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Dividing Lines

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THE MONTH OF APRIL REPRESENTS THAT SEASONAL SPLIT BETWEEN SPRINGTIME AND THE LONG SHADOW OF A WINTER DEPARTING. It's thus appropriate that we turn *Pharm Exec's* attention to a similar borderland, where business principles and practice converge in a mud field of contradictions: what industry thought leaders call an "unresolved policy debate." We prefer to call them dividing lines, three examples of which we bring to your attention as part of our feature coverage this month. What they show is, in our industry, there are always two sides—at least—to every question.

Who is Your Customer? In our Executive Roundtable with four St. Joseph's University Business School alumni responsible for commercial operations, a recurring theme is being "customer centric." Beyond that basic agreement, however, there was a strong sense of uncertainty on how to cope with the sheer diversity of the audiences the industry now needs to serve. This diversity requires commercial teams to pursue costly, customized approaches to market outreach; many are using big data tools to appease one key party: the payer. But a few brave souls still insist the industry will lose its way unless the patient interest is put back at the center of the picture. Tension between these two pathways is palpable: while you can execute a contract with a payer for a quick, definable payoff, building an asset by meeting eye to eye with the patient, at ground level, is a project only for the long-term. The question is can you strive to do both, and serve two masters? Market leadership in a future of non-obvious strategic choices may depend on it.

Diversity in the "C-Suite:" A Dream Deferred? This month's cover feature is our annual take on the Healthcare Businesswomen's Association Women of the Year (WOTY) award, which now has been expanded to three winners in pace with pharma's effort to integrate to all segments of healthcare. Our story provides strong evidence that female leadership is a reputational asset; in an industry associated with the production of a public good, it is also good for business. Yet there is evidence, too, that women are still woefully underrepresented in the top echelons of pharma power—so where is that sense of urgency, to reach beyond the tired expression "as it has been, so shall it ever be?"

The danger is, as a movement matures (HBA's recognition of female talent in the industry now spans 25 years), what was novel can become commonplace. More stimulus is needed, but the direction is wide open to debate. Is the movement promising too much in terms of a culture change? Or should it push harder on the more straightforward economic arguments for diversity in management? One of the most deflating justifications for gender equity I've heard came from Gloria Steinem herself, when she said "it's not that women in the workplace are more moral than men. They've just had less opportunity to act immorally." To move that workplace culture to a better place—maybe more moral, but certainly reflective of the new market demographics—requires that change be felt not just at the top of the food chain, but at the bottom too. That's a harder task, and a much bigger commitment—is the "c suite" ready?

Who You Gonna Call? Not Pharma (Not Yet). Our third feature explores the efforts of Wikipedia, the world's largest online source of health information, to impose some discipline on the legacy it has made—the English language site logs an average 200,000 health visitors a month but only one percent of its content is vetted through external peer review. As the story attests, pressure is on to persuade big Pharma to participate directly in Wikipedia's efforts to improve its standards for completeness and accuracy. As usual, however, the industry must deal with the predictable issue of bias. In this case, the dividing line is drawn on the other side: some Wikipedians just want pharma in, while others want to attach a very big string—to force companies to disclose the results of all sponsored clinical trials, good and bad. Right now, industry seems comfortable deferring any action to the constraints imposed by promotional controls. But, given Wikipedia's vaunting popularity and clout with patients and providers alike, for how long can an industry position based on passing the buck to the regulator be sustained? Stay tuned—this potentially rotten egg is still gestating.

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Ben Comer, Senior Editor

Editor's note: As *Pharm Exec* went to press, we received notice that Dr. Annalisa Jenkins, one of three recipients of the Healthcare Businesswomen's Association Women of the Year (WOTY) award and a subject of this month's cover feature, has left her position as head of Merck Serono's Global R&D Division, effective March 31. A company spokesman reaffirmed Jenkins' role in driving a critical restructuring of R&D strategy and functions that we have detailed in our profile of Dr. Jenkins on Page 25. Her future plans have not been disclosed, but do include receiving the WOTY award as scheduled on May 1 in New York.

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Focus Reports, Sponsored Supplement

Renewed economic growth and a willingness by all stakeholders to work together will be the keystones to preparing Portugal's pharma revitalization.

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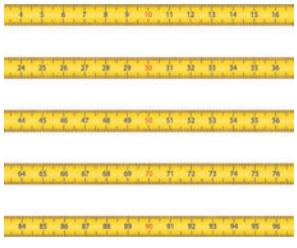


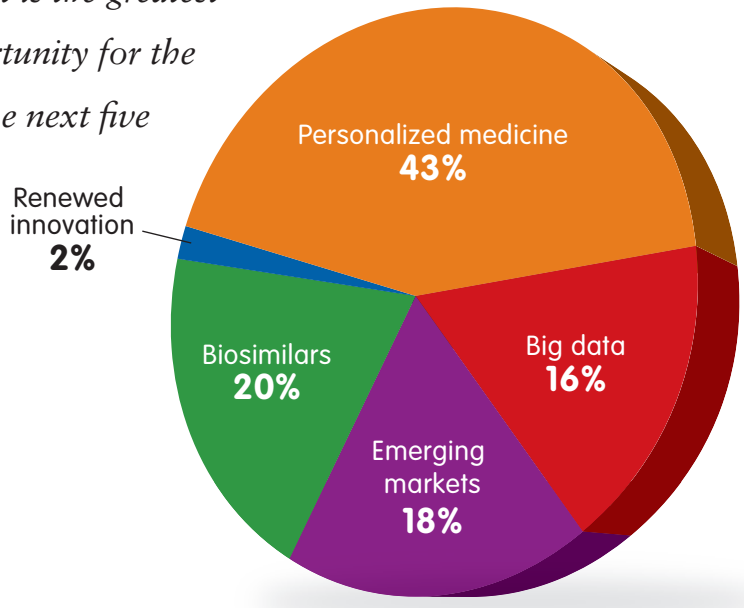
The New Metrics of Market Success
March Issue online
Mason Tenaglia
bit.ly/1h6fGuP

Most-read stories online: February 23 to March 24, 2014

Data Point

Poll data courtesy of online *Pharm Exec* readers between Jan. 21, 2014 and Feb. 10, 2014

Q: What is the greatest opportunity for the industry in the next five years ?



Readers Weigh In

It's important to point out that it cost Gilead $11 billion to acquire Pharmasset and thereby secure the rights to Sovaldi. They still had to pay costs associated with completing development in terms of Phase III clinical trials,managing through the regulatory approval process, and manufacturing. This was all at risk, with no assurance of approval.

Mike Wokasch 2/21/14
"Bringing New Rx Drugs to Market in 2014"
bit.ly/1dsRS5l

I'm guessing that Gilead set the price at $1,000 per day because that's what the market will bear.

David Beasley, 2/20/14
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Michelle O'Connor, 2/20/14
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Front & Center

Designing An Effective And Competitive HUB Model

HUB programs provide support to multiple stakeholders and have a huge impact on patient access to therapy in today's challenging payer environment

In today's market, there are escalating cost pressures and greater demands for affordable, value-based treatment options. Additionally, there are many obstacles to navigating and effectively managing complex product and patient services in an increasingly competitive specialty market.

David Blanc, Vice President of Services at Advanced Care Scripts, an Omnicare Specialty Care Group company, discussed these challenges in his presentation at CBI's Patient Assistance and Access Programs conference on March 5-7, 2014. The collaborative event offered strategies and solutions in effectively managing a brand while ensuring high quality patient services. After David's presentation, entitled "Next Generation Distribution and Support Services to Improve Patient Access," Pharmaceutical Executive met with him to discuss his views.

As specialty drugs become more prevalent, specialty pharmacies and HUBs are being tasked with improving their support services. How are key stakeholders reacting to this industry shift towards specialty products?

As the market shifts, key stakeholders are forced to think differently. Many specialty products focus on smaller populations (as opposed to blockbusters), have a higher than average price, may have payer restrictions, require unique administration and/or have a need for compliance oversight. The cost of specialty drugs and clinical differentiation can impact payer decisions that could lead to unfavorable formulary decisions and higher patient copay responsibility. Stakeholders have to consider these inputs and each unique aspect of their specialty product as they think through the services necessary to commercialize. These services are becoming commonplace and expected. Manufacturers realize offering support programs are necessary to stay competitive. HUBs today are offering multiple custom, integrated services as opposed to a "basic" offering.

Specialty pharmacies and HUBs are being tasked with staying on top of the changing payer environment and making recommendations to their manufacturer clients to further evolve their programs. HUB programs in particular are educating themselves on the expanded Medicaid eligibility and coverage options and other aspects of the Affordable Care Act. As more and more specialty drugs enter the marketplace, HUB programs are refining offerings to ensure their drugs are competitive and their programs are viewed as valuable.

How do manufacturer support programs impact patient access?

Based on how difficult it's become to navigate the payer environment, it's not surprising that more specialty manufacturers are turning to insurance experts for help. When considering "coverage" for a particular medication, it is important to determine whether the patient has insurance that is commercially funded, federally funded, state funded, or low-income subsidized. For patients without insurance, the question becomes: are they eligible for Medicaid or one of the subsidized ACA programs? A good HUB program can help the patient find out what coverage is available to them.

The HUB is responsible for finding the best coverage for the patient – this may be through their medical insurance (AOB or Buy and Bill) or through their pharmacy benefit. Once coverage is identified, the HUB will also address affordability concerns and help the patient navigate additional assistance that they may be eligible for. This includes co-pay assistance programs (discounted drug), patient assistance programs (free drug), or alternate funding sources such as foundation assistance.

The HUB program also has a great impact on patient access through the support it provides to healthcare professionals. Offices that regularly prescribe specialty medication will often have a dedicated team responsible for completing insurance checks and responding to requests for prior authorizations. Many times when the process becomes too cumbersome, physicians switch to an alternative drug that has easier access. A HUB program can alleviate the work in a physician's office and make sure the patient is getting access to the drug that was originally prescribed by the physician. Once a referral is received by the HUB program, a full benefit investigation is done for that patient's specific coverage. If a prior authorization is needed, often times the HUB can initiate or even complete it on behalf of the physician with appropriate documentation on file. If a

prior authorization is denied, the HUB can aid by following the appeals process. They also handle many of the time-consuming and deadline oriented aspects of navigating the payer landscape, alleviating the extra work for physicians.

What should a manufacturer look for in a support program?

A good HUB service does a thorough market assessment prior to making any suggestions for the design of the program. An analysis of the competitor's offerings for co-pay assistance, patient assistance, compliance calls, nurse support hotlines, educational materials, and other support helps create a customized program based on the manufacturer's specific goals and needs. The patient population also needs to be studied; demographics such as age, gender, and insurance coverage help determine the type of technology patients will find comfortable, as well as the expected level of customer contact and the types of patient assistance programs that will be the most valuable. Product characteristics such as method of dosing and dosing frequency are reviewed to determine if patient compliance, transportation, or education are barriers that may need to be addressed. Finally, the market assessment should include a review of the prescriber environment. Most primary care physicians are unfamiliar with filling out referral forms, leaving it up to the patient to fill. On the other hand, many healthcare specialists are more familiar with a HUB referral enrollment and they are eager to take advantage of the support that the HUB provides.

Program design should also be considered. A manufacturer who has taken the time to evaluate the market with a HUB service provider will likely be interested in customizing their plan. The plan design should be able to answer the question: "What is going to increase speed to therapy and generate a higher conversion rate for a better ROI?"

The types of measurement offered by a HUB should be the final consideration when choosing a support program. Many metrics can be used – speed to therapy, patient satisfaction, adherence rate, quality of benefit investigations, appeals success rate, and physician satisfaction are just a few. The important questions are: What information is most important to the stakeholder? And will the program they are partnering with be able to supply and report that crucial information back to them?

Finally, a support program should provide data. The need to trend information and measure success is critical throughout a product's lifecycle. In addition to key performance indicators, market trends can be tracked and should provide information that is both directional and actionable. Trends in enrollment, missing information, prior authorizations, patient copay amounts and persistency are just a few metrics that can inform a manufacturer program of forward thinking ideas for minor or major redesigns. Recognizing changes in trends and being able to react to the market is key in the successful commercialization of a specialty product.

What makes an independent HUB program different from a support program offered at a specialty pharmacy?

The first difference is a HUB program does not actively dispense. Other factors to consider when developing a HUB design are the size of the specialty pharmacy network as well as the importance of speed to therapy. In situations where a very small network of specialty pharmacies (one or two) and the product requires a quick time to dispense, there may be an opportunity to create a "Central Service Provider" or a HUB within the specialty pharmacy.

Products requiring a robust distribution strategy benefit more from an independent HUB that provides consistency and coordination to all program services. A HUB program typically has a team dedicated to a single drug or manufacturer and can move referrals through the investigation, prior authorization, and fill stage, capturing data in a single case management source. This helps consolidate communication with physician offices. A HUB program also has case managers aligned by regions; the physician and patient have a dedicated person they speak with each time an inquiry is made. This is reassuring to both the patients and physicians and allows a relationship to be built based on their needs and preferences.

In designing the appropriate HUB model, the unique needs of each drug therapy must be considered to successfully execute the program. Complex issues including navigating through reimbursement, addressing co-pay challenges, supporting a patient to the appropriate point of dispense and adherence and beyond, have to be viewed holistically. In addition, HUB program models will continue to morph as the healthcare environment is changing, new products are coming to market and technology is evolving.

As vice president of services, David Blanc leads a portfolio of operational business units providing patient access support services including reimbursement hotlines, patient assistance programs, copay assistance programs and specialty pharmacy dispensing and adherence services for a range of physician-administered and self-administered products.

Obama Policies Reshape Pharma Marketing

Health reform initiatives promote transparency, challenge reimbursement.

Although the media coverage of Obamacare has focused on dysfunctional insurance exchanges and unworkable mandates, a number of less prominent but important health reform policies promise important changes in pharmaceutical access, coverage, and marketing. Whether it's greater transparency about pharma interactions with prescribers, new electronic information systems offering prescribing information, more comparative research on treatment options, or limitations on patient assistance programs, the common aim is to better inform prescribing — and to reduce unnecessary outlays on drugs in the process. Add to that new tax and spending plans, and pharma companies, patients, health professionals and payers face considerable challenges.

Reform impacts

An increased focus on the comparative benefits and harms posed by alternative treatments, for example, pressures marketers to provide payers, prescribers, and patients with more credible information on which therapies (including drugs) are most effective — and cost effective. The Affordable Care Act of 2010 (ACA) provides the Patient Centered Outcomes Research Institute (PCORI) with $650 million a year to fund comparative effectiveness research on the outcomes of interventions for back pain, migraine, common cancers, among other conditions, and the program promises to raise multiple challenges to conventional treatment approaches.

Another prominent initiative is to expand the use of electronic health records (EHRs) by doctors and hospitals. This may provide new opportunities for pharma companies to convey information about new drugs to prescribers, explained Mukesh Mehta, vice president of PDR Network, at a recent drug marketing conference sponsored by the Drug Information Association. The rising uptake of EHRs, Mehta explained, expands e-prescribing operations, plus programs to send out refill reminders and to check patient prescriptions, drug allergies, and drug-drug interactions. These systems carry FDA-approved prescribing information, but IT vendors are looking for ways to add on marketing messages from pharma companies.

A troubling prospect is that Obamacare could curb patient assistance programs (PAPs) offered by pharmaceutical companies to help individuals afford expensive medicines. Co-pay cards and discount programs are not allowed for Medicare and other activities defined as "federal health care programs," as the subsidies are considered "kickbacks" from manufacturers to physicians for prescribing certain drugs. Pharmacy benefit managers (PBMs) and insurers complain that such assistance programs really aim to get patients "hooked" on new, more expensive medicines and have been fighting pharma efforts to replace drug samples to physicians with various discount cards.

The question now is whether the Medicare no-pharma-assistance policy also applies to "qualified health plans" sold through the federal exchange.

The question now is whether the Medicare no-pharma-assistance policy also applies to "qualified health plans" sold through the federal exchange. In response to queries from the Senate, HHS secretary Kathleen Sebelius has said that, no, exchange plans are not federal health plans. Yet, HHS also has opposed third-party support (specifically from hospitals and providers) for patient premium payments and "cost-sharing obligations" for fear that will skew the insurance risk pool. That raises questions about the legal status of PAPs.

Jill Wechsler is *Pharm Exec's Washington* correspondent. She can be reached at jwechsler@advanstar.com

The National Health Council has sought clarification on the issue, but the latest rule from HHS on third-party payments failed to resolve the question. Meanwhile, patient groups are pressing for continued access to pharma support, claiming that there are no low-cost alternatives to many of the newer specialty medicines. One strategy is for manufacturers to provide funds to non-profit patient organizations, which then can channel assistance to patients seeking treatment. Payers and PBMs oppose such tactics, noting that PAPs only help patients cover their copays, and insurers still have to shoulder most of the bill for the more costly medicines.

Disclosing payments

Pharmaceutical marketing is the clear target of the Open Payments or "Sunshine" program, which requires manufacturers to submit data to the Centers for Medicare and Medicaid Services (CMS) on transfers of value to physicians and medical centers. After many delays, the program finally is getting off the ground, with pharma companies preparing to submit initial 2013 payment data in May.

But disputes continue over whether and how to value "publication assistance" to clinicians, such as providing medical writing services and other support, and whether such activities should be reported at all. A related topic is the value of journal reprints and other educational materials provided prescribers and whether the program should even count textbooks and journal reprints as "gifts" to doctors. "It's odd," comments John Kamp, executive director of the Coalition for Healthcare Communication (CHC), that while FDA has issued new guidance to clarify appropriate dissemination of scientific and medical publications, CMS reporting requirements raise questions about the value of such information.

Even before the "Sunshine" data comes to light, though, it seems to be having an impact on pharma marketing. The public interest media group Pro Publica unveiled a "Dollars for Docs" report in March indicating a big drop in pharma speaking fees to doctors from 2010 to 2011. This development, says ProPublica, reflects "increased attention from regulators, academic institutions and the public to pharmaceutical company marketing practices."

GlaxoSmithKline made big cuts in this area, and announced last December that it would stop paying speaker fees altogether. But other marketers have not taken that step. And companies say that the decline in marketing outlays may reflect a dearth in new drugs coming to market, as well more generic competition for leading blockbuster drugs – and not the prospect of greater public scrutiny.

Part D controversies

Although the Obama administration has pulled back from adopting major revisions to the Medicare drug program, namely reducing "protected" drug classes and re-examining the "non-interference" clause that prevents Medicare from weighing in on negotiations between drug plans and manufacturers or pharmacies, a number of important policy changes remain under discussion. CMS is examining the effect of reduced copays offered by preferred pharmacy networks and efforts to crack down on "abusive" and "fraudulent" prescribing, primarily of prescription painkillers. And the agency proposes to expand the medication therapy management program for Medicare beneficiaries who use multiple prescriptions to treat chronic conditions, despite concerns about the program's effectiveness. A number of analysts consider MTM a waste of money and support shifting to other payment and quality measurement strategies to improve appropriate medication use by high-cost patients.

