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# Pharmaceutical Executive

**JUNE 2016**

WHERE BUSINESS MEETS POLICY

VOLUME 36, NUMBER 6

## 2016 PHARM EXEC



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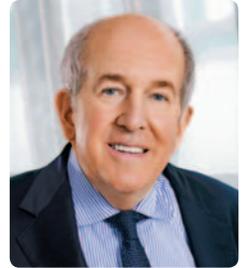
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# Design that Delivers

**CAN THE PHYSICAL SPACES** we work in shape our relationship to the larger world outside? Is a workplace aesthetic founded on the engineered configuration of steel, wood, stone and glass helpful in strengthening a company's morale and mission—extending even to its underlying culture and values? The two questions are getting serious scrutiny from today's big Pharma players as they grapple with the challenge of keeping their employees healthy, productive and engaged. In fact, it's a crucial adjunct to our cover feature this month on why future revenue growth in this industry depends on investing big in that diverse intangible called the "people factor."



**WILLIAM LOONEY**

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To further explore the issue of housing the business enterprise, *Pharm Exec* recently paid a visit to GlaxoSmithKline's four-floor, 208,000 square foot US headquarters at Philadelphia's historic Navy Yard. Home to 1,100 employees, the new office, opened in early 2014, was positioned as the practical expression of a new corporate identity built around a transparent, three-pronged commitment to the patient. Simply put, GSK wants everyone taking a GSK medicine to feel better; live longer; do more.

A survey of employees based at GSK's aging downtown Franklin Plaza high-rise helped shape the Navy Yard renovation led by award-winning Yale University architect Robert Stern, himself an early advocate of energy- and environmentally-responsive design principles. The survey found that colleagues found the existing set-up "demotivating," with its 16-floor vertical accessible mainly by elevator and divided into claustrophobic, low-ceilinged interior spaces that reinforced silos among functions and actually encouraged unhealthy personal behaviors.

In response, GSK opted to build its three mission objectives right into the new design. To advance the commitment to "do more" for patients, the plan set about to raise employee productivity by making access to the facility convenient and easy; providing workers with a variety of shuttle bus, bicycle and other transport options and time-saving retail services; removing interior walls and doors; banning individual private offices; and introducing a natural openness, light and flow among work stations. The design signal to colleagues was manifestly clear: find each other, collaborate and stretch the mind and body in doing so.

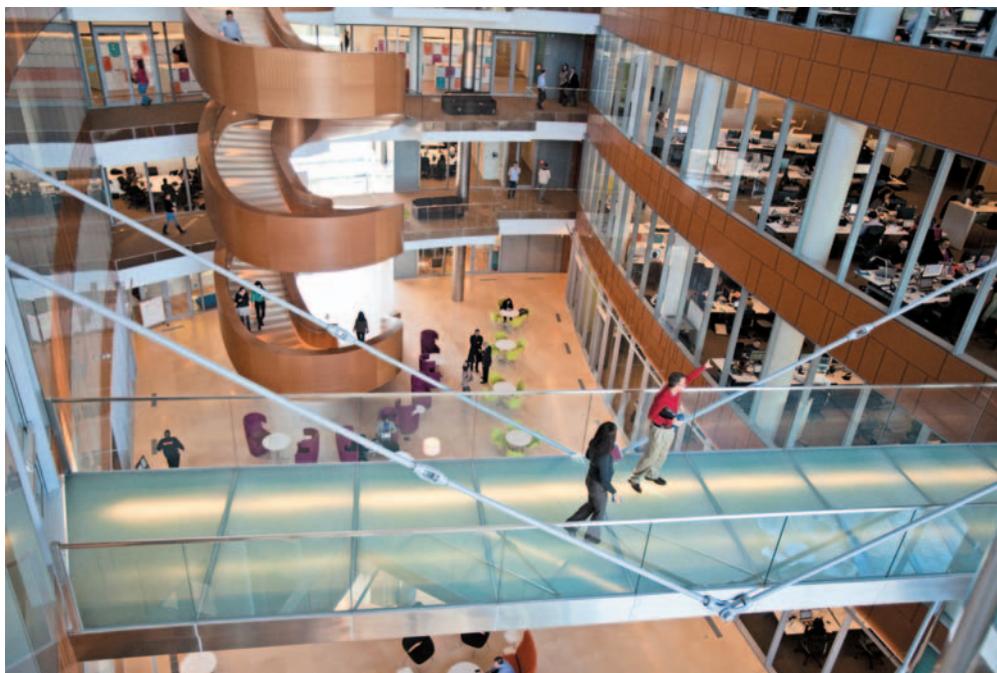
The facility also takes a novel approach to the visual presentation of ideas and information. Instead of a statically positioned display of framed art, GSK opted to use the walls and other surfaces as canvases in themselves, using drawings, words and symbols often used in science to bring sections of the building together—an ever-changing visual stimuli that encourages people to comment, follow and explore what's at the end. This way, the message is reinforced that everything—and everyone—in the building is connected.

The other health-related goals—to feel better and live longer—were expressed in two ways, first by improving on wellness metrics among the GSK workforce and, second, to showcase the company's corporate responsibility as an industry standard-setter on community health, energy conservation and environmental safety. A natural ambience is projected right at the building entrance, in the form of an enormous, light-filled atrium punctuated by a spiral wood stairway resembling the iconic form of the DNA double helix. The central stairs works as a sort of Greek-style *agora*, or meeting place, where employees have no choice but to literally bump into each other. Elevators still exist, but they are purposefully hidden from sight.

The design signal to colleagues was manifestly clear: find each other, collaborate and stretch the mind and body in doing so

Two years on, the results are in.

From the start, the Navy Yard operation has led the US biopharma industry in achieving a progressively lower energy and environmental footprint. The building itself rates a rare "double platinum" LEED status for innovation in energy and environmental design, one of less than 10 (and the sole entry in pharmaceuticals) commercial facilities in the US to do so. Ron Joines, GSK vice president for environment health safety and sustainability, points to other milestones. "We've managed to slash energy consumption to one quarter the level it was at the Franklin Plaza building," he says. "All of our internal materials, from paint to fixtures to machines, are chosen for maximum energy efficiency, and at the lowest level of potentially harmful emissions; the employee parking lot is equipped with chargers for electric vehicles. We think it important for a company that leads in treatments for respiratory disease that our carbon and emissions footprint be as low as possible."



Inside GSK's US headquarters at Philadelphia's historic Navy Yard.

"We've accomplished what we set out to do," says Joines. "We inhabit a built environment that reflects and reinforces our values and what our employees expect when they join GSK." And that pregnant question—whether an appealing workplace ambiance adds heft to those critical markers of corporate identity, culture, productivity, reputation and morale—is being answered in the affirmative. "The bias in the design was to promote human movement and interactions throughout the work day," says Joines. "Our surveys show that at any given time, a third of Navy Yard colleagues are either in motion around the facility, standing or treading in place at their work stations." Considerable investments have been made in these work stations to give colleagues a variety of choices suitable to their desired level of physical activity.

At the same time, in accordance with the company's emphasis on diversity, disabled GSK colleagues benefit from one of the most accessible built environments in the country. It's also a safe place: Joines reports not a single incidence of musculoskeletal injury among staff in the first two years at the Navy Yard site, while the number of reported thefts of company and employee property has dropped from twice a month at the old downtown office to a new record—zero for all of 2015. More important, data from GSK's annual individual employee health risk appraisal reveals an average 56% gain in the amount of movement per employee since the migration to the Navy Yard.

From an employee wellness perspective, GSK's signature initiative is its in-house **Energy and Resilience** campaign geared to helping workers to manage their energy. "We see stress as a major, often

hidden condition that hurts productivity and carries adverse physical consequences. It must be addressed by looking at the individual as a whole person, not just what he or she does at work," Joines told *Pharm Exec*. "The holistic environment we have created here at the Navy Yard is an important contributor to this effort because it actually makes it easier for people to expend their emotional and physical capabilities in a mindful, constructive way."

SMART technology controls that maximize natural ambient light, subtle use of calming, noise-altering audio, and wireless networking and soft phones are the foundation, but the company also offers more than a dozen wellness programs/workshops on site designed to help colleagues manage their lives based on a higher standard of physical and mental awareness.

Looking carefully at the GSK embrace of a new set of aesthetics for the workplace, the company was an early mover on ways that a designed environment might boost those fuzzy ROI metrics on employee engagement, culture and reputation. But other big Pharma players—Novartis and AZ are worth noting here—have adopted the same playbook and the rest of the industry is not far behind.

It's all about alignment—between the spiritual and temporal, between the life mission and the work mission. It's a fact that most people in a knowledge industry like biopharmaceuticals will end up spending the bulk of their lives at work, because there is no fixed time to solve a problem raised by science. The choices are abundant, risks are endemic and answers are most always elusive. So why not make the office a little more like the safe house of home?

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## 2016 Pharm Exec 50

*William Looney, Editor-in-Chief*

Pharm Exec's 16th annual listing of the top biopharma players may look placid on the surface, but, upon deeper inspection, does point to important transitions taking place in the larger business model, including the hidden value of a company's human assets.

### Diversity & Inclusion: A Pharma 50 view

*By Waseem Noor and Saule Serikov*

The industry's diversity commitment remains a work in progress but the benefits—in measurable ROI—are increasingly clear.

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Getty Images / John Lund

### M&A Roundup Forecast: Calm or Crisis Ahead?

*By Peter Young*

Do recent valuation trends in the pharma and biotech M&A and equity markets signal a temporary lull—or a permanent drop? This business trends and outlook report attempts to answer that question.

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*By the BCG Market Access Roundtable Working Group*

A new industry working group explores alternative drug funding options in Europe—and asks key stakeholders in the region to join the discussion.

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### Medical Communications Science Meets Art in MS Battle

*William Looney, Editor-in-Chief*

A new educational and potential prognosis tool for the treatment of multiple sclerosis shows how an accessible, easy-to-see visualization of disease state can serve as the threshold for fresh clinical insight—all geared to the individual patient.

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*Reflector, Brussels Correspondent*

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*Casey McDonald, Senior Editor*

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*Focus Reports, Sponsored Supplement*

While the Italian fashion and automotive industries may steal the global thunder, another sector in Italy flourishes beneath the public's radar. The country's pharmaceutical industry continues to punch above its weight in many areas and has supported Italy's national economy through many periods of weakness.



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May issue online  
Casey McDonald  
[bit.ly/1sHbjzr](http://bit.ly/1sHbjzr)

**Pharma's Value Push: Evidence Matters**

May issue online  
Terry Hisey and Brett J. Davis  
[bit.ly/1WUS4PC](http://bit.ly/1WUS4PC)

**2016 Pipeline Report**

November issue online  
Casey McDonald  
[bit.ly/1QQ8Mwq](http://bit.ly/1QQ8Mwq)

**CEO Snapshot: GSK's Man with a Plan**

May issue online  
William Looney  
[bit.ly/1X8MsSA](http://bit.ly/1X8MsSA)

**HBA's Woman of the Year 2016**

April issue online  
Kathleen Raven  
[bit.ly/1sHddA6](http://bit.ly/1sHddA6)

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## Readers Weigh In

Thank you, *Pharm Exec*, for a well-written article getting inside the head of Pres US at GSK, Jack Bailey. He is a strong, thoughtful, inspiring leader. The current healthcare landscape is frightening at best with decision makers potentially making far-reaching decisions that will affect patient care badly. GSK and Jack Bailey are poised to intercept, adapt, and act on behalf of patients and improving healthcare.

Nancy Mabry, 5/13/16

"Steering the Change: GSK's Jack Bailey"

[bit.ly/1X8MsSA](http://bit.ly/1X8MsSA)

Excellent and timely article. Most pharma clients are still struggling to come to terms with value-based reimbursement and how it is impacting their ROI.

Tony, 5/5/16

"Pharma's Big Push for Value"

[bit.ly/1WUS4PC](http://bit.ly/1WUS4PC)

Obeticholic acid still presents adverse effects and a worsening of the cardio-metabolic profile. It is a real problem for NASH (nonalcoholic steatohepatitis) patients, and not sure that the buzz on OCA will be enough to boost prescription.

Gery DIVRY, 04/29/16

"Who Will Win the Race to Treat NASH?"

[bit.ly/10YteGI](http://bit.ly/10YteGI)

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INVENTIV HEALTH

# Promises and Pitfalls in Calculating Drug Value

There's a stampede to relate prices to broader health benefits, but little consensus on how to do so

**T**herapies able to document to payers and patients that they can extend health, save lives, and slow the growth in health-care spending should be worth a lot, while treatments lacking clinical or economic benefits should charge less. That's the logic behind value-based purchasing and contracting for prescription drugs, a more palatable strategy to industry charging whatever the market will bear.

The hope of biopharma companies is that insurers and health plans will ante up for new miracle drugs able to document high-value life-saving benefits. Payers have covered the stiff prices on many orphan drugs and cancer therapies because they treat small patient populations. But there's been considerable push-back on new cures for hepatitis beneficial to millions of individuals, and for life-saving drugs with very high price tags. A real test will be calculating the value of new cellular therapies, where a one-time treatment may cure a debilitating condition, but at a cost up to \$1 million per patient.

Unfortunately, there's no clear formula for assessing medical gains, particularly over time, and much debate over where and how to calculate the numbers. Medical societies are developing "value frameworks" to support clinical decision-making, but dif-

fer in methods and measures. The National Pharmaceutical Council seeks some uniformity in approaches through development of "Guiding Practices for Patient-Centered Value Assessment Frameworks" (view <http://bit.ly/1WZP29L>).

Steven Pearson's Institute for Clinical and Economic Review (ICER) has become the pace-setter for assessing the value and cost-effectiveness of new medicines, as seen in ICER reports evaluating cancer therapies and PCSK9 inhibitors to control high cholesterol; future analyses are planned for treatments for multiple sclerosis, psoriasis, and non-small cell lung cancer.

An ICER assessment of multiple myeloma therapies adds to the widening debate over the value of new cancer treatments and when and where life-saving benefits are worth the steep prices. ICER says that most of the new myeloma therapies are not worth current prices and some should be discounted more than 75% to meet value targets. That conclusion fits the wave of reports documenting ever-rising prices for cancer therapies and that high spending on cancer drugs in the US limits health gains compared to other countries.

One might think that the new treatments for hepatitis C, which can cure this serious disease much more effectively than previ-

ous medicines and with fewer side effects, would receive high marks for value. However, an ICER assessment in early 2015 found prices far too high for these medicines, despite evidence of "clinical superiority" to existing treatments. ICER advisors recommended strong controls to limit prescribing to patients with advanced liver disease. Utilization has expanded as benefits have become more obvious, and as competition has pushed down rates.

## **CMS strategies**

Drug value assessment fits broader government efforts to shift Medicare and other federal health programs from pay-for-volume to pay-for-value models. The aim is to boost fees to doctors and provider organizations offering quality care that keeps individuals out of hospitals and emergency rooms and extends productivity and life.

Along these lines, the Centers for Medicare and Medicaid Services (CMS) seeks to encourage more use of high-value medicines by testing new reimbursement strategies for Medicare Part B drugs dispensed by clinics and doctors' offices. The proposal, which has ignited a fierce debate over rates and value, would alter current Part B policies that tend to pay physicians more for prescribing pricier drugs. Oncologists contend that the change would penalize them unfairly, and patient advocates and pharma companies fear it would curb access to newer, more costly therapies. Congressional leaders have urged CMS to retract or change the plan, and after receiving some 800 comments, agency leaders say they'll take a fresh look.



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CMS also proposes to evaluate four other “value-based” Part B pricing methods that may not please industry. These include setting a standard “reference price” based on the average price of a group of drugs; indication-based pricing that varies reimbursement according to a drug’s effectiveness in specific conditions; negotiating risk-sharing agreements with manufacturers that link outcomes to price adjustments; and reducing or eliminating patient cost-sharing to encourage use of high-value drugs.

### Rebates and discounts

If pharma companies want to shift the drug pricing debate to “value,” they may have to provide greater transparency in prices after discounts and rebates.

Manufacturers have long complained that drug cost analyses based on list prices overstate real spending, but insist on keeping negotiated rates secret for competitive reasons.

More transparency should help demonstrate that assessments based on net prices bolster drug value claims, as indicated

on prescription medicines in the US rose 8.5% from 2014 to 2015, and brand list prices increased 12.4%, there was only a 2.8% rise in average net prices for brand-name drugs already on the market.

That paltry increase reflects more price competition among brands and aggressive rate nego-

Unfortunately, there’s no clear formula for assessing medical gains, particularly over time, and much debate over where and how to calculate the numbers

by the April report on drug spending from the IMS Institute for Healthcare Informatics. It found that while overall outlays

tiating by insurers and pharmacy benefit managers (PBMs).

Most of the popular proposals to halt pharma “price gouging” do little to promote value. Both Donald Trump and Hillary Clinton support direct price negotiations by Medicare, even though that approach lacks teeth because Part D plans cannot drop important medicines from their commercial plans’ formularies. PBMs have control over formularies, but maintain they will provide better coverage and access to medicines that can demonstrate value to patients and to health plans.

Calculating the value of drugs is challenging and often subjective due to lack of consensus on what to measure, what makes a drug “novel,” and how to balance benefits and harms. Every analyst has individual preferences, and “affordability” can be hard to compare.

The Biotechnology Innovation Organization is airing an ad promoting the importance of breakthrough medicines in extending lives. “How do we place a value on these?” it asks. There are many different answers. **■**

### Value contracting risks fraud, higher rebates

A main obstacle to pharma companies negotiating value-based contracts with commercial plans is that they may run afoul of federal anti-kickback (AK) laws and best price requirements. AK statutes carry significant financial and legal penalties for parties that offer inducements or rewards affecting federal healthcare programs, which could result from contracts that reduce payments and prices based on certain clinical or economic outcomes. And such value-based arrangements with commercial customers could alter how a pharma company calculates and reports “best price” for Medicaid, 340B ceiling prices and the average sales price used to set Part B reimbursement.

To engage in innovative pricing arrangements, pharma companies and insurers are pressing for changes in relevant laws and

regulations. They seek additional “safe harbors” that exempt certain value-based contracting from AK penalties, along with legislation that drops best price reporting for value-based arrangements leading to reduced payments.

Payers also want to know in advance about new, expensive drugs coming to market so they can assess value needed for formulary placement decisions and therapy management programs. But FDA regulations inhibit pharma companies from presenting information to formulary committees and other purchasers about unapproved drugs or indications for fear of violating curbs on off-label communication. Manufacturers and payers agree that such discussion is critical, and legislation moving through Congress would support broader information exchange.

# Front & Center

## State of the Art: Highlights from CBI's 2016 Formulary, Co-Pay and Access Summit

In a world of constant market churn, diligence, data and diplomacy must combine to make industry patient assistance dollars count.

In today's complex commercial environment, drug registration no longer confers a license to print money. In fact, the opposite is true. Market barriers that separate the manufacturer from payers and providers are proliferating to the point where it takes real money and effort to connect a new brand to the ultimate customer: the patient. Access to patients must be built from scratch, using sophisticated financing incentives, consumer engagement and data management tools, spending on which now often surpasses drug maker outlays for clinical development prior to FDA approval. It follows that the expertise to drive patient access has emerged as the competitive differentiator of brand success, right from the launch phase to LOE and even beyond.

As the challenges grow to positioning patients for treatment with the best medicines appropriate to their condition, knowledge of the "access ground game" counts. With this in mind, *Pharm Exec* paid a visit last month to our sister organization CBI's 2016 Formulary, Co-Pay and Access Summit, which it runs in strategic partnership with PSKW, the market leader in brand loyalty relationship-building, whose track record includes managing coupon and co-pay offset programs on more than 230 brands, for companies ranging from the largest global firms to small/emerging biopharmas.

From the start, the two-day peer group exchange has been chaired by PSKW, which provides thought leadership in developing content and strategies for the group. Said PSKW Executive Vice-President Chris Dowd, "it's the original event in the field, the one place where stakeholders can convene to address how tiered formularies, limits on co-pay cards, coupon offsets, and other managed care restrictions end up putting cost before value — another hurdle in the patient journey toward optimal drug therapy."

This year's Summit, held April 5–6 in Philadelphia, offered a strong group consensus around five key findings to help drug makers adapt and thrive through these access challenges:

- (1) **Access barriers and patient out-of-pocket costs imposed by commercial drug plans are real — and growing.** PSKW research reveals that 92 per cent of covered workers are now subject to tiered cost-sharing formularies, while 46 per cent of benefit plans carry high drug deductibles. Both represent an important transition in the escalating access hurdle. The two major PBMs covering 80 per cent of all private-sector workers have increased the number of medicines excluded from their formulary listings to more than 200 this year, compared to 38 in 2012. PSKW's chief data scientist Robert Caprara presented in-house survey data showing that the average retail co-pay for coupon-using patients rose to over \$30 in January, compared to \$15 in January 2013. Nearly 10 per cent of patients experienced co-pays averaging \$100 — per scrip.
- (2) **Co-pay offsets are increasingly popular — particularly among physicians.** With high cost-sharing now an established fact, co-pay offsets are undeniably popular with patients. The number of coupon programs has increased by more than a third, to nearly 600, within the last two years, at an annual cost to drug makers well in excess of \$5 billion. PSKW channel claims data indicate that more patients are enrolling in offset programs independently by going online. The volume of PSKW-contracted coupons coming from the web has risen by nine percentage points — to 28 per cent — over the last year. Physician survey data also reveals that two-thirds believe that co-pay coupons increase adherence to treatment and improve patient outcomes. That's increasingly important for physicians financially, because poor outcomes can lower quality ratings and limit reimbursement from insurers. A larger point is that aggressive managed care tactics to lower the benefit bill represent not only a

shifting of costs to the patient but to the manufacturer as well, whose contributions to patient satisfaction and positive health outcomes often go unrecognized.

