



The BIG patent expiry question: Why sink when you can sail?

Riding the wave of medicine loss-of-exclusivity to gain improved returns

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Executive summary

As a biopharmaceutical product approaches the end of its patent life, executives believe that the product's demise is inevitable and will happen at great speed. They begin to worry about the rapid loss of revenue that will be brought about by the entry of generic alternatives into the market. They believe that there are only two outcomes possible for the product: die quickly or die slowly. This fatalistic outlook motivates the selection of a loss-of-exclusivity (LOE) strategy to achieve a slow demise rather than a quick one.

Starting with an optimistic outlook, particularly with a medicine that has generated multiple billions of dollars in revenue and changed many lives for the better, an aspirational LOE strategy can be developed to weather the storm of generic entry, as well as use the entry of generics into the market as an opportunity to generate more revenue and do more for patients. This article proposes a framework for devising an aspirational LOE strategy, the ingredients needed to create the strategy, and a case study of success.

1. Loss of exclusivity can inspire revenue growth

Loss of exclusivity for a medicine can have a big impact on revenues and profits. Small molecular drugs can lose almost 90 percent of their brand unit share one year after generic entry into the market¹ as generic versions of the drug become available at much lower prices. The entry of generic drugs into the market is therefore generally seen as a wholly negative event that will cause the irreversible and rapid loss of revenue and profit. This view usually drives the selection of a LOE strategy, with the express goal of slowing down the rate at which revenue diminishes post-LOE.

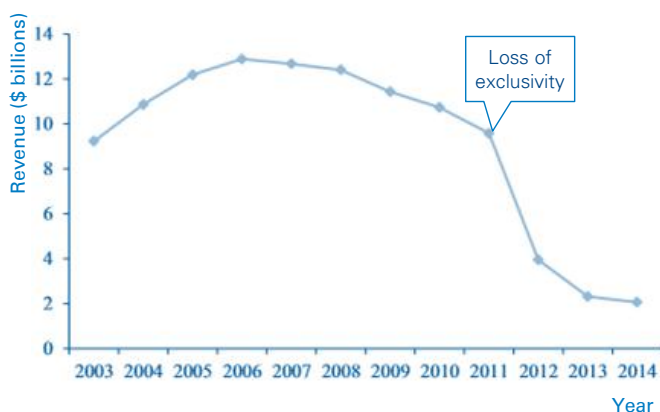
Because of the fatalistic mind-set and negative expectations around the loss of exclusivity of a medicine, the interventional strategy that is usually chosen to be executed cannot deliver sustained positive growth. Since success is considered to be achieved if revenue decline is slow, the strategy selected usually aims to sink the ship slowly.

Thriving rather than declining gently

Companies that are open to changing their perceptions of generic drug entry into the market and are willing to see the event as an opportunity to grow, can develop strategies to achieve growth from the loss of exclusivity of a medicine. In addition to taking advantage of the entry of generics into the market, such a strategy is more likely to be successful if it also enables progress in the therapy area and supports the core goals of external stakeholders. These stakeholders are the patients, prescribers, providers and payers who have become accustomed to enjoying the improved health outcomes provided by the medicine.

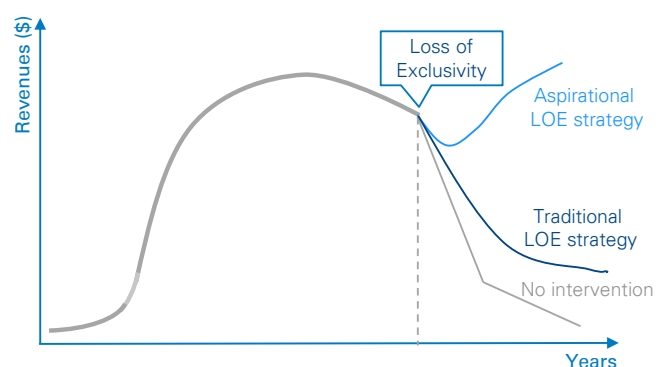
The ideal strategy to deliver growth from a LOE situation will require sufficient time (in advance of patent expiry), investment and a strong multi-disciplinary team to be developed, followed by excellent execution.

Figure 1: Pfizer’s Lipitor® global revenues from 2003 to 2014



Source: Pfizer annual reports

Figure 2: Arbitrary model of LOE strategy outcomes



Source: Arthur D. Little

1 Updated trends in US brand-name and generic drug competition. Grabowski et al 2016

2. Traditional LOE strategies are usually selected to enable gentle sinking

Traditional LOE strategic options

Over the years, proprietary companies have developed different (traditional) strategies to address the consequences of the loss of a medicine’s commercial exclusivity. According to a publication by Raasch², these traditional strategies can be divided into four types – prevention, innovation, extraction and adaptation.

