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Morgan Moments

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TO THE UNWARY, THE JANUARY J.P. MORGAN INVESTOR CONFERENCE in San Francisco bears resemblance to a predatory feast. Like spawning salmon, drugmakers fattened by great science nudge their forward-looking statements upstream—right into the jaws of grizzly investors seeking to score an easy meal. But the big message from this year's Morgan is that, for every start-up salmon caught, dozens more are now making it past the VC bears, propelled by a powerful current of innovation to secure their own destiny in the seed pools of specialty and oncology medicine.

These smaller "stealth pharma" players, most with backgrounds in biotech, are finally beginning to show solid organic growth through focused therapeutics; diversity in the lab; and an intimate, grassroots connection to the patient. The result is what I call the "run of the breakthrough"—drug, of course. Innovative science is the driver, evidenced by the fact that many company presenters at Morgan were hard-pressed to distill all their promising trial data within the 20-plus minute time frames allowed under house rules. Such anecdotal evidence that science is back is bolstered by the latest stats from FDA, where 123 new drug applications (NDAs) were received for review by the agency in 2014, nearly three times the number posted for 2013.

In other words, the drought in FDA drug approvals during the tween years of the new millennium looks now to be over—and it's the small- to mid-size biopharma enterprise that is setting the trend. Of the 41 new drugs licensed by FDA last year, more than half (22) came from players outside the Big Pharma 10, bearing less than household names like Cubist, BioMarin, InterMune, and Amylin. Morgan thought leaders like Juno Therapeutics' CEO Hans Bishop tagged the prominence of smaller companies in the drug innovation ecosystem: while the relentless growth-in-revenue dynamic of big Pharma means they face distraction from having to pad their portfolios with follow-on drugs, start-ups, by definition, "have no choice but to focus on one new thing."

During Morgan, *Pharm Exec* took a closer look at the small biotech space, hosting a Jan. 14 Roundtable with nine US and European-based biotech CEOs. The science around the table was significant, covering unmet needs ranging from Parkinson-related psychosis and other CNS disorders to tumor suppression and antibiotic resistance. The business model of these companies is high risk because commercial advantage is sought in precisely those areas of science where big Pharma and the biotech majors have stumbled. To that end, we observed a lot of contrarian sentiment, along with an unrelenting focus on what's ahead. For example, now that the human genome has been parsed, our CEOs agreed that the inside advantage goes to those who can figure out how individual genes interact, not only as a precursor of disease but as a guide to cures.

Besides the "curse of anonymity" that comes from being small in an industry that values scale and reach, the biggest concern expressed by our Roundtable participants was the future of patient access. Surprisingly, this topic hardly surfaced in the larger discussions at Morgan. Applause for next gen PSCK-9 anti-cholesterol products and multiple new immunotherapies for cancer left no time for any clarifying dialogue on the billions of dollars insurers will have to pay for these large-population breakthroughs. It was left to George Paz, CEO of the largest US pharmacy benefit manager (PBM), Express Scripts, to suggest that the terms of engagement on market-bearing, no-questions-asked pricing and access were shifting nonetheless—and in his favor. Paz touted his PBM as a game-changing innovator—not "the middleman," a word he finds "irritating"—with a commitment to building drug plan designs that will, in the years ahead, efficiently take back many of those billions from the industry. Especially in the specialty/cancer segments, where more attention to moving script share toward the pharmacy [as opposed to the medical) benefit side, could slash spending growth rates "from the high teens to low single digits." Practicing physician oncologists, take note.

With all the talk about blossoming science, it was left to a few congenital cranks to note that new drug sales vs. the cost of capital is lower today than it was two decades ago. Yes, the economics are harsh and, sadly, therefore, the most pregnant question from Morgan was just not asked. If some of the best new science is from the small side of the industry, will innovation suffer when the race for patient access belongs to the biggest and the swift—those with the clout to match and give pause to the PBM?

You'll be able to read more about our biotech RT in our March issue.

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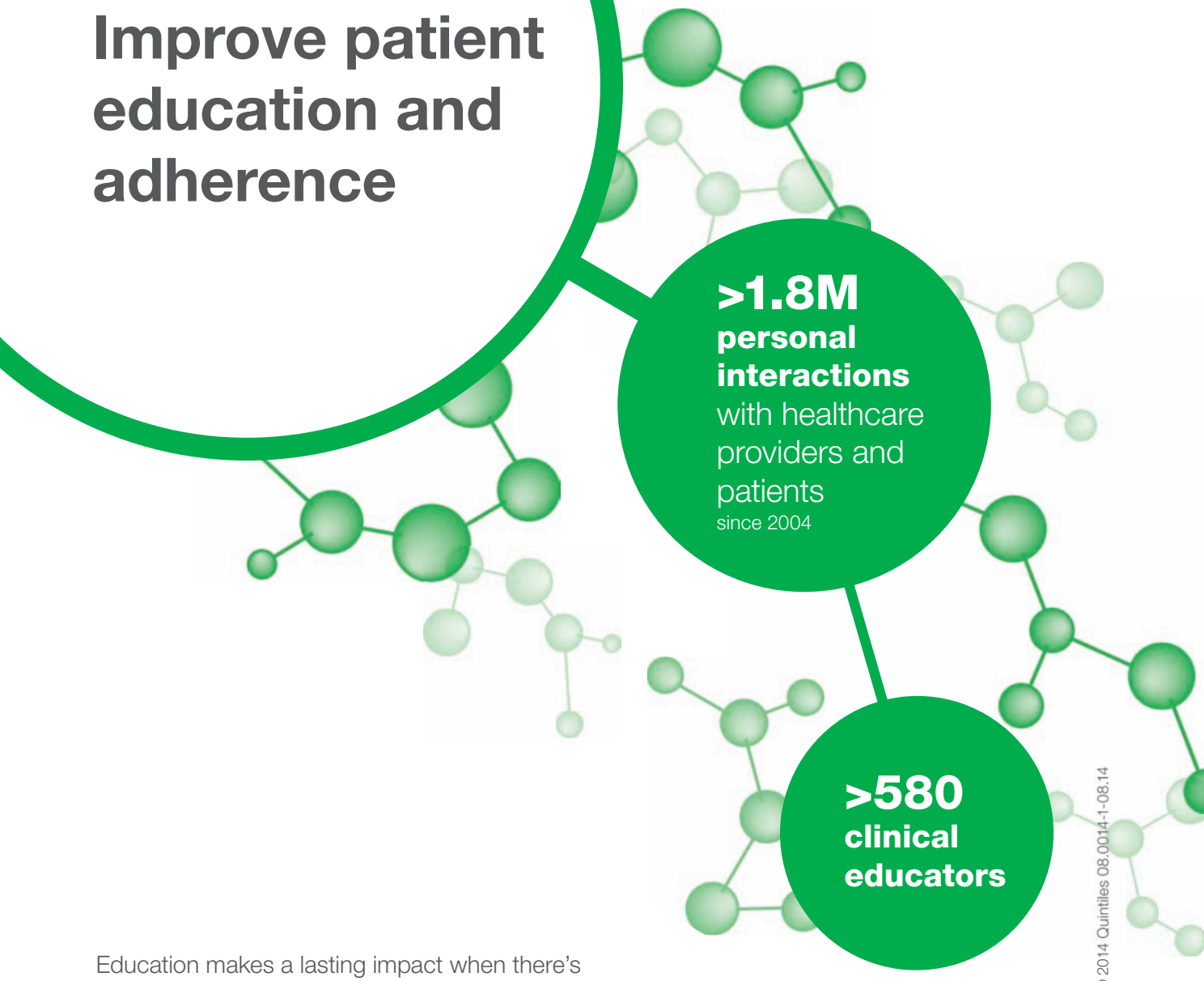

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On The Cover: iStock/Getty Images Plus

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The US drug regulatory system fails to address the country's most urgent medical needs with the resources appropriate for the task. But change is possible.

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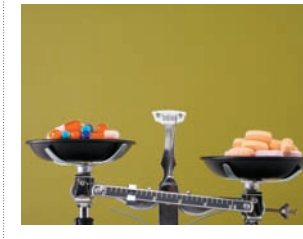

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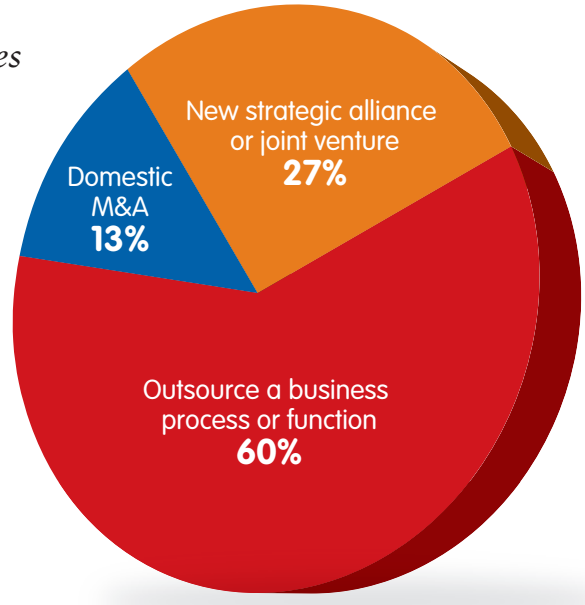
Data Point

Poll data courtesy of online *Pharm Exec* readers between Nov. 4 and Dec. 1, 2014

Q: Which of the following activities is your most important upcoming initiative?



Readers Weigh In

This is a troubling trend because it discourages patient compliance and limits the physician's ability to prescribe the most effective treatment for a specific patient. The co-mingled, high OOP cost-share programs create a catastrophic care type policy that will reduce the value of the policy and discourage appropriate medical care.

Jim Hayes, 12/09/14
"Key Obamacare Actions for Rx Manufacturers in 2015"
bit.ly/1yOgy0a

The price of Gilead's new hepatitis C drug, Sovaldi, has been the topic of much debate. Although Sovaldi cures hepatitis C in more than 90% of those for whom it has been prescribed, the 12-week course of treatment in the U.S. is $84,000, which comes to $1,000 a pill. Gilead, which spends 19 percent of its revenue on research, can profit from sales of Sovaldi.

Asif Raza, 11/25/14
"How Gilead 'Blew Out the Lights' With Sovaldi"
bit.ly/1yyOKbk

Pharma has many other roles to play in the healthcare continuum if they are willing to embrace true innovation and collaboration with providers. However, this will take incredible change on the part of pharma and removing regulatory barriers on Washington's Capital Hill.

Brad, 10/22/14
"The 'Value' of Rx's Under Obamacare"
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*Philipp Cremer, Martin Losch, and Ulf Schrader, "Driving a Transformation in Efficiency," Outpacing Change in Pharma Operations, McKinsey, 2010; Innovation and Continuous Improvement in Pharmaceutical Manufacturing, U.S. Food and Drug Administration, 2004.

Creativity Needed in Drug Pricing, Promotion

Pressure mounts for new drug payment models and greater clarity on economic evidence

The uproar over the cost of new medicines for treating millions of hepatitis C virus (HCV) patients has generated a genuine price war, as the approval of alternative therapies has upped the negotiating clout of pharmacy benefit managers (PBMs) and health plans, pressuring manufacturers to offer deeper discounts in exchange for exclusive formulary placement. The battle over drug pricing also is spurring interest in devising payment strategies that can support biopharmaceutical innovation without busting the nation's healthcare system. There has been some success with "value-based" and "risk-based" payment programs, and now analysts are talking about annuity models that spread payments for medicines over longer time periods.

Insurers are leading the attack on drug pricing, linking rising outlays for medicines to higher premiums. We "cannot sustain blank checks" to pharma companies looking to charge whatever they want, asserted Karen Ignagni, president of America's Health Insurance Plans (AHIP), at the FDA/CMS Summit in December. She noted that drugs still may be a relatively small portion of healthcare spending, but that outlays are growing fast.

One factor is soaring prices for specialty drugs. Amgen's new treatment for a rare leukemia just came out with a $178,000 treatment cost, beating the $120,000 price for Bristol-Myers Squibb's *Yervoy* for melanoma. New gene therapies carry $1 million price tags. But only about 1,000 Americans may be eligible for the Amgen therapy, while new HCV drugs are indicated for millions of patients, bringing total outlays way beyond those for cancer and rare disease therapies. Payers similarly are holding back on approving reimbursement for new, more expensive anti-obesity drugs that may be prescribed for years, and they're worried about more costly diabetes and heart medicines.

The battle over drug pricing is spurring interest in devising payment strategies that can support biopharmaceutical innovation without busting the nation's healthcare system

More competition

Ignagni urged FDA approval of more new drugs, including biosimilars, to promote price competition, and that strategy is bearing fruit. PBM Express Scripts recently announced a landmark deal for a discounted price on AbbVie's new HCV treatment *Viekira Pak* in exchange for exclusive formulary listing. CVS Health followed with an agreement to cover only Gilead's *Harvoni* and *Sovaldi*. Some doctors are unhappy at being limited to one new HCV therapy, but other practitioners seem pleased by the prospect that more patients may receive treatment earlier. Cigna said it's monitoring health outcomes of patients treated with *Sovaldi* and is finding 90% response rates, as seen in Gilead test data.

PBMs seek to improve their negotiating position further by cutting formularies. Last year Express Scripts and CVS dropped dozens of products off their lists, creating less expensive plans with limited formularies and high deductibles, which many employers find attractive, particularly for low-wage workers. And high coinsurance for specialty drugs has become the norm: analysis by Avalere Health reports that many "bronze" and "silver" exchange plans are charging 30% or more coinsurance for specialty medications, primarily to keep premiums low.

Pharma companies fear that plans with high coinsurance and restricted formularies discriminate against sicker patients, particularly those plans that put all AIDS therapies and many cancer meds in the top

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formulary tier. Manufacturers are working with patient advocates and providers to promote comprehensive drug benefits in exchange plans, as seen in comments recently filed by the National Health Council. The group urged greater transparency in formulary descriptions, curbs on limited coverage lists, and more effective "exceptions" processes for obtaining unlisted medicines.

Savings strategies

At the same time, industry is working with payers to explore innovative reimbursement strategies. At the December Summit, Mark McClellan of the Brookings Institution cited "mortgage models" to pay for drugs. Ignagni noted that plans are using bundled payment arrangements and accountable care organizations to achieve savings in cancer care. Avalere CEO Dan Mendelson is looking at programs that spread out the cost of drug treatment over several months and in ways to deal with $6,000 out-of-pocket annual maximums. He also advises pharma companies to align patient assistance programs with plans' interest in adherence and compliance to build access and coverage.

CareFirst of Maryland is testing a program that waives cost-sharing on specific drugs for certain high-cost patients that join a care management plan, reports CareFirst executive vice president Jonathan Blum, former director of Medicare. Patients signing up for coverage through exchanges, Blum noted, tend to be more dependent on high-cost specialty drugs, making it important to integrate drug benefits with cost-of-care models.