- (3) **Facts don't support the assertion that co-pay offset programs undermine efforts of commercial payers to reduce drug benefit costs.** PBMs insist that such programs incentivize reliance on the most expensive branded medicines at the expense of cheaper generics. Not so, says PSKW. A recent poll it commissioned of 600 physicians found they use coupons much more selectively: (1) where a generic alternative does not exist; (2) when a patient's condition requires a mix of medications, involving both existing brands and generics; or (3) as a second line of therapy, after a physician has already prescribed a generic and found his patient did not benefit. Despite claims to the contrary, offset programs are increasingly focused on established brands with a proven record of value in clinical use, not on the newest tier-three or higher formulary-listed specialty brands seen as the biggest drivers of drug costs.

Adds summit chair Chris Dowd, "it also relates to the current situation where price increases for some generics are outpacing those for established brands. This, combined with recognition of the adherence gains from keeping patients on a familiar therapy, is what motivates physicians to use coupons." The result is not more costs but system-wide savings to the insurer. Participants at the CBI event agreed this argument deserves the attention of all parties in seeking a comprehensive solution to the cost curve — it's not an issue drug makers can solve alone. In fact, the industry has little choice today but to face the affordability question about drugs head on. Access programs that help patients save on prescriptions, particularly in managing exposure to out-of-pocket spikes accompanying annual renewal of high deductible plans, help turn the industry message into one of overall value, not price.

- (4) **An effective access co-pay strategy begins with understanding that everything is connected.** In a managed care environment, detailed awareness is required of the market con-

ditions facing each brand. The checklist includes competitive profiling, payer interests, characteristics of the insured patient population, the marketing channel mix, and bid/contracting timelines. Financial risk is trending back to pharma, so it's important to incorporate the cost of wrap-around Hub-like services in budgeting exposure to co-pay offsets; anticipating ways to make that service mix work in negotiations with payers is another priority. And as business models shift under successive waves of market disruption, the roles of each player in the health care ecosystem grow increasingly confused. One big change is how the specialty drug space is becoming more like the competitive primary care segment, with its negotiated, layered and analytics-driven approach to access. In these conditions, an access strategy that is predictable, evidence-based and customized to the preferences of each stakeholder will help your brand stand out.

- (5) **Co-pay programs are an information asset.** Every coupon redemption comes with a wealth of data, which can be leveraged to address the payer interest in real world evidence of value, which is frequently lacking at the higher-priced end of the specialty segment. Good data also helps identify where the drug fits within the clinical treatment algorithms that increasingly determine formulary placements. Wider reliance on EHR will facilitate use of eCoupons and eVouchers, increasing the size of the data pool and its potential as a source of fresh customer insights.

**The key takeaway?** Coupon and other co-pay offset programs are the root and branch of any access strategy because they incentivize demand for the brand, building that share of market allowing you to approach payers, insurers and other stakeholders from a position of strength. Add flexibility in negotiations and a sharp eye on the patient profile and you have an access plan that will make the market come to you — and ensure outstanding brand loyalty.

#### Reference

"An Evidence-based Approach to Understanding the Benefits of Co-Pay Reduction;" PSKW White Paper; June 30, 2015.

# Europe's 'Radical' Regulators Drawn Further into Pricing Debate

Top officials at EMA push the boat out on drug-pricing views

**A**s if the tensions surrounding the cost of drugs were not high enough already in Europe, leading figures at the European Medicines Agency (EMA) opened up the debate even wider in May. Radicals who wield real power at the agency went public with their latest thinking about the role of regulators in the economic aspects of medicines provision—despite the decades-old European Union (EU) taboo about linking pricing with authorizations.

They offer some hints of reluctance for this departure, and suggest their hand has been forced. “Although drug regulators aren’t supposed to be concerned with pricing, they’ve been drawn into an acrimonious debate,” wrote the EMA’s chief scientist, Hans-Georg Eichler, and its executive director, Guido Rasi, in the *New England Journal of Medicine*. They showed no timidity, however, as they enter into the crux of the matter with real gusto, even extending their reflections into the equally contentious area of faster approvals.

## \$\$\$ pain, equal blame

The EMA officials and their co-authors are openly critical of the current situation, and “the growing budget pains

caused by newly authorized products”—with explicit references to recent launches.

“We fail to comprehend prices that, like *Sovaldi*’s, recoup the entire investment within the first few months after a product’s launch but are so unaffordable that patients in need are denied access,” they say, speaking of “financial toxicity” and evidence that “companies tend to charge whatever the market will bear.” And they unambiguously predict that “the market will not bear some of the higher drug prices.”

But their intention is not to put all the blame onto companies. “Regulation drives up R&D costs,” they openly acknowledge. “Regulatory requirements have undoubtedly made pharmaceutical R&D expensive.” They also accept the underlying logic of the current drug development model: new drugs should command prices that reward and provide incentives for R&D investment, they say. “Potentially useful products may not be developed if companies fear they won’t be able to recoup their R&D costs,” they recognize.

Instead, they explore how regulators may be able to exert some beneficial influence. They can’t shut up shop, obviously:

“If we eliminated regulation, the current biopharmaceutical business model would collapse—and so would science-based drug development.” In any case, R&D costs are not the only factor behind high prices. Cutting out some of those regulation-driven costs would still not mean that prices would automatically drop.

“Even pharmaceutical executives admit that this assumption is naïve,” say the regulators. In addition, “robust regulation” is a good thing for all concerned, because it obliges drug firms to meet high standards, and any lowering of standards would be “unwise for both patients and organizations that invest in pharmaceutical R&D.”

## Response plan

So what can they do? Top of their menu is promoting competition, by rapidly approving generics and biosimilars that can drive down prices. And when companies are taking advantage of monopoly conditions for generic drugs, regulator could fast-track additional generic authorizations. As a more challenging approach, they could “ensure that ‘me-too’ products continue to come on the market at a reasonable speed.”

Knowing this is a red rag to the bull of many consumer advocates who routinely accuse drugmakers of marketing products with no added value, the regulators argue that added value is difficult to predict, and “me-toos” can help to drive down prices.

It is in their recommendations for re-assessing the entire process of getting drugs to

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patients that the EMA officials push the boat out furthest, with their support for significant changes. “Clinical drug development is generally an inefficient process,” they state boldly, urging a profound review of “the elaborate superstructure involved”—which, it says, “could be pared down without harming participants.” The iconoclasm doesn’t stop there: conventional development and licensing pathways are also “often economically inefficient.”

Cue an eloquent commercial for the EMA’s recent activities in these areas. And not just the parallel scientific advice sessions it has been hosting where regulators, health technology assessment (HTA) experts, and drug developers discuss pre-marketing clinical trial designs. “Working with HTA bodies and patient groups, the EMA is exploring whether a more flexible development, licensing, and reimbursement approach called adaptive pathways may help companies stagger clinical development costs, generate revenue earlier, and remove some risk from R&D without relaxing the criteria for determining products’ risk–benefit profiles,” they say.

This life span approach to generating evidence “will lower the threshold for financing drug development at a time when prices are coming under pressure,” they argue.

They qualify their adventurous exploration with a disclaimer: “We firmly believe that assessment of quality, safety, and efficacy should remain separate from pricing and reimbursement decisions. Regulators alone cannot solve

the growing problem of high drug prices.”

### ‘Fast’ route no cure-all

But, unsurprisingly, that has not been enough to ease concerns among some of the organizations who are skeptical about the merits of voyaging into these uncharted waters.

One of the first into the fray was the European Public Health Alliance. Its spokesman on access to medicines, Yannis Natsis, took issue with any link between adaptive pathways

The voices of the self-styled “public health community” will have to be taken into consideration, too, if high-level agreements are not to be undone by street-level scepticism

and doing anything about “the high prices of medicines.” There is, he said, no compelling evidence to support assumptions of improved affordability. On the contrary, “some evidence points to fast-track approaches leading to higher prices,” and some serious assessment is needed of the impact. It is not enough to be “working on the basis of an untested assumption,” he said.

Natsis went further in a statement he released days after the *NEJM* article appeared. He claimed that the pilot project the EMA is running on adaptive pathways is a Trojan horse for easing regulatory rigour. Citing earlier expressions of concern from “the public health community” about “the questionable innovative value of these medicines” and “fears about patient safety,” he said

there are “serious questions as regards to public health risks of such an approach.”

He alleged that the adaptive pathways school of thought “seeks to introduce a new model applicable to all drug approvals in Europe by turning the exception—early access—into the new rule,” with the result that the fast-track, light-regulation approach will become the *de facto* approach for approvals for all medicines. This, Natsis warned, would be a fundamental regulatory change through

the back door, without adequate consultation of stakeholders or approval from policymakers. “It is a paradigm shift with massive political impact. Its implications cannot be discussed any longer in side meetings and ... without political accountability and oversight.”

### Breaking point looms

The pressures that Eichler and Rasi perceive are real enough, and will not go away. The dilemmas that drug pricing throws up are exercising senior figures in the pharmaceutical industry, too, and some sort of accommodation or resolution is going to have to be found before long. But the voices of the self-styled “public health community” will have to be taken into consideration, too, if high-level agreements are not to be undone by street-level skepticism. 



# 2016 *Pharm Exec* 50

*Pharm Exec*'s latest annual listing of the top biopharmaceutical players—now in its 16th year—looks placid on the surface. But a restive marketplace and important transitions taking place in the larger business model of healthcare augers poorly for those inclined to read our numbers as a successful adjustment to the world as it is—because it's a sure bet that world is going to be different

**T**hough the companies represented in the top 50 of global sales leaders have remained remarkably stable over time, their relative positioning within the list continues to shift. This reflects the importance that product launches and innovative campaigns to grow existing medications at every stage of the product life cycle now play in building a sales advantage against truly brutal levels of competition. It helps explain why Pfizer resumes its position this year as the industry's prescription sales leader, displacing Novartis in the No. 1 ranking by widening its therapeutic franchise in vaccines—a segment that Novartis recently abandoned—with a strong performance for its multi-indication pneumococcal preventive, *Prevnar 13*.

Further down the list, we also find signs of a pause

in the once heady ascent of what *Pharm Exec* calls the “stealth” players: middle-rank companies with records of product innovation and new-age marketing that could propel them to the top 10. So far, only one of the “stealths” has accomplished that feat: Gilead Sciences, which two years ago leaped from 25th place to 9th last year, with its breakthrough hepatitis C cure breaking all sales records. But, in another sign of the relentless pressure to perform above expectations, Wall Street now says it's time for an encore; without one, the company's continued place on the pole posting of privilege is not guaranteed.

Likewise, the entry of a generic player to the top ranks is still an object on the horizon. Despite the certainty of a larger portfolio as Teva acquires Allergan's generics business, its move to the top 10 is con-

tingent on bucking the threat that price deflation, launch delays, other regulatory challenges and dwindling LOE opportunities pose to the generic sector's overall bottom line.

Ultimately, it's all about the quality and scale of the product franchise—and how effectively that franchise is managed and executed across every element of the biopharma operations playbook.

That's why a special feature accompanying this year's Pharma 50 list highlights what we at *Pharm Exec* continue to insist is the value hidden in a company's human assets. In what is now a global war for talent, commitment

## Ultimately, it's about the quality and scale of the product franchise—and how effectively that franchise is managed and executed across every element of the biopharma operations playbook

to diversity and inclusion in human capital is an across the board competitive differentiator.

Our guest authors at the executive recruitment and talent management firm Russell Reynolds Associates put it succinctly: Diversity is the hardware that brings dif-

ferent machines together. Inclusion is the software that brings the system to life. Well said—and a call to action for every biopharma company who has a place in our Pharma 50 or aspires to it.

—William Looney, *Editor-in-Chief*

Rank	Company headquarters [website]	2015 Rx Sales (USD in mln)	2015 R&D spend (USD in mln)	2015 Top- selling Drugs [USD in mln]
1	<b>Pfizer</b> New York, New York [pfizer.com]	\$43,112	\$7,678.0	Prevnar 13 [5,940] Lyrica [4,839] Enbrel [3,333]
2	<b>Novartis</b> Basel, Switzerland [novartis.com]	\$42,467	\$8,465.3	Gleevec [4,658] Gilenya [2,776] Lucentis [2,060]
3	<b>Roche</b> Basel, Switzerland [roche.com]	\$38,733	\$8,452.1	Rituxan [7,321] Avastin [6,945] Herceptin [6,794]
4	<b>Merck &amp; Co.</b> Kenilworth, New Jersey [merck.com]	\$35,244	\$6,613.0	Januvia [3,863] Zetia [2,526] Janumet [2,151]
5	<b>Sanofi</b> Paris, France [sanofi.com]	\$34,896	\$5,638.2	Lantus [7,089] Plavix [2,140] Lovenox [1,907]
6	<b>Gilead Sciences</b> Foster City, California [gilead.com]	\$32,151	\$3,018.0	Harvoni [13,864] Sovaldi [5,276] Truvada [3,459]
7	<b>Johnson &amp; Johnson</b> New Brunswick, New Jersey [jnj.com]	\$29,864	\$6,821.0	Remicade [5,779] Stelara [2,474] Zytiga [2,231]
8	<b>GlaxoSmithKline</b> Brentford, England [gsk.com]	\$27,051	\$4,731.1	Seretide/Advair [5,625] Pediarix [1,120] Triumeq [1,116]
9	<b>AstraZeneca</b> London, England [astrazeneca.com]	\$23,264	\$5,603.0	Crestor [5,017] Symbicort [3,394] Nexium [2,496]
10	<b>AbbVie</b> North Chicago, Illinois [abbvie.com]	\$22,724	\$3,617.0	Humira [14,012] Viekira Pak [1,639] Lupron [826]

Source: EvaluatePharma® April 2016, Evaluate Ltd, www.evaluate.com

**How the listings were compiled:** 2015 R&D Spend and 2015 Rx Sales analyses were provided by life science market intelligence firm Evaluate Ltd via its EvaluatePharma® service, www.evaluate.com. *Pharm Exec* would like to thank EvaluatePharma® for assisting in the development of this year's Pharma 50 listing. EvaluatePharma® takes sales estimates from leading equity analysts to create a consensus sales forecast, currently to 2022. Evaluate's Sales and R&D Spend figures represent the fiscal year that ended in 2015. For most American and European companies, that means the year ending December 31, 2015. For many Japanese companies, the fiscal year ending March 31, 2016, was used. Historic averages were used in the conversion of companies' native currency to USD.

# Diversity and Inclusion: A Pharma 50 Perspective

*Biopharma's diversity commitment remains a work in progress but the benefits—in measurable ROI—are increasingly clear*

By Waseem Noor and Saule Serikov

Organizations across all industries have begun to recognize that diversity efforts go well beyond simple anti-discriminatory compliance and image campaigns; they provide clear business benefits. Company leaders are creating programs to increase diversity from their board levels all the way down the ranks of the organization.

Underlining these efforts, McKinsey & Company's pivotal paper, "Diversity Matters," published in 2014, looked at the relationship between the level of

diversity, defined as "a greater share of women and a more mixed ethnic/racial composition in the leadership of large companies," and company financial performance, measured as average earnings before interest and taxes (EBIT), for the years 2010 to 2013.

The analysis found a statistically significant relationship between leadership diversity and financial performance. More specifically, the companies in the top quartile for gender diversity were 15% more likely to have above-average financial returns, while the companies in the top quartile for racial/ethnic diversity were 30% more likely to have above-average returns.

Rank	Company headquarters [website]	2015 Rx Sales (USD in mln)	2015 R&D spend (USD in mln)	2015 Top- selling Drugs [USD in mln]
11	<b>Amgen</b> Thousand Oaks, California [amgen.com]	\$20,944	\$3,917.0	Enbrel [5,364] Neulasta [4,715] Aranesp [1,951]
12	<b>Allergan</b> Irvine, California [allergan.com]	\$18,403	\$2,780.7	Botox [1,976] Restasis [1,048] Namenda XR [759]
13	<b>Teva Pharmaceutical Industries</b> Petach Tikva, Israel [tevapharm.com]	\$16,982	\$1,525.0	Copaxone [4,023] Treanda [741] ProAir HFA [549]
14	<b>Novo Nordisk</b> Bagsvaerd, Denmark [novonordisk.com]	\$16,054	\$2,024.2	NovoRapid [3,082] Levemir [2,722] Victoza [2,682]
15	<b>Eli Lilly</b> Indianapolis, Indiana [lilly.com]	\$15,792	\$4,478.3	Humalog [2,842] Alimta [2,493] Cialis [2,291]
16	<b>Bayer</b> Leverkusen, Germany [bayer.com]	\$15,558	\$2,588.3	Xarelto [2,062] Eylea [1,362] Kogenate [1,281]
17	<b>Bristol-Myers Squibb</b> New York, New York [bms.com]	\$14,480	\$4,037.0	Eliquis [1,860] Sprycel [1,620] Daklinza [1,315]
18	<b>Takeda</b> Osaka, Japan [takeda.com]	\$12,565	\$2,776.0	Velcade [1,192] Protonix [840] Entyvio [581]
19	<b>Boehringer Ingelheim</b> Ingelheim, Germany [boehringer-ingelheim.com]	\$12,348	\$2,801.7	Spiriva [3,912] Pradaxa [1,831] Micardis [1,019]
20	<b>Astellas Pharma</b> Tokyo, Japan [astellas.com]	\$10,937	\$1,959.8	Xtandi [2,089] Prograf [1,600] Vesicare [1,128]

# biopharma falling down or turning around?

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Although it proves a correlation and not causation, the paper argues that “more diverse companies are better able to win top talent and improve their customer orientation, employee satisfaction, and decision making, leading to a virtuous cycle of increasing returns.”

Given these findings, we would expect to see the pharma industry diversifying across the globe. And it seems that a handful of Pharma 50 companies are indeed helping lead the way in diversity efforts. A US-based organization called DiversityInc conducts a voluntary survey of company diversity each year and then ranks the companies on four

key areas of diversity management: talent pipeline, equitable talent development, CEO/leadership commitment, and supplier diversity. Individual company data is kept anonymous.

In 2016, more than 1,800 organizations participated in the survey, which is now in its 17th year. Significantly, six of this year’s *Pharm Exec 50* companies are listed: Novartis Pharmaceuticals Inc. (#2), Johnson & Johnson (#8), Abbott Labs (#14), Merck & Co. (#17), Eli Lilly (#26), and AbbVie (#45).

Yet a closer look at the pharma industry shows that, while diversity continues to improve, the Pharma 50, as a

group, is right in the middle of the industry pack when benchmarked against the Fortune 500. In addition, we find striking differences in the levels of gender, national, and ethnic diversity when we look at the boards and executive committees of individual companies. Some are true diversity champions, while others lag far behind. And this disparity persists across regions.

Of course, the definition of diversity differs across geographies. In the US, for example, diversity tends to be defined by gender and ethnicity. In Europe, by contrast, the diversity discussion revolves around gender and

Rank	Company headquarters [website]	2015 Rx Sales (USD in mln)	2015 R&D spend (USD in mln)	2015 Top- selling Drugs [USD in mln]
21	<b>Mylan</b> Canonsburg, Pennsylvania [mylan.com]	\$9,291	\$651.6	EpiPen [1,073] Fentanyl TDS [258] Esomeprazole magnesium [169]
22	<b>Biogen</b> Cambridge, Massachusetts [biogenidec.com]	\$9,189	\$2,012.8	Tecfidera [3,638] Avonex [2,630] Tysabri [1,886]
23	<b>Celgene</b> Summit, New Jersey [celgene.com]	\$9,069	\$2,295.0	Revlimid [5,801] Pomalyst [983] Abraxane [968]
24	<b>Merck KGaA</b> Darmstadt, Germany [merckgroup.com]	\$7,693	\$1,453.5	Rebif [1,995] Erbix [997] Gonal-F [760]
25	<b>Daiichi Sankyo</b> Tokyo, Japan [daiichisankyo.com]	\$7,215	\$1,617.9	Benicar [1,900] Nexium [652] Loxonin/ Loxonin Poultice [382]
26	<b>Valeant Pharmaceuticals International</b> Mississauga, Ontario [valeant.com]	\$7,013	\$333.2	Xifaxan 550 [578] Jublia [338] Wellbutrin XL [320]
27	<b>Otsuka Holdings</b> Tokyo, Japan [otsuka.com]	\$6,728	\$1,595.5	Abilify [2,896] Samsca [346] Abilify Maintena [337]
28	<b>CSL</b> Melbourne, Australia [csl.com.au]	\$6,294	\$563.7	Privigen [2,462] Human albumin [835] Humate P [538]
29	<b>Baxalta</b> Cambridge, Massachusetts [baxalta.com]	\$6,148	\$1,176.0	Advate [2,240] Gammagard Liquid [1,523] FEIBA VH [706]
30	<b>Shire</b> Dublin, Ireland [shire.com]	\$6,100	\$884.1	Vyvanse [1,722] Lialda [684] Cinryze [618]

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nationality. In the workforce in all regions, however, the diversity debate not only relates to demographic criteria such as gender, nationality, ethnicity, and age, but encompasses sexual orientation and the broad experiences, personality types, and work styles of company employees.

### A step further: Russell Reynolds' proprietary research

Using a bottom-up approach, Russell Reynolds Associates (RRA) conducted a proprietary analysis of the *Pharm Exec* Pharma 50 to find out more about diversity on two important organizational levels: the

*board level*, including non-executive and executive board directors, but excluding employee representatives; and the *executive committee (ExCo)* level, including CEOs and their direct reports.

The research was conducted using publicly available information from April 2016, such as BoardEx, LinkedIn, and company websites, and contains data points for over 1,000 individuals.

For the purposes of this analysis, we categorized the Pharma 50 companies into five broad types: big Pharma companies based in the US; big Pharma companies based in the European Union (EU); specialty

pharma companies; pharma companies outside of the US and EU; and privately held pharma companies, primarily in the EU. Our categorization is described in Figure 1 on page 28.

