

## Finding Value in Europe

**Despite growing regulation and shrinking budgets, Europe remains a critical market for branded pharmaceutical companies. L.E.K. Consulting offers three strategies to maximize value capture in increasingly access-challenged markets.**

Taking stock of the global marketplace, pharmaceutical executives face mounting challenges in many core economies. With public debt ratios at all-time highs, many developed countries have instituted austerity measures or significant budget cuts, resulting in growing pricing pressures and restricted market access for pharmaceutical products.

Among developed markets, nowhere is the trend more acute than Europe. The United Kingdom and Germany—two of the top-three European economies—have put an end to free pricing for innovative drugs. Additionally, most countries in the EU are raising the bar on what constitutes an improvement to the standard of care (i.e. product innovations that merit price premiums) and restricting market access through health technology assessments (HTAs), tenders, and other mechanisms. Given these significant headwinds, some question whether the value of commercialization across the traditional European markets is diminishing.

As European economies struggle with shrinking drug markets, the BRIC economies continue to experience outsized sales growth. In aggregate, the BRIC nations are expected to grow 15% per year from 2011 to 2016 in total pharmaceutical sales, while the U.S. will grow just 2.6% and the EU5 (i.e. France,

Germany, Italy, Spain, United Kingdom) will shrink 1.2% over the same period (see Figure 1).

If the European market is so challenging, why not seek value in BRIC countries and other emerging markets? The double-digit growth rates, growing middle classes, and expanded health coverage offer an alluring alternative to traditional markets. However, a closer look at the data suggests that while pursuing high-growth economies is important for future expansion, maintaining a strong presence in Europe is still critical for innovative, branded drug manufacturers.

For *total* pharma spending, the EU5 is expected to decline from 17.6% to 12.7% of the global market between 2011 and 2016, while the BRIC countries are expected to grow from 13.2% to 21.3% of the market during this same period. This shift in market share from developed to emerging, however, is misleading. For *branded* pharma spend, the EU5 will decline from 20.3% to 16.9%, while the BRIC countries are expected to grow slightly from 4.4% to approximately 6.9%. In other words, for higher-margin branded pharmaceuticals, Europe will continue to represent almost 17% of the global market, while the BRIC countries are expected to contribute only around 7% through 2016 (see Figure 2).

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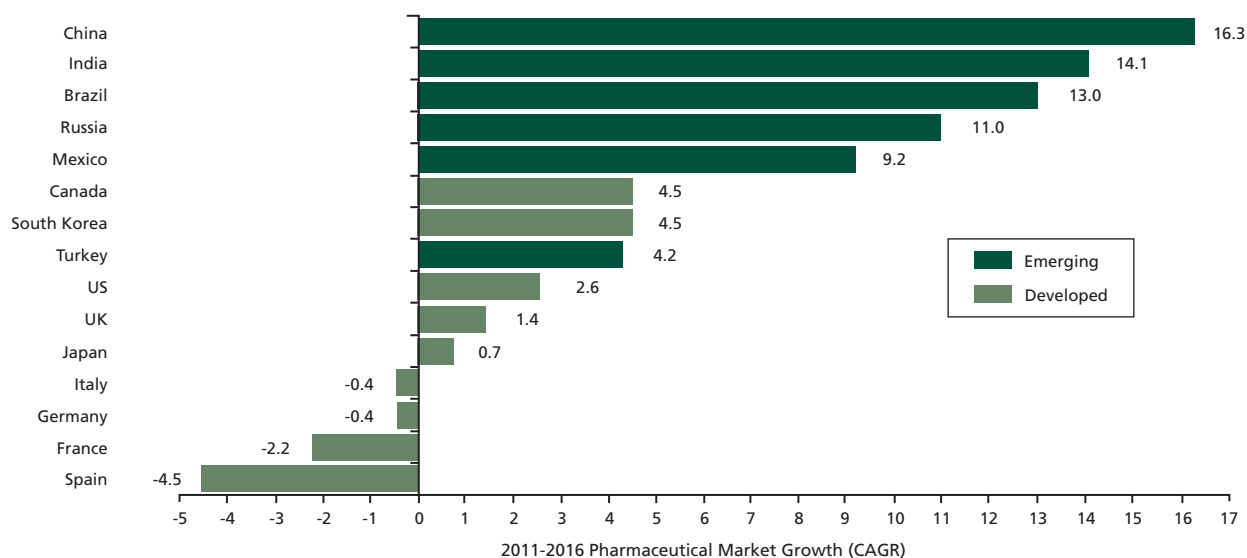
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Figure 1

## Annual pharmaceutical market growth rate (CAGR), 2011 – 2016

The BRIC nations lead the globe in pharma market growth (CAGR), while European economies act as a downdraft on growth.



