

# Rising Up: Part 1

The cost of healthcare is rising at an alarming rate, and this is particularly evident in the US. With European countries gradually replacing 'free-pricing' with the value-based pricing of pharmaceuticals, will the US market be next to make the transition? The first in a two-part series questions whether the industry is prepared for a payer-dominated world

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Graham Scholefield and  
Markus Thunecke at Catenion

Across the globe it has become essential for payers to gain control over dramatically rising healthcare costs. This trend, in combination with three other key drivers, is resulting in the decline of the 'free-pricing' of pharmaceuticals and the rise of value-based pricing, particularly in the European Union (EU) (see Figure 1, page 44). In this article we discuss each of these factors and highlight how recent developments suggest that value-based pricing is coming to the US, the world's largest pharmaceutical market.

## Key Drivers

### Healthcare Costs

The recent 2013 report by the Organization for Economic Co-Operation and Development (OECD) indicates that the ratio of healthcare spending to gross domestic product (GDP) of

OECD countries has risen substantially since 2000 and is projected to increase for the foreseeable future. In fact, it has risen even more than the OECD's most pessimistic scenario put forward in their report published in 2006 (1).

Pharmaceutical sales have contributed significantly to these rising costs, having had a compound annual growth rate (CAGR) of 7.6 per cent in the US over the past decade, with a similar growth rate predicted for the coming decade (2). This trend is putting ever-increasing pressure on payers' budgets, which will eventually be reflected in manufacturers' revenues, if it is not already.

The rising costs of medicines are being driven by changing demographics, for example ageing, as well as the development and pricing of medical interventions. In many ways, the pharma industry is a victim of its own success; for example, Glivec (imatinib) has decreased mortality rates in chronic myeloid leukaemia by five- to ten-fold, to the extent that patients now have a normal lifespan (3). The financial caveat

of this is the large cost of the subsequent lifetime therapy which must be met by the payers.

In addition, the rise of many expensive speciality drugs, which address high unmet needs in small homogenous patient segments – such as crizotinib for five per cent of the non-small-cell lung carcinoma (NSCLC) population costing \$100,000 per annum – has also exacerbated the problem. Indeed, speciality drugs have been forecast to account for half of all US pharmaceutical costs by 2018 (4).

However, the example of Glivec can also be used to show how rising costs are partly of pharma's making. Since the US launch of Glivec in 2001, the annual list price has more than tripled, with a CAGR of nearly 11 per cent, and at the same time the treatable population has more than doubled (5). One can argue that this is akin to 'profiteering'.

Furthermore, there are plenty of examples of new drugs which are no more effective than those currently

marketed, but are still being sold for unwarranted premium prices. One such example is Zaltrap (afibercept) that was recently approved for metastatic colorectal cancer, which despite having almost identical outcomes and higher administration costs to Avastin (bevacizumab), was listed at 2.2 times its price in the US (6). Since healthcare budgets are simply not rising as fast as spending – a situation which has been exacerbated by the recent economic crisis – payers are increasingly looking for value for money in their drug purchases.

**Risk-Sharing Schemes**

Risk-sharing schemes originated from insurers and manufacturers in the US in the 1990s on the premise that a manufacturer’s total remuneration should be linked to the actual performance of their product – in other words its economic value. Three different models have been identified that are in use today:

- Price adjustment based on observed outcomes
- Rebate based on the costs of harm
- Rebate based on the price of the drug

The first two models are the least commonly used – the recent report by A. Sotiropoulos highlights several good examples (7). The final model issues a rebate based on the drug’s list price; one

of the simplest schemes is for Tarceva (erlotinib) in the UK, which provides an automatic credit note for a percentage of its list price. More complicated schemes only provide a rebate if the patient fails to reach a predetermined outcome – such as Velcade (bortezomib), also in the UK.

However, it is the Italians that have really taken up these rebates, with 16 currently operating in the oncology market. Each of their schemes uses progression-free survival after a predetermined number of cycles as its rebate criteria. Their apparent success is, at least in part, due to the web-based national oncology registry (Onco-AIFA). Taken together, these data indicate that risk-sharing schemes are already undermining manufacturers’ revenues and that they are becoming an increasingly popular method of price control.