Our main objective was to investigate the pharma industry's commitment to diversity, as reflected by the diversity of the boards and ExCos of the companies we analyzed, both relative to other industries and within the industry.

We used publicly available distinctions of gender, ethnicity, and nationality to investigate board and committee composition. Within nationality, we typed individuals as being either "national" or "foreign" to the

Rank	Company headquarters [website]	2015 Rx Sales (USD in mln)	2015 R&D spend (USD in mln)	2015 Top-selling Drugs [USD in mln]
31	<b>Sun Pharmaceutical Industries</b> Mumbai, India [sunpharma.com]	\$4,503	\$297.0	Imatinib Mesylate [196] Atorvastatin [178] Absorica [156]
32	<b>Les Laboratoires Servier</b> Neuilly-sur-Seine, France [servier.com]	\$4,470	\$1,121.9	Aceon [706] Diamicron [528] Vastarel [480]
33	<b>Eisai</b> Tokyo, Japan [eisai.com]	\$3,909	\$1,042.7	Aricept [470] Aloxi [370] Methycobal [355]
34	<b>UCB</b> Brussels, Belgium [ucb.com]	\$3,763	\$1,150.5	Cimzia [1,202] Vimpat [753] Keppra [730]
35	<b>Abbott Laboratories</b> Abbott Park, Illinois [abbott.com]	\$3,720	\$137.0	Femelle [26] Geptor [19] Quetidin [13]
36	<b>Fresenius</b> Bad Homburg, Germany [fresenius-kabi.com]	\$3,709	\$375.0	Heparin Sodium [72]
37	<b>Grifols</b> Barcelona, Spain [grifols.com]	\$3,365	\$235.2	Gamunex IGIV [1,057] Flebogamma [655] Prolastin-C [461]
38	<b>Chugai Pharmaceutical</b> Toyko, Japan [chugal-pharm.co.jp]	\$3,297	\$676.8	Actemra [221] Edirol [191] Neutrogen [122]
39	<b>CJ (CheilJedang)</b> Seoul, South Korea [cj.co.kr/cj-en]	\$3,228	N/A	Epokine [23] Mosawon/Mosaone [4] Hepcure [2]
40	<b>Mallinckrodt</b> Dublin, Ireland [mallinckrodt.com]	\$2,976	\$185.1	H.P. Acthar Gel [1,037] Ofirmev [263] Optiray [198]

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organization's headquarters location.

For example, a UK national sitting on the board of a US company would be considered "foreign"; however, a UK individual on the board of a French company would be considered "national," as we have categorized the EU as a single country cluster.

At the outset, we established three hypotheses we wanted to investigate:

» **Hypothesis 1:** Given the dynamic nature of the life sciences industry and the global

breadth of its customers, pharma would be ahead of other industries in terms of board diversity.

» **Hypothesis 2:** Given the globalization of the patient base and of pharma operations, the members of the ExCos of pharma organizations would be more diverse than the boards.

» **Hypothesis 3:** Given their entrepreneurial and innovation framework, smaller specialty pharma companies would be more diverse than big Pharma companies.

## Are pharma boards ahead?

For the first hypothesis, we looked at diversity at the board level for pharma companies and compared it to the diversity of boards in other major industries. As noted earlier, we presumed that the pharma industry would be ahead of many of the other industries in diversity.

For the comparator industries, RRA took 453 publicly traded companies in the Fortune 500 and categorized them into industry sectors. We then analyzed the composition of the board for

Rank	Company headquarters [website]	2015 Rx Sales (USD in mln)	2015 R&D spend (USD in mln)	2015 Top-selling Drugs [USD in mln]
41	<b>Sumitomo Dainippon Pharma</b> Osaka, Japan [ds-pharma.com]	\$2,902	\$684.3	Latuda [920] Brovana [225] Meropen [186]
42	<b>Endo International</b> Dublin, Ireland [endo.com]	\$2,856	\$45.5	Voltaren Gel [207] Opana ER [176] Xiaflex [158]
43	<b>Menarini</b> Florence, Italy [menarini.com]	\$2,836	N/A	Lobivon/Nebilet/ Nebilox [277] Enantyum/Quiralam/ Quirgel [132] Adenuric [93]
44	<b>Regeneron Pharmaceuticals</b> Tarrytown, New York [regeneron.com]	\$2,689	\$1,620.6	Eylea [2,676] Arcalyst [14]
45	<b>Alexion Pharmaceuticals</b> Cheshire, Connecticut [alxn.com]	\$2,603	\$543.6	Soliris [2,590] Strensiq [12]
46	<b>Aspen Pharmacare</b> Durban, South Africa [aspenpharma.com]	\$2,586	\$1.5	Fraxiparine [244] Arixtra [109] Orgaran [24]
47	<b>Mitsubishi Tanabe Pharma</b> Osaka, Japan [mt-pharma.co.jp]	\$2,542	\$609.0	Remicade [573] Talion [141] Ceredist [121]
48	<b>Nestlé</b> Vevey, Switzerland [nestle.com]	\$2,431	N/A	Restylane [394] Epiduo [212] Oracea [206]
49	<b>Meda</b> Somerset, New Jersey [medapharma.us]	\$2,139	\$108.0	Dymista [119] Dona [101] Betadine [98]
50	<b>Hospira</b> Lake Forest, Illinois [hospira.com]	\$2,131	\$247.1	Precedex [139] Hydromorphone Hydrochloride [87] Vancomycin [86]



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**Figure 1: Top 50 pharma companies by cluster**

Big Pharma US	Big Pharma EU	Specialty	Private	Outside US/EU
HQ in the US Rx revenues >USD 10bn	HQ in Europe Rx revenues >USD 10bn	Rx revenues <USD 10bn Niche players, generics, non "pure play" pharma (e.g., Baxter)	HQ in Europe Privately held	HQ outside the US and Europe Japan, China, S. Africa
<ol style="list-style-type: none"> <li>AbbVie</li> <li>Amgen</li> <li>Bristol-Myers Squibb</li> <li>Eli Lilly</li> <li>Gilead Sciences</li> <li>Johnson &amp; Johnson</li> <li>Merck &amp; Co.</li> <li>Pfizer</li> </ol>	<ol style="list-style-type: none"> <li>Allergan</li> <li>AstraZeneca</li> <li>Bayer</li> <li>GlaxoSmithKline</li> <li>Novartis</li> <li>Novo Nordisk</li> <li>Roche</li> <li>Sanofi</li> <li>Teva</li> </ol>	<ol style="list-style-type: none"> <li>Abbott</li> <li>Alexion</li> <li>Baxter International</li> <li>Biogen Idec</li> <li>Celgene</li> <li>CSL</li> <li>Endo International</li> <li>Fresenius</li> <li>Lundbeck</li> <li>Mallinckrodt</li> <li>Mylan</li> <li>Shire</li> <li>Stada Arzneimittel</li> <li>UCB</li> <li>Valeant</li> </ol>	<ol style="list-style-type: none"> <li>Boehringer Ingelheim</li> <li>Chiesi</li> <li>Grifols</li> <li>Menarini</li> <li>Merck KGaA</li> <li>Servier</li> </ol>	<ol style="list-style-type: none"> <li>Aspen Pharmacare</li> <li>Astellas Pharma</li> <li>Chugai Pharma</li> <li>Daiichi Sankyo</li> <li>Dr. Reddy's Lab.</li> <li>Eisai</li> <li>Kyowa Hakko Kirin</li> <li>Mitsubishi Tanabe Pharma</li> <li>Otsuka</li> <li>Sumitomo Dainippon Pharma</li> <li>Sun Pharma</li> <li>Takeda</li> </ol>

Source: RRA analysis of top 50 pharma companies (by Rx revenues); data set for April 2016; employee representatives excluded

**Figure 2: Pharma 50 board composition compared to other industries**

	Fortune 500	Fortune 500 by sector				Pharma 50
		Consumer goods	Financial services	Industrial & natural resources	Technology	
Average board size	10.8	10.9	11.4	10.6	10.7	10.1
% of board seats held by females	20	23	22	17	19	17
% board seats held by ethnically diverse directors	14	15	13	11	11	8
% diverse board seats in terms of nationality	7	9	7	7	6	19

Note: We recognize that the Fortune 500 and Pharma 50 are not directly comparable, as the Fortune 500 includes only US-based companies, while the Pharma 50 is a global categorization that includes North America, the EU, and Asia. Nonetheless, the comparison provides good insights into the diversity levels within the Pharma 50

Source: RRA analysis

each of these companies as of July 2015, when the Fortune 500 lists were announced. For each of the industries, we calculated four factors:

- » The average number of directors on the board of each company ("average board size")
- » The share of board seats held by women ("% of board seats

held by females")

- » The share of board seats held by ethnically diverse directors ("% board seats held by ethnically diverse directors")
- » The share of board seats held by individuals who have a nationality different from the headquarters of the country ("% diverse board seats in

terms of nationality")

The results are found in Figure 2 at bottom left. While we hypothesized that the pharma industry, as represented by Pharma 50 companies, would have strong diversity compared to the other industries, we found—to our surprise—that it generally has less gender and ethnic diversity than the other industries in the Fortune 500.

The average board size within the Pharma 50 does not differ significantly from the board size within the Fortune 500, even when broken out by industry. Yet when we look at gender diversity, the Pharma 50 has a share of female board seats that is well behind that of companies in the other industries in the Fortune 500, with the exception only of the industrial and natural resource industry (with about the same share).

We even found that 16 of the Pharma 50 companies (about one-third) have no women on their boards at all. And while this is true primarily in companies outside of the US and EU, it occurs in all five identified clusters.

In addition, the Pharma 50 lag behind companies in all the other industries in terms of seats held by ethnically diverse directors. Whereas the share of seats held by ethnically diverse directors for the Fortune 500 overall is about 14%, for Pharma 50 the share is around 8%.

In contrast, the international diversity of board seats seems to be stronger in the Pharma 50 companies than in the other companies in the Fortune 500, by a significant degree. We will look further into this variation as we look at the other hypotheses.



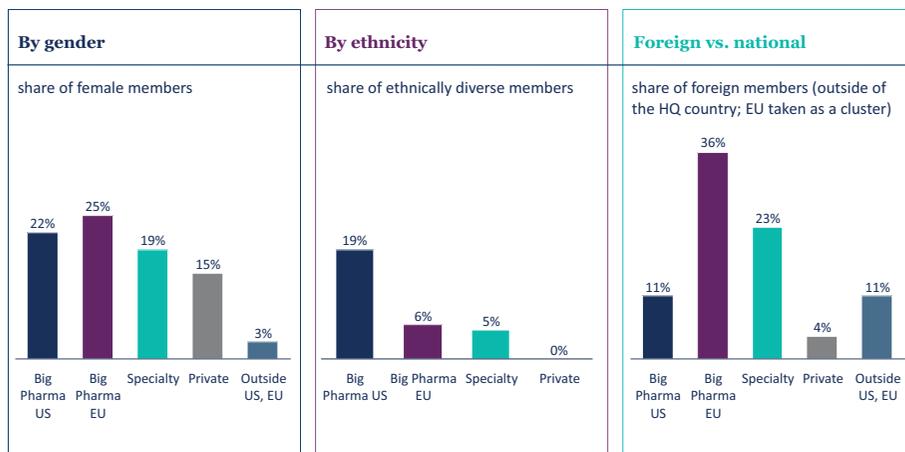
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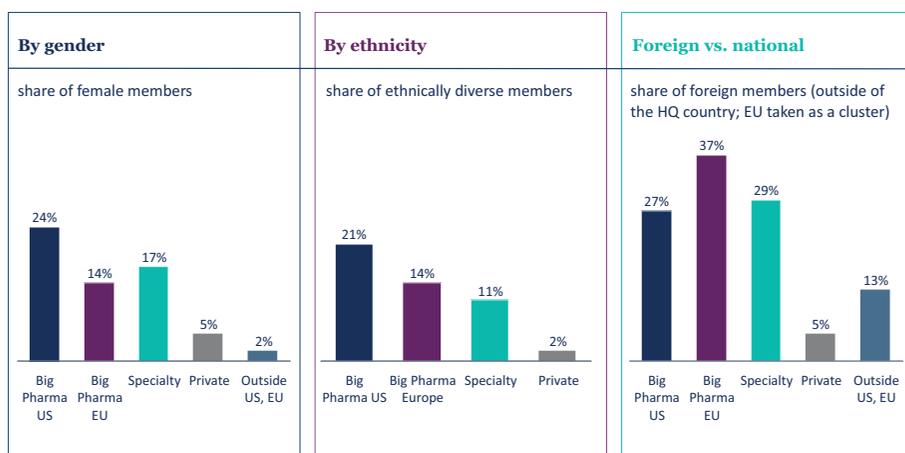
Maybe that's why we have helped to develop or commercialize 81% of all Novel New Drugs approved by the FDA over the past five years. Or maybe our clients just like working with us.

**Figure 4: Diversity across company clusters – board level**



Source: RRA analysis of top 50 pharma companies (by Rx revenues); data set for April 2016; employee representatives excluded

**Figure 5: Diversity across company clusters – executive committee level**



Source: RRA analysis of top 50 pharma companies (by Rx revenues); data set for April 2016; employee representatives excluded

**Are ExCos more diverse?**

For the second hypothesis, we looked within the Pharma 50 companies to examine the diversity of their boards compared to the diversity of their executive committees. We predicted that the make-up of the

individuals in the most senior management positions would be more diverse than that of the boards of the same companies. We once again looked at three dimensions of diversity: gender, ethnicity, and nationality.

For gender diversity, we found that the ExCos of these

companies have even lower female representation. About 12 % of ExCo seats are held by women and 19 of the 50 companies have no women on the ExCo at all. In a surprising finding, therefore, the management teams are generally less gender-diverse than the boards, and this holds true across each of the clusters (see Figure 3 on facing page).

For ethnic diversity, we focused exclusively on US- and EU-headquartered companies. Here, we found that ExCos have a higher share of ethnically diverse members (14%) than do the boards (8%). Within this, however, 53% of the boards and 37% of the ExCos at Pharma 50 companies based in the US and Europe do not have a single ethnically diverse member. By contrast, others have made a significant effort: About 13% of the Pharma 50 boards and 26% of ExCos have more than three ethnically diverse members.

On the nationality dimension, we find that boards and ExCos within the Pharma 50 are almost equally diverse, with numerous nationalities represented. Executive teams have an average of 3.2 different nationalities among the members, while boards have an average 2.6. This strong national diversity may be a reflection of the global nature of the business, which we noted in our hypothesis 1.

In addition, it may be only natural that the Pharma 50 has greater diversity by nationality than the Fortune 500, given it includes the EU, where almost all big Pharma companies have at least one American on the board.

**Figure 3: Diversity on board vs. executive committee**



Source: RRA analysis of top 50 pharma companies (by Rx revenues); data set for April 2016; employee representatives excluded

of their entrepreneurial nature and innovation based approach to therapies.

Our analysis revealed that, in fact, specialty pharma companies are somewhat diverse in terms of gender at the board and ExCo levels, although not quite as diverse as big Pharma in either Europe or the US (see Figures 4 and 5 on facing page). Yet in terms of ethnicity, we find that specialty companies in general have a lower share of diverse board and ExCo members than big Pharma in the US or EU. This may well be because big Pharma companies receive far more public scrutiny than do specialty pharma companies, putting them under pressure to diversify.

**Specialty pharma in the lead?**

For the final hypothesis, we looked to see if there was a variation in diversity among differ-

ent types of pharma companies. We speculated that specialty pharma companies in the Pharma 50 would be more diverse than big Pharma because



# WEBINAR: CONSIDERING BIOSIMILARS

A Panel Discussion Exploring Perceptions and Potential Adoption

Live Webinar: Tuesday, June 7, 2016 at 10 am PDT / 12 pm CDT / 1 pm EDT

**EVENT OVERVIEW**

With FDA hearings imminent and the onset of biosimilars looming, InCrowd's **Considering Biosimilars: A Panel Discussion Exploring Perceptions and Potential Adoption** seeks to share perspectives from biologic prescribers, researchers, and industry experts on the introduction of the new class of drug into the market. In this webinar you will learn:

- Attitudes of current biologic prescribers
- Key considerations for biosimilars adoption, such as pricing of approved biosimilars
- Potential market barriers to biosimilars acceptance.

This panel discussion will be moderated by InCrowd's co-founder and president, Diane Hayes, Ph.D.

**Who Should Attend:**

- Pharmaceutical experts involved in the design, development, and deployment of new drugs

**Key Learning Objectives:**

- To educate attendees on biologic prescribers attitude towards biosimilars
- To open a dialogue between biologic prescribers and pharmaceutical specialists responsible for biosimilars
- To explore the impact of pricing as a key factor in biosimilars adoption
- To help inform and prepare vested stakeholders for the biosimilars FDA hearings

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Looking at diversity by nationality, specialty pharma companies do fairly well, with a 23% share of foreign board members and a 29% share of foreign ExCo members, compared to 11% and 27%, respectively, for big Pharma in the US and 36% and 37%, respectively, for big Pharma in the EU. This is particularly interesting given our finding that big Pharma companies in the US and Europe generally have more diversity on their boards and ExCos than other types of pharma companies, while companies headquartered outside the US and EU have the least diversity.

Perhaps more interesting, when we look outside the clusters, we see that 16 and 14 out of the top 50 pharma companies' boards and ExCos, respectively, have only one nationality represented on their boards—that of the headquarters country.

### Inclusion matters

Although we have focused on diversity in the body of this paper, there is a second very important side to the diversity coin: inclusion. Whereas diversity reflects the different types of individuals resident in a company, inclusion is the glue that brings these individuals together.

Inclusion is essential if companies are to integrate diverse talent into their organizations. When diverse talent is unable to integrate effectively into the organization's culture, there are negative implications for the business, such as increased turnover costs and loss of accumulated knowledge. There is therefore little point in tackling diversity without also solving

for inclusion—ensuring that every person is able to participate and realize his or her full potential. Whereas diversity is the hardware bringing different machines together, inclusion is the software that brings the system to life.

Diversity and inclusion should not be standalone HR initiatives, but included in the overall business and talent strategy. Sponsorship and tangible support from the very top—board- and ExCo-level—are required. Companies will also need a structured approach, including a clear diversity-and-inclusion strategy and roadmap to success. Hiring a chief diversity officer can help, accelerating the process at the highest levels.

To ensure true inclusion, the Pharma 50 companies will also need to understand the areas in which they may have unconscious biases, and take bold moves to address those issues. They will need to embrace new ways of thinking, new styles of behavior, and cultural modifications.

Finally, companies will need to move away from the traditional approach of exclusively measuring demographics and toward a new approach that includes engaging with more sophisticated metrics—especially those that measure the inclusiveness of the corporate culture.

### Reach for equilibrium

We believe pharma companies have recognized the importance of diversity and are working to increase it. We are confident, for example, that if we were to conduct an analysis of the current general managers in place within the top 50 pharma companies in

the leading economies—i.e., the pipeline of next-generation C-level executives—it would reveal an increasing gender diversity. In addition, we believe that other forms of diversity, beyond gender diversity, are growing within these ranks.

This diversity is holding strong here and there on the senior levels. If we look exclusively at board composition over the past 12 years, for example, we see an increase in female representation in top companies, from 13% of the top 10 by sales in 2004, to 24% of the top 15 companies in 2016. In addition, we are already aware of the existence of certain pharma diversity leaders—although all still have a way to go—while others lag significantly behind.

### A call to action

Yet it is essential for all pharma companies to nurture the diverse individuals already in their talent pipelines as these individuals progress throughout their careers; otherwise, such talent tends to fall off the corporate ladder. Let this be a call for action to *Pharm Exec's* Pharma 50: Keep your pipeline diverse, foster inclusion, and make such efforts a business and strategic priority.

Taking these steps will help top pharma companies harness the benefits of diversity to enhance their business performance and capture the gains implied by the 2014 McKinsey study. Whatever they do, it may be some time before they are able to reach an equilibrium—one in which the recognition of diversity's importance is on a level with the actions being taken, and with the diversity—and true inclusion—that results. **PE**



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# Financial Outlook: Hazy

Do recent trends in the pharma and biotech M&A and equity markets signal a temporary lull — or a permanent drop?

By Peter Young

## FAST FOCUS

» Valuations of public pharma and biotech companies declined in the first quarter of 2016, with a major cause being the heavy backlash against the sectors, sparked by numerous negative reports about drug pricing that outraged public and political circles to the point where investors became concerned about regulatory changes that could harm the industry's growth and profit ability.

» The drop so far in 2016 in M&A volume market has been felt more by pharma than biotech. In the first quarter, only 10 pharma deals were completed, worth \$11 billion. During that same period, there were seven biotech deals completed, worth \$5 billion. However, there are pharma deals in the pipeline (as of March 31), 21 in all totaling \$91.4 billion. The biotech M&A backlog is very sparse, with three deals at \$700 million.

» Pharma stock market performance and valuations will remain steady for some time behind an continued influx of novel drugs to the market, but real strides will be hampered by the ongoing fallout from the negative drug pricing campaigns that have suppressed industry economics and investor opinions. On the biotech side, stock market performance and valuations may improve, but not to the exuberant levels experienced in recent years.

**T**he pharma and biotech industries are facing several structural factors specific to the sector itself, as well as external forces that are fostering uncertainty on overall global business and financial conditions. Political risks that could adversely impact investor perceptions about the viability of the industry's long-term investment cycle are becoming more prominent, especially as the US begins a crucial presidential election season. Both major political parties are in the unprecedented position of challenging the industry's historical business model based on the premise that high risk justifies high prices.