But the trend is toward more restricted formularies to manage costs in both private and public plans. And without the option of a specialty tier, PBMs claim that some costly drugs might not get any coverage at all, where not specifically required by law. Insurers generally are more comfortable negotiating discounts and rebates, especially for plans sold through exchanges where beneficiary turnover may be high. And plans appear more willing to test new payment models in Medicare Advantage plans that tend to hold members longer.

The feds were shot down last year in floating proposals to reduce costs in the Medicare Part D program by moderating requirements to cover all drugs in certain "protected classes." Those changes will re-emerge and are likely to gain more support in the next round as more consumers agree to accept less drug choices for lower prices. PE

Communicating with payers

A "front-burner priority" in 2015 for Janet Woodcock, director of FDA's Center for Drug Evaluation and Research (CDER), is to "rapidly re-evaluate" regulation of drug advertising and promotion in light of important judicial rulings related to the First Amendment. She's referring to the *Caronia* decision of 2012 and other cases that have raised questions about whether FDA has authority to block industry distribution of off-label drug information that is not false or misleading.

While marketers hope this thinking will lead to more FDA flexibility for distributing textbooks and sending information via the Internet, industry also is pushing for clearer guidelines on disseminating economic and scientific information to formulary committees, health plans, and other informed entities. The FDA Modernization Act (FDAMA) of 1997 authorized a process under Section 114 for industry to provide "healthcare economic information" to professionals, but FDA never issued guidance to implement the program, partly due to internal agency disagreement over regulation of off-label communication.

The Pharmaceutical Research and Manufacturers of America (PhRMA) issued a white paper in December 2013 urging standards for what qualifies as "competent and reliable scientific evidence" that can support economic claims—and avoid legal and regulatory action. Industry has support on this issue from a spectrum of interest groups, including oncologists and patient organizations that want access to off-label sub-population data to learn more about potential harms and benefits of treatment beyond labeled indications.

PhRMA also seeks a "new regulatory paradigm" that more broadly allows biopharma companies to share data on medically accepted alternative uses of approved medicines—albeit only with specific audiences and appropriate disclosures. Marketers want FDA guidance on how the data should be qualified and described and "clear safe harbors" for disseminating such information. In its guidance agenda for 2015, FDA includes the promotion of healthcare economic information and manufacturer communications on unapproved product uses. But both will have to compete with 88 other topics on the advisory wish list.

Prices, Patents Compete for Attention in Europe

New competition commissioner steps into the unenviable role of trying to solve two particularly contentious pharma firestorms

What attitude will the new European commissioner for competition, Margrethe Vestager, adopt to the pharmaceutical industry? In theory, the personalities of commissioners should have little influence over the way they conduct the business they are charged with. There are laws and there are procedures and there is precedent, so the margin for maneuver might appear limited. But the very nature of competition law can lend itself to subjective judgements, since complex cases often bristle with alternative— and often almost equally defensible—interpretations. There is, in other words, plenty of scope for a personal touch from the holder of that uniquely powerful and autonomous post of competition commissioner, for this is the one field of European Union law where the European Commission has unambiguous authority.

The competition commissioners who preceded this former Danish economic affairs minister certainly imposed their own views, and notably on pharmaceutical industry behavior. It was Neelie Kroes of the Netherlands who, needled by vague allegations of shady deals between innovators and generic firms, instigated the notorious pharmaceutical sector inquiry. And it fell to her successor, the Spanish socialist Joaquin Almunia, to pursue—and take the lead on—controversial decisions imposing massive fines on Lundbeck and Servier for patent settlements that they had reached with generic competitors. Almunia also continued to drive forward the annual monitoring exercise of drug patent settlements that the inquiry sparked, and he claimed year-after-year that the Commission's actions were effectively deterring pacts that harmed consumer interests.

Vestager's reputation for fair-mindedness, impartiality, and independence will be examined partly in light of how much of her time she devotes to resolving the confusion about how the Commission will apply competition rules to patent settlements in the pharmaceutical sector

Taking on Sovaldi

Vestager's first personal public intervention in pharmaceutical matters displays an even-handed approach on the hottest potato in current European pharmaceutical discussions—the price of hepatitis C treatment *Sovaldi*. Virulently industry-hostile members of the European Parliament recently challenged her on what they describe as the "menace to the financing of health systems" posed by the behavior of the product's manufacturer, Gilead, urging her to act against the company for abusing its dominant position. The new commissioner's response was to patiently demonstrate that there were no obvious grounds for an action of abuse of a dominant position. "The Commission is aware of the allegation that prices charged by Gilead in the market for some current or upcoming medicines are too high," she said. But since price-setting in Europe takes place largely at a national level in negotiations between pharmaceutical manufacturers and healthcare systems, "member states are able to exercise their bargaining power," Vestager said. In addition, she cited the European Medicines Agency's (EMA) observation that the market Gilead plays in—for hepatitis C drugs —is a rapidly moving therapeutic area, with several new classes of direct-acting antivirals now in advanced stages of development. "This would seem to suggest that this is a dynamic market," she concluded.

Patent-settlement saga

Vestager's resistance to jumping onto the anti-industry bandwagon that *Sovaldi* has set in motion among European populists was an encouraging sign to company executives, reinforcing the reputation she brought with

Reflector is *Pharmaceutical Executive*'s correspondent in Brussels.

her of a fiercely impartial politician. However, she has inherited a difficult legacy with the patent settlements controls so dear to Kroes and Almunia, and the latest annual report on the issue—it appeared just weeks after she took office—suggests that some of her officials who prepared it retain a stubborn attachment to the industry-hostile views of her immediate predecessor.

Published at the end of 2014, the report amounts to a victory cry from officials jubilant at— they claim—putting an end to unscrupulous and self-serving agreements among rival drug firms to fudge competition so as to favor their own interests at the expense of consumers and health systems. Underlying the many pages of text and tables is a presumption that if an innovator challenges a generic competitor for patent infringement, the correct course is for that case to go to court and to be settled by a ruling—no matter how long that takes and how much that costs. And if the two companies decide that it makes more sense to settle out of court than to pursue the case to the end, there is an immediate suspicion that this is anti-competitive.

The report provides extensive statistics on settlements between originator and generic companies reached during the preceding year, and some densely-argued reviews of points of law. It says it aims to identify settlements that delay generic market entry to the detriment of the European consumer—and "of particular interest are settlements that may lead to a delay of generic entry in return for a value transfer (e.g., a payment) by the originator company to the generic company." It also says it aims at giving an indication of which kinds of settlements may merit further competition rules scrutiny.

But reactions to the report reveal some deep anxieties over its content, its conclusions, and its likely consequences. Much of the information in this fifth annual report is mere repetition of earlier editions—leading some lawyers to accuse the Commission of "copy-pasting." It is also accused of banality, even vacuity—"a face-saving exercise for the Commission," said another leading lawyer in the field. Worse, it lacks clarity, say its critics. Despite reviewing hundreds of settlements, there is still no clear guidance to the industry—notably in its treatment of the concept of "value transfer." It also suffers from contradictions—simultaneously arguing that there is a general principle at stake but that each agreement must nonetheless be treated on a case-by-case basis.

Overall, the Commission is accused of continuing to create confusion in the pharmaceutical sector, discouraging companies from reaching out-of-court settlements. In this way, the exercise becomes counterproductive, say industry sources and numerous lawyers: it inhibits rather than promotes generic competition. Its ambiguities and ill-defined threats condemn many potential generic competitors to choose between the costly and uncertain option of going to court, or simply abandoning their bid to market a generic.

The response from European industry associations has also been highly critical—from innovators and from copyists. The European Federation of Pharmaceutical Industries and Associations (EFPIA) said the Commission was devoting its energies to the wrong task, and should try to remedy "the inefficiencies inherent in today's patent litigation system" instead of creating "legal uncertainty for both innovators and generics without bringing any sensible solution." The European Generic Medicines Association urged "clearer guidance from the Commission," and warned of "a disincentive for companies to challenge patents" an echo of views from its US counterpart on similar cases: the Generic Pharmaceutical Association has consistently argued that "restricting drug patent settlements is not the answer to assuring that consumers are guaranteed the earliest possible access to safe and affordable generic medicines."

Reputation tested

So Vestager faces a challenge. Her reputation for fair-mindedness, impartiality, and independence will be examined partly in light of how much of her time she devotes to resolving the confusion about how the Commission will apply competition rules to patent settlements in the pharmaceutical sector. The two leading cases—Lundbeck and Servier—are still under appeal, and the time could be right for a fresh look at the underlying issues. EFPIA has explicitly urged the new Commission "to act once and for all to tackle the root cause rather than the symptoms" of the "complex and dysfunctional framework for patent enforcement" and the obscurely-motivated competition investigations it has generated.

Her first task might be to review the public statements by the Commission about its attitude to competition in the pharmaceutical sector—which have remained unaltered (and without updating) on its website for more than a year. They contain a perceptible air of missionary zeal, along with complacent reports about the sector inquiry launched in 2008. Vestager could stamp her own personality on that as she opens a new chapter in EU competition law for the pharmaceutical sector. PE


Photo: Thinkstock

The Seven Deadly Sins of Product Launches

As more new products vie for payer and prescriber attention, the stakes around launch success are higher than ever. Here are key traps to avoid in getting things right—when it really counts

By Stan Bernard

The pharma world is currently composed of the "haves" and the "have nots." The haves recognize that the industry has transitioned from the Commercialization Stage ("Pharma 1.0") to the Competitive Stage ("Pharma 2.0") of its lifecycle and have adopted dramatically new and different ways to win. The have-nots continue to compete the same old way, effectively using yesterday's battle plans and approaches to try to win today's brand wars.

Nowhere is this more evident than in product launches. In my experience as a competition consultant, I work with companies and brand teams who consistently launch blockbuster products by leveraging Product Launch 2.0 approaches. Unfortunately, I also witness many other companies who repeatedly make the same launch mistakes. Here is what I refer to as the "Seven Deadly Sins of Product Launches."

Sin #1: Seeking to win the launch year. Most brand teams still try to "win the Launch Year" by conducting a military-style campaign. Once a company receives regulatory approval for their new product, they send waves of infantry-like sales professionals supported by heavy air promotional cover into physicians' offices to battle the competitors' beefed up front-line field forces. At the end of one year, the launch company analyzes IMS sales data to determine the ultimate trajectory of the new product's sales in that market.

Unfortunately, in today's competitive environment, seeking to win the launch year is often two to three years too late. The most successful launch teams conduct an election-style campaign by seeking to win the "Pre-Launch Years." In late Phase II or early Phase III of clinical development, these teams will initiate an election-style campaign to maximize the awareness, advantages, and advocates for their "drug candidate." They create a crescendo of positive perceptions of their new agent to ensure high customer anticipation and demand. Upon approval, doctors and patients cast their votes for the challenger agent with prescriptions to the pharmacy. Today's launch teams can typically project the ultimate sales of a new launch product 12 weeks —not 12 months—after launch.

One of the strongest examples of such an election launch campaign was Gilead Sciences' launch of its hepatitis C virus (HCV) drug *Sovaldi*. Gilead built up so much pre-launch buzz and excitement for *Sovaldi* that many physicians were withholding HCV patients from marketed treatments and "warehousing" them in order to wait to prescribe this new agent.

Sin #2: Trying to win by differentiating your product. In the majority of US Presidential elections, very few voters know the numerous details or specifics of a candidate's policies; they typically vote based on how they generally feel about the candidate and the campaign agenda. Consequently, the most successful campaign parties use a two-step campaign approach. First, they seek to convince the electorate and constituents to focus on their carefully-selected campaign platform issues, particularly the perception of how their candidate would handle these issues. Then they campaign to create the optimal perception of how their party candidate would be best at handling these issues while serving in this leadership role. Essentially, by taking the lead on the campaign agenda, they force rivals to play their game.

Launch teams that create a clear, concise campaign communication platform for their drug candidate usually perform dramatically better than those focusing on countless product details and messages.

In the current environment, pharmaceutical launch teams that force competitors to play their game—according to their own issues, rules, criteria, and timetable—usually win the game. Unfortunately, the vast majority of brand launch teams are still fixated on product differentiation. For example, over the last few years rival novel oral anticoagulant brand teams have focused first on differentiating their agents based on traditional efficacy and safety parameters. In stark contrast, Janssen Pharmaceuticals has forced rivals to play an "indication game." Their launch team campaigned first on the critical importance of demonstrating multiple indications of oral anticoagulants across diverse healthcare settings. Janssen then successfully positioned its new drug candidate *Xarelto* (which it licensed in the US from Bayer) as "the first and only novel oral anticoagulant with six indications approved by the FDA." As a result of this two-step election-style campaign, *Xarelto* became the No. 1 prescribed novel oral anticoagulant in the US.

Sin #3: Using outdated marketing tools and tactics. Many pharmaceutical companies and their partner agencies deploy obsolete launch techniques and promotional tactics. For example, numerous launch teams continue to rely on lengthy product positioning statements, product messages, and sales aids. However, in today's text-heavy, six-second video world, these protracted approaches are tuned out. Doctors, patients, and other constituents today simply cannot keep up with the overwhelming number and amount of different products, trials, data, and details. Consequently, these stakeholders form an overall perception of the different products and select the product with which they feel most comfortable.

Brand teams need to use simpler, more concise communications to convey the optimal perception of a product instead of the details. For example, Janssen used three short "i-Bites" instead of messages to promote *Xarelto* on its website and elsewhere: "proven efficacy across multiple patient types;" "demonstrated safety profile;" and "convenient oral dosing." Launch teams that create a clear, concise campaign communication platform for their drug candidate usually perform dramatically better than those focusing on countless product details and messages.

Sin #4: Focusing on traditional customers. Election strategists know that they cannot win by simply focusing on voters; they have to impact voter influencers or campaign constituents such as the media, political pundits, and major campaign contributors. Similarly, product launch teams need to focus beyond their traditional customer triad of physicians, patients, and payers to engage many other stakeholders. Stakeholders can be defined as those constituents who can influence the perception, access, and utilization of pharmaceutical products.

Stakeholder Management 2.0 consists of several key principles. First, there are numerous types of stakeholders, including but not limited to government agencies, patient advocacy groups, media, analysts, regulatory authorities, politicians, policymakers, professional and lay associations, and many others. Second, their influence can be very different in diverse competitive landscapes and lifecycle stages. For example, Pre-Launch stakeholders are often very different from Post-Launch stakeholders.

Most importantly, today's pharma stakeholders do not exist in silos but rather in a "Stakeholder Ecosystem." They routinely influence and are influenced by other types of stakeholders. Sharing of extensive product information and perceptions has been cultivated by the Internet, which breaks down traditional stakeholder silos and offers timely, comprehensive data to all audiences. The most

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successful launch teams identify, prioritize, and address the stakeholder segments and networks most vital to the launch of their and their competitors' products.

Sin #5: Not anticipating competitive counter-launches. In elections, it is typical for opponents to attack their rivals preemptively, especially early in the campaign when voters are beginning to form their initial impressions of candidates. In fact, many candidates will seek to be the first to pre-position and create a negative impression of their opponent(s), often by negative campaigning and pulling proverbial skeletons out of their rival's closet.