Part D, moreover, could experience additional changes through annual program updates and the federal budget process. The administration's budget plan for 2015 proposes to impose rebates on drugs provided to low-income Medicare patients in Part D plans, to require rebates on drugs that experience price hikes faster than inflation, and to encourage greater use of generic drugs by these "dual eligible" beneficiaries. Another proposal would require manufacturers to provide discounts to cover 75% of the cost of drugs prescribed to patients in the Part D coverage gap – up from 55% discounts proposed in the CMS "call letter" for 2015 that sets rates and policies for Medicare Advantage and for Medicare drug plans for next year. Although these new policies are not expected to gain much traction on Capitol Hill, the budget provides a roadmap to Obama administration goals and spending priorities for the near future. PE

Winners & losers from tax reform

Tax reform is still on the policy agenda, and the latest proposal from House Republicans sounds some alarms for pharma. Most concerning are items to repeal the 50% tax credit for clinical development costs of orphan drugs and to limit deductions for advertising to 50% of outlays. The swipe at advertising is no surprise to John Kamp of CHC, which is working with other marketing organizations to emphasize the importance of advertising to economic growth.

Biopharma companies are more pleased with a separate proposal to make permanent the R&D tax credit, and medical device makers are ecstatic over a provision that repeals the 2.3% medical device excise tax established by the ACA. These proposals are far from enactment, but it's noteworthy that these are Republican options and could move forward with GOP election wins this fall.

Photo: Thinkstock

Whatever Happened To Faster Reimbursement For Generics In Europe?

The plan to accelerate generic pricing and reimbursement has become another tragic European casualty.

Another of those anniversaries in European pharmaceutical regulation has slipped by unobtrusively. It is just a year ago that bold intentions were almost agreed for speeding up the pricing and reimbursement of generic medicines. An outline consensus was reached within most of the European Union's key institutions that the timelines for getting generics onto the market were too long, because there was too much discussion over what they should cost and who should pay for them.

So, instead of the six months that the EU's legislation allowed for, EU officials and the European Parliament took the view that a month should be enough for member states to reach a decision on an application to fix a price for a generic, and a maximum of a month for deciding on whether it could be reimbursed too. It was the culmination of an extensive debate that had featured some striking statistics and some energetic lobbying.

Timeline debate

Research by officials in the European Commission had suggested that it was taking an average of more than seven months for generic medicines to reach the market after the originators lost their exclusivity, and that pricing and reimbursement rules were a factor in that delay. The European Generic Medicines Association (EGA) said its members were waiting an average of 153 days after marketing authorization to receive pricing and reimbursement status, and the range across the EU's member states ran from as little as 14 days to more than 270 days.

In the European Parliament, the influential figure of Antonyia Parvanova insisted that shortening timelines for generic medicines was a key element in the financial sustainability of national healthcare systems. European industry commissioner Antonio Tajani, who launched the proposal to update the EU's 20-year-old rules, said EU member states would benefit from the savings resulting from faster access to generic drugs, and industry and patients would benefit from cutting through some of the red tape currently holding up decision-making. His aides predicted that reducing the time lag would also stimulate price competition, bringing further savings — because originator prices in Europe drop by an average of 20% during the first year after generic entry and 25% in the second year — and by as much as 80-90% in some cases.

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

Why, demanded the advocates of change, was it possible for some countries to complete the entire process in a couple of weeks while others needed the best part of a year? Administrative complacency, they alleged — arguing that without introducing specific shorter timeframes for generics, national authorities would continue treating these products within the more generous schedule designed for the more complex process of considering pricing and reimbursement applications for new medicines. It was just an accident of history, they said, that there was no legislative provision for fast-tracking these decisions; back in the 1980s, when the current EU rules were agreed, generics represented only a tiny proportion of the EU — whereas today they account for some 50% in volume. That damage from that accident should be repaired, they urged, with new rules.

Rule changes mulled

The Commission, therefore, proposed obliging member states to make their decisions within 15 days of an application. It was even ready to consider the introduction of national provisions granting automatic/immediate reimbursement status to generic medicinal products where the corresponding originator already benefits from reimbursement at a higher price — something that roughly 80% of the generic industry had recommended in consultations on the new legislation.

And the parliament broadly agreed. It reinforced the Commission's proposal with a call for "accelerating the entry into the market of generic medicinal products," and beefed up proposed provisions relating to circumventing intellectual property issues. These "should neither interfere with nor delay pricing and procedures for reimbursement of generic medicines in the member states," said Members of the European Parliament (MEPs). The parliament also saw the merit of cutting the timing, although it took a slightly more cautious approach, calling for a more leisurely 30-day deadline — something that was still within an acceptable timeframe for many in the generic industry.

The bid to update the transparency directive is dead in the water, and all those pious expectations of change in the parliament or the Commission are no more than vain hopes.

In fact, the EGA hailed the parliament's vote last February as a triumph, noting that "MEPs have given a positive impulse" to updating the rules (confusingly known as the "transparency directive"). It praised MEPs' support for the introduction of a shorter price and reimbursement approval time limit for generic medicines, and for banning unnecessary complications relating to intellectual property protection or to quality, safety, and bioequivalence.

"European generic medicines manufacturers are pleased that the European Parliament has correctly tackled unjustified delays and market distortions for generic and biosimilar medicines," said Beata Stepniewska, EGA's acting director general at the time.

Resistance stalls action

So why has the anniversary slipped by without much remark? Why were the bold intentions only "almost agreed," and why was outline consensus reached only "within most" of the EU institutions? Because even though the Commission and the parliament were closely aligned, the three-legged stool of EU rules was missing one leg — the Council, where the 28 member states make their decisions. Without the national governments on board, this legislation could go nowhere. And national governments were not — and still are not — on board.

Part of the resistance in the Council came from member states' concerns about being forced to work more quickly. Granting pricing and reimbursement status to generic products automatically or immediately where decisions have been made on the corresponding originator just hasn't caught on — Spain is one of only a handful of member states to have toyed with the idea. Most of the others have no desire to amend the rules so as to shorten the time limits for the pricing and reimbursement of generics. During the consultation process on the proposal,

half of the national authorities and public health insurance bodies that responded took the view that the current time limit of 180 days should be maintained for generic medicines. They say that changes to their current procedures would entail a significant additional burden. As the Commission has laconically observed, "these positions indicate that a reduction of processing times for generic medicines is unlikely to happen across the EU at the sole initiative of member states."

Part of the resistance comes from another direction, more political than technical. The member states just don't want the EU getting too close to their own privileges and rights in deciding on how they handle drug pricing and reimbursement — a reflection of long-standing (and in these more eurosceptic days, a frequently more pronounced) tension at the heart of all EU legislation.

The Commission itself has remarked on the apparent paradox that some countries that already make decisions in 30 days or less for generics are still opposed to legislation on shorter timelines, for instance, Sweden and the UK.

But the paradox is only apparent: both these countries have a strong streak of pragmatic independence, with no enthusiasm for (and indeed a palpable reluctance about) legislation for the sake of legislation. Although EGA's Stepniewska said a year ago that her organization "is looking forward to a swift follow-up of the legislative process and constructive dialogue with the institutions," she hasn't had it.

To all intents and purposes, the bid to update the transparency directive is dead in the water, and all those pious expectations of change in the parliament or the Commission are no more than vain hopes. The initial proposal emerged during the Danish presidency of the EU — and that most famous Dane of them all, who was from Elsinore, might have had the transparency directive update in mind when he said, "Thus conscience doth make cowards of us all, and thus the native hue of resolution is sicklied o'er with the pale cast of thought. Enterprises of great pith and moment with this regard their currents turn awry, and lose the name of action."

Instead, the action, such as it is, in relation to generics has moved away from European pricing rules to European competition rules, and in many respects away from European rules altogether, and back to national rules. The impact of EU competition rules has been seen in the fines imposed over recent months on companies found to have breached anti-trust law in pay-for-delay agreements to keep generics off the market. And the shift to national action on generics is graphically demonstrated by the more limited geographical scope of recent key events.

In France, the authorities imposed a $20 million fine in December on Merck & Co. subsidiary Schering-Plough for attempting to block a rival generic version of its Subutex through systematic denigration; and Sanofi was levied a €50 million fine last May for similar behavior to protect its antiplatelet Plavix. At the same time, Sanofi is fighting a valiant rearguard campaign to limit the damage from the French government's determination to push through generic substitution and price cuts on high-consumption products such as acetaminophen — the active substance in Sanofi's top-selling Doliprane and Bristol-Myers Squibb's Dafalgan and Efferalgan.

Meanwhile, in Germany the latest debate is on whether generics should be exempted from drug price controls — not European controls, but German controls. In Spain, the arguments center on the fact that half of the drugs sold in the country cost only $5 or less, while a new report in Italy argues that it is generics that are keeping the reimbursement bill in check — not in Europe, but in Italy. And, as they say in Europe, "ainsi de suite" — the same trend to a national focus in discussions of generics is visible across the member states. At the same time, the rhetoric of the EGA has moved away — as if in reluctant recognition of the inevitable — from urging faster pricing decisions to more general engagement in the debate about sustainable health systems.

By January, Stepniewska's narrative had moved on to how the generic industry should "seize on opportunities in the current period of austerity to amend its way of thinking and push for significant changes to the regulatory environment." None of the changes she highlighted related to faster reimbursement decisions. As Hamlet himself commented, "The rest is silence. PE

I am 1 in 2 million

I was told that I was hard to find, that there's not many people in the world with my disease. So when they asked me about taking part in a study to understand my condition a bit better, I said yes. Because they made me feel like I could help, like I was needed. And that made me feel part of something much bigger.

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Healthcare's Widening Horizons

For the first time in its 35-year history, the Healthcare Businesswomen's Association recognizes three female leaders in healthcare—each of whom uniquely mirrors the structural diversity of tomorrow's networked pharma landscape. By Joanna Breitstein

After decades of cautious equivocation, there is now a clear business rationale for female leadership in the "c suites" of big Pharma. An industry that has embraced the goal of being "customer-centric" knows that in every health care system around the world, the majority of customers are women. That stereotypical "engaged patient" is more often than not a woman too, one who also serves as an influential provider in emerging professions with the power to dispense, from the pharmacist to the community health practitioner. The data is compelling: three-quarters of the US healthcare labor force is female, while the latest work from the New York-based Center for Talent Innovation provides statistical evidence to show just how much women control the "power of the purse" in treatment decisions.

Future industry profits depend on riding this cresting wave of diversity. Expanding sales geographies and better access to information have combined to bind big Pharma's reputation more closely to societal expectations. And if you want to be seen as "customer facing," it is simply good business to see something familiar when that mirror of perception shines back on your markets.

Nevertheless, the facts say that big Pharma still isn't ready for its close-up. Of the 13 drug companies listed on the 2013 "Fortune 500" list, only one—the generic powerhouse Mylan

Labs, ranked at 374—has a female CEO. The irony is that while the leading consumers of health care are women, the management that oversees development of the products and services to serve those needs remains almost exclusively male.

Yet business does not align with a vacuum; precedent reveals that those who push for change, fill unmet needs and channel it in profitable directions, will eventually assume the mantle of leadership. In an industry in the midst of so much transformation, leaders are emerging that reflect the demographics of big Pharma's polyglot, increasingly globalized business model. For the past 25 years, the Healthcare Businesswomen's Association (HBA) presents an annual Woman of the Year (WOTY) award to a female leader who exemplifies the managerial talent, cultural tone and community perspective required to advance not only our own industry, but the state of healthcare overall. Each of the past 24 WOTY winner has been profiled in the pages of *Pharm Exec* (see box, page 22).

However, for this 2014 silver anniversary, the WOTY award has been expanded to include three leaders across the broad continuum of healthcare. The distinctively unique backgrounds of these women reflect the structural diversity of tomorrow's healthcare—where the successful pharmaceutical company functions as but one element in an interconnected, networked health system, that considers drugs as both an information asset and a platform for services "beyond the pill."

The 2014 WOTY awardees are:

» **Patricia Maryland**, President of Healthcare Operations and Chief Operating Officer of Ascension Health, the largest non-profit provider of hospital and related health services in the United States, and the first African-American woman to hold that position. Ascension is the nation's largest Catholic health ministry, which operates more than 100 hospitals and has over $17 billion in annual operating revenue.

» **Shideh Sedgh Bina**, co-founder of Insigniam, a boutique consulting firm that has served all of the world's largest pharmaceutical companies. An immigrant from Iran, she is an expert on innovation strategy and leading large-scale organizational and culture change initiatives.

» **Annalisa Jenkins**, Executive Vice-President and Head of Global Research and Development for Merck Serono Biopharmaceuticals. A physician and scientist from the United Kingdom, she is the only female head of R&D among the big Pharma companies and was recently named Chair of the Board of Directors of TransCelerate BioPharma, which is coordinating novel industry approaches to the management of clinical trials.

As HBA President Jeanne Zucker commented to *Pharm Exec*, "these three top-flight women underscore what HBA believes is the crucial leadership skill in healthcare today: fostering system-wide collaboration—in drug development, care delivery and service management." In the following profile sketches, *Pharm Exec* examines the path of these three leaders to professional success along with the personal experiences and values that keep them rooted to what many insiders, regardless of gender, still see as a business motivated by the strong will to do good works.

Patricia Maryland: Finding opportunity in crisis

In 2007, Patricia Maryland received what she could only describe as a calling. She was tapped for a new two-pronged position at Ascension Health, as Market Leader for Michigan and President and CEO of St. John Providence Health System (SJPHS). SJPHS is a member of Ascension Health, accounting for 25% of its patients across five hospitals and more than 125 medical facilities in southeast Michigan. It spends significant resources caring for people living in poverty.

Maryland knew it would be a difficult road ahead. Detroit was facing the most economically challenging time in its history since the Great Depression. By 2009, Michigan had the highest unemployment rate in the country; GM and Chrysler had declared bankruptcy, with nearly one million jobs lost across the state. The idea that workers' insurance could pay the healthcare tab for SJPHS was no longer viable.

Great leaders can do more with less, and it was up to Maryland to ensure the health system survived and could continue to meet the needs of the community. This was not a job for the faint of heart. She had to act quickly to slash $70 million in operating expenses while maintaining the mission to serve people in need.

"There was no way to make the cuts and preserve the current operating structure," says Maryland. "We had to do something new for Detroit and for the future…In Detroit, you can get stifled because of the challenges, but instead we looked it as a bold way to extend our creativity. We blossomed in the face of adversity."

Amidst one of the worst economic crises in US history, Maryland, who has a doctorate in public health administration, proceeded to execute a broad vision based on a preventative, patient-centric approach to care. Patricia believed there was a chance to scale up healthcare services so that patients would have a better outcome while saving the system money—all by distributing health care services differently. It centered on providing

an earlier, more interventionist and more holistic approach to care—as Maryland explains, "Our job is to connect the dots and coordinate other services so patients are treated earlier and correctly and thus able to have a better outcome."

It's the type of healthcare Maryland had wished for while growing up, as she watched her mother struggle with diabetes. "My mother had all the complications that follow with diabetes—problems with eyes, nerves, congestive heart failure, and then renal failure, which she died from," she remembers. "We were frustrated when we used the health system; it was always focused on what we needed to do today. We took on each health problem as it surfaced. Care was provided in a silo way. What my mother really needed was a team of physicians to sit with us and review all the things we needed to be thinking about when it comes to diabetes."

Amidst one of the worst economic crises in US history, Maryland proceeded to execute a broad vision based on a preventative, patient-centric approach to care.

Wellness and preventive care attract significant attention, but because it calls on distracted service providers to invest today to obtain results tomorrow, few organizations want to risk leadership in this area for the possible negative short-term impact on budgets. But Maryland knew it was an important element to reducing the overall cost of care. She also saw it as an important shift away from the current unsustainable business model, which is based on a disjointed fee-for-service reimbursement system, which incentivizes physicians and hospitals to treat sick patients rather than performing services designed to keep them well.

The fruits of Maryland's labor is a program called Partners in Care involving St. John's Providence and the Physician Alliance, a network of more than 2,300 physicians in southeast Michigan. Working together, the two groups cut the overall cost of care by shifting treatments away from the hospital emergency room to primary care physicians, who could intervene early on and thus avoid admissions to acute care facilities. The hallmark of the new model is the "medical home"—which is a designated primary physician who meets the patient regularly and focuses on wellness and understanding the needs of the entire family to connect them to the right care.

It was through this hospital-physician organization that SJPHS secured the first commitment on an outcome-based hospital payment model from the large insurer, Blue Cross Blue Shield of Michigan. Under the agreement, St. John's Providence receives higher reimbursement for successful patient outcomes. The agreement sets a new standard of pay-for-performance by encouraging high quality of care rather than high volumes of services, measured by the successful treatment of patients.

Maryland was part of the decision to roll out this model and sell it to Ascension's employees. Over the past five years, her team has proved its mettle with metrics that show the overall cost of healthcare for the Ascension workforce has dropped significantly. The company has now taken the model national with some 150,000 associates now enrolled—

Past WOTY Winners

Year	Name
1990	Karen Katen
1991	Jane Townsend
1992	Joan Keith
1993	Carolyn R. Glynn
1994	Carolyn Koestenblatt
1995	Carol Webb
1996	Lynn M. Gaudioso
1997	Maureen Regan
1998	Kathy E. Giusti
1999	Tamar Howson
2000	Myrtle S. Potter
2001	Carrie S. Cox
2002	Sarah S. Harrison
2003	Catherine Angell Sohn
2004	Christine A. Poon
2005	Lynn O'Connor Vos
2006	Sue Desmond-Hellmann
2007	Meryl Zausner
2008	Charlotte Elaine Sibley
2009	Deborah Dunsire
2010	Deirdre Connelly
2011	Freda Lewis-Hall
2012	Carolyn Buck Luce
2013	Bridgette Heller


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Flashpoint Medica has a real nose for digital. We're setting the standard for digital healthcare communications across a range of strategies, including mobile apps that stop physicians in their tracks, social media that creates a real buzz, and interactive selling tools that can animate both your sales and your sales force.
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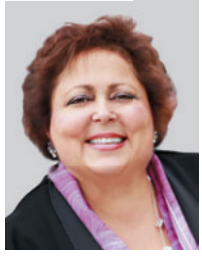
all based on a risky pilot launched in a Detroit on the ropes during the worst recession since the Great Depression.

The lesson for fellow women in the management hot seat? Hard times are often the best time—to think big.

Shideh Sedgh Bina: Culture, interrupted



Shideh Sedgh Bina says the biggest influence on her life was her grandmother. Born in Iran, her world was one where all women were required to wear a veil—a hijab—to cover their head and chest as a sign of modesty and morality. But to Shideh's grandmother, the hijab symbolized much more.

Her father was a doctor and Bina's grandmother dreamed of following in his footsteps. Those dreams were put on hold when at age 13, she was removed from school to help care for her brother. By age 16, she was married.

In 1936, in an attempt to "modernize" the country, Iran became the first Muslim country to ban the veil. But in the community where Bina's grandmother's lived, the women were hesitant to take off their hijabs. Who would be the first?

Shideh's grandmother felt moved to take action. She was young, in her 20s, pregnant, and absolutely terrified of retribution and violence in the small city in which she lived. Still, with her family's blessing, she volunteered. Scared for her life, security came to escort her to a town meeting. It was there that she stood in front of the community and removed her veil. As she talked about why she was removing the hijab, other women began to follow suit. Her reason? She said it was so her daughter, and here she patted her pregnant belly, wouldn't have to put away her dreams like she had.

Shideh was born two generations later and emigrated with her family from Iran to the United States. In 1981, she graduated from the Wharton School at the University of Pennsylvania where she earned a BS in economics. Wharton would eventually recognize her as one of the top 40 prominent business leaders under 40 in the Philadelphia tri-state area.

Following graduation, Shideh quickly became a successful entrepreneur. She went on to lead the New England region for an international training and organizational development firm. In 1990, Shideh co-founded High Performance Consulting, which merged with the Rosenberg Group in 2005 to co-found Insigniam. Today, the consultancy has offices in Philadelphia, Los Angeles, Paris, and Hong Kong, and has worked on projects involving all of the 15 top pharma companies. Bina helps large companies create a stronger internal dynamic that generates breakthroughs in management results—whether that's top line growth, strategy implementation, profitability, or culture change. Her record includes working with management to rethink approaches to speeding new medicines and devices to market and millions of dollars in savings through efficiencies in back channel service operations.

