Roadmap for success in oncology

The worldwide oncology market is projected to outgrow the rest of the pharma industry, becoming the number one therapeutic class in revenue terms by 2011. So will oncology become pharma’s new “holy grail”? Dr Frederic Desdouits, Lionel Delaporte and Dr Stéphane Parnis explain why the outlook is more complicated than that.

Since the launch in 1998 of Roche/Genentech’s Herceptin (trastuzumab) – the first monoclonal antibody marketed in oncology with administration determined by tumour marker testing – many significant advances have been made in the treatment of cancer. The value of targeted therapies/chemotherapy combinations and the potential of adjuvant therapy (drug treatment following surgery to reduce the risk of cancer recurrence) have been demonstrated in the clinic to improve survival rates, notably in breast, lung and colon cancers. The targeted therapy concept – drug treatments developed to preferentially target those signalling pathways that are disregulated in tumours – contrasts with earlier cancer treatments, such as cytotoxics and immunomodulators, which were based on broad-acting mechanisms. Several targeted molecules have shown efficacy in a wide range of indications, including cancers of the breast, colon, lung, kidney and lymphoma, with important survival benefits observed in some of them.

Most innovation in oncology over the past 10 years has been driven by scientific advances, particularly in genomics, transcriptomics and proteomics sciences, otherwise known as the “omics revolution”. Indeed, these major technological advances have lowered the entry barriers in research and have led to the identification and validation of many novel therapeutic targets that were previously unexplored. In addition, improvements in chemical synthesis, the development of molecular libraries and high-throughput screening, advances in preclinical and toxicity studies, progress in the characterisation and production of biological molecules, and the development of oral delivery formulations and cancer vaccines have together accelerated the emergence of very promising drugs and enabled more molecules to be turned into medicines.

One result of these breakthroughs is the start of a fundamental change in the way some cancers are considered. For example, physicians are starting to consider some haematological cancers, such as chronic lymphocytic leukaemia, as chronic diseases. This is not yet true for metastatic cancers, although it is the hope for the coming decades.

So, what are the implications across the wider market? It’s true that significant scientific progress and the high prices commanded by innovative cancer products have encouraged many companies to build and/or strengthen their oncology franchises, but this strategy clearly does not come without its risks.

an attractive marketplace
According to the World Health Organization, the global burden of cancer is expected to grow from 10 million new cases in 2000 to 15 million in 2015. Of these cases, 60% are predicted to occur in the US and Western Europe. The National Institutes of Health estimates that the total cost of cancer in the US was $209.9 billion in 2005. Direct medical costs, including inpatient and outpatient care, drugs and devices, accounted for $74 billion, with another $17.5 billion attributed to indirect morbidity costs (loss of productivity), and indirect mortality costs (loss of productivity due to early deaths) accounting for $118.4 billion. The biggest killers, which include lung, colorectal and breast cancers, currently represent over half of all cancer-related deaths.

Based on current projections, cancer deaths will continue to rise, with nine million people estimated to die from the disease in 2015, and more than 11 million in 2030. Globally, cancer is the leading cause of death of those under 85, and because it disproportionately affects the elderly, oncology expenditure will become an even greater concern in future as a result of the ageing “baby boomer” population.

From a market perspective, in 2006 oncology represented $35.6 billion in global sales and approximately 20% of NCE launches (six out of 31). The oncology market had already more than doubled in size over the five years before 2006, stimulating interest from big pharma and biotech companies. More recently, a remarkable trend has been the rise of oncology-related products as a proportion of all molecules in clinical development. In 1995 this figure was 18%, rising to 25% in 2005. By the end of 2006, cancer drug candidates represented almost 30% of all compounds in development, with more than 650 candidates in late-stage clinical trials (Phase II onwards).

So, it is not surprising that more than 70% of oncology sales today are of products launched over the past 10 years, according to IMS data. In December 2006, 186 drugs were marketed worldwide in oncology, with cytotoxics and targeted therapies accounting for 44% (82 molecules) and 8% (15 molecules).
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Figure 1: Top 10 worldwide therapeutic classes in turnover terms (2006 vs 2011)

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>2005</th>
<th>2011</th>
<th>Trend</th>
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<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Respiratory</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Infectious Disease</td>
<td></td>
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<td></td>
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<tr>
<td>Metabolic</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ophthalmology</td>
<td></td>
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<td></td>
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<tr>
<td>Osteoporosis</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Diabetes/Metabolic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncology/Supportive care</td>
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</table>

Source: IMS Health, analyst reports, Bionest Partners analyses

Figure 2: Patterns in marketed products and development programmes (as of July 2007)

Source: Pharmaprojects, Bionest Partners analyses

respectively. The remainder consisted mainly of hormonal therapies and immunomodulators. Furthermore, cytotoxics and targeted therapies generated respectively 50% ($17.6 billion) and 40% ($14.3 billion) of global oncology sales in 2006, underlining the very attractive premium prices enjoyed by targeted oncology therapies compared with other therapeutic classes.

Oncology drugs represented nearly 16% of blockbusters in 2006 (12 out of 75). The leading products by 2006 sales are shown in Table 1. The US accounts for approximately 45% of the global oncology market, followed by Europe and Japan with 35% and 10% respectively.

These positive market dynamics both reinforce and support the attractiveness of the oncology field, a sector that continues to show considerable potential in comparison to other therapeutic areas. With $6 billion in incremental sales, oncology was the leading growth driver of the pharma industry in 2006, representing around 14% of worldwide pharma industry incremental sales vs 2005.

Oncology showed an impressive 24% growth rate over the previous year, far greater than the global pharma market growth figure of 7%.

Four key factors adding momentum to the oncology market can be summarised as follows:

- Except for certain haematological cancers, there is still no curative...
treatment for advanced stages of cancer, and unmet medical needs are very high;
- Premium pricing is commanded by certain types of products (eg, targeted therapies);
- Recent advances in technologies and better physiological understanding of pathologies have lowered barriers to entry into research;
- Cancer is a priority for many national health authorities and significant investment has been made to improve healthcare screening systems. For example, funds made available to the US National Cancer Institute in 2005 reached over $4.8 billion, an increase of 28% ($1 billion) since 2001.
Consequently, the worldwide oncology market is predicted to continue growing faster than the rest of the industry, with an expected increase in turnover (CAGR05-11) of around 12% (compared with 4.6% for worldwide pharmaceutical sales), reaching $55 billion in sales by 2011. Combined with the supportive care segment, oncology will become the number one therapeutic class in revenue terms ($88 billion in estimated sales in 2011) ahead of cardiovascular drugs (see Figure 1).