Not surprisingly, the same occurs in new pharmaceutical product launch campaigns. Savvy, aggressive companies—most notably Bristol-Myers Squibb and Novo Nordisk—form teams and plans to "counter-launch" against potential new products that threaten their current or future product sales and market shares. Most commonly, rivals will try to form the early first perception of a competitive product by pre-positioning the product in a negative light. Counter-launching companies may deploy many other strategies or actions to preempt new product launches, including legal, regulatory, or payer limitations on market access or specific stakeholder communications and activities.

Many launch teams fail to anticipate these counter-attacks until it's too late. In many cases, launch teams and their partners erroneously want to wait until they have completed most of their clinical trials or product positioning studies before establishing their communication campaign or product positioning. Unfortunately, competitors will not wait to pre-position their new rival. In fact, these counter-launch attacks may come as early as late Phase II or early Phase III of a new product launch. It is essential to prepare for and counter these assaults as early as possible.

Sin #6: Failure to pressure-test the pre-launch plan. One essential way to prepare for counter-launches and overall product launch success is to conduct a series of competitive simulations or business war games 2.0. The new competitive simulations go way beyond traditional war games to incorporate multiple issues, competitors, landscapes, stakeholders, and market factors. Brand teams role-play their competitors and themselves to identify not only competitive insights but—more importantly—a few prioritized strategies and executable action steps to help launch products win in the market.

The best pharma competitors start conducting these simulations in late Phase II trials or early Phase III and continue to conduct them every three to six months in key markets to ensure that the entire, extended launch team is fully prepared for both the launch and competitive counter-launches. These companies usually take a "Multi-Level Competition" approach by considering ways not only to win at the brand level but also at their or their competitors' franchise, portfolio, and corporate level. They may also use simulations for global, regional, or local markets; specific situations, such as the release of new clinical data or a major professional conference; or with certain departments/functions or stakeholder groups, such as medical affairs or payers.

Sin #7: Failing with "Launch Excellence Programs." The most egregious sin of all is companies and consulting firms that actively perpetuate and promote the first six sins in so-called "Launch Excellence Programs." Increasingly, companies are recognizing that many of their product launches have failed to meet corporate and market expectations. As a result, they hire consulting firms or initiate internal launch excellence centers to try to counter this trend. These training programs often teach and embed across the organization the very Pharma 1.0 launch strategies and tactics that caused previous product launches to fail. Consequently, many of these "Launch Excellence Programs" are in actuality "Launch Failure Programs."

Pharma professionals and brand teams that avoid or at least learn from these seven potential sins will dramatically enhance product launch success. As Malcolm Forbes so eloquently stated, "Failure is success if we learn from it." PE

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Keryx's Auryxia: Four Steps to a Successful Drug Launch

By William Looney, Editor-in-Chief

As new drug launches proliferate in the hotly contested specialty therapeutic space, companies are finding that success is often pre-determined by actions that take place very early in the development and commercialization cycle. The vital drivers of success are (1) the quality and depth of interactions with three key influencers—clinicians, payers, and the patient—and (2) harnessing the powerful integrative effects of advanced, state-of-the-art technology infrastructure. Done right, both points can help a new medicine outperform on the timelines to market launch as well as facilitating prompt take-up by practitioners in the market place—ultimately delivering strong P&L in a business where time is money. Has anyone heard of a better source of competitive advantage than this?

"The key to our winning strategy was a relentless focus on leading a niche area rather than trying to be good at everything."

—Greg Madison, Keryx Biopharmaceuticals

One company, Keryx Biopharmaceuticals, offered to share with *Pharm Exec* its own set of best practices, building on the December 2014 launch of its first compound, *Auryxia*, developed to control serum phosphorus levels in patients with chronic kidney disease (CKD) on dialysis. The company devised an integrated four-plank strategy to accelerate its go-to-market launch date, which came only three months after the FDA approved *Auryxia*, on Sept. 5. It included a set of unique clinical trial designs as well as a key opinion leader (KOL) engagement blueprint designed to anticipate the likely actions of patients, payers, and clinicians as the basis for a truly differentiated positioning for *Auryxia* in the marketplace.

In addition, Keryx implemented new cloud-based technology to support the rollout, giving the commercial teams access to customized information and supportive analytics that tackled one of the enduring flaws in traditional launch strategies: poor alignment among internal groups that are supposed to be working together to execute around a packed timeline while being ready to react to unanticipated challenges from regulators, competitors, and environmental changes in the market.

According to Keryx President and Chief Operating Officer Greg Madison, the company began developing *Auryxia* 10 years ago, yet the road to getting the drug on the pharmacy shelf—the specific preparations to go commercial—was accomplished in just 10 months. "Focus and discipline were the two management principles that helped accelerate the launch of *Auryxia* to ensure that the thousands of CKD patients on dialysis with hyperphosphatemia have a new option to help manage their condition."

Madison highlights four process innovations that the company applied to push this new medicine to market:

✓ Build a critical therapeutic niche to address an unmet need

One of the first steps Keryx took toward commercialization was surveying the physician community to uncover the needs of renal disease patients. Keryx quickly learned that good data is not enough to see uptake in the market. Instead, success starts with intelligent clinical trial design in partnership with experts and clinicians who understand the needs of patients.

Keryx strategically designed its clinical trials so it could evaluate multiple comorbidities resulting from CKD, but ultimately found that addressing a very specific unmet need within the CKD disease state would help set the company up for success and, most importantly, help patients. In this case, the niche disease area for CKD is hyperphosphatemia, or elevated serum phosphorus levels, which is often present among patients with end-stage renal disease (ESRD) since the kidneys are not able to excrete phosphate.

✓ Differentiate and provide access

A core component of any biopharmaceutical company's marketing strategy is differentiation.

For Keryx, this meant honing in on a complication in a niche disease state for which there was an unmet need. Patients with CKD on dialysis often experience elevated serum phosphorus and iron deficiency. *Auryxia* was demonstrated to be an effective phosphate binder in clinical trials. In addition to effects on serum phosphorus levels, the pharmacodynamic properties of *Auryxia* has been shown to increase serum iron parameters, through systemic absorption, which is managed by the body's gastrointestinal regulatory mechanisms.

This differentiation didn't stop with brand attributes though; it was also important to consider payer and reimbursement strategies to ensure access to the product.

"We know access to medicines today is challenging, especially in the renal market. As part of our go-to-market strategy, it was imperative that we work with payers to provide patients with affordable co-pays," says Madison. "That's why each *Auryxia* patient will have access to the Keryx Patient Plus program—a comprehensive patient services program that offers eligible patients

with financial assistance, and a dedicated Keryx case manager that provides personalized reimbursement support, including education about the co-pay and patient assistance programs."

✓ Launch with a technology foundation that unites internal-external teams

Keryx began the process of building its commercial technology infrastructure with a simple goal: to enable its field teams to compile, interpret, distribute, and communicate site-relevant information to provide a differentiated customer experience. Keryx's vice president of marketing operations, Abraham Ceesay, knew that establishing its operations in the cloud would meet Keryx's needs in a cost-effective manner, while supporting global expansion and customer-centricity goals. Keryx partnered with Veeva Systems and implemented Veeva Commercial Cloud, a single solution that pulls together customer data and analyses and processes it to create a needs-appropriate platform for multichannel interactions with compliant content, all targeted to give Keryx maximum speed and leverage against the competition.

Ceesay stressed the significance of uniting sales and marketing with technology rather than implementing a system that would impede the groups from sharing information. "Freed from the burden of legacy systems, we were able to quickly set up our commercial infrastructure the right way, the first time, with input and ownership from both sales and marketing," says Ceesay. "They were in on this project from the beginning."

Veeva applications provide Keryx the advantage of a proven, life sciences-specific solution, making it quick to implement without major customization—this proved critical to meeting its aggressive go-to-market timeline. Combined, the cloud-based technology captures all customer interactions across personal and non-personal channels, providing commercial teams with deeper insights about customer targets.

"Our sales teams can hold an ongoing conversation with the customer across all channels, for a seamless customer journey. Sales representatives can follow up on conversations or start new ones seamlessly through a physician's preferred channel using the latest marketing materials without compliance risk. And the system feeds insights from the field directly to marketing, and vice versa, for harmonized, more successful selling," explains Ceesay. "Having a complete view of the customer's experience with the sales representatives, including pre-call, in-call, and post-call activities—has helped us reorient our sales force toward greater focus on customer needs."

Eliminating the barriers between sales and marketing, Keryx's commercial cloud technology delivers a full view of the customer and enables the company to synchronize communications across channels to maximize impact and optimize resources. And, Keryx can change, upgrade, and scale the application as needed, so commercial teams remain agile and are always working on the latest innovations. Specifically, during a face-to-face visit to physicians, the sales rep is equipped to provide a full range of services immediately rather than having to follow up later. Complete results of the sales call, including any digital materials used and customer feedback, are automatically captured to update all Keryx account team members, saving time and improving collaboration. In other words, brand teams can view the interactions in the aggregate to understand the impact of messaging and related activities, quickly modifying the promotional mix as needed rather than waiting months for campaign data. The key is that customer insights are based on actual customer behavior, not derived data pulled from a survey or results from a campaign that ran last year.

✓ Go to where the talent is

But technology or software is not enough without that human touch. Motivated multi-functional teams are required internally and externally to address the demands of the product on all fronts, including commercial, regulatory, medical, as well as technology.

"Keryx took many measures to assemble the right resources and people for its teams," says Madison. "As part of its approach, Keryx expanded its New York-based operations to Boston, a hub of bioscience innovation, to attract and bring together a disciplined and seasoned talent pool capable of collaborating towards its product goals. We engaged a team that had existing experience and knowledge within renal disease. This expertise will add in value to our product launch success."

Madison concludes, "The key to our winning strategy was a relentless focus on leading a niche area rather than trying to be good at everything, including training and motivating our internal associates and fostering a high-performing culture and management style to deliver quality results. Our culture and dedication to the biology of renal disease resembles the agility of a biopharma start-up, very close to its roots. We've got to stay close to the patient due to the fact that our success will ultimately be evaluated by the impact we have on people's lives." PE

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The Hidden Costs of CKD

Chronic kidney disease (CKD) is a complex, burdensome condition that takes a considerable toll on patient health as well as costs to the healthcare system. It is associated with serious chonic conditions like hypertension and cardiovascular disease. CKD is characterized by the progressive loss of kidney function over time, until the organ can no longer remove wastes and excess fluids from the body. The result is often end-stage renal disease, which requires daily dialysis or a kidney transplant. This, in turn, can produce a long list of related complications, including elevated phosphorus levels and iron depletion. It is estimated that more than 450,000 US patients currently suffer from end-stage renal failure and require dialysis.

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The End of Pharma Marketing—or a New Beginning?

FDA licensing approval is often touted as the essential marker of a new drug's success—but what counts far more is the skill of the developer in ensuring physicians, patients, and insurers know about the product to the point they are willing to do three things: prescribe it, pay for it, and use it. Making this connection is the function of the marketer, whose arts of persuasion are being tested by intensifying therapeutic class competition, disclosure rules on promotional spend, and access and reimbursement controls driven by a selective—and often contradictory—definition of "value." In the following Q&A, *Pharm Exec* Editor-in-Chief William Looney talks to two prominent commercial marketing experts, Susan Schwartz McDonald and Sanjiv Sharma, on how this mission critical function must change to stay relevant in bringing the next generation of therapies to the patients who need them.

PE: ***Disruptive change is the central dynamic that drives virtually everything in today's go-to-market toolkit. Can you trace the evolution of how we got to this situation, where the only certainty is uncertainty?***

Sanjiv Sharma: Pharmaceutical history's "modern age" began in the 1970s when a shift from the traditional "sales model" to a "marketing model" converged with an era of exciting science. The next several decades saw a cavalcade of market-leading therapies that revolutionized modern medicine—iconic drugs like *Inderal* or *Mevacor* that have been all but forgotten by later generations of marketers who cut their teeth on the fourth-in-class therapies that followed.

The word "innovation" wasn't yet in vogue, but those days were, in many ways, the best of times.

Looking back, it might be tempting to conclude that early blockbusters of the '80s and '90s were good enough to "sell themselves," but it took genuine marketing vision to make investments in critical outcomes research and blaze the trail for game-changing strategies like DTC. Subsequent decades put marketing to the tougher challenge of promoting drugs whose margins of improvement were more nuanced, but those efforts were still handsomely rewarded so long as healthcare spending remained unchecked.

Susan McDonald: In today's more austere budget environment, customer willingness to pay for minute distinctions is diminishing, while market access trumps marketing savvy as the driver of sales. We might almost be ready to say a eulogy for the very concept of "marketing," were it not for several other equally important trends, including the growing power of the patient, the role of digital technology, and the potential for new paths or processes to speed the transition from bench to clinic. At this watershed moment, we need to be thinking hard about how marketing must be redefined to remain relevant.

PE: ***Posing questions about the "end of marketing" suggests you both are a bit pessimistic about the future of traditional practices in marketing new medicines. Is there a right philosophical and tactical approach for an industry confronting challenges like these?***

Sharma: Our question is inspired less by a sense of pessimism than by a recognition of opportunity, and at the same time, a concern that marketers may not be adapting fast enough to some of the new realities. The signs are everywhere—we're in a period of transition even more profound than that shift 30 years ago from the sales model to the marketing model. The industry is already bidding farewell to the "blockbuster" as we once defined it—i.e., drug therapy for common ailments or widespread prevention—and embracing the concept of niche market products, often priced at a much higher premium. We also know that the regulatory environment will be increasingly inhospitable to drugs that have small incremental benefits; it's clear that payers are looking for differentiating value that they can measure right out of the gate. That explains the swelling ranks of orphan drugs (nearly 200 of which could be approved in the next few years alone), and it also accounts for a new interest in drugs that work very well on only small sub-populations of diagnosed patients. Everyone understands that they need to reframe what commercial success looks like and rethink how to get there. It's not so much that we are defining unmet medical need differently; it's that we are defining solutions differently, in terms of a higher certainty of benefit or showcasing a solution that carries a unique value proposition.

"There is probably no other market with more complex mediation between manufacturer and end-user than the healthcare sector."

—Sanjiv Sharma, InflexionPoint LLC

McDonald: We actually think there is plenty to be upbeat about. One cause for optimism is the science—which ultimately drives everything. Strides in cell biology and advances in proteomics are helping us reconceive big diseases as a series of smaller targets that we aim to hit with greater precision. Science, social policy, and economics are all leading us fundamentally in the same direction—toward a new way of thinking about the drug-value proposition. "Marketing 2.0" in the pharmaceutical industry is no longer about just saying that our product is different and hoping customers will see it that way. It's very much about making it so—and then about finding our way at launch to customers with a "conversation" that actually helps create the value rather than just promoting it. All of which means we need to develop new, end-to-end processes that shape both the "genetics" of our new drugs and the "epigenetics" of the launch environment.