"There's no question on anybody's part that the healthcare industry is in a state of total disruption, which is always an incredible opportunity for transformation."

These corporate transformations are Bina's work, but the first and most important transformation was her own. In the early days of the consultancy, she was charged with, among other responsibilities, business development. But would male clients take her seriously? Shideh was scared of taking on the assignment and possibly hurting the bottom line. It was then one of her partners told her something she would never forget: "He said, 'We are in the business of breakthroughs, thinking outside of what is traditional, separating old beliefs and assumptions,'" says Shideh. "You have to make a choice: You are either going to become the culture or interrupt the culture. This bit of wisdom became my mantra."

Bina's grandmother took off her hijab with the goal of a better future. Given all the challenges in healthcare today, Shideh says, executives have the same opportunity to scrap the veil imposed by conventional wisdom, to envision a better future—and act.

"There's no question on anybody's part that the healthcare industry is in a state of total disruption, which is always an incredible opportunity for transformation," says Bina. "There is a group of executives that see it for what it is, take the ball and run with it and in doing so shape the future around their own vision."

Precisely this is what Bina says is so exciting about being in healthcare right now—there is an opportunity to change society and build a new platform for healthcare. So what distinguishes the executives that are willing to shape the future versus those that are just reacting to it?

"With all of them, there is fear—risk is inherent in disruptions," says Bina. "Except there is a certain group of people who are willing to step away from the fear and give themselves permission to envision something bold

and inspiring. For those people, being proactive actually reduces the risk."

It is statements like those that show how deftly Bina is able to channel emotion. Shideh says it wasn't until she was married with children, in her 40s, that she was really able to tap into that compassion. People who know Bina say she is not afraid to wear her heart on her sleeve. She shares herself and is not afraid to be vulnerable in the work environment.

"What is in your heart?" asks Shideh. "Trust that it doesn't make you soft, it makes you more effective."

Annalisa Jenkins: Remaking a global organization

Dr. Annalisa Jenkins came of age during the 1980s in the United Kingdom. It was a time when the two most powerful people England were women – Prime Minister Margaret Thatcher and Queen Elizabeth II. Looking back, Jenkins attributes her ambition to the social context of her upbringing.

"Growing up where the most visible and prominent leaders of my country were women showed me the power of role models," says Jenkins. "I think women gain their ambition largely through role models so seeing successful women is important for young girls."

Jenkins came from a military family. She wanted to be a doctor, and saw the British Royal Navy as an opportunity to help pay for school. She graduated in Medicine from St. Bartholomew's Hospital London and upon graduating earned her medical degree from the University of London. She trained in Cardiovascular Medicine in the UK National Health Service, at the front lines of universal public health care.

In 1991, following family tradition, Jenkins entered the Royal Navy. She was only the third woman to serve as a medic, the only female in her intake class that year, and would be the first female to serve on the front lines of combat. Jenkins would rise to the rank of Surgeon Lieutenant Commander.

"During my naval career I was constantly in an environment that I was the only woman on the team or one of very few," says Jenkins. "I was constantly adapting to my environment and working out to how to conduct myself in order to be accepted and respected, and therefore be able to contribute and make a difference."

"I know what it feels like to be in an organization that has challenges and that is questioning the sustainability of the R&D model."

The most unforgettable moments in the Navy were during the Gulf War. Jenkins was serving with the Minesweeper Squadron, working with the unit to advance into the northern part of the Persian Gulf, clearing mines so that the American aircrafts could follow. At night, the Iraqis would launch missiles at them, and Jenkins didn't know if she would make it out alive. It was there that she learned some of her most important lessons of leadership.

"The role of the leader is to engage and energize—to make others want to follow you," says Jenkins. "Being in the military is about building high performance teams, and leveraging leadership that can allow people to overcome what others thought was impossible."

Annalisa was married and became a mother to two children. She had intended to make her career in the Navy, but when she was handed an 18-month oversees deployment, she couldn't bear the thought of taking it with young children in tow. Instead, she decided in 1997 to join Bristol-Myers Squibb as a Cardiovascular Medical Advisor, based in the UK.

Jenkins was immediately identified for rapid advancement. Over the course of her 14 years at BMS, she took on a new responsibility every 2-3 years, often in a different part of the world. She had a leadership role and accountability for nearly 60 countries. In 2008, she was promoted to Senior Vice President, Global Medical, where she oversaw the company's Medical Division worldwide.

In 2011, Annalisa took a career jump, leaving the familiar BMS and her string of proven successes to join Merck Serono, a division of Merck KGaA, based in Darmstadt, Germany. Recruited by Dr. Stefan Oschmann, then-president of the company, by 2013 she was promoted to Executive Vice-President and head of Global Development & Medical.

Jenkins was hired, in no uncertain terms, to lead the transformation of Merck Serono's R&D. There was a crisis in productivity following the 2007 acquisition of the Swiss-Italian, family-owned Serono by Merck KGaA. She calls it the "Sleeping Beauty syndrome." Ten or 15 years ago, the company had fallen asleep in a pretty good place, she explains. But with the slumber induced by good times, the industry had changed. Now, Merck Serono had several costly and high profile late-stage failures and regulatory setbacks.

Are you asking the right questions?

IT may have the answers to some of your toughest business challenges.

Perhaps it's time for pharmaceutical executives to ask themselves a question—and then have an honest conversation about how IT may be impeding instead of driving their basic business strategies.

Let's start by recognizing some fundamental realities. Competitive and regulatory pressures are driving major change across the pharmaceutical industry. Companies must adapt quickly to new demands on how they relate to consumers, fill their drug pipelines, and run their businesses.

Astute leaders also now know they risk missing out on once-in-a-generation opportunities unless they get some clear answers on things—such as data management, analytics, mobility, and other emerging technologies.

So ask yourself: Isn't it time for a clear, far-reaching talk with your IT colleagues?

IT's changing role

To appreciate how technology can help pharma compete in a changing market, it may help to understand how IT itself has changed. For a generation of pharma leaders, IT was the invisible support group that maintained the infrastructure but did not really understand the business or its fundamental requirements.

In today's environment, however, it's not enough to just keep the lights on.

Pharmaceutical companies need IT solutions that address their most pressing needs. The good news is a New Style of IT is now emerging. It is an approach that leverages new models and capabilities to help executives meet some of the biggest challenges pharmaceutical companies have ever faced.

This emerging approach to information technology focuses on integration and speed to value. It is built on a range of powerful new technologies, including cloud, mobile computing, Big Data, and robust IT security. This new style rests on a converged and FDA-compliant infrastructure that is fast and flexible—and is changing the way technology is delivered, paid for, and consumed.

Pharmaceutical companies that embrace this new IT environment can position themselves to compete and succeed.

The hard questions

But first, you may need to ask some tough questions about your organization and IT partners.

Outcomes: How can pharmaceutical brand leaders communicate with their reimbursement teams to meet the demands of the pay-for-performance environment?

Pipeline: Are you ready to optimize your pipeline portfolio management in the face of stronger, globalized competition?

Personalized medicine: Can your IT infrastructure provide the insights needed to compete in a more personalized, consumer-centric, and genomics-based pharmaceutical marketplace?

Mobility: Do you have the infrastructure needed to support a mobile, collaborative pharma workforce?

Safety and regulatory: Is your organization prepared for the strategic and technological demands of safety and regulatory changes from the FDA, EU, and other sources?

The right answers

Solutions are out there if companies embrace the new more collaborative, analytic, and data-oriented approach to information technology. Here is just an overview of how emerging technologies are meeting specific challenges in our industry.

Outcomes: Pharmaceutical companies can now leverage powerful, new analytical capabilities to capture and understand structured and unstructured outcomes-based data. HP also can support post-market studies and enhanced outcomes research aligned with Health Economics Outcomes Research (HEOR) Reimbursement initiatives.

To support the pay-for-performance economic model, companies also must streamline and strengthen their entire value chain. HP leverages SAP HANA capabilities to capitalize on cloud, Big Data, and mobility. HP offers rapid-deployment capabilities to meet horizontal supply chain needs and specific pharmaceutical sector requirements.

Pipeline: To accelerate the crucial drug development process, companies can deploy SAP-as-a-Service to ensure real-time support for target discovery, pre-clinical development, and other research-and-development efforts.

Advanced information retrieval capabilities give companies faster and more reliable access to high-value scientific data—including internal research in web- or document-based formats, and external research from Reuters Medical News, The Pink Sheet, and other sources. Personnel can research those sources by grammatical formulations, word proximity, and document meaning.

Personalized medicine: Powerful life sciences-oriented decision support platforms enable pharmaceutical organizations to better analyze patient and clinical survey data, speech, and focus group inputs. R&D groups can leverage advanced healthcare analytics capabilities to gain greater insights into patient disease groups and the potential for targeted therapies among a specific patient cohort.

Mobility: Modernized, cloud-ready applications give sales, R&D, and other personnel seamless anywhere/anytime access to corporate assets and services. HP cloud solutions position pharma organizations to embrace a secure, yet collaborative, R&D approach across business, industry, and academic environments.

Private and hybrid cloud solutions burstable scalability meets the computing demands of genomic and other R&D efforts. HP open cloud analysis and storage platform enables transparent research while also providing end-to-end process standardization, integration, and workflow automation.

Regulatory: Changing and more stringent requirements from the FDA, EU, and other regulatory bodies require pharmaceutical firms to improve safety, surveillance, and compliance capabilities. HP can assist with a robust, cost-effective ability to mine information published about a product on social media, and can help pharmaceutical organizations respond appropriately. A flexible, modular security and data governance approach promotes cross-company collaboration while protecting enterprise Internet Protocol assets.

Open the conversation

There can be no serious doubt: The shifting healthcare environment means dramatic changes in how pharmaceutical companies develop and commercialize their products.

Consider this: In our private lives, many of us already embrace a more open, tech-savvy lifestyle—from mobility and smartphones to social media and data-driven offers that meet our unique needs. Yet many in the pharmaceutical industry have yet to fully leverage technology in the professional setting. That needs to change.

In this emerging world, delivering better outcomes to patients will be the key to generating measurable value for a pharmaceutical company. To do that, companies must find new and better ways to collaborate, innovate, and optimize their commercial product pipelines.

Information technology is not a magic bullet—but IT can be an important part of pharma's competitive arsenal. At the very least, pharmaceutical executives should be talking to their IT departments and their strategic partners about how to translate technology into real differentiation and measurable competitive advantages.

So call your CIO. Lunch is on you.

Contact HP to help you get the conversation started
life_sciences@hp.com

Make it matter.

"This was not an agenda of 'steady as she goes'," says Jenkins, of joining the company. "This was going to be a transformation effort and every part of the R&D ecosystem had to change."

"Women are consistently rated as better leaders, and the industry is in need of these leaders to reshape it."

For Annalisa, the answer lied in enabling efficient innovation. This meant re-organizing and rationalizing the global footprint of the company, which had not been done following the merger. There were a staggeringly bureaucratic complex of 66 regions, each of which had been operating separately. She worked to connect all the functions, in the midst of a broad restructuring. Serono's headquarters in Geneva, Switzerland was closed, a painful step; meanwhile, new hubs of innovation were established in Boston, Darmstadt, Beijing, and Tokyo.

"It was a remarkable journey," says Jenkins. "I knew we could do it because I'd come from a company that had done it. I know what it feels like to be in an organization that has challenges and that is questioning the sustainability of the R&D model. But fast forward, it feels great to go through a transformation and come out as a winning team."

Now, with a more united, global organization on a stronger footing, Annalisa is envisioning a key role in the next phase for Merck Serono. It includes a focus on emerging markets and capturing future growth opportunities, she says. Indeed, with 30 per cent of its prescription medicine sales in emerging markets, today the company's derives a higher percentage of its sales from emerging markets than any other US or European-based pharmaceutical company. That in itself has called for a radical departure from the old ways of interpreting key market drivers.

At a time when Jenkins is spending more of her time envisioning the next stage of Merck Serono, she still remains studious about the past. "In times of true transformation, senior leaders recognize you have to stretch and go into a different direction. Diversity was clearly high on the agenda when the company's direction changed course," says Jenkins. The company's decision to hire her, and also another female, Dr. Belén Garijo, who recently succeeded Stefan Oschmann as President and CEO, transformed what had previously been an all-male management team. "It is this diversity that provides an expanded platform for sustainable innovation."

Three women, three ways forward

Annalisa Jenkins recently published an editorial in *The Economist* where she wrote, "Who is leading R&D throughout the world today? The short answer is 'men, basically.' Men in life sciences senior management outnumber women about 6-to-1. And who's leading R&D in the biopharma industry, specifically? This time the answer is "men, almost exclusively." Among the world's top 20 biopharma companies by revenue, just one has chosen a woman to head its R&D efforts…As that one woman, I can say unequivocally that the members of my gender are vastly under-represented at leadership levels in biopharma and, for that matter, in life sciences R&D organizations generally."

Finding out why women tend to start out equally with men in the labs of pharma but gradually fade in the transition to the upper ranks of the corporate R&D hierarchy is a topic that has attracted the scrutiny of think tanks like the Center for Talent Innovation, among others. Expect more to come on that.

Shideh Bina believes the big issue facing women's progress is culture and mindset. While forward-thinking executives are eager for gender and ethnic diversity, there is still a disconnect. "My experience today is that there is very little in the way of countermoves against women--people no longer say women don't belong in the C-suite," says Bina. "But we are socialized to think and act that inadvertently make the opening smaller for women and minorities to advance. We need to adopt employment practices so we don't hire peers in a way that creates a self-fulfilling cycle in the workforce. It behooves us to pay a lot of attention to this so we get to a place where we don't need to pay attention."

Bina notes the list of other challenges preventing women from reaching the highest leadership positions are all too familiar, including the difficulties associated with having a successful career and raising a family. "Still, it's important to solve the problem. Women are consistently rated as better leaders, and the industry is in need of these leaders to reshape it."

For Patricia Maryland, the path to women's progress is best forged through active sponsorship and mentoring – each of the three say this was a critical factor in their own success. As such, being among the few women at the top, all eyes are upon them. Says Maryland, "As an African America woman, I am aware of the need to set the tone for accountability and achievement. I feel an absolute level of responsibility. The tone is always set by those that precede you." PE

Joanna Breitstein can be reached at joanna_breitstein@yahoo.com.

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The Trials of Commerce

Four commercial line executives serve as our jury of peers on what's in store for the future of pharma.

A critical function of *Pharm Exec's* Editorial Advisory Board [EAB] is to provide us with a perspective on what really counts in the business of big Pharma today—at the front lines of the competitive war for market share, how do you differentiate, align strategy with capabilities, motivate winning teams, and deploy resources efficiently, all toward the ultimate objective of building sustainable sources of growth, for the long-term? To help answer this question, *Pharm Exec* convened on Jan. 30 a panel of four alumni from our EAB meeting host, St Joseph's University Business School Pharmaceutical and Healthcare Marketing Program, each representing the commercial operations side of the business, from drugs to consumer products to vaccines. The following contains highlights from the discussion, including input from other members of our EAB community. The big lowdown? Marketing today is so competitive, management only gets one shot to get it right—and if you are not listening to the patient first, you fail.

— William Looney, Editor-in-Chief

PE: *Each of you has moved up the ranks on the commercial side of biopharmaceuticals, from serving on the field force to a management assignment with direct P&L responsibility. How has your work and the requirements for success changed over the course of your career? What are the key drivers of competitive differentiation today versus when you started in the industry?*

Joe Truitt, Achillion Pharmaceuticals: I began my career in 1989, as a sales representative. At that time, the selling proposition in pharmaceuticals was relatively simple. Prescribing decisions were made at the physician level. Now the market has evolved into a much more complex environment, with many more stakeholders involved in the process. Prescribing decisions are impacted by payers, governments, physicians, specialty

pharmacies, PBMs, and patients. Each of these segments requires a targeted commercial plan in order to succeed.

PE: *Isn't it all still a question of how much scrip you can get physicians to write for the product? Has the situation really changed that significantly?*

Truitt: Due to the complexities of access and reimbursement, physicians are no longer the only decision makers in prescribing. We have to understand the road map to access and reimbursement very early in the development of a compound to ensure the required data is available to support the launching of a new drug. If this planning is not executed during the clinical phase of drug development, there is a risk that physician uptake could be limited due to barriers to access. For example, health technology assessments conducted by governments now play a vital role in shaping everything from the design and location of clinical trials to the final go-to-market launch strategy. Six years ago, there was no IQWiG agency in Germany to influence the decision on a domestic reimbursement price for a new drug, the outcome of which guides actions by payers in many other countries.

PE: *What other key drivers of change can you identify from the time you entered the industry?*

Gerianne DiPiano, FemmePharma Health Care: My area, women's health, is a reflection of changes that have dramatically altered the position of patients in relations with providers. Social media platforms have empowered patients to make their own therapy choices. Nine out of 10 consumers access information on the web before they see a primary care practitioner. Buying decisions are made every time a patient looks his condition up on Wikipedia. Yet industry research indicates that half of the top 50 biopharmaceutical companies in the US lack a strategy to address this change, such as through active involvement in these online community networks.

List of Participants

Helen Bourret, Specialty District Sales Manager, Amarin Biopharmaceuticals

Gerianne DiPiano, CEO and President, FemmePharma Health Care

John Furey, Global Franchise Head, Vaccines, Baxter Healthcare Corporation

Joseph Truitt, Senior Vice President and Chief Commercial Officer, Achillion Pharmaceuticals

ing countries have embraced social media more proactively than in the US, largely because there are few institutions to advance their view; many people feel disenfranchised from the health systems. New digital technologies provide an outlet.

Despite the high profile being given to the patient, our industry has far to go to before we are truly "patient centric." Market access is the hot field in big Pharma today because it reflects our adjustment to the ascendency of payers. Market access is designed

We have to understand the road map to access and reimbursement very early in the development of a compound to ensure the required data is available to support the launching of a new drug.

—Joseph Truitt, Achillion Pharmaceuticals

John Furey, Baxter Health Care: Based on my 20 years in the biopharma and vaccines business, I can point to three transformative changes. The first is the shift in the science, from classic chemistry to biology. This has significant implications for the business, because when you are managing a biologics enterprise, how you manufacture and supply the product is as critical as marketing and market access. Securing the supply chain is a function that traditional managers did not need to focus on—you were just trained to sell doses. The product turned up. Today, a more holistic approach is required. Knowledge of the process is vital.

The second big change is the necessity to think beyond the home market, to emerging markets and the globalization of most functions in the biopharma enterprise. This change makes it all the more important to understand the patient, in all his/her diversity. In fact, patients in emerg-

to give payers a front row seat in the design of our R&D pipelines. But shouldn't we first be asking what is most important to patients? The huge financial bets on the next generation of biologics demand that we have a better understanding of just how the patient will use the product. This is not a question that can be answered with a reimbursement strategy. You have to dig deeper and determine the conditions under which a patient will use a drug: are there structural or institutional hurdles to integration of the new medicine in the patient's system of care?

The third transformation is around the talent needed to succeed in a very complex business environment, where there is no fixed blueprint for success. The road to the "c suite" is no longer one of starting out "carrying the bag" in sales, then advancing to commercial operations and eventually leading a business segment. Rather, it's all about earning

multiple assignments in different aspects of the business, and in varied geographies. You want to be the person who can readily see how all these activities are interconnected. There is a war underway for talent that has a fuller understanding of the business and the capability to operate on the basis of a global point of view.