Source: IMS, BMI, L.E.K. analyses

Additionally, several factors are further concentrating potential value within traditional European markets:

- 1) Per capita, branded pharmaceutical spend in the EU5 is expected to remain far above the BRIC countries for the next decade. The most innovative drugs, particularly biologics, are skewed even further toward developed countries, as emerging markets prioritize highly prevalent and public health-focused diseases (see Figure 2).
- 2) Growth in emerging markets is heavily driven by volume increases due to more widespread and better coverage. While the markets are large, pricing and margins in emerging economies can be as challenged (and often more so) than Europe under austerity.
- 3) Emerging countries offer their own set of challenges for market access, from higher regulatory and government influence on health priorities, to preferential access for domestic manufacturers.
- 4) The populations in the BRIC countries are highly distributed, often making physical access and commercial promotion challenging and expensive.

The opportunity in emerging markets should not be overlooked, yet it cannot replace the profit potential for innovative, branded drugs in the EU5. Emerging market strategies should augment, not replace, a European strategy (see Figure 3).

## The Pharma Growth Agenda: Optimizing Market Entry Opportunities in Europe

To take advantage of favorable opportunities in Europe, manufacturers must revise their commercialization and development strategies—maintaining the current focus on efficacy and approval, but also paying close attention to market access and pricing dynamics.

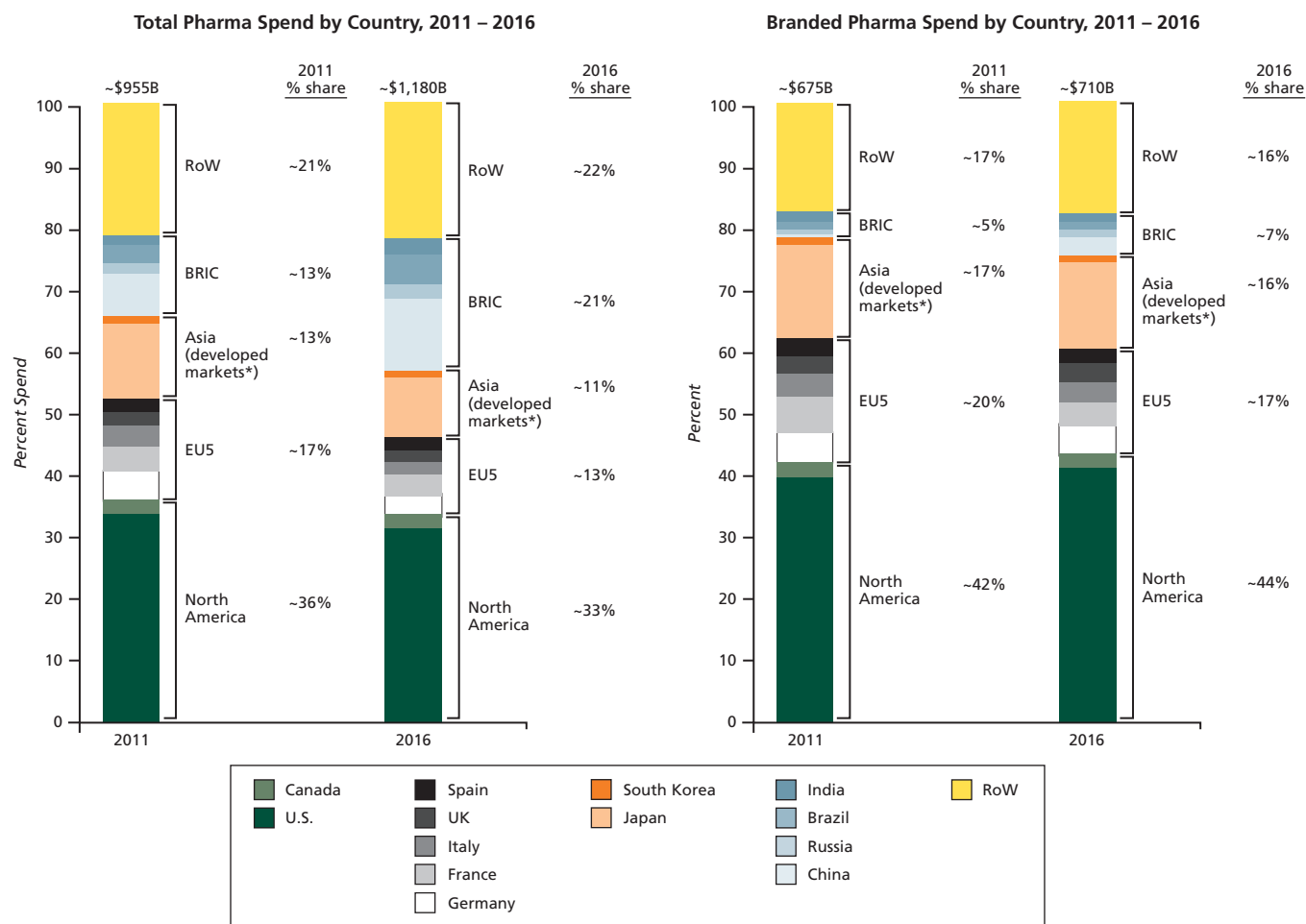
In our work with biotech and pharmaceutical companies around the globe, L.E.K. Consulting has observed three key strategies that top-competing players use to maximize their franchise value in Europe.