**Real World Clinical Data**

Onco-AIFA is a good example of how the proliferation of information technology has facilitated the creation of valuable real world datasets. Since 2006 this registry conducts mandatory surveillance of all Italian oncology patients treated with a variety of novel chemotherapy drugs, allowing individual patients and their associated outcomes to be efficiently tracked. Datasets like this also exist in the US – for example, the databases of

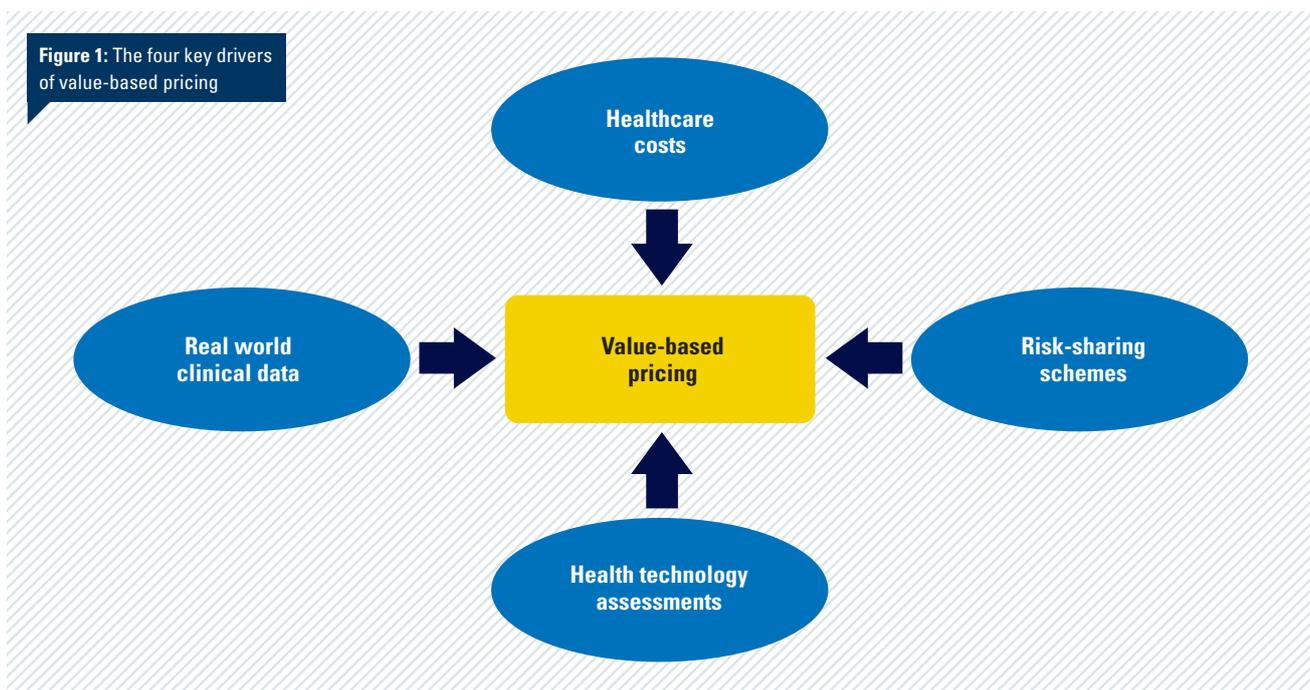
insurers Kaiser Permanente and United Health Group – and elsewhere in Europe, each with millions of patients.

In the short-term, this data will greatly facilitate the use of outcome-based pricing as more states and insurers adopt the necessary technology to track individual patients and their associated fate, allowing for efficient rebate collection. In the long-term, the increasing quality and scope of patient datasets, such as Onco-AIFA, will open up the possibility of revising the cost effectiveness valuation of a treatment in an ongoing manner as ‘real world clinical data’ becomes available.

Preliminary analysis of seven novel cancer drugs in nine indications using Onco-AIFA data suggests that real world progression-free survival of cancer patients is on average 30 per cent less compared to the corresponding clinical trial data (8). Should this translate into overall patient survival, manufacturers could potentially face significant list-price reductions, or even market exclusion in favour of competitor compounds.

**Health Technology Assessments**

Health Technology Assessments (HTAs) are on the rise, particularly in the EU.



Previously, market access was largely a 'one-step' procedure involving gaining a marketing authorisation from the European Medicines Agency (EMA). The past decade has seen the rise of a two-step procedure, whereby after the EMA grants a marketing authorisation, the medicine can also be subjected to a HTA by a member state – notably the National Institute for Health and Care Excellence (NICE) in the UK, Institute for Quality and Efficiency in Healthcare (IQWiG) in Germany, Italian Medicines Agency (AIFA) in Italy and Haute Autorité de Santé (HAS) in France. This not only contains an economic element, but also requires the new medicine to be evaluated against the current standard of care in the country, as opposed to the placebo comparison demanded by the EMA, which dramatically raises the bar for market penetration of new medicines.