PE: ***What is the single most important change needed in our industry to create that value and realize the potential of "Marketing 2.0?"***

McDonald: Given that much of the marketing cycle is now focused on launches, you've got to start the discussion by talking about the "epigenetic" factors that influence the health of a brand. By Phase III, the drug development process has pretty much dealt you a hand and now you have to play it.

So what must pharma marketers today do differently? The single most important change requires a transformative, born-again credo that replaces traditional "product-focused" marketing with a "customer-focused" model. Customer focus is something that receives much lip service but is actually challenging to adopt and execute with consistency. It's not enough to just say it; you have to live it. To walk that walk, companies, need to be rethinking not only about how they go to market, but just as much, how they are organized to develop and launch their products. Customer focus is something that has to be embedded in the business culture.

In a product-focused marketing model, everything is all about you— what your product does and how it suits you to deliver your product and your message. A customer-focused marketer takes a hard look at what customers want and

need, really assimilates it, and then looks closely at his own way of operating through that customer lens. Customer-focused marketing is not just about looking for points of existing alignment or trying to change the customer so he fits your world, which has been the defining modus operandi of traditional product-focused marketing.

"The sales force has been a very good hammer for our industry, but we are starting to recognize that not every sales problem is the same sort of nail—or needs to be hit quite so many times."

—Susan McDonald, NAXION

The first thing it requires is listening to, and really hearing customers, even when what they tell you seems at odds with your conception of commercial success. Simply calling your market research "customer insight"—which has been all the rage since the start of the millennium—doesn't get you all the way there. It's what you do with the answers. People have a tendency to keep asking the same question over and over until they get an answer they like. In our travels, we've both seen many valid insights discarded or ignored because they didn't fit the marketing team's aspirational view of the market, and it seemed too hard to make good use of them. Part of the problem, of course, is that our end-user, the patient, really doesn't want to take medication. It feels like a form of bondage. Patients complain about that sense of diminished autonomy all the time and they often abandon therapy simply to regain their "freedom." As a result, we have gotten used to discounting some important things our customers have been telling us all along.

The concept of customer focus is an especially complex and challenging one in the pharmaceutical industry because we have less freedom with respect to how we "engineer" our solutions and what we say about them. And if you try to take a lesson from Steve Jobs' missionary approach to innovation in the digital space, you have to acknowledge that there is always a paradox between giving customers what they appear to want or say they want, and giving them what you know they ought to want, or what they really will want once you use innovative technology to retrain them. In other words, you have to be sensitive to the risks that customer focus, if not applied imaginatively, will perpetuate the status quo in a way that profits no one.

If years ago, we had actually listened to customers when they told us that they didn't like monthly dosing because it was too hard to remember, we'd have really missed the boat. Some people did miss it. The trick is to hear what customers want to experience since they can't always evaluate the mechanisms you are developing to get them there. That is precisely what Steve Jobs understood better than most people. Whether or not he did market research was beside the point; he knew what to look and listen for when he thought about "customer needs."

PE: ***What does "customer focus" mean in a complicated market ecosystem like healthcare, with different types of customers who don't necessarily have the same agendas or priorities?***

Sharma: By the time you get to market, the DNA of a drug is already fixed, but there is still a great deal we can do to influence the customer experience at launch and after. The question is: what and who is meant by "customer?" There is probably no other market with more complex mediation between manufacturer and end-user than the healthcare sector. Clearly both payers and clinicians continue to control market access, though in very different ways. But the single biggest change we've seen in this market is the growing power of the patient, who is now very much in the conversation, thanks to digital information and social media.

Another critical change is dwindling sales access to providers, and looking ahead, a future in which they will have less decision-making latitude than today. (We're going to set aside payers for the moment because their definition of value is relatively straightforward, even though their calculations are sometimes opaque.) The theme, of course, is clear. Information delivery is changing everything. Information is no longer just about the product; it is an integral part of the product, and it is even an integral part of the distribution system, too. That's true in just about any market we can think of.

But because we are talking about an alignment of needs between pharmaceutical marketers and multiple customer groups who interact in complex ways, we need to be thinking not just in terms of traditional product positioning—i.e., what is the most persuasive thing we can say about our product?—but rather, we need to be thinking about "value zones" drawn more broadly and more holistically, based on how the overall product proposition maps to the complex profile of customer needs, objections, and routine behaviors. It is not just about identifying key benefits; it is also about understanding and dealing with limitations in a constructive and realistic way. That requires us to look for the areas of easy alignment and—potentially even more important—pay close attention to those borderline areas where alignment in any direction could conceivably be

improved if we're willing to revisit our assumptions or adjust the solution we offer customers. Ethnographic insight on provider environments and patient lifestyles can play a key role here, but really, value-zone modeling is not about a method of research, it's about a method of thinking.

To set the stage, we have to develop a dynamic market map for every product depicting those alignments and anticipating how different customer groups will enable or impede one another. That allows us to devise a unique customer value strategy for every launch that reflects the interplay of patient, provider, and payer. Every new product needs one of those models, built on market intelligence that predicts vectors of influence and patterns of alignment across the market, because different customer groups overhear what we say and react very much to one another. This new world is multi-dimensional, not flat.

PE: ***What are the practical implications of using this kind of" value zone map" to guide launch strategy?***

Sharma: What ties it all together is, of course, communications. For marketers living in the information age, that's the critical tool in the kit. If we think in terms of customer solutions, then how and when we communicate about our product, and what sort of ongoing dialogue we have with customers, are not just tactics—they are value drivers that differentiate our brand. Everyone agrees that the patient is increasingly at the center of this ecosystem because the patient is clearly more engaged, accessing more information and shouldering more of the cost. Patients need to be made aware of options in order become activated, and they also need to find information when they leave the provider's office with a script or a recommendation in hand. The data suggest that patients are far more likely to do a drug search after an MD visit than before, and that what they learn in those searches will influence the rate of script fulfillment.

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Just as important—maybe even more so—is what happens after the script is filled. We believe that pharma manufacturers have to be thinking in terms of customer relationship management (CRM) as a strategy, beginning with the information they deliver at launch, the co-pay subsidies they offer, and the ongoing support they provide to patients in order to cultivate loyalty. Sanofi now has a chief patient officer. We believe that this sort of thinking, and the willingness to translate it into organizational structure, is critical.

One key challenge is that patients have traditionally "trusted" pharmaceutical companies less than many other information sources because they believe them to be self-interested. And it happens that the pharmaceutical industry as a whole has never done a very good job of image management. The industry has been so busy managing its relationship with regulators that it has never paid serious attention to the broader public in a way that some other industries have done. Ironically, it's partly because the pharma industry refuses to recognize that patients are as scared and resentful about drugs as they are grateful for them—again, the "bondage" idea.

But one dynamic in this new environment is the potential to redress that balance. Payers are increasingly going to take a lot of heat for "withholding" premium therapies which patients might want but can't afford. Co-pay support and patient engagement programs have the potential to change that, and help patients believe that pharmaceutical manufacturers are looking out for their interests. We don't need to be the villain in the piece anymore.

In order to make this work on the individual brand level, you've got to structure your launch in a way that optimizes the "value zone map" and then you've got to engage with patients immediately after launch to understand how the experience is unfolding for them so you can remap based on *in vivo* experience, if you need to. Even within the first few months of launch, you need to seek out patients who have failed to fill scripts or abandoned therapy to get the best shot at early course correction—whether it's access issues (including distribution), titration challenges, or critical information gaps. Companies can't be afraid of adverse event reporting here or they will miss a very important opportunity.

PE: ***Given the importance of communication as a CRM platform, what is the right role for the sales force in a new digitally enabled environment—especially since provider autonomy will almost certainly diminish in the coming years?***

McDonald: Clearly, we need to think about communications as the key to CRM with all our customers, which means we also need to rethink how we engage with providers too—not just because we're resource-constrained, but because we need to optimize their experience. As we've said, information is a critical component of that experience. The sales force has been a very good hammer for our industry, but we are starting to recognize that not every sales problem is the same sort of nail—or needs to be hit quite so many times. Personal promotion is never going to be completely replaceable in our industry, but what we are seeing now is a long overdue correction. The future of marketing in our industry requires us to think strategically about where the sales force can be most effective—for instance, in introducing paradigm shifts—and where other tools, especially digital channels, can deliver better ROI. That can mean shifting resources away from traditional selling to digital communication serving up information when customers really want it, and not when it's convenient to deliver. Several successful launches, including the first major launch in the woman's healthcare space in many years, have used that to very good advantage.

Digital selling also gives us the agility to manipulate messages and formats, and then track the results with analytic tools that link click-through messaging (patients) or online details (providers) to prescribing trends by community. Nimble communications represent a win-win that can bring customers and marketers into the same value zone. And we'll get better at it if we use digital channels as a way of learning about marketing effects, not just as a way of disseminating our messages. Digital strategies are not just megaphones, they're telescopes.

The use of more cost-effective and convenient methods of communication with customers can only become more critically important as networks become more accountable for cost of care, and individual providers themselves justify less direct investment. We are, by now, quite accustomed to pleading our case and cutting deals with payers. Once provider networks assume more of the cost and risk, we can expect a more centralized, cost-based decision-making process from them too—but structures, philosophies, and cultures will differ. It's very early days, and we need to be studying their evolution like good anthropologists so that we can decipher patterns of internal influence within, and respond appropriately. Long term, this trend may create new opportunities for influence mapping within large organizations, and inspire an approach to sales force deployment that places greater priority on institutional knowledge than specialized product knowledge. Specialized product knowledge can be delivered in a variety of ways once we know the lay of the land.

PE: ***Do the same rules apply for more specialized therapies, like orphan drugs, or in oncology, where evidenced-based principles appear to leave much less room—or need—for new ways of thinking about customer value?***

Sharma: It's true that drug marketing inhabits a therapeutic continuum from "authoritarian" science on one end to customer "democracy" and self-direction on the other. Sometimes the evidence is so clear and the clinical constraints or obligations so compelling, that marketing has only a small corner seat at the table. No one is going to argue that a drug that meaningfully extends life for melanoma or ovarian cancer patients will owe its commercial success to marketing. Even so, we are seeing evidence that drugs which extend life are sometimes being rejected by patients because the cost-benefits are not persuasive—whether the calculus is based on financial considerations or quality of life. Oncologists tell us that these conversations are occurring more often in their office, which means, in effect, that every aspect of the customer's own micro-environment will influence their experiences and their therapy choices. Information and empowerment are going to become increasingly important there too. The entire business model of the Cancer Centers of America hangs on that understanding.

PE: ***Looking back upstream, to earlier stages in the commercialization process, what needs to change there in order to get a head-start on customer-focused launch marketing?***

McDonald: In consumer products marketing, we preach the gospel that marketing needs to guide product development, not merely optimize it. And of course, it's much easier to do that with engineered technologies where more can be controlled. For years, the industry has been mindful about the potential for guiding clinical trials by using marketing intelligence to value alternative indications or endpoints, and some companies are more proactive than others, but the process, overall, has lacked consistency, discipline, and coordination. So the time has come to really walk that walk too—by shifting from a discovery mindset to an engineering mindset, where everything comes together sooner in a more coherent, systematic way. We certainly can't de-risk the process entirely, but our preclinical molecular screenings need to be more ambitious so we can really advance the best compounds with improved candidate selection and better molecular engineering.

We also need to make some critical organizational changes by restructuring our commercial and clinical functions so that they are truly integrated, not just "collaborative." Too often, there is both a commercial team and a clinical development team and the two may seem to walk down the path arm in arm but in practice, those teams are

not always thinking or seeing quite the same things.

More work also has to go into the development of a disciplined minimum acceptable product profile (MAPP) and target product profile (TPP) in the earliest clinical stages. Even Phase II profiles need to be modeled in ways that give us greater clarify of understanding around what it might mean to miss or exceed the mark. The quality of that research is often subpar for a variety of reasons: poor internal communication, poor communication with research consultants, and poor planning, among other things. Some of our newer techniques allow us to build models with smaller sample sizes but in order to take advantage of those tools, you need a team that is thinking very hard in a structure that maximizes information exchange, candor, and collaboration.

This shift from discovery to engineering mindset will also be enabled by sophisticated biomarker technology and better biochemistry screening to tailor drugs very early on for appropriate subgroups and market applications. We're going to have to think about this in reverse, by the way—not developing drugs and looking to biomarkers to confirm benefit, but developing biomarkers to guide our development path. To get full ROI on our investments, we need clinical trials strategies that shift from one-size-fits-many to a more segmented approach, in which you prove higher, or more predictable, value for smaller groups of patients. There is much talk about personalized medicine these days but at the moment, that's really a misnomer. To borrow an old marketing term, it's really about segmented medicine—deconstructing the market into clinical subgroups with biomarkers suggestive of a particular therapeutic solution.

PE: ***Does the credo of "customer focus" mean that pharma companies need to reinvent themselves more broadly to become "healthcare solutions" providers—and, if so, what scope of innovation is required to accomplish it?***

McDonald: Frustration is inspiring a lot of creative thinking about what pharma companies should really be in the business of selling. It's one thing to say that you are going to provide data and tools that support your drug, and quite another to say you are going to manage patient health solutions with a portfolio of drug and service options, including behavioral interventions. Are pharma companies properly structured and situated to design those holistic solutions, or do they really need to focus on designing the "plug-in" technologies that support broader health initiatives? Is the pharmaceutical company of the future an Apple that creates environments or an Intel that powers them?

The answer depends on whether, as an industry, we are willing to broaden our innovation mandate and make it our business, literally, to scan the environment for disruptive technologies that restructure various aspects of healthcare delivery. Once again, that kind of disruption is not going to come from bench science, it's going to come from bioinformatics.

Consider the call by the XPrize for smartphone-enabled diagnostics that match or improve on physicians' clinical assessments. That challenge is the logical extension of a trend we are already seeing among consumers: evidence of a growing appetite for information about their bodies that they can use to guide daily decisions or second-guess professional ones. Digital measurement and data modeling technologies that can routinely measure and interpret physical information blurs the line between patient and consumer—and it will extend their autonomy whether or not the healthcare system or its regulators think that's a good idea. Information, including esoteric information, gets cheaper and more accessible by the day. All the stakeholders in this system will need to think about how to organize themselves around new channels and vectors of information that bypass established authority and release patients from that sense of bondage they experience. At the top of the old-fashioned benefit ladder for consumers is control over the destiny of their bodies. We've been hearing customers say it for years but we never paid serious attention to it.

Sharma: There is an important message here for pharmaceutical companies of the 21st century. Already the big companies are leaving much of the drug discovery process to smaller, more nimble organizations. Part of their mandate needs to be scanning the environment for disruptive technologies and thinking about ways of integrating them with products they bring to market. IBM Watson-type computing has the potential to truly customize dosing, for instance, in a way that gives reality to personalized medicine. The possibilities are as numerous as the number of disruptive technologies we can spot, and the odds of success are daunting—especially in a regulated industry where optimal consumer health is the ultimate benchmark of success.

