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VOLUME 38, NUMBER 3

THE VALUE EQUATION

New Perspectives on Outcomes-Based Healthcare

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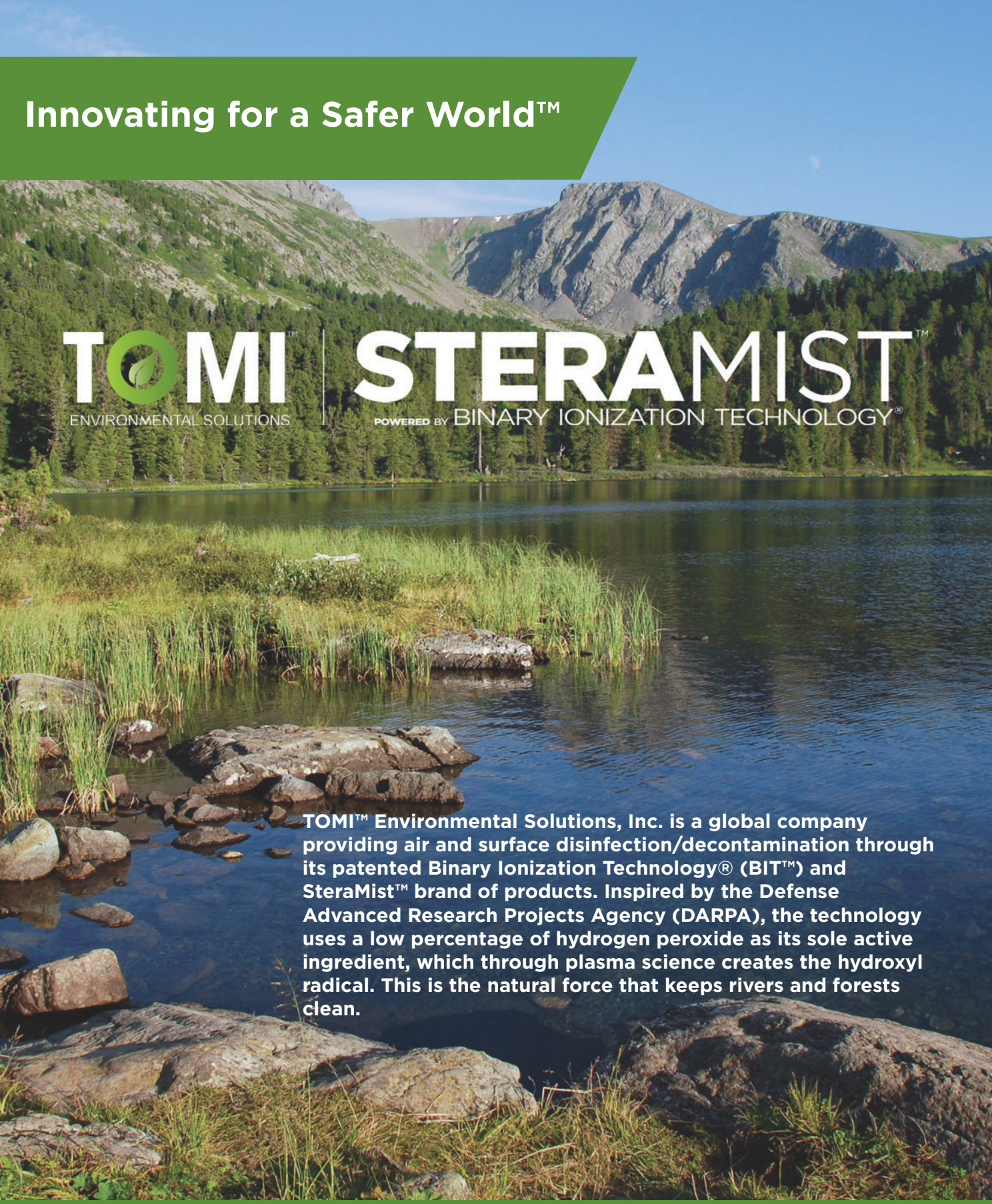

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The Law of Unintended Consequences

WHEN NAVIGATING THE NEW TERRAIN OF VALUE-BASED PRICING AND CONTRACTING, is there such a thing as an intended consequence? The word consequence is somewhat negative, used as a word substitute for punishment with children. As in, "if you do this, there will be consequences." It's more of a PC term meant to affirm decision-making skills and you don't want to use the word "punish" for a child because it sounds extreme. But I digress, and also included the question from the panel I attended on outcomes-based contracting, which is featured on page 14. What are the unintended consequences around this type of contracting? It's very complex, just on the cusp of leaving its nascent stage, and involves multiple stakeholders. It's not simple and there are consequences.