Prevention strategies aim to delay or temporarily deter generic entry. Here measures such as pediatric patent extensions, which typically provide an extra six months of exclusivity³, are used to delay the inevitable. This is an approach that most companies use (sometimes in combination with other strategies) for their products facing loss of exclusivity.

Innovation strategies are deployed to avoid competition altogether by creating or developing something that can be protected by a patent. This involves developing a new indication or a line extension, patenting a new step in the manufacturing process, etc.

Extraction strategies involve extracting the most value from the product while it is protected by a patent. To maximize revenue, companies sometimes invest in aggressive promotion to increase sales as much as possible before exclusivity is lost. In

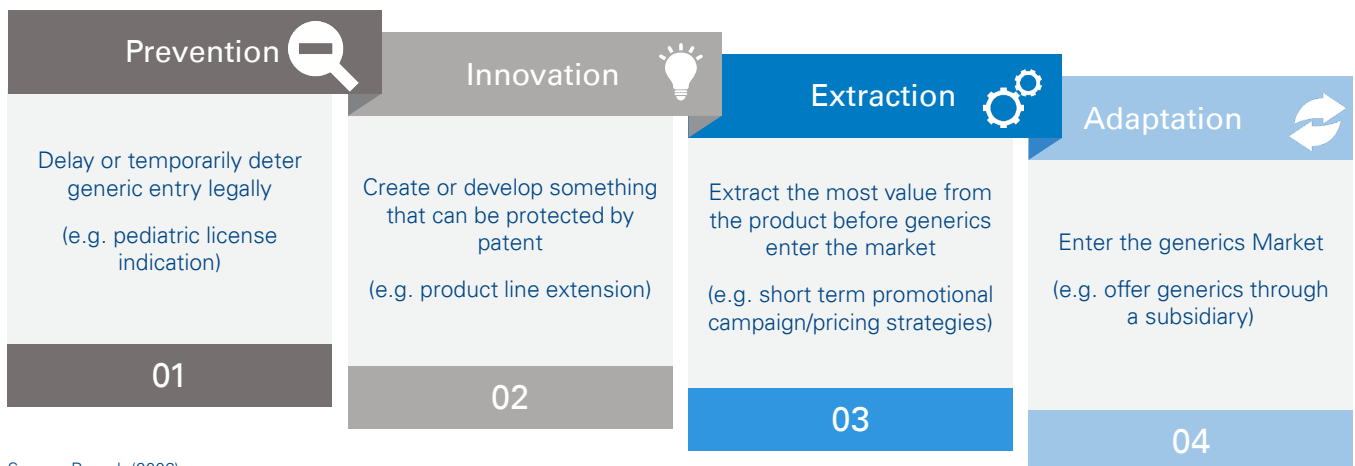
addition, prices can be increased for segments of the population that are not price-sensitive. To maximize profits, companies may choose to reduce promotion of the drug to the bare minimum (e.g., via digital channels) while sales are still strong and brand loyalty can carry the product along until the patent expires.

Adaptation strategies involve entry into the generics market either by producing a branded generic product with a view to targeting different segments with different products depending on their price sensitivity, or by creating a subsidiary that launches a generic version and capitalizes on first-mover advantage – i.e., launches ahead of other generic alternatives.

Objective: Decline slowly

There are some examples of successful implementation of traditional LOE strategies to achieve business objectives. However, because most companies look at the loss-of-exclusivity situation from a fatalistic perspective, their expectation of what success should look like is impaired, and therefore a slow decline in revenue becomes the main objective. Consequently, the traditional strategy selected can be defensive (sometimes passive), one-dimensional, inward looking and focused on short-term financial outcomes.

Figure 3: Traditional strategic options for LOE



Source: Raasch (2006)

2 Raasch C (2006). Der Patentauslauf von Pharmazeutika als Herausforderung beim Management des Produktlebenszyklus. DUV, Wiesbaden
 3 Better Medicines for Children. European Medicines Agency 2015

3. You can sail through to revenue growth with an aspirational LOE strategy

Aspirational LOE strategy

A more positive outlook is required to take advantage of a LOE situation to achieve growth. And if growth is the objective, then any old traditional strategy will not do. What is needed is an aspirational LOE strategy.