Still, this puts the onus on pharmaceutical companies at the highest level of management to be on the look-out for relevant technologies of all kinds and be organized to make the most imaginative commercial use of innovation—platform as well as product; and digital as well as clinical. This way of thinking and behaving is what we will need to get past this emerging era of Marketing 2.0 to the next quantum leap—which is quite likely to require the reinvention of the pharmaceutical company. Whatever enabling technologies drive that reinvention, we can be assured that delivery of enhanced customer experience in the very broadest sense will be both the driver and the measure of success. PE

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Meeting Unmet Medical Needs: The Disparity Dilemma

The US drug regulatory system fails to address the country's most urgent medical needs with the resources appropriate for the task. But change is possible

By Christopher-Paul Milne and Kenneth I Kaitin, Tufts Center for the Study of Drug Development

Although prescription drugs comprise a relatively small percentage of overall healthcare expenditures at 10%, they, nonetheless, represent the primary point-of-contact between the majority of the US population and the healthcare system; while 62% of Americans fill a prescription in any given year, only 8% typically experience a hospital stay. Thus, in an era of health reform, when a primary concern for decision-makers at all levels—policymakers, public health officials, practitioners—is how well our system is meeting the medical needs of the population, focusing on the role played by prescription drugs is essential.

In the US, oversight of new drug development and approval is the responsibility of the FDA. In 1997, the FDA Modernization Act expanded the agency's mission to go beyond *protecting* the public from unsafe protects, to also *promoting* public health, by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner.

While the overall number of approvals for new molecular entities (NMEs)—i.e., innovative new drugs with active ingredients never previously approved by the FDA—has varied from year-to-year over the last three decades, a concerning trend has emerged. Among the top five therapeutic areas—infection (e.g., antibiotics, antivirals), cardiovascular (e.g., hypertension, heart failure), central nervous system disorders (e.g., Alzheimer's disease, schizophrenia), metabolism & endocrine diseases (e.g., diabetes, enzyme deficiencies), and oncology (e.g., blood cancers, solid tumors)—approvals of NMEs have decreased significantly in two areas (infection and cardiovascular), remained static in two others (central nervous system and metabolism & endocrine), and increased in only one area (oncology). (See chart on facing page).

Worrisome trend

Why should we be concerned about this trend? For two reasons. The first is that the trend is not in sync with public healthcare needs. While cancer is certainly a major health problem, it is neither the nation's No. 1 health concern, nor the most urgent in terms of unmet medical needs. In contrast, infection and cardiovascular disease, two therapeutic areas representing notable unmet needs, had significant decreases in the absolute and relative numbers of

NME approvals. Cardiovascular disease is the nation's No. 1 killer in terms of overall mortality, while infection is the No. 1 threat (e.g., drug-resistant pathogens and newly emergent infections such as SARS and Ebola), with the potential to impact a sizeable portion of the US population.

The second reason for concern is that the trend runs counter to FDA's mission—which is defined by Congress, who thus shares some responsibility for supporting it. In principle, regulatory bodies should be addressing public health needs with resources proportionate to the challenges at hand—this is what agencies strive for, and what citizens should expect. If this is not being done, then agency priorities and resource allocations should be examined, and recalibrated if necessary.

The NME approval trend is perplexing, because while FDA controls how many and how fast products reach the marketplace, it is the pharmaceutical industry that controls what drug candidates enter the development pipeline. The two therapeutic areas that have remained static in recent decades—CNS and metabolism & endocrine—represent areas with substantial market potential (e.g., mental health was tied with cancer as one of the four most costly conditions in the US during the decade of the 2000s, whereas by the end of the decade, diabetes topped the charts with $40 billion more healthcare costs annually than cancer). Despite the enormous market opportunity, however, the number of NME approvals in these two therapeutic areas has been static, in each area equaling only half the number of oncology approvals. At a time when there is increasing availability of prognostic and diagnostic technology available for CNS disorders, as well as drug delivery and drug-device innovations in metabolism & endocrine diseases, the continued dominance of oncology, at 30% of the pipeline, is both economically and medically out of balance.

Top 5 Therapeutic Areas for NME Approvals

	1984 – 1993	1994 – 2003	2004 – 2013
Anesthetic/Analgesic	30	31	N/A
Anti-Infective	58	77	35
Cardiovascular	69	71	36
Central Nervous System	25	34	28
Oncology	N/A	46	60
Metabolic/Endocrine	N/A	31	25

Comparing the number of new molecular entity approvals during three time periods.

Economic dictates of supply and demand, and what the market will bear, explain some of industry's high level of interest in oncology drugs. Over the last 10 years, the average price for oncology treatments has risen sharply. While high prices act as a "pull" incentive for oncology research and development (i.e., they increase the likelihood of sufficient return on investment and thereby act as an R&D incentive), regulatory initiatives aimed at speeding development and review times serve as equally powerful "push" incentives (i.e., they lower the financial and logistical barriers, and reduce the risk of entering the field of research).

Regulatory bodies should be addressing public health needs with resources proportionate to the challenges at hand—this is what agencies strive for, and what citizens should expect

Another reason for industry's focus on oncology is that the enormous investment in basic research by the National Institutes of Health and other funding sources has led to greater understanding of the pathophysiology and genetic mechanisms of many cancers, which provides exciting new and fertile areas for commercial product development. Also, the field of cancer research, over the years, has benefitted from a very effective patient advocacy movement. The American Cancer Society, for one, has been described as "the single most effective disease-based lobby in American pharmaceutical regulation."

Regulatory spark

The regulatory environment has had a substantial impact on the introduction of innovative new medicines in certain therapeutic areas. Over the past 25 years, a large number of regulatory initiatives have been implemented to speed the development and review of drugs for life threatening and severely debilitating medical conditions. As one would expect, drugs to treat cancer have been some of the major beneficiaries of these initiatives.

It's not surprising that at a time when the out-of-pocket costs to develop a new medicine exceeds $1 billion, many companies would be drawn to areas that receive favorable regulatory treatment. This has certainly been true in oncology. In the 2000s, oncology drugs represented 32% of all priority reviews (i.e., those drugs considered by the FDA to offer important therapeutic gains, and receive a six month review time, compared to 10 months for standard drugs), 53% of all accelerated approvals (i.e., drugs eligible for conditional approval based on surrogate, or indirect mea-

sures of benefit), and 50% of all fast-track designations (i.e., breakthrough drugs that receive increased access to scientific interaction with the FDA during the development period). In sum, oncology drugs received 45% of all FDA special program awards (i.e., priority review, fast-track designation, and accelerated approvals). The relationship between regulatory initiatives designed to speed access to important new medicines, and industry's focus on oncology is supported by the fact that if you look at the number of oncology approvals during the 10-year period before FDA's special regulatory programs were implemented (1984 -1993), oncology was not even in the top five therapeutic areas for approvals.

There is a critical need for public debate about what our R&D priorities should be; the FDA should then be authorized to use special regulatory programs to incentivize companies to focus efforts in these areas

Unfortunately, it is a zero-sum game. FDA has often voiced concern that it has been asked to do more over the years without a commensurate increase in resources allocated by Congress. Sometimes, as FDA itself has pointed out, this imbalance results in performance deficits in one area of responsibility to the detriment of another. Nonetheless, change is possible. For example, under the Generating Antibiotic Incentives Now (GAIN) Act, antibiotics intended to treat drug-resistant pathogens may be eligible for several incentives, including fast-track designation and priority review, as well as five years of market protection from generic competition, once approved. Just two years since passage of the GAIN Act in mid-July of 2012, industry participation in the program has been robust, with 52 designations awarded for 35 unique molecule development programs, according to FDA's Blog. Regrettably, however, not every disease area can have its own GAIN Act. Political will and patient and public advocacy are often lacking, and resources at the FDA are finite.

Two steps toward change

To address a broad swath of unmet medical needs and to boost innovation in those areas, we offer the following two-step policy recommendation. The first step is to create a National Commission on Medical Priorities. The Commission would be comprised of experts from government, academia, industry, and the medical establishment, and its responsibility would be to assess the country's immediate and long-term health needs, and review the innovation landscape to determine whether current public and private R&D efforts are appropriately focused on those needs. One of the beneficial outcomes of the Commission would be to spark a national debate and raise public awareness of this country's most urgent medical needs.

The second step is to create within the FDA an Office of Special Regulatory Programs. The new Office's aim would be to design and implement a prioritization process to determine which drugs may be eligible for one or more of FDA's fast-track programs, thereby garnering a greater share of the agency's resources. The prioritization process would triage new drug candidates based on level of unmet medical need, using the recommendations of the National Commission on Medical Priorities as a guide. To help subsidize these activities, sponsors of candidate drugs would pay an application fee to the FDA. The application would explain why the drug candidate should be considered a priority, and why it deserves to receive special attention by the agency. If the new Office determines that a drug candidate is eligible for one or more of FDA's special regulatory programs, the sponsor would be exempt from paying any additional application or user fees. It is likely that drug sponsors would be attracted to such a program, because it would provide an opportunity to receive FDA attention and advice during the development process, and an expedited review of the new drug application, ultimately leading to quicker time to market.

Despite the enormous public and private investment in R&D to bring new drugs to market, there are urgent medical needs in the US that remain unaddressed. In fact, in disease areas associated with some of the highest levels of morbidity and mortality (e.g., cardiovascular disease), the number of innovative new medicines approved over the last three decades has actually declined.

To address this deficit, there is a critical need for public debate about what our R&D priorities should be, and then the FDA should be authorized to use special regulatory programs to incentivize companies to devote resources and focus their efforts in these areas. The creation of a National Commission on Medical Priorities, to identify areas of urgent medical need, and an FDA Office of Special Regulatory Programs, to ensure that those drug candidates that address those needs benefit from FDA's fast-track programs, would be two important steps in the right direction. All that is required to affect such change is political will and public support. PE

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Biosimilars: Finding the Right Path to Differentiation

How will companies market similarity in a way that differentiates from the innovator brand? Customer experience may be the key

Biosimilars are coming. How will biosimilar value-added marketing measure up to the innovator behemoths? Value needs to extend far beyond modest price reduction and will be measured by a unique set of expectations coming to the US.

If you're planning to bring one to market, claiming a coveted share of the $169 billion biologic market[1]—of which biosimilars are forecasted to reach up to $35 billion by 2020[2]—will mean stretching beyond conventional practices. It's a new frontier that requires a shift in both approach and mindset. For those planning to market a biosimilar, the types of strategies that may have served companies well in the past with small-molecule generics will likely need retooling to effectively compete.

A challenge at odds with itself

Marketing a biosimilar brings a unique set of challenges, the most fundamental of which feels like a contradiction: On the one hand success depends on proving similarity; on the other you've got to differentiate to win. This requires a stepwise approach—first you have to fully establish similarity in the minds of physicians in order to gain receptivity to discussions about differentiation.

As marketers, we've been conditioned to quickly get across our point of differentiation. But doing so too fast with a biosimilar can lead to tune-out if you haven't passed the first hurdle on similarity.

Establishing trust

Education is a big part of shoring up trust in biosimilars. Although awareness and familiarity with biosimilars among physicians are increasing, there is still much work to be done on the education front—particularly since these levels vary quite a bit by specialty and by country. According to a survey conducted by the Alliance for Safe Biologic Medicines, most physicians, while "familiar" with biosimilars, have only a basic understanding of them and many can't tell you what one is. That signals a lot of market conditioning to be done as the patent cliff for major biologics looms.

Biosimilar marketers and their agencies need to push well beyond competitive parity with the experience they deliver

And while willingness to consider prescribing a biosimilar—which is likely tied to familiarity—is growing year over year, according to a recent US and pan-European survey among rheumatologists,[3] the reasons cited for not considering them include barriers that can be overcome through fundamental education: doubts about purity, questions relating to clinically meaningful differences in efficacy, immunogenicity, and other safety concerns.

These underlying reasons for doubt and concern are very much different versus a new molecule or mechanism of action, and market conditioning needs to reflect that. Creating a communications plan that effectively preempts concerns and instills confidence in what clinicians can expect of your biosimilar in clinical practice is essential. It requires that you keep your finger on the pulse of shifts in awareness, perceptions, and attitudes on a near-constant basis.

The good news is that physicians are quicker to extend their trust about a biosimilar to companies that have a long-established history in a particular category. So if you've got an established heritage, be sure to leverage it. If not, be prepared to invest more heavily, as it may require greater effort and resources to secure trust.

'If it's the same, why should I prescribe it?'

This is where companies need to get creative and really stretch. Most likely you're going up against an innovator biologic heavyweight that's not only tried and trusted, it already comes with a virtual treasure trove of value-added programs and materials for patients. Take, for example, AbbVie's *Humira*

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(adalimumab), Amgen's *Enbrel* (etanercept), and Sanofi's *Lantus* (insulin glargine). These companies have all invested heavily in relationship-building in the medical community as well as development and deployment of patient support resources.

Hence, "If it's the same, why should I prescribe it?" is a fair question. And, given that you're not likely to meet the 50% to 70% reduced-price expectation of a generic or a 1st or 2nd-tier formulary status in the US that comes with little or no patient co-pay, you've got to offer a differentiated value proposition (and don't expect physicians, payers, or consumers to go easy on you with something soft). This is where commercialization planning and marketing get exciting.

Unless your financial targets are set at a commodity level, delivering marginal benefits won't be enough. Biosimilar marketers and their agencies will need to push well beyond competitive parity with the experience they deliver. Value expectations are high in biosimilar categories and higher still where entrants may include biobetters. The value delivered needs to be genuinely transformative—helping healthcare providers to deliver better care that improves outcomes and/or significantly increases patient satisfaction.

Finding a different approach to differentiation

Embracing the catalysts that can lead to transformational differentiation is an important first step for biosimilar brands. Consider, for example:

- Expanding the inner circle of idea generators to include thinkers who can offer forward-looking perspectives on the emerging and near-future world of health management. This includes health-tech thought leaders and, in some cases, healthcare futurists—both of whom can more quickly see opportunities for truly differentiated value solutions.
- Partnering with innovators in the field of market research discovery to help reframe how brand teams look at customer problems. Traditional research framing leads to predictable learnings, which, in turn, puts brand teams on a path to fall back on marketing models not geared toward the complexities and demands of biosimilar markets. We've got to learn to do things differently starting upstream in the strategic planning process.

While there aren't clear-cut paths that lead to success for biosimilars in general, there are areas of exploration from which success is likely to rise.

Differentiation needs to play out on a better experience

One prospect for differentiation is improvement to device delivery technology, which FDA guidance on biosimilars clearly allows for. Because biological molecule size usually requires that it be delivered via injection, opportunity exists to improve upon the innovator product's delivery device without affecting the safety and efficacy. Since the device is often a major component of the daily patient experience—particularly for chronic conditions such as diabetes and rheumatoid arthritis—this can represent a compelling point of differentiation for your biosimilar brand.

