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CLOSER TO THE MARK: Focusing on the Market Environment to Improve Pharmaceutical Revenue Forecasting

- Financial analysts have done a poor job in forecasting pharmaceutical product revenue.
- A critical evaluation of recent product launches reveals significant opportunities to improve revenue forecasting by focusing on the market environment.
- Analysts have the opportunity to improve forecasting by identifying the competitive ecosystem that will surround the product as it is commercialized.
- In each ecosystem, good forecasts occur when analysts place emphasis on identifying the value of patient benefits relative to future competitors as seen by decision makers who influence therapy selection.

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The Poor Record of Pharmaceutical Product Forecasting

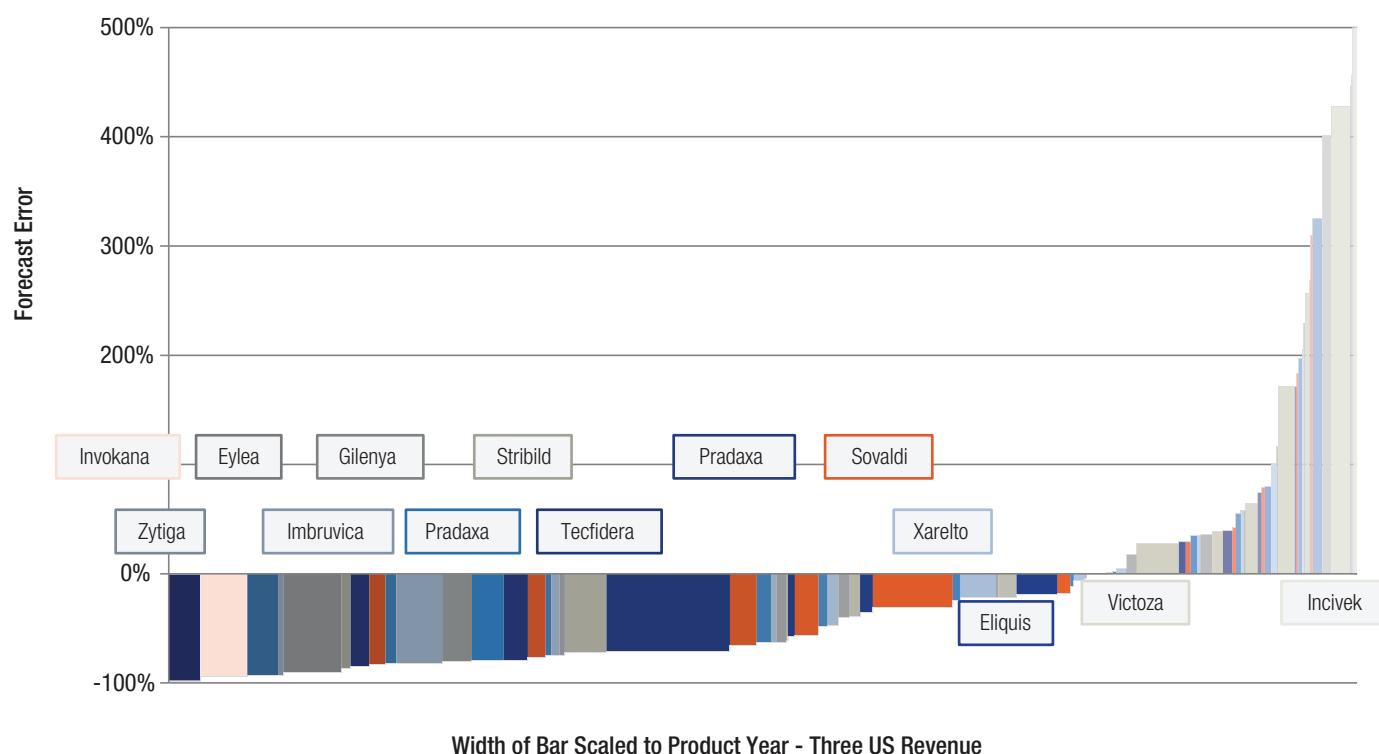
Forecasting revenue for pharmaceutical products is a challenging endeavor. The ultimate projection represents a combination of estimates applied to a range of uncertain factors. Forecasters must make judgements regarding the treatable population, the pace of product adoption, launch timing, reimbursement design, pricing, and the level of supporting promotion. It may not be surprising, then, to find a poor track record for pharmaceutical revenue forecasting. Figure 1 compares the actual US revenue for 84 pharmaceutical products in their third year in the market and a consensus of analyst forecasts for year-three sales that was made one year ahead of launch.¹ Only 39 of those forecasts fell within a range of 50% to 150% of the actual results. In 13% of the observations, the forecast was more than three times the actual sales.²

Other analyses have highlighted similarly disappointing performance of pharmaceutical revenue forecasters, but these analyses have provided little guidance on why the forecasts are so poor.³ The goal of this paper is to take the next step and identify some of the main drivers of forecast errors. We believe that revealing the gross unreliability of forecasts without identifying the drivers of the errors is similar to giving an employee a poor performance review without also providing an accompanying development plan. The only way to improve future forecasts is to critically evaluate the poor performance to date, identify what is prompting the errors, and develop strategies for overcoming those factors.

So, why are the forecasts so bad? Isn't this a highly transparent industry

Figure 1

Pharmaceutical Forecast Accuracy
 (Comparison of Year-Three Actual US Sales to Estimates From One Year Ahead of Launch)



¹ Our source for consensus forecasts is EvaluatePharma®. The commercial database provides mean value average for US and global sales. US values were used on our analysis to minimize the impact of changes in launch timing across geographies.

² Interestingly, consolidating the forecasts to build expectations for the market as a whole provides a surprisingly accurate forecast. The median error in our sample was -1%. The cumulative value of forecasts totaled 80% of the actual year-three results. These observations offer some comfort to financial investors

with a well-diversified portfolio of investments, but little value to strategists responsible for making brand level investment decisions. The large variance in forecasting accuracy is even more concerning to corporate development and licensing leaders faced with making product specific decisions in an environment that is clearly subject to wide errors.

