Beyond Lifecycle Management – Optimizing Performance Following Patent Expiry

PREPARED BY:

Edward Tuttle, Andrew Parece, and Anne Hector
Analysis Group, Inc.

July 2004

ANALYSIS GROUP
ECONOMIC, FINANCIAL and STRATEGY CONSULTANTS

Beyond Lifecycle Management – Optimizing Performance Following Patent Expiry

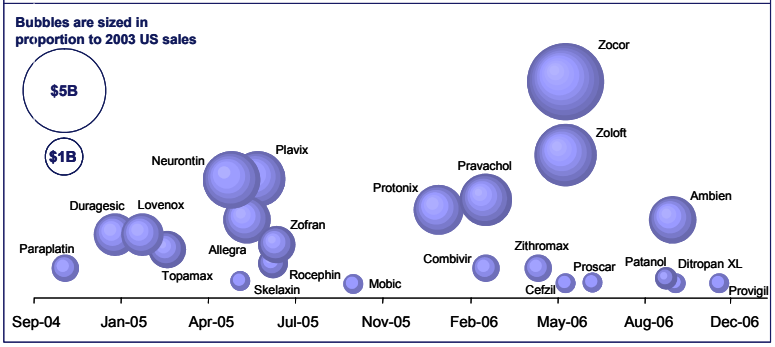
INTRODUCTION

In a well-known example of generic drug entry following patent expiry, when generics to Eli Lilly's anti-depressant Prozac were introduced in 2001, its volume fell precipitously –it lost 73% of its share of new prescriptions within two weeks, according to the Congressional Budget Office. The Federal Trade Commission reports that between 1984, when Congress passed the Hatch-Waxman Act to encourage generic participation in the prescription drug industry, and 2002 the share of total prescriptions filled with generics has risen from 19% to 47%. Today, that figure is widely reported to be above 50%.

Based on review of recent patent expiry data, such rapid losses of revenue for brand owners (and eventual reduction in costs for payors, as generic prices are eroded by additional generic entrants) appear to be getting more common over time. Generic companies are becoming stronger and more sophisticated and payors are becoming more effective in their efforts to influence the way prescriptions are written and filled. Review of data from the most expiries suggests that pharmaceutical brands are losing more share, on average, in the first 12 months following generic entry today than they did several years ago.

Figure 1 – Major U.S. Patent/Exclusivity Expiries 2004-2006

The U.S. pharmaceutical market is set to experience a record number of significant patent expiries over the next two years. Although the timing of individual losses of exclusivity is uncertain, several large generic markets will undoubtedly result. With careful planning and analysis, manufacturers of brand name pharmaceuticals can maximize the value of their patented molecules



Sources: SG Cowen Pharmaceuticals Report March 2004, Company Reports

Patent expiry and generic entry are of great interest to pharmaceutical companies today, as Figure 1 illustrates. Products with U.S. sales totaling above $15 billion are scheduled to face generic entrants for the first time in 2005. The difference between a more rapid and less rapid drop in share could translate into a revenue difference of several hundred

million dollars for a blockbuster product. At a time when new FDA approvals have been slow and R&D costs rising inexorably, patent expiry puts added pressure on pharmaceutical companies already squeezed by rising costs and public pressure on pricing.