Each of these three drivers depends on the ability of the industry to stay innovative. Such an outcome is not guaranteed. In the average big Pharma R&D budget, a significant portion of funding can be devoted to fixed costs and life cycle management of existing products. It raises a serious issue of how much money is really available to fund the next wave of innovation. Everyone is looking for novel, low-risk vehicles to generate investable ideas, such as in-house VC operations.

Helen Bourret, Amarin Biopharmaceuticals: My career has been entirely in sales. When I joined the industry 15 years ago, it was the land of good and plenty. Products were approved, regularly and on time. The product was automatically covered and reimbursed; formulary listing was not an issue. It was an environment uniquely suited for the blockbuster phenomenon. Today, we face an entirely different situation. Generics are dominant in nearly every class, so by default we have had to become experts in formulary positioning and politics. Sales and commercial teams must be conversant in dozens of managed care plans, most of which operate on the basis of strict prescribing guidelines that accord generics status as first-line treatment. These plans define "new products" as anything up to 5 years old.

On the relationship side, which is critical to those engaged in selling anything, contacts with physicians and providers are controlled to the point where, assuming you get access, the conversation has to be treated like a script. And when you have the meeting, more than three quarters of all physicians will limit it to two or three minutes. What do you say in two minutes? You can count the words; each one had better carry value. The strategy must be to identify the physician's incentives under the benefit plans he or she works with. For example, if you can show how prescribing a therapy will raise the practice's patient satisfaction score within that plan, then the physician will listen. And you have to build other contacts—with the nurses, community health workers, and others who pull the patient's charts.

Basically, the sales professional today is seen as redundant. The challenge is to overcome that perception by showing physicians how you can help them meet their obligations to the PBMs and payers. Being able to differentiate your product in a world of "me too" medicines is equally vital.

PE: *Given the consensus that the business climate today is markedly tougher, can we cite instances where a change proved disruptive to your commercial model? How did you respond and what was the outcome, in terms of shaping your own career?*

Truitt: Prior to my current position, I was given responsibility to position an orphan drug for launch. What I quickly figured out was that, for this launch, engaging the patient was going to dramatically influence the success of the launch. This was a disruptive, eye-opening development, as it contrasted to my previous exposures on the commercial side. It took us awhile to figure how to move the focus to the patient, but we succeeded. We put a product manager in place whose sole assignment was to work with patient groups. We sought out patients in focus groups, listened how they wanted to receive therapy, and incorporated their ideas in the contracts we negotiated with our specialty distribution partners. We actually served as a concierge in a "high touch" approach to drug delivery.

I would summarize our learnings from the process as follows. Pay attention to the disease community. Show them that what you have is clinically distinctive, advances the standard of care in a way that is tangible to the patient experience, and is appropriately priced. Acting by example, prove that patient expectations identified through the trial phase will be incorporated post-launch.

PE: *Will you leverage any of these learnings in your current role as a developer of new treatments in the very competitive field in HCV? Many of the emerging therapies promise to increase the cure rate for hepatitis C from drug interventions to upwards of 90%, from less than 50% today. The patient benefit is clear.*

Truitt: The level of innovation in this disease area is astounding—drugs now coming on the market promise to take patients from an HCV infection to cure in only 12 weeks. As a smaller company, we think there is an opportunity to carve out some "blue ocean" space in this field by focusing on what the patients with this disease really want.

PE: *Any other examples of addressing a disruptive change or transition in your career?*

Furey: Prior to joining Baxter, I served as general manager for an MNC's vaccines business in China. I arrived there and promptly discovered that the conventional model for selling medicines in China—lots of "boots on the ground"— was not working as well for vaccines. Government played a dominant role as the lead purchaser of vaccines and controls on traditional marketing practices in this segment were growing, leading me to pose the question why we on the vaccines side needed to rely purely on the mass mobilization approach. Government influence was so strong it could determine if

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you even had a sales channel to work in at all. In that case, market access would be irrelevant.

Recognizing these distinctions, we reconstructed the sales force around a new "customer solutions team" concept to work with government procurement agencies on transparent targets supporting China's five-year health sector development plan. For example, we emphasized the ability of pneumococcal vaccines to reduce pneumonia among young children and the elderly. It was a closely coordinated, patient-centric approach that acknowledged the role centralized health planning plays in penetrating the Chinese market.

The disruption that matters most to me—and which I might hesitate to describe as innovative—is the massive downsizing of the industry sales force over the past decade.

—Helen Bourret, Amarin Biopharmaceuticals

This is a model—non-traditional, built around a new generation of stakeholders—that is relevant not only to China but to most of the industrialized countries as well. Public-private partnerships centered on high-value, innovative vaccines and biologics is certainly the avenue we are taking at Baxter. Last year, we began a 20-year partnership with a Brazilian state-owned company, Hemobras, to produce our recombinant factor VIII therapy for hemophilia so the country can move away from reliance on older, blood-based treatments. This relationship will allow the Brazilian government to upgrade the standard of care for the country's 10,000 hemophiliacs while also supporting the Brazilian biotech industry to leverage its capabilities from this technical transfer to spawn newer technologies.

Bourret: The disruption that matters most to me—and which I might hesitate to describe as innovative—is the massive downsizing of the industry sales force over the past decade. The challenge to those of us in the sales function has been to minimize the damage from the loss of so much accumulated expertise, especially as the implementation of these reductions in force has often been delegated to third-party consultants. Important issues like customer impact, retention of long-standing client relationships, legal and regulatory compliance, internal organization alignment, and staff morale, don't get the proper attention from senior management. The disruption has led to the loss of many high quality contributors. Company reputation is damaged: to fill the gap, you have to go to a physician who had the same rep, often for a decade or more, and try to start over again. In a larger sense, the question is whether any of this advances the claim of so many companies that the patient is at the center of their business? As a manager, my response is to do all that I can to establish continuity and restore trust. I work consistently with my team to get everyone on the same page.

PE: *Looking ahead, what can you identify as the most "mission critical" function that executives will need to successfully navigate this transition in the biopharma business model?*

Truitt: The key mission critical function is the ability to digest and synthesize multiple streams of information. An important example would be the ability to manage the increasingly complex process of completing clinical trials, on a global basis; and finding the best way to position a new product for maximum market access, in multiple countries worldwide. In the old era, structuring the trial, filing for registration, and securing market uptake could all be approached separately, in sequence. Looking ahead, we have to anticipate during the proof-of-concept stage what our trial design will look like, what comparators we will select, and what evidence is needed to position the product for reimbursement. The other step is to establish our launch order in a way that reinforces— not dilutes—our market access priorities as we roll the product out.

Di Piano: There is a great deal of innovation locked up in smaller companies. The problem is the lack of resources to fund it. There will be a premium on people who have the financial, operational, and communication skills to either create partnerships or take a company public. Making a case for the start-up is not easy, so the ability to do that is going to be a prized attribute for anyone in this business. Confidence and assurance is also needed to confront the negative headwinds from the VC community, whose engagement once gave small companies a runway to the future. Now the VC players want all their risks guaranteed—not only does a company like my own have to show it can generate revenue on a consistent basis, it has to shine on key profitability performance metrics like EBITDA. The ripple effect here is that big Pharma wants highly structured transactions, with milestones that shift more of the risk to the smaller partner. In summary, people with the smarts to overcome these institutional deficits and secure the capital to grow an asset internally are going to be in high demand.

There is a great deal of innovation locked up in smaller companies. The problem is the lack of resources to fund it. There will be a premium on people who have the financial, operational, and communication skills to either create partnerships or take a company public.

—Gerianne DiPiano, FemmePharma Health Care

Furey: No one skill or attribute is going to dominate as "mission critical." That said, process capabilities—getting all the functions in an enterprise to work together—will be very important to achieving business targets. It used to be that a good clinical profile coupled with commercial and promotional muscle was sufficient to move the markets. Today, many additional factors must apply to a seamless launch; there are more moving parts. But getting large organizations aligned behind the strategy and to identify and then execute around the right tactical measures is not as easy as it sounds. It may seem trite to state it, but we need to ensure the entire organization is working toward the right end point. It is surprising how often companies miss the mark by presuming that if you tick a box, results will follow.

Another factor that underscores the importance of process is the externalization of big Pharma R&D pipelines. This requires a high level of "street smarts" and sensitivity among managers in building successful partnerships. Big Pharma must strive for balance: expectations based on internal markers must not be so rigid as to starve a small and medium-sized partner of the oxygen—from know-how to capital—it needs to thrive and realize the potential of the partnership. Finding mutual benefit from the connection between big Pharma and the smaller biotechs is critical to the future of innovation, particularly in generating the resources to ensure the best new science is funded.

Bourret: Selling will remain the principal way this industry competes for profits. The sales rep is not going away; there will still be boots on the ground. What is changing is the role of the rep, who is going to be positioned as a knowledge asset and a service provider beyond the pill itself. The value of the relationship between the rep and the customer is going to be quantified. A few pharma companies are trying to make loyalty a metric of performance. Educating sales professionals to conform to this new model is not going to happen overnight; for some the transition will be painful. And there is a question whether this criteria is sufficiently objective to serve as the basis for compensation involving large numbers of professionals. Asking a physician to assess what amounts to a sales rep's personal and emotive skills is subjective. It might help determine what value the rep brought to the relationship, but it's worth emphasizing here that a sales professional is ultimately hired to sell. Going that extra mile, doing the right thing beyond the transaction itself, may—or may not—make a difference in generating prescriptions.

PE: *What does the group feel about the pace of this change? Will the next five years bring still more rapid transitions or are these transitions likely to occur at a slower rate?*

Truitt: Achillion is active in the HCV space. I can say I have never worked in a segment that has innovated at such a furious pace. Three years ago, the science to treat this condition had given us a single direct acting antiviral, pegylated interferon, and ribavirin that provided cure rates of approximately 70%. Today, we have combination therapies for hepatitis C that have demonstrated cure rates near 100%, at a high level of safety and tolerability.

Progress in the science has been rapid and we anticipate continued change and improvement. What counts is building a nimble organization that can move quickly to seize opportunities as the science evolves.

PE: *The implication of these new therapies is you may be obliterating a chronic disease in the course of a single 12-week course of treatment. The traditional paradigm of financial success in biopharma is selling a drug that patients must take as maintenance therapy, for years or even a lifetime. As you cure these patients, won't the financial opportunity go away?*

Truitt: My experience is that with every new treatment that advances the standard of care, we underestimate the prevalence of the condition. We think hepatitis C is under-diagnosed. And you also have to factor in the time it takes to get all those patients into treatment. Our forecast models at Achillion project a multi-billion dollar market for this next generation of hepatitis C products extending well into the next decade, in the US alone. This doesn't include additional markets with large patient populations like China, Japan, and other parts of Asia.

PE: *Will the business model of the future move us further toward the "virtual company" concept in which efficiency depends on outsourcing many key activities and functions to a third party?*

DiPiano: The virtual or extensively outsourced company model has great appeal among investors and shareholders, and I don't see that changing, particularly in small companies like my own. Infrastructure is expensive. Investors like the idea of being flexible and to cut SG&A expenses when things don't work out. Pivot is the word that comes to mind: it's easier for a CEO to shift course if you don't have 5,000 people working for you.

PE: *Another benefit of being virtual is the ability to access a huge talent pool of people who have left industry jobs, for one reason or another. Consultancies filled with ex-industry people can be retained on a project basis, avoiding the high fixed costs of employment. It's a great model, as the client also benefits from the varied background of these people rather than keeping people who might only know how to do one thing.*

Bourret: At many small companies, major internal functions are outsourced, such as sampling, benefits, payroll, etc. In addition, sales representatives and managed care managers can work on a contract basis. The focus is on building a strong in-house management team with the mindset and flexibility to multi-task. People have to be prepared to rise to the occasion. The largest companies are often preoccupied by strategic issues at the top of the decision chain and thus can devote less attention to the troops on the ground—the field force. This is an omission that small players make at their peril.

PE: *A larger question shaping the future is the origin of those new drug pipelines that promise so many breakthrough products. Licensed-in products seem to be in the ascendant. Can licensing replace the productivity flaws that seem to inhibit traditional in-house R&D?*

Truitt: It makes sense to spread your opportunities—you can't invent everything in-house. The key is deciding when and how to transition assets into your portfolio. It's a decision that must be taken on a case-by-case basis.

PE: *Your emphasis on the business being centered on the patient has been very consistent today. Is the industry taking heed, in your view?*

Furey: Progress has been made, but there is much still to be done. One example is market access, which has emerged as a new, high-profile function in big Pharma organizations. In many cases, this integrative, more holistic approach to addressing the customer has not worked out well. Why? I believe it's because the overall mindset in marketing and commercial operations continues to neglect the patient—market access is not designed to be patient centric. Such programs were created in reaction to the rise of the payer. It is a company centric response. We don't think consistently and strategically about where the patient fits in this equation – what does he or she get, beyond our own specific needs?

The aim of any deal must be to do something good for patients. That's the ultimate test of market relevance and it usually takes five or six years for the partners to confirm that their joint efforts paid off.

—John Furey, Baxter Healthcare Corporation

DiPiano: A good licensing program requires management to root out "the not-invented-here" syndrome. The big multinational company I worked for prior to launching my current business had a reputation as a bad partner. It needed to own every part of the deal, which was always scrutinized first for its tax implications. Such ground rules made it very difficult for any smaller partner to ink a transaction that is remunerative and sustainable.

Furey: Companies able to build "win-win" partnerships will secure a competitive advantage against those that choose to stay solo. The issue is managing the adjacencies: a licensing deal has to make sense to your core market mission or there is the danger the business will get too broad too quickly so that you lose focus. It's worth recalling the aim of any deal must be to do something good for patients. That's the ultimate test of market relevance and it usually takes five or six years for the partners to confirm that their joint efforts paid off.

DiPiano: I agree, but there are other factors at work, beyond this rigid commercial mindset. We are afraid to speak to the end-user of our products – the patient – because the law says our main interlocutor has to be the regulatory agencies. Yet consider the fact that all the top leadership of the FDA is active on Twitter. It is ironic that the regulators can interact directly with patients but we – the regulated – cannot. When real dialogue depends on the intervention of a third party, it's harder to put the patient in the center. PE

William Looney is *Pharmaceutical Executive*'s Editor-in-Chief. He can be reached at wlooney@advanstar.com.

Photo: Thinkstock

Fixing Wikipedia

Can Pharma overcome its natural aversion to undocumented risks and join a growing effort to make the world's leading online health information resource more relevant to providers and safer for patients?

By Peter Houston

As I started writing this, my 77-year old mother-in-law was taken ill; she had suffered a silent ischemia. A few days in hospital and she was back home, tired but on the mend. One of the medications prescribed was Warfarin. She wasn't especially happy—the name rang a rat-shaped bell for her—so I suggested a quick Google search to find out more. Close to the top of the results list, we found Wikipedia's page on the anticoagulant.

With one search, my mother-in-law and I joined the millions of people who turn to the Internet for health information every month and end up on Wikipedia, "the free encyclopaedia that anyone can edit."

According to *"Engaging Patients Through Social Media,"* a survey report released in January by the IMS Institute for Healthcare Informatics, Wikipedia is now the leading single source of healthcare information for patients and healthcare professionals.

The report shows that the top 25 Wikipedia healthcare pages were each accessed more that 2 million times in a 12-month period, with the Tuberculosis page topping the list at 4.2 million visits a year. Patients are using the site throughout their healthcare journeys, not just when treatment starts or changes. Healthcare professionals

(HCPs) also use it to research specific conditions, especially for rarer diseases that are less well understood at the general practice level.

As many as three-quarters of patients with Internet access in the United States search for healthcare information online; in Europe, the figure is as high as 80%. Almost half of US physicians using the Internet for professional purposes reference Wikipedia; it could be as high as 75% in Europe.

Searches don't necessarily start on Wikipedia, but a high percentage end up there. A recent post on the eConsultancy digital marketing blog reported that Wikipedia entries are likely to feature heavily in any web search, second only to brand names or related URLs. eConsultancy's *"Wikipedia and SEO"* post claims that where searches are focused on more generic information, disease states for example, Wikipedia is likely to rank first.

Wikipedia scores highly with search engines which, like the general public, trust its content, recognize the breadth of information it contains and its global, multi-lingual nature. The free-to-access content is generally regarded to be of a high standard, especially when compared with information available through un-moderated social platforms like Facebook and Twitter.

The fact that patients turn to the Internet, and ultimately Wikipedia, for health information is not surprising. The IMS Institute report spotlights a growing need for pharma to consider engaged patients who want information that is reliable, up to date and understandable. Wikipedia is right there, with almost 4.5 million articles in English and growing at the rate of 800 pages a day. While not perfect, it is the most comprehensive encyclopaedia in human history.

Fact gaps

But it's the "not perfect" part that worries people in this risk-averse industry we call pharmaceuticals. The rub is the general public and HCPs are regularly accessing occasionally inaccurate and potentially dangerous health information online. "The combination of trust in Wikipedia and its vulnerability to both mistakes and author bias has caused concern…" say the IMS Institute's *"Engaging patients"* authors.

Patients are using Wikipedia throughout their healthcare journeys, not just when treatment starts or changes. Healthcare professionals (HCPs) also use it to research specific conditions, especially for rarer diseases that are less well understood at the general practice level.

Wikipedia itself makes it very clear that the information on the site is not necessarily accurate. At the top of its general disclaimer page, in big, bold capital letters, it says **"WIKIPEDIA MAKES NO GUARANTEE OF VALIDITY."**

The page emphasises the fact that Wikipedia is an "open-content collaborative encyclopaedia," meaning that anyone with an Internet connection can alter its content. The last sentence on the general disclaimer page says, "If you need specific advice (for example, medical, legal, financial or risk management) please seek a professional who is licensed or knowledgeable in that area." This doesn't seem to be putting off patients, carers and physicians turning to the site for health information. It's what patients and practitioners do with this information that raises the prospect of Wikipedia becoming a public health problem.

Can you trust a crowd?

As things stand, it looks unlikely that Wikipedia has the manpower (volunteer editors are 90% male) to fix this problem. Tom Simonite wrote in the *MIT Technology Review* last year that the volunteer workforce that built the English-language Wikipedia peaked in 2007 at more than 50,000 people but had fallen to about 30,000 in the middle of 2013. These are the active editors that are the only real defense against vandalism, hoaxes, and manipulation.

In his article, "The Decline of Wikipedia," Simonite says problems with a "crushing bureaucracy" and an "often abrasive" atmosphere deter the recruitment of new blood that could broaden and improve the service.

That doesn't mean that the Wikipedia community is ignoring the problem of unvalidated medical information. WikiProject Medicine, a loose coalition of 500 volunteer editors, most with some level of medical or pharmaceutical expertise, has set out to try to correct some of the problems with health-related content on English Wikipedia.

The group, including experienced medical editors, is aware of Wikipedia's shortcomings. Veteran Wikipedian Anthony Cole is a participant in the group and says, "We are very conscious of our responsibility at or near the top of every search-engine result."

The work of the group centers on assessing and reviewing articles. Members are encouraged to improve articles against style guidelines developed specifically for medical articles and add high-quality references wherever possible.

(Spong) thinks the industry uses concerns over regulatory transgression as an avoidance strategy, but challenges it to change. "The industry repeatedly lays claim in its corporate communications to a commitment to enlarging the store of humanity's health and well-being. We, the healthcare consumers of the Internet, respectfully request to cash in that promissory note."