### 1. Rigorous Product Selection

Beginning in early clinical development, manufacturers face ongoing decisions over which programs to advance and which to cut. Traditionally, as programs in the lab advanced toward early clinical development, manufacturers have relied on scientific rationale (e.g., mechanistic potential, toxicity,

Figure 2

While BRIC countries are expected to experience strong growth in *total* pharma spend, forecasts show they will only contribute ~7% of *branded* pharma sales by 2016. Further, despite shrinking market share, Europe is expected to continue to be a major revenue center for *branded* pharmaceutical companies.



PK/PD, and selectivity endpoints) to guide development decisions. However, as market access requirements continue to become more rigorous, scientific metrics alone are no longer sufficient to justify program advancement.

To correct the problem, many biopharma manufacturers have reset product/program review criteria to incorporate a broader set of evaluation metrics—metrics that force them to build a stronger case for both scientific potential as well as commercial viability earlier in a product's development.

This initial commercial case should include:

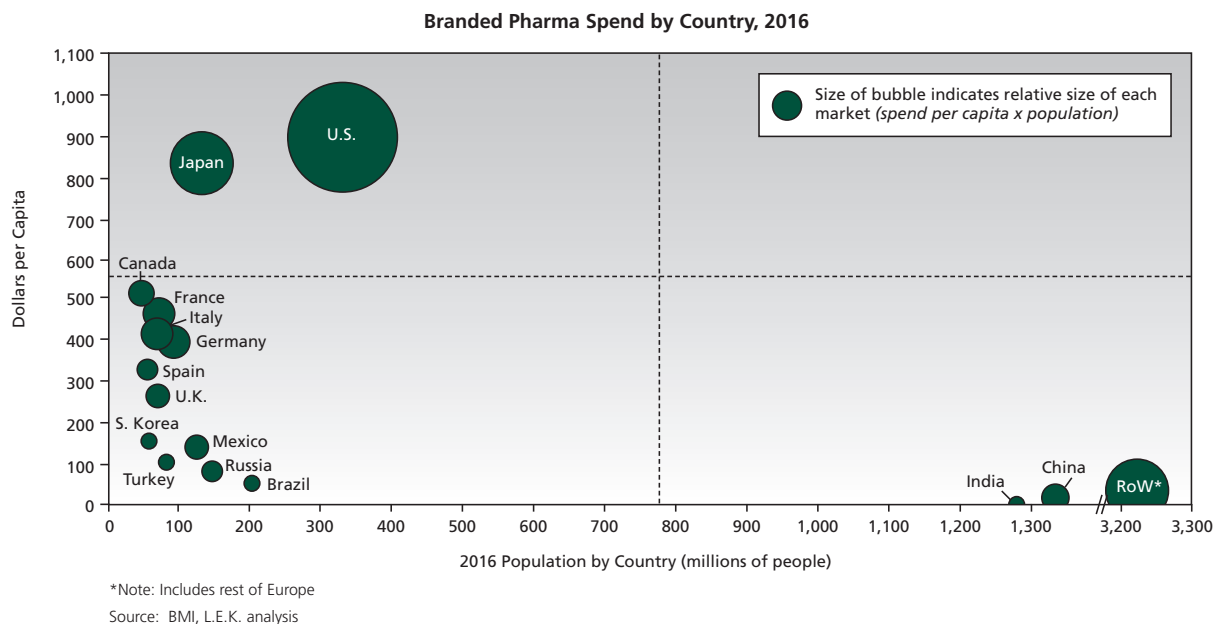
- An initial hypothesis about product positioning within each targeted market (e.g., a first-line therapy versus