Does all this mean oncology is becoming the new holy grail of the pharma industry? True, the market dynamics are very attractive and numerous players continue to invest significantly in this new "El Dorado", but few will actually enjoy success in line with their expectations. Increasing financial constraints on payers and fierce competition are the early seeds of a (r)evolution that should radically change the economics of this market.

deal with complexity, and focus

Key to successfully discovering, developing and launching a new oncology drug is the management of complexity. Oncology is one of the main science-driven specialties in medicine, with highly technical products and multifaceted patient management. This makes research and commercialisation in this area particularly complex and unpredictable. To make matters even more complicated, many teams are competing not only with similar approaches, but also with different approaches to the same targets and/or the same cancer. And with more than 200 different types of tumour, companies are faced with a difficult, and sometimes uncharted, web of possibilities and decisions.

“One of a kind” therapeutic area
Cancer is not a single disease; rather it consists of numerous different diseases characterised by uncontrolled cell growth that may be triggered by external (eg, chemicals, viruses, radiation) and internal (eg, hormones, immunity, genetic) factors. Consequently, there are many heterogeneous indications associated with a wide range of unmet medical needs and incidence rates, as shown in Figure 2. Primary prostate, breast, lung and colorectal tumours are the most common forms. While a favourable prognosis is more likely in these cancers if they are diagnosed early and/or if the patient is a candidate for an operation, there is still no curative drug treatment for advanced stages of disease. Thus, unmet medical needs remain and available treatments are not entirely satisfactory.

At the other end of the incidence spectrum, tumours of the oesophagus, stomach, liver and pancreas, and advanced melanoma, are less common in the west.

Unfortunately, the five-year survival rates in this group remain very low, reflecting the intrinsic nature and related scientific and clinical challenges of these tumours. It is also a sign of the relative lack of industry interest in pursuing R&D in these indications over the past 10 years, (with the exception of melanoma which is probably over investigated relative to incidence).

In the middle area of Figure 2 are the haematological cancers, which affect a large number of patients and encompass many disease categories broadly classified as lymphomas, multiple myeloma and leukaemias. Survival rates associated with these conditions are generally moderate, (although some leukaemias such as CML have very high survival due to the availability of drugs like Novartis’ Gleevec (imatinib)).

There is a plethora of treatments which can be used by physicians, and with varying levels of efficacy. As touched on earlier, products range from broad-acting therapies such as cytotoxics, immunomodulators and hormonal therapies to the targeted therapies such as angiogenesis and pathway inhibitors (see Table 2). Analysis of late-stage clinical trials reveals ongoing enthusiasm among oncology players for broad-acting therapies. These products represent the biggest therapeutic class among late-stage drug candidates (56% of the total), with cytotoxics at the top of the pile.

However, emerging targeted therapies are leading to a paradigm shift in oncology: cancer is transforming from a uniform collection of organ-based diseases into subsets of biologically differentiated patients. This change is being fuelled by a greater understanding of the molecular mechanisms of carcinogenesis, leading to a large variety of therapeutic approaches.

To add to the possibilities (and the complexity), cancer drugs are mostly prescribed in settings combining several compounds. Most frequently, the cancer treatment “backbone” consists of two or three chemotherapy agents. Historically, these compounds have belonged to classes such as the alkylating agents, antimitotic agents or antimitabolites. As already mentioned, the oncology space has recently witnessed the progressive appearance of molecules with more targeted mechanisms of action, resulting in many more combination opportunities. By following this “add-on” strategy (described later), new players now have to

<table>
<thead>
<tr>
<th>Product</th>
<th>Generic name</th>
<th>Company</th>
<th>2006 sales ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituxan</td>
<td>rituximab</td>
<td>Roche/Genentech</td>
<td>3.3 billion</td>
</tr>
<tr>
<td>Herceptin</td>
<td>trastuzumab</td>
<td>Roche/Genentech</td>
<td>3.2 billion</td>
</tr>
<tr>
<td>Gleevec</td>
<td>imatinib</td>
<td>Novartis</td>
<td>2.6 billion</td>
</tr>
<tr>
<td>Avastin</td>
<td>bevacizumab</td>
<td>Roche/Genentech</td>
<td>2.4 billion</td>
</tr>
<tr>
<td>Taxotere</td>
<td>docetaxel</td>
<td>Sanofi-Aventis</td>
<td>2.3 billion</td>
</tr>
<tr>
<td>Eloxatin</td>
<td>oxaliplatin</td>
<td>Sanofi-Aventis</td>
<td>2.2 billion</td>
</tr>
<tr>
<td>Arimidex</td>
<td>anastrozole</td>
<td>AstraZeneca</td>
<td>1.5 billion</td>
</tr>
<tr>
<td>Gemzar</td>
<td>gemcitabine</td>
<td>Lilly</td>
<td>1.4 billion</td>
</tr>
<tr>
<td>Zometa</td>
<td>zoledronic acid</td>
<td>Novartis</td>
<td>1.3 billion</td>
</tr>
<tr>
<td>Casodex</td>
<td>bicalutamide</td>
<td>AstraZeneca</td>
<td>1.2 billion</td>
</tr>
<tr>
<td>Zoladex</td>
<td>goserelin</td>
<td>AstraZeneca</td>
<td>1.0 billion</td>
</tr>
<tr>
<td>Enantone</td>
<td>leuprorelin</td>
<td>Takeda</td>
<td>1.0 billion</td>
</tr>
</tbody>
</table>

Source: company data
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**Table 2: The wide spectrum of available oncology drugs**