³ Cha, M., Rifai, B., Sarraf, P. Pharmaceutical Forecasting: Throwing Darts? *Nature Reviews Drug Discovery* 2013; 12: 737-738

where product launches are anticipated years in advance? Can't the financial analysts draw insights from the availability of detailed information on thousands of previous products? Aren't there extensive sources detailing the epidemiology for both highly prevalent and ultra-rare conditions? The answer to all of those questions is yes, but it appears analysts require something beyond access to these robust data sources.

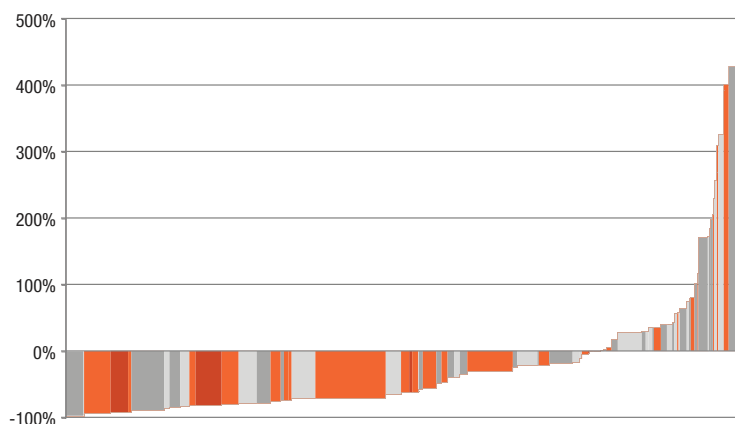
There is no simple path to identifying drivers of forecast errors. Interrogation of the data reveals no systematic mis-steps related to ultimate product revenue, designations of product novelty, product pursuit of small patient populations, or the size of the company launching the product (Figure 2).

With this as a backdrop, we hypothesized that it is more than the characteristics of the product that influence forecast accuracy. Looking into the market situations that have led to poor forecasts and the cases where analysts did a better job we have concluded that much of the error can be explained by forecasters' low level of appreciation for the market context into which the product will launch. Simply stated, we know that **good forecasts occur when analysts can accurately project the patient benefits of a product relative to future competitors as seen by decision makers who influence therapy selection.**

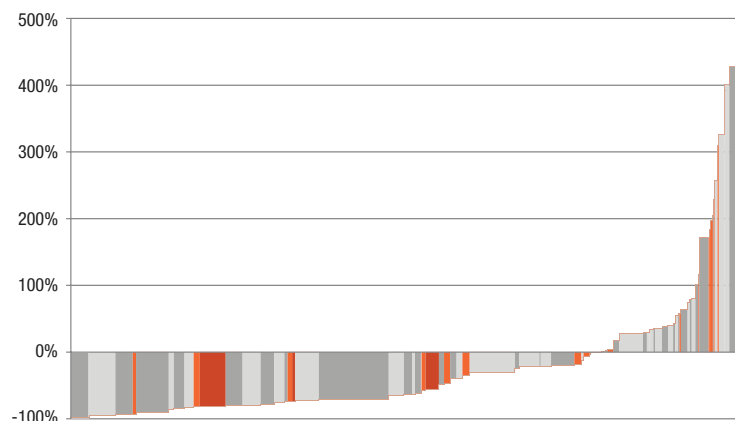
That principle also offers guidance on the circumstances that provoke forecast inaccuracy. Poor results occur when forecasters misunderstand the true relevant patient group, when the perspectives of groups other than the true decision makers are over-weighted, and, most importantly, when there is insufficient consideration of the anticipated competitive environment. It appears that many forecasters focus on opportunities for the product as if it were the only change to the market. Less attention is paid to other factors that will upset the status quo. In reality, rich and varied streams of innovation often converge on a pharmaceutical market within a very short period of time. A new entrant may face competition from multiple products applying a similar mechanism of action or from alternatives exploiting different mechanisms. That new product may also enter a strategic environment where the power of influencing parties is changed—notably, one where expectations for access and reimbursement are destabilized by changing behavior of payers.

Figure 2

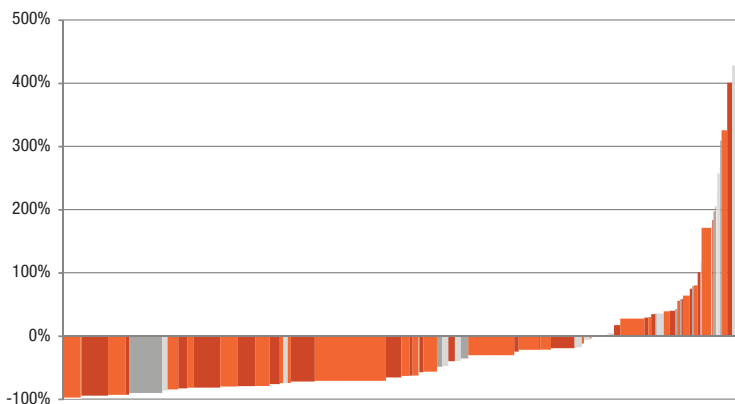
First-in-Class Products
(shown in red and orange)



Orphan Products
(shown in red and orange)



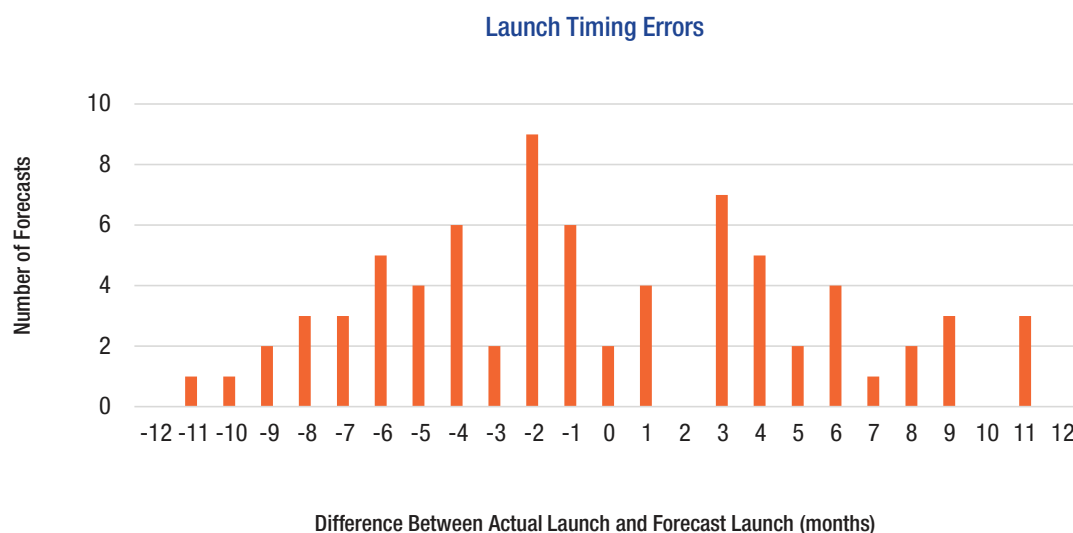
Products Launched by Top 25 Pharma Companies
(shown in red and orange)