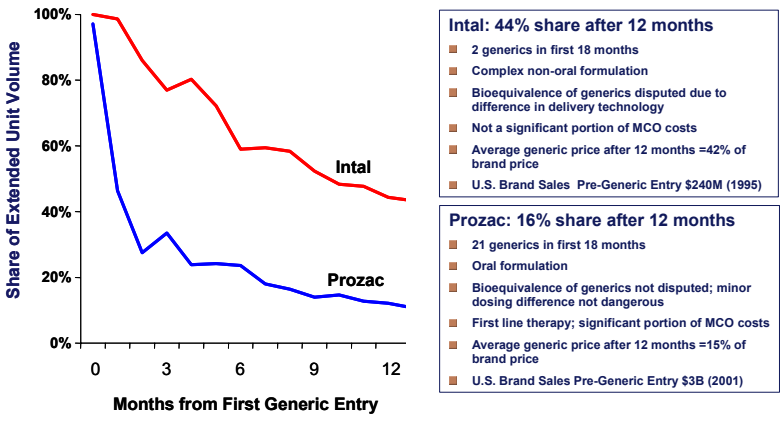
BEYOND LIFECYCLE MANAGEMENT

Not surprisingly, a variety of lifecycle management tactics have been pursued aggressively by many manufacturers. If brand equity (and prescriptions) can be transferred to a follow-on or derivative product, even a reformulation or new delivery system, a franchise can be sustained. Switching the prescription brand to an over-the-counter product, where possible, also provides a new venue for sustaining revenue.

These tactics notwithstanding – and great effort has certainly been devoted to them – the bulk of the expiring brand revenues will at some point give way to generics. The question for a pharmaceutical company is: How quickly? And a key corollary to this question is: If a company can predict how fast brand revenues will erode, are there different tactics it should employ depending on the answer?

Figure 2 – Post-Expiry Share: Two Case Studies

Prozac and Intal show two very different patterns of what can happen to the share of a branded drug after it goes off patent



Pharmaceutical brands are not all equal. As Figure 2 illustrates, the rapid erosion of Prozac (an antidepressant) can be contrasted with that of another drug, Intal (an asthma treatment), which eroded far less quickly. Brand managers generally know intuitively

that some products have attributes that make rapid switching less likely. We note in Figure 2 some of the characteristics of Intal that may be related to its lower losses vs. generics – the complex metered dose inhalant system, for example.

The challenge, though, is not just to recognize this potential but to forecast it effectively. This challenge is compounded by the aforementioned increase in share losses associated with more recent expiries. The effect of timing as well as of the other circumstances which may affect post-expiry performance must be accounted for. Because investment decisions – continued promotion, or a clinical trial investigating the therapeutic equivalence of different forms of a drug, perhaps – depend on arriving at a reliable forecast, this problem is an important one. As generics enter, brand teams must grapple with a planning and forecasting regime very different from that during the patent life and where new and evolving strategic options, such as the possibility of an authorized generic, are on the table.

FORECASTING SHARE WITH GENERIC ENTRANTS – THE RELATION OF PRODUCT AND CLASS ATTRIBUTES TO POST-EXPIRY BRAND POTENTIAL

Given the wide range of possible outcomes when a brand faces generic entrants, determining the brand's intrinsic potential for share retention is critical to making the right strategic choices about post-expiry options – things that are within the brand manager's control. What are the key factors that are associated with share retention and how can the brand manager make better estimates of the brand's potential to optimize its post-expiry strategy?

In our research, we have found that there are several product and therapeutic class attributes that are more strongly associated with share retention than others. Understanding these attributes and their relationship to the brand's potential to retain share, an informed brand manager can better determine what strategies will be most effective once generics enter. The key attributes affecting brand share retention can be grouped into two categories: product attributes, and class or category attributes.

Product attributes – Generally, products that are more difficult to manufacture have higher potential for share retention. If fewer manufacturers are able to produce products of a certain type, the product has the potential to experience fewer generic entrants and retain higher share. This phenomenon has historically applied with certain advanced

delivery systems – the osmotic pump technology in Procardia XL, for example – and it is likely to come into play more frequently over the next few years as biologics such as erythropeitin begin to lose exclusivity.

Another attribute associated with share retention is the complexity or risk associated with administering the product. It is not surprising that physicians might be more conservative, payors less demanding, and entrants less aggressive in therapeutic categories or products with high risks or challenging titration issues. The blood-thinning drug Coumadin has had few generic entrants and sustained high sales for many years, due in part to the risks associated with its narrow therapeutic index.

