the entire genome, they can point to new regions for research and validate or rule out mechanisms in human populations without conducting clinical trials.

Take the case of cholesterylester transfer protein (CETP) inhibitors. Experience with statins shows that high-density lipoprotein (HDL) is important in heart disease. So researchers assumed boosting HDL would reduce the risk of myocardial infarction, but trials of several CETP inhibitors showed no positive effect.<sup>130</sup>

Why not? The trouble is that HDL concentrations don't vary greatly from one day to the next, or even from one month to the next. So HDL is an excellent early predictor of heart disease, but correlation isn't the same as causation.<sup>131</sup> And, thanks to genomics, we now have an answer to the question. Researchers used Mendelian randomisation to analyse the link between 15 genetic variants known to affect HDL and the incidence of myocardial infarction. Their findings strongly suggest that alleles that raise HDL don't cut the risk of heart disease.<sup>132</sup>

**Figure 2 Most pharma companies spend a very small percentage of their budgets on target selection and validation**



Sources: PhRMA Annual Member Survey, 2011, and PwC research

## Making the most of genetics and genomics

At present, genomics plays a relatively small role in the lab, as one recent survey of 21 large pharma companies shows (see Figure 3).<sup>133</sup> Indeed, we estimate that the industry spends just \$6 billion a year – less than 7% of its total R&D investment in 2011 – on such research.

But this is an area of study that's advancing very rapidly. Witness the fact that scientists lately identified some four million gene switches in the DNA that was once dismissed as 'junk'.<sup>134</sup> So we believe that, by 2020, pharma could be investing as much as 20% of its R&D budget in genetics and genomics for discovering and commercialising new drugs.

It will also draw on a growing number of population-based studies with well-characterised phenotypes. The UK government plans, for example, to release blinded clinical data on the 52 million patients enrolled in the National Health Service (NHS).<sup>135</sup> And, by 2020, online genetic testing companies will be another key source of information (see box, **Grassroots research**).<sup>136</sup> Together with better biomarker screening technologies and cheaper genomic technologies, this will help pharma decipher the messages encoded in our genes.

It won't be easy, given that there are 21,000-odd genes in the human chromosome, matched by a roughly equal number of RNA-producing segments, with promotion, silence, regulation and interaction of both, as well as epigenetic influences. There's also far more pleiotropy (where one gene affects multiple phenotypic traits) than most scientists initially expected. So some of the insights the industry's unearthing will require years of multi-disciplinary research before they can be used to create new medicines. And, since most companies are currently organised by disease area or indication, as well as being geographically scattered, they'll need to remove the barriers to information sharing.

But despite all the challenges, pharma will be in a much better position to dissect the molecular basis of many conditions by 2020. It can then start developing targeted medicines to treat them, much as it's now doing with cancer. An example? Several studies have identified four 'de novo' mutations that cause autism.<sup>137</sup> Once the list of genes grows, and they're assembled into pathways, it may be possible to diagnose autism through molecular defects and develop an effective therapy for a disease whose underlying pathogenic mechanism is currently obscure.

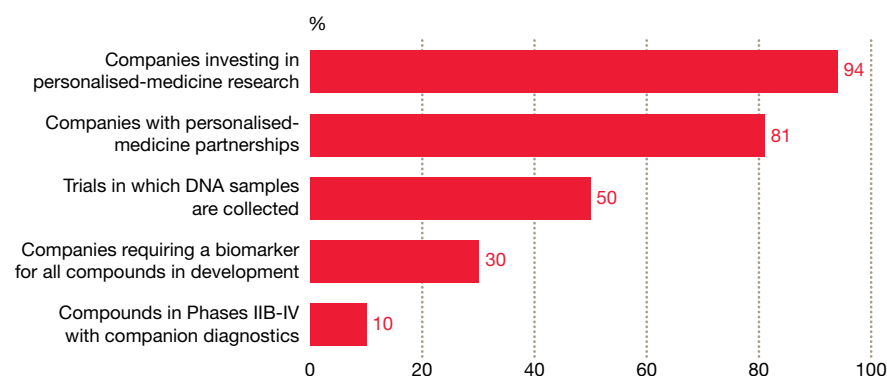
## Grassroots research

Social media sites offer a totally new source of genetic and phenotypic data – and one many drugmakers are turning to. Personal genomics provider 23andMe is among the pioneers. The company invites the people who use its testing service to share information about their medical history and lifestyle and contribute it to genetic research.

23andMe recently bought CureTogether, which started as an online platform to help people with chronic pain share their experiences. CureTogether now has more than four million phenotypic data points on more than 500 conditions.

The combination could be a powerful one. 23andMe has already built a major database of genetic data on Parkinson's disease. It's also collaborating with the Scripps Research Institute and Michael J. Fox Foundation for Parkinson's Research. And, in June 2012, it secured its first patent, based on the discovery of a variant in the SGK1 gene that may offer protection against Parkinson's disease in individuals who carry the high-risk LRRK2 G2019S mutation.

**Figure 3 Few companies are currently capitalising on the full power of genomics**



Source: Tufts Center for the Study of Drug Development

## Focusing to play

We've discussed the importance of investing more in the early part of the drug discovery process and capitalising on the potential of genomics. But there are several other steps pharma companies can take to enhance their productivity. The first is to become more selective about the therapeutic areas they cover.

A lot of companies try to investigate numerous diseases and spread themselves very thin. We think it's better to focus on a few areas, prune your portfolio accordingly and bolster your expertise by hiring or collaborating with the best people in your chosen fields of research.

Many pharma executives now recognise the merits of 'open innovation' (**see box, A problem shared is a problem solved**).<sup>138</sup> The industry majors are actively linking up with universities. Some companies are also joining precompetitive discovery federations, where public and private institutions pool resources to overcome shared scientific bottlenecks. The international Serious Adverse Events Consortium

(iSAEC) is one such instance. iSAEC has already identified various alleles associated with drug-related liver toxicity and skin rashes in patients taking individual therapies. It's now exploring several cross-drug alleles that could cast light on the underlying biology of drug-induced SAEs.<sup>139</sup>

A number of historical rivals have entered into co-development pacts, too. Novartis and Amgen are jointly investigating a therapy for breast cancer. Similarly, BMS and Roche are collaborating on a melanoma product.<sup>140</sup> And, in September 2012, 10 leading companies formed a non-profit organisation called TransCelerate BioPharma to solve common drug development problems.<sup>141</sup>

We believe this pattern will continue and that, by 2020, most precompetitive challenges will be tackled collectively. But collaboration with fellow experts is only part of the equation. The other part is specialisation: focusing on a select range of diseases, rather than trying – and failing – to cover all the bases.

## Cutting to the chase

It's equally important to devise a clear path to clinical proof of concept for all compounds entering development and test them in humans as soon as possible, using the best tools for selecting subjects and endpoints. Biomarkers have a significant contribution to make here by narrowing down the subset of patients on whom a molecule should be tested and exposing defects more rapidly. So they should be treated as an integral part of the route to market, rather than being bolted on in late-stage development.

Some companies might also want to consider novel forms of testing, such as n-of-1 trials (where a single subject receives two treatments in an alternating fashion) and in-life trials. Most organisations still focus on performing traditional randomised controlled trials, believing that's what the regulators favour. But the EMA has explicitly stated that it's prepared to consider evidence from pre-planned, sequential n-of-1 trials.<sup>142</sup> And the FDA recently approved Xarelto for the prevention of strokes in patients with atrial fibrillation on the basis of a large in-life trial.<sup>143</sup>

## A problem shared is a problem solved

Open-innovation platforms such as InnoCentive and Kaggle are gradually changing the way pharma conducts research. The Pistoia Alliance also draws on the collective wisdom of pharma and informatics experts from a wide range of organisations to devise and document best practice in R&D. And Sage Bionetworks acts as a matchmaker for computational biologists.