Probably the most well-known HTA is NICE, which is the gatekeeper to arguably one of the most important European markets due to its prices being extensively referenced by other countries. The UK Office of Fair Trading estimates that 25 per cent of global medicine sales reference English prices, while more than 90 per cent of EU countries reference English prices directly or indirectly to some degree (9, 10).

NICE evaluates the efficacy of a new treatment in comparison to the current standard of care, quantifying the economic cost of any observed benefit. This is then set against a 'willingness to pay' threshold to determine if the medicine is recommended for use in the National Health Service (NHS). The current method involves calculating the cost per quality-adjusted life years (QALYs) gained from a novel medicine versus the current standard of care. If NICE does not recommend a technology then it acts as a *de facto* rejection and is consequently not significantly prescribed within the NHS (11).

Taking these four drivers together, it is clear that pharma companies face an increasingly difficult market environment with future price reductions coming from the increasing prevalence of outcome-

based rebates, potentially revised cost-effectiveness benefits derived from real world clinical data, and continuing HTAs. Therefore, it is of paramount importance that market access intelligence is integrated into drug development decisions to ensure both market penetration and sales maximisation in the future.

### The US Market

In order for value-based pricing to become a reality in the US, it must be driven by the three major market forces: the public, politicians and private insurers. There are several lines of evidence to indicate that these forces are aligning towards ascribing an economic value to current and future medicines.

The world-leading Sloan-Kettering Cancer Centre has refused to prescribe Zaltrap for metastatic colorectal cancer due to unjustifiably high cost, indicating that doctors are prepared to take a stand against unjustifiable medicine expenditure (12). In response to this, the companies marketing the drug have offered a 50 per cent discount on the list price. However, since patient co-payments are often linked to the list price, there is continued resistance from doctors to prescribe the drug. The Sloan-Kettering is highly regarded among physicians, and thus any decision taken by it is likely to affect prescription rates, not just in the US, but also internationally. Two years prior to this, in 2010, the political establishment took affirmative action when the Affordable Care Act was signed into law by President Obama. This established the Patient-Centred Outcomes Research Institute (PCORI) which allocates \$3.5 billion of funding for cost-effectiveness research through to 2019 (13).

This development becomes even more significant when you take into account the stance of private sector insurers. A survey by the PwC Health Research Institute indicates that 80 per cent of US insurers said that "manufacturers must demonstrate a clear clinical benefit for their products compared with current branded and generic treatments, and demand clear proof of cost savings" (14). Over half of insurers said they "rely on

independent data to evaluate drug effectiveness," for example the kind of research funded by the PCORI. Finally, 16 per cent of insurers said they "have adopted new payment and contracting arrangements such as outcome-based payments and risk-sharing agreements," with a further 37 per cent indicating they expect to adopt them within the next three years (14).

A separate survey at a recent US insurance conference – attended by around 60 executives from different insurers – indicated that cost control is their number one strategic imperative, followed closely by providing a customer-centric service, a view strongly compatible with value-based pricing (15).

Taken together, these developments indicate there is a public, private and political will to push for the transition to value-based pricing within the US. Therefore, the manufacturers that integrate payers' needs into their clinical development decisions will be the ones that survive and dominate in the payer-driven market of the future.

### Value-Based Pricing

We have conducted a survey of the oncology market in the UK to ascertain how successful pharma has been in fulfilling payers' needs (see Figure 2). We found that the proportion of oncology label indications recommended by NICE has been very poor; for labels marketed in 2012 just one out of seven were recommended. Furthermore, virtually every oncology drug recommended by NICE since 2005 has been subject to a risk-sharing scheme, which has been kept confidential in most cases. These data seem to indicate that, thus far, the pharma industry has failed to successfully integrate payers' needs into product development – a finding that is unlikely to be solely restricted to oncology.

In May 2012 we conducted interviews with ten Vice Presidents or Directors, who all oversee market access functions, from several top-20 pharma companies in order to gain some insights into the ability of the industry to clear this value-based pricing hurdle in the future.

Despite all of the interviewees stating that they undertook in-depth studies of payers' needs, only one fifth indicated that payers' needs drove mid-stage clinical development decision making, while half of the interviewees indicated that balancing payer value demonstration with time, cost and feasibility constraints remains a significant challenge.