One circumstance meriting special attention is whether the manufacturer has been successful in developing or licensing a follow-on product in the class. Follow-on products, as well as OTC options, are of course considered well before the brand's patent protection expires, and are important to maximizing the brand's potential. Just as the brand manager carefully considers follow-on options in planning a franchise strategy, he must be aware of these factors in interpreting data from prior patent expiries. In most cases, a brand's share erosion is accelerated by the introduction of a new brand by the same manufacturer, e.g. AstraZeneca's launch of Nexium to follow Prilosec. If this is not recognized and accounted for when interpreting historical data or identifying appropriate analogs, the brand manager may come to incorrect conclusions about the brand's post-expiry potential.

Class Attributes – Attributes of the therapeutic class are also critical to the brand's potential for retaining share post-expiry. For instance, if there has already been a significant number of generic entrants to the class, one might expect a weaker effect from a new generic, both on the brand and the class overall, as some degree of shifting to the pre-existing generics may have occurred.

Category conditions cannot be overlooked. A brand possessing attributes associated with share retention may be in a category with new brands or even a new therapeutic class poised to enter at about the time its patent protection expires. The post-expiry share loss experienced by Pepcid, a leading H2 agonist for treating acid reflux disease, was accelerated in part by the entry of proton pump inhibitors into the category.

In addition to new entrants, the prescribing environment, including managed care benefit structures (three-tier copayments, prior authorization, step edits, etc.), state Medicaid preferred drug lists (PDLs), and Medicare coverage/reimbursement are constantly changing. Given these considerations, and their impact on the therapeutic class, a brand's potential and the range of strategic options may be vastly different from the situation in which the underlying category is "stable". Modeling these dynamics is an essential step in defining the optimal post-expiry strategy.

Table 1 presents a list of these and other attributes, observable prior to patent expiry and generic entry, which we have found to be associated with increases in post-expiry share.

Table 1 – Examples of Product and Class Attributes Associated with Higher Post-Expiry Brand Share

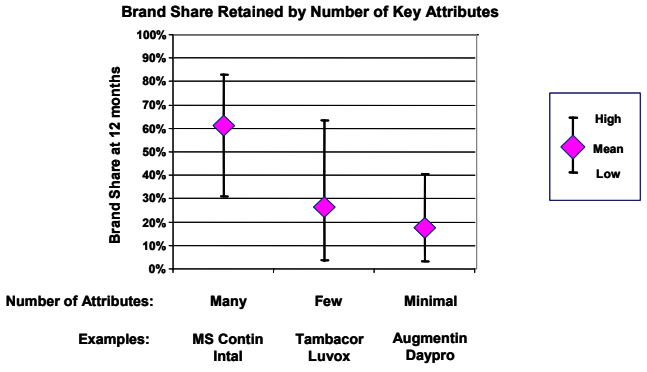
- Less interchangeable with other brands
- More potential for risk, adverse outcomes
- Lacking a follow-on product
- Prescribed by few physicians, i.e. specialists
- Harder to produce technically
- Less recent date of expiry
- Part of a class with many prior generics
- Less subject to managed care control
- Smaller category size
- Part of a class with less new brand activity

We have found that the role these attributes may play in post-expiry brand share can be a topic of considerable debate within pharmaceutical companies. Analyzing a set of approximately 30 recent expiries, however, we find a clear correlation between the presence of certain of these attributes and the brand's retained prescription share 12 months following generic entry.

Figure 3 shows the relationship between several of these attributes and retained share. The products are grouped according to the number of key attributes they possess: several, few, and minimal. The figure shows that products possessing more of these key attributes – e.g., MS Contin or Intal – have maintained more share once generics have been introduced.

Figure 3: Relationship Between Brand Share Retained and Product Attributes

The relationship between certain critical product attributes and the share retained by brands is evident based only on the number of attributes. Through multivariate regression techniques to isolate these effects and account for other relevant factors a robust forecasting model can be developed.



The discussion of attributes and factors affecting potential for share retention is not intended to be exhaustive, nor have we attempted to quantify the relative impact of these factors in the limited space available. However, our research has shown that these factors can be the basis for rigorous and powerful multivariate models that use these attributes as inputs to estimate brand share, and allow scenario analysis of the brand's strategic options.