An aspirational strategy is progressive, multidimensional and addresses both internal and external drivers while focusing on short- and long-term business objectives. Furthermore, an aspirational strategy has to see the entry of a generic competitor at least partly as an opportunity, rather than as a wholly negative event. For a product that is generating annual revenues of at least \$1 billion, it is worth going beyond the approach of tentatively selecting a traditional LOE strategy that can deliver a slow decline. A major product should have a LOE strategy that can deliver growth. Aspirational LOE strategies are developed to deliver growth by adhering to the following principles and meeting the associated criteria:

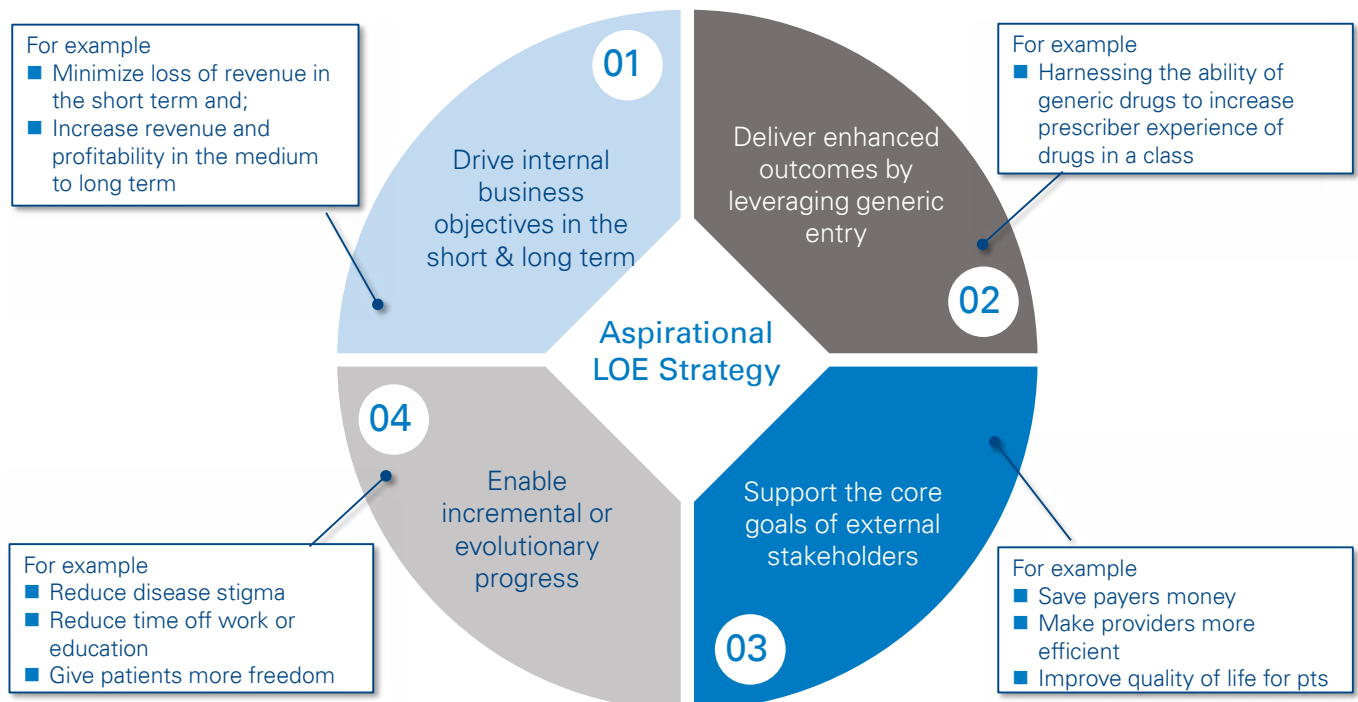
Don't take the money and run – drive ambitious short- and long-term business objectives

In most cases, traditional LOE strategies tend to be very focused on short-term financial gain or a managed decline of revenue. An aspirational strategy must achieve pressing short-term objectives (e.g., maintain revenue/profit, prepare the way for a product launch in the future) and then be able to deliver ambitious longer-term objectives as well. For example, a longer-term ambition (after an initial loss of revenue) could be to return to peak sales levels in 3-5 years.

Don't be scared of competition – achieve enhanced outcomes by leveraging generic entry into the market

Inherent in the thinking around an aspirational LOE strategy should be the expectation that generics will enter the market, and that their coming will, in some way, enhance the results of the aspirational strategy. For example, this could be that

Figure 4: Framework for designing an aspirational LOE strategy



Source: Arthur D. Little

the entry of generics will change prescribing behavior or patient numbers favorably, among other possible outcomes. An aspirational LOE strategy should be poised to capitalize on the anticipated change brought about by generic entry into the market.

Don't just look after number one – support the goals of external stakeholders




At the time a medicine is coming to the end of its patent life, if it has achieved or exceeded peak expectation in sales, there will be many patients on the medicine and many prescribers relying on it as part of their treatment offerings. An aspirational LOE strategy should go beyond safe-guarding the finances of the proprietary company and cater to the needs and goals of the broader stakeholders of the medication.