In addition, four out of ten of the interviewees also indicated that there is a poor understanding of the importance of payers' needs across the organisation. Finally, an independent survey by the Health Research Institute showed just seven per cent of US insurers are 'very confident' in the economic and comparative effectiveness data provided by drugmakers (14).

Taken together, these data indicate that pharma companies remain relatively unprepared to successfully adapt to a payer-dominated reimbursement landscape. This translates into a significant proportion of potential future sales being 'at-risk' due to a significant likelihood of failing to clear the high payer hurdle after a new medicine gets marketing approval.

### Conclusion

In this article we have discussed the ongoing transition to value-based

pricing with examples from not just the EU, but also the US, pointing towards the possibility that HTAs are going to become a reality in the world's largest drug market. We end on the observation that the pharma industry seems relatively unprepared for this change, thereby exposing a significant proportion of their future sales to the risk of payer rejection.

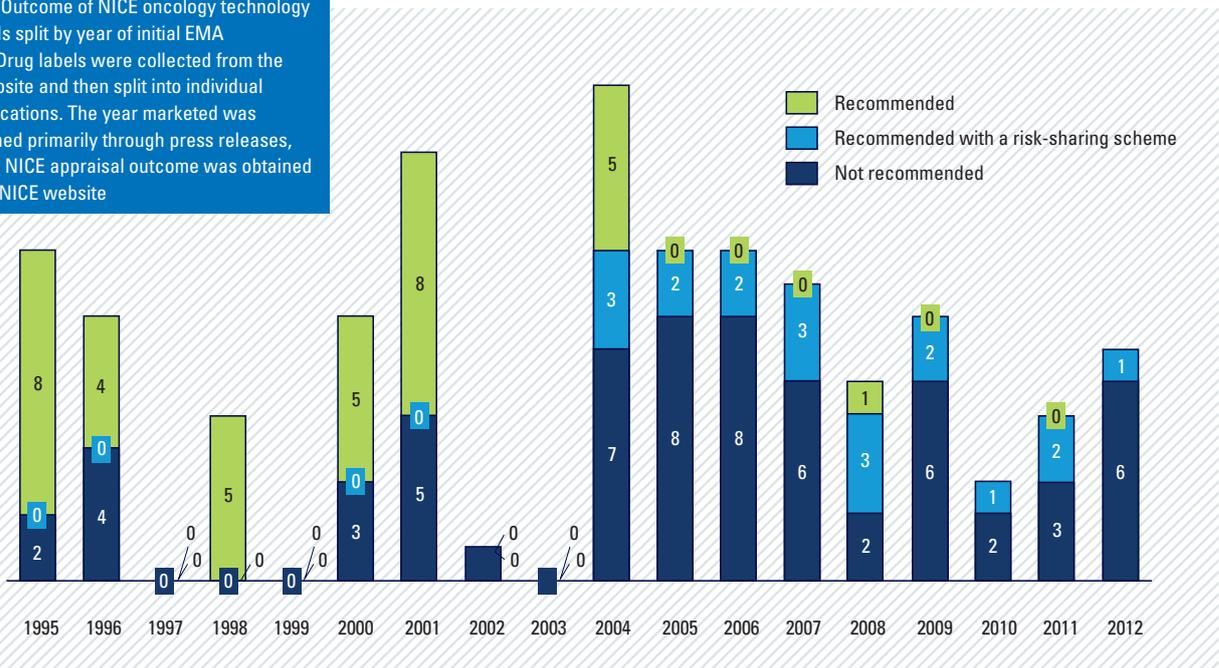
In part two of our article, we will discuss a methodology that pragmatically integrates payer needs into R&D decision making. This highlights a project's future sales-at-risk within payer scenarios, allowing for the cost-benefit evaluation of various options which mitigate this risk. This analysis will aim to facilitate sound decision-making by key strategic leaders in the industry.

#### References

1. OCED, Public spending on health and long-term care: a new set of projections, 2013
2. Centers for Medicare & Medicaid Services, The National Health Expenditure Accounts (NHEA), 2013. Visit: [www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/nationalhealthaccounts/historical.html](http://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/nationalhealthaccounts/historical.html)