Figure 4 – Attribute-based Simulation of Post-Expiry Brand Share

One type of forecasting model uses a two-stage approach in which certain attributes are first used to estimate the number of generic entrants and the relative price of the generics and brand over time. A second stage uses the outputs of the first as well as other attribute data to forecast the resulting share of the brand and the generics

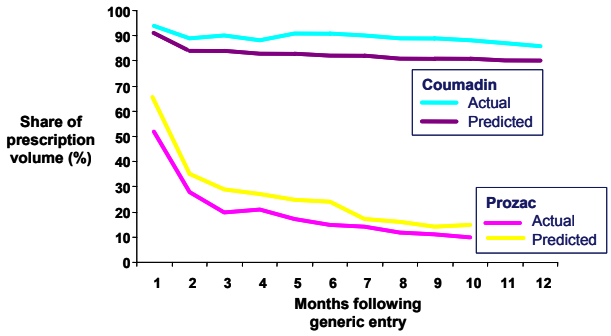


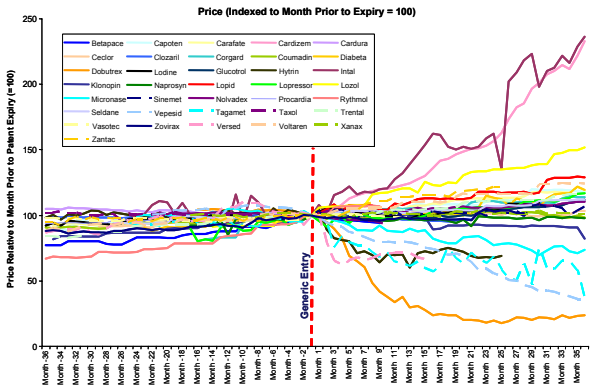
Figure 4 shows the actual and estimated share erosion based on one of the models we have developed, illustrating both a product that has retained significant share (e.g., Coumadin) and one that has seen much more substantial share erosion (e.g., Prozac). After carefully assessing and identifying a brand's key attributes, it is possible to apply the model to estimate the likely share that will be retained for products facing patent expiry. For example, this model would suggest that products that possess many of the key attributes discussed earlier, such as Lovenox, will be able to retain substantially more share than others that possess none of these attributes, such as Cefzil.

Attribute-based forecasting models such as these can be complemented by market research with physicians focused more specifically on the issues relevant for a specific product and class. It is typically the case that such models can be enhanced if the brand team has a good approximation of the number of potential generic entrants through ANDAs filed or market intelligence.

Another factor relevant for forecasting is the potential effects of different pricing strategies by brand name and generic manufacturers. Using models which account for product and class attributes as well as the number of entrants, we find that the decline in prevailing generic prices is fairly predictable over time. The pricing choices made for brands themselves have varied widely – with most having increased brand price after generic entry (see Figure 5). There is some evidence these decisions have not always been made optimally. In the case of, Dobutrex, for example, in which a brand appears to have sought to drop price to retain more share against generics, the brand has lost virtually as much share as we would predict with a steady price.

Another important factor to consider is the interaction of generics with other brands and other therapeutic classes. Generics may expand the molecule share of the class (i.e., by drawing share from other brand name agents in the class or by drawing new, untreated patients to the class). Generics also may expand the class share of a broader therapeutic category (e.g., generic ACE-inhibitors possibly expanding the ACE-inhibitor share of the anti-hypertensive category). Understanding the degree to which a generic entrant could expand the molecule or class, versus gaining share from the brand, is essential to determining the brand potential. Analyzing data from prior patent expiries myopically

Figure 5: Brand Price Movements Have Varied Substantially Post-Expiry



Note: Drugs with pre-expiry annual sales in excess of $100 million whose patents expired since 1995. IMS data

(i.e., looking only at the share of molecule) in some cases will result in a biased estimate of the true potential for the brand.

In summary, the attributes most important for a specific brand and class need to be assessed in the context of that brand's situation – the lifecycle strategies it may have implemented, the intrinsic product and class attributes influencing its potential for share retention, and the unfolding dynamics of its therapeutic category. The brand manager who carefully considers these questions will be much better positioned to identify an optimal post-expiry strategy.