<table>
<thead>
<tr>
<th>Drug type/class</th>
<th>Mechanism of action</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>blood cell factors</strong></td>
<td>stimulate proliferation, differentiation and mobilisation of blood cells</td>
<td>increase blood cells, which allow more aggressive chemotherapy administration and decrease infection</td>
</tr>
<tr>
<td><strong>chemopreventive agents</strong></td>
<td>prevent carcinogenesis or stimulate apoptosis of precancerous cells</td>
<td>chronic treatment of pre-malignant conditions to prevent cancer progression</td>
</tr>
<tr>
<td><strong>chemotherapies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>alkylation agents</td>
<td>kill cells by directly attacking DNA</td>
<td>certain carcinomas (breast, lung, ovary, prostate), chronic leukaemias, Hodgkin's disease, lymphomas</td>
</tr>
<tr>
<td>anti-tumour antibiotics</td>
<td>bind with DNA and prevent RNA synthesis</td>
<td>wide variety of cancers</td>
</tr>
<tr>
<td>antimetabolites</td>
<td>block cell growth by interfering with certain development activities; halts normal development and cell reproduction</td>
<td>acute and chronic leukaemias, choriocarcinoma, tumours of the breast, GI tract, and ovary</td>
</tr>
<tr>
<td>hormonal agents</td>
<td>modify growth of hormone-dependent cancer cells</td>
<td>breast, prostate cancer</td>
</tr>
<tr>
<td>nitrosoureas</td>
<td>kill cells by inhibiting changes necessary for DNA repair; cross blood-brain barrier</td>
<td>brain tumours, lymphomas, malignant melanoma, multiple myeloma</td>
</tr>
<tr>
<td>plant (Vinca) alkaloids</td>
<td>block cell division during mitosis</td>
<td>leukaemia, breast, lung, and testicular cancers, lymphomas neuroblastoma</td>
</tr>
<tr>
<td>immunotherapies</td>
<td>boost immune system function</td>
<td>IFN and IL-2 for kidney cancer; many others in development</td>
</tr>
<tr>
<td>targeted therapies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>angiogenesis inhibitors</td>
<td>block formation of new blood vessels</td>
<td>colorectal cancer; in development for others</td>
</tr>
<tr>
<td>tyrosine kinase inhibitors</td>
<td>inhibit growth factor receptor-linked enzyme activity</td>
<td>NSCLC, RCC, CML, GIST</td>
</tr>
<tr>
<td>monoclonal antibodies</td>
<td>block interactions of cell-surface receptors with their ligands</td>
<td>breast cancer, non-Hodgkin's lymphoma, CLL, colorectal cancer, NSCLC, numerous in R&amp;D</td>
</tr>
<tr>
<td>supportive care</td>
<td>add-on drugs used to enhance efficacy or improve side-effect profile of agents</td>
<td>prevent nausea, pain, mucositis</td>
</tr>
</tbody>
</table>

Source: University of Pennsylvania's OncoLink

multiply clinical trials in order to identify the most optimal combinations and enter treatment backbones.

**Many areas left to explore**

In a recent study, the authors plotted the relationship between the number of oncology products, the frequency of cancer and the level of medical need (see Figure 2). Both marketed drugs and molecules in late-stage clinical studies were considered. As a result of this analysis, three main segments within the cancer market were identified as follows:

A. The “big and crowded segment”, comprising breast, prostate, colorectal and lung cancers.

B. The “significantly investigated segment where unmet needs remain”. This includes renal cancer, lymphoma, multiple myeloma, leukaemia, head and neck, ovarian and cervical cancers.

C. The “challenging niches”, such as brain, stomach, oesophagus, liver and pancreatic cancers, and advanced melanoma.

The “big and crowded” segment A is the most important in terms of approved drugs. It offers potentially high margins for companies because both incidence and/or survival rates in breast, prostate, colorectal and to a lesser extent lung cancer, are sufficiently high to allow long-term use of products in a significant number of patients. Advanced stages of breast, prostate and lung cancers have comparable incidence and five-year survival rates, but there are slightly more drugs available for breast cancer. One reason could be that surgery and cryotherapy (the therapeutic use of cold) provide physicians with effective and well understood therapeutic alternatives for the management of prostate cancer. The relatively good median survival rates observed in colorectal cancer are probably the result of earlier detection compared with other cancers, permitting successful use of surgery. This similarly applies to breast cancer, which shows a much higher median survival rate than colorectal.

From a pipeline perspective, the key drivers behind the relatively high level of R&D activity in breast, prostate and lung cancers are slightly different. In lung cancer, improving the efficacy of treatments remains the number one priority. The incidence of lung cancer is increasing sharply due to smoking habits and it has one of the poorest prognoses. This therapeutic area is one of the most difficult to address, but potentially it is also one of the most profitable. In breast cancer, efforts are focused on improving efficacy (ie, survival), with other work aiming to reduce side-effects. And in prostate cancer, significant R&D is concentrating on the discovery of molecules to manage HRPC (hormone resistant prostate cancer), the new clinical challenge in this area.

Segment B consists of cancers for which treatments are available, but which still pose a challenge as five-year survival rates remain average to low. Leukaemia and lymphoma, with the highest number of approved drugs, and ovarian cancer belong to this segment.
Looking at R&D pipelines, it is apparent that these indications are still attracting the interest of companies, and they could fuel competition in these markets in the coming years. In this segment, the authors identified several cancers with a surprisingly high number of products (both marketed and under clinical investigation) in relation to their incidence in the overall population. These were renal and ovarian cancers, multiple myeloma and leukaemia. It is interesting to note that competition in renal cancer has increased dramatically since the recent approvals of the first oral angiogenesis inhibitors (Bayer Schering Pharma’s Nexavar (sorafenib) and Pfizer’s Sutent (sunitinib)).

Segment C, the challenging niches, groups together a series of cancers with relatively low incidence and five-year survival rates, and a limited number of product approvals. These include pancreatic, liver, stomach and oesophageal cancers, advanced melanoma and, to a lesser extent, brain cancer. The lack of therapeutic options is clearly the result of economic considerations, although these niche cancers could in theory interest newcomers and/or small players as the medical need is huge. The main challenge in these cancers remains poor survival rates, which make it difficult to prove therapeutic efficacy. However, pancreatic cancer and advanced melanoma could become highly competitive segments in the near future. Many players have molecules targeting these indications and the number of products under clinical evaluation is increasing.

Finally, the limited number of drugs for cervix uteri, corpus uterus and testicular cancers is in part due to the significant success rate of surgical intervention for these diseases. It is not surprising to see very few molecules under development for these indications.

Increasing complexity in drug development

For most companies, the cost of conducting oncology clinical trials is significantly increasing, calling for more informed strategic decision-making. In particular, when initiating the development of a new cancer drug, companies are faced with the following choices:

- The "add-on" vs the "switch" strategy (ie, the addition of a new molecule within a treatment backbone, or the replacement of at least one molecule in the backbone);
- The "blitz" vs the "domino" strategy (ie, the development of several indications at the same time, or the linear step-by-step approach).

We are currently seeing an increase in the number of drug combinations in the major oncology indications, offering physicians many therapeutic alternatives. This is mainly a result of the add-on strategy, which involves testing a new drug in addition to the backbone in a particular indication. This strategy not only increases complexity from the perspective of doctors, but also changes the way pharma and biotech companies must address the development of new drugs in cancer.