LISA HENDERSON
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No one pharma company or health payer has the magic formula for outcomes-based contracting. The articles we present in this issue focus primarily on challenges and real-life tips for getting started. Other articles contributed to this issue focus on the need for pharma to completely re-engineer its pricing models. Again, consequences are coming.

In a recent webinar (http://bit.ly/2FAwbjU), PwC presented the idea that if pharma did not provide sustainable engagement with value-oriented customers, the consequences would be negative. Specifically, if pharma comes to the table with weak or unproven value propositions, such as programs too focused on short-term pharma upside: price, volume, adherence, Rx durability; too narrowly focused on cost offset or cost-effectiveness evidence generation; an approach with limited willingness or ability to customize; limited investment horizon; or without any meaningful pharma risk.

Other negative consequences, says PwC, could come with too many operational impediments, such as around regulatory concerns (anti-kickback, HIPAA); data sharing and technology; too much implementation responsibility left to health system; or overly complicated contracting requirements.

Many of these concerns are discussed by the panel members and are offered as insights to help companies take those steps toward sustainable value-based engagement. But let's tackle some of the unintended consequences.

Significant changes to incentive alignment. What is one company's revenue stream is another company's inefficiency. If you make it more efficient, someone is going out of business. That is a simple concept, but doesn't make it easy to negotiate. There is going to be disruption, noted one panel member; we just don't know what it looks like yet.

If drugs are going to be paid solely on effectiveness, will companies only focus on drugs that will be successful? We know how much drug development costs, and we know how many programs fail to make it all the way to approval. Companies prevail because they are "rewarded" financially for those few successes. If companies only pursue outcomes acceptable to payers, where will innovation come from?

Who has the responsibility for making sure patients play their part in the outcomes scenario? If a patient doesn't take their medication, or if comorbidities or other medications cause imbalances in the result, who bears that problem?

Technology. Who has the data, how do you integrate the data, who interprets the data, how is data managed, measured, and modeled? This isn't so much unintended as completely necessary and discussed further in the articles this month. PwC goes as far as describing ways that value-based engagement and contracting becomes predictive through analytics. This may be true, but in the interim, agreeing on these terms and processes is a big elephant.

The Cobra Effect is well-documented on the Internet as an example of unintended consequences. In Imperial Britain, the government was concerned about the number of venomous cobra snakes in Delhi. So it offered money for every dead cobra, which successfully resulted in a large number of dead snakes. Eventually, however, people began to breed cobras for the income. When the government became aware of this, the reward program was scrapped, causing the cobra breeders to set the snakes free. As a result, the wild cobra population further increased.

In a closer-to-home page from potential unintended consequences come from one of the scientists who discovered CRISPR (http://bit.ly/2EUvCo9). She noted "there's been discussion about this [...] around the use of gene drives in insects like mosquitoes to control the spread of disease. On one hand, that sounds like a desirable thing, and on the other hand, I think one, again, has to think about potential for unintended consequences of releasing a system like that into an environmental setting where you can't predict what might happen."

The world may be paved with good intentions, but unintentional results are always around the corner.

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Value-Based Contracting

The Quest to Measure Up

Michelle Maskaly, Senior Editor

Outcomes-based contracting could be a potential game-changer in linking drug cost with value, boosting healthcare efficiency, and ensuring that appropriate patients benefit from innovative medicines. But several complex challenges remain in the bid to make this model a mainstay.

12

Pharma: Meet Your New Neighbors

Lisa Henderson, Editor-in-Chief

Executives from diagnostics, payers, pharma, and patient care companies recently got together to share stakeholder insights on outcomes-based contracting.

14

(L-R) Marc O'Connor, of Curant Health; Jerry Conway, of CDx Diagnostics; and Harry Vargo, of Aetna, pose after taking part in a recent panel at the CBI Outcomes-Based Contracting conference in Philadelphia (Photo: John Halpern). Not pictured, but part of the panel discussion, was Sachin Kamal-Bahl, of Pfizer.

Risk Sharing, Italian Style

Julian Upton, European and Online Editor

With Italy's system of outcomes-based agreements now well-established, the world's major markets will be studying the country's progress in the area more closely, as new disruptive forces in healthcare come increasingly to the fore.