a more advanced line of therapy targeted to a specific patient population).

- The opportunity for *meaningful* differentiation over the current standard of care and other products in development (e.g., novel MoA, better efficacy, improved safety/tolerability profile, or new RoA).
- The role the molecule may potentially play in the manufacturer's overall commercial plan (e.g., can it be folded into a core therapeutic franchise or is it external to current commercial competencies).

**Figure 3**

Pharma spend in countries such as China and India are driven by broadening access to basic medicines aimed at addressing public health needs, demonstrated by high spend overall but low per-capita spend. The EU5, on the other hand, continues to have relatively high spending per-capita (behind the US, Japan and Canada), and are expected to remain strong drivers of branded pharma sales through 2016.



While these criteria themselves are not novel, it has become increasingly critical to incorporate commercial criteria early. As programs advance through clinical development, both the scientific and commercial rationale for advancement must be reviewed continually, with increasingly rigorous hurdles for advancement. Failing a positive result, the commercial development teams need to stand ready either to cut the program at the earliest possible stage of development, or accept a lower return if the product is carried through to launch.

By changing the product development gating criteria to include a high standard for what constitutes a valid commercial case earlier in the process, taking a consistent and rigorous approach to product review, and being willing to cut under-performing programs manufacturers can make more effective go/no-go decisions at much earlier stages of development. This scenario optimizes resource allocation, and begins the critical process of building the commercial case.

#### KEY STRATEGY SUMMARY: Rigorous Product Selection

- Accelerate the incorporation of commercial considerations in program evaluation metrics earlier in the development cycle
- Raise the bar for what constitutes a valid commercial case that justifies program advancement
- Be consistent in your product review approach, and failing a positive result, cut the program(s) at the earliest possible time

#### 2. Commercially Relevant Evidence

Commercial viability is no longer a matter of regulatory approval. Patient-relevant outcomes, health economic analyses, and highly engaged discussions on relevant metrics and comparators of care are now the gold standard for attaining market

access. Regulatory approval and commercial market access are increasingly parallel rather than serial processes.

The threshold of “patient-relevant outcomes compared to standard of care” can be seen in several decisions from NICE in the UK. Sanofi’s Multaq (for atrial fibrillation) was initially rejected as too expensive with no incremental benefit, and was not approved until a safety benefit compared to the second-line therapy was demonstrated. Similarly, NICE recommended against Merck’s Daxas (for COPD) and has asked for more evidence of reduction in COPD exacerbation as an add-on to current therapy. Lastly, NICE rejected Novartis’s Gilenya (for MS) initially because the data submitted was compared against a placebo and Avonex, not Tysabri, its likely primary competitor.

For those products with moderate improvements in benefit, health economics are increasingly the gating factor for access. NICE rejected Janssen’s Zytiga for castration-resistant prostate cancer, reversing its decision only after more aggressive discounting. Similarly, Novartis’ Xolair was initially recommended for use in the UK, until changes to the dosing schedule and new mortality data reduced its cost-effectiveness and caused NICE to pull its recommendation. Then, following further data analysis and a revised patient access scheme—which included additional price discounting allowances—from Novartis, NICE reversed themselves again, and reinstated their recommendation for the use of Xolair in the treatment of severe, persistent confirmed allergic IgE-mediated asthma. The environment has shifted the burden-of-proof for access and price premiums to the manufacturers, which need robust health economic evidence to support their ongoing market access.

Beyond high clinical thresholds and health economics data, we further recommend early and detailed conversations with market access authorities. Germany’s IQWiG has rejected multiple drugs for not using the G-BA defined “appropriate comparator.” GSK’s Benlysta for SLE, Biogen Idec’s Fampyra for MS, and Boehringer Ingelheim’s Trajenta for type 2 diabetes were all negatively recommended because they deviated from the preferred comparator. While some of these rejections were the result of the dynamics of implementing a new system in Germany, these cases highlight the expanding role of access authorities in Europe (and around the world).