Government agencies are getting in on the crowd-sourcing act, too. The US National Center for Advancing Translational Sciences and industry partners Pfizer, AstraZeneca and Lilly are tapping the nation's 'brightest

minds' to test various compounds that have been studied in humans but shelved, to see whether new uses can be found for them. And, in September 2012, the US President's Council of Advisors on Science and Technology recommended setting up a network of industry representatives, academic researchers, patient and consumer groups, physicians and insurance companies to address specific challenges. The proposed Partnership to Accelerate Therapeutics would have three major functions: to fill key knowledge gaps in the science, technology and methodologies underlying drug discovery and

development; to improve the clinical trial process; and to clarify the development pathway for innovative medicines.

Open innovation will solve a number of pharma's problems. It will help the industry become more pioneering by allowing it to share pieces of the biochemical jigsaw that would otherwise be sequestered in separate organisations and call on researchers in all walks of life. It will also cut research costs by reducing unnecessary duplication, as well as sparing patients from exposure to molecules other organisations already know don't work.

Both forms of testing can provide insights that traditional trials can't yield. N-of-1 trials are particularly useful for detecting variations in efficacy. Data from individual patients can be aggregated and analysed to extract broader inferences.<sup>144</sup> In-life trials reveal how well a product works in the real world and provide proof of its economic value (see Table 1).<sup>145</sup>

Conducting in-life trials isn't easy. Many doctors working in community practices don't have any experience of participating in clinical trials, so they need to be trained. Most such trials also require larger samples to cover losses from patients dropping out. And it's often harder to interpret the results, both because practitioners are free to treat patients normally and because some patients may be taking multiple medications.

So in-life trials aren't a substitute for randomised controlled trials. And, managed badly, they simply drive up costs. But that's not what we're advocating here. The point we're making is that pharma should be conducting different kinds of trials to answer different questions. And it should be doing both as efficiently as possible, using an increasingly sophisticated electronic infrastructure (see box, **The real McCoy**).<sup>146</sup>

Moreover, since the emphasis healthcare payers put on evidence of comparative effectiveness will only grow, the industry should be collecting that information before it goes to market. Conducting such research poses challenges at any time (e.g., selecting the most appropriate comparator, dose and administration regime, study population and endpoints for comparison).<sup>147</sup> But doing it when a drug has just been launched is even harder because of rapid changes in the characteristics of the user population during the early phase of marketing.<sup>148</sup>

**Table 1 These are the core characteristics of traditional, n-of-1 and in-life trials**

	Traditional trial	N-of-1 trial	In-life trial
<b>Goal</b>	To establish clinical validity: does the intervention work?	To measure variability: does the intervention work in an individual patient?	To establish clinical utility: does the intervention work in the 'real' world?
<b>Setting</b>	Experimental: hospital or academic medical centre	Normal: community-based care	Normal: community-based care
<b>Participants</b>	Carefully selected to maximise patient compliance	Single subject	Representative of everyday clinical practice
<b>Intervention</b>	Strictly enforced fixed regimen	Alternating treatments	Flexible, as in daily life
<b>Comparator</b>	Placebo or directly competing therapy	Placebo or directly competing therapy	Usual care, including least expensive/most effective treatment
<b>Data points</b>	Clinical endpoints	Clinical endpoints, quality of life, use of resources and costs	Clinical endpoints, quality of life, use of resources and costs
<b>Outcomes</b>	Condition-specific, often short-term surrogates or process measures	Condition-specific, with periodic re-testing for longitudinal studies	Long-term measures that reflect disease progression and broad range of outcomes

Sources: S. Treweek & M. Zwarenstein, 'Making trials matter: pragmatic and explanatory trials and the problem of applicability'; PwC

## The real McCoy

Several healthcare providers are piloting remote monitoring schemes. The British NHS is rolling out one such project: 4,000 patients with chronic diseases will be given touchscreen phones that can monitor their health and vital signs remotely.

Some of the biosensors in development can also be used for point-of-care diagnosis. Israeli chemical engineer Hossam Haick has, for example, built an artificial 'nose', which detects various cancers by picking up disease markers that move from the bloodstream into the lungs and get exhaled.

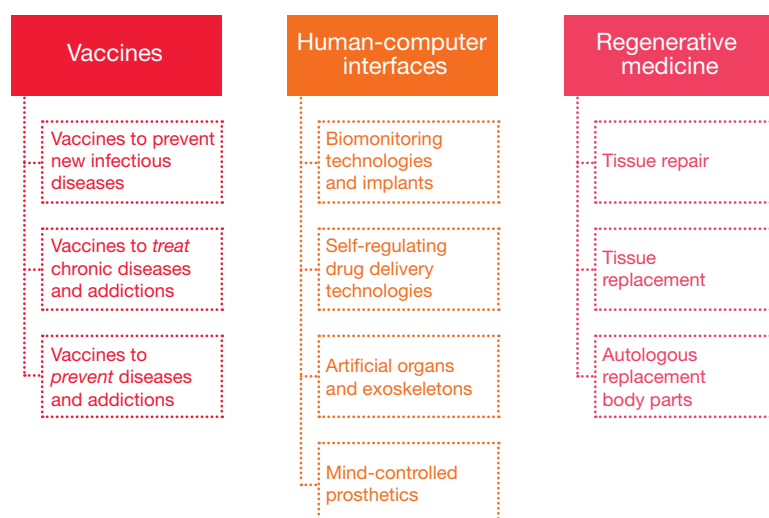
The race is now on to develop a Star Trek-style medical 'tricorder'. In the long-running TV series, fictional USS Enterprise medical officer Dr 'Bones' McCoy could diagnose a patient's condition simply by scanning his body. Global telecoms equipment provider Qualcomm has recently thrown down

the gauntlet with a \$10-million prize for the first person who builds a tool capable of capturing 'key health metrics and diagnosing a set of 15 diseases'.

Meanwhile, new audio technologies will transform the way in which patient data is captured and categorised, if inventors like Steve Goldstein have their way. Goldstein, who heads acoustics specialist Personics Labs, recently filed a patent application for an 'always-on' headwear recording system that automatically records audio and files the recording in a separate storage device. By 2020, such technologies will be used to compile EMRs. The doctor will wear an in-dwelling hearing device that automatically records patient consultations and stores the information so that it can easily be retrieved to provide a synopsis of previous visits or a full patient history in real time.



**Figure 4 New forms of medical intervention are in the pipeline**



Source: PwC

## Turning to new treatment types

We've talked about what pharma can do to improve the speed and skill with which it develops new medicines, but those aren't the only aces in the deck. Just as the insights provided by genomics are one reason to feel optimistic, so is the progress scientists are making with new forms of medical intervention (see Figure 4).

The industry's options are increasing, as these new avenues open up – and some forms of intervention could be particularly helpful in dealing with the HONDAs who consume a disproportionate share of healthcare resources. New drug delivery technologies could reduce non-compliance, while new vaccines and regenerative medicine could provide a way of preventing or curing certain chronic conditions.