18

'Outcomes' Deals: A Look Inside

Christen Harm, Associate Editor

13

Tech Dive in OBC Waters

22

Market Access

Innovating Pharma Pricing Model

By Juan F. Rivera and Caitlyn Macdonald

Drawing from implementation lessons and successes in other industries, possible strategy shifts to pharma's pricing playbook are explored.

24

Executive Profile

A Bold Path Etched in DNA

Michael Christel, Managing Editor

Markus Warmuth, CEO of cancer genomics company H3 Biomedicine, speaks with *Pharm Exec* about being part of a new wave of biotech business leaders, who let the science chart the course.

30

NEWS & ANALYSIS

Washington Report

8 Public, Policymakers Seek Full Pharma Disclosure
Jill Wechsler, Washington Correspondent

Global Report

10 Showdown Approaches On Europe Research Incentives
Reflector, Brussels Correspondent

STRATEGY & TACTICS

Commercial Strategy

35 The Personalized Genetic Profile: It's Time to Align
By Craig Wylie and Prashanth Prasad

INSIGHTS

From the Editor

3 The Law of Unintended Consequences
Lisa Henderson, Editor-in-Chief

Back Page

51 Setting the Standard in Medical Affairs
Michelle Maskaly, Senior Editor

Correction

In the article "Image Fix: Lessons from the Field," published in the February 2018 issue of Pharmaceutical Executive, the company affiliation given for Mark Alles was incorrect on second reference. Mr. Alles is the CEO of Celgene; he is not affiliated with Shire.

Country Report: India

38 Pharmacy to the World?
Focus Reports, Sponsored Supplement

The global importance of the Indian pharmaceutical industry and the affordable generic drugs it produces is indisputable. But despite its evolving international role, India's domestic healthcare system remains underperforming and undercapitalized.

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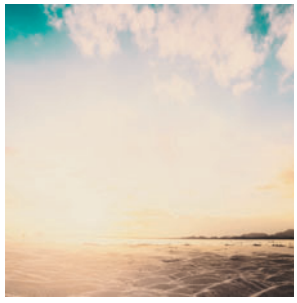

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■ This is the type of information that helps us to make informed business decisions, I appreciate you sharing.

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■ The list of obstacles keeps growing for #bigpharma: Pharmaceutical Executive's Jill Wechsler says 2018 could prove to be a "tumultuous year" for the industry. #HEOR #HealthCare #ACA #Pharma

HealthEconomics.Com, @www_healthecon, 1/9/2018
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WHERE SPECIALTY PHARMACY MEETS

Full Disclosure Demanded for Pharma Industry

The public and policymakers seek more transparency in pricing and product development

There's a mounting clamor for an end to the secrecy surrounding prescription drug pricing, promotional activities, regulatory decisions, and research findings. Stakeholders on all sides believe that more information on drug discounts and rebates is key to reining in payer and patient outlays for medicines (see sidebar on facing page). States are expanding provisions in the Federal Open Payments or "Sunshine" program that tracks industry payments and gifts likely to influence prescribers. And more timely and complete information on product safety aims to prevent patient harm, as do efforts to make drug labeling more informative.

The FDA recently adopted a policy to inform the public more quickly about adverse events and product recalls and the agency will watch to see if that generates unwarranted alarms or gets high-risk products off the market more effectively.

The full disclosure movement has gone global, moreover. The European Medicines Agency (EMA) seeks to provide more detailed clinical trial data, despite industry protests. And the China FDA recently proposed a plan to issue and disseminate more information regarding the regulatory review and approval of new drug applications.

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Revealing rejections

A main transparency issue involves access to information on the status of drug applications and FDA's decision-making process in both denying and approving submissions. Consumer activists and free market deregulators alike want to see the complete response letters (CRLs) FDA sends manufacturers that essentially delay or reject an application and outline what additional clinical or manufacturing information is needed to achieve approval. FDA currently posts summaries and some data when it approves a new drug or biologic for market. But current rules prevent agency disclosure of information on products that fail to pass muster, ostensibly to protect trade secrets or confidential information, and manufacturers want to keep it that way.