Don't be content with treatment-as-usual – be progressive

At the point of LOE, a successful medicine would have addressed one or more (mainly therapeutic) challenges, however, there will be other challenges (e.g., convenience and treatment efficiency challenges) that can be addressed with minor modifications to the original form of the medication. An aspirational LOE strategy must look to address some of the challenges that are within reasonable reach of the medicine facing loss of exclusivity.

An illustration of treatment progress could be made using a very effective pain medicine in tablet form, taken three times a day, with constipation and medication addiction as potential side effects and lactose as one of its excipients. This medicine could be transformed into a slow release capsule that is taken every 72 hours, is lactose-free hence suitable for people who are lactose-intolerant and has no risk of addiction or constipation as potential side effects.

Figure 5: Selection process for LOE strategies

Strategy selection process	Key differences in the process of LOE strategy selection	
	Traditional strategy	Aspirational strategy
 <p>Perception of generic entry into the market</p>	<ul style="list-style-type: none"> ■ Generic entry seen as wholly negative ■ Revenues and profits are expected to diminish rapidly 	<ul style="list-style-type: none"> ■ Generic entry seen as partly positive and a potential opportunity ■ Revenues and profits may be impacted negatively in the short term but can certainly benefit in the longer term
 <p>LOE commercial objective</p>	<ul style="list-style-type: none"> ■ Slow down the decline of revenue and profit from the product 	<ul style="list-style-type: none"> ■ Grow revenue and profit from the product
 <p>Strategy to achieve LOE objective</p>	<ul style="list-style-type: none"> ■ Traditional strategy <ul style="list-style-type: none"> – Prevention – Innovation – Extraction – Adaptation 	<ul style="list-style-type: none"> ■ Aspirational strategy <ul style="list-style-type: none"> – Bespoke to the product and therapy area – Designed using the aspirational strategy framework

Source: Arthur D. Little

4. Case study: Execution of an aspirational LOE strategy

Risperidone (Risperdal®) was the biggest single contributing asset in the Johnson & Johnson (Janssen) pharmaceutical portfolio in 2007, generating \$3.4 billion⁴ in sales that year. Risperidone is used in the treatment of schizophrenia as well as other mental health illnesses. Before risperidone's patent expired in 2008, an aspirational LOE strategy was implemented to mitigate the consequences of medicine patent expiration. Core to that strategy was the use of advanced technologies to enhance the benefits that a risperidone-based product could deliver, and to address more challenges than Risperdal in its tablet form could address. The products developed after Risperdal were Risperdal Consta®, Invega®, Xeplion®/Invega Sustenna® and Trevicta®/Invega Trinza®. Consta, Xeplion and Trevicta are based on cutting-edge technology used to develop intra-muscular formulations which have delivered significant progressive leaps in the management of schizophrenia.

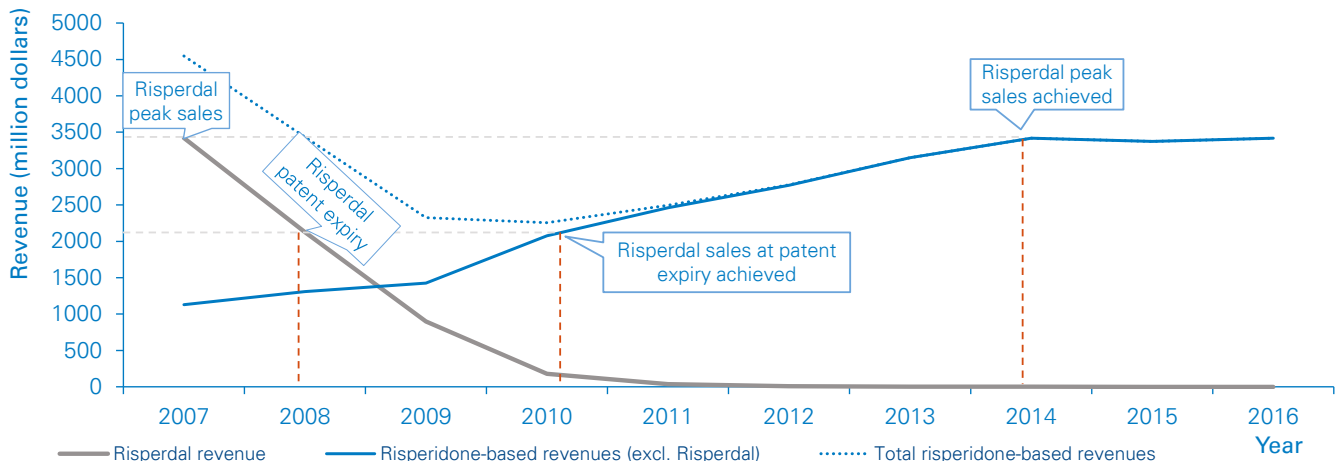
Risperdal Consta® is a twice-weekly injectable of risperidone which builds on the strength of risperidone as an effective medicine. It reduced the frequency of administration to address poor adherence (which is a major cause of relapse in schizophrenia), and sought to tackle the stigma of schizophrenia by providing injections into the arm rather than the buttocks, among other benefits. A patient needs to have received risperidone tablets before they can be transferred to Risperdal