OPTIMIZING POST-EXPIRY PERFORMANCE

Among the set of decisions managers must make as they determine the optimal path for a brand losing exclusivity, we see two critical choices:

1. Whether to participate in the generic arena with an authorized generic product
2. How aggressively – if at all – to support the brand with investments aimed at differentiating it from generic competitors (e.g., pricing, promotion level and mix, studies)

The first of these questions is currently generating a wave of interest as brand owners begin to pursue this approach more aggressively and generic companies challenge what has been perceived as a move limiting their incentive to launch generics as rapidly as

possible. We address both questions here, building on the understanding of the brand's intrinsic potential that comes from the attribute-based assessment covered earlier.

1. Authorizing a Generic

The "authorized generic" is a recent development in post-expiry strategy. An authorized generic is created when the manufacturer of a drug soon to lose exclusivity contracts with a generic company to sell an "authorized" version of the molecule, in some cases supplying the product to the authorized generic company. Particularly in those instances where a legal challenge (under paragraph IV of the Hatch-Waxman Act) creates the potential for the first generic to enjoy a 180-day exclusivity period, brand owners have begun to utilize this "join rather than fight" approach.

A number of branded pharmaceutical companies, including Bristol-Meyers Squibb, GlaxoSmithKline, Johnson & Johnson, and Pfizer have drawn a great deal of attention for their launched or planned authorized generics in recent months. This strategy is new, regulatory opinion is still evolving, and long term results have yet to be observed. However, evaluation of a notable early case and the underlying dynamics of brands and generics offer useful insights.

GlaxoSmithKline's Paxil (paroxetene) offers an illustration of the authorized generic option. GSK contracted with Par to sell a generic version of Paxil. In September 2003, Par launched its generic simultaneously in the market with a generic from Apotex, the manufacturer that had challenged GSK's patent under paragraph IV and that anticipated a 180-day exclusivity period if it prevailed.

By launching concurrently with Apotex, Par gained access to the typically higher generic prices of the first 180 days, though its presence may have brought the prevailing generic price lower than it would have been with Apotex alone during that period. In addition, Par gained the opportunity to establish early contracts and distribution with pharmacies that might persist, helping it sustain share after other generics have entered.

This arrangement clearly appears to have benefited Par. Apotex, by contrast, was forced to share what might have been a period of generic exclusivity prior to the entry of other generic companies. Not surprisingly, manufacturers in Apotex's position have objected to these arrangements. To date this year, generic companies have filed four citizen's petitions with FDA regarding authorized generics, all of them rejected. In its most recent

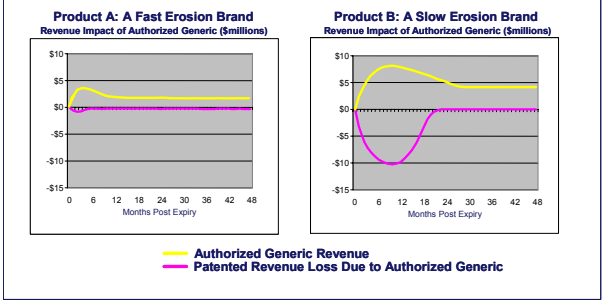
ruling, FDA stated that the entry of the authorized generics and the resulting lower drug prices benefit the American consumer. This situation will continue to evolve but, at present, regulatory sentiment favors the benefit to consumers over any losses of generic exclusivity.

What about GSK? Depending on the terms of its contract with Par, the authorized generic appears to give it an ongoing royalty stream from generic paroxetene which would supplement the post-expiry brand revenues from Paxil. Is it worth it? We will not examine the public policy factors that might sway a brand owner like GSK but limit ourselves to the financial consideration – specifically, are there circumstances where losses of revenue from the brand name drug would outweigh the royalty stream from the authorized generic?

To explore this issue, let's consider two hypothetical cases. Product A in Figure 6 represents a fast-eroding blockbuster. Product B, by contrast, represents a comparably sized but slower-eroding product attracting fewer generics.