The switch strategy aims to move a superior drug rapidly into the backbone and thus into the guidelines of medical societies. This strategy is the fastest route to producing a cornerstone therapy. For instance, Sanofi-Aventis’s strategy for Elixitin (oxaliplatin) in colorectal cancer was to go head-to-head with Pfizer’s Camptosar (irinotecan), the gold standard at the time. With better clinical outcomes, Elixitin rapidly advanced from second- to first-line treatment and stole a leading share of the market.

Another example is Gleevec from Novartis, which was approved in chronic myelogenous leukaemia in 2001. Before the arrival of this tyrosine kinase inhibitor, the main treatment options for this rare haematological cancer were alpha-interferon (which showed mild to high efficacy, but serious side-effects), Bristol-Myers Squibb’s Hydrox (hydroxyurea, which showed poor efficacy and mild side-effects), and medullar grafting (which was capable of definitive cure, but was associated with a very high mortality). With high efficacy and relatively low safety concerns, Gleevec proved itself in this niche market and is now the gold standard.

Not all drugs can show superiority. In fact, most of the time switch strategies are used to replace one treatment component with a similar product that demonstrates an improvement in safety or convenience only.

Positioning a drug in the treatment backbone is a strategic decision and can be critical to its success. For instance, Avastin and Imclone Systems’/Merck Serono’s Erbitux (cetuximab) for colorectal cancer were first developed with Pfizer’s irinotecan (in the period 2000-03), which was swiftly replaced by Sanofi-Aventis’s oxaliplatin (after 2003). If Merck Serono had chosen to combine its Erbitux with oxaliplatin first, it probably would have had an edge over Roche’s Avastin.

There are also collateral benefits associated with a product becoming part of a backbone. Not only does the drug become a standard, but its use is automatically boosted by clinical trials of other therapies seeking to prove added efficacy. The best illustration of this point is Avastin, which is becoming a backbone therapy in several cancer types. In addition, an increasing number of trials of other cancer compounds now also involve this anti-angiogenic drug.

The other strategic choice is whether to favour the “domino” or the “blitz” approach. The latter involves testing several new drugs in parallel in a large number of indications and even in several settings. On the other hand, the domino strategy involves developing a drug in only one indication (large or niche) first and then, when the product is marketed, extending the indications (to other cancers and/or higher lines). While pharma companies have traditionally applied the domino strategy, there seems to be a more recent trend towards the blitz approach.

Based on the authors’ analyses, an average of 3.5 clinical trials per molecule are conducted by companies active in oncology. Very few firms choose to develop their molecules in a single indication (although there seems to be a trend among the newer and smaller companies to explore fewer indications per molecule, which is instinctive given that they have limited resources to carry out trials). Well established companies generally conduct three or four parallel studies per molecule, while the most active players, such as Johnson & Johnson and Merck & Co may run up to seven. For example, it is striking to note that Merck has about half as many oncology molecules as AstraZeneca, yet it is running the same number of programmes.

The domino strategy offers several advantages, particularly for a small company and/or a newcomer in the cancer field:

- Marketing authorisations can first be obtained in a relatively less crowded market, or in an indication for which demand is high;
- The approach limits risk by focusing resources on the most promising indication;

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- Marketing authorisations can first be obtained in a relatively less crowded market, or in an indication for which demand is high;
- The approach limits risk by focusing resources on the most promising indication;
Clinical development costs are comparatively low because patients and clinical trials are limited in number. The blitz strategy, meanwhile, offers advantages of its own, in terms of both R&D and marketing:

- It allows a more rapid ramp-up in sales;
- It raises the number and the level of barriers to entry in the indications concerned (future competitors have to demonstrate non-inferiority, and recruitment of patients could be more difficult, notably if the population size is limited);
- Companies can leverage their marketing efforts toward physicians, with a greater focus on future indications and/or off-label use of the drug;
- To a lesser extent, it increases the level of awareness among physicians and contributes to the company’s science-driven image – oncologists appear to view this as a critical criterion for prescribing.

However, the blitz strategy is more risky as it requires a better understanding of the biology of the drug. In addition, it is more costly because clinical trials require large numbers of patients. The blitz strategy is thus most suited for drugs with relatively low toxicity. From an ethical perspective, a very toxic drug cannot be tested in many patients before it demonstrates efficacy in at least one indication. In addition, when placing many bets, companies commit to very high costs. As efficacy is by definition unknown before testing, this strategy requires a minimum acceptable level of toxicity to succeed. Avastin’s clinical development is a standout example of a successful blitz strategy (see Box 1 on page 7).

Based on the authors’ analyses, two additional issues regarding clinical research are noteworthy. First, the clinical development of targeted therapies could be further optimised. There is a high level of temptation among pharma companies to develop targeted therapies in the same way as broad-acting treatments, such as cytotoxics, meaning that they have not been optimising the chances of success of their molecules. In the past, several examples have highlighted a preference among some pharma companies to target overall populations (driven by profit), rather than specific populations of patients (patient stratification) – and this has sometimes led to statistically insignificant clinical results. Historically, this situation has resulted in some dramatic failures, the misfortune of AstraZeneca’s Iressa (gefitinib) in lung cancer being a good example. Today, even if some companies continue to favour this risky strategy, others such as Amgen (Scrin No 3344, page 16) are taking bold steps towards stratification, thus developing a competitive edge.

Second, patient recruitment is becoming increasingly difficult from both quantitative and qualitative perspectives. The growing number of cancer therapies (both approved and in development), and the resulting boom in oncology-focused clinical research, means that pharma companies are increasingly finding it difficult to convince key opinion leaders (KOLs) to participate in their trials.

Moreover, due to the development of add-on strategies, it is now common to count up to three or four lines of treatment function of indications. As a result, patients included in clinical trials are increasingly frail and refractory. Indeed, for ethical reasons, clinical trials are limited to patients for whom available therapies have failed to demonstrate therapeutic benefits, and they mainly concern patients who have previously relapsed on two or three lines of treatment.

**take risks and be able to adapt**

*Limiting attrition of R&D projects*

Several promising drugs have recently encountered setbacks, highlighting the challenges that pharma companies increasingly have to face. For instance, Bayer Schering’s Nexavar (sorafenib) failed in one pivotal Phase III trial in first-line NSCLC. In the same indication, AstraZeneca’s Recentin (cediranib) failed to progress into Phase III due to toxicity. Witness also the problems faced by Pfizer’s anti-CTLA4 therapy for melanoma.