Valuations of pharma and biotech companies in the public and M&A markets soared up until August/September of last year because of positive industry developments, the search for high-growth potential products, and the restructuring activities of the industry. More recently there have been a number of setbacks in public trading valuations due

to the volatile equity markets and the negative publicity about drug pricing and other factors affecting the M&A markets.

The volume of M&A activity and IPOs has fallen dramatically in the first quarter of this year. This raises two critical strategic questions for the biopharma “C-suite:” What caused this fall in volume and valuations? Is the current trend temporary, or is it going to be around for the long-term—even a permanent aspect of the financial landscape in a maturing business?

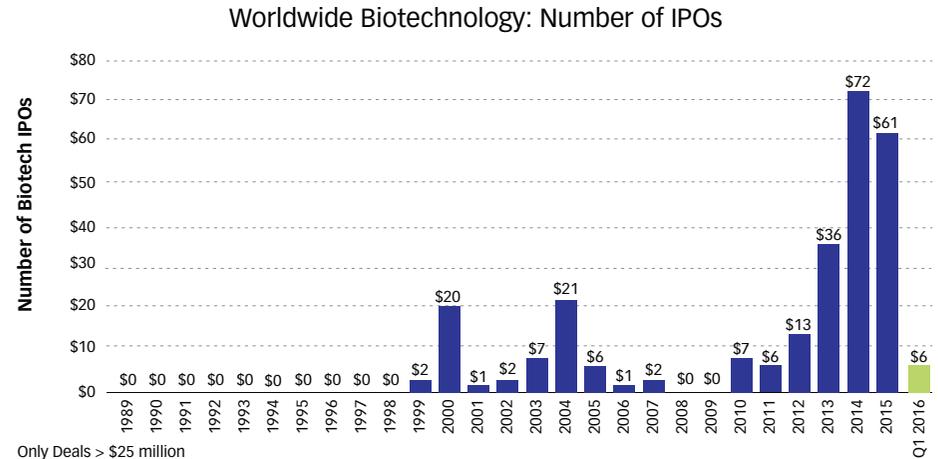
### The Stock Market and IPOs

The overall stock market fell significantly in January and February, but staged a vigorous recovery in March. As a result, the first quarter of 2016 saw the S&P 500 up 2.3% from the beginning of the year and the FTSE 100 increased by 1.3%.

Unfortunately, the pharma and biotech industries did not do as well.

During that period, the valuations of public U.S. Pharma declined slightly, but the European ethical pharma, generic, and specialty pharma companies declined more dramatically. During the first quarter, the Young & Partners (Y&P) US Pharma index decreased by 0.5%, the Y&P European Pharma decreased by 7.9%, the Y&P Specialty Pharma index decreased by 11.6%, and the Y&P Generic Pharma index decreased by 11.3%.

The biotech industry fared even worse. The Y&P Large Cap Biotech, Y&P Mid Cap Biotech, and Y&P Small Cap Biotech indices decreased by 13.3%, 22.4%, and 21.2%, respectively, far worse than what happened to any of the Y&P pharma indi-



• The number of IPOs surged starting in 2013 when the market fell in love with biotech companies, but volume started to fall in late 2015 and has fallen dramatically in the first quarter of this year.

ces. On the other hand, we are not even close to the trough levels from a number of years ago.

Very negative sentiment about the biotech and pharma industry was a major cause, as the media published numerous stories about drug pricing, to the point where investors became con-

cerned about government and regulatory changes that would harm the industry’s growth and profitability. This was accentuated by the traditional bashing that the drug industry tends to receive during presidential elections in the US, since the politicians find the pharma industry an easy target to blame for high healthcare costs.

On the equity financing side, secondary equity offerings and IPOs of biotech companies have been at all-time highs in recent years. Pharma secondary equity offerings have been steady and IPOs are much less common.

### The biotech industry had reached highs in the equity markets that many observers felt were excessive and hyped

cerned about government and regulatory changes that would harm the industry’s growth and profitability. This was accentuated by the traditional bashing that the drug industry tends to receive during presidential elections in the US, since the politicians find the pharma industry an easy target to blame for high healthcare costs.

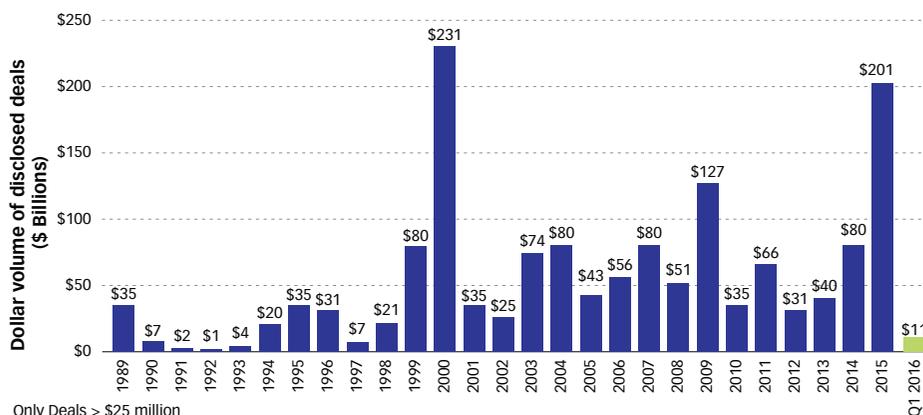
Of course, it is also true that the biotech industry had reached highs in the equity markets that many observers felt were excessive and hyped. This made the biotech fall even steeper than it otherwise would have been, hence the bigger drop in biotech

Pharma equity issuance in the first quarter of 2016 was \$5.3 billion versus \$32.7 billion for all of 2015, a significant decline on an annualized basis. There was only one pharmaceutical IPO in the first quarter of 2016—by Shield Therapeutics PLC, a specialty company based in the UK. It closed on Feb. 12 for \$47 million.

Biotech equity issuance in the first quarter of 2016 fell more dramatically, with only 31 equity offerings worth \$3.2 billion completed compared to 206 offerings worth \$20 billion during 2015.

In terms of IPOs, in the first quarter of 2016, only six biotech

Dollar Value of Worldwide Pharma Acquisitions



Only Deals > \$25 million

• The value of deals was low for most of the 1990s, escalated in 2000 and has been healthy but volatile since. 2015 was very strong due to several mega deals closing, anchored by the Allergan/Actavis deal. There was a dramatic fall in Q1 2016.

IPOs were completed that raised a total of only \$0.5 billion in new equity, well below 2015 levels when 61 biotech IPOs were completed totaling \$5 billion.

## The market will tend to favor certain areas of new development such as genome editing and immunotherapy

Hence, it is fair to conclude that the equity market has turned cold for pharma and even more so for biotech.

What factors will change the trajectory of the equity offering calendar and activity from the current subdued and selective market to a more robust one? First, the overall equity market will have to show a great deal of strength. There has already been a recovery of the overall equity markets that started in March and we expect that to continue. Second, the sentiment toward the biotech and pharma industries has to improve. We feel this will happen, but not until the US presidential elections are over, there is relief from the negative press about drug pricing, and certain industry structural challenges improve. It

may take more than a year or two before we see these sentiments turn around. Continuation of the current innovation renaissance, exemplified by a high volume of

FDA and European Medicines Agency (EMA) approvals, alone, will not be enough.

Meanwhile, good companies that have successful clinical trials and commercial successes will be able to go public or issue follow-on equity, but it will be selective and at valuations below the peak levels of 2014 and 2015. The market will also tend to favor certain areas of new development such as genome editing (CRISPR) and immunotherapy.

### The M&A market

The drop in the M&A market volume has been even more dramatic in pharma and less severe in biotech.

In the first quarter of 2016, only 10 pharma deals were completed, worth \$11 billion, versus

56 deals completed, worth \$200 billion, during all of 2015. From an annualized point of view, this represents an astonishing decrease in the dollars and the number of deals.

There was only one large deal completed, the \$5 billion acquisition of Dyax by Shire.

The backlog of transactions has also fallen dramatically.

As of March 31, the value of the pharma deals announced but not closed was \$91.4 billion (21 deals), so there are deals in the pipeline. Notable announced transactions include Teva's \$40.5 billion acquisition of Allergan's generics business, Shire's \$36 billion acquisition of Baxalta, and Mylan's \$10 billion acquisition of Meda.

But the pipeline fell from \$240.4 billion (16 deals) at the end of December, with the terminated Pfizer/Allergan deal constituting a large part of the drop. The high volume of pharma M&A in recent years has been driven by both strategic and financial factors. Drugmakers are acting as both buyers and sellers, forming strategic alliances, and swapping assets as well as they shore up their core businesses, exiting non-core units, buying to build or buying to cut costs, and using or seeking US tax inversion advantages. A few of these factors have weakened or are no longer viable practically.

Historically, biotech M&A activity has almost always been modest compared to the pharma industry, with small spurts of activity from time to time. In 2015, there were 31 biotech M&A deals completed, worth \$18.2 billion.

In the first quarter of 2016, there were seven biotech M&A deals completed, worth \$5 bil-



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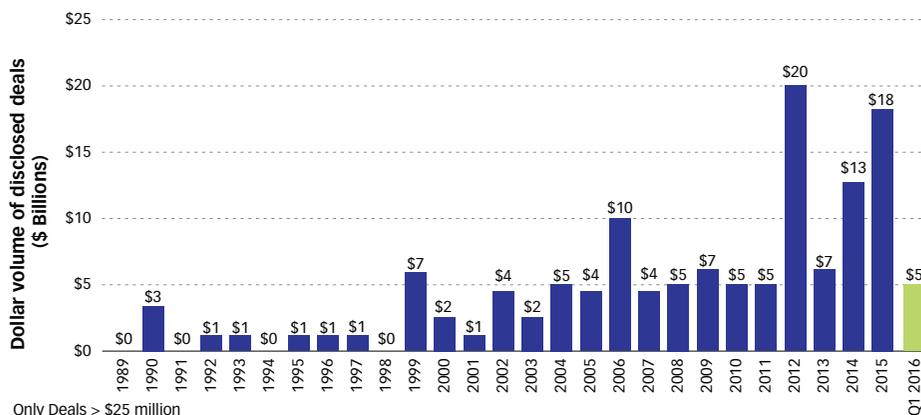
#### Key Take-Aways:

- Importance of MSLs in generating and communicating real-world data and insight
- Critical role of MSLs in liaising with physicians and KOLs
- How MSLs can help identify potential obstacles in pathway effectiveness
- Case study: The successful deployment of MSLs and the results achieved for a small biotech company

**For technical questions** about this webinar, please contact Daniel Graves at [daniel.graves@advanstar.com](mailto:daniel.graves@advanstar.com)

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### Dollar Value of Worldwide Biotechnology Acquisitions



• Since 1999, M&A activity has been fueled by pharma acquisitions of biotech companies and biotech consolidation. Dollar volume was high in 2012, 2014 and 2015 due to one large deal in each of those years.

lion. This represents an annualized pace that is slightly lower on a number-of-deals basis and slightly higher on a dollar basis.

But the biotech M&A backlog is very sparse. As of March 31, 2016, the value of deals announced but not closed was very modest at only \$0.7 billion on three deals.

**Expect the disappearance of a large portion of the pharma M&A market that was driven by tax-inversion and the strategy of buying companies and raising their product prices and/or cutting R&D**

What has caused the drop? In the case of pharma M&A, a large factor was the US Treasury rule changes that make tax-inversion deals (singular and serial) much more difficult to do. Although many feel that the recent tax rule changes were aimed squarely at the Pfizer/Allergan deal, the structural changes will affect a wide variety of attempts at tax-inversion transactions. In addition, the strategy that many organizations

have been using where they acquire companies, increase their product prices, and, in some cases, slash their R&D expenditures is now under attack as a result of the governmental scrutiny around drug pricing. Many of the larger deals have been based on one or more of these three strategies.

Valeant Pharmaceuticals is an example of a company that relied heavily on all three methods (tax inversions, price increases, and reductions in R&D) and is in serious trouble now as a result.

**What will the future bring? Pharma M&A and financing**

Y&P believes that the pharma industry stock market performance and valuations will be

steady at the current levels for some time, as the industry continues to show its ability to develop and commercialize new drugs. But real improvement in the outlook will be held back by the overhang from the negative drug pricing campaigns that will continue to suppress industry economics and investor opinions.

Equity financing has been less important for pharma companies, so the continued movement sideways at a lower level will not be damaging to their market positioning.

On the M&A front, expect the disappearance of a large portion of the pharma M&A market that was driven by tax inversion and the strategy of buying companies and raising their product prices and/or cutting R&D.

Fortunately, there is enough activity that is driven by restructuring of portfolios, additions of revenues and product lines, and geographic expansions to keep the overall M&A activity at a healthy, but less frothy level.

**What will the future bring? Biotech M&A and financing**

The biotech story will be a bit different. The biotech industry stock market performance and valuations may improve, but not to the exuberant levels that were experienced for the last couple of years. Some of the underlying reasons will be similar to the pharma industry—the overhang from the pricing problems and the negative publicity. But the biotech industry has hit a valuation bubble that will be harder to recreate in the next few years.

As explained earlier, the equity financing market will continue to be available for com-

panies that are showing good data and in areas that the market is excited about, but valuations will continue to be subdued relative to the previous peak valuations until the negative sentiment about the industry subsides. This could take one or more years or even longer to change.

On the M&A front, we expect the biotech M&A market to rebound to higher, but still traditionally modest levels. The biotech M&A market has been less driven by the tax-inversion phenomenon and more by the desire on the part of pharma and specialty pharma to acquire promising biotech drugs going through FDA approval. Partnering will continue to be a non-M&A alternative to achieve these goals, but

## The biotech M&A market has been less driven by the tax-inversion phenomenon and more by the desire on the part of pharma and specialty pharma to acquire promising biotech drugs going through FDA approval

the weak equity issuance market for biotech companies (including IPOs) will make it harder for these firms to raise cash with high valued public shares. This will drive many of them to sell themselves to big Pharma earlier than they would have during the last couple of years.

Y&P believes that the current stock market, equity financing, and M&A markets

are suppressed, but they will rebound, but not to the levels they were at last year and the year before. The entire sector depends heavily on reputational goodwill from key stakeholders, especially regulators and payers that hold the reins on granting market access to the numerous new products now coming out of industry labs. This is a historical reality that shows no signs of going away. **PE**

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# Science Meets Art

## Mapping the Topography of MS

A new educational and potential prognosis tool for the treatment of multiple sclerosis shows how an accessible, easy-to-see visualization of disease state can serve as the threshold for clinical insight—all geared to the individual patient

By *William Looney*

**W**hen strict scientific rigor is combined with the visual artistry of data display, something wonderful can occur in the all-too-human practice of medicine. Knowledge becomes accessible—and therefore, useful—in helping health-care professionals (HCPs) better understand and communicate the clinical manifestations of disease in the individual patient.

Examples of this synergy between art and medicine remain rare, however, which explains why a new collaboration between a prominent academic expert and a leading medical communications agency has attracted the attention of a diverse

array of stakeholders active in the study and treatment of multiple sclerosis (MS), a complex, unpredictable and debilitating neurological disorder affecting some 2.5 million patients worldwide.

The project—the “Topographical Model of Multiple Sclerosis” disease simulation app—scored its latest win on March 21, when an independent jury organized by the 4A’s, the top trade association representing the US ad agency business, bestowed its first Health and Wellness Partnering Award to the two collaborators, Dr. Stephen Krieger, assistant professor of neurology from the Icahn School of Medicine at Mount Sinai, and Harrison and Star, the New York-based global health-care medical communications agency. Christian Bauman, chief creative officer at Health4Brands,

and a member of the jury, told *Pharm Exec* “our recognition of this work demonstrates the appeal of simple visual metaphors that connect the patient directly to his or her condition. Healthcare is the last bastion in advertising where a quick, creative visualization of something inordinately complex carries the most meaning for busy clinicians and their patients.”

The “Topographical Model of MS” is based on research conducted by Krieger, an MS specialist and neurologist at Mount Sinai’s Corrine Dickinson Center for MS. Krieger, a protégé of Center Director Dr. Fred Lublin, who pioneered development of the four clinically accepted phenotypes used to characterize the course of MS in patients, has built on this important definitional work in MS to create a model that visualizes clinical course and disability accumulation in this highly individualized disease.

Krieger sees disease manifestation in individual patients as a continuum, a heterogeneous interplay between relapses and progression that contributes to a variable expression of symptoms and potential disability in MS. This can include motor and/or sensory symptoms, bowel and/or bladder dysfunction, cognitive impairment, fatigue, and depression. The manifestation of these symptoms varies from patient to patient and can be quite unpredictable.

### See to believe

According to Krieger, any help in identifying—and thus explaining to patients—the role of underlying lesion topography in the manifestation of symptoms is critical to explicating the

## Krieger sees disease manifestation in individual patients as a continuum, a heterogeneous interplay between relapses and progression that contributes to a variable expression of symptoms and potential disability in MS

disease course of MS in each patient. More broadly, it might guide future improvements in diagnostic accuracy across a spectrum of disease.

In an interview with *Pharm Exec*, Krieger said he hit upon the idea of a topographical tool to map this condition to address two challenges simultaneously. “One challenge in clinical practice is that it is difficult to predict the course of MS given the variability of disease factors in each individual patient. It’s an accepted fact that no two patients with MS are precisely alike, so part of the goal behind this tool was to depict disease course in an individualized way. This brought to mind that each patient has a unique underlying disease topography.”

“The second challenge,” Krieger continues, “is the difficulty that clinicians have in relating information about MS

disease course to their patients. How can we teach our patients to understand what they are undergoing on a day-to-day basis? Or what they can expect to see next?”

The key to offering more clarity, according to Krieger, is helping patients to understand why it is that some lesions, based on their location and severity, cause relapses and symptoms while others remain hidden, below the “clinical threshold.” Symptoms also manifest differently over the course of the disease. Some result from acute relapses caused by new inflammatory lesions; some occur due to a temporary worsening of symptoms, which can be brought on by stress, infection or fever; while other symptoms reemerge as the disease progresses and can persist as chronic disability. Krieger points out that “under-

### FAST FOCUS

» The Topographical Model of Multiple Sclerosis simulation app recently won the 4A’s first Health and Wellness Partnering Award. The tool is a result of a collaboration between Dr. Stephen Krieger, an MS specialist and neurologist, and global healthcare medical communications agency Harrison and Star.

» Krieger’s idea for the invention was sparked by the need to address two challenges simultaneously: the difficulty in predicting the course of MS given its variable disease factors in individual patients, and the difficulty that clinicians experience in relating information about MS disease course—what is does specifically on a daily basis—to their patients.

» Taking Krieger’s vision, Harrison and Star formed a team of medical writers, database experts, medical illustrators, 3D imagers, UX designers, and digital programmers to develop a prototype for the Topographical Model of MS app. It took nine months to complete. The tool provides a visualization of the clinical course of MS based on the topographical display of disease factors commonly experienced by the individual patient.



standing the differences in these clinical experiences can help with overall management of MS and to address patients' emotions, fear and uncertainty that pervades this condition."

Krieger knew instinctively that accomplishing these two goals depended on rendering information through some type of arresting visual that could capture the attention of patients and initiate an informative dialogue between patients and clinicians. An animated video was his initial thought, the outline of which he sketched out on notebook paper. In presentations to scientific audiences on his research, Krieger also began talking up the need to rethink how clinicians approach patients with MS, empowering them to better understand both the complexity of the disease and their individual goals of care. This, he said, was best advanced through a modeled "map" as a springboard to conversation, adjustable to the individual's disease topography at a given point in time.

### Seatmate summit

Like many collaborations, it was a chance encounter that ended up providing the lift to Krieger's scribbled sketch notes. Karin Cook, senior vice president and associate creative director for Harrison and Star, happened to find Krieger as her seatmate on a flight returning to New York from a medical meeting on MS in Kansas City. Harrison and Star served as the ongoing creative force behind Teva's top-selling brand, *Copaxone*, for 16 years. The two got to chatting and Krieger pulled out his sketchbook to describe the concept he was trying to animate.

Says Cook, "My immediate reaction was 'stop-listen-let's talk'—because visualizing complex scientific data is exactly what Harrison and Star does. So we agreed to meet again back in New York when he could look at some examples of our work."

That discussion quickly produced a consensus that a short video wouldn't be sufficient to achieve Krieger's goal of transforming the way clinicians and

patients talk about disease progression in MS. "Karin and the Harrison Star team convinced me that to change how patients view this disease we needed a highly interactive app with the capability to visually depict the damage from CNS lesions and relate that directly to the diversity of the disease process in individual patients," Krieger relates.

### Creative test of will

"At Harrison and Star, we saw this as a brain-twisting challenge that would test a lot of our assumptions about the best use of technology," says Cook. "We wanted to demonstrate that being able to actually interact with a disease could change people's understanding of it." In other words, doing good for the MS map was also good for keeping the agency's creative *bona fides* fresh.

To implement Krieger's vision, the agency put together an internal cross-functional team of medical writers specializing in MS, database experts, medical illustrators, 3D imagers, UX designers and digital programmers—all on a *pro bono* basis. Development of the prototype for the "Topographical Model of MS" disease simulation app took nine months to complete. As promised, the iPad app (see image above) presents a visualization of the clinical course of the disease based on the topographical display of disease factors commonly experienced by the individual patient.

### A pool and its peaks...

In Krieger's model, the CNS is depicted as a pool, with a shallow end and a deep end representing increasing functional

reserve and the water's surface denoting the clinical disease threshold. Using 3D imagery to represent key disease factors, the app can show the disease course in MS as having both effects from the base of the pool—with new inflammatory CNS lesions emerging as “peaks”—and also from the surface of the water as functional reserve in the CNS is lost and the clinical threshold declines.