Moving the Starting Line

Even one year ahead, forecasters' expectations for launch timing was imprecise. As shown in Figure Box 1, analysts often missed the true launch date by several months. Reviewing the data for trends, there was, in fact, a correlation—albeit a very weak one—between forecast errors and the number of months error in the expected launch date. For products where the launch date was sooner than anticipated, forecasts for year-three sales tended to be underestimates. For products launching later than anticipated, the forecasts tended to be overestimates. This is consistent with expectations as more months in the market would allow the product more time for product adoption. However, this factor by no means provides a dominant explanation of the forecast error.

Figure Box 1



Good forecasts occur when analysts can accurately project the patient benefits of a product relative to future competitors as seen by decision makers who influence therapy selection

Drawing lessons from products launched in the US during the period 2008 through 2013, we have identified seven characteristic market circumstances that proved particularly challenging for forecasters. Each of these situations is represented by a commercial example where expectations for selected products fell far from the ultimate realities. We conclude each review with observations on how forecasters might have better anticipated the market results and suggest approaches for making better estimates in similarly structured situations in the future.

We believe much better forecasting is possible, and one key opportunity for improvement can be found by investigating the drivers of these unsuccessful forecasting efforts of the past.

Oncology Pricing: A Series of False Peaks (so far)

In oncology, there has been a tendency to under-forecast year three sales (figure 3). Overall, year three revenue estimates for oncology products were 56% of the actual performance. For products treating solid tumors, the forecasts averaged 31% of the actual value. Two factors contributed to the underestimates for these products. First, these products tended to have an earlier launch than was expected. On average, solid tumor oncology products launched 7.4 months sooner than had been expected in the month one year ahead of launch. Across all of the products in our database, moving an extra six months down the adoption curve would be expected to increase sales between 20% and 30%.

Much more important than the launch timing expectations, forecasters seem to have underestimated the pricing potential for oncology assets launched during this period. Figure 4 shows a progression of forecasts for US pricing for Yervoy®, Xtandi®, Zytiga®, Zelboraf®, and Imbruvica® during the period one to four years ahead of launch. At the point one year ahead of launch, analysts were projecting pricing that was often one half or even one third of the eventual launch price.

In retrospect, the market's inability to successfully anticipate pharmaceutical pricing should not be surprising. First, this has been an area of substantial controversy. Year after year, observers remark on the unrelenting growth in pricing of innovative therapies. This is often paired with comments regarding the impossibility that the trend will continue. Yet, to date, in many orphan diseases and in oncology, each new launch is priced at a premium to its predecessors. Quite reasonably, the analysts have hedged, applying limits to their price estimates.

Better forecasting will require an improved ability to anticipate the pricing levels that pharmaceutical companies will be able to achieve. Those responsible for forecasting must begin to think like payers. They must evaluate product benefits as they compare to the available alternatives. Where possible, they must investigate how organizations such as the Institute for Clinical and Effectiveness Research (ICER) and the National Comprehensive Cancer Network (NCCN) have judged the value of similar product benefits.⁴ Finally, forecasters must

Figure 3

Solid Tumor Therapeutics
(shown in red and orange)

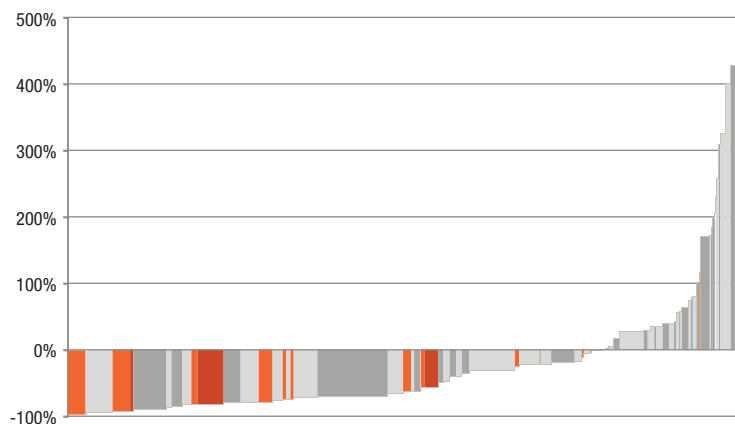
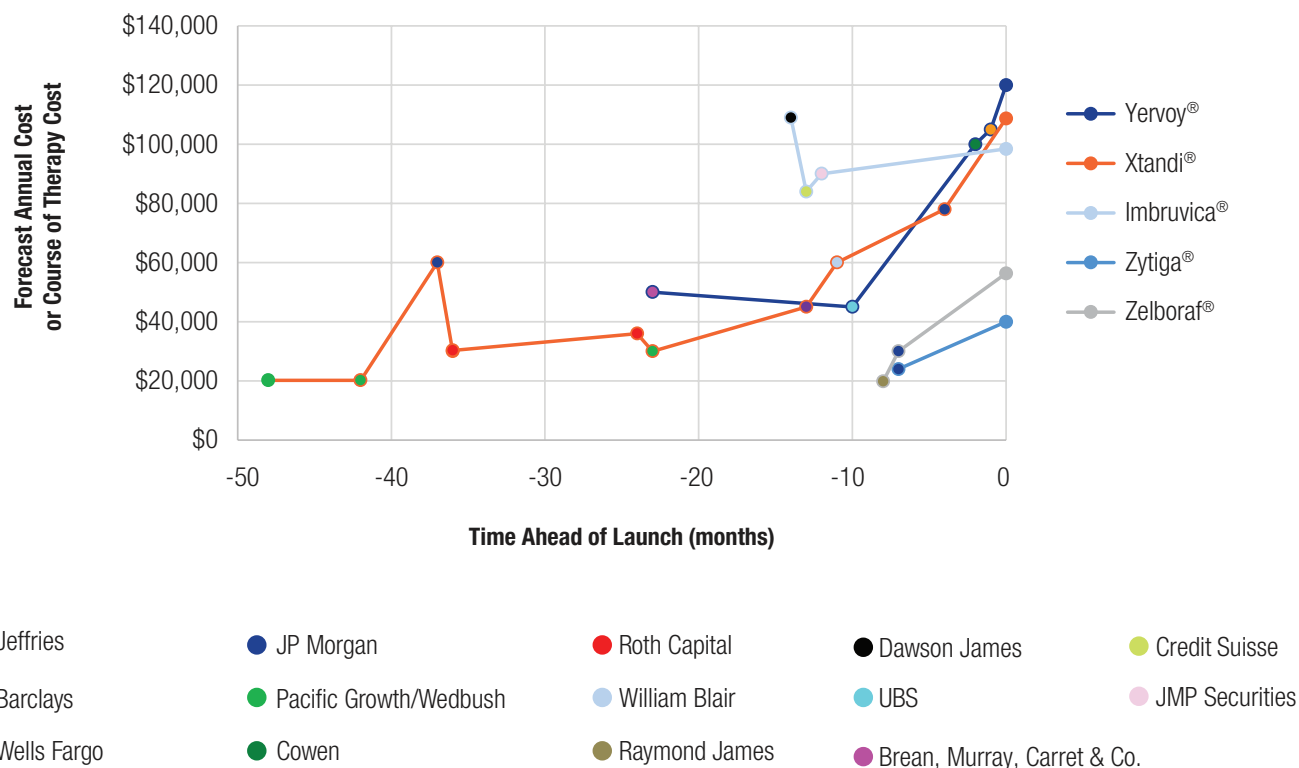