The authors calculate that success rates in oncology are three times lower than the overall industry average, and the situation is getting worse. For a cancer drug candidate entering Phase I, the average probability of it eventually reaching the market is 3.2%, compared with around 8-9% for the overall industry. Several factors could explain this difference:

- On the research side, more and more novel approaches are being explored in anticancer drug development. Over 40% of cancer drugs in development are directed against novel mechanisms, and almost 70% of the targets that are being investigated in discovery are innovative. The price to pay for innovation is of course the risk of failure attached to it;
- In oncology there is a dearth of adequate preclinical models and translatable preclinical biomarkers, which in some other therapeutic areas are used for early target validation;
- There is often a lack of robust biomarkers that can be used to show proof-of-concept and to gauge whether meaningful therapeutic targeting is occurring in early-stage clinical evaluation. This is particularly true for drug candidates targeting innovative mechanisms;
- In oncology, Phase II results are of a different nature from those needed for registration. In Phase II, products usually show tumour shrinkage and the endpoint is usually tumour response. Fine tuning is used to find an active dose with low system toxicity. In Phase III, the drug is challenged on its global biological impact and the endpoint becomes disease-free survival or often progression-free survival, a much more complex outcome.

To make the situation even trickier, success rates in oncology have been declining over time. The authors tracked the evolution of attrition rates from the mid-1990s to the early 2000s. Between

<table>
<thead>
<tr>
<th>Table 3: Recent oncology-driven M&amp;A deals</th>
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<tbody>
<tr>
<td><strong>Buyer</strong></td>
</tr>
<tr>
<td>Novartis</td>
</tr>
<tr>
<td>Amgen</td>
</tr>
<tr>
<td>Genzyme</td>
</tr>
<tr>
<td>Eisai</td>
</tr>
<tr>
<td>Celgene</td>
</tr>
<tr>
<td>Roche</td>
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<tr>
<td>Takeda</td>
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</table>

* transaction in progress
1996 and 2000, cumulative success rates from first-in-man trials to registration decreased from 4.1% to 3.2%. This increasing rate of failure is due to a sharp decline in Phase II productivity (from 38% to 21%) and, to a lesser extent, Phase III productivity (from 41% to 34%). However, products that do reach the registration stage have a better chance of success (up from 57% to 83%).

More systematic use of biomarkers in R&D projects and better patient selection should help pharma companies to address this challenge. Indeed, biomarkers can reveal drug targets and optimise earlier the selection of drug candidates that interact with these targets for further development. Another way of thinking about this is to have better selectivity of R&D projects in which companies favour development of true innovation rather than me-too compounds.

Manage changes in standard protocols
As described above, oncology is not a typical therapy area; things are changing more quickly than in any other therapeutic indication. With over 70 oncology molecules currently in Phase III trials (and taking into account attrition rates), more than 20 new molecules should be launched within the next four years. As a result, physicians will employ new drug combinations, with varying degrees of success, and most protocols may have to undergo exhaustive rewriting. The successful oncology players of the future will be those that can anticipate protocol evolution now, design the most relevant clinical trials accordingly, and take advantage of developments at competitor companies.

One example is the approval of Bayer Schering’s Nexavar in liver cancer. After the company announced positive results from its SHARP Phase III trial (which assessed the efficacy of the oral angiogenesis inhibitor in hepatocellular carcinoma), most competitor companies in this space (some of which also had products in Phase III) had to stop or redesign their clinical trials. Indeed, physicians demanded that Nexavar be positioned as the new gold standard for hepatocellular carcinoma management and required other players to compare their new drug candidates with that product.

So, oncology players should run head-to-head clinical trials, instead of comparing their molecules with the historical gold standard. Up to now, this risky strategy has only been tried by few companies, one example being Pfizer, which is conducting a Sutent vs Avastin Phase III trial in combination with paclitaxel in the first-line treatment of metastatic breast cancer.

Deal with price pressure
In 2000, oncology drugs accounted for approximately 3.5% of global pharmaceutical market sales. By 2006, this figure had increased to over 5.5% and it should reach 7% by 2011. This trend is directly linked to the significant and rapid penetration of certain targeted therapies such as Rituaxan, Herceptin, Gleevec, Avastin, Erbitux, Sutent and Nexavar. It is also a result of the high prices enjoyed by these drugs and their analogues.

Generally, price is not directly linked to the incidence of a particular cancer, meaning that a rare cancer does not automatically warrant an expensive drug. However, a clearer relationship between price and incidence can be seen for biologicals compared with small molecules. Recently approved drugs with new mechanisms of actions (eg, pathway inhibitors) and/or biologicals have benefited from high prices, with annual treatment costs of $20,000-40,000 becoming increasingly common. This has made the blockbuster model relevant to oncology, but will it be sustainable for payers? Clearly not! With the growing number of patients receiving such therapies, and the high profitability of these drugs (gross margins for biologicals are often 80-90% of sales), healthcare systems will not accept these prices for very long. This seems somewhat ironic considering that many companies that try to access the lucrative oncology market do so because of the high prices granted to innovation in this area.

With cost containment policies being pursued in most industrialised countries, cancer drugs (like all therapies) are expected to come under increasing pricing pressure in the near future. Three factors will contribute to the growing pressure on cancer drug prices in particular:

- The very rapid growth of cancer treatment spending as part of total healthcare expenditure as mentioned above;
- The increasing number of products resulting from competition among a greater number of players;
- The expected increase in combinations of costly drugs. Combinations of two biologics and/or of two targeted therapies (biologics or small molecules) are becoming more common in clinical trials. For example, Avastin is currently being tested in Phase III in combination with Tarceva (erlotinib) as a treatment for lung cancer, and with Erbitux in colorectal cancer. If such combinations are approved, the higher prices will clearly become unsustainable for healthcare systems.

Box 1: Roche’s blitz strategy for Avastin clinical trials
For its anti-angiogenesis drug Avastin, Roche designed a very aggressive development plan, targeting most of the main solid tumours with a vascular network, and directly in the first-line indication (see Table 4 overleaf).

Avastin demonstrated a strong competitive advantage on three grounds:

- Indications sought in parallel. Roche/Genentech developed Avastin in parallel in most cancer types from an early stage, while most competitors concentrated their resources on one cancer type before expanding their development programmes. Avastin is in first-line clinical trials in six cancers (including the three most common cancers) vs three for Bayer Schering Pharma’s Nexavar (only one main cancer) and one for Pfizer’s Sutent.

- Full set of combination trials. Avastin is in a comprehensive set of combination trials with all the current gold standards, with the aim of becoming the backbone therapy in as many tumour types as possible. Competitors’ products are generally being tested with only one or two gold standards by tumour type.