3. Gambacorti-Passerini C, Antolini L, Mahon FX *et al*, Multicenter independent assessment of outcomes in chronic myeloid leukemia patients treated with imatinib, *Journal of the National Cancer Institute* 103(7): pp553-561, 2011
4. Taylor L, Specialty drugs 'to account for 50% of all US pharma costs by 2018', *PharmaTimes*, 2013. Visit: [www.pharmatimes.com/article/130405/specialty\\_drugs\\_to\\_account\\_for\\_50\\_of\\_all\\_US\\_pharma\\_costs\\_by\\_2018.aspx](http://www.pharmatimes.com/article/130405/specialty_drugs_to_account_for_50_of_all_US_pharma_costs_by_2018.aspx)
5. Kantarjian H, Price of drugs for chronic myeloid leukemia (CML), reflection of the unsustainable cancer drug prices: perspective of CML experts, *Blood* 121(22): pp4,439-4,442, 2013
6. Bach P, Satlz L, Wittes R, In cancer care, cost matters, *The New York Times*, 2012. Visit: [www.nytimes.com/2012/10/15/opinion/a-hospital-says-no-to-an-11000-a-month-cancer-drug.html?\\_r=1](http://www.nytimes.com/2012/10/15/opinion/a-hospital-says-no-to-an-11000-a-month-cancer-drug.html?_r=1)
7. Sotiropoulos A, Pricing pharmaceuticals by outcome, 2011
8. Jirillo A *et al*, A new proposal of drug pricing based on value for effectiveness in real practise oncology, ESMO Congress Vienna, 2012
9. EU Directorate-General, Differences in costs of, and access to, pharmaceutical products in the EU, 2011
10. The Office of Fair Trading, The pharmaceutical price regulation scheme – an OFT study, 2007

**Figure 2:** Outcome of NICE oncology technology appraisals split by year of initial EMA licence. Drug labels were collected from the EMA website and then split into individual label indications. The year marketed was ascertained primarily through press releases, while the NICE appraisal outcome was obtained from the NICE website



11. Thornhill MH *et al*, Impact of the NICE guideline recommending cessation of antibiotic prophylaxis for prevention of infective endocarditis: before and after study, *BMJ* 342: pp2,392-2,392, 2011
12. Grisham J, *The New York Times* commends memorial Sloan-Kettering's stance on a costly cancer drug, MSKCC, 2012. Visit: [www.mskcc.org/blog/new-york-times-commends-msk-stance-costly-drug](http://www.mskcc.org/blog/new-york-times-commends-msk-stance-costly-drug)
13. PCORI, How we're funded, 2012. Visit: [www.pcori.org/about-us/how-were-funded](http://www.pcori.org/about-us/how-were-funded)
14. Taylor L, US study warns drugmakers over cost/effectiveness data, *PharmaTimes*, 2012. Visit: [www.pharmatimes.com/article/120521/US\\_study\\_warns\\_drugmakers\\_over\\_cost\\_effectiveness\\_data.aspx](http://www.pharmatimes.com/article/120521/US_study_warns_drugmakers_over_cost_effectiveness_data.aspx)
15. OVUM, US insurance execs choose cost control as strategic imperative, 2013. Visit: [www.ovum.com/2013/04/02/us-insurance-execs-choose-cost-control-as-strategic-imperative](http://www.ovum.com/2013/04/02/us-insurance-execs-choose-cost-control-as-strategic-imperative)

## About the authors



Graham Scholefield is an Analyst at Catenion where he has worked on various projects in the fields of economic modelling, portfolio evaluation and strategy and biomedical innovation. In addition, he has taken a keen interest in pharmaceutical market access, pricing and reimbursement. He holds a PhD in Biochemistry from the University of Newcastle in the UK, where he investigated the regulation of DNA replication initiation for which he was awarded the University Doctoral Prize following several publications in world-leading journals. Graham also holds an MA in Medical and Molecular Biosciences from the same university. Email: [graham.scholefield@catenion.com](mailto:graham.scholefield@catenion.com)



Markus Thunecke is a founding Senior Partner of Catenion. He has helped numerous clients around the globe in the pharmaceutical and medical products industries create a competitive advantage, and is a frequent speaker at conferences on R&D strategy and portfolio management. Markus holds a PhD in Biochemistry from the University of Heidelberg, where he generated transgenic animal models for Alzheimer's disease. He also has three years of research experience within the central nervous system field at Schering AG. Markus started his consulting career in 1997 at Mercer Management Consulting before joining a strategy consulting boutique, Theron, and setting up Catenion in 2003. Email: [markus.thunecke@catenion.com](mailto:markus.thunecke@catenion.com)

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Director, Marketing & Special Projects  
Phone: +1 (905) 286-6270  
Mobile: +1 (647) 234-3395  
Email: [diezzi@therapurebio.com](mailto:diezzi@therapurebio.com)