Figure 4

Progression of Analyst Forecasts for US Oncology Pricing



⁴ Senior M. Scoring Value: New Tools Challenge Pharma's US Pricing Bonanza, In Vivo October 2015 10-16

anticipate how product adoption behavior will change if payers respond to increased pricing through higher levels of patient cost sharing or increased access restrictions.

More Like a Speed Boat than an Aircraft Carrier

When putting together a forecast, analysts often start by estimating the peak share expected for a product and then building an adoption curve estimating how quickly that peak share will be achieved. Many have become accustomed to a familiar S-shaped curve reflecting a progression through early adopters, general use, and laggards. In the past, the rationale for the S-curve adoption model has applied reasonably well to large primary care markets where tens of thousands of prescribers must be converted to a new product option.

The evidence suggests the S-curve adoption model is not as effective in anticipating the uptake in specialty markets where an innovative product has clear advantages over the existing options. Two situations in our data set exemplify the need to adjust the models used for anticipating product adoption.

First, consider the case of Eylea® (aflibercept). Eylea is a human antibody fragment that is used in the treatment of age related macular degeneration (AMD). The requirement for intravitreal administration substantially limits the number of prescribers who are responsible for the selection of Eylea. At the time of the product's introduction, ophthalmologists were either using Lucentis® (ranibizumab) or Avastin® (bevacizumab) for treating AMD. Lucentis had received an FDA approval in 2010, required monthly injections, and had an annual cost of \$24,000. Lucentis and Avastin are anti-VEGF (vascular endothelial growth factor) drugs that have a similar molecular structure. Rather than pay the high price of Lucentis, many ophthalmologists had turned to using very small doses of Avastin, often supplied by a compounding pharmacy that prepared the product. Genentech, the supplier of both Lucentis and Avastin had taken efforts to position safety advantages and demonstrated efficacy of Lucentis as compared to Avastin.

Interest levels and awareness of AMD treatment options were exceptionally

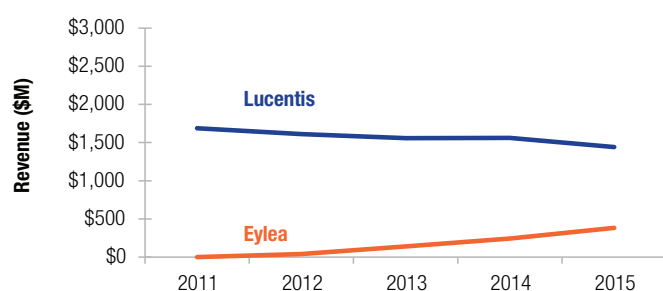
high, both because the introduction of Lucentis brought a breakthrough option to physicians and because the commercial positioning relative to Avastin had touched deep emotional nerves within the ophthalmology community. At the time of launch, one would be very hard pressed to find a treating ophthalmologist who lacked awareness of Eylea and the key points of differentiation. Eylea required three initial weekly doses, but then moved to a schedule of once-every-eight weeks administration. The per-injection price was \$1,850 vs. \$2,000 for Lucentis, meaning the annual cost of treatment could be \$8,000 less for Eylea.

Rather than slowly migrating prescribing to Eylea, physician prescribing pivoted. As shown in Figure 5, the early adoption of Eylea was not the steady build up characteristic of the early stages of an S-curve, it was a rocket blast off, and Eylea sales dramatically exceeded expectations. Concurrently, there was a modest drift downward in sales of Lucentis. It appears the key advantages for Eylea were mostly appreciated relative to compounded Avastin. While this adoption has continued to expand over time, it is remarkable to view the characteristic rounded shape of a rapid-uptake curve. High awareness of meaningful differentiating characteristics that were appreciated by a concentrated set of decision makers led to almost unprecedented dispersion of specialist adoption.