Krieger has spent much of the past year presenting the Topographical Model at grand round talks and professional medical conferences, including an open poster session attended by nearly 500 neurologists at the April 2015 annual meeting of the American Academy of Neurology. The novel hypothesis at the core of this work, that progression recapitulates a patient's underlying disease topography, is the subject of ongoing academic research.

### ...Leads to more light

Notes Krieger, “The significant thing about the model is it renders the current clinical framework for MS in a sharper light, making it more applicable to the experiences of the individual patient. We are not making new claims about the biology of MS. What the model does is to show the heterogeneity of this disease—and how much of its propensity to cause disability is hidden from view.”

Krieger also cites the novelty of the app devised by the Harrison and Star team. “Using a gaming engine to drive a 3D visual depiction of a disease state as complex as MS was tremendously innovative,” he says. “To my knowledge, it had never

“More people in medicine today recognize the power of dynamic data visualization to help bridge the communication gap between patient and provider.”

— KARIN COOK

been done before in this format, as an educational tool for patients and professionals.”

The best models appear deceptively simple, even when depicting something extraordinarily complex. To achieve this balance, the team translated clinical data for a wide range of disease parameters into pixels and leveraged real-time simulation technology to allow users to vary the severity and rate of these metrics. The spirit of scientific inquiry inspired the team to imagine a future beyond the task before them. Says Cook, “We wanted the app to function for educational purposes as a dynamic visualization; but we also wanted to anticipate how the technology could potentially be used in the future—that someday, once empirically validated, this could be used as a prognostic tool.”

### Next steps—and a test run

Until then, a plan to run a demo version of the Model on the iTunes platform is in the works. According to Cook, reaction to the Model's test run has been solidly supportive. “I think more people in medicine today recognize the power of dynamic data visualization to help bridge the communication gap between patient and provider,” says Cook.

For the advertising community, her message is equally succinct. “As creatives, we hunger to solve big problems, and getting to use technology to advance scientific thinking has had an electrifying effect on what we know we are capable of doing,” she says. “Working with a creative agency that is steeped in the science behind the disease, inside and out, can really make a difference.”

To Krieger, however, challenges still await. “The science behind this model remains to be empirically validated and peer-reviewed in order for it to become a standard part of MS practice.”

Once that is done—no small feat in itself—the app can be made available to the MS community, empowering patients through a better understanding of their disease with the hope of supporting their treatment goals. But that's not all. “If the model's potential is fully realized, my hope is we can actually approach this disease in a way that has real implications for improvement in clinical trial design, recruitment and results,” Krieger predicts.

Time will tell. But thanks to this unique collaboration between a single committed researcher and an agency committed to creative innovation, the outcome is not going to depend on serendipity alone. 

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# Market Access in Europe: Building Health Equity Through Better Outcomes

A new industry working group explores alternative drug funding options in Europe—and asks key stakeholders in the region to join the discussion. With public financing for healthcare continuing to be a challenge, the time for a new approach to market access is not when, but now—and how

**T**here is a growing awareness within the European Union that healthcare systems are socioeconomically vulnerable. Many stakeholders recognize that far-reaching changes are required in order to ensure sustainable patient access to high quality healthcare in the future. Opinions differ, however, on how countries should address the economic pressure without limiting access to care.

Current approaches to managing healthcare budget constraints remain piecemeal, putting broad patient access to innovative treatments across Europe at risk. To optimize the quality of care as well as achieve cost efficiencies, the total healthcare value

chain across stakeholders should be addressed. The current focus on innovative treatments falls short. In addition, current efforts do not address the high variation of health outcomes among different healthcare providers within and across countries—a fact that is unknown to most patients.

In order to address the sustainability challenge and improve the quality of care, healthcare systems ought to shift their focus to patient-relevant outcomes that use existing resources more effectively, and explore alternative funding sources to alleviate the burden on publicly funded systems.

## Convening power

The Boston Consulting Group (BCG) Market Access Roundtable is a forum that brings together senior pharmaceutical leaders in market access and serves as a platform for interactive discussion on industry level topics.

In light of the ever more pressured healthcare systems in Europe, the Roundtable created a working group to explore and analyze financing of novel therapeutics in Europe beyond traditional approaches. This paper summarizes the outcome of the work conducted over the past year, and proposes two strategies designed to promote efficiencies through better outcomes and increase options for additional system-wide funding.

## Statement of problem

**European healthcare systems are increasingly unable to provide equal access to specialized care—yet there is still no broad discussion involving all stakeholders**

European healthcare systems are under pressure today and in the near future the situation is expected

## Working Group Members

*(And co-authors of this report)*

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\* The opinions expressed in this paper are solely those of the authors and do not represent the positions of the organizations they are a part of.

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##### **Casey McDonald**

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There is an abundance of data available which companies can leverage to support more precise asset valuations and more robust expectations about return on investment – but they rarely do. Overlaying technical probability of success in clinical development with market access drivers can help companies establish a more realistic picture of an asset's value.

This webinar will outline the factors driving asset valuation under different clinical program designs and will present strategies to optimize expected value of the compound/ indication.

#### Key Take-Aways:

- How to use insights from how competitors have performed in market access and pricing negotiations.
- Understand how asset valuations can support informed strategic decision-making and clinical program design.
- Learn from a case study presented by Grünenthal how early HTA insight can help improve knowledge of real product value and how this knowledge can be used to optimize the clinical development approach.

**For technical questions** about this webinar, please contact Daniel Graves at [daniel.graves@advanstar.com](mailto:daniel.graves@advanstar.com)

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to become even more challenging. Across the European Union (EU), factors such as an aging population and increased incidence of chronic diseases are stretching healthcare systems, requiring greater healthcare spending at a time when there is increasing economic pressure on public funding.

At the same time, advances in scientific and technological research are opening up new, promising treatments for previ-

ously deadly diseases manageable, prevented and cured some serious illnesses, and even eradicated some diseases outright.

Today, many so-called primary care diseases are well treated at reasonable costs. Similarly, increased diagnostic possibilities and new medical devices have expanded our diagnostic options and surgical interventions.

There is a growing sentiment that healthcare systems feel the impact of specialty care on their budgets already and are at the edge of their means

ously difficult to treat diseases, increasing the demand on already constrained healthcare budgets. As a consequence, European countries either have to spend an increasing share of their GDP on healthcare or limit access to some aspects of it to contain costs. As the sustainability of healthcare systems is contested, societies must contend with questions such as, “what level of healthcare access is appropriate/expected?” and “how should healthcare be financed?” Yet despite growing concerns, the lack of a broad discussion involving all stakeholders is painfully apparent.

**While a funding gap could be detrimental to all aspects of healthcare delivery, access to new, innovative, and specialized care seems to be particularly at risk**

Scientific progress over the past several decades has made many

Currently the biggest unmet medical need is for care for complex specialty diseases such as cancer, Alzheimer’s disease, and immunological disorders. In response to this, over the last few years, the biopharmaceutical industry has shifted its research efforts to developing new treatments for specialty diseases. In 2014, almost 50% of newly FDA-approved drugs were specialty drugs, whereas 10 years ago this was below 30%.

At the same time, as scientific focus shifts toward developing new, innovative medicines to treat the highest unmet medical need, payers and systems increasingly find themselves unable to appropriately fund specialty care treatments due to the fragmentation of drug budgets and constraints on total healthcare budgets. As a consequence, healthcare systems have focused efforts to

control spending on medicines, as drug budgets are easily targeted. These efforts clearly cast doubts on healthcare systems’ ability to maintain and expand access to new, innovative treatments in the future.

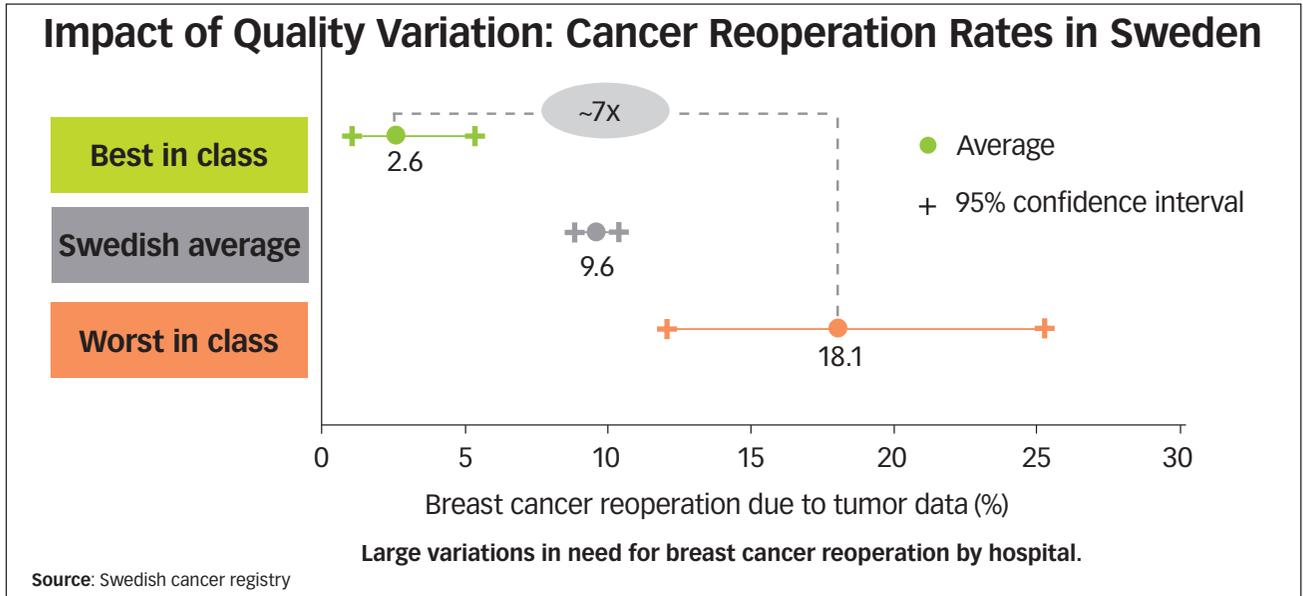
There is a growing sentiment that healthcare systems feel the impact of specialty care on their budgets already and are at the edge of their means. Inevitably, payers will put more emphasis on cost containment in previously less scrutinized areas such as cancer care, and, therefore, limit the expansion of patient access to life-saving specialty treatments.

## Two overarching observations

### 1.) **Current approaches to containing costs remain piecemeal and siloed—and result in unintended unequal access to medicines across Europe**

Unable to sustain increasing healthcare expenses given increasing public budget constraints, most countries in Europe have deployed measures to limit healthcare expenditure growth. Since 2003, there has been continued pressure on healthcare spend, but it has accelerated in the years following the financial crisis. Total healthcare spending growth in EU was reduced from 7% in 2003 to 2008 to 3% in 2008 to 2012.

Enacted initiatives remain piecemeal and often only look at particular parts of the healthcare budget, failing to address the issue in a comprehensive manner. Expenditures on prescribed medicines have garnered the most attention,



despite accounting for only about 13% of total healthcare spend. Inpatient/outpatient care provision accounts for a majority of total healthcare spending.

In the area of health technology assessment (HTA), despite widely agreed-upon definitions of “health technologies” that include medicines, diagnostics, devices, and medical procedures, the vast majority of HTA agencies focus largely on medicines and not other significant areas of healthcare spending. As a consequence, investment in medicines shrank by about 2% while overall healthcare expenditures grew by about 3% from 2010 to 2012 across most markets in Europe.

Varied implementation of efforts to contain healthcare costs, for example, delaying access through a later launch, usage limitations through reimbursement decisions, or spending caps, led to wide inconsistencies in access to medicine. Not surprisingly, the cost of reduced access is disproportionately affecting those least able to pay.

Looking at population size-controlled volume consumption of innovative medicines across Europe, we observe a thirtyfold difference between the countries with the lowest and the highest consumption of innovative anti-diabetics in 2012. Volume usage patterns broadly follow the GDP/capita distribution, with Luxembourg using most and Bulgaria least.

Even today, patients in Europe have very differing health prospects depending on in which country they fall ill, which puts in question the very idea of a pan-European equity in healthcare.

**2.) Patients are not guaranteed the best available treatment**

Health outcomes for the same condition or treatment can vary dramatically between countries and even within countries across different providers. Patients, and more strikingly, health systems officials, seem unaware that the choice of healthcare provider can have a dramatic impact on health outcome.

Data from the Swedish cancer registry reveals that breast cancer patients are up to seven times more likely to require reoperation depending on in which hospital they are treated. Looking only at university hospitals, the difference between best and worst in class is still more than threefold (see chart above).

Such outcome variation is common across Europe. For example, in the UK, patients receiving primary hip replacement surgery in the lowest-ranking hospital are six times more likely to require emergency readmission within 28 days than patients receiving care in highest ranking one.

Such vast variation suggests that pockets of care-providers have developed superior treatment standards, and thus deliver better outcomes while others fail to provide their patients with the best possible care. Contrary to popular belief, better outcomes don't have to come at an increased cost. As providers look to deliver holistic care that focuses on improving outcomes, costs to the healthcare system

can also be reduced. One example is the tracking of cataract outcomes and identification of best practices in Sweden by a national registry that improved postoperative endophthalmitis rates by 80% while reducing costs by 1%. In Germany, “Gesundes Kinzigtal” tracked

approach to sustainable access to specialty healthcare in the future.

Broadly, there are two approaches to ensuring healthcare systems are able to maintain and expand access to specialized, innovative healthcare in the future:

## Continuing the piecemeal approach to a large problem is failing all stakeholders: patients, providers, payers and pharmaceutical companies

outcomes and optimized care for chronic patients with a focus on prevention and wellness. This reduced mortality rates by 53% and resulted in a saving of €151 per patient.

### Rethink financing of specialty care

The discussion on how we, as society, ensure the continuous provision and expansion of access to specialized care is a pressing one. Current cost and funding outlooks paint an unsustainable picture for the future, and in many European countries the funding and access situation is bleak. Clearly, current approaches to cost containment have not been successful.

Continuing the piecemeal approach to a large problem is failing all stakeholders: patients, providers, payers, and pharmaceutical companies. A broad debate on what level of healthcare access is appropriate or expected and how such healthcare should be financed is required to foster a holistic

» **Better utilization of existing resources**

» **Enabling additional funding/payment options**

Better utilization of existing resources targets unnecessary or ineffective healthcare spending. An estimated 30% of total healthcare spending in the US is unnecessary. This share may be lower in Europe, yet it is still far too large to be ignored. Putting resources to better use could limit or even prevent the growth of healthcare costs for many years.

But even with better utilization of current funding, maintaining and expanding the quality of and access to healthcare might not be possible everywhere in the EU. As public funding pools are already limited, it would be wise to explore whether additional funding from non-traditional (such as non-public) funding pools could help relieve the pressure on public healthcare systems.

It is widely acknowledged in academia that given the large differences in national healthcare systems in the EU and the

current funding levels and sources, there is no silver bullet for European healthcare. This white paper attempts to lay out different options to improve the utilization of existing resources, and proposes alternative funding options which could support and supplement public funding more effectively.

## Our two proposals

### 1. **Better utilization of existing resources**

Current levels of healthcare funding could go further if resources were used more effectively. The European Commission writes, “Efficiency gains could translate into a 0.5% reduction in the annual growth rate of public health expenditure, eventually halting the increase in the public healthcare expenditure-to-GDP ratio in the EU over the long-term.” The World Health Organization (WHO) already in 2010 pointed out that “At a conservative estimate, 20–40% of health resources are wasted.”

Ineffective use of resources has many causes. Key among them are unnecessary or ineffective tests, lack of appropriate early diagnosis and intervention, and dysfunctional patient pathways, including treatments either driven by “defensive medicine” or by misaligned incentives of the reimbursement system. To address suboptimal use of medicines, healthcare payers are starting to implement measures to drive down the inefficiency in the prescribing and use of medicines. In Italy, for example, the payer reimburses the cost of certain cancer drugs after response is

ascertained by the physician and documented by means of a therapy registry.

Many pharmaceutical companies are open to contributing to better use of medicines through so-called pay-for-performance reimbursement schemes. Under such reimbursement agreements, the payer only pays for the medicine if it provided a substantial, pre-defined patient outcome. The healthcare system thus only bears the cost for positive outcomes. Key to establishing pay-for-performance systems are outcomes registries to track how patients respond to certain treatment options. Unfortunately, only certain diseases in a few European countries are tracked to date.

The key to any approach to better utilizing existing funds is a focus on outcomes to define the optimal use. Luxembourg, for example, is now asking whether the assessment of the performance of health systems should focus on the effectiveness of healthcare (specifically outcomes), as a main contributor to healthcare quality and better health of the population.

A focus on outcomes ensures that healthcare systems as a whole focus resources on the most important goal: to improve patients' health. At the same time, a focus on outcomes can also reduce costs. We believe that if patient-relevant outcomes are measured in a transparent and standardized way, a focus on outcomes could push all healthcare providers to provide care equal to best-in-class in the most cost-effective way.

In 2005, Sweden began to collect data on whether hospitals were adopting best practice when treating acute coronary

syndrome. Data showed that a 13% improvement year-on-year was being achieved. When the findings were made public, and individual hospitals named, the year-on-year improvement jumped to 22%. Furthermore, in the U.S., a registry was created to track outcomes and best practice implementation of cardiac care. The end result was a 73% reduction in the risk of dying from a cardiac-related cause.

As these examples illustrate, there is great value in measuring and reporting outcomes across healthcare providers, treatments, and medicine in a standardized and transparent way. Making outcomes data publicly available would lead to a healthy competition for patients. Patients selecting the provider with the best track record would reward the best providers with higher volumes, which in turn drive down the costs. The Martini Klinik in Hamburg, Germany, became the largest prostate cancer center in Europe through better patient-relevant outcomes, and can now offer lower-cost treatments.

Further, an outcomes focus enables providers to learn from each other and drive lower-performing providers to adopt better practices and standards. An outcomes focus can thus improve equity, quality, and cost of care across all providers and treatments if implemented across the healthcare value chain.

Given the broad benefits, the Luxembourg Presidency of the Council of Europe (2015) proposes to pursue the discussion by stressing access and outcomes. However, in some European countries, better utilization of existing resources may

not be enough, as current total public healthcare spending does not provide adequate access. Additional funding options have to be explored in order to safeguard patient gains and maintain access to innovative treatment options across Europe. Outcomes tracking and optimization can build the foundation for alternative, additional funding options.

## **2. Enabling additional funding options**

A system-wide focus on transparency of outcomes could also open the door to more targeted, non-traditional funding mechanisms. Focusing on outcomes provides a clear value-for-money picture of alternative funding options. All approaches to healthcare funding in the future would require an understanding and demonstration of the return on investment, in this case, the health outcome. Only when the healthcare system can clearly articulate what works will we be able to attract other, supplementary funding for certain aspects of care provision. In turn, alternative funding sources are likely to require the entire healthcare value chain to track and optimize outcomes to deliver a value-for-money promise.

Given the different healthcare and healthcare funding systems, disease types, and treatment options, a range of potential non-traditional funding options is feasible. We acknowledge that many of these non-traditional funding mechanisms are already in place across the EU in pockets (out-of-pocket, private insurance, pay-for-outcomes). *However a public debate on the role they*

could play in the future is missing. We also recognize that not all options are viable in all markets, but in the spirit of initiating a debate, we take a holistic approach without focusing on any given EU healthcare system. We have proposed a range of potential solutions that could enable additional investment in healthcare and help fund future innovation. We are not suggesting that any one solution could work in isolation or for all European countries. Most likely, a combination of these potential solutions will be required across Europe, depending on the current makeup of a country's healthcare funding levels and systems.

#### OUT-OF-POCKET/CO-PAYMENT

Perhaps the simplest form of expanding private support for healthcare expenses could be

through expansion of out-of-pocket or co-payments. Historically, out-of-pocket payments have been used mostly as a tool to control the overuse of medicines and healthcare services. Through such out-of-pocket payments, payers encouraged spending limits by asking patients to pay a share of the costs. However, an extension of out-of-pocket contributions could also have a more direct effect by supporting healthcare funding.

One option could be to invite a greater share of private funding to cover primary disease treatment, and as a consequence, public funds would provide broad access to life-saving critical care and innovative specialty products. Medicines for primary diseases would be most suitable for higher out-of-pocket/co-payments given the

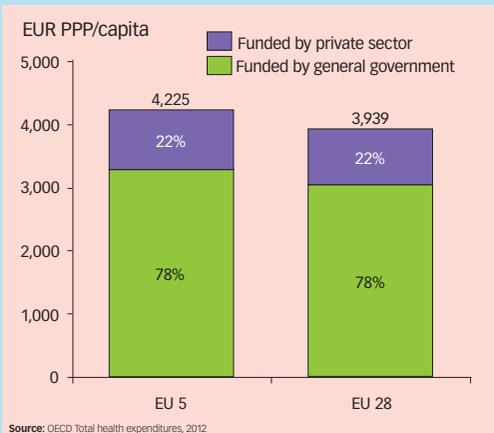
lower price range and often more elective usage pattern. The cost burden for primary care patients would certainly increase, yet patients would receive better access to potentially life-saving treatments should they need them. Maximum absolute co-payments would certainly have to differ per country due to different GDP- and income-levels.

An increase in out-of-pocket and co-payments could be funded by the patient directly, covered by new private insurance policies targeted towards these expenses, or by employer coverage. All these options require individuals and patients to make decisions about their healthcare options, therefore they need to be well informed about the benefits and risks of all the treatment options at hand. Today, patients are often

## Public Healthcare? Europe's Multi-tier Models

While the majority of funding for European healthcare systems stems from public sources, one in every five Euros spent on healthcare in the EU comes from a private source, according to the latest OECD health statistics.

### Funding Glance



There are two broad types of European healthcare systems—tax-funded systems (Scandinavian countries and the UK) and social insurance models (Germany and France). In both systems, private funding plays a considerable role.