Consta. Therefore, when generics came into the market, the total pool of patients receiving risperidone tablets (both branded and generic), as well as psychiatrists' experience, could only increase and boost the uptake of Risperdal Consta.

To build further on Risperdal Consta, Xeplion®, a once-monthly injectable medication was developed from the active metabolite of risperidone (called paliperidone). Xeplion went further to address non-adherence, reduce bed days in hospital, and support patient recovery and return to work/education (due to increased flexibility of administration to fit around a patient's life). A patient is eligible for treatment with Xeplion if they have shown a response to risperidone or paliperidone any time in the past. This means that as generic risperidone or paliperidone is used increasingly, the pool of patients to be moved to Xeplion can only grow in numbers.

In line with the aspirational strategy, Trevicta®/Invega Trinza® was launched after Xeplion. Trevicta is a paliperidone-based drug that is administered four times a year (once every quarter) and brings with it a number of benefits over Xeplion. From a generic-entry perspective, a patient needs to have received a number of administrations of Xeplion to qualify for Trevicta. It means that a generic version of Xeplion will help to develop the pool of patients that qualify for treatment with Trevicta.

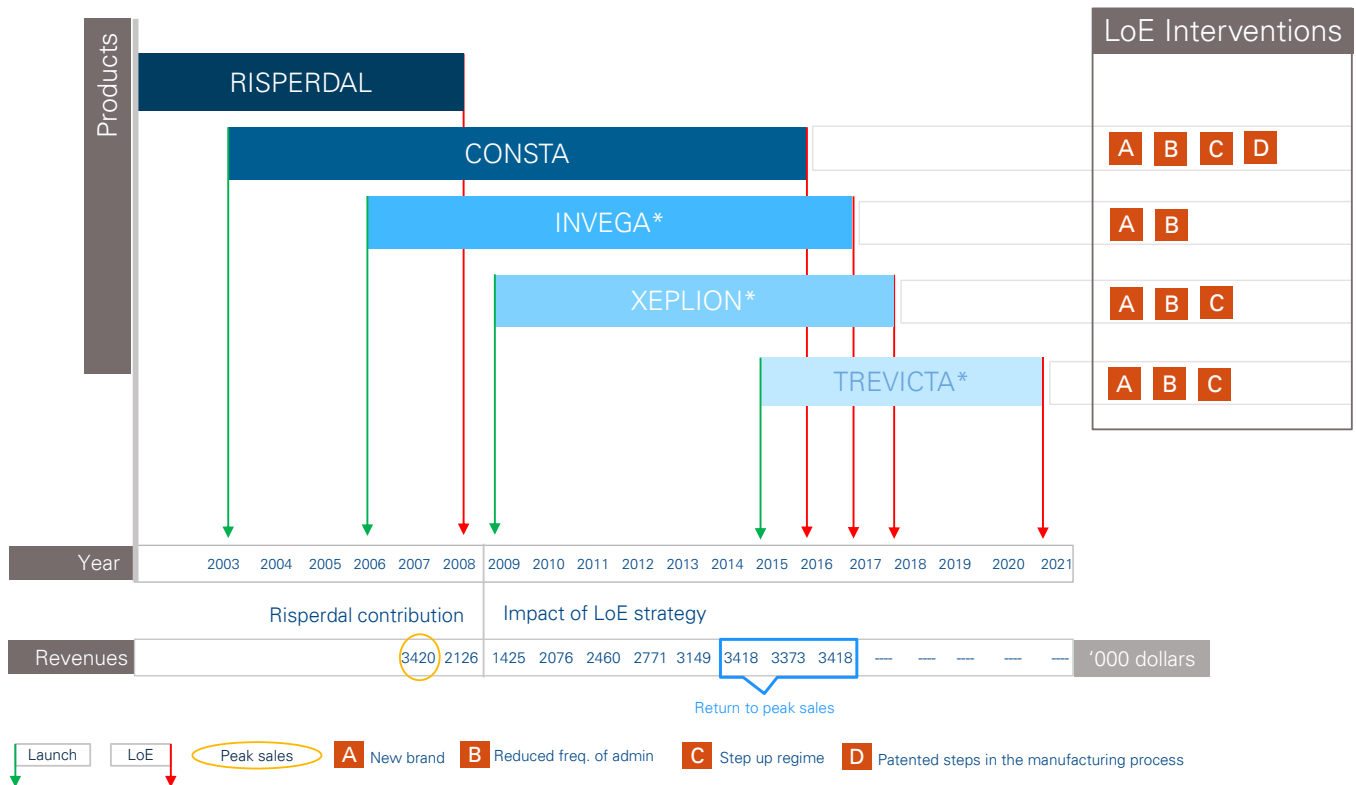
Figure 6: Effect of Risperdal LOE strategy on 'risperidone' revenues