Figure 6 – Revenue Impact of an Authorized Generic Varies with Brand Potential

An authorized generic may yield positive revenue and return for the majority of drugs going off patent. A prototypical, fast-eroding brand (Product A) attracts sufficient generic entrants that the addition of an authorized generic has little impact on brand revenues. For slow-eroding brands (Product B), the situation is more complex – fewer generics are expected to enter the market and an authorized generic could substantially erode patented revenues. With Product B, while the authorized generic may ultimately generate greater revenue (and NPV), in the short run, the brand name pharmaceutical manufacturer may profit more by foregoing a generic and defending the brand.



Both Product A and Product B would benefit from the royalty stream of an authorized generic (the yellow line in Figure 6). Product B's royalty stream would be higher due to the presence of fewer generic companies. However, we also must evaluate any incremental erosion of the brand revenue (the pink line in Figure 6). In a category where many generics will enter and the branded drug share will erode quickly (Product A), the addition of one more generic – the authorized one – would not typically result in

substantial additional erosion of brand revenue. In this case, an authorized generic is likely to be unambiguously favorable financially.

Product B illustrates a more complicated dynamic. In this instance, the authorized generic does materially affect brand sales. The additional generic and the enhanced generic price erosion has the effect of increasing total generic share at the expense of the brand. In such a circumstance, it may take substantially longer for the authorized generic deal to break even for the brand owner – or, depending on the contract terms, it may not be worthwhile.

It is critical to understand the attributes of the product and the expectations for post-expiry performance in advance of striking any authorized generic deal. Table 2 lists some of the most important circumstances for success of an authorized generic. As noted earlier, there may be other factors influencing an authorized generic decision. For example, it may be the case that a choice to authorize a generic with one brand will have implications for other brands in the company's portfolio. These factors, beyond simply the financial trade-off for the brand in question, must also be taken into account.

Table 2 – Circumstances Favorable to Issuing an Authorized Generic

- **Product has a predominance of attributes associated with fast erosion**
- **The product and market are substantial and possess characteristics likely to attract multiple generic entrants**
- **Ability to identify a strong licensing partner**

2. Continuing to Support the Brand (or Not)

As we have seen, an authorized generic can benefit consumers or payors by hastening price and share erosion, and also benefit brand owners to the extent that cannibalization of brand sales does not outweigh royalties. In addition to the decision on whether to participate in the generic arena, the brand owner must also decide whether to continue investing in the brand itself.

While the historical norm – and likely the right answer for many products – has been to withdraw essentially all investment from brands at or before expiry, this question should

be carefully considered. Where there are product and class attributes that correlate with high share retention, some amount of continued investment may be warranted.

The case of Intal, discussed earlier, provides one example where continued investment was likely merited. Intal is a mast cell stabilizer (anti-inflammatory) used primarily for asthma. The delivery mechanism was not a widely diffused technology at the time (1995), and relatively few companies were able to reproduce the product. The first generic entrant did not use an identical delivery technology, and Fisons, Intal's manufacturer, made an investment in communicating information about these differences. Intal maintained over 40% share 12 months post expiry (Figure 2) and as late as 2002 was still generating significant revenue.

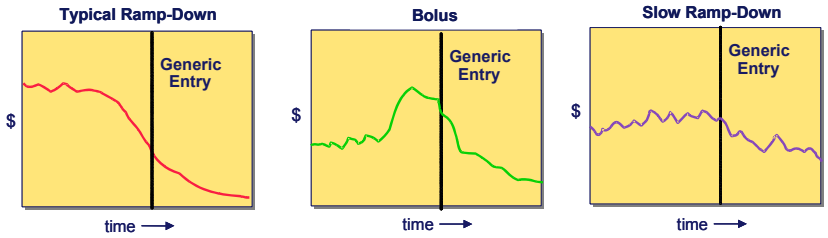
There are other examples of manufacturers successfully differentiating and maintaining a branded product post expiry. Coumadin (warfarin) is a well-known example. Armed with a number of the intrinsic attributes associated with share retention (e.g., mortality risk, dosing concerns, few prescribers), DuPont and then BMS continued to promote the product, supported by studies and communication of the data to agencies and payors. Although such circumstances are relatively rare, we anticipate more in years to come, particularly as biologics lose exclusivity.