European healthcare systems on average receive 22% of their funding from private sources. In countries with lower GDP per capita levels, the private funding is often driven by the countries' inability (and/or unwillingness) to provide adequate public healthcare for their citizens. Individuals are forced to pay a high share of their healthcare expenses out of pocket; so people unable to cover treatment costs do not receive the care they need. In stronger economies, however, the private funding share is also driven by individuals who seek better or faster care through private insurance or private care options. It seems healthcare stakeholders have quietly embraced co-funding of the increasing healthcare expenditures, while political debate largely ignores the issue of private funding.

Private funding contribution is not a new phenomenon; over the past decade, private funding levels remained mostly constant. In 2003, the share of private funding in EU5 was already at 31%.

not fully aware of new treatment options and the benefits of innovative treatments or how much treatments and doctor visits cost.

A higher share of out-of-pocket funding could in turn trigger a broader focus on outcomes, as patients who co- or self-fund treatments will carefully examine which treatments they are willing to invest in. Scrutinizing the perceived cost/benefit ratio of treatments from the patient perspective immediately forces healthcare providers to focus on the most effective use of resources and could trigger additional pressure to move towards an outcomes-focused healthcare system.

#### **PRIVATE MEDICAL INSURANCE**

Private medical insurance to either supplement or replace public healthcare coverage is available in many European countries. In France, 95% of the population bought supplementary (or top-up) insurance to receive additional or better care, and in Germany 11% of people opt out of the public system and buy private insurance instead, while another estimated 22% complement their statutory health insurance with private insurance. As their presence grows, private insurance models are increasingly being debated. Given the history of public healthcare in Europe, private insurance models are often still viewed negatively, for fear of them paving the way to a “two-class” healthcare system. Yet despite often being cited as a challenge to equality in healthcare, individuals are open to funding a share of their health expenses privately in order to receive additional, faster, and/or better care.

Private insurance could come in different forms. Supplementary

insurance would ensure additional services or faster access above and beyond the care provided by the public system. Alternatively, individuals could opt out of the public system and seek only private insurance (potentially with a government subsidy—as these people are no longer a cost item to the public system). Finally, private insurance could cover specific services or treatments such as rehabilitation.

The common benefit of all insurance options is that they provide some relief to the public system and thereby help ensure that public systems can provide and expand access to adequate healthcare to its citizens. Higher private insurance levels would help ensure that all patients receive the best care possible for life-threatening accidents and illnesses. Key to a broader engagement with private insurance is that patients and lawmakers understand how private insurance models could be part of the solution.

Similar to out-of-pocket payments, increasing the role of private insurers will trigger a broader emphasis on outcomes and optimal utilization of resources across the healthcare value chain. Opening up options for private insurance thus not only helps increase the total investment in innovation, it also helps reduce the total costs of the public healthcare system.

#### **EMPLOYER-SUPPORTED HEALTHCARE MODELS**

Better access to innovative healthcare not only benefits each individual, employers also stand to gain from a healthier workforce. Healthier employees are more productive, as many studies have highlighted. And while high quality preventive care can help employees avoid sick leave in the

first place, the possibility of early detection of diseases can also do away with the necessity for invasive treatments which require employees to take longer leaves. For employees who suffer from diseases that cannot be prevented at an early stage, innovative therapies can shorten the time an employee spends in treatment, away from the workplace.

As employers clearly benefit from expanded access to healthcare, it is not unreasonable to require greater support in the form of funding. In addition to helping mitigate the sustainability issue, making employers part of the solution would have positive secondary effects. For one, employers would have an even greater incentive to focus on preventing ailments in their workforce. In many cases, prevention is cheaper than treatment. Secondly, it would involve employers more in establishing healthier workplaces and promoting a healthier lifestyle.

Deeper employer support for public healthcare systems could take several forms. Governments could mandate that employers above a certain size provide supplementary health insurance to their employees. Such an approach could lead to employers buying supplementary insurance coverage from private insurance providers (similar to the US model). Employers are able to bundle the coverage of many individuals, thus negotiating better rates than individuals can. This also plays a role in reducing overall healthcare costs. Another option would be to require a contribution from employers directly with the proceeds supporting the funding of the public healthcare system.

## These are initial thoughts on what new payment models could look like. A more detailed debate with all relevant stakeholders at the table is required to define and test new models

### NEW PAYMENT MODELS

Even with additional funding models in place, curative medicines and gene therapies will continue to pose challenges for payers. Curative medicines, as the name suggests, cure diseases, while gene therapies treat disorders by replacing, inactivating, or introducing genes with a single injection. Next to the obvious health benefit for the patient, such medicines and therapies relieve the healthcare system of all future costs it would have faced over the period of the disease or the lifetime of the patient (for example, ongoing treatment, hospitalization, and/or future surgery). Providing such curative care to all eligible patients quickly goes beyond predefined healthcare budgets, as we have witnessed in many countries where access to new hepatitis C virus (HCV) drugs has already been achieved.

To find new solutions to fund such treatments we have to look at healthcare not as an expense, but as an investment. Investments (for example, buying a house) carry a high upfront payment, but the benefits are enjoyed throughout the asset's lifetime. Curative medicines also require an initial investment and provide a continuous benefit thereafter. An investment is often co-funded by third parties who provide debt. Similarly, one could explore whether a third party could provide debt to finance the initial investment which the payer could then amortize over a period of time and thus

staggering the cost of one time investment (for example, gene therapy, HCV clearance) over several years of benefit.

Alternatively, health savings accounts could enable patients to save a portion of the funds required to cover future healthcare investments. In such a model, individuals could pay into a specialized health savings account and accrue the funding for future treatments. Of course, many individuals may not be able to save enough to cover larger surgeries or cancer treatment if they are needed within a few years. Therefore, such health savings accounts would also aim to cover common/primary care diseases, while the public system covers the more cost-intensive surgeries and specialty care.

Similar to expensive one-time curative treatments, the treatment of lifelong chronic diseases increasingly poses financial burdens on Europe's healthcare systems. Thanks to medical and technological advancement, more and more previously fatal diseases can be managed as chronic diseases.

These are initial thoughts on what new payment models could look like. Clearly a more detailed debate with all relevant stakeholders at the table is required to define and test new models.

It is, therefore, not a question of either better utilization of existing resources or looking for alternative funding options. Both approaches are required, given the different starting positions and

intricacies of healthcare systems in Europe today and given that they reinforce each other. A focus on outcomes to better utilize existing resources builds the foundation for alternative funding sources to participate in funding healthcare. In turn, private funding sources only invest in treatments with positive outcomes, which forces healthcare systems to track outcomes very closely.

### Initiating debate: The time is now

The current situation of healthcare funding in Europe is not sustainable. An aging population, the increase in chronic disease, and the development of new, specialty treatments, all add to an already stretched public healthcare budget. At the same time, current efforts to contain costs are piecemeal and siloed, focusing on single elements of the overall value chain rather than taking a holistic view.

A shift to outcomes-focused healthcare, where all stakeholders focus on improving outcomes, can result in better care for patients and better utilization of existing resources. In addition, the need to explore alternative funding options is also becoming evident.

While we acknowledge that current healthcare systems across Europe all have different starting positions and face different challenges, and that no single solution is universally applicable, we do believe that European societies need to begin a discussion on healthcare financing now. Any change in financing healthcare will require considerable time—decades rather than years—and strong political/societal willingness for change. **PE**

# A Digital Prescription for the Pharma Industry

How companies can better integrate valuable data across business functions to meet rising value-chain demands

In two years, 93% of US doctors will be using electronic medical records—up from 30% two years ago—and 97% will have electronic access to treatment protocols, more than double the rate in 2011, according to Bain research (see chart below). Most US healthcare providers and payers also will go digital over the next five years.

That profound shift (among others) has pharmaceutical companies pouring money into digital tools and initiatives to keep pace, but a lot of those investments are wasted. Why? The initiatives are scattered and unfocused. At one global pharma company, we found more than 200 digital projects and 2,000 related websites, many of which lacked the necessary coordination. The leadership team had no overview of the various activities and, as a result, derived little benefit from them.

In order to make digital tools pay off across a complex value chain, pharma companies have to do a much better job linking data, analytics, workflow, and connectivity. The real value comes from integrating internal data smoothly across business functions and with external data systems. A handful of digital forerunners lead the way, developing integrated strategies, making smart use of real-world data, and investing in a great digital customer experience.

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## Big data's 'real' deal

Let's look at how that kind of approach works with real-world data. Increasingly, real-world data is disrupting the traditional approach to medical reimbursement as payers demand evidence of efficacy beyond the lab. In the future, only companies that use real-world data to demonstrate superior outcomes for new drugs will generate attractive returns.

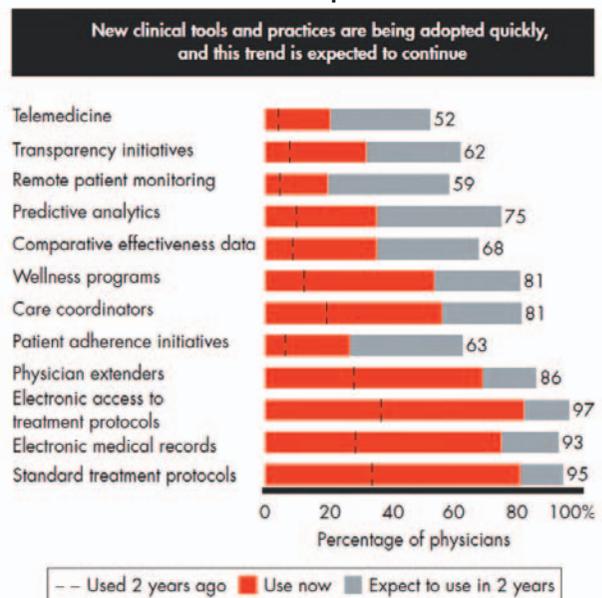
Big Data analytics, for example, helps pharma companies to harness real-world data to accelerate drug discovery while also providing valuable health economics and outcomes data for access, pricing, and safety. Bayer invested in generating real-world data for its anticoagulant *Xarelto* to

address concerns about bleeding as a side effect. It used data from existing disease registries and funded new studies. The real-world trial of 6,784 patients showed 96 out of 100 subjects did not experience any major bleeding or related side effects, which helped convince payers to reimburse patients and accelerated the drug's acceptance in the market.

Most pharma companies lack the real-world data to benefit from analytics, modeling and simulation. Without it, all research trends look equally interesting. Combined with the right tools, however, data becomes a torch in the darkness. The companies that are working on harnessing real-world data on a large scale are poised to reap big gains. According to a recent forecast by IMS Health, the top 10 pharma companies could each unlock up to \$1 billion in value by tapping into real-world data.

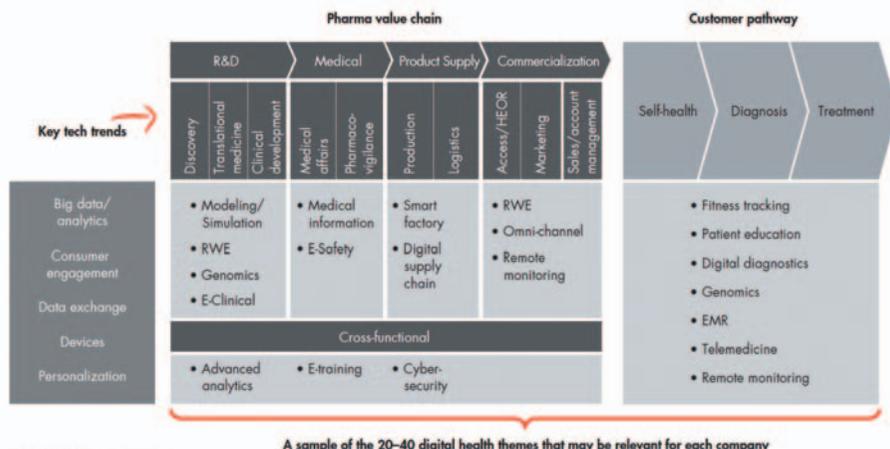
But even the biggest players will need strategic partnerships to obtain it. Clinical trials represent

## Growth Spurt



Source: Bain Front Line of Healthcare Survey, January 2015

## Dissecting the Digital Journey



Note: RWE=real-world evidence  
Source: Bain analysis

only a sliver of the world's health-care data. As the industry and governments adopt data tools such as electronic medical records and patient reporting platforms, they will increasingly partner to create rich troves of real-world data.

time online for professional reasons than with pharma sales representatives. As payers and providers increasingly seek medical information online and embrace outcomes-driven healthcare, digital forerunners are participating

Without real-world data, all research trends look equally interesting. Combined with the right tools, however, data becomes a torch in the darkness

To harness real-world data, forerunners invest in comprehensive digital platforms that integrate internal data with external data systems, linking, for example, regulatory affairs, clinical research, and marketing. These platforms include the capability to semantically normalize and clean data from vastly disparate sources that are intended for widely varying uses.

### The experience effect

In addition to implementing advanced data platforms, successful companies get closer to customers, patients, and other stakeholders by offering them a positive digital experience. Bain research shows physicians already spend significantly more

in these new models of clinical decision making.

The leaders use an omnichannel approach and personalized marketing to build a digital customer experience and increase their reach while significantly raising return on marketing and sales investments. Cost-effective technology tools help companies move from a siloed view to an integrated view of customers, ensuring messages are consistent and aligned as communication channels proliferate.

Merck & Co. embraced a new multichannel approach to launch *Januvia*, a drug for type 2 diabetes, making extensive use of the Internet and other new media for prelaunch education, as well as targeted communication to doc-

tors through representatives and online physician marketing, promotion, and communication. That strategy helped *Januvia* rack up sales of more than \$750 million in its first year and hit blockbuster status one year later.

Personalized marketing harnesses digital connectivity and data to address the individual consumer directly in real time with offers that are based on individual behavior and preferences such as over-the-counter treatments for sports enthusiasts or pregnant women. Pfizer offers a free mobile app called Pfizer CVM to increase awareness of cardiovascular problems such as blood pressure, diabetes, and cholesterol.

Real-world data and digital customer experience are two fields where digital forerunners are making great strides. But a digital strategy can affect the entire value chain. Improved transparency with customers and suppliers, for example, can help companies minimize working capital and improve forecasts. One helpful way to think about digital options is to break them into a manageable number of thematic clusters. These clusters become a useful roadmap of digital opportunities, helping leadership teams focus on the areas most important to them (see chart above).

### Set priorities

There is no right answer about where to start the digital journey. What's important is choosing a few high-priority areas that represent the greatest return for the lowest cost, risk, and investment of time, based on a company's strategy. Leadership teams that set clear priorities now will be able to cut through the digital noise and develop competitive advantage in a changing landscape. <sup>PE</sup>

A close-up, profile view of a man's ear on the left and a woman's nose and mouth on the right, set against a light blue background. The man's ear is in sharp focus, while the woman's features are slightly out of focus.

**IN OGNI  
CURA,  
IL FARMACO  
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L'INIZIO.  
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**CON L'ASCOLTO E LA CONDIVISIONE  
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# ITALY

## *A tradition of resilience*

### Part I

Amongst the myriad of globally recognized luxury brands promulgated by the Italian fashion and automotive industries, another sector flourishes beneath the public's radar. True to form as a national champion, Italy's pharmaceutical industry punches above its weight in many regards and has supported the national economy through many a period of weakness. Following the period of volatility brought on by the 2008 financial crisis, Italy entered a recession during 2011, seeing the economy contract 4.9 percent from the beginning of 2012 to the end of 2014. Meanwhile, Italy's pharmaceutical production increased by 38 percent from 2009 to 2014, driven by a 71 percent increase in pharmaceutical exports, reaching EUR 20 (USD 26.6) billion in exports and EUR 29 (USD 38.5) billion in total production.

This sponsored supplement was produced by Focus Reports.

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As such, “commentaries over the last one-and-a-half years in the nation’s newspapers, economic studies and official central bank reports all attribute the return to growth this year to two core economic sectors,” according to Massimo Scaccabarozzi, president of the pharma industry association Farindustria; “the automotive and pharmaceutical industries.” Commensurate with its role in helping the Italian economy return to growth in 2015, Scaccabarozzi explains that the Italian pharma industry is “second in the ranking for industrial production [of pharmaceuticals] in Europe after Germany, but number one when ranked by [pharma] production per capita.”

This path to the success that the industry is currently experiencing began long before 2009. “The global pharmaceutical industry was born in Italy,” affirms Aldo Braca, president and CEO of the internationally



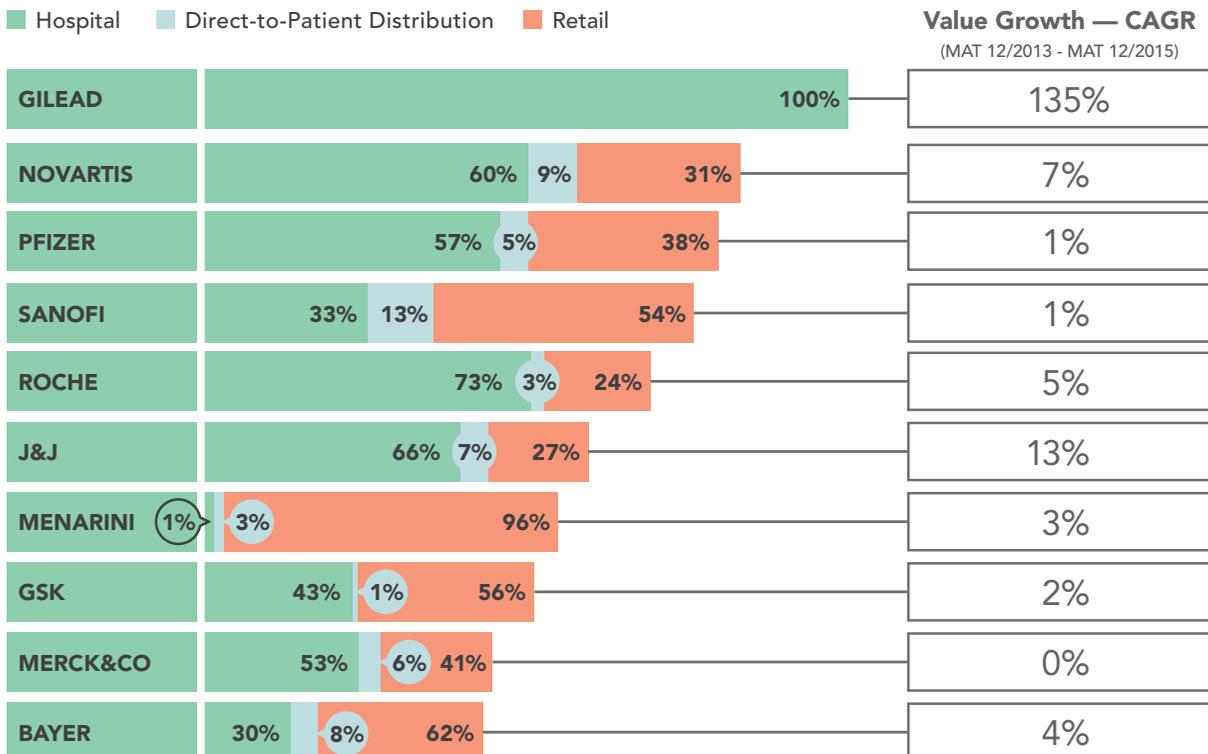
**Beatrice Lorenzin, minister of health;**  
**Luca Pani, general director, AIFA**

renowned oncology CDMO, BSP. “Farmitalia Carlo Erba and Lepetit were among the first pioneering companies about eighty years ago. Unfortunately, they did not receive much backing from the government, so were never able to flourish to their full potential. Nonetheless, these two entities planted the initial seeds for many Italian firms to develop into what they are today. Looking at the history of large-scale global players, such as Pfizer and Roche, many have been linked, in some way or another,

to these two foundational Italian companies.”

Owing to this remarkable heritage, Italy possesses a wealth of experience in pharmaceutical production, a strong culture of excellence in the field, and a robust manufacturing base that has enabled the industry to capitalize on significant growth opportunities in the past seven years. As Minister of Health Beatrice Lorenzin states, “healthcare represents 12 percent of our GDP and we are the second European hub, behind Germany, in both the pharmaceutical and medical device sectors. We could easily become the first, beating the Germans.” Nevertheless, the Italian industry’s current position might just as easily be lost; as the opportunities fueling this current boom may be transient. These opportunities stem from an indefinite shift in global demand away from low-cost

**INNOVATION IS DEFINING LEADERSHIP OF THE SECTOR**



Source: IMS Health IMFMFODPC.

pharmaceutical products and from APIs originating in emerging markets like India and China towards higher quality European sources. At the same time, Italian manufacturers face a reasonable cost profile relative to German, French, and British companies; in part due to the weaker macroeconomic context.

However, without a flagship global player to lead the Italian pharmaceutical industry, the backbone of the industry today remains small to medium sized, often still family-owned, companies. Osvaldo Ponchiroli, CEO of OP Pharma, confirms that, “it is true that there are a number of well-known Italian companies, which are family-owned, that have attained massive success.” He attributes this to “in-depth, insider knowledge, accumulated over decades and combined with a strong ingrained aptitude for strategic long-term vision.”

## AN UNSUSTAINABLE STORY

Analogous to other EU states, the Italian government is deeply concerned about the long-term sustainability of healthcare spending and maintaining universal healthcare coverage; “hospital pharmaceutical spending is EUR 1.8 (USD 2.0) billion out of control” warns Minister of Health Beatrice Lorenzin. This number may rise due to the large number of high-cost innovative therapies that have recently or will soon be coming to market and the country’s ageing population. 21.25 percent of Italians were over the age of 65 in 2014, behind only Japan and Germany.