Wikiproject Medicine is currently focusing on 85 articles deemed to be of top importance, striving to get them to at least Wikipedia's "B" standard, where the content is mostly complete and accurate without major problems. To date, Wikiproject Medicine has achieved this for 80% of the targeted articles. It has also set a target for 80 up-to date "Featured Articles" (Wikipedia's top quality ranking) and 300 "Good Articles," that have passed an official review.

Vet and verify

While this work is incredibly valuable, it seems like a drop in the ocean. That's why Cole would be delighted to see the pharmaceutical industry get involved.

He says, "Wikipedia is just waiting to have good content written onto it. If a pharma company produces a model encyclopaedia article conforming to our arcane but not impossible norms, under the Creative Commons 'CC-BY-SA' license, nothing will prevent it from being adopted wholly if we don't already have the article, or in part if that part improves an existing article."

Cole is not overly concerned that pharma companies will overrun Wikipedia with information that smacks of self-promotion. Problems only arise when companies try to force something into the encyclopaedia that doesn't conform to Wikipedia's rules. He says the "secret" to successfully adding content is to make it good content; companies will only face difficulties when they try to slant content or edit articles directly.

"My perception, and that of at least one other veteran medical editor, is that, so far, the companies have been no problem at all to us," says Cole. "I don't think I've confirmed one instance of company editing in eight years here, and where I've suspected it, it has been benign."

Cole does however, have an alternative—he would like to see paid editors reviewing medical articles on Wikipedia. The idea is that named, highly-regarded scholars review for accuracy, balance and comprehensiveness articles that have reached Wikipedia's top "Featured Article" standard. Those that pass review would then be locked down. Future editors, rather than working on the "approved" version, would update non-public drafts, which would only replace the locked version after it had passed another expert review.

The funding for these paid editors would come from relevant non-profits whose mission includes public education, with oversight provided by relevant scholarly and professional societies. Cole would give preference to benevolent foundations or government agencies, but doesn't discount a role for non-profits funded by pharma. He believes this approach would also overcome one of Wikipedia's biggest problems—the reluctance of experts to contribute.

"Because any Randy in Boise can do what he likes to our articles, experts just don't bother," says Cole.

Randy is the archetypal "relentless but uniformed" Wikipedia editor first mentioned in a 2006 *Wired* essay. Cole says few academics are willing to waste their time composing a brilliant article only to have it descend into drivel as well-meaning amateurs or academics from outside the discipline "correct" it. "And they don't have the time to argue with Randy for weeks about why vaccines don't cause autism," he says.

Cole believes that if this model was adopted it would not only improve the quality of content on the site, it would also increase the volume of quality content. With a new, reliable class of Wikipedia article developed, genuine experts would be happy to write for Wikipedia, for free.

"Members of the different disciplines would informally adopt the articles in their areas of interest, producing a thousand times the quantity of quality content than even the pharmaceutical industry could afford to pay for," says Cole.

However, it is funded; the idea of delivering approved medical content on Wikipedia makes perfect sense, but change at Wikipedia happens slowly.

Late last year, a discussion started on the Wikiproject Medicine pages around the idea of adding disclaimers to all medical articles on Wikipedia. Common sense you might think, but the discussion thread around wording, positioning and design of any disclaimer runs to almost 40 screens and ends without any consensus almost three months later.

What should Pharma do?

Until a system of article review and approval is created, and accepted,

Cochrane's Long Coattails

One way to improve the reliability and rigor of health information supplied through Wikipedia is expanding its line of vision to include outside partners. An effort to do just that is now underway, through an informal working link agreed in February between WikiProject Medicine and the Cochrane Collaboration, an independent advocate for accuracy, credibility and transparency in the dissemination of health research. Founded in 1993 as a non-profit and based in the UK, Cochrane operates as a global review network of 31,000 volunteer epidemiologists, physicians, statisticians and research scientists—many from prominent academic health centers—located in more than 120 countries. And although the group has been in existence since 2004, in 2012 it moved to formalize its legal status by incorporating as a non-profit in the state of New York.

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Boost for WikiProject

The agreement between the two organizations seeks to raise the quality and integrity of the medical information furnished through Wikipedia, where, despite its mass popularity, less than one per cent of its content is subjected to external peer review. Cochrane experts will furnish WikiProject Medicine editors with advice on raising standards for organizing material and evaluating its suitability for the general public. In addition, Cochrane is offering to provide the editors with 100 free accounts that grant access to the full Cochrane Library, consisting of more than 5,000 Systematic Reviews conducted by the network's researchers on drugs and other types of medical interventions. Finally, funds have been procured to create a new full-time position, Wikipedian in Residence, to serve as liaison between Cochrane staff and WikiProject editors.

Mark Wilson, Cochrane's new CEO, told *Pharm Exec* "this is a fantastic way to make our information accessible to more people, in an easy-to-digest format." Although Cochrane is widely known among big Pharma companies for the scope, detail and accuracy of its Systematic Reviews, few are aware of the liaisons Cochrane has forged with patients and the general health care community. Recently, Cochrane established a department at its Oxford UK headquarters to coordinate these relationships—the goal is to make the Cochrane Reviews more relevant to lay viewers without sacrificing professional standards. "We are vying to serve the soaring numbers of online health consumers with the best and most accurate information available," says Cochrane press officer Katie Breeze.

James Heilman, a leader of the WikiProject Medicines team, says the Cochrane link will go far in raising the credibility of medical information sourced through Wikipedia. He notes that the effort to reach out is not new: WikiProject already has information exchange relationships with the National Institutes of Health, the World Health Organization, the University of California/San Francisco School of Medicine, and Cancer Research UK, among others. Talks are also underway with the Centers for Disease Control in Atlanta. And although the group has been in existence since 2004, it recently moved to formalize its legal status by incorporating as a non-profit in New York in 2012.

Finding the patient voice

Heilman was frank in telling *Pharm Exec* that making medical information more accessible does not necessitate a weakening of professional standards. "Half of our editors come from outside the medical practice community; some of our best, most authoritative and frequently sourced material has been written directly by patients," Heilman said. "What counts is finding the best way to use language most appropriate to the audiences we are speaking to, and that requires embracing a diversity of sources." He gave Wikipedia's widely cited postings on Crohn's disease and the kitogenic diet for epilepsy patients as examples.

It's those trials ... again

However, It is still less than clear how big Pharma fits into this picture. WikiProject is aware of the many legal constraints on what industry can communicate. As noted elsewhere in this story, it does not have an agreed standard to certify that such material adheres to its broader guidelines requiring that sourced information be "non-biased." Heilman told *Pharm Exec* the uncertainty might be a reflection of the industry's own ambivalence about sharing its data. "I'd say that if industry wants to be involved in the revolutionary changes now taking place in health care information, the best way to start is to formally end the practice of selectively publishing the results of its sponsored trials. Such action would go far to remove the taint of 'publication bias' that makes it harder to verify and incorporate this kind of material as a source."

— William Looney, Editor-in-Chief

"If industry wants to be involved in the revolutionary changes now taking place in health care information, the best way to start is to formally end the practice of selectively publishing the results of its sponsored clinical trials."

—James Heilman, WikiProject Medicine editor WIKIPROJECT MEDICINE

should pharma companies take the task on themselves?

Given the broad usage of Wikipedia content by big Pharma's target audience, the site's presence at the very top of the search engines and company focus on ROI, you might have thought they would already be courting Wikipedia aggressively. Easier said than done—there isn't really a Wikipedia to talk to.

Cole describes it as "an incoherent bunch of individuals with radically different opinions on just about everything, especially on the best way forward." But he and other Wikipedia medical editors are keen to discuss the best way to ensure the reliability of pharmaceutical content while safeguarding the independence and neutrality of the encyclopaedia. "I believe all large companies should have one or two Wikipedia experts on their payroll," he says.

This is an idea put to the industry in an open letter from Hungarian Medical futurist Bertalan Meskó, in June 2012. His idea was simple: pharmaceutical companies should name an employee who could make 100%-transparent edits to Wikipedia entries related to their own products. Two years on, he says has had acknowledgement from several pharma companies that this is the correct way for them to tackle Wikipedia content, but none have actually done it.

Social business evangelist and STweM health conversation blog author Andrew Spong is a strong supporter of the pharma Wikipedians concept, but doesn't think companies recognize Wikipedia as a business-critical need. He thinks the industry uses concerns over regulatory transgression as an avoidance strategy, but challenges it to change.

"The industry repeatedly lays claim in its corporate communications to a commitment to enlarging the store of humanity's health and well-being," says Spong. "We, the healthcare consumers of the Internet, respectfully request to cash in that promissory note."

His hope is that pharma companies will ultimately take on their own Wikipedians, especially as he thinks the regulatory "smokescreen" is falling away. Spong pointed to the February 2014 informal guidance on digital communications from the UK's Prescription Medicines Code of Practice Authority. "When an industry's own regulators observe that pharma could consider taking a more "proactive" role with regard to Wikipedia, the only conclusion one can reach is that the industry is being too conservative in its approach," he say.

A moral duty

Like Wikipedian Cole, Spong doesn't see any major conflict in pharma companies getting involved in the creation and editing of Wikipedia content. Contrary, he believes whatever public health risk there is in Wikipedia content would be mitigated rather than exacerbated by the industry's direct involvement.

"The active curation of all entries relevant to its business would provide each pharmaceutical company with a copper-bottomed means of becoming the authoritative source of information on the Internet about its own products," Cole says.

He believes Wikipedia's value to pharma should be self-evident.

"In my opinion, the pharmaceutical industry has a moral and ethical duty to assume an active role in the editing of relevant Wikipedia entries," he says. "The trust-generative, credibility-boosting benefits that a visible and enduring commitment to editing Wikipedia in a balanced, approvable manner would also bring are secondary, but surely also valuable."

Whether or not Wikipedia ever delivers on WikiProject Medicine's ambition of providing free access to the sum of all medical knowledge, I am optimistic that the quality of information on the site will continue to improve. In the long-term, the Wikipedia community will find a way to work with the pharmaceutical industry, HCPs, patient groups, non-profits, professional agencies and regulators to validate its medical content.

In the meantime, I would refer the public and HCPs to the advice given in Tom Simonite's *MIT Technology Review* article. Treat Wikipedia the way you would an urgent care center, not as a replacement for established medical advice but as a cheap and fast place to go first. "A place to get you pointed in the right direction," Simonite writes. Like Simonite, I think Wikipedia does a pretty good job at that. PE

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Regional Trends In Bioinnovation investment

Can the Cambridge growth model be duplicated?

By Amanda Christini and Kenneth Kaitin

Bioinnovation has been a key driver of US economic development, with notable examples of success in California's Bay Area and the Boston/Cambridge nexus in Massachusetts. Over the past two decades, hundreds of thousands of jobs have been created through start-up companies and the large multinational anchor companies that attract ancillary support services, including venture capital. Today, many other jurisdictions—both in the United States and abroad—are seeking to replicate this productive ecosystem to support their own economic growth.

It is thus timely to ask: How have these regions become so successful in this space? What factors contribute to their dominant strategic position? What lessons can be applied to help other regions grow their bioinnovation assets? Noting the mutual benefits that pharma companies, academia and government obtain from these successful precedents, we identify the necessary foundations for a strong biotech ecosystem and explore a potential strategy blueprint using Philadelphia and the state of Pennsylvania as a case study.

The seeds of growth in bionnovation are rooted in four stakeholders: Academic medical and research centers (AMCs); biotech and pharma companies; investors, including VCs; and local, state and federal government institutions. Each of these stakeholders has dramatically different priorities and goals (see Figure 1).

Maximizing the value of these relationships depends on identifying the areas where goals and mission align. While it may appear that the areas of overlap are small, they carry transformative potential. Breaking down silos that thwart the ecosystem of innovation is thus critical to success. For example, AMCs' mission is typically focused on excellence in research, teaching and patient care. But another key part of their mission is to translate basic medical breakthroughs, which are largely funded by public money through institutions like the National Institutes of Health (NIH), into improvements in medical care. These improvements are usually commercialized by the private sector, generating revenue growth and more jobs. Likewise, while VCs are focused primarily on return on investment to their limited partners, that investment remains a viable avenue to achieve substantial investment multiples. Since 2008, average multiples for VC-backed private biotech companies via M&A transactions have been increasing, while the biotechnology IPO market is starting to open up again. Ten IPOs were listed in the first five months of 2013, the largest number in nearly a decade.

While pharma and biotech firms must focus on shareholder return, there is often a paucity of internal assets to leverage this goal. So this, too, requires an effort to engage with other stakeholders through pre-competitive collaborations with AMCs that provide access to potential new pipeline assets. Finally, for governments, bioinnovation carries a multiplier effect by adding to the tax base and creating jobs through innovation-friendly urban infrastructure. The evidence shows that an interactive matrix supporting innovation has become mandatory for top-line growth in sectors vital to 21st century competitiveness.

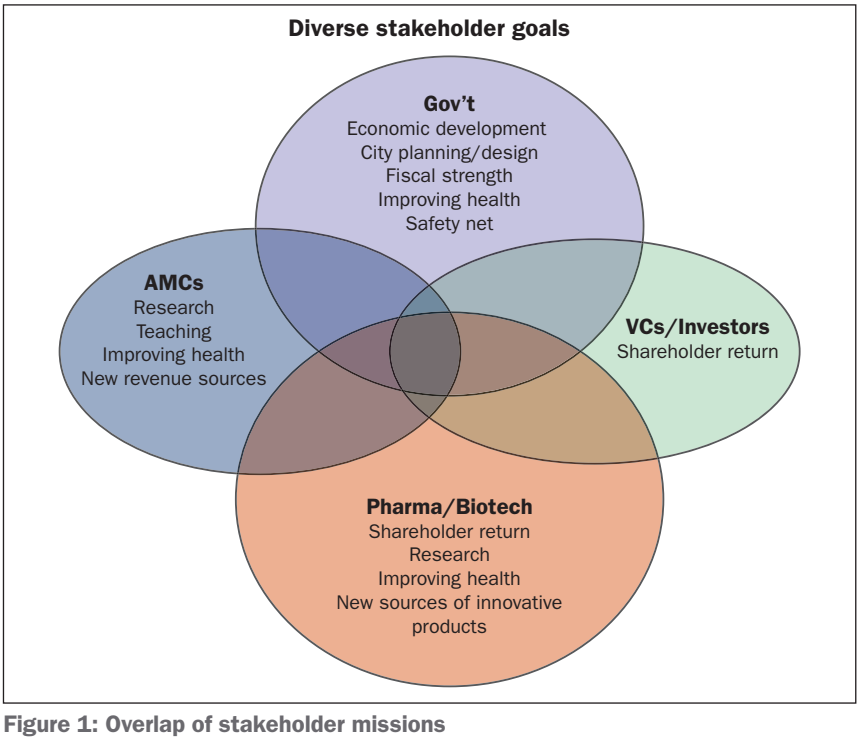

Figure 1: Overlap of stakeholder missions

The Cambridge Model

This success story begins with the universities and AMCs in the region, specifically MIT, Harvard University, Whitehead

Institute, Tufts University, Boston University, University of Massachusetts, and their associated medical schools, medical centers and business schools. Among these institutions, MIT stands out with a vision of entrepreneurialism that was far ahead of its time. Specifically, MIT encouraged faculty to create start-ups and to collaborate with industry partners. Its Office of Technology Licensing has achieved some impressive metrics, with nearly $150 million in revenue, 16 start-ups and 199 US patents. More important, companies founded by MIT alumni employ 3.3 million people and generate revenues of approximately $2.2 billion annually. Some 6,900 MIT alumni firms are headquartered in Massachusetts and generate $164 billion in annual revenue within the state.

With MIT as the standard-bearer, neighboring institutions are moving toward relatively low-friction strategies that facilitate more bioinnovation. There is a critical mass of top-tier academic institutions in the Boston region that offer experience, talent, IP and vision that can turn invention into value. Resources derived from here are supporting critical research at a time when NIH funding is declining. Approximately 20% of MIT's overall research budget is derived from corporate partnerships, a figure far in excess of most peer institutions.

With this academic legacy as a stimulus, large multinational companies like Novartis and Sanofi, began locating their US research headquarters in Boston, Cambridge and surrounding suburbs. In addition, there are substantial home-grown successes, such as Biogen (now Biogen-Idec), Genzyme (now a wholly-owned subsidiary of Sanofi), Millennium (acquired by Takeda in 2008), Vertex, and Alkermes.

This influx of established companies and crop of new university-based start-ups requires vast amounts of capital. Of the 14 most active VCs worldwide in the biotech space, four are located in the Boston area, six in the Bay Area and two in New York; the remaining three are in Europe. The four VCs in the Boston Area—Third Rock Ventures, Atlas Ventures, MPM Capital (based in the Bay Area and in Boston) and SR One—have raised a total of $745M to invest in mainly local ventures. Interestingly, however, of the top ten VC deals in 2012 in terms of dollar value, only one company, Bluebird Bio, was in the Boston area, while seven were in California, reinforcing the regional bias inherent in VC investing. This is important, because once a region dominates on access to capital, it creates a positive feedback loop where dollars continue to flow into ventures led by known managers with strong track records of facilitating lucrative VC exits.

A final element in the Cambridge story is proactive government. The state of Massachusetts, through its fiscal policies and life sciences initiatives, has created a positive business environment for the industry. An example is the 10-year, $1-billion Life Sciences Initiative enacted in 2008. As part of this initiative, the Massachusetts Life Sciences Center (MLSC) was created to implement the program. Its goals are to strengthen the state's role as the international leader in life sciences, create high-skill/high-paying jobs, attract investment dollars and support innovation and entrepreneurship.

The MLSC is structured around a diverse Board of Directors and Scientific Advisory Board charged with allocating a $500 million capital fund, a $250 million tax incentive program and a $250 million investment fund. As of February 2013, $359 million has been committed and used to leverage $1.03 billion in matching investments. Funds provide direct support for research, new investigators, recruitment of top talent to universities, industry/academic research collaborations, start-up capital to early-stage companies, and capital investment for infrastructure support. MLSC has made 77 awards totaling $56 million in tax relief to companies, who have pledged, in turn, to add 2,800 new jobs to the existing 80,000 life sciences jobs in the state. Outside the MLSC program, the state and local authorities have invested in a land use policy that includes new, open corporate space design, common green space, high-quality public transport, mixed residential/corporate neighborhoods, and use of the Boston area waterfront that fosters business collaboration.

Can Cambridge Be Cloned?

Despite the fact that bioinnovation has flourished in Massachusetts and California, other parts of the country continue to struggle. This raises the question: can their success be replicated? To provide an answer, we examine how various engagement strategies play out among each of the four stakeholders that nurture biopharma innovation.

» **Educating AMCs.** Researchers, clinician-investigators and administrators are the source of all university-based innovation. Understanding this fundamental concept is the first step toward change; in fact, it begins with mobilizing the strength of this "grassroots" network. One way to do it is to encourage researchers to learn more about basic operational realities involved in translational research, including cost, timelines, and regulatory considerations; the process of due diligence to determine the value of an invention or business concept; intellectual property; and sources of funding. Educating this group toward a basic level of business acumen is critically important, but this is seldom done in most AMCs.

Investigators should be aware of where funding in today's environment is coming from, and to the extent possible, align their research interests with funders' goals and interests. They should get external business advice as "quality control" for their strategy, starting with the real world value of their innovation. Most importantly, researchers must be their own advocates: they must talk often and openly with other stakeholders to monitor the process and identify improvements.