## Moving the needle with new vaccines

The induction of antibodies by prophylactic vaccination against infectious diseases has been the most effective medical intervention in human history.<sup>149</sup> Bill Gates recently acknowledged as much when he called on the World Health Assembly to make this 'the Decade of Vaccines' and set some basic goals: eradicate polio in the 1% of the globe where it remains; develop five or six new vaccines; and build a system capable of delivering vaccines to every child. That, he said, would 'save 4 million lives by 2015 and 10 million lives by 2020'.<sup>150</sup>

Advances in vaccinology are providing the tools with which to develop more effective vaccines for a much wider range of diseases. With structure-based antigen design, for example, X-ray crystallography is used to determine the three-dimensional structure of an antigen-antibody complex and then computational protein design is used to engineer an antigen.<sup>151</sup>

New delivery technologies are also expanding the ways in which it's possible to insert antigens into the immune system. Researchers at the University of Oslo have developed one approach that uses electrical impulses and DNA code to trigger a molecular reaction. The technology has two major advantages; it dispenses with the need for an adjuvant and produces a much quicker, more powerful immune response.<sup>152</sup>

A new generation of vaccines is now in the pipeline. Some of them aim to treat infectious diseases like malaria and HIV or antibiotic-resistant pathogens like MRSA.<sup>153</sup> Others aim to treat chronic or acute conditions and addictions. Vaccines for a wide range of chronic illnesses, including diabetes, obesity and cardiovascular disease, are already in clinical development.<sup>154</sup> Several cancer vaccines are also showing considerable early promise, one such instance being a 'universal' vaccine that operates on the principle of training a patient's body to recognise and destroy tumour cells by itself.<sup>155</sup> And work on vaccines to curb nicotine and cocaine addiction is likewise well underway.<sup>156</sup>

Many of these new vaccines for non-infectious conditions are designed to slow down, as distinct from curing or preventing, disease. But it's prophylactic vaccines that represent the industry El Dorado – and here, too, there's been progress. Novartis recently filed for approval of a vaccine that protects infants against meningococcal disease, for example, while GSK has commenced Phase III trials on a recombinant vaccine for preventing malaria.<sup>157</sup> And Inovio Pharmaceuticals is testing a synthetic DNA vaccine that might both treat and prevent infection with HIV from clade B, the subtype of virus mostly seen in North America and Western Europe.<sup>158</sup>



## Building bionic bits

The realm of man/machine interfaces is proving equally exciting. Scientists at Massachusetts Institute of Technology (MIT) are, for example, developing a 'smart tattoo' with a nanoparticle ink that can track glucose levels in patients with diabetes.<sup>159</sup> And researchers at China's Chongqing University have built a prototype temperature-controlled drug release system using titanium nanotubes covered in a layer of hydrogel.<sup>160</sup> Both have obvious uses in pharma.

Meanwhile, the US Department of Energy Office of Science is spearheading efforts to develop a device containing hundreds of microelectrodes that can be implanted in the eyes of people blinded by retinal disease.<sup>161</sup> Swiss researchers are developing a wheelchair driven via electrodes placed on the skin in a skullcap. And animal tests have been conducted in which devices are implanted directly into a nerve to process and transmit signals wirelessly to an external object.<sup>162</sup> British professor of cybernetics Kevin Warwick has even tested a neural implant on his own nervous system.<sup>163</sup>

## Growing new parts

With regenerative medicine, it may eventually be possible to do away with some biomechanical aids altogether. Several tissue-repair products, such as Dermagraft, are now on the market. But that's just the first step. The second is tissue replacement, using 3D bioprinters to print living tissue with 'ink' derived from human cells.

Various organisations have already made headway in this field. In late 2010, for example, US biotech firm Organovo created the first blood vessels to be bioprinted using cells cultured from a single person. It's also successfully implanted bioprinted nerve grafts into rats and hopes to start human trials of bioprinted tissue by 2015.<sup>164</sup>

Replacing damaged neurological tissue and entire organs is, of course, the end goal – and, despite the enormous challenges, it's no longer a far-fetched fantasy. In January 2012, scientists at the General Hospital of Chinese Armed Police Forces began a Phase II trial on the use of umbilical cord stem cells in treating motor neuron disease.<sup>165</sup> And, in June 2012, US biotech company Advanced Cell Technology started testing retinal pigment epithelium made from embryonic stem cells to treat Stargardt's disease, a condition that destroys the central vision of the eyes.<sup>166</sup>

But perhaps the best illustration of what scientists can achieve comes from a remarkable international collaboration in mid-2011. Doctors at Stockholm's Karolinska Institute completed the world's first synthetic organ transplant, using a trachea 'grown' on a scaffold at London's UCL Medical School and soaked in stem cells from the patient's bone marrow in a bioreactor made by Harvard Bioscience.<sup>167</sup>

## The return of the blockbuster

So conventional pharmacological agents – personalised or otherwise – aren't the industry's only hope. On the contrary, its options are getting steadily wider and, by 2020, we think there will be far more diversification. But many of these options will require profound changes in R&D, manufacturing and distribution.

When human cells and tissues are tested in animals, for example, there's a cross-species immune response that complicates the findings. In addition, the way the cells are distributed in the bodies of healthy and diseased animals often varies, which may have a bearing on the safety endpoints that are used. Testing gene and cell therapies in humans poses other problems, including the risk of undesirable mutations and transmission of the transplanted gene to germ-line or transplacental cells, although the latter has never yet been observed.<sup>168</sup>

There are unique challenges with the manufacturing and characterisation of cell and tissue therapies, too. Living cells are unstable, which means it's essential to assess the effect of biological variability on each stage in the manufacturing process. Moreover, cell and tissue therapies can't be terminally sterilised, and cryopreserving the starting cell source or final product could impair its quality.<sup>169</sup>

In short, many of these new therapies will require much more complex development, manufacturing and distribution processes than those used to produce conventional medicines. Yet they will also generate enormous clinical and commercial value. A prophylactic vaccine for a common chronic condition or stem cell therapy that cures a neurodegenerative disorder won't earn revenues from repeat prescriptions. But it will command a very much higher price precisely because it provides a *permanent* solution. Such products will be tomorrow's blockbusters.

## Keeping an open mind

Whatever diseases and forms of medical intervention a company decides to focus on, though, and whatever methods it chooses to discover and develop new treatments, one thing's vital: keeping an open mind until clinical proof of concept. It's always painful to see a beautiful hypothesis slain by an ugly fact. It's even more painful when that hypothesis has consumed a lot of money.

# Portfolio management: Choosing the best jam

*“If you must play, decide on three things at the start: the rules of the game, the stakes and when it’s time to quit.”*

Chinese proverb

## Flummoxed by all the flavours

In 1995, social scientist Sheena Iyengar set up a tasting booth in a US food store and pretended to be a supplier of gourmet jams. Every few hours, she switched between a selection of six flavours and 24. On average, customers tasted two flavours, regardless of the size of the assortment.

Now here’s the nub. Only 40% of customers were drawn to the small selection, whereas 60% stopped by the large one. But 30% of those who’d been given a choice of six flavours purchased a jar of jam, while only 3% of those who’d been given a choice of 24 flavours did so. Confronted with two dozen samples, most people were paralysed by indecision.<sup>170</sup>

Choosing which drug candidates to progress through the pipeline is far more difficult than choosing which kind of jam to buy, and a lot more rests on the choice. Yet many pharma companies are behaving like the customers in that food store – with one major difference. Rather than walking away without purchasing anything, they’re buying a jar of jam in every flavour.

**Table 1 The biggest pharma companies have numerous projects in their pipelines**

Company	Pre-clinical	Phase I	Phase II	Phase III	Total
Abbott Laboratories	40	35	51	16	142
Amgen	21	47	74	14	156
AstraZeneca	27	80	116	27	250
Bristol-Myers Squibb	57	94	114	23	288
Eli Lilly	22	62	126	24	234
GlaxoSmithKline	46	115	217	44	422
Johnson & Johnson	30	48	73	15	166
Merck & Co.	35	60	82	35	212
Novartis	27	79	225	50	381
Pfizer	71	92	120	31	314
Roche	49	127	133	37	346
Sanofi	33	64	80	31	208
<b>Total</b>	<b>458</b>	<b>903</b>	<b>1,411</b>	<b>347</b>	<b>3,119</b>

Source: EvaluatePharma. Phase III figures verified by cross-referencing EvaluatePharma data with latest available company-reported pipelines and ClinicalTrials.gov

Note: Excludes abandoned and suspended projects.

The bitter taste of failure

We discussed the scientific factors behind pharma’s declining R&D productivity in chapter 4. Managerial factors play a big role, too, and one of the biggest factors is poor decision making. As Table 1 shows, many of the industry leaders have more than 100 projects in Phases II and III. Most of these projects are destined to fail.