Technology-based experiential differentiation can, of course, be extended to support services, too. The near-daily advances in the health-tech space offer a vast range of possibilities that can serve personal health management needs from next-generation wearable gear to "smart" at-home health monitors. Partnership with the health-tech community is just another option to deliver a differentiated value experience.

For most biosimilar manufacturers, meeting the ever-increasing value expectations will require new strategic planning models. It's not about abandoning the models that have led to success in the past; rather it's about adjusting the formula to identify ways in which differentiated value can be delivered. From the marketing research perspective, this means not only assessing customer wants and needs very differently, but also from new vantage points. For example, taking a more holistic view of the end customer—zooming out to look beyond the patient-only aspect of their experience.

The expectation of customers today is that the value experience will be highly personalized. Often this involves bringing culture to the forefront in order to provide a very different foundational context both to understand patient beliefs and behaviors and influence them. In taking a more holistic approach, marketers are able to deliver differentiated value solutions that help patients fit the condition into their lives, not their lives into the condition. This is where the bar is set and, for many conditions where biosimilars are in development, there is tremendous opportunity to deliver on this expectation.

Winning will take fortitude—and more

Reportedly, there are currently more than 700 biosimilars in development by a diverse range of companies spanning big pharma to major generics companies. And with some innovator biologics having up to 20 or more biosimilars in development, there's no doubt competition will be intense. Beyond navigating the legal and regulatory uncertainties, which is no small feat, winning will require significant resource investment as well as a strong commitment to differentiate in new, innovative ways. PE

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Adapt or Die: Leadership Lessons from the Battlefield

The Army General who led the Iraqi 'surge' campaign cites nine lessons that pharma leaders can apply in today's come-from-behind struggle for market share

I have been privileged over the past several years to be associated with senior executives from the pharmaceutical industry. I have been impressed by their passion and commitment. They have an intense desire to do well and to make a significant contribution to our society.

The pharmaceutical industry is essential to the innovation that leads to new cures and treatments for patients worldwide. I find myself amazed when I research your organizations and discover the sheer number and scope of medicines that you are bringing forward at great risk and significant up-front cost. You make a difference everyday, and I am sure that alone is very rewarding. It is important to our nation that the pharmaceutical industry continues to thrive. I am convinced that a key element of this is effective, adaptive leadership.

I have been blessed to be a leader at many levels. I graduated from West Point in 1977 and embarked on a 35-year military career, culminating in command of all the US Army installations, representing a annual budget of $12.3 billion and with responsibility for the welfare of some 120,000 staff. I commanded a division in combat in Iraq as part of the Bush Administration's troop surge initiative, as well as the largest operational force in the US Army when I commanded III Corps and Fort Hood Texas. I went to West Point because I couldn't afford to go to school anywhere else. When I left the Academy, I was convinced that I was only going to be in the Army for five years. That five years changed to 35 years, because it went from being a job, to a profession, to a passion. I loved the opportunity to lead folks in the accomplishment of important work. In the military, that work was our national security. It was protecting our freedoms and our way of life. In your business—pharmaceuticals—it is guaranteeing our future by focusing on our health and well being.

When I retired from the military, I decided to write a book that would capture my leadership experiences and lessons learned. I took 35 years in the Army and four years at West Point and condensed it to nine leadership principles, with a focus on faith and family. The book is entitled *Adapt or Die: Leadership Principles from an American General.*

Adaptive leadership is relevant to all segments of society, but it is especially critical to the pharmaceutical industry. It is imperative to build adaptive leaders and adaptive organizations. In today's environment, circumstances change almost continuously. Resources that were counted on are no longer available. Weather, war, natural disasters all impact what we are doing day to day.

I tell folks in my public presentations that if you slept well last night, you're not paying attention. We are a nation at risk. Just look at today's newspaper. The terrorist organization ISIS is growing. They are well resourced and well equipped, and they reject our freedoms and our way of life. Russia is threatening Eastern Europe. We have domestic terrorists amongst us who are trying to destroy our society.

The pharmaceutical industry needs adaptive organizations—and adaptive leaders to run them

A world of change

The pharmaceutical industry is highly volatile. When I was at the US Army War College, we talked about a world that is VUCA (volatile, uncertain, complex, and ambiguous). That defines what your business is about. Today, yours is close to a trillion-dollar industry worldwide, which rivals energy. There is a steady shift to technological advances. Delivery of care methods are changing. Electronic medical records are evolving, and the data in such records may eventually be accessible to the patient directly through wearable devices or skin implants. Availability of healthcare is changing, with recent policy changes leading to greater demands. Global markets are changing, driven in large part by an aging population. There is greater competition. Evolving business models are leading to strange bedfellows. It takes 10-12 years to bring a drug to market, at high cost: $2.3 billion on average. And there is always the looming "patent cliff,"

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when branded drugs come off patent and open up the door for generics. Taken together, what this means is the pharmaceutical industry needs adaptive organizations and adaptive leaders to run them.

The title of my book was carefully chosen. In the military, if leaders and organizations didn't adapt, folks literally died. In corporate America, if leaders don't adapt, organizations will self destruct—the analogous experience of "death in life."

Nine ways to lead

I don't want that to happen to our nation's pharmaceutical industry. What you do is too important. In that vein, I offer up some observations to enable you and your organizations to be more adaptive.

Terms of engagement. Engaged leadership is critical. It is really all about the people. Leaders should love their subordinates like they love their own children. The pharmaceutical workforce deserves leaders who care, who give colleagues the predictability that allows everyone to contribute their best and perform with confidence. But today's pharma CEO must ask intrusive questions to learn more about the workforce. It is critical to remember that leaders must be careful what they ask. There is no such thing as a casual conversation if you are a leader. If your employee tells you something based on your question, they expect that you will respond by doing something.

Strength in stability. Anyone who works for an employer five days, every week, deserve predictability. Constantly changing rules is a severe degradation to workforce morale. Leaders must protect their employees from changing circumstances, and give them as much freedom to thrive as possible. Before things are changed, leaders must analyze the impact of that change. I find much of the turbulence inside a company is self-inflicted.

Leaders must focus on opportunities, not obstacles. They must maintain a positive attitude even in times of crisis. They must search for the "silver lining" behind every unforeseen event. They must shield their workforce from any problem, and turn every event into an opportunity and not an obstacle.

Leaders must demonstrate work-life balance. They must show their employees that it is OK to focus on their families. It is possible to both work hard and play hard. It is all about time management, and focusing on important things. While on active duty, I was called the Family First General. I placed programs in place to force folks to take advantage of available time. I demanded that everyone be allowed to go home for dinner, by 6 p.m., and to leave at 3 p.m. on Thursdays to have more time with the family, and not to work on weekends except with my approval. It caused everyone to be more efficient with how they spend their time at work, and gave everyone much-needed time with their families.

Decision time—why rush? Leaders must decide when to decide. Too many times leaders make rash decisions, merely because they do not want to appear to be indecisive. The first decision a leader must make is when does the decision have to be made. Decide when to decide first. Then take advantage of all available time to research the decision, seek input from everyone involved, and talk to folks about the idea in advance to see how well it will be received. Don't rush it.

Downward mobility. I am convinced that leaders must look down, not up. Too many folks spend their work days trying to impress their boss. They ignore their employees. Your employees will take care of you if you take care of them. Focus on their needs, on their welfare. They will surprise you with what they can get accomplished.

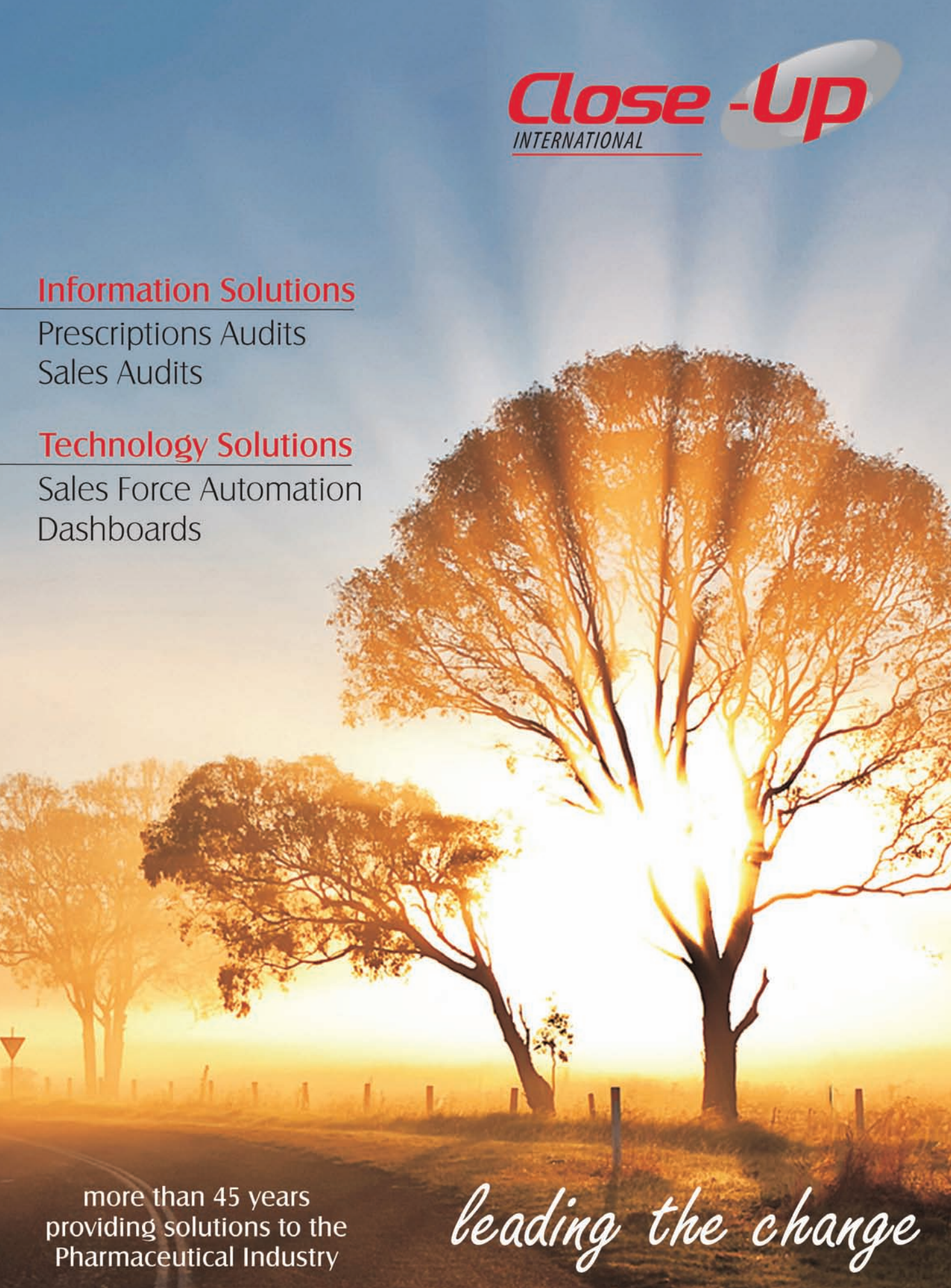
Demand, don't demean. In order for an organization to be high performing, leaders must be demanding, but not demeaning. It is OK to demand adherence to high standards. When goals are accomplished, do the appropriate recognition and then "raise the high bar." Also, set goals that are just beyond reach to motivate increased performance. However, leaders don't need to be demeaning to do that. There is no need to belittle someone, to rant and rave, or use profanity. Be nice, but ensure the work gets done.

Open communication. Make it a point to have an effective counseling program in your organization. Require leaders to routinely sit down with their employees and discuss job performance. This has to be done at least quarterly. Tell folks how they are doing and what you expect of them. If they meet or exceed the standards, recognize them. If they fail, give them additional training or coaching to try and improve their performance. If they still fail, then let them go.

Seek a supportive mix. Leaders should always celebrate diversity. Not just social acceptance, but true celebration. Take a close look at who is in your "inner circle." If they look just like you, you are limiting yourself. True, it is easier to surround yourself with folks who act like you and think like you. However, all you get from such people is a reflection of yourself. Intentionally surround yourself with people from different age groups, genders, races—all have something distinctive to offer.

Mentee, mentor. Companies that have a vibrant mentor program do well. Everyone should have a mentor, and everyone should be a mentor. It is how companies grow and flourish. I believe the definition of a mentor is someone who has three characteristics. They are accessible, they listen well, and they truly care. Encourage your employees to seek out mentors. Have them determine what they would like to do as they progress in the company, and then pick a mentor who has already achieved those goals. Encourage your employees to be a mentor. Rarely have I seen formal mentor programs succeed.

Have a blast. Leaders should have fun. If the leader isn't having fun, no one is having fun. When people are having fun and enjoy what they do, they are more productive. They look forward to coming to work. If you look closely at the companies that people most like working at, they all have programs to encourage having fun. PE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ARGENTINA
Beating the Cycle

Argentina has experienced six severe economic crises since the great depression, and as a result, Argentinians have become excellent problem solvers. With extensive scientific and engineering expertise, creativity and ambition, the industry has established a pattern of strong growth in times of plenty, and minimizing losses during periods of inflation and recession, in effect "beating the cycle." Along the way, the top Argentinian labs have developed into a powerhouse pharmaceutical industry that rivals the multinational sector domestically, and has taken a position of leadership in markets across the region.

A LOCAL'S MARKET

Truly diamonds in the rough, the top Argentinian pharma and biopharma laboratories are forces to be reckoned with wherever they do business. "Argentina is one of the few nations worldwide that has a domestic pharma industry that dominates the international pharma sector in terms of revenue; seven out of the ten top firms are Argentinian, and 60 percent of the market value is sold by Argentinian laboratories," explains Francisco Cervo, the general manager of Elea. Patrice Fuster, the general director of Sanofi Argentina, clarifies that these national companies "are not nationals in the traditional sense, as they are giants; they are regional

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companies, exporting their products around the world. They have an extremely strong presence and are very competitive in Argentina, and their brands are incredibly strong." One of these domestic giants, Roemmers, stands significantly above the rest, with more than nine percent of the market, nearly twice that of the next highest grossing competitor, Bagó. Argentia, a company of the Roemmers group led by Esteban Echenique, entered the nutraceutical market after the acquisition of Metabolic Cla and recently incorporated Menarini's products into their portfolio, another example of the dynamism of the Roemmers Conglomerate, lead by Eduardo Macchiavello, CEO, Roemmers. Echenique explains their strategy : "to focus on chronic products, the cardiology area mainly focused on antibiotics, and with our cardio branch our market share grew from the 13th largest to the 8th (and climbing) at this point in time." Argentia is the fastest growing company in the IMS ranking of the 50 biggest companies in Argentina.

This market is also unique within the region, as it has developed as a branded generics market with very low pure generics participation, at just ten percent according to IMS, the lowest level in the region. Norberto Bonaparte, the founder and CEO of Close Up International, explains that "until 2002, physicians could legally prescribe a specific branded product, and today a brand name is usually included alongside the generic name on the prescription." As such, "most labs carry out extensive and dynamic marketing strategies and actions," according to Bonaparte, and Eduardo Neira, country president for AstraZeneca Argentina, says Argentina has a "consumer driven market that pays more interest to brands rather than new molecules," because the brand is seen as a "stamp of quality."