- First-rather than second-line. Roche/Genentech went straight into first-line therapy, whereas in cancer

pharma companies usually start by concentrating on later-stage patients before moving up to the first-line setting. Avastin is a first-line treatment in several major cancer types, while competitor companies have more than half their drugs as second-line therapies. This may be striking given that anti-VEGFs have so far shown better efficacy in earlier stages of cancers than in late stages and that first-line settings provide a much larger patient pool.

This innovative approach gave Avastin a firm advantage over all its main competitors. As a result, renal cancer is today the only indication in which Roche’s product is beaten by other anti-angiogenesis drugs and we do not foresee a threat from competitors before 2010 in lung, colorectal, ovarian, pancreatic or breast cancers.

Having positioned Avastin on top of the chemotherapy backbone, Roche is now trying to reverse this situation. The product is becoming the core of the backbone on top of which pathway inhibitors are tested. This strategy is illustrated by the series of combination Phase II trials underway evaluating Avastin plus EGFR inhibitors in NSCLC, RCC, metastatic breast cancer and head and neck cancers.
### Table 4: Anti-VEGFs in late-stage development

<table>
<thead>
<tr>
<th>Product</th>
<th>Company</th>
<th>Colorectal cancer</th>
<th>NSCLC</th>
<th>Breast cancer</th>
<th>Prostate cancer</th>
<th>Renal cancer</th>
<th>Ovarian cancer</th>
<th>Liver cancer</th>
<th>Pancreatic cancer</th>
<th>Brain cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avastin (bevacizumab)</td>
<td>Roche/Genentech</td>
<td>approved (first-line)</td>
<td>approved (first-line)</td>
<td>approved (first-line)</td>
<td>Phase III (second-line)</td>
<td>pre-registration (first-line)</td>
<td>Phase III (first-line)</td>
<td>n/a</td>
<td>Phase III (first-line)</td>
<td>Phase II</td>
</tr>
<tr>
<td>Nexavar (sorafenib)</td>
<td>Bayer Schering Pharma</td>
<td>Phase II (second-line)</td>
<td>Phase III (first-line)</td>
<td>Phase II (second-line)</td>
<td>approved (second-line)</td>
<td>approved (second-line)</td>
<td>approved (first-line)</td>
<td>Phase II</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Sutent (sunitinib)</td>
<td>Pfizer</td>
<td>Phase III (second-line)</td>
<td>Phase III (second-line)</td>
<td>Phase III (second-line)</td>
<td>Phase II (second-line)</td>
<td>approved (second-line)</td>
<td>n/a</td>
<td>Phase II</td>
<td>Phase I</td>
<td>n/a</td>
</tr>
<tr>
<td>axitinib</td>
<td>Pfizer</td>
<td>Phase II</td>
<td>Phase II</td>
<td>n/a</td>
<td>Phase II</td>
<td>n/a</td>
<td>n/a</td>
<td>Phase III</td>
<td>n/a</td>
<td>Phase III</td>
</tr>
<tr>
<td>Zactima (vandetanib)</td>
<td>AstraZeneca</td>
<td>n/a</td>
<td>Phase III</td>
<td>Phase II</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>Phase II</td>
</tr>
<tr>
<td>pazopanib</td>
<td>GlaxoSmithKline</td>
<td>Phase I</td>
<td>Phase II</td>
<td>Phase III</td>
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<td>Phase III</td>
<td>Phase II</td>
<td>Phase I</td>
<td>Phase II</td>
<td>Phase II</td>
</tr>
<tr>
<td>BIBF-1120</td>
<td>Boehringer Ingelheim</td>
<td>Phase I</td>
<td>preclinical</td>
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<td>Phase II</td>
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<tr>
<td>CDP-791</td>
<td>UCB</td>
<td>n/a</td>
<td>Phase II</td>
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<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>motesanib (AMG706)</td>
<td>Amgen</td>
<td>Phase I</td>
<td>Phase II</td>
<td>Phase II</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>VEGF Trap (aflibercept)</td>
<td>Regeneron/Sanofi-Aventis</td>
<td>Phase III</td>
<td>Phase III</td>
<td>n/a</td>
<td>Phase III</td>
<td>n/a</td>
<td>Phase II (second-line)</td>
<td>n/a</td>
<td>Phase III</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Source: Pharmaprojects
Moreover, because lifecycle management is very important in the oncology space, it is common to find 3-4 granted indications for one oncology product. This means that the treatable population (and underlying costs) will significantly increase throughout the lifetime of a molecule, making a price reduction inevitable.

In response, some pharma companies are exploring new ways of working within payers’ financial constraints. The 2007 decision of the UK National Institute for Health and Clinical Excellence (NICE) regarding the management of relapsed multiple myeloma with Johnson & Johnson’s Velcade (bortezomib) is a standout example. Last September, NICE’s appraisal committee said that patients who showed a full or partial response to Velcade should remain on treatment funded by the NHS, whereas patients who showed less than a partial response should be taken off treatment with the cost reimbursed by the manufacturer.

Interesting developments also took place in France when the country’s healthcare system switched from free to regulated prices. The introduction of a “tarif de responsabilité” for expensive (e.g., oncology) drugs set the basis for drug prices on which hospitals are reimbursed. In addition, the implementation of the “marge de reversement” for costly drugs encourages hospitals to actively negotiate prices with pharma companies. Finally, in future, all costly drugs are likely to be included in a “groupe homogène de séjour” in which prices are defined and managed by the health authorities.

**properly assess generic threats**

Additional pricing pressure is coming from the generics sector: such products have already eroded sales of former leading oncology drugs such as cisplatin, doxorubicin, paclitaxel and tamoxifen.

Broadly speaking, small-molecule oncology drugs are more exposed to the generic threat than biologicals. (Biosimilars will compete as “me-too” drugs when they enter the market and therefore will not lead to such a drastic erosion of sales as in the case of small molecule therapeutics.) The risk is especially low for monoclonal antibodies given their structural complexity and the resulting IP protection afforded to these molecules.

Within the next five years, several significant oncology drug patents will expire: Sanofi-Aventis’s Taxotere, AstraZeneca’s Casodex and Arimidex and Lilly’s Gemzar, for instance, are particularly exposed. Based on oncology attrition rates, these companies cannot expect to gain more than two or three new approvals in oncology before 2011. Finding new products to make up for lost sales will be a tough challenge, particularly for Lilly and Sanofi-Aventis, which have not shown much enthusiasm for striking deals in this therapy area.

