New Ecosystems In Pharma: Maturing Markets Mean New Models Are Needed

To succeed in today’s pharma market, companies need to integrate three considerations: where there’s unmet need, where innovation is likely to gain acceptance, and what payors need. Oliver Wyman’s ecosystems framework provides a differentiated view of opportunity and value that can help companies adapt and shape their strategies.

Pharma companies are under pressure. What were favorable tailwinds a decade ago – abundant innovation, relative pricing freedom, benign public and regulatory attitudes – have turned into headwinds. Safe, effective generic therapies are available for many diseases, raising the bar on innovation. Payors are pushing back, restricting the use of expensive new therapies if they don’t show economic benefit. Regulators, stung by widely publicized product failures, are increasingly cautious. At the same time, the science of drug development is getting harder as the industry targets diseases like Alzheimer’s or diabetes, where the biology is less understood and treatment pathways are more nuanced. While the industry remains highly profitable, growth has stagnated. What was once an advantaged economic formula is no longer sustainable.

Although the challenges are self-evident, pressure for change is uneven. Despite slowing growth and weaker pipelines, most of the industry’s largest companies remain enormously profitable. The churn of patent cliffs and new drug launches means that stagnation in one franchise co-exists with explosive growth in another. In addition, the serendipity of science is a continual challenge to focus, as new molecules show promise in unplanned areas. “Whole enterprise” solutions won’t work, and pharma execs can’t abandon the profitable core for risky experiments. No one has laid out a clear path for transforming the enterprise – where to initiate change and what direction it must take.

Pharma companies are not standing still. Many have established smaller, narrowly focused research units, responsible for innovation in a highly targeted area, or independent franchises with broad business responsibility and entrepreneurial leaders. (See “AstraZeneca Rebuilds R&D Amid Growing Near-Term Pressures” — IN VIVO, June 2011.) And companies increasingly rely on external collaborators as a critical component of the innovation engine. Yet even as they innovate, they continue to think of drugs in traditional categories – by body geography (respiratory, cardiovascular), technology platform (small versus large molecule), business model (Big Pharma versus specialty versus biotech), or customer segment (primary care versus specialist).

The problem is that these segmentation schemas miss important differences in how opportunity has changed across diverse pharma markets. They shed little light on where opportunity is to be found or what it takes to win. To say that you are “in oncology” is no longer a defining statement. And though it may be biologically meaningful to lump depression, schizophrenia, Parkinson’s, and Alzheimer’s disease under...
a “neurosciences” label, it ignores fundamental differences in how those conditions are treated – and provides almost no help in building a successful business. What’s needed is a multidimensional approach that identifies patterns of difference beyond traditional segmentation. In developing strategy and a business model, it is crucial to understand disease-specific context: What is the therapeutic headroom, given generic or non-drug alternatives? How rich is the technology pipeline? What is the economic burden of treating the disease, and how is it distributed across drug therapy, in- and out-patient care, and broader morbidity and mortality? Who is the primary decision maker about drug therapy, and what matters most to them?

**A NEW WAY TO DEFINE AND DIFFERENTIATE OPPORTUNITY**

In this article we describe Oliver Wyman’s “ecosystems” framework, which offers a novel segmentation of drug markets and yields new insight into how opportunity in pharma is changing. To develop this segmentation, we posed three fundamental questions about the nature of opportunity in different drug markets:

- Where is there remaining medical need?
- Where are drugs continuing to gain traction with new innovation?
- Where is there opportunity for a strong value proposition to payors?

Specifically, we examined 125 diseases that account for 79% of overall health care spending in the US, and pharmaceutical segments that account for 94% of drug sales globally. To characterize unmet medical need, we assessed overall disease prevalence, the complexity of the treatment paradigm in each disease, and criticality as measured by morbidity and mortality. To address innovation traction, we assessed therapeutic headroom in efficacy, safety, and ease of administration; the density of the R&D pipeline; and the power of branding. And to address the value proposition, we analyzed overall medical spend in each disease, the cost of treating individual patients, total spend on drugs specifically, and the ratio of drug spend to overall medical spend. (See Exhibit 1.)

We used these measures to cluster different diseases into “ecosystems” that share common characteristics with respect to unmet need, innovation traction, and potential value proposition to payors. As traditionally defined, ecosystems are complex systems of interconnected elements that interact both cooperatively and competitively. The ecosystem framework accounts for the primary concerns of the key health care stakeholders – patients, payors, providers, and manufacturers – and provides an integrated view of opportunity that will help companies to understand how to adapt and shape their competencies to match their selected target opportunities.

