

Getting "PERSONALIZED"

Sure, there are reasons why personalized medicine hasn't taken off yet—but they're not the ones you might expect. Stop worrying about shrinking the market for your drug, and start figuring out how the "test and treat" business model works

By Peter Keeling & Mollie Roth

After a decade of hype and expectancy, personalized medicine is still in the process of "becoming." The science is there, but it's still in the process of being perfected. With new entrants such as Pfizer's Selzentry for CCR5 trophic HIV, and the relabeling of Warfarin to include genomic-dosing data, the industry is moving beyond the mere promise of targeted therapies—and thankfully, moving

the discussion beyond oncology and the over-hyped Herceptin case.

New York Times columnist Olivia Judson recently asked: So why hasn't personalized medicine yet hit it big? In part, it may be a simple matter of timing. In a *Spectrum* report, one industry commentator estimated that "[i]n 10 years, about 20 to 25 percent of new products in the pipeline will depend



to some degree on a related test.”

The greater problem, and perhaps the biggest barrier to realizing the promise of personalized medicine, might be perceptions about the potential of these drugs held by the pharma industry itself. Most companies have a difficult time seeing therapies targeted toward specific genotypes—which depend on diagnostics to guide prescribing decisions—as anything more than a way to enhance R&D productivity within the currently challenged “one-size-fits-all” model of drug development.

Somewhere along the way, the pharmaceutical industry decided that the market segmentation implicit in targeted therapies necessarily translates into fewer patients and, therefore, reduced returns. But in reality, personalized medicine has far greater potential and much broader applicability than just an R&D enhancement. The industry needs to overcome the divergent business models between pharma and the diagnostic industry, and learn how to harness the marketing dynamics embedded and largely unexplored within personalized medicine.

Pharma companies can go beyond viewing personalized medicine as just an R&D productivity tool to understanding how it can reshape market dynamics, alter a drug’s marketing trajectory, and drive sales—possibly even in the face of generics competition. In fact, if managed and positioned correctly, tailored therapeutics can even offer a return on investment (ROI) equal to drugs developed under the one-size-fits-all model.

Convergence: Mind the Gap

While many of the leading pharma and diagnostic companies have outwardly embraced the idea of personalized medicine, how to get such therapies translated into practice is a very different question. The two industries have developed very different business models, which are culturally, strategically, and

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financially distinct, and their junction during co-development and clinical decision-making is a much more difficult and complex prospect than simply working side-by-side.

The difficulty in working together is particularly exacerbated when dealing with personalized medicine, which requires the diagnostic and pharma industries to overcome not only a cultural and strategic divergence, but also a technological divergence of therapy and diagnostic. Historically, when the two industries have attempted to work together the results have been suboptimal. In one notable case, diagnostic and pharma companies agreed to co-develop and co-market a targeted therapy, but the diagnostic partner ultimately sued its pharma partner when it found out that drug reps were telling physicians that they didn’t need to use the test.

To make personalized medicine a reality, the pharmaceutical and diagnostic industries must learn to work together, as interdependent partners motivated around and by the same value proposition. Other industries have showed the value of this convergence. Take, for instance, the marriage of computing and hardware manufacturers like Nokia and Motorola, which have developed mobile-based television broadcasts. Companies such as these offer a good example of how integrated thinking and development processes can lead to coordinated, market-driving products.

Within the field of healthcare, other

prototypes of integrated development exist, such as drug-eluting stents for cardiovascular management and the integration of robotics and prosthetics. But these examples are not sufficient for most pharma companies. Time and again, executives and development teams brush aside analogies from other non-targeted drugs or other industries, asking, “What about other personalized medicines? How have they achieved this goal?”

The answer is that with only approximately 14 targeted therapies on the market across all disease areas, there are simply not enough examples from which to draw a roadmap sufficient enough to guide business practices and development decisions. Companies that wait for a well-traveled path built by their competitors will simply be the last to capitalize on the benefits of the new technology.

At present, the idea of developing and launching a test alongside a therapy is either resisted by the individual drug development teams or undertaken on an “if we have to” basis. One of the most common, self-limiting, and damaging ideas within drug development teams is the desire for a hands-off approach to a companion diagnostic strategy under the simple rationale that “we are not a diagnostic company.”

It remains to be seen whether pharma companies will acquire their diagnostic partners or continue to try and create strategic partnerships. Whatever the model, both sides need to learn how to integrate their divergent development and business models to effectively co-develop and launch personalized medicines.



Change Your Thinking

If there's anything the industry should have learned from Vioxx, Rezulin, and other highly litigated one-size-fits-all drugs, it's that pharmaceuticals developed for mass market conditions don't always serve mass markets. A drug being given to 1,000 patients that is only effective in 500 patients is not a treatment for a patient population of 1,000. It is a drug that is only appropriate for 500 patients—and while those additional 500 people may provide an early ROI, they are likely to discontinue the drug after receiving little or no benefit or, worse, experiencing an adverse event.

Personalized medicines offer companies the opportunity to shift from focusing on less precise ideas of market share to focusing on the share of patients who would actually benefit from the drug or drug class. Well-planned personalization will ensure that a drug reaches as close to 100 percent of its target patient population as possible—and more importantly, in the current era of abysmal industry reputations, only reaches the patients for whom that drug will actually be effective.

Forget the idea that segmentation results in smaller markets. Personalized medicines may actually allow a company to reach beyond those 500 patients, and potentially beyond the 1,000 treated with the one-size-fits-all drug. According to IMS Health, prescribers are more likely to use a drug that comes with a test—at a rate of 70–90 percent more than other more traditional drugs—because the test provides greater evidence of likely positive patient outcome.