Yet, thus far, the Italian government has been highly successful at managing costs, with public healthcare spending accounting for 7.1 percent of GDP versus the 7.9 percent average of the ‘Big Five’ EU



Walter Ricciardi, president, ISS;  
Massimo Scaccabarozzi, president,  
Farmindustria

countries, and pharmaceutical expenditures as a proportion of GDP roughly 30 percent below those of France and Germany according to Farmindustria. Bloomberg rated the Italian healthcare system the third most efficient in the world in 2014 with an ‘efficiency score’ of 76.3; Singapore scored 78.6, while France was in eighth as the next most efficient European country, with 64.6.

As such, Massimo Scaccabarozzi, president of Farmindustria, has been working to communicate that “if



Cody and Kolten, living with Gaucher disease

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you add up what [the pharmaceutical industry] gives back in terms of investments, R&D, salaries, and taxes you get to EUR 13 (USD 14.4) billion,” which is quite comparable to the country’s EUR 15 (USD 16.6) billion RX market, which has contracted significantly from a peak of EUR 17.2 (USD 22.8) billion in 2010 (IMS data). Prices have similarly fallen, with an average pack costing EUR 9.6 (USD 10.7) in 2015 versus EUR 11.4 (USD 15.1) in 2010. Given



**Paolo Casati, managing director, Santen; Giorgio Pisani, general manager IBSA**



these trends and the pharma industry’s economic contribution to the

country, many industry leaders have argued that the government should stop framing the industry purely as a cost to be contained. Pfizer country manager Massimo Visentin says, “there needs to be a broader shift in attitude towards viewing pharmaceuticals as part of the solution, rather than purely as a cost.” Scaccabarrozi has been central in encouraging this perspective shift, and contends, “we have succeeded in changing the government’s perception of the industry,

## Faster than first appearances



**Francesco Scopesi, managing director, Shire**

Shire’s Francesco Scopesi has a rare insight into many aspects of the Italian healthcare system. “In spite of some of the lowest prices in the entire region,” Scopesi says Italy’s “health system is actually highly advanced.” While formal marketing and reimbursement processes may take more time than in other European countries, he points out that “there are laws in place enabling access to a product prior to official approval status under regulations 326 and 648, which mean that you can respond to unmet needs earlier than you might think, just so long as the product and patients satisfy certain conditions. This means that, when there is a pronounced medical need that is recognized, then the Italian system is capable of delivering. There are thus some very appealing characteristics that the medical community very much appreciates.”

As a key stakeholder in the management of rare diseases, Scopesi says that “the authorities, for their part, constitute a reliable partner that is sensitive to the issue of rare diseases. Obviously cost-control is a priority for state actors, but we are always able to identify points of convergence and they do prove receptive in understanding the benefits we can deliver to patients.” Moreover, the authorities have generally supported Shire’s pioneering efforts in home care. Starting in 2008, Shire initiated a home delivery program for “enzyme replacement therapies in [Fabry’s] patients’ own homes rather than requiring them to travel hundreds of kilometers to a specialist hospital every couple of weeks.” Scopesi adds that, “over time we have scaled up the program to include Gaucher disease patients and even introduced

a ‘follow-me’ aspect so that patients travelling abroad in certain other European countries such as Germany can receive their infusions abroad from a third party. As you can imagine, these sorts of initiatives transform lives and greatly enhance patient satisfaction.”

Fabio Andreola, country managing director at Baxalta concurs, saying “overall, Italy treats rare diseases very well, and patients have good access to orphan drugs relative to most other countries, and moreover “in principle, all stakeholders in Italian healthcare - from centralized authorities to regional institutions - are aligned on the fact that rare diseases and orphan drugs require special attention.” However, he warns that “in actuality many individuals within the public sector remain very focused on minimizing costs, which can make it a challenge to effectively validate and communicate the value of the innovative therapies we offer.” As such, companies commercializing orphan drugs “must be able to demonstrate the value that their products bring to patients and the healthcare system in a highly credible and transparent way,” to assure market access discussions progress as rapidly as possible to limit “delays [that] come at a significant and avoidable cost to patient wellbeing.”

However, Celgene VP and general manager, Pasquale Frega, highlights the role of patient groups in Italy, “the Italian system is quite limiting in the way it allows companies to work with patient groups... there is still a very limited role for patient associations in the decision-making process.” This is a particular issue for patients with rare diseases, as in such situations they often become more knowledgeable about their particular condition than many of their physicians. As such, Frega hopes that “the government changes the way in which it approaches patient associations and includes them more prominently in the decision-making process.”



and pharmaceutical costs are very different and, when the government is working to meet budgetary targets, “it is very difficult to close a hospital while it is much easier to introduce measures such as our current payback system where we pay back around 50 percent of the budget overruns incurred as a result of overspending. Unfortunately, this does not only put a cap on the system’s expenditures, but also on innovation, as well as to patients’ access to it.”

This payback system has become a bone of contention between the

pharmaceutical industry and the government and is now a major consideration for potential investors. Boehringer Ingelheim’s country president, Anna Maria Porrini, says that she “can understand” the rationale behind the government trying to contain costs and bring health expenditure under control, but notes that “this mechanism where we pay for part of the expenditure naturally makes us think long and hard about continuing to invest in the country.” “If we have to repay a certain amount

of money, that means that we cannot use that money to invest. This is quickly becoming a vicious cycle, which we feel must be broken soon,” she adds. Pfizer’s Visentin recalls that working with the government to find new solutions has become a key priority, so much so that there was a “meeting between our CEO, Ian Read, and Prime Minister Renzi and Minister Lorenzin last September, in which he discussed the need to find an alternative to the current payback mechanism that places the country in such an unfavourable position compared to other more competitive European markets.”

Given the relative scarcity of public funding for pharmaceuticals, many innovative stakeholders have actually begun to encourage the use of generics and biosimilars, which currently account for only 20 percent of market value and 50 percent of volume. Leonardo Vingiani, director of Assobiotech, argues that, “it is vital that we save money through generics, in order to finance innovation [and] without these savings, we will not be able to innovate sufficiently to effectively maintain our traditional standards of healthcare.” Novartis’s global strategy corresponds directly with Vingiani’s argument. As country president Georg Schroeckenfuchs points out, Novartis offers “high quality generics through Sandoz and leadership in biosimilars as well. This allows us to contribute proactively to the establishment of an overall more sustainable healthcare system. The generics and biosimilars that we provide can go towards freeing up resources that can then be reinvested in real innovation.”

According to a study commissioned by Assogenerici, as much as EUR 1.4 (USD 1.6) billion in retail spending could be saved through the wider use of generics in Italy. These savings would however go to consumers and would not directly impact public budgets. Generics and biosimilar

## A Virtuous Circle



**Massimo Di Martino,** president and managing director, Abiogen

“Abiogen is proof that Italy can be competitive in pharmaceutical manufacturing,” claims CEO Massimo Di Martino. “Back in 2010 we manufactured 18 million units, but last year I am proud to say that we surpassed the 35 million-unit mark. This year, our intention is to push the boundaries even further and hit 40 million units.”

Martino believes that this competitiveness is “a natural consequence of the dramatic strictness imposed upon the Italian pharma industry in the early 2000s when both indigenous players and the in-country affiliates of the multinationals alike were subjected to

a whole array of measures from price cuts to the claw-back to restricted market access. This actually obliged the Italian pharma industry to restructure prior to the global financial crisis and ironically ended up serving us well. Italian manufacturers were compelled to invest a lot in upgrading their facilities and in securing authorizations to penetrate new markets as it was necessary to look for revenues outside of the home country as a way to stabilize revenues and diversify risk.”

This put Italian manufacturers like Abiogen in a position where they “can compete well against any Central or East European outfit on both cost and quality for third party manufacturing contract.” He admits that “obviously no European facility can compete outright on price with the Asian basket of countries such as India and China, but there are still many advantages to be leveraged from manufacturing closer to home and Italian producers, with their well-earned reputation for quality, can exploit this reality,” and at the same time can engage in various forms of innovation to differentiate their products. Through partnerships, Abiogen has been able to engage in the “development of fresh formulations, new indications and optimized delivery techniques,” which has had the added value of exposing his team “to new ideas and technologies intrinsic to such ventures has enabled us to maintain our capacity for innovation and to raise our game in terms of optimizing the ways we conduct our manufacturing.”





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FOR THOSE  
WHO CARE,  
IMAGINE CARE  
AND RECEIVE  
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**Eugenio Aringhieri, CEO, Dompe;**  
**Paolo Zambonardi, managing director,**  
**Ferring**

penetration in hospital channels may lag behind some other European markets, but Accord's managing director Massimiliano Rocchi explains that for the "traditional chemotherapies, the market-share in terms of volume varies from 60 percent for Epirubicin to 100 percent for fluorouracil. All the rest fall somewhere in this range," and for the hospital market in general "volumes and consumption are flat and the price is declining due to competition." He further explains that "today, the adjudication process [for

tenders] is one hundred percent based around price," but that this should be changing as EU directive 24/2014 "states that hospitals should change this to be compliant with the 'Most Economically Advantageous Tender' process," which will theoretically encourage hospitals to offer the best value, not the lowest price.

Given the unsustainability and costs of attachment to branded products, the situation is evolving. Osvaldo Ponchiroli, CEO of OP Pharma, notes that "the Italian generics market has seen double-digit growth in the past decade... [and] this growth is set to continue. Generics penetration is still low in Italy compared to other European countries, and given the unrelenting budget constraints, the generics market will only continue to grow, as these drugs represent a critical element of the solution to the problem of maintaining budget sustainability."

Unfortunately, an attachment to

original pharmaceutical products is not the only inefficiency within Italian healthcare. For one, there is significant room for improvement in preventative healthcare; according to MSD Italy's CEO Nicoletta Luppi, "the WHO has been very severe with Italy, as coverage among the population is falling rapidly." For MSD, she says, "our first objective therefore needs to be to help the authorities to get coverage rates up to the required standard. Approval of the National Vaccination Plan is the best way to do this, especially considering its relatively low expense compared to the large costs which could be avoided through its effective implementation."

Professor Walter Ricciardi, president of the Italian National Institute of Health (ISS), highlights that, in the battle for managing costs in healthcare, one of Italy's greatest assets is not being fully utilized. Much like the budgetary situation, "the data

## GENERIC TRIGGER DECLINES IN THE PRESCRIPTION RETAIL MARKET

NEW CHEMICAL ENTITIES (NCES) OFTEN RESTRICTED TO NON-RETAIL CHANNELS



Source: IMS Health – Multichannel 2015 – Public prices.

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**Enrique Häusermann, president, Euro Generici (Stada);  
Massimiliano Rocchi, managing director, Accord Healthcare;  
Federico Seghi Recli, managing director, Molteni**

we provide is being used in silos, so the Ministry of Finance is using our financial data, while the Ministry of Health is using the data on healthcare indicators.” As such, while the ISS has “plenty of data, our system is severely underestimated, undervalued and underused,” and he asserts that “we need to start breaking down these silos in order to gain new insights on the state of the healthcare system, and so provide decision makers with the appropriate tools to make smart decisions.”

costs continue to spiral out of control will not be sustainable, or correct.” That said, Italy clearly possesses the tools needed to improve operational efficiency within the national healthcare system, and current healthcare spending efficiency is already respectable within Europe.

### **THE MAMBO ITALIANO**

Part of the prestige attached to the “made in Italy” brand stems from the

In essence, the pharmaceutical industry has made clear progress in cutting costs of innovative drugs in recent years, with total RX expenditures actually decreasing. As Pfizer’s Visentin puts it “saving in pharmaceuticals while hospital sector

sheer level of creativity and attention to detail of Italian workmanship. End consumers may not have reason to wonder where this lauded Italian flexibility and creativity derives from, but those more familiar with the country witness a culture that prides elaborately creative, intricate, and sometimes convoluted methods over a simpler path.

The Italian market access scenario for pharmaceutical products provides a fitting example. Professor Luca Pani, director general of the Italian Medicines Agency (AIFA), recounts that AIFA “was originally established with the idea of calculating the risk-benefit and benefit-to-price ratios of new drugs within the very same institution.” A sensible and eye-catching model that “differentiates the Italian regulatory apparatus from its equivalent European counterparts.” For Pani, this “ability to fully negotiate the national registration for a drug ‘under one roof’ has become a real asset, rendering AIFA the sole negotiator for public reimbursement.” Unfortunately, the situation is not quite that simple. As Ferring Italy’s CEO Paolo Zambonardi details that, “right now, once approval is secured from the EMA, it takes a further six to nine months to get a decision of pricing at the national level before then going to the 21 different regions each with their own peculiarities and distinctive health systems.” Some regions are faster than others, ranging from a matter of weeks up to two years. Zambonardi concludes “the end result is a loss of approximately two years patent and today that results in big damage to your profit margins but, more importantly, it is a problem for the patients who do not have access to innovative products to treat their diseases while they wait.”

Professor Walter Ricciardi of the Italian National Institute of Health (ISS) explains that this anomalous situation arose out of ill-thought-out modifications to the national constitution back in 2001. “Essentially, the provision of healthcare was delegated to the country’s 19 regions and two

Molteni Farmaceutici is a privately held pharmaceutical company founded in 1892 with a strong knowledge and experience in control substances and a wide spectrum of pharmaceutical products for the treatment of pain and drug addiction.



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autonomous provinces, and the state did not retain sufficient competencies to maintain a homogeneous, effective and efficient system in the country.” Instead, as Ricciardi puts it, “heterogeneity proliferated, resulting in a wildly imbalanced public health landscape with certain regions blessed with world-class care, while others languish blighted by dysfunction.” In his eyes, “the only way to ensure the country’s continued ability to maintain universal coverage is to refashion the governance model.” Such an eventuality may soon reach fruition with constitutional amendments already under discussion in parliament, which would ultimately require ratification by referendum later in the year.

IMS managing director Sergio Liberatore has another perspective on the complexity of the Italian pharmaceutical market. As he explains, “the entire marketplace is much more granulated than in many countries,” and is served by 240 wholesalers alongside direct sales between some pharmaceutical companies and pharmacies, “and that translates into a high demand for connecting up the dots, which happens to be our specialty.” Liberatore admits that “the complexity of the Italian marketplace creates a lot of work for us,” and as such, while Italy has the seventh largest pharmaceutical market worldwide, IMS Italy is in fact the third ranked affiliate within the IMS global organization.

Given the fact that getting market access for a product nationwide can require 20 sets of negotiations, one with each of AIFA and the 19 regional authorities, foreign companies must enter the market with a careful approach. Simona Falciai, general manager for Shionogi’s recently established Italian affiliate explains that the company started building their European “base in 2012, primarily focusing on developing and registering innovative medicines for the European market, focusing on Germany, Spain and Italy.” Falciai notes that “Italy is one of the most challenging countries for market



**Alberto Chiesi, president, Chiesi;**  
**Massimo Visentin, managing**  
**director, Pfizer**

access policy,” but contends “AIFA has made important improvements, the timing for centralized approved drugs is much faster now. If you want to have reimbursement, it naturally takes longer to go through the reimbursement process, but the timelines for reimbursement have also been shortened from roughly over a year to six to nine months nowadays. I think a remaining challenge is the predominate regionalization in Italy.” With these remaining challenges, Falciai says that “we will focus on women’s health in the first few years of our presence while working on the clinical research and market access strategy for our new specialist pipeline,” including one very promising product that Shionogi expects “to launch in 2020, but we need to start now with our market access strategy to understand what will be required from the payers in order to get optimal access to this drug.”

Another Japanese company, ophthalmology specialist Santen, is in a similar position with regards to their entry into Italy. General manager Paolo Casati explains that “Santen entered the Italian market being entirely focused on glaucoma,” and the company will be “expanding our portfolio in a smart way,” by first building “a strong portfolio in ophthalmic pharmaceuticals as a foundation for the affiliate.” This strategy is “especially relevant as we have four new ophthalmic treatments arriving over the next few years, and three of those address unmet needs.” As such, Casati is “working to establish the brand of Santen” in Italy as “one of the very top companies of reference in our area... especially in terms of

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**Sergio Liberatore, managing director, IMS Health; Fabrizio Greco, managing director, AbbVie; Paolo Marcucci, CEO Kedrion**

relationships with KOLs and the scientific community,” although it’s clear that the global brand is already known in Italy as “a customer survey showed that most of the KOLs in Italy knew Santen before we arrived in the market.” Once Santen Italy establishes itself as a key player in ophthalmology, Casati will begin “looking at the introduction of a wider, more diversified portfolio over time.”

Although Daiichi Sankyo has been established in Italy for several years, Antonio Reale, CEO of the Italian affiliate, has also had reason to refocus as the company’s global R&D focus has shifted from primary to specialty care, with the first such innovative product, Edoxaban, expected to launch soon. Reale explains that due to this shift, “we decided in 2013 to move away from the traditional “push” marketing model to

a “pull” model, driven by the needs of our stakeholders. Specifically, it meant switching from a largely tactical approach to a strategic mind-set and to implement a new, more agile and flexible structure better able to respond quickly to all the external changes and challenges.” According to Reale, the key aspect of this transformation “was the decision to build the new market access team from the ground up,” and to focus “on attracting and recruiting capable resources from the outside” for these roles, because the organization “desperately needed to obtain expertise in this new area.”

## MADE IN ITALY

Regardless of external challenges, the Italian pharmaceutical industry is clearly equipped for success, in terms of physical capital, expertise, and culture. To start with, Italy already has a reputation for quality and workmanship upheld today by luxury automotive and fashion brands, which can be traced to the country’s centuries of experience producing wines, olive oil, and leather of the finest quality. AIFA’s Pani affirms that “there is a “Made in Italy” element in pharmaceuticals which is just as significant as it is in cars for Ferrari, or in leather for Gucci. We are incredibly good at using numerically controlled machines, such as those used in pharmaceuticals, and there is a very strong SME network in the country. The quality of the drugs these companies make is outstanding, accurate up to 99% and passing every external test.” Recipharm Italy’s CEO Giorgio Bruno concurs, going so far as to say that, “the Italian stamp is important for our success and our reputation at the international level.”

Signalling the quality and technical sophistication of Italian pharmaceutical manufacturing is the presence of several multinational facilities producing highly innovative drugs for the global market. Georg Schroeckenfuchs, Novartis country president, illustrates this fact by saying that “in the cardio-metabolic therapeutic area we have a stand-out product in Entresto, which has attained great success in treating chronic heart failure. Interestingly our worldwide production of this particular product is carried out here in Italy and demonstrates our local competitiveness in manufacturing vis-à-vis other Novartis manufacturing sites worldwide.” Novartis’ generics division Sandoz also has facility in Roverto, which had “an export budget of USD 113 million in 2015,” and, according to Sandoz managing director Manlio Florenzano, is “dedicated to the production of API (Acid Clavulanic, Acid Mycophenolate and Tiamulina).” Moreover, Florenzano reiterates that “as part of our long-term strategy we continue to upgrade and modernize our facilities: in 2015-2016 alone, EUR 5 (USD 5.5) million was invested in technological innovation to ensure the highest standards of quality.”

Other big-pharma and big-biotech players with significant manufacturing presences in Italy include GSK with two

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**Simona Falcial,**  
general manager,  
Shionogi

facilities, Pfizer with four following the integration with Hospira, a Lilly facility which produces a third of the company's global insulin supply, and Boehringer Ingelheim. Boehringer Ingelheim president

Anna Maria Porrini explains that the company's manufacturing presence in Italy is through subsidiary "Bidachem SPA, which manufactures APIs and plays an important role in the provision of our innovative drugs. It is considered a strategic production site by the Boehringer Ingelheim group and as such we invested EUR 70 (USD 90) million back into the plant in the past five years, and continue to invest around EUR 10 (USD 11.2) million each year in order to keep the facility up to date." AbbVie's Italian

manufacturing plays a similar role within that organization, as general manager Fabrizio Greco notes, "the Campoverde manufacturing site has been chosen as the global production site for one of the three active ingredients in our revolutionary treatment to eradicate Hepatitis C. The AbbVie interferon-free therapy against hepatitis C is an important research milestone that can improve the lives of 160 million patients worldwide. All these elements position our manufacturing site as one of the highest performing and most competitive in the AbbVie manufacturing landscape." Similarly, Baxalta country managing director Fabio Andreola explains that "our plant in Rieti is a state-of-the-art plasma fractionation plant that has been expanded significantly over the last few years, supplying other Baxalta worldwide with plasma, to process into branded plasma-derivatives. In terms of technology, this site is quite advanced even within the

context of Baxalta's innovative global manufacturing network."

Italy is also home to an assortment of internationally competitive CDMOs that work closely with these leading multinationals. Aldo Braca's BSP is one, as, from the time he founded the organization, "our key objective was to be a CDMO which specializes in a particular segment... we wanted to carve out a specific segment of the market for ourselves." Citing the global pharmaceutical industry's shift from cardiovascular products toward oncology in the last decade, Braca explains that BSP offer their clients "a strong value proposition ... because we solve one of the major challenges of the conjugation process," within their highly specialized oncology facility at, so specialized that outside engineering groups are not allowed within the facility, as according to Braca "we consider our plant to be intellectual property." The focus

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for the CDMO is currently on the construction of two new immunotherapy plants that they aim to have operational by 2019.

Leading global CDMOs including Patheon, Catalent, Famar, and Latina all have at least one facility in the country, while Sweden based Recipharm now operates four facilities in Italy following their acquisitions of the Corvette Group and Mitim in October 2014 and February 2016 respectively. Recipharm's Bruno explains that what his clients look for in a CDMO "partner is quality, efficiency, capacity and reliability. The price is important of course but it is not the most crucial factor. Flexibility is key because clients routinely face market fluctuations and they expect us to be able to act and react accordingly." Italians, he says, "place a great emphasis on flexibility. This is why Italian CDMOs in general have a great reputation around the world. We are very flexible in catering to the needs of our customers." Between reputation, expertise, and hard work Recipharm Italy is clearly doing something right, as Bruno admits that "at the moment, we operate with full capacity in all plants that belong to the Recipharm umbrella in Italy – from Biologici to Mitim."