**Exhibit 1**

**The Ecosystem Framework**

Our study yielded ten distinct ecosystems that collectively encompass most of human disease and virtually all of the potential markets for drug therapies. Starting at the highest level, these ten ecosystems can be grouped into three clusters of opportunity, varying by the degree of change that is required from the traditional pharma business model. (See Exhibit 2.)

Starting on the left, the first cluster is closest to the traditional markets for drugs and currently represents 21% of health care spend and 43% of drug spend. These ecosystems require less
change in the model for discovering, developing, and commercializing medicines. In the short run, they encompass the most robust opportunities for pharmaceutical companies. Hub of Innovation is a set of hard-to-treat, critical diseases. They currently have few treatment options, but are where research is gaining traction. The very small patient populations in Rare Diseases often share a common genetic profile or mutation and are treated with very expensive, chronic therapies that replace missing proteins or repair damaged tissue. Drugs Are Core consists of highly prevalent, often chronic conditions (diabetes, hormone-positive breast cancer) for which drugs are an important part of the standard of care, but there is significant unmet need and high long-term health care spend; these conditions are a major area of focus for the pharmaceutical industry today. Drugs are not yet a major part of the treatment paradigm for the chronic conditions in Help Desperately Needed, but – with successful innovation – have strong potential to become so.

The next cluster of ecosystems (representing 25% of health care and 36% of drug spend today) consists of a set of conditions for which there is more limited forward-looking opportunity for drug companies. Proceed With Caution includes smaller disease markets with a partial standard of care but significant unmet need due to intractable disease biology. Payors may not support the premium pricing needed for a positive return on R&D investment, so success here will require not just a step change in efficacy or safety, but a radically lower cost model for R&D and commercialization. Yesterday's Blockbusters includes conditions that were the heart of pharma markets fifteen years ago (e.g., depression, hyperlipidemia, migraine). These large disease segments still drive massive spending on drugs, but top-line growth is limited by the steady advance of generics and increasing payor sophistication. There is opportunity in these markets – for example, by targeting patients with intractable disease or better integrating drugs with other treatment modalities. But it will be difficult to exceed an already high standard of care, and payors will demand substantial health outcome evidence to grant access; even then, novel therapies will be relegated to second line and older, cheaper therapies will influence a price ceiling. Brand Central includes patient-directed conditions (e.g., acne, fertility control) in which sales of branded products persist despite near-universal availability of generic substitutes. The opportunity here is to leverage better consumer segmentation and to target non-medical wants and needs – more personalization, greater convenience, more satisfying patient experience, etc. But with pricing limited by generic substitutes, innovation will need to be faster, cheaper, and virtually continuous.

The last three ecosystems represent the least robust opportunities for traditional biopharma companies, and while they account for 33% of current health care spend, they drive less than 15% of drug spending. In these ecosystems, an entirely new paradigm is needed. Acute Killers includes a set of conditions where high patient mortality and highly intensive clinical interventions make it difficult for drugs to gain traction. Despite substantial R&D investment in some areas (e.g., stroke, acute renal failure), few drugs are used for anything beyond palliation or sedation, and we see limited routes for drugs to enter the treatment paradigm without a revolution in disease understanding. In Cut & Stitch the standard of care is effectively driven by non-drug treatments. This is the realm of the surgery and outpatient clinic, and drugs are again limited to supportive care. Finally, Pharma Graveyard includes a set of conditions in which there is significant use of medicine, but cheap, safe, and inexpensive generics address virtually all medical need. For all three of these ecosystems, the available room in the standard of care is so limited, or the cost and risk to address unmet need is so high, that today there is simply no economically viable role for new drug innovation that follows traditional models.

**Cancer Isn’t a Singular Disease**

As an example of the segmentation approach, consider prostate and lung cancer, two of the “big four” solid tumor types. Historically, companies see both diseases as residing within the oncology franchise – after all, they’re both treated by medical oncologists, they’re commonly treated with a combination of surgery and other therapy, and they’re highly prevalent cancers. However, they have important differences. (See Exhibit 3.) In prostate cancer, the treatment paradigm includes watchful waiting before expensive branded therapies are used, leading to lower total medical expense per patient. In lung cancer, patients are treated more aggressively, but with a mix that includes both high-cost novel drugs and a range of less expensive chemotherapeutics. These differences mean that these diseases should be approached differently. A prostate cancer strategy must focus on providing incremental value to payors through solutions that are clearly superior or on treating patient niches with high unmet need (e.g., HRPC, currently seeing a wealth of clinical activity). Meanwhile, the higher therapeutic headroom in lung cancer suggests that there are more areas in which to win. Placing these nominally similar diseases in different ecosystems brings out important context on the nature of the opportunity they offer.