FDA Commissioner Scott Gottlieb addressed these issues at a January forum to discuss a "Blueprint for Transparency at FDA" issued in March 2017 by a group of experts organized by the Johns Hopkins Bloomberg School of Public Health (view: http://bit.ly/2EVoXpp). Gottlieb announced a new pilot to test the impact of FDA posting more detailed data from clinical study reports (CSRs) of approved drugs, asking that sponsors of nine new products voluntarily provide CSR data, protocols, and statistical analysis plans on their pivotal studies. FDA also aims to better track drug studies through the R&D process to review and approval by adding the ClinicalTrails.gov identifier (NCT) number to all clinical data submitted to the agency.

However, Gottlieb hedged about publishing CRLs, proposing instead to further explore FDA's authority to disclose these documents, while evaluating the feasibility of redacting and releasing a subset of CRLs that raise important public health issues. While he acknowledged that some information in CRLs might enhance the appropriate use of marketed products, Gottlieb noted that redacting proprietary information from these letters is burdensome and that much of the data may not be useful. Meanwhile, FDA officials emphasize that pharma companies are perfectly free to publish CRLs and other confidential information on their own and should do so, especially information important to patients and prescribers.

The Hopkins Blueprint further recommends greater disclosure of FDA's evaluation process for new drugs, generics, and biosimilars, including what products are in the review queue and why certain applications are not approved. The rationale is to help avoid research studies not likely to succeed, reducing costs and waste and unnecessary patient exposure to potential harm. The experts also want FDA to have authority to correct misleading information issued by manufacturers, such as incomplete factors underlying a CRL, and for the agency to disclose results from clinical trials for approved products when sponsors fail to do so.

These issues are not new and have been discussed and debated by FDA and stakeholders for years. The agency launched a Transparency Initiative in June 2009 under former commissioner Margaret Hamburg, which has led to FDA online "dashboards" that track agency actions and programs, including inspections, recalls, imports, and compliance actions. A "Drug Trials Snapshots" initiative posts data from clinical trials on products approved in recent years. FDA has expanded access to agency enforcement reports and adverse event data and has made its guidance development process more visible and efficient.

Sponsors, furthermore, are listing more studies on the ClinicalTrials.gov website, although the record is weaker for timely disclosure of research results for newly approved medical products. Under pressure to share more research data to avoid repeated errors and waste and support more efficient clinical research, biopharma companies are providing qualified researchers with access to confidential clinical research data. And some sponsors are pledging to publish new research reports only in open-access journals.

More timely and complete information on product safety aims to prevent patient harm, as do efforts to make drug labeling more informative

While policymakers and industry struggle to refine transparency, continued expansion of information available through the Internet, social media, and smart phones—some of it inaccurate or biased—erodes traditional controls over public disclosure of data on drug testing and production. Reports of adverse events and enforcement actions emerge online quickly, as do claims of both patient harm and of miracle cures. These developments raise questions about the value of limits on what FDA can or cannot disclose regarding products or manufacturers and highlight the importance of more forthright industry disclosures about marketing and results. PE

More sunshine on prices and rebates

The black box environment surrounding drug pricing, rebates, discounts, and coverage policies is under attack on all sides as policymakers and consumers rail against skyrocketing drug costs. Multiple federal and state reform proposals seek to expand disclosure of manufacturer list prices, discounts to pharmacy benefit managers (PBMs), and "exorbitant" price increases, particularly for older, low-cost medicines. California and Nevada have enacted laws requiring manufacturers to disclose price hikes above certain levels, and Maryland proposes to establish a commission to set maximum reimbursement for expensive new drugs and those with excessive price hikes.

The Trump administration's budget proposal for 2019 seeks to shed light on drug pricing and reduce out-of-pocket outlays for seniors by requiring Medicare Part D plans to pass on to beneficiaries a portion of the discounts and rebates negotiated with PBMs. The budget also looks to alter reimbursement for drugs covered under Medicare Part B, and it proposes a demonstration that authorizes five state Medicaid programs to negotiate prices directly with manufacturers, utilizing closed formularies and an exemption from best price reporting.

A recent report on "Reforming Biopharmaceutical Pricing" from the White House Council of Economic Advisers (CEA) outlines the need to reform a number of opaque drug pricing issues, including how the Medicaid Best Price program actually may boost prices for commercial plans, that reimbursement for Medicare Part B drugs encourages doctors to prescribe higher-priced therapies, and Part D policies that raise reimbursement for certain medicines.

Pharma companies like the idea of plans returning rebates to beneficiaries as a way to defuse push-back against price controls, but are up in arms over another measure enacted by Congress that significantly boosts the portion manufacturers pay for coverage of drugs in the Part D coverage gap, or "donut hole." That change is slated to cost industry billions, while saving money for health plans and Medicare.