Source: Arthur D. Little analysis, J&J annual report

1 J&J 2009 annual report

Figure 7: Implementation of the aspirational LOE strategy for risperidone



*Based on paliperidone which is an active metabolite of risperidone
 Source: Arthur D. Little analysis, J&J annual report

Figure 8: Risperidone LOE strategy meets the aspirational LOE strategy criteria

Aspirational strategy criteria	Outcomes of the risperidone LOE strategy
Drive internal business objectives in the short and long term	<ul style="list-style-type: none"> Loss of revenue from risperidone was minimized in the short term Revenue was returned to pre-LOE levels within 2 years Revenue was returned to peak sales levels within 6 years
Deliver enhanced outcomes by leveraging generic entry	<ul style="list-style-type: none"> Patients need to have some exposure and response to the risperidone/paliperidone molecule before receiving Risperdal Consta or Xeplion therefore generic entry for risperidone supports an increase in the pool of patients for the long-acting medicines
Support the core goals of external stakeholders	
<ul style="list-style-type: none"> Patients 	<ul style="list-style-type: none"> Patients with schizophrenia want to achieve recovery and be free from the burden of medicines. The launch of the long-acting medicines ensures that non-adherence does not jeopardize patients' recovery and medication burden is significantly minimized
<ul style="list-style-type: none"> Providers (Hospitals and HCPs) 	<ul style="list-style-type: none"> HCPs want patients to get the best from existing treatments therefore the launch of risperidone/paliperidone-based long-acting medicines ensures that patients can continue to receive trusted medicines with HCP interactions at reasonable intervals Hospitals want to be efficient with scarce resource and hospital beds are a very scarce and expensive resource. Xeplion ensures that a patient can be discharged early from hospital without compromising their treatment. Xeplion also reduces the rate of re-hospitalization
<ul style="list-style-type: none"> Payers 	<ul style="list-style-type: none"> Payers want patients to be treated and recover fully with no relapses. Non-adherence is one of the biggest causes of relapse in schizophrenia. The risperidone/paliperidone-based long-acting treatments help to prevent non-adherence and relapse
Enable incremental or evolutionary progress	<ul style="list-style-type: none"> The LOE strategy for risperidone helps to address non-adherence by reducing frequency of administration gradually from 365 administrations to 4 administrations per year. The strategy also progressively changed medication administration to the point where a +/-14 day window is now available to take medication. This fits the medication around the patient and supports holidays, return to education and return to work The strategy helped to reduce the stigma of schizophrenia by providing injections that can be given in the arm rather than in the buttocks. This is really helpful especially with patients that have paranoia as one of their schizophrenia symptoms.

Source: Arthur D. Little analysis

5. Time, money and talent are needed to build an aspirational LOE strategy

In most cases, no growth is expected from a medicine facing loss of exclusivity so no meaningful investment is made in the product. Most companies leave the LOE discussions until late into the product life cycle and many consider LOE to be an issue for the Established Brands or Marketing function. To achieve growth, an aspirational strategy needs to be developed with 3 key ingredients – sufficient time, financial investment and a strong multi-disciplinary team.