ARGENTINA IN FACTS & FIGURES	
Population (2013)	41.45 million
GDP (2013)	USD 609.9 billion
Total Healthcare spending (2012)	8.5% of GDP
Annual Retail pharmaceutical spending (October 2014)	USD 6.1 billion
Pharmaceutical plants	110
Foreign owned Pharmaceutical plants	17
National Labs share of total market (2014)	57%
OTC share of total market (2014)	10%

The significance of brands to the Argentinian consumer, and the strength of many of the top Argentinian brands, has limited the ability of multinational companies to penetrate the market on their own. According to Ernesto Felicio, the executive director of the research-based pharmaceutical industry association CAEMe, which is celebrating its 85th anniversary in 2015, there has been "an increase in joint initiatives between local and international companies" in recent years; many of these joint initia-




From left: Esteban Echenique, General Manager, Argentia, Alberto Alvarez Saavedra, President, Gador; Luis Rodriguez, Director General, Gador; Francisco Cervo, Director General, Elea

tives have taken the form of product licensing and co-marketing agreements. Mariano Sanchez, lead healthcare partner at KMPG Argentina, explains "the increasing prevalence of distribution and licensing agreements between multinational and Argentine laboratories" is the result of several policies that caused local labs to build "better distribution and marketing infrastructure and [made] investing in manufacturing capabilities in Argentina" less attractive to outside investors.

In today's market, "multinational companies often want to launch products in countries like Argentina, but lack the sales force to properly market the products," Cervo explains. "Since only the top five or six firms have sufficiently large sales teams," he continues, "there are only a few competitors for this [co-marketing/licensing] business that we must contend with overall, across all therapeutic areas." The demand for local partners is so great, that for Gador, "in Argentina, nearly 40 percent of our sales are licensed products at this point," according to the company's general director, Luis Rodriguez.

PHARMACEUTICAL EXCEPTIONALISM

"The pharmaceutical industry has been one of the most dynamic sectors in the Argentinian economy, and is now an engine of economic growth, employment, scientific knowledge and applied technology," says Alfredo Chiaradia, the general director of CILFA, the chamber of Argentinian pharmaceutical industry that recently celebrated its 50th anniversary. "Pharma in Argentina comes from a very rich and deep-rooted tradition, triggered by the early emergence of many national family businesses, many of them now over 100 years in the country. All that was achieved in spite of the frequent volatility associated with the evolution of the economy at large." Janssen's finance director for Janssen Latin America South, Alejandro Smolje, assures that this pattern still continues, saying "in spite of the country's often volatile economy, the industry has enjoyed adequate growth over the past few years."

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From left: Emb. Alfredo Chiaradia, Director General, CILFA; Ernesto Felicio, Executive President, CAEMe

While the industry has outperformed other sectors in recent years, Mariano Sanchez, the partner in charge of healthcare at KPMG Argentina, points out a few external and structural factors that have contributed to the industries success. "Following the crisis in 2001," he explains, "a significant number of multinational pharmaceutical companies started to sell their production facilities in Argentina," and a few years later the government "put in place the controls on imports that we see today, and instituted the 'national preference' policies in many parts of the healthcare industry." As a result, "some of the larger local companies were able to acquire high-tech manufacturing facilities from multinational companies at liquidation prices, and then were given a privileged position in the market and protected from foreign competition." The pharma industry also benefits from several other governmental support measures, including low rate investment credits awarded for Argentina's bicentennial in 2010 and scientific, engineering and financial support for R&D from the ministry of science and technology, and the national research council (CONICET).

Offsetting these measures of support however, are the price controls on pharmaceutical products, which have not adequately taken into account the effect of the country's high inflation rate. "For several years, the price of pharmaceutical products in Argentina has been lagging behind the increase of prices of everything else (raw materials, salaries, etc.)," says Juan Pablo Bagó, the general director of Grupo Bagó's pharmaceutical business in Argentina. "With the inflation rate of around 25 to 27 percent per year [over the last four years], prices of medicines have only increased by an average of 14 percent per year," Bagó explains. With profit margins being squeezed, quarterly price negotiations with the ministry of economy and public finance led by Augusto Costa, the secretary of commerce, are of critical importance for vendors, and the chambers representing the industry in these negotiations—CILFA, CAEMe, and COOPERALA—have seen their responsibility increase substantially. However, Daniel Varde, Deloitte's head of healthcare and life sciences for Latin America, notes that while margins "have been shrinking, they are still reasonable," because Argentinian "prices are quite high relative to other countries."

However, as Varde also admits, "surviving in this environment has forced companies to overhaul their strategy, so that they can effectively reduce costs, or at least limit their growth, without losing revenue." Furthermore, he argues that while reducing costs, "it is critical for companies to grow their revenues by launching new products and developing more exports," which provide the added benefit of revenue diversification. However, he also points out the fact that developing these revenues means "there are R&D, registration, and marketing costs that cannot be cut and in some instances, must be increased in the short term." Accordingly, several CEOs have quoted aggressive goals for export growth, with Lab Richmond aiming to exports from 14 to 50 percent of revenue in the short-term, Gador hoping to increase substantially from 20 percent, and Bagó planning on reaching 75 percent from their current level of 45.

The OTC segment is another area that holds a lot of potential for growth in the Argentinian pharma market, as this segment only accounted for 10 percent of total retail revenues in 2012. Bagó says that the share of OTC products will "increase on an annual basis," and that "the current market situation is not due to regulation," but the fact that "very few companies are currently focused on the OTC market." German Heiken, the general manager for Genomma, agrees, and points out "companies like us, mainly focused on OTC products, are quite rare in Argentina." Bagó sees this gap in the OTC market as a key opportunity for the firm's growth, and as such the group is "investing more than ever in this type of product," and he is confident that "in the near future OTC will be definitely one of our leading lines in the Argentinian pharma market."

HEALTH & PHARMA "ARG-ECONOMICS"

Consisting of a patchwork of overlapping insurers, providers, and often-inconsistent systems, the Argentinian healthcare system is closely entwined with the local industry and the incentives of multinational players. In reality, the system is fragmented along more than just geographical lines as there there are three separate systems of healthcare providers: the public systems (managed independently within each province) including public hospitals and health centers, the private health system, and a system of healthcare centers operated by Pami, the Argentinian social security health insurance agency for senior citizens. While Pami and the public system are self-funded, private healthcare services are covered by both private insurance providers and union-based health insurance plans called "obras sociales" or "social work insurance," which are themselves generally outsourced to private insurers. Raul Pistorio, executive director of Farmalink, clarifies that currently, "healthcare coverage level is as follows: 46 percent through agents of social security, 39 percent some of the different services provided by the public sector, and finally about 15 percent the private sector."

According to Mariano Sanchez, partner in charge of healthcare at KPMG Argentina, this fragmentation has reduced the efficiency of healthcare spending, indirectly contributing to the system's high levels of debt and payment risk for pharmaceutical players. He highlights several structural and procedural inefficiencies, pointing out that when the unions outsource the 'obras sociales' to private insurers, "there is an extra margin generally included by the union," and that "in many cases people are covered by more than one payer, yet there is no harmonization between the systems."

From left: Eduardo Neira, Presidente, AstraZeneca; Alejandro Smolje, Finance Director, Janssen; Maria Gabriela Pittis, Country Manager, Shire

However, despite posing certain risks to the pharmaceutical industry, the healthcare system itself offers an excellent standard of coverage to Argentinians. Healthcare spending was 8.5 percent of GDP in 2012, according to the World Bank, and Brazil and Uruguay are the only Latin American countries to surpass

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What does it take to lead in Argentina?

Patrice Fuster, Director General, Sanofi

Edgardo Vazquez, General Manager, Pfizer

Mariano de Elizalde, General Manager, Sandoz

Doing business in Argentina presents a host of challenges that managers do not often face in other markets. Confronted by high and volatile inflation, controls on imports and exchange rates, and a political system with a track record of interventionist policies, they must direct their companies through a sea of uncertainty and around a wide variety of obstacles. When asked what qualities are most needed in a manager for an Argentinian business, Mariano de Elizade, general manager for Sandoz in the south cone, answers "patience and constant flexibility to adapt to daily changes are the most important qualities you have to show," a sentiment echoed across the industry. "Managing a company effectively in this environment of uncertainty can be exhausting, as doing so requires one to continuously ask or suppose 'what if?'," says Luis Rodriguez, general director for Gador, adding that beyond planning for contingencies, "we have to be prepared for all of the above, and thus must be quite conservative."

Multinationals face a particular dilemma in selecting managers for Argentina, as their top talent globally may not be the most suitable for the job. "Learning and understanding all of these challenges and risks would take an outsider months at a minimum," says Edgardo Vazquez, country manager for Pfizer Argentina. He explains that as an Argentinian citizen, his "ability to navigate all of these issues and achieve a reasonable balance between the risks and rewards in Argentina makes me an asset to Pfizer globally." Daniel Varde, healthcare and life sciences partner from Deloitte Argentina adds that "the dynamics here are different and often seem counter intuitive to outsiders," and that "it is usually advisable to make use of local managerial talent."

While many multinationals such as Pfizer have taken this approach, a few such as Sanofi have not. Patrice Fuster, general manager of Sanofi Argentina, points out that the HR cycle and company culture must be taken into consideration. "Some companies run a shorter cycle, in the hopes that new blood and fresh ideas will stimulate growth," he says. "Others prefer a longer cycle so that their country manager has the opportunity to build a local network and put down roots in the local community and provide an aspect of stability." In an environment that puts a high premium on creativity and flexibility, bringing an outsider with a fresh perspective and who is less constrained by knowledge of the barriers and obstacles in the Argentinian market can present certain advantages, as long as their management team is able to provide the necessary local knowledge and experience.

this level of spending, at 9.3 and 8.9 percent respectively. "Access to medicine in Argentina is among the best in the world," explains Hugo Sigman, CEO of Grupo Chemo and its parent company Grupo Insud. "On one hand, there are many national programs that help the population to receive medicine, such as Plan Remediar, which supplies 40 million free units to health centers around the country, as well as Plan Nacer. The government delivers free medicine to 100 percent of people with AIDS, chagas, and other illness. Additionally, if you are a patient in a hospital you receive free medicines. Today, there are 18 compulsory vaccines in Argentina that are free, universal and obligatory. All citizens with pensions receive free medicines or medicines with minimal cost."

Regarding access to innovative and high-cost treatments specifically, "many Argentine citizens today have access to specialty or high technology products due to a solid reimbursement system," explains Alejandro Smolje, the finance director for Janssen Latin America South. "Through HMOs, more than 70 percent of the population has access to these high tech products. This is not unique, but certainly different from the situation in many other Latin American countries." Smolje also adds that Janssen has "been able to launch new, innovative and high-quality products on numerous occasions due to an emphasis on a long-term strategy focused on unmet medical needs," and Eduardo Neira, country president for AstraZeneca Argentina concurs, saying "market access in Argentina is outstanding: we are often among the first countries [worldwide] when it comes to new drug releases."

Among the innovative and often high cost treatments that the Argentinian healthcare system is able to provide, the government has recently made progress with regards to orphan drugs for rare diseases. "Argentina passed a law in 2011 that is still being implemented, which explicitly requires the private and social insurance organizations to provide support for rare disease treatment," explains Gabriela Pittis, the general manager for Shire Latin America South. Furthermore, recognizing the "phenomenon unique to rare diseases, which is that through Internet research and participation in patient associations, the patients quickly come to know far more about their condition" and its management "than most of their physicians, health

Dr. Raul Pistorio, Executive Director, Farmalink

management organizations, and regulatory authorities." The same law "created a central committee, which includes patients as members, to coordinate activities such as neonatal screening and patient registries." Overall, she concludes, "progress in Argentina is moving more quickly than in many other countries in the region, and current treatment standards are very high."

NEXT STOP ON THE EXPORT EXPRESS; FIRST WORLD MARKETS

According to Federico Trucco, CEO of Bioceres, Argentina's "strong tradition in biological sciences" is a key factor behind the success of the country's domestic pharma companies at the regional level in recent years. As "the only country in Latin America with three Nobel laureates in the field," the country has a large "pool of talent, who lead in biopharmaceuticals because of their renowned expertise," that the pharma and biotech industry has recruited heavily from. Antonio Bouzada, president and founder of Eriochem, reinforces this claim by saying that "our biggest asset is our strong pool

Figure 2: Ranking of Top 20 companies

		Volume	Share volume	USD Sales	Market Share
1	Roemmers	55,879,630	8.11%	$554,108,756	9.08%
2	Bayer	45,238,857	6.56%	$212,347,002	3.48%
3	Gador	30,270,402	4.39%	$267,888,456	4.39%
4	Elea	29,245,217	4.24%	$260,442,964	4.27%
5	Bagó	28,307,312	4.11%	$288,268,967	4.73%
6	Montpellier	25,305,491	3.67%	$198,799,360	3.26%
7	Genomma	22,936,368	3.33%	$81,822,326	1.34%
8	Pfizer	21,415,673	3.11%	$165,559,249	2.71%
9	Casasco	19,752,175	2.87%	$250,913,980	4.11%
10	Baliarda	19,106,937	2.77%	$214,235,175	3.51%
11	Investi	18,176,596	2.64%	$146,074,588	2.39%
12	Andromaco	17,658,563	2.56%	$118,313,009	1.94%
13	Nutricia Bago	17,459,310	2.53%	$64,989,379	1.07%
14	Bernabo	17,450,849	2.53%	$134,492,723	2.20%
15	Boehringer Ing	17,427,972	2.53%	$135,800,593	2.23%
16	Raffo	17,379,050	2.52%	$229,850,428	3.77%
17	Mead Johnson	16,973,145	2.46%	$27,014,100	0.44%
18	Ivax Argentina	13,474,176	1.96%	$181,638,793	2.98%
19	Cassara	11,786,065	1.71%	$41,158,796	0.67%
20	Glaxosmithkline CH	11,505,028	1.67%	$43,998,194	0.72%
	Top 10	297,458,062	43.17%	$2,494,386,235	40.89%
	Top 15	385,631,352	55.96%	$3,094,056,526	50.72%
	Top 20	456,748,816	66.28%	$3,617,716,837	59.31%
	Total market	689,106,095	100.00%	$6,099,971,049	100.00%

Source: IMS Health Argentina (oct 13 to oct 14 data) Retail Market

Regional Leadership Beyond the Private Sector

The state-owned laboratory Hemoderivados, which is part of the National University of Cordoba, is a unique public institution. One of the most technologically and scientifically advanced institutions in Argentina, Hemoderivados produces a broad portfolio of plasma products, injectable generic pharmaceuticals and bone tissue products. Hemoderivados currently has several biotech protein products in the pipeline, including recombinant factor IX, thrombin, fibrinogen and fibrin glue, as well as other generic pharmaceuticals, tissue products, and organ conservation liquids.