Conversely, the arrival of generics in the oncology space could also bring some benefits. As discussed previously, many cancer therapies are combinations of 2-3 compounds, so replacing one component with a generic would lower the overall price of the “cocktail.” This in turn would make it more feasible to increase the price or dose of the other components, or even to add a new compound.

So, what level of benefit in terms of efficacy (e.g., progression-free survival or overall survival improvement) compared with current protocols should justify a price premium? This is the question both payers and pharma companies should bear in mind.

**sell effectively**

While the successful development of drug candidates is crucial, so too is effective selling taking into consideration the specifics of the oncology market. Three factors are key to achieving this goal:

- Meet all oncology market access requirements to secure registration, premium pricing and reimbursement in a timely manner as well as maintain prices of existing drugs;
- Ensure alignment between affiliate organisations and targeted prescriber segments regarding their respective needs;
- Optimise interactions between companies’ corporate management and their local affiliates.

To meet market access requirements, pharma companies have to:

- Ensure access to and get the full support of international and national KOLs;
- Secure product registration by aligning and updating clinical comparators according to the rapidly evolving medical guidelines;
- Anticipate any pricing and reimbursement (P&R) system changes, in particular for expensive oncology drugs;
- At an early stage, integrate P&R as a critical component of the product strategy and clinical development plan by maintaining ongoing relationships with payers;
- Strengthen the P&R dossier by clearly defining and qualifying the size of the reimbursed population vs the regulatory population and strengthen health economic studies highlighting the financial benefits/value of the drug in its competitive universe;
- Develop risk management programmes to monitor serious adverse events.

Where possible it is important to integrate marketing, medical, sales and business intelligence functions dedicated to oncology into a single business unit. This offers several advantages:

- One multi-disciplinary team shares the same business objectives with clear roles and responsibilities assigned;
- Internal miscommunication is avoided;
- A customer focus approach is employed, leveraging the operational expertise available within the business unit.

However, the sales and marketing situation is becoming complicated by the evolving nature of prescribers. For some time, European patients have been treated not only by oncologists but also by “organ-specialist” physicians, and a similar trend is emerging in the US. This movement cannot be overlooked because the two groups demonstrate quite distinct prescribing habits.

Put simply, in most countries “pure oncologists” take care of such indications as breast and colorectal cancers, leukaemias and lymphomas. By contrast, pathologies such as lung, prostate, bladder or renal cancers more often come under the remit of specialists, such as pneumologists and urologists. Things are further complicated by differences in cancer care from one region to the next. For example, in Germany breast cancer is treated by gynaecologists rather than oncologists, whereas the opposite is true in the US.

These distinctions not only impact on the required marketing and sales forces, they also influence product sales. Pure oncologists are accustomed to integrating new drugs into their practice rapidly, whereas penetration tends to be slower among the organ-specialist physicians,
mainly due to a lack of management of serious adverse events (eg, hand-foot syndrome, cardiovascular toxicity) associated with targeted agents. This calls for greater marketing efforts directed toward the latter group, in particular, concerning the management of the side-effects associated with cancer drugs.

Hence, developing and implementing appropriate medico-marketing platforms and tools to reach targeted prescriber segments is also a key factor. A parallel can be drawn here with other highly technical therapeutic areas, such as AIDS and immunology. In these segments sales forces have been adapted to target GP practitioners: AIDS tri-therapy, for instance, is now prescribed in most countries by GPs even if hospital KOLs continue to play a major role. To a lesser extent, the arrival of subcutaneous formulations of biological disease-modifying antirheumatic drugs (DMARDs) in rheumatoid arthritis, such as Abbott’s Humira (adalimumab), Schering-Plough’s Remicade (infliximab) and Bristol-Myers Squibb’s Orencia (abatacept), has opened the door to ambulatory care. Even if GPs are not yet fully involved in prescribing these drugs, the hospital-to-ambulatory shift will contribute to the modification of marketing approaches in much the same way. In this regard, it is also important to intensify local/regional partnerships to respond to KOL needs regarding clinical trials.

Lastly, companies need to optimise interactions between corporate HQ and their local country affiliates. In order to achieve this, corporate functions have to provide full support to their local affiliates regarding P&R, as well as give them flexibility around the deployment of the global strategy. Affiliates need the freedom to adapt local clinical study development according to the needs of stakeholders. Corporate functions should also facilitate communication and best practice sharing.

This can be achieved using two models – the centralised and the decentralised (regional) marketing organisations – and there is a steady shift towards the former. This trend can be expected to continue as:
- The number of clinical trials increases sharply, covering multiple indications;
- Larger patient samples are required to obtain statistically significant data;
- Management of clinical trials becomes increasingly complex as described above.

As a result, companies will have to take an increasingly systematic approach, for which the centralised model is better suited. A centralised marketing organisation consists of a top-down decision-making process, in which a corporate-level team defines the rules for all the country subsidiaries. This approach requires a clearly empowered corporate team that drives relationships with leading international KOLs and sets the precise framework for clinical trials: studies are designed at the corporate level, with few modifications at the local level. This approach is well suited to the blitz strategy discussed earlier.

On the other hand, a decentralised marketing organisation consists of a locally-driven decision-making process. Highly decentralised approaches do not always allow close control over the design of trials. Nevertheless, on the positive side, local affiliates that are allowed some degree of breathing space can develop strong relationships with local KOLs, as well as implement clinical trials required by local physicians.

get a foothold in biotech

Biotech companies are fuelling innovation in oncology more than ever before. Over 70% of cancer drugs currently in late-stage clinical trials originated in biotech labs. Over 80% of the recombinant proteins or biological peptides/proteins currently in Phase II/III clinical trials were originally discovered by biotechs. Further evidence of the impact of biotech on cancer innovation will no doubt come in the form of small interfering RNA (siRNA) and gene therapies should these technologies deliver their potential. In fact, after the currently available kinase inhibitors and anti-angiogenic drugs, mTOR inhibitors, inhibitors of histone deacetylase (HDAC) and toll-like receptor agonists seem to be the most promising agents. They have demonstrated potential therapeutic activity against a broad range of tumour types, with favourable safety profiles relative to other therapies. They rely on induction and enhancement of the body’s own natural anti-tumour responses and acceleration of immune system recovery after chemotherapy or radiation treatment.