The new set of market access hurdles—critical for positioning new products for optimal market access and pricing—will require manufacturers to involve their commercial and regulatory teams much earlier in the development process than has historically been the case. Understanding commercial positioning, patient-relevant benefits and health economics as a product progresses through development is a new imperative; clinical trials must be designed to target the relevant endpoints and patient segments necessary to address regulator and payer needs.

#### KEY STRATEGY SUMMARY:

##### Commercially Relevant Evidence

- Engage regulatory and payer bodies to define relevant clinical endpoints and appropriate comparators earlier in the development process
- Design clinical efforts to capture appropriate patient-relevant outcomes and health economic data which support product differentiation
- Communicate a product’s value proposition to key regulatory and payer stakeholders continuously through its development

### 3. Continuous Differentiation

Finally, to maintain a competitive position post-launch, manufacturers will need to redouble their efforts to differentiate through evidence. Following approval and initial price setting, manufacturers must continue to conduct clinical, economic, and post-hoc meta-analysis studies to demonstrate long-term safety and efficacy, as well as strengthen core economic arguments. This data must be communicated through a variety of touch points—including the national market access and pricing organizations—and timed to coincide with recurring pricing reviews dictated by national reimbursement bodies.

For example, German regulators now offer newly launched products one year of free pricing prior to their initial HTA review

and formal price setting. Building a value dossier that supports continued premium pricing and communicating it to key stakeholders within the first year is critical to maintain a strong market position in Germany. France offers compassionate use access to markets, but expects all drugs to be reviewed for benefit and economic impact after five years. While it does so less frequently, the UK also revisits market access as data emerges (e.g., Xolair). This periodic post-marketing review will force manufacturers to invest in continued clinical and economic evidence development.

Lipitor—the largest drug by total sales over the last ten years—offers a good case study of evidence-based market positioning. In its heyday, Lipitor was the best-selling drug in the world, a position Pfizer did not take for granted. The sheer volume of post-launch studies the company sponsored and conducted dwarfed those of their main competitors. Pfizer's strategy of differentiating through evidence created an insurmountable market position for their drug, allowing it to maintain preferred status in the face of intense branded and generic competition.

#### KEY STRATEGY SUMMARY: Continuous Differentiation

- Maintain market position by strengthening and communicating ongoing long-term safety, efficacy, and health economics data
- Evolve the commercial and communication model to engage payers and involve medical education more robustly

Some speculate Pfizer is repeating this strategy with the imminent launch of Xeljanz for rheumatoid arthritis. Early reports show Pfizer's initial approval submission dossier is one of the most extensive ever submitted, and further studies are already in the works for RA, as well as other indications.

Judging by Pfizer's efforts to build a clear and forceful case for preferred access and premium pricing, Xeljanz may be Pfizer's 'second act,' their next big blockbuster drug.

Roche similarly employed ongoing evidence development efforts to support its case that Lucentis was safer and more efficacious for wet AMD than Avastin. While the body of evidence is mixed, Roche invested in data generation and is adopting a similar approach to defending its biologics franchises (Avastin, Rituxan, Herceptin, Lucentis *et al.*) against biosimilars.

### Conclusion

With emerging markets not yet able to replace the value generated by Europe, the first question for most innovative drugs should be, "How do we succeed in Europe?" rather than "Should we play the game in Europe?" To maximize your chances of success in the Europe of austerity, we recommend the following:

**1) Rigorous product selection:** Accelerate the incorporation of commercial requirements in the development process. Raise the bar on commercial gating factors. Eliminate programs that do not meet commercial requirements without delay.

**2) Commercially relevant evidence:** Engage payer authorities early with scientific, patient-relevant outcomes, and economic evidence. Control the conversation on metrics and comparators.

**3) Continuous differentiation:** Resting on the laurels of past evidence is increasingly risky. For market access, positioning against competitors and defense against biosimilars, ongoing evidence generation will become the norm. These developments also necessitate an evolving emphasis in commercial efforts, with payer engagement and medical education increasingly critical.

The rules are changing and value capture is becoming increasingly difficult everywhere. However, adapting to the evolving commercial requirements and succeeding in Europe still offers a critical geographic component not easy to replace elsewhere.



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