One priority often overlooked is to detect and eliminate barriers to cooperation. Often, these exist to protect IP or to promote ethical behavior. This requires a revisit of long-standing policies like IP ownership, equity ownership by founders, reach-through rights and conflicts of interest. An extension of this point is developing rigorous standards for fiscal responsibility while being reasonable and creative in negotiating terms with licensees, start-ups and industry collaborators. Too often these institutions insist upon prohibitive financial terms and structures that are non-starters for a partnership. Institutions with traditional, non-entrepreneurial cultures should look at peer institutions that have established bioinnovation-enabling policies without compromising their academic missions; examples include MIT, University of California at San Francisco, Duke University, Stanford and the Cleveland Clinic.

Faculty should be recognized and rewarded for achievements related to entrepreneurship, in the same way that they are for securing grants or publishing in peer-reviewed journals. Equally important is striking a balance between basic research and translational work—do not forsake the former for the latter. Finally, AMCs and universities must provide resources for their entrepreneurs, including infrastructure to support basic and clinical research, regulatory and business support, and funding in the form of grants or, more interestingly, venture funding in exchange for an equity position.

» **Pharma, biotech and other industrial partners.** Private industry is increasingly interested in working with other stakeholders. More than 350 life sciences academic-industry deals/partnerships were agreed in 2012, predominantly in cancer (15%), infectious disease (14%), diagnostics (15%) and neurology (12%). The top academic institutions in terms of deal flow included Harvard and the University of Texas, with seven each; University College of London and University of California system, with six apiece; and Broad Institute (MIT and Harvard), with four. Nearly all of these deals were discovery-stage, platform-based collaborations.

Pharma and biotech companies also engaged in a substantial amount of M&A activity, with 27 acquisitions in 2012. Only six of the acquired companies were at the preclinical stage, four in Phase I and the remainder in Phase II or higher. Similarly, total licensing deals continue to decline from 2010 levels, with the vast majority in the discovery or post-Phase II space. This leaves a gap in partnership activity and corporate funding for innovative technologies in the critical pre-proof-of-concept area. It reflects the increasingly low-risk tolerance of potential partners. Very early stage deals are cheap and large payments are back-ended, thus allowing partners exclusive access to a potentially valuable platform for very little upfront investment. Post-Phase II deals are sufficiently de-risked and provide an opportunity to add a near-term clinical asset to often dwindling pipelines. Everything in between is too risky and too expensive. In addition, the most active therapeutic areas in terms of deal volume—oncology and infectious disease—represent areas where regulatory reforms, such as breakthrough designation, make the development timelines more attractive than in other areas.

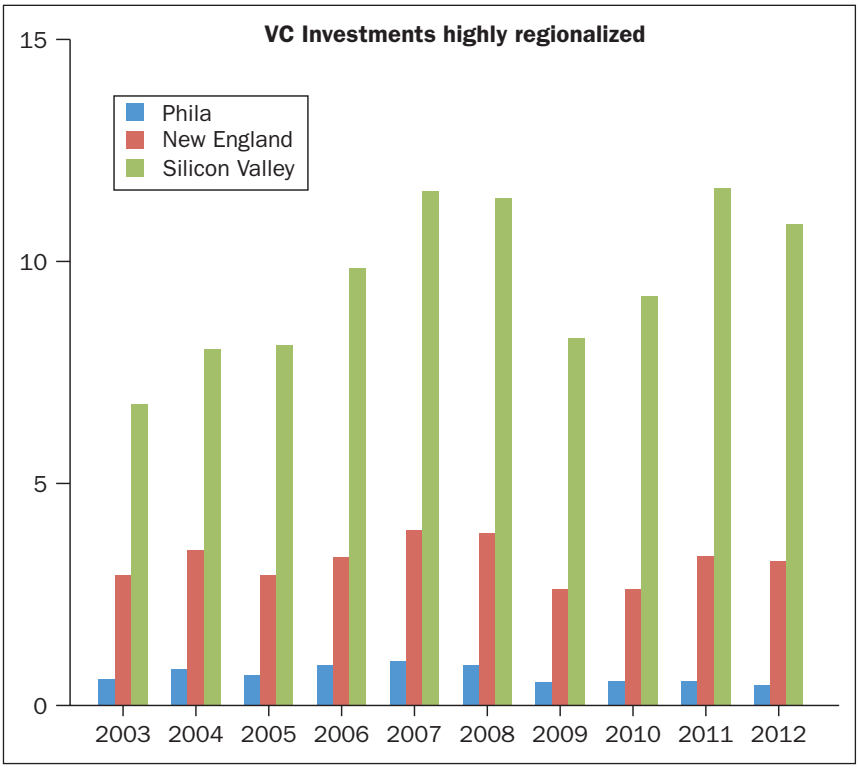

Figure 2: Regional trends in VC investment 2003-2012

In parallel, VC arms of pharma and biotech companies are becoming more active in earlier-stage investments that often fall outside the scope of the parent company's interest and mandate. In fact, of the 14 most active VC firms in life sciences in 2012, five were venture arms of pharmaceutical companies: Novo Nordisk, Novartis, Pfizer, SR One and Shire, which together represent a total of more than $1.1 billion in potential investment dollars.

While it is difficult to imagine pharma and biotech companies altering their

risk-tolerance profiles on new deals given shareholder pressures, a reasonable avenue to maintain early-stage investment for start-ups and access for their partners would be for pharma and biotech companies to shift a portion of their substantial cash reserves into venture investment vehicles. These investments are most typically part of a syndicate of other VCs that further reduces risk but preserves potential ROI and access to early-stage, truly innovative technologies.

» **Local and state government agencies.** Many analyses indicate that to be competitive in the bioinnovation landscape, governments must build infrastructure, offer tax incentives for businesses to relocate and add jobs, and fund grants and other direct investments in research. Yet with slow recovery from the 2008 financial crisis continuing, local and state government leaders are under considerable pressure to maintain budget neutrality.

Given the Massachusetts example, creative government intervention is a powerful tool. Moreover, public support goes a long way to bridge the gap between discovery and proof-of-concept that is currently hobbling much of the true innovation in the life sciences.

» **VC funding.** The final piece of the life sciences ecosystem puzzle is equity financing, provided typically by a robust VC community. At least three important trends have emerged over the past five years. First, VCs and their investments are highly regional (see Figure 2 on previous page). Second, with a few important exceptions, such as Third Rock Ventures, VCs are not investing in the translational research phase, but rather the peri-proof-of-concept phase. Third, relatively few new start-ups are being funded; the bulk of VC investments are going to follow-on rounds in existing portfolio companies.

Moreover, in 2012, the amount of VC investment in young, innovative life sciences companies fell to its lowest level in nearly 10 years. This holds true both in the United States, where funding was 4% lower than 2011, and in Europe, which saw a substantial drop of 31%. In addition, this cash is spread over fewer deals, 156 in 2011 in the United States, and highly concentrated into a handful of biotech hubs. This reflects the zero-risk tolerance of many VCs and their limited partners, the overall downturn of the investment markets since 2008, a paucity of quality management teams for start-ups, and, until very recently, inability to access public markets for exit. With biotech IPOs at their highest level in years, strong data supporting ROI, and the overall stock market at an all-time high, perhaps we will see greater risk tolerance among VCs and a return to their roots of funding novel research and new innovation. If so, this will be vital to extending the locus of a strong bioinnovation ecosystem.

Philadelphia: The Next Cambridge?

The Cambridge example shows the necessity of engaging and incentivizing all stakeholders to create and maintain a successful and thriving bioinnovation ecosystem. Philadephia and the state of Pennsylvania is as an interesting counterexample, with similar parameters to Cambridge and Massachusetts. Philadelphia has four top-tier AMCs and universities (University of Pennsylvania, Temple, Thomas Jefferson and Drexel); the second-highest level of NIH funding by institution (Penn); many multinational pharmaceutical companies and large biotechnology companies; and a small concentration of early-stage biotech and life sciences companies. The state's second-biggest city, Pittsburgh, is home to the University of Pittsburgh School of Medicine, a top-ten medical school and ranked sixth for NIH funding, and Carnegie Mellon, a leading engineering school.

Despite this, the city and state is not considered a vibrant hub of bioinnovation. Why? Our premise is that the four key stakeholders have not yet been fully engaged in this goal.

AMCs in PA don't make realizing the value of their innovations a strategic imperative; none of the top ten AMCs most active in spin-out formation are in PA, despite the fact that Penn ranked third in European and sixth in US patents issued to it in the eight-year period ending in March 2013. In contrast, MIT ranks far below Penn in the number of patents issued, but was the second-most active, behind the UCAL system, in spinning out new life sciences companies.

In addition, there is a limited amount of VC funding available. While many pharma and biotech partners make their homes in the Philadelphia area, their deals in the last several years are focused geographically in Cambridge and Silicon Valley. Gov. Tom Corbett has spoken openly about making life sciences investment a priority in PA, but there are few tangible results to date. The much discussed "D2PA" program—discovered in PA, developed in PA—allocates just $10 million in the current state budget to invest in new companies. The Life Sciences Greenhouse and Ben Franklin groups, funded by the state to invest in new technologies across all industries, have invested only $23 million into 33 seed and 23 pre-seed companies, and $17 million into 40 companies, respectively, since 2003. Gov. Corbett has put forward several tax incentive plans that will take effect over the next several years and has convened a panel of business leaders to discuss approaches to building and supporting a bioinnovation ecosystem in PA. Taken together, however, these initiatives pale in comparison to the strategies taken by states with highly successful life sciences hubs. If bioinnovation is going to succeed in unleashing new growth in PA, more must be done to incentivize each of the four stakeholders to make investments—and take risks. PE

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Photo credits: Olga Palaga

PORTUGAL: Preparing the New Portugal

When PharmaBoardroom came to Portugal in 2007, price cuts, payment delays and changes to the health system with each successive government were but the first indications for the pharmaceutical sector that troubled times were ahead: four decades of political and financial mismanagement had resulted in Portugal's economic stagnation. When the country requested a financial bailout by the IMF in spring 2011, the country quickly came round to face reality. Adaptation was paramount to the recovery of this economically ravaged nation, and government and industry quickly sought to find new solutions to the crisis. In 2014, renewed economic growth and a willingness by all stakeholders to work together will be the keystones to preparing Portugal's revitalization.

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Then-White House Chief of Staff Rahm Emanuel commented in 2009, "You never let a serious crisis go to waste…it's an opportunity to do things you think you could not do before." This mantra parallels the mindsets of many in Portugal's pharmaceutical industry today. After serious downturns in the last few years, the country is poised for restoration. While many believe that returning to the environment in the years preceding the crisis is not likely, there is immense hope for a return to respectable market levels.

From left: Heitor Costa, Executive Director, APIFARMA; Eurico Castro Alves, President, INFARMED; Manuel Teixeira, Secretary of State for Health

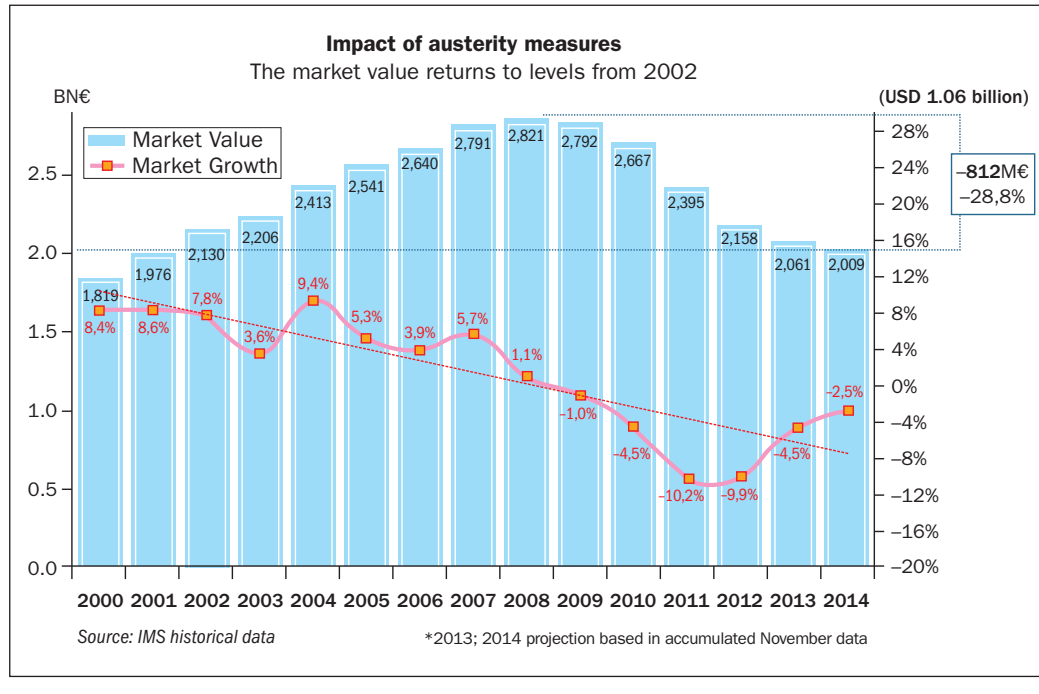
WHAT WENT WRONG?

Portugal's austerity measures for healthcare are similar to those across Europe, but are more extreme because of the country's bailout. As health plays a major role in Portugal's budget allocation, the pharmaceutical industry has been targeted as an area for cutting costs. "Imposing the lowest prices in Europe based on reference countries, creating restrictive access measures, and refusing to compensate new medicines are all easier than merging hospitals or changing policy at the level of the Ministry," says Heitor Costa, executive director of Portugal's pharmaceutical association APIFARMA. He believes that it is easier for the health system to make cuts in the area of pharmaceuticals, the majority of which are reimbursed by the country's government, than in other areas. The troika of the Central European Bank, International Monetary Fund (IMF), and European Commission have set a goal for government spending on healthcare to be limited to only one percent of GDP, one of the lowest in all of Europe. As such, the pharmaceutical industry created a memorandum of understanding (MoU) that stipulated the industry contribute EUR 600 million (USD 780 million) in savings back to Portugal's healthcare system between 2011 and 2012. This was followed up with a similar MoU for 2012-2013.

This agreement was critical to ensuring stability in Portugal, especially for innovative companies. "We try to work closely with Portugal's regulatory authority INFARMED and the Ministry of Health to find best ways to bring innovation to Portuguese patients," remarks Gisella Dante, general manager of Janssen Portugal. "Participating in APIFARMA is also critical; we believe in the protocol, and Janssen believes this is an important tool in terms of placing everyone together to determine a solution for the government, industry and ultimately the patients. This protocol was also the first of its kind in Portugal; no other industry has given money back to the government. Many companies had to work hard internally to make this protocol work for two consecutive years; but it represents a real partnership."

"APIFARMA maintains a stance of dialogue, which always prevails," says Eduardo Pinto Leite, vice president of APIFARMA and director general of GSK Portugal. "The industry is here because it has been given a license to operate for society. Although conditions are rough, particularly with lack of debt payment and slowness of innovation entry, the Ministry of Health knows the industry is here to stay. With that in mind, we have always supported dialogue."

"Partnership between the health system and the pharmaceutical industry



A TIMELINE OF REFORMS

2007	6% Reduction – Ordinance n° 30-B/2007	(Jan.)
	System of price caps – DL.65/2007	(May)
	5%, 9% or 12% Reduction applied to generic drugs with a market share of: 50% ≤ Q < 60%, 60% ≤ Q < 70% e Q ≥ 70% – Ordinance n° 300-A/2007	(May)
2008	Review under the new pricing methodology – DL.65/2007 and Ordinance n° 300-A/2007	(Apr.)
	30% Price cut for generic drugs maximum prices – Ordinance n° 1016-A/2008	(Oct.)
2009	Review under the new pricing methodology – DL.65/2007 and Ordinance n° 300-A/2007	(Apr.)
2010	Reduction resulting from the transfer of margins for pharmacies and wholesalers at 3.85 factor - DL.48/2010	(Jun.)
	7% Average price reduction on drugs, in accordance with the pricing methodology review - Ordinance n° 312-A/2010	(Jul.)
	20-35% Price cut for some generic medicinal products	(Aug.)
	6% Mandatory Discount in Retail Price for all reimbursed medicines - Ordinance n° 1041-A/2010	(Oct.)
	7.5% Price cut for biological medicines Despatch n° 18419/2010	(Dec.)
2012	New pricing methodology with a new set of reference countries (Spain, Slovenia and Italy), new marketing margins for wholesalers and pharmacies, and new generic prices (50% below the RRP of the reference product, or 25% if the wholesale price is less than 10€)	(Jan.)
	Downward prices review for branded drugs 1/April by the application of the new reference countries (Spain, Slovenia and Italy) - DL.112/2011	(Dec.)

Source: Price Legislation DL - Decree Law

must be more than noble intentions and enthusiastic words," notes Secretary of State for Health Manuel Teixeira. "Despite specific missions and frequent divergent approaches, health system activities and pharmaceutical interests have symbiotic connections. Bearing this in mind we are open to discuss balanced and affordable partnerships that give patients equal access to valuable treatments."

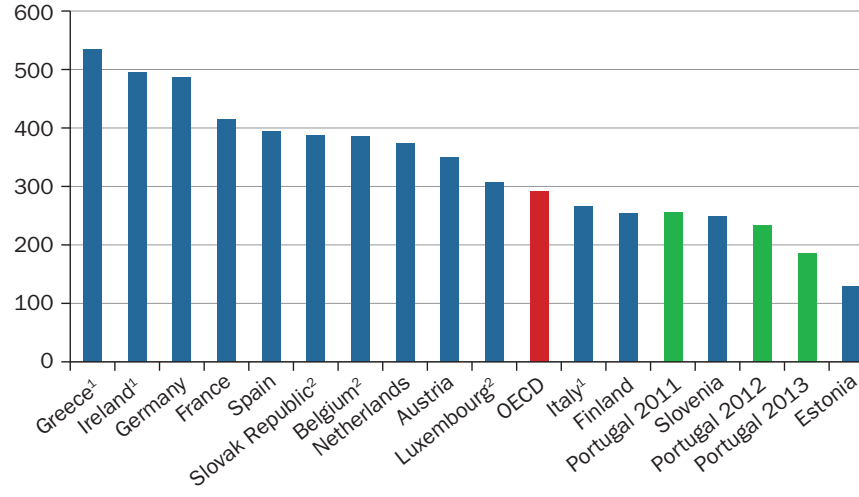
The industry's protocol to provide savings for the healthcare system over the last two years has seriously affected the introduction of new drugs into Portugal. For the last two and a half years, an extremely limited number of medications have been accepted for reimbursement. "Portugal has been part of Europe for a long time, but it feels like the country is leaving Europe because of this lack of access to new medicines to fulfill unmet medical

Eduardo Pinto Leite, General Manager, GSK Portugal

needs," continues APIFARMA's Costa. "Sustainability is one of the main preoccupations of all companies here and elsewhere in Europe. The industry should share risks in that sustainability while still maintaining access to innovation; the state currently designs the market for each company, which creates uneven competitiveness and is generally incomprehensible."

"The government has very demanding concrete targets to achieve, of which the industry is aware," says Nelson Ambrogio, managing director of Bayer Portugal. "There is a collaborative spirit between government and the industry, and there are clear challenges for issues like innovation approval. The period between marketing authorization and access to medicine in Portugal is almost 500 days. This figure is more than one year for approval in many other European countries."