Capturing the most promising oncology innovations through in-licensing activities is now essential for pharma and big biotech. Large companies bring financial muscle to the table, and can therefore accelerate the development process and support the blitz strategy. Additionally large partners can contribute:
- Proven expertise and knowledge of the oncology arena;
- Capacity and capability to support late-stage clinical development and commercialisation;
- Increasing willingness to set up partnerships with biotech companies;
- Capacity to manage complexity;
- Access to KOLs.

That said, the partnering arena is highly competitive, and successful licensing calls for a unique blend of both scientific and business expertise. Among other things, licensees need to develop proactive mindsets; ensure rapid decision-making; continuously screen potential opportunities using a prioritisation process; and use relevant tools to define the “right price” for in-licensed or acquired assets.

Recent M&A deals point to significant activity within the oncology sphere. The authors’ analysis of pharma/biotech acquisitions valued at over $50 million in addition, there is now mounting evidence supporting the synergy between HDACi and numerous other therapies (eg, kinase inhibitors, chemotherapeutic agents, protease inhibitors, and radiation therapy) in a broad range of cancer indications. Positive clinical results in a wide range of haematological and solid tumours have been obtained and HDACi products have demonstrated attractive efficacy/safety ratios in comparison to other chemotherapies. Among the most promising are those being developed by Merck & Co (vorinostat), Novartis (panobinostat), Topotarget/Curagen (belinostat) and Methylgene/Pharmion (now Celgene) (MGCD0103).

Among first-in-class molecules under development, toll-like receptor agonists represent other promising agents. They have demonstrated potential therapeutic activity against a broad range of tumour types, with favourable safety profiles relative to other therapies. They rely on induction and enhancement of the body’s own natural anti-tumour responses and acceleration of immune system recovery after chemotherapy or radiation treatment.
between January 2006 and December 2007 demonstrated oncology to be the principal focus of interest, accounting for 25% of deals. Infectious and autoimmune diseases followed at 21% and 12% respectively. Within this period, the total value of closed oncology deals came to $9.6 billion. Some of the most significant transactions are summarised in Table 3 on page 6.

synergies with other markets
This discussion has so far focused on the therapeutic oncology market. However, it is important also to consider the supportive care and in vitro diagnostic (IVD) segments, each of which has its own distinct growth trends and presents clear opportunities for synergy with the therapeutic sector.

With over $19.3 billion in sales in 2006, supportive care was the second-largest market segment (34% of total sales) after therapeutic oncology drugs. Accounting for 62% ($11.9 billion) of total segment sales, anaemia care agents (eg, erythropoietins and colony stimulating factors) were the leading therapeutic classes in revenue terms, followed by the opioids ($2.6 billion), the anti-emetic drugs ($2.4 billion) and the bisphosphonates ($2.3 billion). The supportive care market is expected to grow annually by 6.3%, reaching over $33 billion by 2011.

Many widely-used cytotoxic agents lack tumour specificity and therefore cause a wide range of serious side-effects, such as nausea, anaemia, and neutropenia. As such they sustain the market for treatments including recombinant erythropoietin (EPO) and granulocyte colony stimulating factor (G-CSF). Among the anti-emetic drugs, 5-hydroxytryptamine type 3 (5-HT3) antagonists are the gold standard for preventing acute nausea and vomiting induced by chemotherapy or radiotherapy. With $1.6 billion in worldwide sales in 2006, GlaxoSmithKline’s Zofran (ondansetron) was the clear market leader in this area, but it is now being threatened by the entry of generics. The other main competitors are Roche/Genentech’s Kytril (granisetron), Sanofi-Aventis’s Anzemet (dolasetron) and MGI Pharma’s Aloxi (palonosetron).

The bisphosphonate market has faced significant changes over the past decade with the launch of third-generation therapies such as Novartis’s Zometa, the entry of generics and potential clinical repositioning. However, bisphosphonates are still the standard of care for treating the bone metastases that are particularly frequent in breast cancer (occurring in 65-75% of patients). In addition they are now under clinical investigation for bone metastasis prevention.

In parallel, worldwide sales of molecular diagnostics, immunoassays and immunohistochemistry products exceeded $2 billion in 2006. In vitro diagnostic products encompass a wide range of applications from less sophisticated technologies (eg, occult blood, histology stains) to very advanced immunoassays and nucleic acid testing covering various aspects of disease management (from screening to monitoring and prognosis evaluation). Much research has been conducted over the past decade to gain a better understanding of cancer mechanisms. This has led to significant improvements in IVD tests within the oncology domain, in particular urine, faeces, blood, or tissue-related tests (eg, immunoassay and immunohistochemistry) detecting the presence of cancer biomarkers; and genetic tests detecting abnormal DNA/RNA sequences indicative of cancer.

Now, many tumour markers are part of common treatment practice, but they are only available for a limited number of cancers. In 2006, immunoassay products were the market leaders (63% of total sales), while immunohistochemistry and nucleic acid testing (NAT) products lagged far behind, accounting for 19.2% and 18% of total IVD sales respectively. In vitro cancer diagnostic sales are expected to grow at a double-digit rate (14.1%) over the 2006-2011 period to reach about $3.9 billion. The NAT domain should register the highest growth with an expected CAGR of over 20% by 2011.

In addition, the expected boom in personalised medicine should prove to be a significant driver of this market segment. Companies investing in such technologies, such as Roche with Herceptin and Novartis with Gleevec, are likely to be the oncology winners of the future, even if the concrete applications of personalised medicine as yet remain limited. In addition, developing an oncology portfolio combining therapeutic treatments with supportive care or in vitro diagnostics could be an interesting option for oncology players to pursue.

healthy prospects
Oncology is clearly a very attractive marketplace: it is expected to grow at twice the pace of the global pharma market over the next few years and it continues to be driven by significant unmet medical need. However, the market is becoming increasingly complex, cancer drug development is becoming more difficult and risky, and high prices will be difficult to sustain in the near future. Indeed, payers will come up against increasing financial constraints, and as a result will probably require more evidence of efficacy and patient stratification as they seek to absorb the cost of treatments. At the same time, drug development costs can be expected to increase significantly and patient recruitment will become a hurdle. Moreover, the threat from generics will become a reality and several best-selling brands will soon face drastic sales erosion.

Based on these considerations, the industry can expect a significant reshaping of the oncology landscape over the next five years – the future winners will be those players that are willing both to invest and to accept the underlying risks. There is no magic spell to succeed in oncology, but companies can be successful if they properly manage the risks related to this complex market, meet all market access requirements, ensure alignment between affiliate organisations and target prescriber segments, optimise interactions between corporate teams and local affiliates and if company assets allow, implement an aggressive partnership strategy with biotech companies.

References

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