Consider the case of Takeda's Actos, a PPAR agonist for the management of diabetes. In 2005, it was used to treat around 1.5 million US diabetics. According to Evaluate Pharma, the company had a 50 percent market share—putting the “hypothetical” to-



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tal patient pool at three million diabetics.

However, epidemiology studies showed that there were actually almost nine million US patients with insulin-resistant diabetes at that time, a significant percentage of whom could hypothetically have benefited from Actos. Why weren't they switched to Actos? The answer, perhaps, goes back to physicians' reluctance to switch their patients' therapies, even when they're not achieving optimal results. But the additional confidence and higher degree of evidence seen through a diagnostic test may be just what the doctor ordered. Thus, by actually segmenting the market and by treating that segment more efficiently, companies have the potential to access patient numbers that are at least similar to the blockbuster model.

Market Dynamics: The Rise of SUVs

There aren't many examples of marketing and sales strategies that showcase how pharma should promote the “test and treat” paradigm, but the introduction of sport utility vehicle (SUV)-type vehicles does provide an analogy of how a high-capital industry with long development cycles used converging technologies and segmentation to dominate a new niche.

In the early 1980s, Ford's and Chevrolet's SUVs were fully enclosed, two-door pickup trucks used mainly by outdoorsmen. American Motors (AM)

came late to the market, and didn't want to compete head-to-head against more established brands.

Instead, they saw a way to differentiate from the competition. AM designed an SUV with four doors, cargo room behind a second row of seats, and a chassis that rode high like a truck but handled like a car. Immediately, AM's Jeep Cherokee appealed to urban families. And by differentiating the product for these consumers, AM carved out a powerful new market while retaining their loyal customers, who still just wanted their standard truck or car. In 1980, SUVs held just 0.1 percent of the US automobile market. But the introduction of the Jeep Cherokee forever recreated the typical urban family vehicle, and SUVs increased their share to 3.6 percent of the market by 1989.

But differentiation can be a powerful tool, and can be used by more than one competitor. Later, Ford capitalized on AM's design changes and created an SUV with many of the same parts and the same chassis as the light pick-up truck, but used differential pricing to charge up to \$10,000 more per vehicle.

The automobile industry, too, faced a lack of direct analogues on which to predict success. At first blush, it would have seemed that, given the niche market to which such vehicles would have been marketed and the increased costs of creating such vehicles (including the ad budgets required to “educate”



consumers about the need for these trucks), this would have been unduly onerous—certainly not profitable.

Indeed, the industry spent a collective \$9 billion on advertising SUVs from 1990–2001, as reported in Keith Bradsher's book, *High and Mighty: the Dangerous Rise of the SUV*. But ultimately, the investment paid off. By May 2007, the midsize SUV represented a full 11.3 percent share of the US automobile market share, according to J.D. Power and Associates.

Market Dynamics: Personalized Med

Let's break down the components of the SUV example to understand how this strategy applies to personalized medicines.

Show how it's different The pharmaceutical industry redefines markets as drugs mature, face competition, or go off-patent by using the standard "Four Horsemen" of differentiation—efficacy, safety, convenience, and cost effectiveness. This product differentiation can result in the ability to cap-

ture greater market share, charge higher prices, deflect competitive initiatives, command greater buyer loyalty, and stimulate earlier trials and referrals of products.

It is already well understood that the simple step of differentiating your product in the crowded clinical marketplace—whether through better dosing, reduced adverse effects, or greater efficacy—can greatly increase returns for comparably small input. Personalization represents the possible Fifth Horseman, and is an effective and

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powerful tool to segment and define clinically meaningful patient populations for whom the drug works.

Lock in patients Physicians can be fickle. Research shows that their prescribing choice is highly sensitive to drug rep visits, direct-to-consumer advertising, price, and the availability of therapies with more convenient dosing schedules. Look at Fosamax, the gold standard osteoporosis drug built to last as the market leader through a series of improvements to its dosing profile to a once-weekly dosing. Even so, it lost 15 percent of its market share within three years to Actonel, when it launched in 2000 with a more convenient once-monthly dosing.

Personalized medicines can create market security to guard against these common, competitive threats. If a therapy is targeted at a specific patient group based on a particular genetic difference, it will be very difficult to substitute products, and physician commitment and loyalty are likely to be high. First entrants are likely to capture and hold onto market share to a much greater degree than one-size-fits-all drugs. And the benefits of a "targeted" lock on patients is highly likely to confer the same market security as that bestowed in mature markets on leading brands.

Accelerate adoption Research by DiMasi shows that, historically, the average time to peak sales for drugs is 4.5 years. This adoption curve is lengthened when looking at diagnostics, which historically have slower market diffusion and adoption than drugs.

The Confidence to Prescribe

Years ago, people working in the industry would talk about personalized medicine as a paradigm that would offer physicians the ability to "predict and prevent" diseases. In reality, personalized medicine today is more about "test and treat"—but even so, it's changing medicine in ways that few had imagined.

The most recent example lies with the approval of Oncotype DX, a CLIA-approved, reverse-transcription polymerase chain reaction test that predicts the recurrence of breast cancer in early-stage patients. Physicians can use the test, manufactured by Genomic Health, to determine which breast cancer patients should take adjuvant therapy in addition to anti-estrogen therapy. The test can point the way toward the most appropriate treatment, and also helps predict the likelihood of the benefit of adjuvant chemotherapy in these patients.

Certainly, the Oncotype DX test will help save lives and reduce unnecessary and expensive medication in the oncology space. But less anticipated was the impact the test has on improving patients' and physicians' confidence in their treatment plan. A recent study of nearly 90 patients who had been treated by 17 oncologists at four medical facilities found that the Oncotype DX test results increased physicians' confidence in the final treatment plan in 76 percent of the cases. (It also influenced treatment choices in 32 percent of cases.)

—Joanna Breistein