In the broader arena of more "average" products, the question is less likely to be whether such an aggressive post-expiry marketing and promotional campaign is merited but instead whether *any* form of investment – a small study on therapeutic equivalence or a "bolus" of promotional activity just before generic launch – should be undertaken. For example, if a delay with a planned follow-on creates a substantial "gap" between the original product expiry and the launch of its successor, the brand owner needs to consider the merits of remaining engaged in the category during that period.

The variance in appropriate responses to patent expiry is illustrated by an examination of the patterns of promotional activity in recent expiries. Three patterns emerge, as illustrated in Figure 7. The first, showing a sharp drop in activity beginning well before the first generic competitor enters, is typical but hardly universal. We also observe both the burst of late-life activity represented by the "bolus" and the sustained investment associated with a product like Coumadin.

Figure 7 – Patterns of Brand Promotional Investment at Generic Entry

Based on an analysis of detail, sample, journal, DTC and other spending for a group of recent patent expiries, we observed considerable variance from the most typical pattern of rapid promotional pull-back in advance of generic entry. The alternative patterns are observed in instances where brands have the potential to retain more share, based on intrinsic attributes of the product and class, or where specific events (such as a "bridge" to a delayed follow-on product) make continued promotion appropriate.



An effective model for post-expiry performance should consider the impact of continuing promotion and other forms of investment in the brand, after accounting for the attributes and category dynamics influencing the brand's potential. Such a model can be highly valuable for a wide range of products, helping to assess underlying potential and customer responsiveness where existing models of brand performance are often ill-equipped to account for generic entrants.

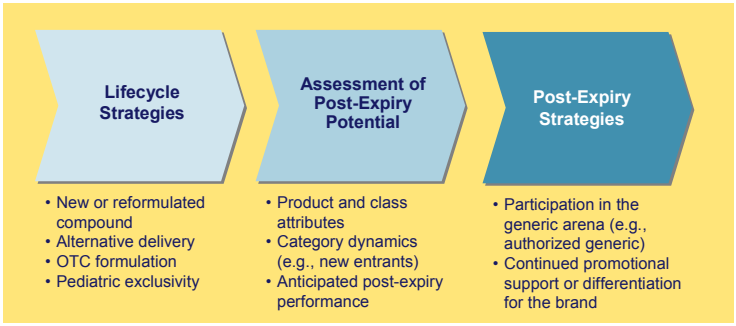
SUMMARY

More active, systematic management of brands facing loss of patent protection is essential for branded pharmaceutical companies today. As more high revenue brands, including biologics, lose exclusivity and as generic companies continue to grow in sophistication and strength, brand owners should look beyond traditional lifecycle management to ensure that post-expiry options are being fully evaluated.

Beyond Lifecycle Management – Optimizing Performance Following Patent Expiry

Figure 8 – Pharmaceutical Brand Management Beyond the Product Lifecycle

The first phase of patent expiry management is typically to deploy all reasonable lifecycle extension options as depicted in the first block of this diagram. As generic entry approaches, however, it is essential to understand the brand's post-expiry potential and to use that insight in evaluating the full range of post-expiry options available.



Understanding the intrinsic potential of a brand is, in our view, an essential complement to the pursuit of the familiar lifecycle options of follow-on or reformulated compounds. A systematic, attribute-based approach to simulating post-expiry performance, as highlighted in the middle block in Figure 8, allows more informed consideration of appropriate post-expiry options – both in terms of continued brand support and generic participation. This fuller picture is what we believe every brand manager should be addressing as the product's lifecycle advances toward expiry.

Note: The views expressed in the article are those of the authors and do not reflect positions of the firm or its affiliates.

Edward Tuttle and Andrew Parece are managing principals, and Anne Hector a vice president, of Analysis Group, an economics, financial, and strategy consulting firm.