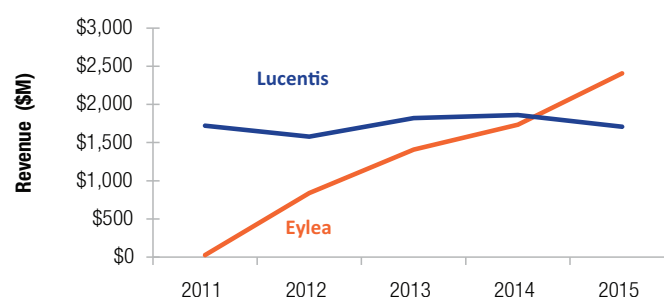
A similar pattern was observed when oral therapies for multiple sclerosis were introduced. Here, three different products were introduced to the US market in the period from 2010 to 2013, Gilenya® (fingolimod) from Novartis in 2010, Aubagio® (teriflunomide) from Genzyme in 2012, and Tecfidera® (dimethyl fumarate) from Biogen Idec in 2013. These products, each leveraging a different mechanism of action, presented notable improvements in relapse rates for MS patients, but each also presented the potential for significant side effects. Anticipating that physicians and patients would cautiously incorporate these options into their treatment paradigm, analysts projected gradual uptake curves. Instead, year three sales for all three products dramatically exceeded forecasts (see Figure 6). Interestingly, more recently, analysts have struggled with over-forecasts in this category. For Tecfidera in particular, the high early sales have proved to be the start of a rounded, rapid-uptake curve, not the first steps of an enhanced S-shaped curve progressing to ever-greater product revenue.

Figure 5

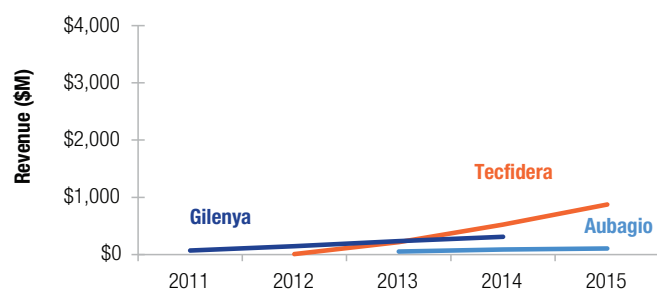
Eylea/Lucentis Analyst Expectations for US Sales
(Expectations one year prior to Eylea launch)



Eylea/Lucentis Actual US Revenue

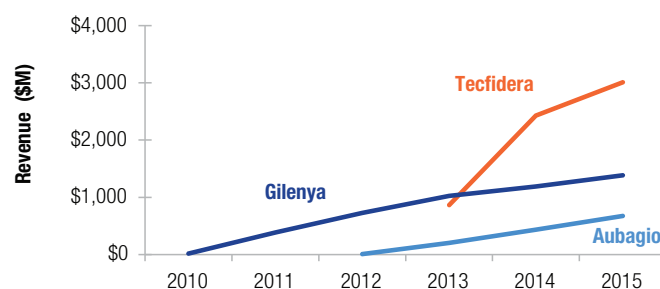


Source: EvaluatePharma

Figure 6
MS Analyst Expectations for US Sales
(Expectations one year prior to launch)


Note: Aubagio expectations estimated 21 months prior to launch

Source: EvaluatePharma

MS Actual US Revenue


Despite the important learnings from the review of the AMD and MS markets, it would be a serious mistake to suggest that rapid uptake is the new norm for all pharmaceutical launches. In fact, as specialty product launches are accelerating, conditions in primary care markets are making it more difficult for new products to gain early traction. Here, information about new alternatives needs to reach a wide group of physicians, and patients are substantially less involved in researching emerging treatment options. Finally, payers have demonstrated less willingness to quickly position innovative cardiovascular and diabetes products on their formularies. Forecasters are then wise to anticipate slower S-shaped adoption curves to primary care even as they are incorporating faster adoption in specialty categories.

Clash of Titans – Anticipating Performance When Large Companies Compete

In late 2010, cardiologists eagerly anticipated the entry of several new treatment options for their patients who experienced atrial fibrillation. Because of the substantial stroke risk, many of those patients were treated with warfarin, a vitamin K antagonist that had originally been launched by Bristol Myers in 1954. While the treatment provides a meaningful reduction in stroke risk, there are several downsides to warfarin therapy. The product is administered through subcutaneous injection, and it is difficult to determine appropriate dosing. Patients receiving a dose that is too high suffer a substantial increase in bleeding risk.

At the end of the first decade of the 2000s, three innovative products were progressing through development. Boehringer Ingelheim was in the lead with Pradaxa® (dabigatran) a direct thrombin inhibitor. Xarelto® (rivaroxaban) being developed by a collaboration between Janssen and Bayer and Eliquis® (apixaban) marshaled by a teaming Bristol-Myers Squibb and Pfizer were close behind Pradaxa. Ultimately, Pradaxa was approved in October of 2010, Xarelto in November of 2011, and Eliquis in December of 2012.

There is a high level of similarity across these products. The major indication for each was expected to be stroke prevention in nonvalvular atrial fibrillation⁵ and each development program had used warfarin in the comparator arm. Because Pradaxa was expected to launch late in 2010, expectations for meaningful revenue began in 2011. Further, analysts anticipated modest product uptake in the early years of promotion. Although US sales for Pradaxa exceeded expectations, analysts were correct in assuming the product's revenue performance would be tempered by the entry of additional oral alternatives.

As shown in figure 7, once in the market, Xarelto quickly took a leading position. Did Xarelto offer new levels of efficacy or safety? Was it some share driving commercial strategy from Janssen? No, to a great extent the big difference was dosing. Xarelto is taken once a day while Pradaxa and Eliquis require twice daily administration. While the forecasts suggest analysts recognized that once-a-day dosing presented Xarelto with a marketing advantage, it appears they did not anticipate the level of the product's rapid adoption.

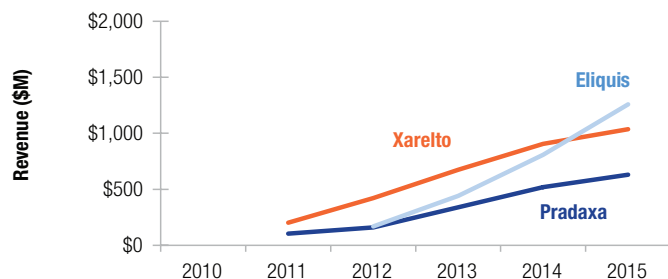
Launching more than a year after Xarelto and suffering the same twice-a-day dosing disadvantage as Pradaxa, expectations for Eliquis might have been tempered. However, potentially emboldened by the early performance of Xarelto, analysts projected the product would rapidly reach US sales levels above \$1 billion.