Attrition rates in clinical trials have climbed steeply over the past two decades. What’s more instructive, though, is when – and why – so many molecules have foundered (see Table 2).<sup>171</sup> The high percentage of products pulled for strategic reasons in Phase II suggests that one problem may be overlapping activity between companies with very similar compounds in the pipeline. That’s grounds for greater collaboration.<sup>172</sup> But there’s a second, and far more serious, issue.

Between 2007 and 2010, 83 compounds failed in Phase III or during the submission process. Analysis by CMR International shows that 66% of them fell near the final post because of insufficient efficacy: 32% were no better than a placebo; 5% were no better than an active control; and 29% showed no real benefit as add-on therapies.<sup>173</sup>

In short, the researchers concluded, many companies seem to be pushing candidates that display only marginal efficacy in Phase II proof-of-concept studies into Phase III trials. Many also seem to think that success in one disease will translate into success in a different disease, without firm evidence that the mechanism of action is still relevant.<sup>174</sup>

Table 2 Failure rates in clinical trials have soared in the past 20 years

	Attrition rates		Current reasons for failure
	1990	2010	
Phase I	33%	46%	
Phase II	43%	66%	Insufficient efficacy (51%) Safety concerns (19%) Strategic issues (29%)
Phase III	20%	30%	Insufficient efficacy (66%) Safety concerns (21%)

Sources: Fabio Pammolli et al., ‘The productivity crisis in pharmaceutical R&D’; Steven M. Paul et al., ‘How to improve R&D productivity’; and John Arrowsmith, ‘Trial watch: Phase II failures: 2008-2010’; ‘Trial watch: Phase III and submission failures: 2007-2010’; and ‘A decade of change’

So pharma’s spending vast sums of money buying jars of jam in every flavour, only to find that most of them don’t pass muster. To quote equities analyst Andrew Baum, it’s ‘failing late, failing more and failing expensively’ – and that’s caused ‘some world-champion value destruction’.<sup>175</sup>

Why? We think it’s because many companies don’t really understand the relationship between risk and value. They’re also over-optimistic and, as a result, they’re trying to do too much.

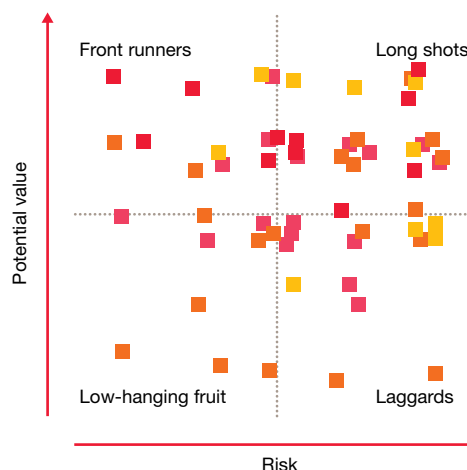
## Deciding on the rules, the stakes and when it's time to quit

What should such organisations do? Their options are limited, since they can't conjure up new molecules. But what they can do is prune their portfolios to focus on the compounds with the greatest probability of success. We recommend using two yardsticks: therapeutic expertise and the risk/value ratio of each compound in the pipeline. Plotting the correlation between risk and value helps to separate the frontrunners from the long shots, and the low-hanging fruit from the laggards (see Figure 1).

Of course, most companies do consider the risk and potential value of the molecules in their portfolios, but they rarely draw on all the information at their disposal. When they measure risk, for example, they generally concentrate on technical risks: how novel a target or mechanism is, the degree of confidence in rationale and so forth. They spend much less time considering commercial risks like market access or whether a product offers *enough* improvement on the existing alternatives (see Table 3).

Similarly, when they measure potential value, they don't give sufficient thought to what payers or providers think. One problem here is that there's no consensus definition of outcomes for some diseases – and thus no common way of assessing the value a new medicine might generate. But most companies don't discuss the issue with healthcare payers and providers. There are a few honourable exceptions. GSK now consults health officials and insurers at least five years before a medicine's due to leave its labs. And, in 2011, Sanofi brought in Medco Health Solutions to stress-test its entire Phase I development programme.<sup>176</sup> Such companies are still in the minority, though.

Figure 1 A clear risk/value framework helps companies make better decisions



Source: PwC

Table 3 The risk/value equation has many dimensions

Potential value	Risks	
	Technical and regulatory risks	Commercial risks
What's the prevalence of the disease?	How complex is the disease?	How many other companies are working on the disease?
How serious is the disease?	How new is the biological target? What are the implications of hitting it?	How many other treatment options exist?
What's the cost of treating individual patients?	How new is the mechanism of action?	Is the product better enough, given the competing therapies?
What's the total medical spend on the disease?	What's the level of confidence in rationale?	Is it better enough, compared with normal care?
What are the generic and non-drug alternatives?	What pharmacokinetics and/or bioavailability issues exist?	What's the product's economic profile, relative to that of the competing therapies?
How useful is the product?	Do we know enough about the disease population, pathophysiology, pharmacological properties of the compound etc. to use modelling and simulation?	Will healthcare payers and providers want to use it? And what incentives will they require (e.g., patient access schemes, add-on services)?
How much safer, more effective or easier to use is it, relative to competing therapies?	Will the product need a companion diagnostic to get approved?	Will healthcare payers and providers be prepared to pay for the product? If so, how much?
What is its unique selling point, relative to the alternatives?	How far is it from proof of concept? And is there a clear development path?	What will healthcare payers and providers require to buy it (e.g., outcomes data, discounts, risk-sharing contracts)?
How might it reduce overall healthcare costs?	Will the product require a complex manufacturing process, formulation and/or packaging?	Will patients take the product as prescribed?
Can it command a premium price?	What are the likely pre-approval regulatory hurdles and post-regulatory requirements (further studies, risk management etc.)?	What future opportunities exist, (e.g., line extensions and OTC formulations)?

Source: PwC

*Good investment managers constantly keep an eye on their portfolios*

### ***Building a balanced portfolio***

The next step is to build a balanced portfolio, just as investment managers try to do when they're managing financial assets. Responsible investment managers don't bet all their clients' money on risky assets that might, with luck, deliver a big return. They combine a few highly speculative investments with bread-and-butter stocks that will generate a steady income.

But many pharma companies assume they should be concentrating on the molecules with the greatest potential revenues. They also underestimate the risks, or overestimate the potential value, of the products in their pipelines. That's partly because they rely on the opinions of the researchers involved – who naturally 'talk up' the projects they're working on. So it's essential to appoint an independent committee of senior executives to decide which products to pull and which to progress, and to be completely objective during the appraisal process.

Moreover, this isn't an exercise that should be done once or twice a year. Good investment managers constantly keep an eye on their portfolios, buying and selling assets on a regular basis to maintain the balance between risk and potential value on which they've decided. Most pharma companies, by contrast, only review their portfolios every six months.

Admittedly, drug candidates aren't as volatile as shares. Nevertheless, a clinical pathway can be completely redesigned in six months, as we noted earlier. So it's crucial to monitor the drug portfolio continuously and dynamically – and to be decisive.

Adopting a more discriminating approach has two advantages. First, it frees up resources for the candidates a company chooses to focus on – which increases the odds of getting them to market. Second, it helps the company reduce its R&D costs. And even if it only succeeds in lowering its cost base without increasing its output, it's still improved its productivity.