**The Pharma Industry in the Ecosystem Context**

As we look at the industry arrayed across the ten ecosystems, we see patterns that put the industry’s current challenges in perspective. Exhibit 4 provides a picture of industry revenues by ecosystem over time, as well as a view of how the share of total revenues in each ecosystem has shifted. (The universe of pharma spend captured in this analysis totaled approximately $545 billion. Of that, approximately $31 billion fell outside of the ecosystems classification.) The surprise is that well over half of current sales are in ecosystems where the current industry model is increasingly less relevant and under challenge. Five of these ecosystems – Pharma Graveyard, Cut & Stitch, Acute Killers, Yesterday’s Blockbusters, and Brand Central – require a fundamental rethinking of the innovation and selling models. Pharma companies will be challenged to offer a value proposition that moves the needle for payors. This is not to say that there isn’t opportunity for pharma companies – just that it won’t be accessed by traditional approaches.

Also striking is how little of the overall market sits in ecosystems where the existing model has strong traction. Hub of Innovation and Rare Diseases comprise less than 8% of overall pharma sales today. While it is not surprising that these relatively nascent markets are a small...
component of current global revenues, the fact that virtually every pharma company has announced a shift in focus to the disease areas that make up these two ecosystems raises questions about the depth of the opportunity over the long term. We believe that traditional R&D and commercial approaches apply in these diseases, but they are not large enough to sustain growth for the entire industry.

It is also clear that, despite a broad strategic reorientation toward specialist, high-need categories, there is substantial remaining opportunity in markets that are maturing. Two ecosystems, Drugs Are Core and Help Desperately Needed, represent large, deep markets for drugs. They include crowded, complex disease areas – breast cancer, rheumatoid arthritis, congestive heart failure. In many of these conditions, a partial standard of care is in place, raising the bar for innovation and potentially reducing the size of the prize for new therapies, which may be limited to a specific subpopulation or later stages of therapy. These areas have relatively high therapeutic headroom and they remain a high priority for payors, representing some 23% of total medical spending. (See Exhibit 5.) Payors will look favorably on therapies that advance the standard of care and drive better health value – better outcomes and less overall cost (no mean feat).

Today’s industry leaders need to be relentless in building and sustaining new competencies in specific areas. Companies must adapt and shape these over time – some toward higher science, others toward greater clinical integration, and still others toward fast-cycle, consumer-directed innovation.

**Exhibit 3**

**Ecosystems And Disease Comparisons**

SOURCE: Oliver Wyman Analysis

**Exhibit 4**

**The Industry Ecosystem Profile**

**Pharma Industry Revenue By Ecosystem**

SOURCE: Evaluate Pharma 2010; Oliver Wyman Analysis

The ecosystem framework is most powerful in diagnosing and guiding strategic and business model decisions within individual companies. Exhibit 6 provides a current snapshot of the sales of the Top 20 pharma companies arrayed against the ecosystem framework.

This top-level industry view demonstrates that true focus is elusive. Most companies have a broad footprint that spans multiple ecosystems, with the average company maintaining a significant
Pharma Business models

Presence (>5% of sales) in five or more ecosystems. This is not surprising given the scale of these companies and their history of acquisitions. But it is a considerable challenge, even for the largest companies, to spread business focus and investment across such divergent markets. Compared to companies in many other industries, pharma companies have been less active in adjusting their business portfolio – exiting mature, commoditizing sectors to fund investment in higher-growth sectors. A key difference is that in pharma, mature, slow-growth areas often remain highly profitable, masking their challenges and helping to fund R&D investment elsewhere. Nevertheless the resulting business model conflict is significant and a strong inhibitor of focus.