Pfizer and Bristol-Myers Squibb implemented an aggressive commercial investment strategy for Eliquis. At \$219M in 2014, direct-to-consumer spending for Eliquis ranked third among all pharmaceutical products and far exceeded the levels for the other two oral anticoagulants. Similarly, the amount of speaking and consulting payments to physicians for Eliquis were reported to be among the highest in the industry. Supported by this heavy commercial investment, sales in the US alone would position Eliquis beyond the \$1 billion blockbuster-qualifying threshold in 2015.

⁵ The products are also effective for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE)

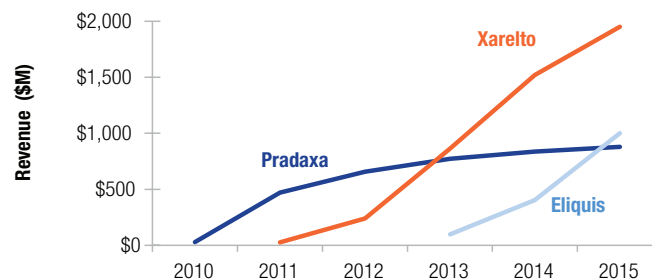
Figure 7

Anticoagulant Analyst Expectations for US Sales
(Expectations one year prior to launch)



*2015 Pradaxa estimate based on expectations 7 months prior to launch

Anticoagulant Actual US Revenue



Source: EvaluatePharma

This Clash of Titans example offers several quick lessons for industry forecasters. Notably, we see the importance of constructing the forecast in two steps. First a view must be established of how a new set of options will compete with existing therapies. As in the case of the oral anticoagulants, when there are important benefits over existing treatments, heavy promotion of multiple competitors often leads to a rapid shift to the new alternative. The combined US revenue for Pradaxa, Xarelto, and Eliquis in 2015 exceeded forecast by \$900M.

Once an estimate for the overall shift to new products has been developed, forecasters must build a perspective on how competition among the new entrants will play out. The large commercial investment applied to Eliquis highlights the challenge in projecting share allocations. When multiple, similar products enter a market together, the situation inspires a period of intense commercial innovation. With product characteristics and clinical performance, in-depth information is available years ahead of a product's launch. Far less advance information is available regarding marketing strategies and commercial tactics. Analysts must, then, build expectations based on each company's commercial effectiveness and previous levels of promotional investment.

More work remains for forecasters as new strategies continue to play out in the oral anticoagulant market. In October of 2015, Boehringer Ingelheim received approval for a reversal agent for Pradaxa. Providing a solution for patients who suffer major bleeding or require invasive surgery, this product could shift share back to the product that ushered in the oral anticoagulant era. On a different front, the launch of Daiichi Sankyo's Savaysa® (edoxaban) represented entry of a fourth alternative. In such a market, the temptation will surely be felt for one or more players to pursue low pricing strategies in the form of aggressive payer discounts.

Innovation Battlefield

The commercial opportunity for each newly launched pharmaceutical product depends on its ability to demonstrate meaningful differentiating

characteristics from the therapeutics that are in the market. As time moves on, the competitive set changes. Then, instead of facing the standard of care that existed at the time of launch, the product must withstand competitive challenges from each new wave of innovation. Nowhere has this dynamic been more evident than in the market for hepatitis C therapies.

Here, in 2011, both Incivek® (telaprevir) from Vertex and Victrelis® (boceprevir) from Merck received approval. When paired with interferon and ribavirin, these very effective NS3/4A inhibitors had been shown to eradicate the virus in 60% to 70% of patients infected with specific genotypes of hepatitis C. Both products took off quickly, and Incivek achieved sales of more than a billion dollars.

Incredibly, the extraordinary launch for these products was followed by a crash that was just as remarkable. By its third year in the market, sales of Incivek sales had fallen below \$500M. Year three sales for Victrelis were \$158M. There was no new safety concern. There were no manufacturing interruptions. The driver of sales declines in the single agent NS3/4A class occurred because a better option, Sovaldi® (sofosbuvir), a NS5B nucleotide inhibitor, offered patients better efficacy and a shorter treatment period. The performance of Sovaldi and Gilead's combination product follow on, Harvoni® (ledipasvir 90mg/sofosbuvir 400mg), was so superior to the earlier products that both Incivek and Victrelis were removed from the market by 2014.

Sovaldi's exceptional clinical performance was not a surprise. Given the long clinical trial requirements and the expectations for regular scientific updates, the entire infectious disease community was anxiously awaiting the product's launch. The revenue forecasts for Sovaldi were not, however, paired with anticipated declines for Incivek and Victrelis. In fact, as 2011 came to a close, some held enough confidence in future revenues of Victrelis that they were willing to purchase royalties held by Dendreon for intellectual property that had supported the product's early development.⁶

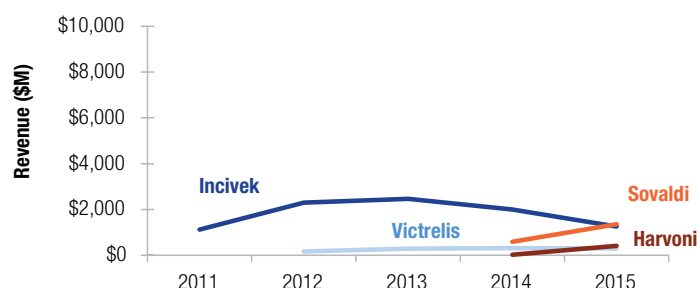
⁶ Timmerman L. Dendreon Pulls In \$125M By Selling Royalty Slice of Merck's Hepatitis C Drug, Exome, December 6, 2011

Years ago, forecasters could use a product's early commercial performance to reliably sketch out its future revenue. To do so in an innovation battlefield like hepatitis C will result in false hopes for familiar trajectories of early entrants. Only so many patients will be treated and it makes no sense to presume steady growth of a later entrant will occur concurrently with market preservation of products already being sold. We see a similar

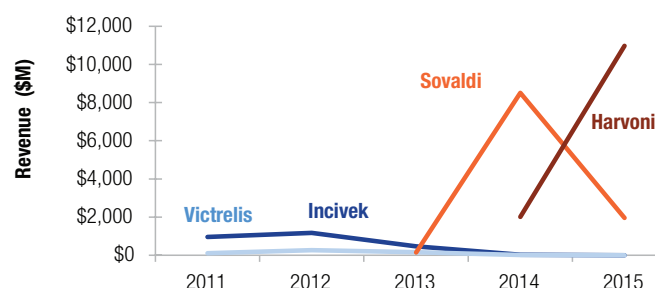
pattern emerging in markets for biosimilar products. In many individual cases, and in the market as a whole, we see analysts anticipate adoption of biosimilars while suggesting little effect on the originator products. Those sales are going to have to come from somewhere, and we doubt that the primary source will be market expansion.