Catalina Massa, Executive Director, UNC Hemoderivados

Most remarkably, the public laboratory is currently a critical source of blood-protein products for several countries outside of Argentina. The executive director of Hemoderivados, Catalina Massa, explains that "the social role of Hemoderivados has two somewhat separate aspects: one is to produce expensive medicines at a more affordable price, the other is to produce medications that are not currently being produced by anyone in our country, or in the region," while the ultimate goal of the organization "is to help the south cone region of Latin America reach self-sufficiency for plasma and blood products." At present, the organization exchanges plasma for plasma products with Chile, Uruguay and Ecuador, with 35,000kg of the roughly 140,000kg of plasma that they currently fractionate coming from these countries. Hemoderivados is currently in the process of signing a new plasma exchange agreement with Paraguay that should be finalized by the end of the year.

Laboratorios Hemoderivados, Cordoba

"I think it is quite clear that there is significant potential for mutually beneficial cooperation on other issues," says Massa, giving the example of the organ conservation liquids that the lab is currently developing, as there is currently no producer of these products in the region. "Once we develop enough capacity to meet Argentina's needs, our next objective will be to meet the demand for the region, while cooperating with their own health authorities."

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of human resources, and the cultural commitment to excellence in work; business might not be the most efficient or professional in Argentina, but when people are expected to meet a certain level of quality in their work, they meet it," allowing this company and many others "to achieve and maintain the standards necessary to export to some of the more regulated markets."

Carlos Grzelak, General Manager, Glenmark

Trucco also says that he believes the industry's core strength has been in "producing existing technology at a lower cost with high quality," and "pursuing state-of-the-art pharmaceuticals to generate competitive production platforms," and Bouzada hopes that "in the future, we will be able to leverage these strengths [in production technology] and take a strong position as generic players in the more regulated markets." "The problem for the other markets," he says "is that our products are neither the cheapest, nor the very highest quality." This trade off has encouraged many Argentinian firms to pursue niche product types and difficult-to-produce products, including added-value generics, also known as super-generics, and biosimilar APIs and products, as their higher operational costs are less of a disadvantage in these underserved and technologically demanding areas.

At present, "the main destination for our exports is clearly the Latin American market," says Alfredo Chiaradia, the general director for CILFA, before adding "despite that, Argentine products reach almost every corner of the world," mentioning Southeast Asia, Eastern Europe, parts of Africa, Lebanon, Pakistan and Kazakhstan as important markets for the industry. "In terms of export growth, the last years have seen the value of our exports increase about 15 percent per year," according to Chiaradia, and "in 2013 total medicines exports reached a level of USD 900 million."

The next step for many firms, which they are just beginning to reach, is to enter the US and EU as generics and biosimilar players. While many labs are currently FDA and EMA compliant, only a few have actually been officially certified. Eriochem is one of the few, having received its FDA certification letter in October 2014, and is currently the only national laboratory in Argentina with FDA certification for injectable products. Lab Richmond is one of those on the cusp, as the company recently built a new plant that, according the president Marcelo Figueiras, has "the latest technologies and complies with international standards required for the production of pharmaceutical products according to PIC/S GMP," and "is prepared to [be] certified by the EMA and the US FDA." Similarly, Edgardo Taraciuk, vice president of Tuteur Argentina, explains that the firm's "state-of-the-art" plant has applied for EMA certification, along with several other labs.

Of course, among the most sophisticated laboratories in the country are the 17 plants owned by multinationals. Despite the economic and political risks that have discouraged many foreign companies from investing in the country, the excellence of Argentinian scientists, chemical engineers, and other professionals has convinced several firms to develop or acquire plants in the country that supply their regional or global operations.

Sanofi's plant in Mirador

Among these firms are Sanofi Pasteur, AstraZeneca, Glenmark, Catalent, GSK, Pfizer, and others. Eduardo Neira, country president for AstraZeneca, explains that the company's Argentinian facility produces "many injectables and everything related to the anaesthesia line," as well as "different types of ointments and creams," in addition to several other products manufactured in the country via a third party. Glenmark's global oncology business is actually based in Buenos Aires, which "serves as the hub for development, manufacture and distribution of injectable oncology drugs for the entire organization," according to country manager Carlos Grzelak.

AN INNOVATIVE MODEL FOR INNOVATION

What is Argentina's biggest barrier to true innovation? "Argentina doesn't have enough capital to adequately invest in R&D without taking unreasonable levels of risk," says Mauro Bono, President of Savant, "although we arguably have the required scientific expertise." Furthermore, most Argentinian firms have very limited access to global capital and credit markets due to the economic and political risk that foreign investors must carry. Local laboratories must face these same risks, and thus are relatively conservative in their investment projects in general, with two of the most innovative firms in the country, Gador and Bagó, investing only four and five percent of their revenue in R&D respectively. As such, in the past innovation has been limited to incremental product innovations, and process innovations on the manufacturing side.

These instances of innovation, as well as other more radical research projects that Argentinian firms are currently involved in, have been achieved under a unique collaborative model. Since companies are unable to fund high-risk pre-competitive research, the public sector, namely the ministry of science and technology, "has filled that gap in terms of providing significant funding for pre-competitive research," explains Federico Trucco, CEO of Bioceres. This funding is distributed through two different mechanisms: first through public research organizations including national universities and the Argentinian National Scientific Research Council (CONICET), who often collaborate closely with the private sector for R&D, and through government grants for specific projects.

CONICET employs over 8,000 researchers, and is filing an increasing number of patents each year, with 42 applications in 2010, 79 in 2011, 93 in 2012 and 94 in 2013, with 26 percent of all patents in the field of 'health'.

Beyond patents, technology, and early-stage research, public organizations also provide private companies with human resources in many cases. "In general, they help us by carrying out some of our development work for us so we don't have to carry the entire load ourselves," explains Francisco Molinari, CEO of Amega Biotech, referring to national universities, such as the National University of Litoral and National University of Cordoba,

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two organizations that they currently have projects with. In return for this assistance, Amega "helps them with their research strategy and provides them with certain technology or biological samples."

Eriochem is leading a particularly intriguing project at the moment, for which they have enlisted the assistance of Amega Biotech and the National University of Litoral. Antonio Bouzada, president and founder of Eriochem, explains that the "idea relies on the fact that many types of cancer tumors preferentially absorb a particular cholesterol lipoprotein as they grow due to a mutation on one of their receptors." Eriochem is "seeking to imitate this lipoprotein using biotechnology, which is the step that Amega Biotech is helping with, so that we can then attach a chemotherapy drug to it, our leading candidate being docetaxel." There have also been recent initiatives to stimulate and facilitate collaboration in Argentina, such as the inaugural Bio Argentina event in October 2014 hosted by the chamber of biotechnology, which brought together over 900 professionals from across the industry to discuss the strategic future for Argentina's biotech industry, and serve as a platform for researchers to present research proposals to the chamber's member companies.

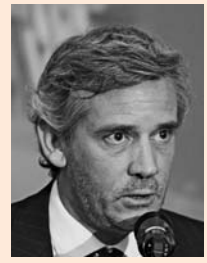
BOLD BIOTECH BUSINESSES

As one of the areas in which Argentina's pharmaceutical sector is more competitive globally, biotech has been the most exposed to global trends. Alfredo Chiaradia, the general director of CILFA, expects that "in terms of the type of products we export, we follow the global trend in the expectation that by 2016, half of the top-selling drugs in the world will be of biotechnological origin. In 2012, six of the twenty bestsellers were from this source," compared to only two in the year 2000. However, another key global trend, being changing regulatory standards and demands, has also had a significant effect on the structure and strategy of Argentinian biotech firms.

From left: Francisco Molinari, CEO, Amega Biotech; Hugo Sigman, CEO, Grupo Insud; Mauro Bono, President and Founder, Savant; Santiago Garcia Belmonte, Chairman, Biosidus

Argentinian Multinationals on the Horizon?

There are few Argentinian firms that truly have the potential to become multinationals. Several are strong regional players in Latin America, with operations across the continent, and others export products worldwide to as many as 40 or 50 countries, but generally lack fully-owned affiliates in non Latin American markets. Close Up International and Grupo Bagó are two of the few Argentinian firms that have the potential and ambition to become truly global players.



Juan Pablo Bagó, General Director Pharma, Bagó

Close Up was "the first company in the world to provide audits and reports in the prescription market," and its "internationalization process began right after the foundation of the company in 1968, when we challenged ourselves to go to Brazil and Mexico," says the founder and president of the company, Norberto Bonaparte. Today, the company audits prescriptions in Latin America and Spain, and develops and manages CRM systems for customers around the world, in roughly 70 countries. Bonaparte continues, saying that while "Close Up is a well-respected company throughout Latin America and has a wide percentage of coverage in the region," the company's goal "is to expand globally, especially in the northern hemisphere."

Norberto Bonaparte, CEO, Close Up

Key figures of Bago group

Bagó, a strong regional player with 18 affiliates across Latin America and plants in Argentina, Bolivia, Chile, Uruguay and Mexico, also has a significant presence in other parts of the world. The firm currently has four affiliates outside of Latin America, in Pakistan, Russia, Sri Lanka and Ukraine, with 11 manufacturing facilities strategically distributed between Argentina, Bolivia, Brazil, Chile, Colombia, Pakistan and Uruguay. Juan Pablo Bagó, general director for the group's pharmaceutical business in Argentina, says that the group currently envisions "a turnover of 75 percent coming from international markets" within the next five to ten years. Furthermore, being one of the few Argentinian companies to have discovered a new molecular entity (talniflumate, in the late 1960s) the holder of 85 patents developed over 15 different countries, and having achieved USD 1 billion in sales in 2012, Bagó is the perhaps the only Argentinian pharmaceutical company with the potential to develop a blockbuster drug that could catapult them into the global top 50.

"Regulatory standards are increasing worldwide, so regardless of whether we choose to compete in developed markets or emerging markets, we face increasing levels of scrutiny," explains Santiago Garcia Belmonte, president of Biosidus. Francisco Molinari, CEO of Amega Biotech, agrees that "regulatory burdens on final dosage form manufacturers, in even the most unregulated markets, have increased substantially," and points out that in many cases, this has caused clients to demand "a lot of information and analysis from API producers that is pharmaceutical in nature, as they can't handle these challenges themselves. Now our clients are asking us for the 'complete solution.'"

With these new demands from their clients, both firms have had to take a new strategic direction. "Previously, we placed the most emphasis on our transgenic animal research for API production," explains Belmonte, "and in 2010, we made the decision to focus more on final-dosage forms and recombinant proteins." Amega Biotech, which operated primarily as an API producer until five years ago, has similarly become "a pharmaceutical manufacturer of a wide range of finished dosage forms." The two companies' strategies differ at this point however. Amega Biotech is working hard to enter the US and EU markets, while Biosidus's "core objective is to become the leading biosimilars in emerging markets," according to Belmonte.

Photos: Thinkstock

Pharma Memes

The interesting dynamic of industry-targeted memes in social media—still a quiet treading ground for pharmas

Pharma and life science (PLS) companies spend massive amounts advertising their wares to a wide range of consumers, including patients and healthcare professionals. Because of perpetual regulatory uncertainty about how to do so in the modern/social media sphere, pharma's voice is awfully quiet outside of traditional venues like print, TV, in doctors' offices and at professional events.

Memes are tough to control no matter what industry you're in. (If you don't know the term, Google it before reading Richard Dawkins' *The Selfish Gene*, published in 1976—a great read by the way!) And in the highly regulated, to put it mildly, environment of pharmaceutical marketing, it's safe to say that PLS companies are very limited at creating, using, and controlling these rapidly moving and dynamic idea vehicles.

Clearly, Internet memes are mostly critical of the industry, and PLS companies remain quiet. You won't see Gilead tweeting much (or responding to tweets) about drug pricing. Meanwhile, companies enter discussions in less-regulated industries. For example, @MonsantoCo joined Twitter three years before @LillyPad and has tweeted twice as many times.

This is not to say that sans regulation, social media and the industry would suddenly get along (i.e., you can't blame everything on regulation).

Negative memes

Profits

#PharmaProfits doesn't return many tweets, but the idea that greedy pharma companies are reaping too high profits by way of robbery is widely shared. Huffington Post article—almost 20,000 Facebook shares or likes and over 650 tweets: **huff.to/1n5M6pj**.

Pharma spend: Marketing vs. R&D

Not to be overly meta here on the topic of marketing, but a widely held meme is that PLS companies ought to spend more on R&D and less on marketing.

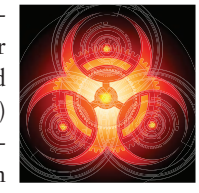
Pharma does spend more on marketing than R&D, references this BBC article: **bbc.in/1qrtWAe**.

Still, on the topic of drug marketing, this petition to the FDA to ban direct-to-consumer advertising looks to be approaching 52,000 online signatures: **bit.ly/1t7I0Fx**.

#TaxInversion

One of pharma's most controversial topics of the last few years has been inversions. This Rolling Stone article has been shared on Facebook and Twitter over 13,000 times: **rol.st/VQImQN**.

#Ebola



Media has been positive and negative for the industry (and western governments) regarding Ebola. Clinical trials have been gearing up with initiations announced this week by J&J, which is good.

But as vox.com wrote in December, as far as Americans could care, the Ebola meme lost muster by December: **bit.ly/1CBRIEp**. The article received more than 3,500 shares on Twitter and Facebook.

Casey McDonald is *Pharm Exec*'s Senior Editor. He can be reached at cmcdonald@advanstar.com.

Positive memes

Clearly, patient advocacy groups communicate well.

#IceBucketChallenge

$115 million raised—enough said.

But PLS companies have had to be a little more creative, sometimes edgy to start conversations.

Pfizer's "Get Old" campaign has certainly been an attempt to tackle various aging and health topics head on. **#FOGO** (fear of getting old) doesn't quite have the same popularity as YOLO (you only live once) or #BOGO (buy one get one), but it's an interesting angle: **https://www.getold.com**.

Searching #FOGO and Pfizer does make me nervous that I'll start getting more Vi&GRa% emails in my spam folder. And #viagra commercials are a completely separate meme.

Breathless Moments

Bayer's "Breathless Moments" campaign raising awareness about chronic thromboembolic pulmonary hypertension (CTEPH) certainly has its appeal. The company, along with the Pulmonary Hypertension Association, announced CTEPH Awareness Day in a November press release followed by a three-month photo contest to evoke "inspirational moments in our lives" that can leave us breathless.

Of course, illustrating that social media may not be pharma's strong suit, @pharmaguy pointed out that breathlessmoments.com is owned by a wedding photographer: **bit.ly/15DYI5p**.

In addition to the website conflict and poor search engine optimization, there is little-to-no activity on Facebook or Instagram.

Pharm Exec will wait to see how the photo contest unfolds, but, meanwhile, I might have to include some Instagram pics of my own #nofilter. PE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