Public Expenditure on pharmaceuticals per capita
both retail and hospital markets



Source: *OECD health data*
1. Cannot be separated and includes medical non-durables. 2. Prescribed medicines only.
Euro zone countries BCDE Indicators 2009 (or nearest year) Portugal 2010,2011 Infarmed Reports Ambulatory; 2013 Target MOU for 2013

From left: Robin Turner, General Manager, Roche Portugal; Rui Carrington, CEO, OCP Portugal

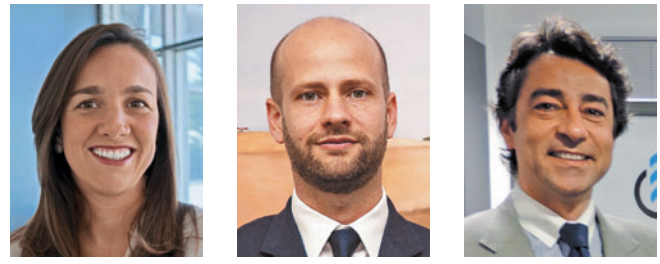
Part of this issue revolves around the complex regulatory system of Portugal, which pharmaceutical companies often struggle to comprehend. Eurico Castro Alves, president of Portuguese regulatory authority INFARMED, is making efforts to help streamline many of INFARMED's processes, such as the implementation of an autonomous and integrated national system for the evaluation of health technologies. "This system will be the basis for the decision on public funding for medicines and medical devices according to their cost-effectiveness," says Castro Alves. "The goal is to ensure equity in national access to medicines and medical devices, making available better suited treatments to the clinical situation of each patient, and correlating them to the resources of the national health system." Additionally, INFARMED also played a key role in the creation of the Forum of Portuguese Speaking Medicines Agencies (FARMED). "Through this project and through mutual cooperation," comments Castro Alves, "the objective is to move towards a more convergent regulatory framework, strengthening national capacities to promote and ensure access and rational use of quality, effective and safe medicines, contribute to the sustainable development of the sector and the respective health systems, and promote the elimination of barriers to such development."

TAKING THE HIT

Between Portugal's two main distribution channels of hospitals and pharmacies, hospitals have suffered in particular. As the pharmaceutical industry's largest customer, it has been critical for government to work with pharmaceutical companies to find solutions. Robin Turner, general manager of Roche Portugal, likens the relationship of the industry with the market to a marriage: "Sometimes they struggle because of money." This struggle has been quite severe in some cases; public hospitals in Portugal owe more than EUR 1 billion (USD 1.3 billion) in debt to the pharmaceutical industry. As the largest hospital-based pharmaceutical company in Portugal, Roche was owed a colossal amount. As a consequently, Roche "reluctantly introduced a new commercial policy for the 25 percent of hospitals that had the longest outstanding payments," recalls Turner. "These were hospitals that owed us between 500 and 1500 days. We insisted on cash payment until the historic debts were paid back. It was a resounding message to the marketplace to address the issue and promulgate change. Happily today, all historic debt has been paid back to Roche. We therefore have a clean slate

and the payment discipline of hospitals is at a stable and acceptable level."

Pharmacies have also endured their struggles as well. In 2008, the ambulatory market was valued at EUR 2.8 billion (USD 3.6 billion), while today its market size is the same as it was in 2002, representing a EUR 812 million (USD 1.06 billion) loss, or roughly 29 percent. Rui Carrington, CEO of local pharmaceutical distributor OCP Portugal, indicates that the model pharmacy shop as it is known today and patient accessibility to drugs have been affected as a consequence. "It is possible that punctual short-term market supply problems arise because of economic conditions or lack of financial capacity to support pharmaceutical distribution, shortage of bank credit and continuing reduction in market value," says Carrington. In order to fix problems across the supply chain as a result of these factors, Carrington suggests increased collaboration between distributors and pharmacies as well as increased productivity among all players. "Reducing the actual level of credit from wholesalers to pharmacies would be a start. This would require banks to provide credit lines that allow both to restructure their debts," recommends Carrington. "We need to at least maintain the current margins of pharmaceutical distribution and progressively increase the fixed part of it to cover the major part of operational costs. This is the best way to ensure compliance with GDP and the Statute of Medicines, and to preserve the model."



From left: Gisella E. Dante, General Manager, Janssen Portugal; Nelson Ambrogio, Managing Director, Bayer Portugal; Rui Ferreira Dos Santos, Country Manager, Almirall Portugal

"Transparency mechanisms are needed across the entire supply chain," concludes Carrington. "Compensation measures to support operational costs across the supply chain can prevent and manage supply shortages. Transparency and reliable information about quantities available from manufacturers can also make a difference. Defining a 'life-saving' list of medicines that all players should commit to, granting Public Service Obligations (PSO) would also help. Transparency and exchange of reliable information about real needs, availability, quantities and deliveries should be the guiding principle."

In response to the crisis, the Portuguese affiliate of Spanish pharmaceutical group Almirall took a courageous decision to stop all commercial activity at the beginning of 2011 in response to a mature portfolio and strong erosion of sales. "Since 2011 we do not have any field force promoting products," explains Rui Ferreira Santos, country manager of Almirall Portugal. "My small team here is focused on the access of new products we were expecting from our own R&D and licensing agreements. Thus, in response to the crisis, rather than work on mature products, we prepared the market and ground to bring new products."

Ensuring a strong performance in clinical trials is also important for Portugal to recover. "The strategic value of clinical research for Portugal is now being recognized by the Portuguese government and by INFARMED," says Janssen's Gisella Dante. "Recently, some important initiatives have been put in place such as the launch of the National Platform for Clinical Research and INFARMED and the Portuguese Central Ethics Committee are assuming a leading role within the EMA

Voluntary Harmonization Procedure. On the other hand, there are a growing number of hospitals setting up clinical research units in order to increase their effectiveness in this field. In 2013, for the first time in years there was an inversion in the negative trend regarding the number of clinical trials approved annually. The signs are encouraging and Janssen has been fully engaged in this process."

"Clinical trials are a way of ensuring early access to innovation, obtaining clinical expertise and are one way to attract investment to the country," says Amgen Portugal country manager Ramón Palou de Comasema. "As a country, Portugal has significant potential to improve in terms of implementation of clinical trials. The expertise of clinicians in hospitals here is unprecedented. However, we need to improve processes. The most important part of this is to ensure that in the future, companies will continue to invest in Portugal."

GENERICS: HEADROOM FOR INNOVATION?

In PharmaBoardroom's first coverage of Portugal in 2007, generics represented 16 percent of the pharmaceutical market, a tremendous feat considering laws for generics had only been implemented a few years before. Today, generics represent nearly 40 percent of the market in count units, and according to the MoU, the aim is to increase this to 60 percent by the end of 2014.

Moisés Apura, General Manager, Ciclum Stada

Using generics as a means of cost-cutting for a fragile health budget seems like an easy go-to option for Portuguese health authorities. "Portugal has budget constraints, and can only spend around EUR 1.7 billion (USD 2.2 billion) for medicines every year," says Paulo Lilaia, president of Portugal's generic association Apogen and CEO of local flagship generics company Generis. "If we want to be able to buy innovative therapeutics that add value, we must save money somewhere."

Between 2008 and 2013, price cuts resulted in a 75 percent decrease in generic prices, resulting in significantly lower prices for generics compared to Portugal's new reference pricing countries of Italy, Spain and Slovakia. This also makes it difficult for generic companies to justify selling in a country where profits would be so low. By contrast, originator prices have only decreased 6.1 percent since 2009, creating an unsustainable gap between originators and generics.

From left: Paulo Lilaia, CEO, Generis; Francisco Velez, Director General, toLife

According to Francisco Velez, director general of generics player toLife, innovative companies benefited for many years because Portugal only had process patents, and the balance of product patent protection changed when generics were introduced in Portugal. "The time between the end of a process patent and the beginning of a product patent's start on the market is too long and generates confusion, which leads to doubts about the market. Until one and a half years ago, toLife, which was acquired by Catalan pharmaceutical group Esteve in 2007, simply had "preliminary injections of registered products in INFARMED. If any innovative company was aware of such product registration, that company could stop the approval program through an administrative court. Such courts are not the right place to decide on patents. I had products approved in 2007 and they have just hit the market this year because they were blocked by the court, sometimes with no reason. We lost huge market opportunities, since otherwise we would be first place in the market."

Portugal Report

João Madeira, General Manager, Mylan Portugal

"The generic medicines business model was focused on high prices and the commercial terms you could offer to pharmacies in particular," states Mylan Portugal general manager João Madeira. "Of course, when you do not have the market developed to the point of pharmacy-based decisions (which you would expect in a substitution market), and when you start adopting strategies and tactics that do not correlate with the profile of that market, you will fail. Focusing business on pricing and commercial strategies alone, without creating the landscape to de-stigmatize generic medicines and increase its understanding by physicians and patients is dangerous." Generic medicines used to be under a branded prescription-based business: "physicians prescribed, drugs were shipped to pharmacies with a script, and pharmacies would typically dispense whatever was in that script," continues Madeira. "That definitely did not help to build the generic medicines marketplace in Portugal, and did not allow for a proper understanding of the value of having a developed generic medicines market in Portugal nor the need for the authorities to leverage this market."

Lagoas Park in Oeiras, where many multinational pharmaceutical companies are based in Portugal

"The problem is that many stakeholders are involved in the decision-making process," comments Moisés Apura, general manager of generics business Ciclum Farma, which is owned by Stada Group. "Furthermore, pharmacists have lost so much profit in the last three years as they are remunerated through a percentage, so they prefer to sell originators over generics. Doctors lose the power to follow patients due to mandatory INN prescription, especially since the brand dispensed at pharmacies may change every month, complicating patients' compliance. That is why doctors prefer to prescribe originators. If the law

Redefining crisis management

"During the throes of Portugal's economic crisis, Servier Portugal actually created an international center for research that conducts several studies across Portugal for old and new products. This center was created as a symbol and a demonstration to doctors, authorities and internal collaborators that the company is truly investing in Portugal, and is here to stay not just to sell medicines but to also be a strategic partner." (José Albino Mendes, general manager, Servier Portugal)

José Albino Mendes, General Manager, Servier Portugal

"As a company that operates in very specific markets, the first challenge I encountered was to provide a more global personality to the company, and to make it more visible in the market and to stakeholders, local industry and the Ministry of Health. The internal implementation of governance boards that were not available at that time was also a priority. By developing such boards, as well as functions, job descriptions, and communication flow, these simple aspects assisted in the development and motivation of the company's employees." (Nuno Brás, general manager, LEO Farmacêuticos Portugal)

Nuno Brás, General Manager, LEO Farmacêuticos Portugal

"I had to change the way BMS relates with authorities. It used to be a spot type of relationship, in which a reimbursement or issue was discussed with the authorities. It is a model that no longer works for the entire industry, and I strongly believe that you need to have a different way of interacting with stakeholders. You need to really think about collaboration of partnership; what projects or elements are critical for them so that we can work together towards common goals." (Valentino Confalone, general manager, BMS Portugal)

Valentino Confalone, General Manager, BMS Portugal

"Bene operationally launched the Portuguese affiliate in 2010, when Portugal's pharmaceutical industry was experiencing its worst year ever, followed by two more years of even worse performance. In spite of these issues and some public's skepticism towards our optimist attitude, Bene has enjoyed continual success in Portugal because of the company's product reliability. Ben-u-ron, our main brand, has been the brand of confidence for several years in a row because of our commitment to the people through confidence, trust and quality." (Frank Tischler, Managing Director, Bene Farmacêutica)

Frank Tischler, Managing Director, Bene Farmacêutica

changed so that doctors could manage what is best for a patient and follow the prescription and the margin to pharmacy is settled by fixed value instead of percentage, perhaps generics would be prescribed more frequently."

Furthermore, according to Aurobindo Portugal country manager Pedro Merlini, clear timeline definitions also need to be established in Portugal. "Companies need to know exactly when an originator is launched, registered, when changes are made to its indication, and when its patent protection ends. Without that clarification, a fair market is almost impossible," he notes.

NATIONAL PRIDE

While multinational pharmaceutical companies have been forced to make the necessary adjustments to maintain their presence in Portugal, national pharmaceutical companies in Portugal have a different story. Despite the country lacking any "big pharma" players, many of the mid-sized companies in Portugal have continued to thrive despite the national crisis by looking at new outlets for growth.

Pedro Merlini, Country Manager, Aurobindo Portugal

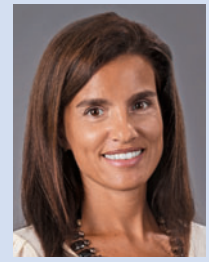
According to António Donato, vice president of Tecnimede Group, cluster-based strategies would be useful for the Portuguese health ecosystem. "Organizations must focus on building an identity for a cluster, enhancing innovation though joint R&D projects, as well as focusing on business development, exports, joint acquisitions and international cooperation," he says.

"As a result of local economic crises the issue of internationalization is becoming more and more important for Portuguese companies, remarks Donato. "The pharmaceutical market is heavily regulated, and differences in regulatory systems typically lead to restrictions on the

Big players, big responsibility

With all its divisions combined, Novartis is the biggest player in the Portuguese market. In 2013, the company invested EUR 4.8 million (USD 6.2 million) in clinical trials, and between 2009 and 2013 saw a 70 percent increase in R&D. This year, the affiliate plans to launch nine new clinical trials.

Cristina Campos, CPO Head & Country President, Novartis Portugal answers our questions:



Cristina Campos, CPO Head and Country President, Novartis Portugal

What is the importance of clinical research for Novartis Portugal?

Novartis Portugal is building capabilities internally by bringing the right people into the organization as well as upgrading the current skills of our workforce, allowing us to have the best medical team in the industry. By overcoming process barriers currently in the market, we can speed up the approval clinical trials in Portugal and ensure Portugal's attractiveness for clinical research. Novartis has 20 ongoing clinical trials, enrolling 400 patients in Portugal. We are therefore one of the biggest sponsors of trials in this country, doubled in size and scale compared to a few years ago. I believe we can still do much more if the government can ensure some stability and simplified processes. This will allow the subsidiary to be seen as a reference for other countries and to make Portugal a more attractive country for clinical trials.

Is there a burden of responsibility in committing to the Portuguese population as the biggest player in the market?

With all five Divisions, Novartis serves more than one million patients and consumers in Portugal. This is a huge opportunity, and our aspiration is to be seen as the most respected and trustful player in the sector. From quality and compliance standards to the excellence of the delivered programs in the market, there is a huge burden of responsibility. Given our big scope and diversified portfolio and pipeline, Novartis Portugal has an obligation to be a role model in positioning the pharmaceutical industry as a respected and collaborative player in the Portuguese economy and society.

Bial: The Portuguese high flyer

- Founded in 1924
- R&D unit established in 1993
- Products are distributed in 52 countries worldwide
- Therapeutic areas include musculoskeletal, CNS, cardiovascular, antibiotics, respiratory and immunotherapy
- Largest national company in the Portuguese market

António Portela, CEO, Bial

Bial made headlines in October 2013 when their antiepileptic drug Zebinix (marketed in the United States as Aptiom) was approved by the Food and Drug Administration for commercialization in the US, the first ever Portuguese-developed drug to do so. Already commercialized in Europe since 2009, Bial has invested EUR 300 million (USD 390 million) and the last 13 years in developing Aptiom. "It was a huge challenge for the team, which had no experience in developing drugs and submitting them to regulatory authorities," remarks Bial's CEO António Portela. "This project helped transform Bial from a local to an international company." For a family-owned company, Bial's R&D and internationalization investments are enormous. Portela attributes this to the company's ability to think in the long-term: "We hope that the revenue from the development of Aptiom will allow us to invest in continuing to develop our pipeline and our presence in international markets."

Bial's facilities in São Mamede do Coronado

registration of medicines or establishment of new companies, which significantly impacts entry in some markets. Regulatory challenges are economic in nature, and are a consequence of issues like barriers to trade and internationalization. As such, cooperation and discussion with INFARMED and other competent authorities are crucial to the evaluation and definition of how Portuguese companies can enter foreign markets."

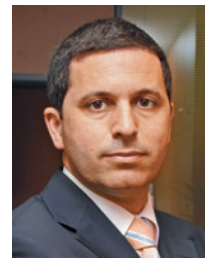
Diversification is also critical for many companies. As an example, local player Tecnifar accumulates roughly 75

From left: António Chaves Costa, CEO, Tecnifar; António Donato, Vice President, Tecnimede Group; Pedro Ferraz da Costa, Chairman of the Board, Iberfar

percent of its sales from the in-licensing of drugs from multinational companies, relying on its flexibility to adapt to the needs of each individual partner. António Chaves Costa, CEO of Tecnifar, says "the company aspires for a diversification of partnerships to avoid being dependent on a specific franchise from one partner. Whenever an opportunity arises to complement the in-licensing business, the company looks for specific brands or products available for acquisition."

"Between 2010 and today, Tecnifar diversified its risk by moving beyond pharmaceuticals, specifically beyond prescription medication," continues Costa. "The company recently

developed competencies in diagnostic imaging services, including cardiology and gastroenterology imaging, and the OTC, nutraceutical and medical device areas." Tecnifar has also partnered with local biotech startup Technophage for the last six years to strengthen R&D. "We finance the investigation, contribute with project management and regulatory affairs, while they provide the brains and investigators for a project in the bacteriophage area. This commitment to R&D is a pillar of Tecnifar and we cannot present ourselves solely as a commercial company with a sales force, even when talking with potential partners."



Hernâni Sério, General Manager, Fresenius Kabi Portugal

"While the pipelines of pharmaceutical companies today are quite complicated due to loss of patents, opportunities arise for businesses like Tecnifar to partner with those companies that had to reduce their presence here," concludes Costa. "Our company has been in Portugal for many years; we know all the stakeholders and the market well enough to partner with a company with no budget for their continued growth."

BUILDING BLOCKS

Similarly, manufacturing may also present opportunities for continued growth, particularly given the low cost of production and high quality in Portugal. Despite a shrink in the manufacturing industry, the possibility for a comeback is more real due to government initiatives designed to relax labor laws and reindustrialize Portugal.

Every multinational pharmaceutical company with production capacity has abandoned their facilities in Portugal over the

Building an affiliate from an affiliate

Jaba Recordati was formed in 2006 through the acquisition of local pharmaceutical company Jaba by Italian multinational Recordati. The company is primarily focused on ambulatory products in the areas of cardiovascular, urology and pain. Jaba Recordati's general manager Nelson Pires has worked hard to grow the company since he arrived four years ago.

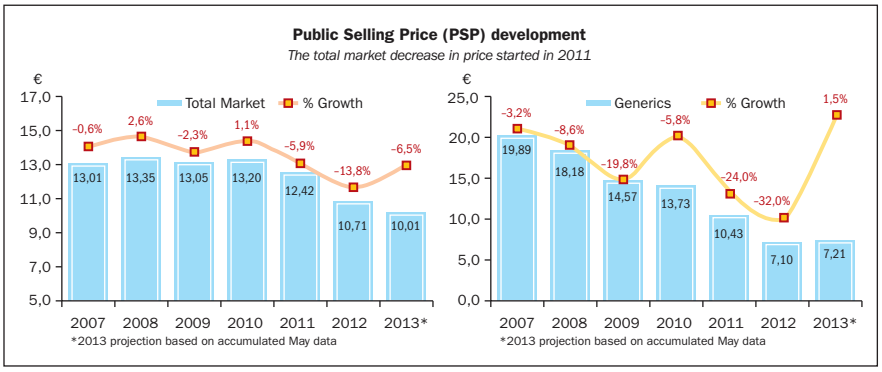
Nelson Pires, General Manager, Jaba Recordati

"Most top companies are focused in the hospital business, and their margins come from this area," says Pires. "Therefore, there is a big opportunity for companies focused on ambulatory products and specialist products sold in the ambulatory market by specialist doctors." As such, "the company is financially sustainable and is probably one of the best companies in terms of value in the stock market."