Figure 8

Hepatitis C Analyst Expectations for US Sales (Expectations one year prior to launch)



Hepatitis C Actual US Revenue



Source: EvaluatePharma

A Lack of Segmentation

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder in which immune complexes accumulate in various organs. Subsequent inflammation of the organ systems causes tissue injury and a variety of disease presentations including skin rash, arthritis, joint pain, and pulmonary or renal complications. The underlying cause of SLE is not well understood and physicians must rely on a number of rating scales for diagnosis. The two most widely used scales are the SELENA-SLEDAI which is built on an assessment of twenty-four symptomatic factors and the BILAG which comprises observations to an 86-question survey. A patient's disease severity is summarized through the assignment of a SELENA-SLEDAI or BILAG score.

In 2011, patients and investors anxiously awaited the launch by Human Genome Sciences and its partner, GSK, of Benlysta® (belimumab), a monoclonal antibody inhibiting the B-lymphocyte stimulator (BLyS). When launched, Benlysta would be the first new therapy for SLE in over fifty years. Analysts were tremendously enthusiastic with some anticipating global sales could quickly rise to over \$3 billion.

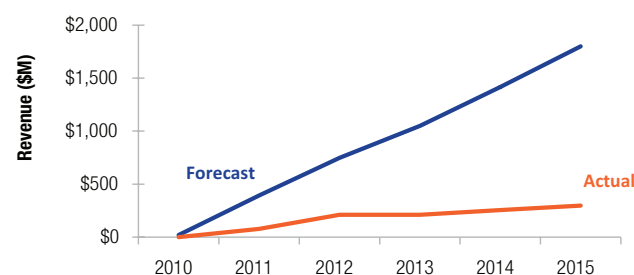
At the time of the launch, many analysts commented on the scarcity of reliable information on the prevalence of lupus in developed countries. Nevertheless, most ultimately landed on a US prevalence number somewhere around 350,000. Less explored was the question of which of these patients would receive meaningful benefit from Benlysta. Studies of the drug had only required that patients have a SELENA-SLEDAI score greater than six. This represents patients with a fairly mild level of disease, many of whom are well managed through the use of generic products such as steroids or hydroxychloroquine. The area of truly important unmet medical need in SLE is for severe patients. Severe patients make up approximately 25% of those diagnosed with SLE.

The pricing of Benlysta was set in the US at approximately \$36,000 per patient per year. That pricing level would presumably offer important benefits for severe patients or significantly delay the onset of more severe disease in moderate patients. However, neither of these conditions existed. At the time of launch, Benlysta performance in severe patients had not been demonstrated. More importantly, physicians are most concerned about the benefits to specific organ systems in severe patients, and controlled studies in these areas were in very early stages. For patients with moderate disease, Benlysta offered only modest benefits and the trials specifically pointed out the lack of benefits in African American patients.

Figure 9 shows forecast and actual performance for Benlysta for the three years following product launch. In the chart, the underperformance relative

Figure 9

Benlysta Actual and Analyst Expectations for US Sales (Expectations one year prior to launch)



Source: EvaluatePharma

to forecasts is dramatic. Physicians simply did not see a benefit for the target patients that warranted the product's very high price. The lessons are clear. Forecasters cannot project the value for one group of patients to others. Benlysta is an extreme case where patients' and the market's desperation for a product to address a long standing area of significant unmet need resulted in an unforgivable sequence where estimates of the value of benefits to one group of patients (those with moderate SLE) were determined based on the needs of a different group (those with severe SLE) and then applied to both groups. The reality, seen through the retrospective analysis of Benlysta, is that better estimates are built when analysts consider each patient segment independently and anticipate adoption based on the benefits each will receive.

Late Entry to Specialty Class

For as long as there have been multiple entries within a class of pharmaceutical products, forecasters have sought to identify the relationship between order-of-entry and market share. Some, emphasizing the differentiation in product characteristics, development strategies, and marketing investment have argued against the predictive power of launch sequence on product revenue. Countering this, at least one recent article has demonstrated that meaningful insights can be drawn when information on the length of time between product launches and competitors' relative marketing investment is incorporated in the order-of-entry model.⁷

A closer look suggests that order-of-entry models are most successful when considering alternatives for high-prevalence conditions treated by primary care physicians. In those categories, physicians are likely to be less discerning regarding subtleties in clinical study design, and prescribers may be more influenced by differences in marketing investment. The models do not hold up as well in specialty markets. There, the prescribing is concentrated in a smaller set of more deeply informed decision makers.⁸

Bosulif® (bosutinib), introduced by Pfizer in 2012, is an inhibitor of BCR-ABL used in the treatment of chronic myelogenous leukemia. Along with Sprycel® (dasatinib) from BMS and Tasigna® (nilotinib) from Novartis, Bosulif is positioned for patients who experience disease progression following treatment with Gleevec® (imatinib). Analysts had understandably modest expectations for Bosulif as the third entrant for second line treatment. Moreover, soon after launch, additional competition was anticipated from Iclusig® (ponatinib), a product being positioned for CML patients exhibiting a highly specific genetic signature. Even with these low expectations, Bosulif year-three sales is among the worst performances relative to forecast. Going forward, analysts will be well advised to explore closely the expectations for late entrants to specialty categories. Unless they have evidence that there is a compelling reason for physicians to adjust well established prescribing behaviors, it is unlikely these products will capture even the modest share that might be anticipated for late entrants in the primary care setting.

Payer Power

In 2014, Express Scripts added a new weapon to its armamentarium for managing prescription drug spending. Prior to this time, formulary managers relied primarily on tiered copayments, step edits (a requirement to use a cheaper product option before being prescribed a more expensive alternative), and requirements for prior authorizations.⁹ In that year, the company introduced the first list of product exclusions. Applying the guidance of a panel of clinical experts, Express Scripts populated the exclusion list with products that were determined to offer insufficient incremental value as compared to lower cost alternatives. In addition, Express Scripts used the threat of placement on the exclusion list to motivate concessions from manufacturers in highly competitive categories.