This view also highlights the large stake that most companies maintain in maturing markets destined for slower growth. Across the top 20 pharma, 55% of the average company’s revenues are drawn from ecosystems that are no longer a good match for the traditional innovation and commercialization model (represented in blues and yellows in Exhibit 6). Two of the top five pharma, Pfizer Inc. and Merck & Co. Inc., sit with more than 75% of sales in these lower density areas.
### New Ecosystems In Pharma

#### Hub Of Innovation
- Difficult disease, involving critical body systems that must survive treatment
- Markets with high unmet need
- Lower sensitivity of payors

**Representative Diseases**
- Brain and Spinal Cancer
- Liver Cancer
- Multiple Myeloma

#### Rare Diseases
- Very small patient populations
- Chronic and expensive therapies, where available
- Treatment to date primarily focused on protein replacement

**Representative Diseases**
- Cystic Fibrosis
- Bone Cancer
- Lipodoses

#### Drugs Are Core
- Diseases that drive a significant portion of pharma revenues today
- Drugs are a key part of current therapy, but the level of remaining unmet need is high
- Focus of industry innovation today

**Representative Diseases**
- Alzheimer’s Disease
- COPD
- HIV/AIDS

#### Help Desperately Needed
- Chronic, progressive diseases with high payor interest
- Ample therapeutic headroom
- Complex biology with many druggable targets

**Representative Diseases**
- Ischemic Heart Disease
- Pulmonary Heart Disease
- Lymphoma

#### Proceed With Caution
- Complex chronic diseases with narrow therapeutic index
- Lower payor interest due to smaller populations
- Treatments are not well targeted; and industry has struggled in R&D

**Representative Diseases**
- Hepatitis B, C
- Lupus
- Psoriasis

#### Brand Central
- Includes diseases where the patient is a critical decision maker
- Symptomatic diseases with reasonably effective therapies
- High use of generics

**Representative Diseases**
- Acne
- Attention Deficit Disorder
- Incontinence

#### Yesterday’s Blockbusters
- Huge portion of drug spending, now declining with waves of patent expiration
- Chronic, symptomatic conditions
- Increasing use of generics

**Representative Diseases**
- Anxiety, Depression
- GERD
- Migraine

#### Acute Killers
- Unexpected diseases with often-fatal outcomes
- High clinical intensity in treatment
- Limited opportunity for drug therapy

**Representative Diseases**
- Acute Renal Failure
- Septicemia
- Stroke

#### Cut And Stitch
- Surgery is often curative to fix or remove the problem
- Drugs are used to manage complications and provide comfort
- Novel approaches (i.e., regenerative medicine) could get traction

**Representative Diseases**
- Appendicitis
- Joint Derangement
- Uterine Cancer

#### The Graveyard
- Something is “wrong” that can often be fixed with a pharmaceutical
- Markets are heavily penetrated by generics
- Payors typically guide patients to therapies that are least expensive

**Representative Diseases**
- Acute Bronchitis
- Ulcer
- Allergies
This is not surprising given that today’s sales are a reflection of historical strategy, not current strategy, but it runs counter to the professed strategic orientation for most companies that emphasize “high innovation” medicine. Looking forward, Merck is forecast to expand rapidly in more innovative markets through 2015, but Pfizer’s ecosystem profile is projected to remain relatively stable.

Our core contention is that it is more important to be structured appropriately for your target markets than to focus on a particular ecosystem. Of the top 20 pharmas, only one, Novo Nordisk AS, has significant sales in three or fewer ecosystems (and even Novo is exploring new areas like inflammation, which could eventually dilute its focus). The analysis in Exhibit 7 looks at total shareholder return for the top 20 pharmas, ranking them by portfolio focus, or the proportion of sales in similar ecosystems (the three broad clusters in Exhibit 2). We see that the most focused quintile outperforms the least focused in any time period over the last 10 years. The point is not that top performers focus only on the most innovative or highest need clusters. Rather, more focused companies appear to have found ways to structure their businesses to extract superior performance in any economic conditions.

**ROCHE AND BMS: BENEFITS OF ECOSYSTEMS FOCUS**

Two companies in the large pharma cohort – Roche and Bristol-Myers Squibb Co. – stand as examples of having shifted the majority of their portfolio into the innovation-dense ecosystems. Exhibit 8 illustrates the sustained effort required to achieve this sort of strategic repositioning.