## BALANCING AT THE PRECIPICE

With a stellar reputation and the highest pharmaceutical production per capita level in Europe, the Italian industry currently holds a strong position within the global pharma industry. However, several industry stakeholders have voiced concerns regarding the sustainability of prevailing strategies. Despite emerging markets having been a key growth market for many Italian manufacturers in recent years, Alberto Chiesi, president of Chiesi reflects that, "further development will pose a challenge as these economies naturally evolve to drive an economic protectionist policy, usually raising

## "Hospital-territoriality"



**Gabriele Baccelli,**  
country manager,  
Orion Pharma

Excerpt from interview with Gabriele Baccelli, country manager for Orion Italy

"In Italy if you want to be active in the hospital market, you need to know the territory very well. We have 20 different regions, with 20 independent healthcare systems, and this is different to what Nordic companies are used to. Here in Italy everything can be completely different from hospital to hospital so we had to communicate to our management that it was possible to operate effectively and profitably using a heterogeneous strategy, as long as we had the right team to implement it.

Right now, our customers are not only taking care of patients, they also need to organize their department, manage budgets, reorganize their operations on the territories and perform many other tasks. This means it is important to not only communicate the value of the drug directly, but also to talk about the patients they are managing and how they do this. If in that environment you can show that your drugs are sustainable and add value to the entire organization, rather than only the patient and the customer in an isolated fashion, you can succeed.

This is what makes the hospital market completely different from the territory market. In the respiratory sector for example your main competence is to find the time and the people to get as much contact as you can. This is because in these crowded markets the only added value is contact. That is not true for the hospital market, and it is why many companies which tried to face the hospital and territory market with the same strategy failed utterly.

Now, in two years we have completed 75 percent of the rollout of our drugs to the Italian regions which means that in some hospitals the patient has had access to our drugs for almost two years and in some other hospitals they are not yet available. Stakeholders need to come together to improve the regulatory environment, to make the quality of healthcare more homogenous. This will be to the benefit of both our patients and the industry."

local content requirements." "The consequence is either delocalization of manufacturing capabilities or concluding agreements with domestic manufacturers to license out production," he predicts. Meanwhile, Leonardo Vingiani, director of Assobiotech, raises different concerns pertaining to small molecule products, fearing that, "in five to ten years, our exports of pharmaceutical and medical products, which are currently at record levels,

will disappear as emerging markets such as India and China catch up in the quality of their own production." "Biotech products are much more difficult to produce, and this is where our future on the international export stage will be found...Now is the time to be investing in the development of these capabilities," he counsels.

As such, for Italy to remain a relevant global pharma production hub, significant additional investment will



**Georg Schroeckenfuchs, country president, Novartis; Aldo Braca, president & CEO, BSP Pharmaceuticals**

be needed. Unfortunately for Italy, past success and a tradition of pharmaceuticals alone may not be enough given the competitive financial incentives offered in many jurisdictions. As Pfizer's

in an FDA approved plant, normally takes between 12 and 15 months," while "companies in other countries that are achieving exactly the same in a matter of days." Marcucci concludes that, "this is simply not conducive to managing an industrial business."

However, Marcucci is quick to make clear that "despite the bureaucracy, restrictions and import delays and external competition, there is a lot of knowledge embedded within Italian suppliers, technicians, and R&D. In a relatively small space in Tuscany, we have three high-ranking universities that are focused on medicine, pharmacy and biotechnology, which are attracting a lot of students from all over Italy... It is decidedly appealing to be part of such an environment." Still, "It would be so much easier if the bureaucracy were better aligned with the industry needs and modus operandi."

### STAYING AHEAD OF THE GAME

There is a palpable degree of inspiration and vision throughout the Italian pharma manufacturing sector that distinguishes the executives leading Italian companies and affiliates. The strong desire to maintain the level of growth and success that has been enjoyed over the last seven years, and the pressure to remain a vibrant source of growth to support the national economy, all appear to play a function in stimulating the famed Italian propensity towards

Massimo Visentin notes, "Headquarters looks at countries as a whole, and for Italy that means they base their evaluation on both the production and commercial side as a single organization." Thus, the potential of the local market, and the extent to which innovation and investment is rewarded, may play a significant role in determining the future growth of the Italian pharmaceutical sector.

Italy's regulatory environment can sometimes place Italian firms at a competitive disadvantage in international markets, a fact that certainly decreases Italy's ability to compete for investment. Kedrion's CEO Paolo Marcucci explains, "our regulations are often fundamentally different to the rest of Europe," and "there are peculiarities that make Italy very complicated and businesses more expensive to run." For example, he recalls that, "to obtain an import permit to Italy for an intermediate from plasma manufactured



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**Antonino Reale, managing director, Daiichi Sankyo; Paolo Cionini, managing director, Leo Pharma; Nicoletta Luppi, managing director, MSD**

flexibility and creativity. Nonetheless, while Italian executives face the same challenges created by the same global trends as their colleagues do in other markets, a surprising majority seem to have clear and decisive ideas about what they are going to do to stay ahead.

Eugenio Aringhieri, CEO of Dompé has demonstrated decisive leadership more than anyone else in the industry. As he explains, “it became very clear to me that the pharmaceutical industry is splitting off into two very different directions and that the industry’s main protagonists will have to choose one path or the other. There can be no middle ground or third way. Either your leadership relates to your capability to offer the best price and to outcompete

your competitors by offering an equivalent performance at a lower cost. Alternatively, you can go down the route of leadership through your capacity to innovate and be the first mover in bringing latest generation technology to market.” Given this situation, he had to decide which route would be most successful for Dompé, a traditional Italian family company that in Aringhieri’s words was “a local, primary-care orientated company connected by commercial alliances.” Pivotaly, Aringhieri concluded that the way forward for Dompé would be “leadership through innovation,” and thus today he is “in the midst of transforming Dompé from a local pharma company to an international biotech entity.”

Dompé is far from alone in this shift towards innovation, as Leonardo Vingiani, director of Assobiotec, says that over “the last six years, we have had an important shift in the image of innovation as a driver of our country’s competitiveness. This is something new for Italy, and it has a lot of implications, in the attitude towards research, towards innovation and innovative products and in the public’s perception of patents.” Vingiani further explains that, “the magnitude of this shift can be seen through the number of companies which have joined our association, which thrives on innovation. In 2009 we had roughly 70 members, today we stand at more than 140.”

One such member is Kedrion Biopharma, a globally competitive leader in plasma derivatives. CEO Paolo Marucci explains that the firm’s 15 percent annual growth rate has been “driven by hyperimmune globulins, for which we are leaders in the US and worldwide. Kedrion is internationalizing its business by building a new “a new plant dedicated to the production of a 10 percent immunoglobulin that will be launched in 2020” in the US, but Italy will continue to be central to the production of their most advanced products; “our production sites in Hungary and in the US carry out the relatively easy first part of the fractionation process, whereas the complex, high-value purification step takes place in Italy.”

For many mid-sized Italian firms, successfully innovating in life sciences is becoming increasingly challenging. Aside from the rising average cost of bringing an innovative drug to market, Aringhieri highlights that while “traditionally R&D has been performed in-house within the larger firms,” today “the sheer complexity of innovation today demands a wholly different approach. We’re talking about mastering the arts of nanotechnology, biotechnology, genomic and proteomic systems and much more. Not even big pharma can aspire to cover all of these bases within their own laboratories. It’s simply neither economically nor organizationally efficient.” Thus, for Italian firms with less access to capital than big pharma, successfully innovating requires new strategies.

The key to these new strategies lies in “the rapidly

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Recentemente Daiichi Sankyo sta focalizzando la sua attenzione verso settori terapeutici dove i bisogni di cura rimangono ancora insoddisfatti, come lo sviluppo di farmaci anticoagulanti, di trattamenti antitumorali e per il diabete.

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developing nexus between networking and innovation within the pharma industry,” according to Aringhieri. He says “it’s far better to develop real mastery in a specific competence and to blend that with a strong network linking you in to the best specialists in all the other fields relevant to the technology that you are innovating,” and as such his priority for Dompé has “been to link up our own in-house capabilities with best-in-class actors all around the world by building up and maintaining a formidable network of partners.”

Partnerships and collaboration have proven equally important for developing successful and competitive incremental innovations. Molteni CEO Federico Seghli Recli, says that for his company, which “ranks among the largest manufacturers of opioids pharmaceuticals in Southern Europe,” the “strategic direction is to accelerate internationalization in the niche

market of drug addiction where there is still a clear room and opportunity for a pan-European player.” He explains that from 2008 Molteni started working “with Archimedes (now a subsidiary of the ProStrakan Group)” to develop a fentanyl nasal spray; the two companies worked together “on conducting the regulatory trials, and had the product approved by the EMA in 2010. At that time, we decided to make this large investment, and it has proven very successful. We have the exclusive manufacturing rights for Europe, and we are in the final stages of extending this geography to other territories outside Europe.” This collaboration with Archimedes was only the beginning of a larger “strategic partnership with ProStrakan with whom we expect more projects to come beyond the manufacturing of PecFent.”

IBSA Italy plays a major role within the organization as Italy is the compa-

ny’s top market and serves as a global production hub. IBSA has employed a similar strategy focused on delivery technologies; CEO of the affiliate, Giorgio Pisani, says that the company does “not employ the traditional approach to research” and that instead their products are “enhancements of generics” where innovation trends coalesce around “improvements to production technology and delivery systems.” For example, Pisani explains that star product, Flector, was the first transdermal use of diclofena which was developed by their researchers in Lugan and represents the type of “small, but smart innovations that revolutionize patients’ livelihoods” that the company is becoming increasingly renowned for.



**Giorgio Bruno,**  
general manager,  
Recipharm

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**Mario Marazziti, president of the XII Social Affairs Commission, Chamber of Deputies; Osvaldo Ponchioli, CEO, OP Pharma**

In fact, this product's potential is so significant that it was also registered in the United States and distributed by Pfizer. Devising such innovations entails forging new types of collaboration and the continual acquisition of new skill sets. Pisani explains that, "patch technology is the main reason we bought Bouty," and as with Flector and other products arriving last year, "it was crucial to develop a very strong connection with the pharmacy channel." Bouty alone afforded them immediate access to ten thousand pharmacies. Moreover, the same transdermal technology is also used to produce a product for Novartis, namely Voltadol.

## **CLOSING THE GAPS**

The path from scientific discovery to safe and approved product is long and fraught with risk and challenges, and the optimal development path often means a candidate travelling across several geographies. Yet, there are many advantages to having access to support within a more concentrated environment; without this access, science parks and technology hubs would not exist. Italy as a country has fantastic expertise in many areas, yet historically many innovators have had to leave the country in search of funding. Today many of these gaps are being closed, and as a whole the Italian life science community remains a highly competitive destination for R&D investment.

Italy's scientific leadership potential is clear to see through examining the portfolios and pipelines of leading Italian innovators. Alberto Chiesi explains that Chiesi "achieved approval for our new regenerative product Holoclar, which will stimulate the regeneration of the cornea, the

transparent area forming the front of the eye, which will help patients to regain vital eyesight. This is the first stem cell based product approved in Europe!" This product was developed by Italian scientists at the Center for Regenerative Medicine in Modena. Professor Luigi Naldini, director of the San Raffaele Telethon Institute for Gene Therapy, shares another example of cutting edge biopharmaceutical science taking place in Italy, this in partnership with GSK, and explains that "our successful experience with ADA-SCID gene therapy was the basis for our institute's alliance with GSK, and together we are developing what could become the first ex-vivo gene therapy to be approved anywhere in the world."

These two examples illustrate a point that Leonardo Vingiani, director of Assobiotech, makes clear when he declares that, "here in Italy, we truly have amazingly talented scientists." However, beyond being talented and productive, Vingiani contends that Italian scientists "have consistently proven

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## Gerrymandered Generics

Why is generics penetration so low in Italy? Enrique Hauserman, CEO of Eurogenerici (a subsidiary of STADA), explains that “the root cause of this situation was the system which was introduced in 2001, which did not take into consideration the penetration time for new generics, and caused generics companies in the market to compete against each other. There was also no incentive for prescribers or pharmacists to prescribe generics.” IMS managing director Sergio Liberatore adds that “the patent cliff arrived with a lag-time of two to three years in Italy as the patent protection legislation was introduced rather later than in many other countries,” and as such the generics segment “is still playing catch-up comparatively with other mature European economies in terms of penetration and market value.” Generics policy was updated in 2012 with the introduction of the Balducci law, which Hauserman explains, “obliged prescription of acute therapies according to international non-proprietary names (INNs), as well as for cardiovascular therapies for new patients.” Partly due to this policy, retail sales of unbranded generics in Italy expanded from 12.1 percent per annum from 2009 to 2014, despite a 2.2 percent contraction of the retail market for reimbursable products over the same time period.

That said, generics penetration remains abnormally low, with unbranded generics accounting for only 26.5 percent of off-patent drugs sold in 2014 (by volume). Additionally, 85 percent of the generics market is controlled by just five companies according to Hauserman; Doc Generici the

only Italian firm among this group. However, although generics companies have relatively low market share in Italy, their presence on has an undoubtedly greater effect today than previously. “In the past, when there was less competition to be faced down from generics, patent expiry was not so much of a big deal,” says Ferring Italy CEO Paolo Zambonardi, but “nowadays, the moment a patent reaches expiry you can expect a price decrease of 30 percent minimum.”

Sandoz’s Manlio Florenzano explains why “the substitution-logic that works well in many European markets has clearly been less effective in Italy... Firstly, the legislation tends to treat former originators and generics in very much the same way. When a patent expires, we negotiate the price with AIFA and then innovative companies tend to drop their prices accordingly to the point where the substitution logic loses its relevance... It’s therefore quite easy to get sucked into a race to the bottom on pricing.” Liberatore continues, “Italians remain very brand conscious and pharmacists are obliged by law to ask customers to choose between either the branded originator or generic. The difference in price is then borne by the customer, but in many instances this is a price that consumers prove willing to pay.”



**Manlio Florenzano,**  
country head  
and managing  
director, Sandoz

that they are able to do as well as others, with less resources. It also has to do with the fact that the cost of a researcher in Italy is 30 percent less than in Germany, France, or the UK, and a full 50 percent less than in the USA.”

A particular strength of the Italian scientific and academic industry is the strong focus on facilitating and optimizing translational research. Many of Italy’s top scientists work within research institutes, the leading example being the San Raffaele Scientific Institute (SRSI) attached to the San Raffaele Research Hospital. Professor Manuela Battaglia, vice director of the diabetes research institute (DRI) within the SRSI, explains the “SRSI itself is centered on the mission of translational medicine. The key feature of the SRSI is the coexistence of laboratory, hospital and university, which is a rare

occurrence even globally. Very tangibly, it is uncommon for a researcher to be able to cross a street and obtain patient samples for use in the laboratory, and our interactions with researchers in the US have impressed on us the rarity of our work situation.” Naldini explains that the value and synergy of this arrangement stems from the fact that for basic scientists “it is crucial to speak to a clinician early on in the development process. Scientists need to know if their idea is realistic or not as soon as possible.”

Focusing on bringing research into the clinic at an early stage has been a successful strategy for the SRSI according to Naldini, who explains that one of the aspects “which greatly contributed to our success was the establishment of in-house manufacturing capacity. Early on the SRSI spun off what is now

MolMed SPA, a company which still provides us with the pharmaceutical products needed to conduct our gene therapy trials.” The SRSI’s relationship with MolMed is far from the organization’s only relationship with the pharmaceutical industry; vice-director of the DRI Professor Lorenzo Piemonti explains “very practically speaking, industrial collaboration made up 13 percent of our operational budget from 2008 to 2013.”

Separately from collaborating with Italian academic researchers, several big pharma companies have ended up with R&D facilities in Italy over the years, often through M&A activities. While some have scaled back or closed such research centers following integration and consolidations, others have maintained a strong R&D presence in the country, in part due to the cost effectiveness.



**Luca Guidotti** deputy scientific director, **San Raffaele Scientific Institute**; **Luigi Naldini**, director, **Telethon Institute for Gene Therapy**

Boehringer Ingelheim's president Anna Maria Porinni explains that their "research facility employs 38 researchers working hard to develop new chemical entities. The center has been very productive in terms of new molecules reaching the pre-development stage, with 14 new chemical entities reaching this milestone in the last 5 years." Similarly, Novartis once operated an important vaccines research center in Siena, which was transferred to GSK as part the global division swap between.

With a big pharma R&D presence and strong life science research institutes that work closely with the industry and specialize in translational research, the major gap remaining in the life science environment predominantly affects entrepreneurs. Vingiani explains that "the problems stem from a financial market that is not as mature as these companies might deserve," as "in Italy we are still lacking venture capitalists specialized in biotech." As such, "In the past, Italian scientists have had to go to Switzerland, France, and Germany to find the funding they need," however this method presents challenges as well as most foreign VC firms say "they need a leading local investor to oversee the daily status of the projects in-country." Progress is underway, but Italian entrepreneurs will have to wait for a few more years before specialized VC firms are more accessible. Capital is still relatively

accessible however, because, as Vingiani puts it, "with its new patent agreements, tax credits and support for hiring PhDs, this is a good time to invest in the country. The atmosphere is very good here, and the government is very supportive, so we are excited about the future."

Looking ahead, the future is bright for Italy, although not without challenges. Luckily for Italy, Italians are well versed in adapting to change and finding inventive, if not straightforward, solutions to tricky situations. Leading Italian scientists also appear to rapidly be developing a more entrepreneurial spirit to complement, and fuel, their academic prowess. For those willing to leave handling the Italian eccentricities to the Italians, it seems to be a pretty profitable place to do business in; the world-class wine, top-class gastronomy, and eye-catching fashion are all just a bonus. 🌟

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# Cancer's Disruptive Dozen

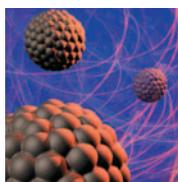
The World Medical Innovation Forum presents its second list of breakthrough technologies—this time focused on oncology

**T**he healthcare technology news corps took out its wide-angle lens once again to capture a gaggle of experts on stage at April's World Medical Innovation Forum in Boston. In its second season, Partners Healthcare played host to more than 1,000 industry leaders convened on the topic of cancer. (Last year's focus was neuroscience; 2017 will target cardiovascular).

Once again, the conference headlined its Disruptive Dozen—12 technological advances that the surveyed faculty members identified as having the greatest potential to enhance care in the next decade. We highlight a few of them here.

## #12: Nanotechnology

Engineering at the nano scale offers promise to cancer treatment and diagnosis as well as in the research setting. Ligand-directed nanoparticles may be directed to specific tumor cells for precision drug delivery, minimizing harm to healthy cells and side effects.



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## #11: Redefining Value



The cost of innovative treatments remains on everyone's mind, even for those doing the innovating. Novel patient-cen-

tric metrics and the merging of big data, shared and transparent, with new analytic capabilities, will be key. The Partners are optimistic that the future will bring better management of "complexity of cancer," part of which will be "finding alternative payment models."

## #9: mHealth

Mobile devices, wearables, etc.



promise to do great things in medicine. But how will they play in cancer? Tracking patients outside of the hospital for changes and adherence will be one. Cancer care apps offering supportive care could offer "personalized social support." Rapid response to specific side effects of chemotherapy is one way digital and mobile technology is already being tested.

## #7: CRISPR



Clustered regularly interspaced short palindromic repeats (CRISPR) are triggering hysteria among researchers (and mainstream media) at the amazing potential to edit the genome with ease. Therapies may ultimately target cancer cells directly or empower immune cells in the fight.

## #4: Machine Learning and Computational Biology



Cancer specialists face a daunting task just to keep up with the latest research. The literature is just one thing to consider. Add to that the reams of data each patient will bring to their check up, from a genomic analysis to step-counting wearables. Machine learning will be necessary to enable personalized care and to give an assist on accurate diagnoses.

## #1 and #2: Immune Modulators and Cellular Immunotherapy



Immunology earned the top two spots from the Partners faculty. At #2, checkpoint inhibitors, like our Brand of the Year, *Opdivo*, are already proving their worth, and more candidates and combination strategies have oncologists thrilled. Time will tell how many more patients can benefit as cure rates are expected to improve and more cancer types are being targeted. And causing even greater excitement, at #1, was cellular immunotherapy, namely CAR-T technology. Genetically altered T-cells turned into cancer seeking missiles has researchers and the investment community simmering, especially given impressive response rates in patients who had stopped responding to all other interventions.

Check out the *Disruptive Dozen* full report here: [bit.ly/1NWu8Df](http://bit.ly/1NWu8Df) 



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## Strategic considerations for clinical development programs in emerging biopharma

At small biotech companies, the race is on: investor demand, regulatory complexity, crunched timelines, stakeholder pressures, and limited resources are just a few of the challenges. Yet another challenge is finding suitable partners capable of providing both flexibility and access to the capabilities your product and company desire, while aligning to your budget. By examining your product development through the lens of an investor, it becomes clear that early planning and design are crucial to navigating your clinical studies and commercial pathways.

Rick Sax, a leading expert in integrated drug development, will be discussing the strategic considerations you should consider in order to navigate the clinical development of your product as an emerging biopharmaceutical firm:

- Design with the end in mind, from drug discovery, IND, through approval
- Perspectives: investors vs stakeholders vs market
- Balance investment opportunity & risk
- Understand the healthcare system and your market
- Thinking ahead without investing major resources
- Key questions to ask yourself and your team throughout development

Key takeaways:

- Clinical-Commercial convergence and good design practice should sit at the heart of drug development
- Harness the power of information to inform the development process
- Think about what guides investments and how you can demonstrate value

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**Lisa Henderson**

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