CVS soon followed Express Scripts' lead and prepared an exclusion list of its own, and the number of products on the list has grown. For Express Scripts, there were 44 products on the 2014 list and 80 on the 2016 list.

Placement on the exclusion list has a meaningful direct negative effect on product sales. Moreover, it demonstrates that a product may face poor receptivity from other decision makers. Now more than ever, forecasters must incorporate expectations for payer's appreciation of a product's differentiation. The evidence suggests this factor is not being adequately incorporated. Nine products launched in the period that we evaluated were included in either the Express Scripts or the CVS 2015 exclusion list. In seven of those cases, US forecasts for year-three sales were overestimated, often by wide margins.

Caution regarding forecasts for less well differentiated products is similarly supported by reviewing the performance of products that were designated "addition to class" in an FDA supported paper reviewing trends in the industry's level of innovation. With 17 "addition to class" products in our research set, revenue for US year-three sales was overestimated for 11.¹⁰

Closing

Getting pharmaceutical revenue forecasts right is important. These projections steer both long term and short term investments, and expectations for commercial results underlie many regulatory incentive programs that are designed to encourage investment in areas that would otherwise be neglected. This paper began by reviewing the industry's unacceptably poor forecasting track record. Unexamined, the record will not get better, but with careful review of the circumstances surrounding each missed forecast, we believe there is a large and valuable opportunity for improvement.

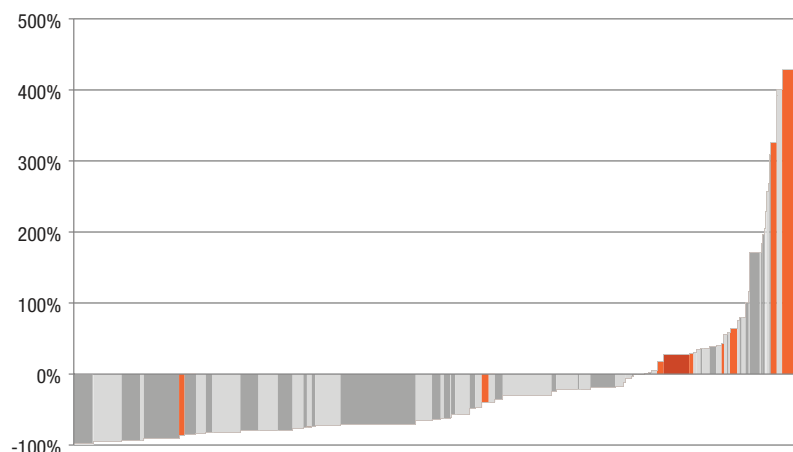
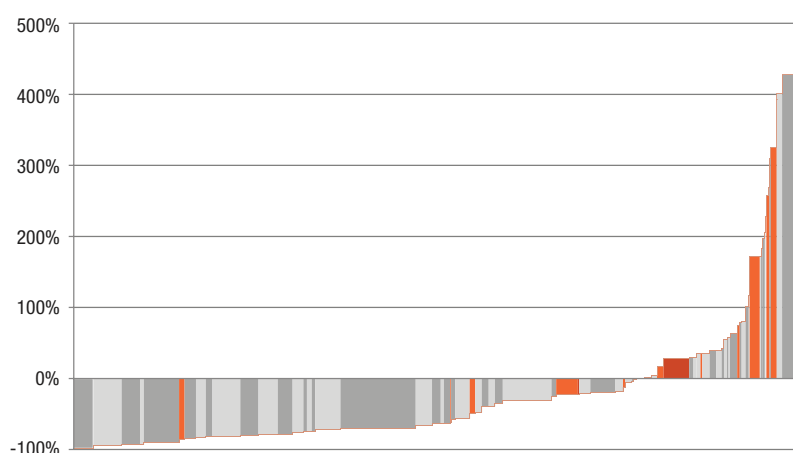
Each of the subsections above describes a market ecosystem surrounding the launch of a pharmaceutical product. The situations that are reviewed are by no means exhaustive. Other products face other circumstances, and in many cases a new product will launch into an environment where the patterns from more than one of these ecosystems will play out concurrently.

⁷ Regnier S. Ridley D. Forecasting Market Share in the US Pharmaceutical Market, *Nature Reviews Drug Discovery* 2015; 14: 594-595

⁸ Longman R. The Shrinking Value of Best-In-Class & First-In-Class Drugs, *In Vivo* July/August 2015 8-12

⁹ Bonifant B Kelly K Reimbursement: The New Biopharma Investment Hurdle, *In Vivo* June 2010

¹⁰ Lanthier M. Miller K. Nardinelli C. Woodcock J. An Improved Approach To Measuring Drug Innovation Finds Steady Rates of First-In-Class Pharmaceuticals, 1987-2011, *August 2013* 32:8 1433-1439

Figure 10
Products on Express Scripts or CVS Excluded List
(shown in red and orange)

Addition to Class
(shown in red and orange)


Despite the different conditions in each of the ecosystems, a fundamental lesson emerges. If they are to be more successful, forecasters of pharmaceutical product revenue need to transport themselves into the future competitive environment and objectively evaluate how decision makers will respond to the then available options. This is not a simple task as it requires understanding both the objectives of decision makers and their relative influence, all within the context of uncertain clinical and regulatory developments. It is, however, a task that will be more effectively performed when a meaningful effort has been applied to research how the market played out in similarly structured earlier markets. Only with this type of pattern thinking—about the market ecosystem—not about the individual product—will there be meaningful improvement in pharmaceutical forecasting.

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About Triangle Insights Group

Headquartered in Research Triangle Park, Triangle Insights Group, LLC is a strategy consulting firm providing guidance on the most critical business issues to leaders in life sciences organizations. The firm's approach combines deep knowledge of the industry across therapeutic areas and functional groups, with a dedication to creativity and disciplined critical thinking. Recommendations from Triangle Insights Group are original, relevant to the industry environment, and supported by rigorous analytics. Clients of Triangle Insights Group include large pharmaceutical companies, emerging biotechnology firms, diagnostics manufacturers, medical device companies, and private equity investors.

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