*Thinking like an investor helps executives see their business as others see it*

**Thinking like an investor**

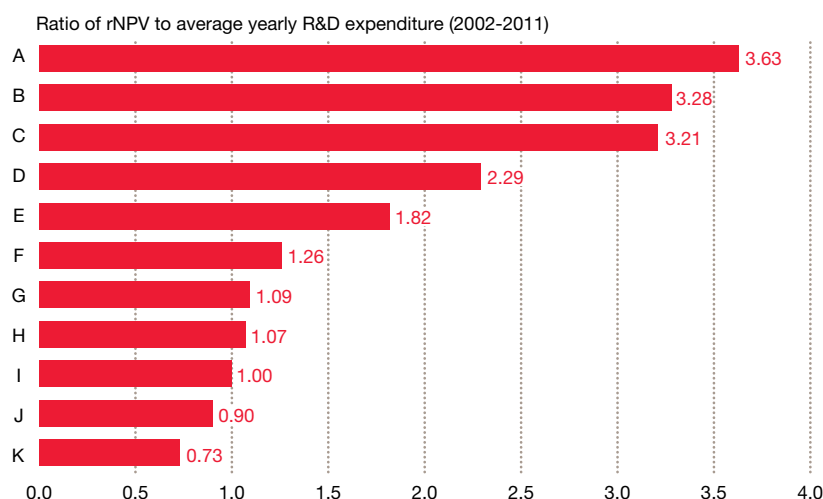
It's not enough to look at a company's R&D portfolio in isolation, though; senior management should also consider how strong or weak it is relative to those of other companies in the sector. When investors decide where to put their money, they compare different companies – and the competition for capital has become intense, following the global economic downturn.

Thinking like an investor helps executives see their business as others see it and expose hidden assumptions. We'll focus on the quoted industry majors, using risk-adjusted net present value (rNPV) analysis – now the standard technique for valuing pharmaceuticals – to illustrate what we mean.

Examination of the pipelines of the 11 industry majors shows there are significant differences in the quantity and quality of the key candidates they have in Phases II and III (i.e., those to which analysts have assigned an rNPV).<sup>177</sup> That, in turn, means there are significant differences in their total pipeline rNPV. But the sums the 11 companies invest in R&D also vary, so it's the relationship between their R&D expenditure and pipeline rNPV that really counts. In **Figure 2**, we've compared the two, using average annual expenditure over the past 10 years to eliminate significant changes in spending from one year to the next.

This simple comparison shows that three companies have a pipeline rNPV of more than three times their average annual R&D outlay over the past decade. Conversely, two have pipeline rNPVs that are *less* than their average annual investment in R&D.

**Figure 2 The ratio of pipeline risk-adjusted NPV to R&D expenditure differs considerably from one company to another**



Sources: EvaluatePharma and PwC analysis

Note: The rNPV of each pipeline is the aggregate rNPV of all the products in Phases II and III to which analysts have attributed a value. The rNPV of each product has been calculated using consensus sales forecasts to 2018. Sales beyond 2018, costs and resulting cash flows have been projected over the life of each product to 2032. Terminal growth methodology has been applied to calculate the value of any cash flows after 2032. All R&D costs have been treated as 'sunk'.



Some of these disparities are due to differences in the extent to which the 11 companies in-license compounds rather than generating them organically. R&D costs are typically expensed via the income statement, whereas upfront in-licensing fees and milestone payments are typically capitalised and amortised over the useful life of the resulting products.

The kinds of therapies a company focuses on are also a factor, as is the spread of its assets. The trials required for primary-care products are often larger and more costly than those required for specialist products. And a company with a lot of late-stage assets will probably be spending more on trials than one with a lot of assets in earlier stages of development.

But the variations are too marked for this, alone, to explain them. In **Figure 3** we've therefore looked more closely at the composition of each company's late-stage pipeline. We've divided the key candidates in each portfolio into six clusters, ranging from the most valuable (those with an rNPV of > \$1 billion) to the least valuable (those with an rNPV of < \$125 million).

Company A has 10 key molecules in late-stage development and four of them have an rNPV of > \$1 billion. These compounds collectively represent four-fifths of its total pipeline rNPV. Company J has also concentrated on the top end of the value spectrum, but it has far fewer key candidates in late-stage development.

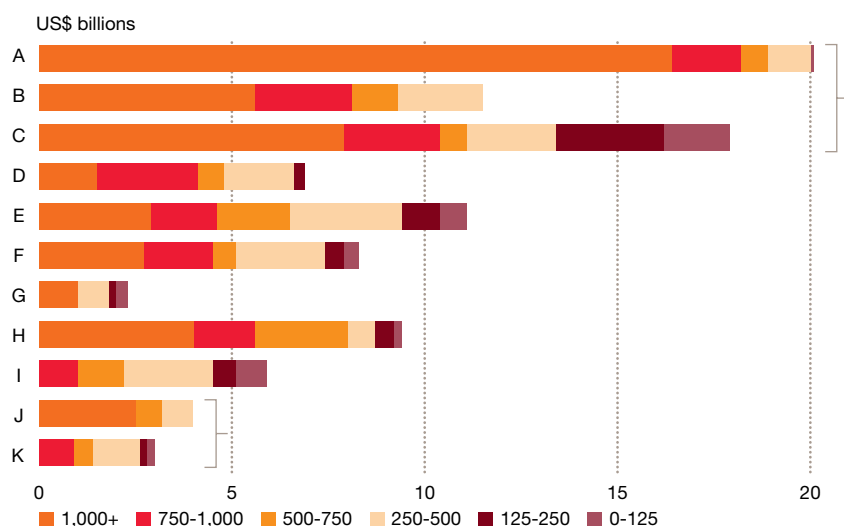
Companies B and C have cast their nets more widely. Even so, more than 40% of their pipeline rNPV comes from compounds with an rNPV of > \$1 billion, whereas company K has no such compounds in its portfolio. In fact, two-fifths of its pipeline rNPV comes from products with a potential value of < \$500 million.

So what accounts for these differences? We believe two factors – therapeutic focus and the ability to manage risk – have played a big role. Company A has been very selective. It's pursued a low-risk, high-value strategy and controlled its risks by combining critical mass with rigorous portfolio management, whereas companies B and C have managed their risk by spreading it. Both are developing a wider array of products in a wider range of therapeutic areas. Both have also recognised the merits of including 'bread-and-butter'

molecules in their portfolio mix. Handled badly, this strategy can dilute a company's focus, but their pipeline rNPV suggests that B and C are striking the right balance.

In other words, the three industry majors with the most promising pipelines (measured in terms of rNPV) have decided on the rules by which they're playing and stuck to them. That's what we think all pharma companies should do: weed out their weakest compounds, with disciplined and continuous portfolio management; concentrate on the frontrunners, with some bread-and-butter molecules to provide stability and a few long shots that might generate really high returns; cut their R&D costs; and communicate what they're doing effectively. Winners know when to double-down on their investment, but they also know when to quit.

**Figure 3 The way value is distributed differs widely between companies**



Sources: EvaluatePharma and PwC analysis

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## Corporate culture: Culprit and cure?

*“The ultimate measure of a man is not where he stands in moments of comfort, but where he stands at times of challenge and controversy.”*

Martin Luther King, Jr.

The values, beliefs, habits and management style that determine how people in an organisation think and behave have a profound bearing on its decision-making processes. And when the environment in which the organisation operates alters, these characteristics often need to alter, too. Yet most pharma companies still rely on a corporate culture that prevailed 20 years ago.

The 1980s and 1990s were a period of relative economic stability. Today, there's much more economic volatility. The global distribution of wealth is also shifting, with the rise of the growth markets and greater gender equality.

Demographic and epidemiological trends that were still on the distant horizon in the early 1980s have simultaneously come to the fore, while new communication technologies have empowered individuals. In the Facebook era, patients can see – and say – more about the organisations they deal with, and the medicines they take, than at any previous time in history.

Pharma's business model has also altered almost beyond recognition. In the 1980s and 1990s, it made medicines for chronic diseases, marketed them to doctors and focused on turning them into blockbusters. These days, it's concentrating on specialist medicines, which it markets to healthcare payers – who use different, and more rigorous, selection criteria (see Table 1).