For much of the decade between 1995 and 2005, BMS focused heavily on what we now define as Yesterday’s Blockbusters, with Pravachol (pravastatin), Plavix (clopidogrel), and other primary care medicines contributing the majority of revenue. But after notable setbacks in its portfolio and a major management shakeout, BMS embarked on a major strategic initiative to shift its focus to high-need specialty markets and biotechnology. This was a challenging process, requiring significant workforce reductions, divestiture of non-core businesses (e.g., Mead Johnson nutrionals, Oncology Therapeutics Network, BMS Medical Imaging), and a series of partnering deals to share risk and access broader funding. (See “Bristol Spins Off Mead Johnson in Stock Swap, Finally Pure Biopharma” — IN VIVO, December 2009.) But after nearly a decade of repositioning, BMS is now seeing the rewards of an increased focus on higher-density markets. Recent successes such as Yervoy (ipilimumab) and Sprycel (dasatinib), and a healthy R&D pipeline including potential blockbuster Eliquis (apixaban) are reflected in the recent performance of BMS stock, which appreciated more than 32% in 2011, compared to 8% for its peers (as measured by the 2011 performance of the AMEX Pharmaceutical Index).

For its part, Roche provides a counter example to the general pattern that larger companies participate in more ecosystems. Through a decade of portfolio repositioning, Roche has steadily increased its presence in the Help Desperately Needed ecosystem, demonstrating a strong track
record as an innovator in large markets with high unmet need, notably oncology. Roche’s focus was reinforced by the purchase of Chugai and Genentech, which brought control of an industry-leading portfolio of protein therapeutics for conditions with high unmet need. Roche’s past successes are no guarantee for the future, but the company is notable for the continuing shift in its innovation focus, moving from the larger and better-served oncology markets (like breast cancer) into areas of higher unmet need in the Hub of Innovation, with therapies like anti-FGFR3 and pertuzumab targeted at multiple myeloma and metastatic ovarian cancer; Roche is also building in the non-oncology part of Hub of Innovation, with therapies in a range of autoimmune diseases, including multiple sclerosis and lupus. These therapies offer the potential for step-change improvement in outcomes that will be demanded in increasingly crowded specialty markets.

One final insight from the ecosystem profile of individual companies: serendipity is the enemy of focus. The pipelines of Roche and BMS – our poster children for conscious portfolio repositioning – illustrate the point. (See Exhibit 9.) While both companies show an increase in R&D programs targeting the highest-need areas, they also show a disproportionate number of programs – upwards of 30% of molecules in development – focused on partially or well-served diseases. These molecules target areas that both companies have publicly shifted away from. Whatever opportunity they offer will likely be constrained. In fact, if you look at the drugs BMS and Roche expect to launch, both companies look less focused than they do when you look at current sales. BMS and Roche both show great discipline in managing their portfolios. The fact that they continue to advance programs in non-core areas highlights a challenge: Pharma companies find it difficult to terminate or sell off R&D programs and are reluctant to abandon areas of traditional strength. Whatever the cause, this persistent muddying of focus suggests that most companies still have room to prune the portfolio (extracting value for non-core programs through other means) and better align investment with targeted areas of opportunity.

We don’t suggest that companies reorganize by ecosystems; in general, even the largest phamas lack sufficient density in any particular ecosystem to use it as a central organizing concept. We do not intend it as a prioritization tool, to blindly decide which markets are “good.” We do not see it being useful in guiding the operations of individual functions; in particular, it would be inappropriate in discovery operations, which naturally segment by system biology, and for which traditional segmentation schemas are more natural and actionable.

So, how do we recommend the framework be used? Principally as a tool to integrate thinking about the nature of opportunity for a drug in a specific market: What is the relative importance of factors driving unmet need, the traction for innovation, and the value proposition to key stakeholders? How much attention should we pay to these different elements in setting strategy? What are the key value drivers of opportunity for a particular disease? What are the critical challenges that must be addressed in a winning business model for a particular disease?

As markets continue to mature and diversify, companies will need to differentiate their strategies more than they have in the past. The ecosystems framework provides an integrated view of opportunity and value that can help companies adapt and shape their portfolios: Which disease areas will be platforms for growth, and which cash cows to fuel investment? Is the future competency model aligned with the portfolio? Where and when will there be need for breakthrough science, greater clinical integration, or fast-cycle, consumer-directed incremental innovation? No company can be the best at more than a few things – even the largest players will need to choose where they will play and then relentlessly build world-class competencies that match their areas of focus.

Jerry Cacciotti is a partner and head of the life sciences practice, Bill Shew is a partner, and Parie Garg is an associate partner at Oliver Wyman, a leading global management consulting firm. E-mail Jerry.Cacciotti@oliverwyman.com.

**Related Reading**
“Bristol Spins Off Mead Johnson in Stock Swap, Finally Pure Biopharma” — IN VIVO, December 2009
“AstraZeneca Rebuilds R&D Amid Growing Near-Term Pressures” — IN VIVO, June 2011

**Access These Articles Online:**
www.ElsevierBi.com