Start early

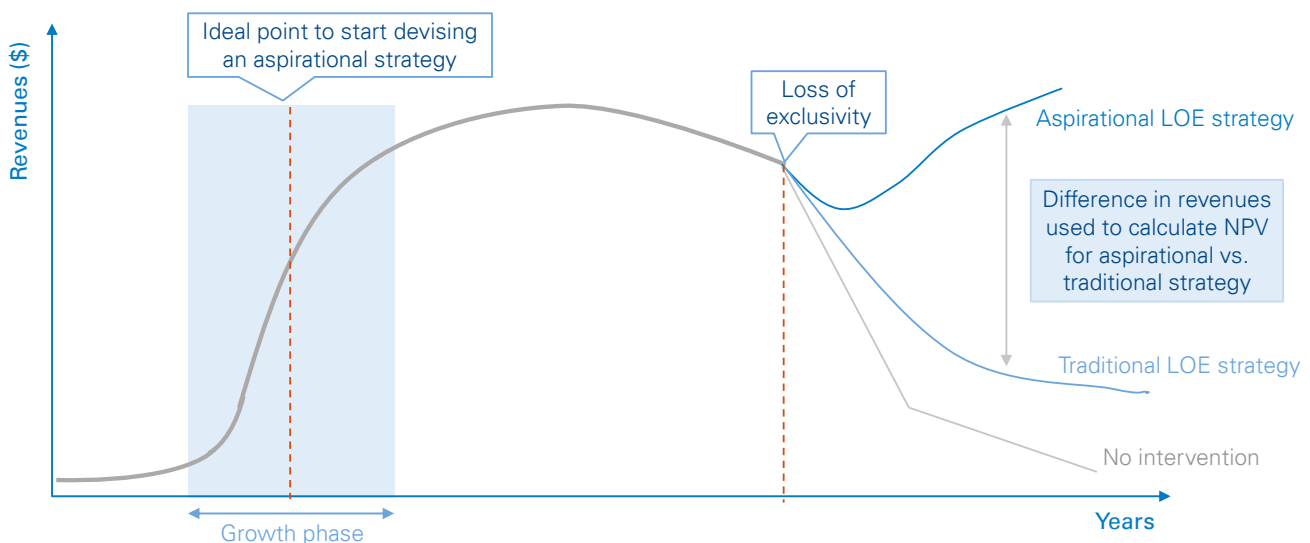
Many companies undermine the commercial performance of their medicine by making LOE plans with 1-2 years to LOE. It is imperative to start developing the LOE strategy of a medicine as early as possible. Ideally, the process should begin in the middle of the growth phase of the product life cycle. The middle of the growth phase (usually around three to four years after launch) is a reasonable point to be able to assess the potential of the medication and forecast its financial trajectory with some degree of confidence. The assessment and forecast will help to develop a business case for maximizing the value of the medicine. An early start provides time to allow for all possible

alternatives to be considered and tested before the final strategy is agreed upon. Failure to start early enough in the product lifecycle will mean that certain options could be unworkable due to the time it could take to do things such as to develop/test a new technology.

Secure investment

Companies have finite resources, so financial investments tend to be prioritized for good opportunities supported by compelling business cases. For a medicine delivering \$1 billion or more annually, the tendency can be to see it as a cash generator for other projects. The business case for an aspirational LOE strategy, therefore, has to show that the company will stand to improve shareholder returns by reinvesting some of the generated income back into the same medicine. Also, the business case has to show how reinvesting in the medicine will bring returns that exceed the hurdle rate of the company and deliver a positive Net Present Value (NPV) that is higher than what may be expected from pursuing a traditional strategy. From a risk perspective, the fact that the company already has a great reputation with prescribers and patients in a therapy area,