But despite such seismic shifts, the organisational culture at many pharma companies has changed very little – or, if it has changed, some people suggest, it's only changed for the worse. “The Big Pharma culture has been homogenized, purified, sterilized, whipped, stirred, filtered, etc. and lost its ability to ferment the good stuff required to innovate,” life sciences venture capitalist Bruce Booth argues.<sup>178</sup>

Booth isn't alone in blaming the industry's declining scientific productivity on cultural influences. In one recent survey of 150 R&D executives, 54% cited lack of creativity as a key organisational issue, while 53% cited lack of coordination between the R&D and commercial functions.<sup>179</sup>

Why this cultural sclerosis? One possible reason is the fact that most of the industry's top executives learned their business while the blockbuster model reigned supreme. They were also promoted from within, or recruited from similar companies, and naturally tend to reinforce the existing culture because it's the one in which they feel comfortable.

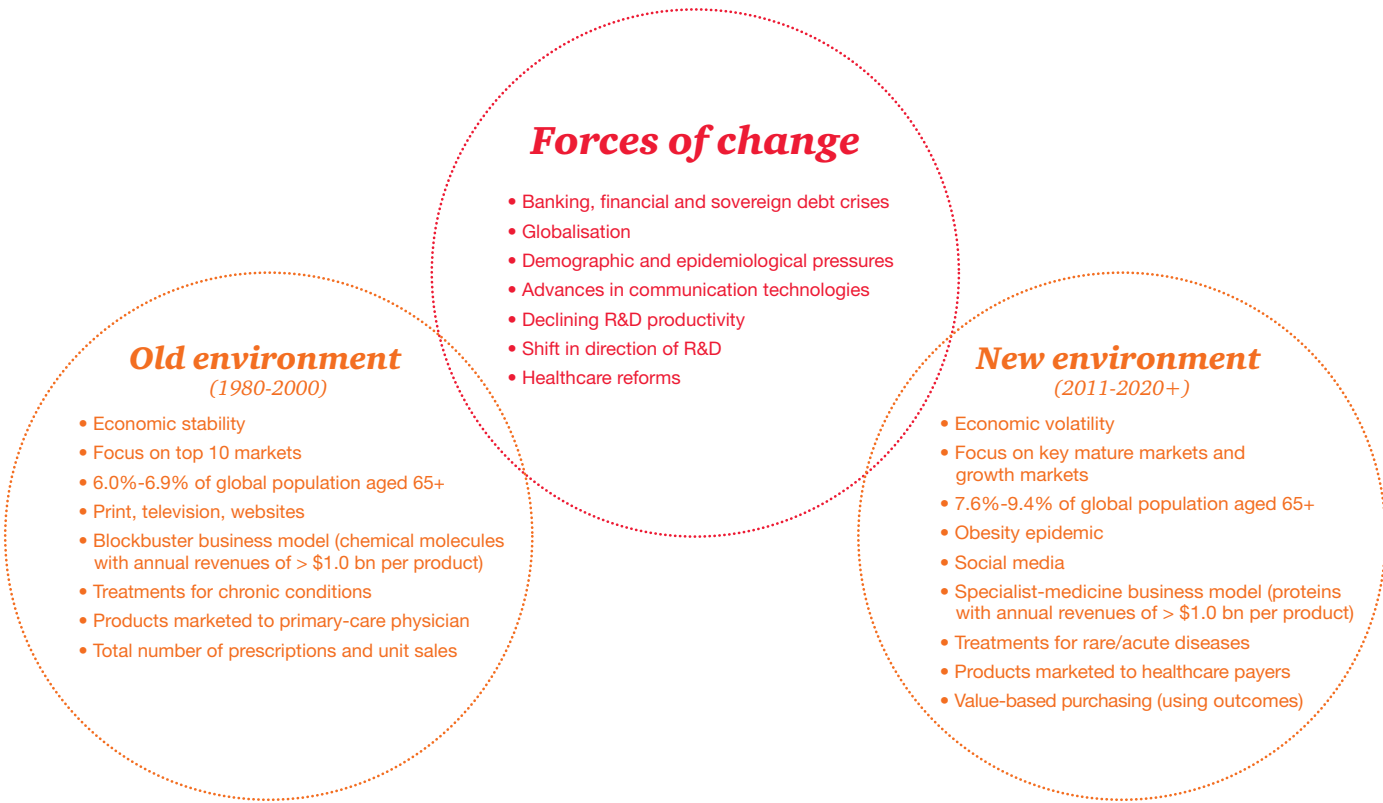
That’s slowly changing with the appointment of a number of younger executives keen to embrace new ways of doing business and growing internal acceptance that the existing state of affairs can’t continue. As revenues, profits and share prices fall, and redundancies become more widespread, many employees have recognised that the old days are truly over.

But shorter periods in office are also an obstacle. In 2000, the average tenure of a chief executive was 8.1 years; by 2010, it was down to 6.6 years.<sup>180</sup> It’s lower still in pharma, with a typical tenure of

4.8 years for the chief executive and just 3.6 years for the head of R&D.<sup>181</sup> This presents particular problems for an industry whose product development cycle is at least a decade. In essence, the incumbent management has to make major decisions it can’t see through to the end.

To sum up, then, today’s top pharma executives face a formidable test. They must pilot their companies through turbulent waters, drawing on experience acquired in very different circumstances, without any leeway in which to make mistakes.

**Table 1    The context in which pharma operates has changed dramatically**



Source: PwC

*Successful innovation requires strong leadership, commitment and solid decision-making*

### **Creating a more innovative culture**

So what can the industry's senior figures do? We believe there are a number of changes they can initiate to foster a more creative corporate culture and reinvigorate their companies.<sup>182</sup>

### **Bring fresh blood into the top team**

Successful innovation requires strong leadership, commitment and solid decision-making. It also requires an open mind and the courage to experiment – both traits that are harder to find in companies where most of the management comes from the same mould.

There's relatively little gender or racial diversity in the top echelons of most pharma companies, although the industry's not unusual in this respect. Only 10.5% of the 3,933 pharma and biotech directors in the BoardEx global leadership database are women. Similarly, only 10.2% of the 1,500 who disclose their nationality come from countries outside North America and Europe. A mere 55 come from the BRIC economies. But, with globalisation and the rise of the growth markets, many pharma companies will need to recruit more widely.

Some organisations might also want to consider hiring first-class executives from other industries, although they'll have to exercise considerable care. Pharma depends on specialist knowledge more heavily than most other industries, and bringing in outsiders hasn't always proved a positive experience. That said, hiring from a broader talent pool gives a company access to new ideas and methods, which helps it thrive in periods of turmoil.

### **Set clear rules and stick to them**

Both employees and shareholders need to know where they stand, so it's crucial to set clear ground rules. Internally, senior management should specify the sort of innovation it wants, how it plans to measure innovation and the trade-offs it's willing to make. It should also make sure the right resources are in the right places.

Externally, senior management should let investors know how much the company plans to spend on R&D over the next few years – and stick to its guns in the face of short-termism. Jeffrey Immelt, the highly respected head of General Electric, has long followed this policy. "Over a 10- or 20-year time period, the businesses that are hard to do had the best returns," he says. "So the arithmetic works over time."<sup>183</sup>

### **Lessen the layers**

Too much bureaucracy stifles creativity – and big pharma companies tend to be very bureaucratic. We recommend eliminating as many layers of middle management as possible, minimising the number of committees and creating autonomous R&D teams that report straight to the top. Locating these teams in biotech clusters can also stimulate innovation.

But the main point is to remove roadblocks. Every R&D team should be given a specific challenge, budget and timeframe, and then left to get on with the task without having to plough through vast quantities of paperwork, grapple with the latest management craze or worry about surviving the next cull. If a team doesn't deliver, it should certainly be held accountable – but not before it's had a chance to do its job.

### **Recruit non-conformists, build networks**

Most companies, pharma included, focus on recruiting people whose ‘faces will fit’. Yet it’s sometimes better to hire the ‘wrong’ people because they’re the ones who’ll challenge the status quo. There’s a lot of research to show that mavericks play a major role in innovation.<sup>184</sup> They’re typically independent-minded, passionate about what they do and willing to break the rules. Such people can therefore be a great source of inspiration, although managing them isn’t easy.