Part of Jaba Recordati's strategy involves expansion to the Portuguese-speaking African countries (PALOP), primarily Angola, Mozambique and Cape Verde. Pires plans to create Jaba Recordati affiliates in these countries, starting with Angola. "It is not normal for an affiliate of a multinational to become its own small multinational," Pires states. Like many other companies in Portugal, Jaba Recordati has taken advantage of its cultural and linguistic connections to these nations to expand business. "We supply European health technology to African countries, training health technicians and doctors, and sponsoring congresses and scientific activities," continues Pires. "Most companies solely export without creating local links, whereas I believe we should create an internationalization business to create local value. After establishing a local affiliate with the right partner, we can develop a link with local stakeholders."

past couple of decades, except German company Fresenius Kabi. The organization purchased local manufacturer Labesfal in 2005, and this has turned out to be a very strategic move on Fresenius Kabi's part. "Through this acquisition we acquired all the complexity, size and content of Labesfal, as well as the knowledge, expertise and resources that Labesfal had in the field of IV generics," explains Fresenius Kabi Portugal general manager Hernâni Sério. "The company wanted to create a competence center in Portugal for the development and production of IV drugs, and in doing so the company increased its position in the pharmaceutical sector in Portugal and became one of the biggest providers of IV drugs for the hospital sector." As of today, Fresenius Kabi is the biggest exporter of pharmaceutical products according to the National Statistical Institute of Portugal, and its facilities are approved to produce for Europe, Latin America, Middle East, and Asia-Pacific.

Similarly, Portugal's health-related exports have actually been experiencing year-on-year increase for a number of years; in 2012 sales from medicine exports finished at EUR 600 million (USD 780 million), and EUR 700 million (USD 910 million in 2013. Including other related products like medical devices, 2013 totaled EUR 1 billion (USD 1.3 billion). Latin America and the Portuguese-speaking African countries (PALOP) are often targeted first because of Portugal's historical connections to these places. For CMO Iberfar's president Pedro Ferraz da Costa, "Iberfar's fastest area of growth and biggest opportunities today are in Angola, where we have a 140-person operation with USD 40 million turnover, a partnership with two other companies and a 20 percent growth rate. The government is trying to expand healthcare to a bigger part of the population and it is working. The price level and margins are very high, so it is a healthy business with expansion possibilities. From Angola we think we can build up an operation that would cover southern Africa."

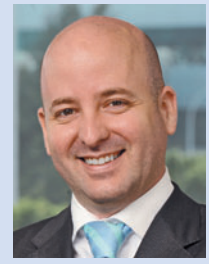


CAN SCIENCE = PROFIT?

Portugal is frequently hailed for the excellence of its scientific output, given the outstanding quality of the numerous research institutes that exist in this relatively small country. "The country has grown significantly in terms of research and PhDs, the younger generations are highly educated, and Portugal has some of the best ranked universities in the world for healthcare and engineering," comments Pedro Gonçalves, Secretary of State for Innovation, Investment and Competitiveness under the Ministry of Economy of Portugal. "But we need to be able to transform that knowledge more actively and effectively into creating an economy that is technologically more advanced, and into products and services that incorporate more

Orphan drugs and austerity

In Portugal's continuing struggle to adapt its reimbursement system, orphan drugs are at the center of the debate. Health authorities in Portugal have not updated Portugal's reimbursement system in decades, and thus are not adapted to the modern realities of innovative medications like orphan drugs. This presents some challenges for companies specialized in this niche. Fermin Rivas Lopez, the Spanish country manager of Celgene Portugal, remains optimistic. "It's less difficult to defend the use of Celgene's products since we bring value and strong data regarding survival and clinical value of products," says Rivas. "Since Celgene's products are orphan drugs, the number of patients and budget for hospitals is lower. I think that we are in a very good position to defend the use of our drugs given the low level of budget impact, and high level of investment in Portuguese clinical trials." The Portuguese affiliate conducted seven clinical trials in 2012 and increased this number to 11 in 2013.



From left: Ramón Palou de Comasema, Country Director, Amgen Portugal; Fermin Rivas Lopez, Country Manager, Celgene Portugal

Amgen's Portuguese affiliate is in a similar situation. "Amgen needed to maintain its current structure in terms of product sales and work on new products in our pipeline to be approved in Portugal," explains fellow Spanish expatriate and country director of Amgen Portugal Ramón Palou de Comasema. "In reality, it has not been easy to provide access to innovation in Portugal in the last year. Nevertheless, Amgen has been successful in the last few years in demonstrating to the authorities the benefit of our molecule products first for patients in terms of clinical value and savings to the health system, which holds true for all companies." Specifically, Amgen was able to reimburse three of its products in Portugal over the last four years. With 14 clinical trials ongoing in Portugal today, Amgen is also a leader in bringing clinical research to Portugal.

added value. I am responsible for the instruments that give incentives to create such policies, namely incentives to utilize the human resources the country is graduating. For example, the Ministry of Economy recently introduced a fiscal benefit commonly used by the pharmaceutical industry, in which expenses that companies incur for PhDs are accounted for 120 percent. That means there is a 20 percent gain from which research centers and companies can benefit."

"Portugal's R&D environment is outstanding," comments Joaquim Cunha, executive director of Health Cluster Portugal (HCP). "However, in order to succeed, our R&D institutions may need to adjust their strategies slightly to be aligned with the needs of the market."

HCP is a collaborative platform founded in 2008 that brings together more than 130 members across the Portuguese health value chain, including universities, R&D institutions, hospitals, and major private healthcare groups, along with national and multinational pharmaceutical, medical device and ICT companies. The main driver for its foundation was the belief in the scientific and technological progress witnessed in Portugal over the last twenty years. Cunha believes that by defining the country's strengths and focusing its efforts on those strengths, combined with proactive international networking, Portugal can have a dominant role in the life sciences industry globally. "Three key words embody HCP's goals: innovation, collaboration and internationalization," continues Cunha. "The ultimate design is to turn knowledge

into value, within the Portuguese health value chain, while focusing all of our efforts on the global market." Specifically, oncology and neuroscience could be the pivotal areas of health science in which Portugal could excel.

BIOTECH: SMALL BUT GROWING

Daniela Coutu and David Malta, founders of Cell2B, point out that "economically, the cost of doing business in Portugal is much lower than other emerging biotech countries, even Ireland. Portugal could be a hub for biotech with high standards of quality and lower investments to develop products. Translating basic science into commercial products therefore might be slightly easier here."

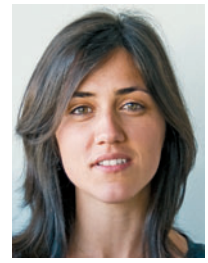
According to Nuno Arantes-Oliveira, president of Portugal's biotech association P-BIO, the weakness of the biotech sector, especially with regard to the 30 or so biotech companies in Portugal focused on health, has been the companies' lack of capacity to grow beyond the early stages of development. "A few years ago, there were some barriers to entrepreneurship for startup companies but this is now changing and it is relatively easy to start a technology-based company in Portugal," says Arantes, who notes that Portugal needs to create the best con-

Top 20 Pharma Companies by Sales, September 2013	
1	MSD
2	Novartis
3	Pfizer
4	Bial
5	AstraZeneca
6	Servier
7	Bayer
8	Sanofi
9	Boehringer Ingelheim
10	GSK
11	Generis
12	Ratiopharm
13	Lilly
14	Menarini
15	Medinfar
16	Merck
17	Janssen Cilag
18	Vitoria
19	Jaba Recordati
20	Abbott

Source: IMS Health

From left: Joaquim Cunha, Executive Director, Health Cluster Portugal; Pedro Gonçalves, Secretary of State for Innovation, Investment and Competitiveness





From left: Nuno Arantes-Oliveira, President, P-Bio; David Malta and Daniela Couto, Co-Founders, Cell2B

ditions for the best startup biotech companies to grow as if they were located anywhere else in the world. "Today there are facilities, incubators, seed funding and venture competitions, which allow for creation; now the issue is growth. There are no large private venture capital funds that invest heavily in Portuguese biotech. Historically there has been some state venture capital that dabbles in several industries and private generalist venture capital from banks. The recently created Portugal Ventures seems to be an example of the state rationally investing in specific fields including biotech."

"My vision is one of consolidation, focused on the creation of critical mass, which is not exclusive to biotech; rather they should be part of a movement to specialize the country in problem-driven objectives," concludes Arantes. "In biotech, because some of our companies are at an early stage, they are flexible enough to go along with the trend. If it becomes logical that Portugal can be the best in the world in, say, one specific rare disease, perhaps there are several biotech companies that are developing technologies that could shift into that focus."

José A. Aranda da Silva, General Manager, Formifarma

PREPARING THE NEW PORTUGAL

Portugal may have struggled through some truly difficult times in recent years, but hitting rock bottom has certainly provided the wake-up call necessary for the country to bounce back. "I believe the market will return to normal levels in the next few years, but the industry must also change by having the capacity to add value of products in the market and health system," says José Aranda da Silva, general manager of local consultancy Formifarma. "We must also invest more into convincing authorities about the value of drugs, and shy away from the idea that health and medicine are economic burdens."

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"Market-Based" Price Controls In India?

Three strategic implications for pharma pricing strategies in India

India's Department of Pharmaceuticals (DoP) released the Drug Price Control Order (DPCO) in May 2013. It increased the number of drugs on the National List of Essential Medicines (NLEM) from 74 to 348 and offers new paradigms for determining and enforcing price ceilings while maintaining stable drug supply. Biopharmaceutical companies that do business in India need to carefully evaluate the consequences of this legislation.

The DPCO has three primary aims: expanding the NLEM, authorizing the National Pharmaceutical Pricing Authority (NPPA) to regulate prices of India's NLEM, and authorizing the NPPA to regulate price increases of non-essential medicines. The DPCO uses market-based mechanisms to set price ceilings. It works differently, depending on how many products are in a category:

- If a drug is one of many drugs within a given product category, the price ceiling is the simple average of the prices of all drugs that have at least 1% of market share within that category (plus a 16% pharmacists' margin).
- If a drug is the only one within a given drug category, the new price ceiling for that category will be a fixed percent, based on price reductions in similar categories.

Moving forward, all drugs in a product category must be priced at or below the price ceiling or the manufacturer will face monetary penalties. If a drug's price is already below the price ceiling, a price increase is prohibited. The NPPA, however, currently has no mechanism to officially penalize an offending manufacturer. For all NLEM-listed treatments, yearly price increases must be in line with or below the wholesale price index.

The Indian government has also reserved the right to mandate continued production for up to 12 months, to require quarterly drug production reports, and to require six months' notice before production of a given drug ceases. The regulation also exempts all drugs developed and patented in India from price control as a means of incentivizing India-based research and development.

The DPCO results in three key implications for pharmaceutical and biotechnology companies in India, as well as for the country as a place for future clinical R&D:

- Fewer "branded generics."
- No let-up in pricing pressure for non-NLEM drugs.
- No dramatic change in MNC R&D investment in India.

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Fewer "branded generics"

To understand how this new policy will impact prices within the Indian market, consider the following three cases:

- Because **Novartis' desferrioxamine mesylate** is the only drug within its product category, it experiences price reduction as a fixed percentage of its current price. In order to determine the price reduction for desferrioxamine mesylate, the NPAA considers the average reduction in similar product categories. For desferrioxamine mesylate, the price reduction will be 24.80%, the average price reduction for antidotes. This will reduce the price per unit from its current R170.40 to R128.14.
- **GlaxoSmithKline's hepatitis B vaccine** is significantly more expensive than the other seven options. Because the new price ceiling is determined by an arithmetic, and not a weighted average, the price ceiling for hepatitis B vaccines will force the price of GSK's vaccine significantly down from over R300 to a maximum of R87, a roughly 75% reduction.
- **A local manufacturer (Pavior Pharmaceuticals) offers a more expensive factor VIII concentrate injection than the only alternative, Baxter's cheaper version.** According to clearly outlined DPCO policy, the new price ceiling for factor VIII concentrates will become the average of current prices, or about R5400. Baxter's factor VIII is priced well below where the new price ceiling would be, so Baxter will not face mandatory price reduction. This is a particularly interesting

case, as the DPCO aims to impact high-priced branded options that compete against a set of generic and "branded generic" alternatives. Baxter's product has over 90% of market share, so the price ceiling will not have any impact on the category spend.

In order to understand the reach of the DPCO's price reduction policies, one must fully understand the India market. Consumers and physicians in the country are very brand-conscious, even when it comes to medications. As a result, higher drug prices don't necessarily lead to lower market share. Indeed, for almost half of the product categories under the DPCO (47%), the most commonly used drug is also the most expensive. Consider the hepatitis B vaccine market from case No. 2. GSK's product, despite being the most expensive by a wide margin, has a disproportionate 26% market share. This is because market share and price are not inversely related in this product category as would typically be expected. Thus, this category demonstrates DPCO's potential success. Though GSK's drug is the only therapy that will face significant price reduction due to its high market share, the weighted average of prices in this category will be slashed in half from R140 to R70.

As a result of the DPCO, price differentiation for NLEM-listed medications will become increasingly difficult. More importantly, the DPCO may impact locally-manufactured generic alternatives as it reduces the price of the MNC branded options, thus decreasing the price gap and perhaps making the MNC brand more attractive. As price differentiation within each product category decreases, so too does the potential for a middle tier, products that are neither the most nor the least expensive in the category of "branded generics." This will lead to a decrease in the overall number of "branded generic" NLEM products across all categories.

Recent IP Precedents in India

Patent issue	Product by Manufacturer
Compulsory licensing	Nexavar by Bayer
Revocation due to lack of inventive step	Sutent by Pfizer Pegasys by Roche
Revocation due to improper filing procedure	Herceptin by Roche
Revocation due to new version of molecule therapeutically not superior (Section 3d)	Glivec by Novartis Tykerb by GSK Ganfort by Allergan
Denial of alleged patent infringement against generic	Tarceva by Roche Januvia by Merck

No let-up in pricing pressure for non-NLEM drugs

An estimated 70% of the India drug market is not listed on the NLEM and will not face new price ceilings or mandatory price reductions. However, medicines not listed on the NLEM will only be permitted a 10% annual price increase. In addition, pricing opportunities remain limited by patient affordability and the threat of compulsory licensing. The Indian government has a history of implementing compulsory licensing and revoking patents for drugs it considers too expensive. Nine drugs for either cancer or diabetes have faced patent problems ranging from compulsory licensing to revocation of patents to denial of patent infringement in India (see chart). These patent problems have led to cheaper generic alternatives for high-cost medicines in India, and have also positioned India as a country in which exceptionally high-priced therapies are unlikely to launch successfully.

MNC R&D investment in India will not change dramatically

The DPCO incentivizes India-based research and development of drugs. However, the likelihood that this will influence investment decisions by MNCs is negligible. MNCs often have established R&D centers outside of India. Since revenue from NLEM drugs for MNCs in the context of their global revenues is very small, it is very unlikely that many of these companies will make a large R&D investment in India because of the DPCO.

Next steps

The Indian government is heavily involved in regulating prices for medicines in India by using the DPCO to set price maximums for essential medicines. Going forward, the Indian government may also look to other larger areas of the pharmaceutical/biotech market to introduce new and increased regulation to make medicines more affordable. To be successful in a changing India market, manufacturers need to constantly review the changing policy landscape and reassess their India strategy carefully. PE

Sickle Cell Disease In Three Acts

Is there a happy ending in store for sickle cell patients?

The first act in the story of sickle cell disease, one of the oldest known genetic diseases, is not a happy one. Aside from a very small number of young patients undergoing successful bone marrow or stem cell transplants, there is no curative treatment. Other drugs address the disease according to which symptoms present most urgently, or serve as short-term solutions for a long-term problem.

Sickle cell disease prevents one of the body's most fundamental resources—the blood—from adequately transporting oxygen to the tissue, which can result in organ damage and many other related complications. A sickle cell related vaso-occlusive "crisis" can be extremely painful for patients, and deadly in some cases. Both quality of life and life expectancy are reduced for sickle cell patients, even when the disease is optimally managed with existing therapies, blood transfusions, vitamin regimens and a host of other precautions.

Beyond the medical pathology of the disease, sickle cell patients in the US—a population of 100,000—also face a social stigma. They often require strong opioids, and the disease is commonly recognized as a "black disease," or one that only plagues minorities, which isn't true. The intermittent pain crises that most patients experience usually result in an overnight stay at the hospital and a heavy dose of pain meds. Once stabilized, they return home until the next crisis strikes.

However, a quorum made of new pipeline therapies, public research investments, and a renewed sociopolitical focus on the disease is attempting to pen a redemptive second act for sickle cell patients. With a successful Phase 1 safety study completed, Abraham Abuchowski and Glenn Kazo, who serve as CEO and president of Prolong Pharmaceuticals, respectively, are currently working with sickle cell patient associations and foundations to determine which efficacy studies would have the largest impact on sickle cell patients' co-morbidities, and their lives in general.

In February, a Sickle Cell Disease Congressional Caucus was formed, led by Charles Rangel (D-NY), Danny Davis (D-IL) and Tim Scott (R-SC). The stated goal of the caucus is to "increase support for the largely underfunded disease" and to "address barriers in access to and development of crucial treatments."

Also in February, FDA convened its fifth Patient-Focused Drug Development meeting, this time on the subject of sickle cell disease. At the meeting, patients were asked to speak openly about treatment options for sickle cell, and also which effects of the disease matter most. Kazo, who attending the meeting, says two key messages emerged from those discussions. The first is that "drug development in the sickle cell area doesn't usually look at co-morbidities, or the related diseases that sickle cell patients actually suffer from," says Kazo. "The other challenge is enrolling patients in clinical studies."

Prolong's approach to sickle cell is to improve overall oxygenation, which gets at the underlying disorder in sickle cell disease. The company's lead product, Sanguinate, is an infused bovine pegylated hemoglobin molecule that Prolong hopes will address the most severe complications facing sickle cell patients. Abuchowski, Prolong's CEO, was instrumental in the development of pegylation technology decades ago, but back then the oxygen delivery characteristics of the hemoglobin protein, human or animal, weren't well understood. Plus, errant hemoglobin in the blood stream is toxic, as any clinician will tell you.

What's special about cow hemoglobin? Aside from obvious sourcing problems related to the need for large quantities of human blood, Abuchowski says human hemoglobin is extremely unstable compared to bovine hemoglobin; what makes hemoglobin especially toxic in the blood is when it splits apart. "Hemoglobin is a four sub-unit protein…those subunits break apart in human hemoglobin, but in bovine they do not," says Abuchowski. "In the genetic engineering space, everybody thought anything human is best, but that's just anthropomorphic egotism. Just because it's human doesn't make it the best."

Prolong's Sanguinate, a play and reversal on the verb exsanguinate (defined as the action or process of losing blood), isn't being positioned as a blood substitute, which Kazo describes as a fool's errand. But Prolong will attempt to distinguish Sanguinate from other products in development by going beyond the treatment of a single symptom to address co-morbidities related to poor oxygen delivery, the root cause of vaso-occlusive crisis and many other debilitating effects of sickle cell disease.

Nearly 150 open studies targeting sickle cell disease are currently listed at ClinicalTrials.gov, underscoring patient need and industry's interest in addressing it. For patients and their families, a truly disease-modifying therapy could hold the curtain up long enough for a third and final act: the cure. PE

Ben Comer is *Pharm Exec*'s Senior Editor. He can be reached at bcomer@advanstar.com.

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