Figure 9: Preparing an aspirational LOE strategy



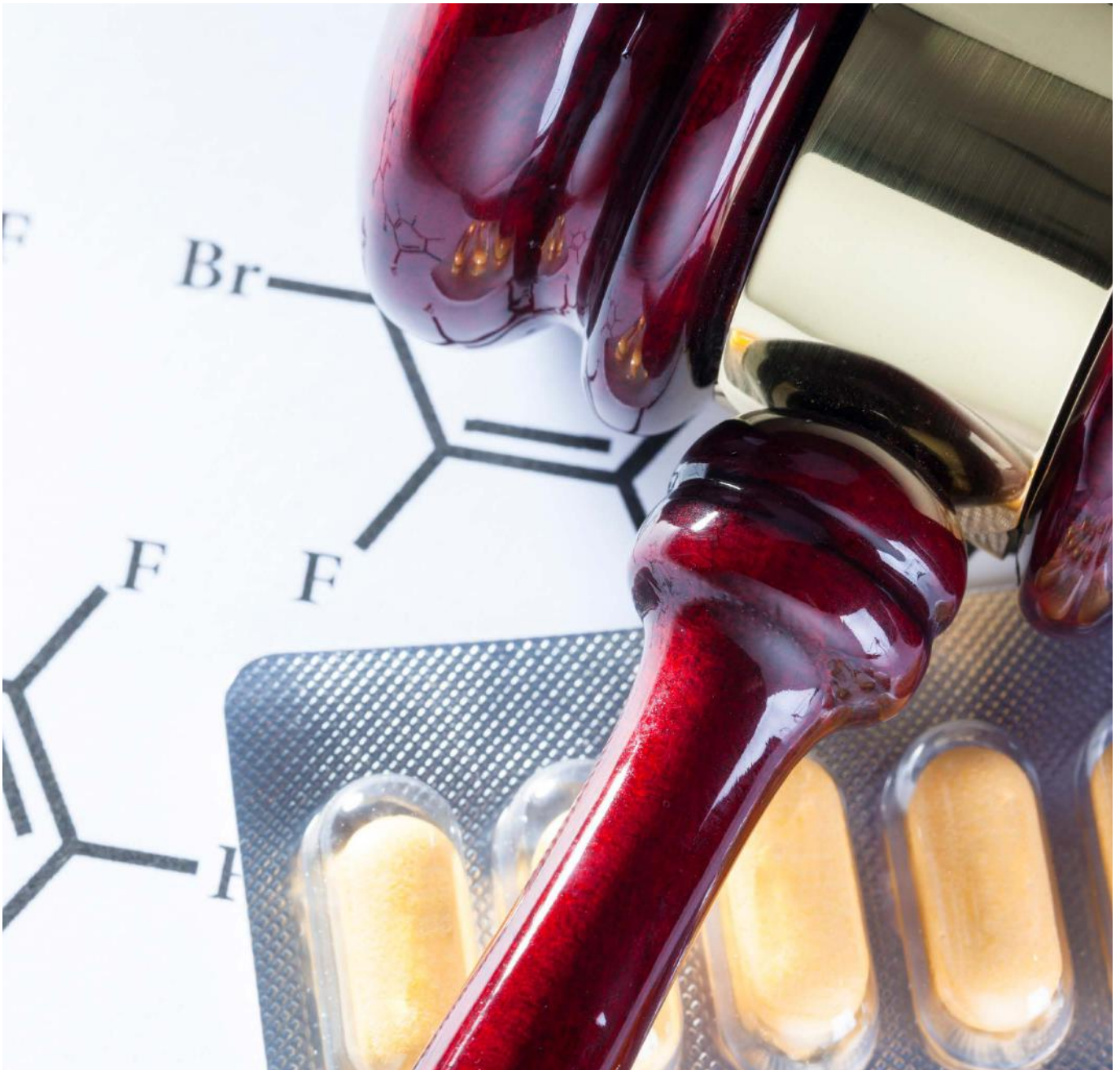
Source: Arthur D. Little analysis

plus the fact that the molecule is well known and trusted, gives some advantage to the business case for an aspirational LOE strategy around a successful medicine.

Build a winning team

A strong multi-disciplinary team is needed to devote its collective energies to creating an aspirational LOE strategy. As the core medicine is already in the market and the post-LOE version may require enhancements, it is important to have input from the full spectrum of disciplines spanning R&D, supply chain and market access/commercialization, rather than just from

the marketing or established brands function. This will ensure that the medicine is looked at from all angles to see how more value can be gained. Restricting the LOE discussions to the commercial end of the value chain will significantly limit the range of LOE options that could potentially be generated for the medicine. The strategy development can be greatly assisted by internal and/or external LOE experts who can help the team with frameworks and ideas to harvest and synthesize their collective intellectual output, as well as bring insight from the wider biopharmaceutical LOE ecosystem.



6. Why sink when you can sail?

In managing the loss of exclusivity of a successful medicine, a change of mind-set (from fatalism to optimism) will lead to a change of objectives (from managed revenue decline to revenue growth), and this will influence the strategy that is required to achieve the objective (an aspirational LOE strategy rather than a traditional strategy). Traditional LOE strategies have their place in trying to mitigate the adverse financial outcomes that follow the expiry of a medicine's patent. These strategies may be relevant in cases in which the uptake of a medicine is respectable but not outstanding, or the science in the therapy area is expected to advance considerably in the years after product launch. However, if a medicine is unique, delivering rapid revenue growth and expected to remain a compelling treatment option for prescribers and patients, that medication would benefit from an aspirational LOE strategy.

Seize the opportunity

With an early start, the right financial investment and a strong multi-disciplinary team, biopharmaceutical companies can create aspirational LOE strategies for great medicines. These medicines can continue to build on the success they gained during the period of commercial exclusivity. Rather than manage a decline in revenues, biopharmaceutical companies can capitalize on the entry of generics into the market to achieve revenue growth, while bringing progress to the therapy area and meeting the needs of all stakeholders.

So if you have a medicine that is generating (or has the potential to generate) over \$1 billion annually, you can begin to prepare to sail rather than sink. You should seize the opportunity and begin to prepare an aspirational LOE strategy.

Notes



Notes



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