But, ultimately, innovation isn’t dependent on individuals; it’s the product of networks of people, both within a company and outside it (e.g., partners, suppliers and customers). That’s especially true of pharma, where new sciences like genomics are so complex that unravelling the insights they offer requires a multi-disciplinary approach. So it’s equally important to build networks that cut through the barriers between different business units and organisations, and encourage genuine collaboration to get access to the best science.

Numerous open-source R&D initiatives have been launched in recent years and some of them have been very successful. Yet significant cultural hurdles remain. One big stumbling block is fear of sharing intellectual property, even though collaborating provides opportunities for developing new assets.<sup>185</sup> A second is the industry’s ‘reluctance to let go of unnecessarily individualistic business processes’.<sup>186</sup>

### **Use the right measures and rewards**

Many pharma companies measure and reward the wrong things. For example, they use purely financial criteria to measure innovation. They reward researchers for getting new molecules to the point immediately prior to testing in man – which encourages those researchers to push unviable compounds further down the pipeline. And they promote their best scientists to management positions, although scientific expertise is no guarantee of managerial competence.

In our experience, it’s better to use a measurement system that combines financial and non-financial metrics (like motivation and commitment). That system should also be flexible enough to measure different kinds of innovation and easy to understand. Similarly, it’s better to reward scientists only when a molecule reaches proof of concept or when they solve serious problems. This encourages them to focus on creating compounds with a real chance of success in the clinic. It also strengthens the links between R and D.

But it’s not enough to reward success; it’s equally important to promote a ‘fail early, fail cheaply’ mindset by providing incentives for terminating weak candidates as fast as possible. Punishing failure socially or economically discourages risk-taking and dampens creativity.

### **Times of challenge and controversy**

A company’s culture alters only when the people who work in it alter how they think, talk, decide and act – and that happens only when top management shows the way. It’s now more imperative than ever for pharma’s business leaders to blaze a new trail.

The industry is going through a period of profound change. Any company that wants to weather the transition will have to focus on delivering value, not charging high prices. It will have to supplement its products with services. And it will have to become an integral part of the healthcare continuum.

The smartest and most charismatic executives already know this. They’re building organisations with the courage to explore and flexibility to thrive in different conditions. Others continue to preside over companies that hark back to a more comfortable past. Yet the ultimate measure of an enterprise – as it is of the people who lead it – is not where it stands in ‘moments of comfort’, but where it stands at ‘times of challenge and controversy’ such as now.

*It’s now more important than ever for pharma’s business leaders to blaze a new trail*

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# Conclusion: From vision to decision

*“Almost anything can be turned around: out of every ditch, a path, if you can only see it.”*

Hilary Mantel

The next few years may look bleak for pharma, but we're convinced that the following decade will bring a golden era of renewed productivity and prosperity. We've discussed our vision of the future in earlier Pharma 2020 papers. Our focus here is on how companies can reach 2020 in a position to deliver better outcomes and profit from the changes that lie ahead.

The paramount challenge is to create more value for patients, providers and payers – and thus for shareholders. Clearly, the route each company takes will depend on its individual aims and circumstances. Nevertheless, there are a number of common imperatives.

- Every company will have to provide real-world data on the outcomes its medicines deliver, and that will entail setting up a suitable infrastructure to capture such data.
- Every company will have to decide how much (if anything) to invest in the growth markets, where to invest and what strategies to pursue in the countries it targets. The biggest markets might not be the most profitable ones, for example, and the costs of setting up a local manufacturing arm might outweigh the additional custom.

- Every company will have to be more selective about the diseases it addresses. Many will also have to consider the implications of investing in new treatment types, such as vaccines and regenerative medicine.
- Every company will have to invest more heavily in genetics and genomics, and revise its R&D processes to improve its scientific productivity. That will involve sifting through a plethora of new technologies, singling out the best and making sure they're properly integrated.
- Every company will have to collaborate with academia, governmental and non-governmental organisations, fellow life sciences companies and other stakeholders, such as the regulators and patient groups, to get access to the best science and eliminate waste.
- Every company will have to be more discriminating about the candidates it advances through the pipeline and courageous enough to dump the junk *before* racking up big bills.
- Every company will have to make sure it behaves ethically at all times and is an organisation others want to associate with. That means being open and honest rather than treating compliance with the regulations as a cost of doing business.
- Every company will have to transform its corporate culture to foster innovation and address the needs of patients, payers and providers in the twenty-first century.

There is indeed a path out of every ditch for those who can only see it. That path may be hard – strewn with impediments, forking in unforeseen ways, demanding decisions that are very difficult. But those companies that survive the journey will reap significant gains. In another decade, they'll have the scientific and technological edifice to start developing medicines that render some of the most serious diseases from which we now suffer curable.



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# Key national indicators

	Projected population in 2020 (millions)		Economic indicators		Personal affluence (% of adults with net worth, 2010)				Public health (% of population with access, 2010)	
	Total	Aged 60+	GDP, 2011 (US\$ bn)	Per capita health spending, 2010, US\$	Under US\$1,000	US\$ 1,000-10,000	US\$ 10,000-100,000	US\$ 100,000+	Clean water	Improved sanitation
<b>North America</b>										
Canada	37.2	9.3	1,737	5,222	10.0	10.3	31.0	48.7	100	100
United States	337.1	75.6	15,094	8,362	3.5	23.8	36.5	36.2	99	100
<b>EU-Big Five</b>										
France	65.9	17.3	2,776	4,691	0.3	10.5	49.4	39.7	100	100
Germany	81.0	24.5	3,577	4,668	13.1	14.6	30.4	41.9	100	100
Italy	61.3	17.9	2,199	3,248	0.0	41.4	41.4	55.5	100	100
Spain	48.7	12.2	1,494	2,883	1.1	18.0	47.9	32.9	100	100
United Kingdom	65.8	16.1	2,418	3,503	0.3	12.2	40.9	46.6	100	100
<b>BRIC economies</b>										
Brazil	210.4	29.6	2,493	990	21.0	41.1	34.1	3.7	98	79
China	1,387.8	241.0	7,298	221	6.8	59.6	31.8	1.8	91	64
India	1,386.9	135.9	1,676	54	42.8	50.1	6.6	0.4	92	34
Russia	141.0	31.2	1,850	525	24.0	51.4	23.5	1.1	97	70
<b>Fast followers</b>										
Argentina	43.9	7.2	448	742	22.0	43.5	32.3	2.2	96+	90
Egypt	94.8	9.6	236	123	18.1	54.1	26.7	1.1	99	95
Indonesia	262.6	28.8	846	77	24.8	53.0	20.3	2.0	82	54
Mexico	125.9	15.4	1,155	604	18.5	41.8	35.8	3.9	96	85
Pakistan	205.4	15.1	211	22	30.8	59.3	9.7	0.2	92	48
Poland	38.4	9.7	514	917	8.3	36.4	50.4	4.9	100	90+
Romania	21.0	5.0	190	428	17.8	50.0	31.1	1.2	84+	72+
South Africa	52.6	5.1	408	649	24.1	42.7	29.6	3.6	91	77
Thailand	72.1	13.2	346	179	34.8	53.7	11.1	0.3	96	96
Turkey	80.8	9.8	778	678	13.8	38.6	43.7	3.9	100	90
Ukraine	43.0	10.0	165	234	42.5	53.4	4.0	0.1	98	N/A
Venezuela	33.3	3.8	316	663	20.0	45.4	32.7	1.9	92+	91+
Vietnam	96.4	12.0	123	83	34.8	55.1	9.9	0.2	95	76
<b>Asia-Pacific</b>										
Australia	25.2	5.6	1,488	4,775	0.3	9.8	31.8	58.2	100	100
Japan	124.8	42.7	5,869	4,065	0.0	6.2	42.7	51.1	100	100
Malaysia	33.0	3.7	279	368	10.7	38.3	46.8	4.3	100	96
New Zealand	4.8	1.1	162	3,279	5.0	22.5	38.7	33.9	100	100
Philippines	109.7	8.6	213	77	34.4	52.2	13.1	0.4	92	74
Saudi Arabia	33.6	2.4	576	680	11.7	37.7	46.1	4.4	N/A	N/A
South Korea	49.8	11.5	1,116	1,439	0.4	7.1	64.6	17.9	98	100
United Arab Emirates	9.2	0.4	360	1,450	0.1	9.8	52.8	37.3	100	98

Sources: United Nations Population Division, International Monetary Fund, World Bank, World Health Organisation, Credit Suisse Global Wealth Databook, UNICEF, Business Monitor International, PwC research



Risk factors (% of population)			Impact of non-communicable diseases (% of deaths)					Market indicators			
Adult smokers	Overweight or obese males aged 15+ (2010)	Overweight or obese females aged 15+ (2010)	All NCDs	CVD	Cancers	Resp. diseases	Diabetes	Pharma sales at constant exchange rates, 2011 (US\$ bn)	Pharma sales at constant exchange rates, 2020 (US\$ bn)	Generics market share, 2011 (% of total sales)	Generics market share, 2020 (% of total sales)
19.5	66.9	59.5	89	33	30	6	3	26.6	31.1	17.6	23.9
27.0	80.5	76.7	87	35	23	7	3	337.1	424.8	23.7	32.4
29.9	48.0	36.9	87	30	31	4	2	48.7	49.5	13.1	18.1
25.7	67.2	57.1	92	45	26	4	3	55.1	57.6	19.1	28.3
23.0	55.0	40.0	92	41	28	5	4	34.6	29.0	6.7	10.3
29.9	57.9	49.8	91	33	27	9	3	28.0	19.2	7.3	14.7
21.0	67.8	63.8	88	34	27	8	1	38.3	38.6	21.9	26.9
17.2	54.0	60.3	74	33	16	6	5	25.6	57.3	16.0	33.8
28.1	45.0	32.0	83	38	21	15	2	66.9	175.8	64.2	58.7
14.0	20.1	18.1	53	24	6	11	2	15.6	48.8	72.2	72.7
39.1	46.5	51.7	82	62	13	2	0	20.7	45.1	37.0	41.1
27.1	77.7	71.2	80	33	20	10	3	7.6	24.2	9.8	14.1
19.4	64.5	76.0	82	39	11	3	3	3.1	8.4	27.3	36.5
24.2	9.9	27.1	64	30	13	7	3	6.0	12.9	40.0	50.2
15.9	73.6	73.0	78	28	13	6	13	13.0	26.2	12.1	18.1
19.1	22.8	29.5	46	25	7	5	1	2.0	4.5	65.5	63.3
30.3	50.7	44.3	89	48	26	3	2	11.3	16.9	41.6	39.9
32.4	37.7	40.6	91	59	19	3	1	4.2	8.1	22.6	24.7
31.7	41.3	68.5	29	11	7	3	3	3.7	7.7	29.2	38.5
23.7	28.3	39.9	71	27	12	7	6	4.3	7.0	50.9	49
31.2	47.9	65.7	85	49	18	9	2	10.2	19.7	34.3	41.2
28.8	41.2	48.5	86	66	11	2	0	3.4	8.6	49.2	51.5
18.0	74.4	67.3	66	31	15	3	6	5.5	20.9	35.2	50.6
23.8	7.5	12.2	75	40	14	8	3	2.4	7.2	50.0	55.9
16.6	75.7	66.5	90	35	29	6	3	13.3	15.1	13.8	24.8
23.4	29.8	16.2	80	32	31	5	1	127.4	148.7	9.1	19.5
21.5	64.1	42.2	67	32	15	7	2	1.8	3.7	30.0	33.3
19.9	73.9	74.2	91	37	29	7	3	1.1	1.2	17.9	25.1
28.3	22.2	33.6	61	30	10	5	4	2.9	4.1	17.1	34.2
12.5	63.1	65.9	71	42	9	3	6	4.5	9.1	7.7	13.8
27.7	51.5	51.0	82	29	30	5	5	14.8	21.7	31.8	34.1
20.5	66.9	71.6	67	38	12	2	3	1.5	3.1	15.1	18.5

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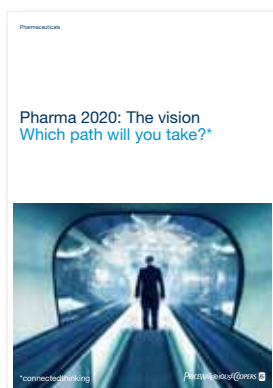
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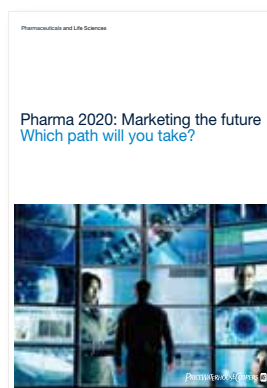
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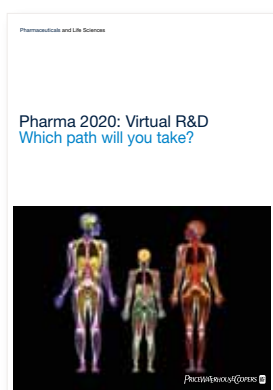
## Previous publications in the series



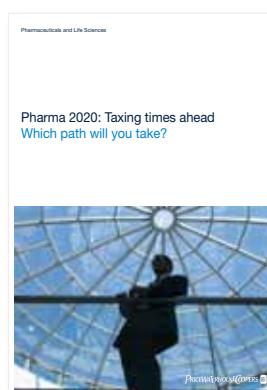
Published in June 2007, this paper highlights a number of issues that will have a major bearing on the industry by 2020. The publication outlines the changes we believe will best help pharmaceutical companies realise the potential the future holds to enhance the value they provide to shareholders and society alike.



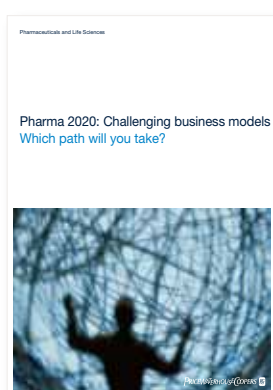
Published in February 2009, this paper discusses the key forces reshaping the pharmaceutical marketplace, including the growing power of healthcare payers, providers and patients, and the changes required to create a marketing and sales model that is fit for the 21st century. These changes will enable the industry to market and sell its products more cost-effectively, to create new opportunities and to generate greater customer loyalty across the healthcare spectrum.



This report, published in June 2008, explores opportunities to improve the R&D process. It proposes that new technologies will enable the adoption of virtual R&D; and by operating in a more connected world the industry, in collaboration with researchers, governments, healthcare payers and providers, can address the changing needs of society more effectively.



The fifth report in our series, published in December 2009, focuses on the opportunities and challenges from a tax perspective. It discusses how the political, economic, scientific and social trends currently shaping the commercial environment, together with the development of new, more collaborative business models, will exert increasing pressure on effective tax rates within the industry. It also shows how companies can adapt their tax strategies to support the provision of outcomes-based healthcare and remain competitive.



Fourth in the Pharma 2020 series and published in April 2009, this report highlights how Pharma's fully integrated business models may not be the best option for the pharma industry in 2020; more creative collaboration models may be more attractive. This paper also evaluates the advantages and disadvantages of the alternative business models and how each stands up against the challenges facing the industry.



In our sixth release of the series, published in February 2011, PwC discusses how pharma companies must develop different supply chain models, learn to use supply chains as a market differentiator and revenue generator, and recognise how information will drive the downstream flow of products and services.

All these publications are available to download at: [www.pwc.com/pharma2020](http://www.pwc.com/pharma2020)

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