Showdown Nears on Europe Research Incentives

Scope of supplementary protection certificate (SPC) could change

What goes around comes around in keeping competitors away from profitable medicines, just as in anything else. And now Europe is locked in a battle over whether to roll back some of the protection it gave drug innovators in the last century.

It is a good bit more than a quarter of century since European drug industry bosses, fearful of the way that lengthening pre-approval processes were eroding their patents, started pushing European Union legislators to give them some relief. And it is just 25 years ago that they won the first in a series of victories, with the grant of a supplementary protection certificate that offered restoration of up to five years of a patent term. Over the intervening years, the supplementary protection certificate (SPC) has itself been supplemented by other EU legislation similarly intended to protect the rights of innovators to profit from their efforts—notably the orphan medicines scheme.

But in the coming weeks, the EU is going to have to decide if the degree of protection it has provided is really in the interests of patients and society—or just gives drug firms an easy ride. Some of the SPC could be shaved off. And the benefits under the orphan medicines scheme may be squeezed.

The driving forces include concern among national paying agencies and their government ministers about the costs of healthcare, growing public distrust of the drug industry's ethics, and a wider societal shift in attitudes to enterprise, innovation, and reward. All three elements came together in the influential conclusions reached by European health ministers in 2016 that it was time to review some of the benefits that the EU had been handing out.

New medicines may pose challenges "regarding the assessment of their added value, the consequences for pricing and reimbursement, [and] the financial sustainability of health systems," the ministers agreed. In particular, they pinpointed the need to ensure that incentives for innovation, including SPCs, data exclusivity, market exclusivity, and protocol assistance, were "proportionate"—and should not "encourage inappropriate market behavior of some manufacturers and/or hamper the emergence of new or generic medicinal products." And they noted concerns that "this system may be imbalanced and that it may not always promote the best possible outcome for patients and society."

Conversation advances

In consequence, ministers told EU officials to ensure a "fair distribution of incentives and rewards and if necessary consider revision of the regulatory framework." Nearly two years after that instruction was given, that is the task that health and industry officials in the European Commission are bringing closer to completion, with the publication due shortly of a comprehensive study. The stakes are high. And the discussions are generating a lot of heat.

As the European Public Health Alliance (EPHA) remarked recently, "For the Commission, the current study is too big to fail. That the EU ministers asked for it from the Commission sets a precedent which cannot be overlooked. Such a study was politically inconceivable three years ago. It underlines the severity of the affordability problems faced by health systems."

Organizations such as EPHA, with a tradition of skepticism about drug industry behavior, have lined up with those governments keen to rein in any "inappropriate market behavior" by drug firms—such as The Netherlands, which was one of the principal influences on those 2016 conclusions. Understandably, the research-based drug industry has been energetically arguing the case for retaining incentives as a necessary prompt for innovation. In the middle ground are EU countries—such as the UK and Germany—with strong domestic drug industries that help support jobs and exports, who defend the concept of an effective intellectual property environment "for supporting and promoting access to innovative, safe, effective, and quality medicinal products."

But the debates have become all the more complex because the increasingly powerful European generics industry has come out strongly in favor of chopping back the SPC—setting it on a collision course with its col-

REFLECTOR is *Pharmaceutical Executive*'s correspondent in Brussels

leagues engaged in research. Some of this was set out in *Pharm Exec*'s sister publication, *Pharmaceutical Technology Europe*, which in December highlighted the conflicting views on the impact of introducing a Bolar-style waiver to allow generic competitors to manufacture stocks prior to the expiration of the SPC on an original product they wished to copy.

The battle rages on with a seemingly endless stream of position papers, briefing documents, and backgrounders littering the streets of Brussels, each offering a further permutation on the consequences for jobs, sales, profits, research, and competition both within the EU and beyond, based on one or another option being adopted at the level of the EU or by national governments (archetypically, in the EU, decisions on what type of SPC waiver may be granted to generic firms is decided at the national level).

The Commission, which has been repeatedly accused of dragging its feet in completing its task, has even brought the public into the picture with the recent announcement of a consultation on the linked question of how the man in the street feels about EU support for orphan research—accompanying a targeted consultation of member states, NGOs, business, health technology assessment bodies, and academia, with a conference scheduled for early 2019.

So far officials are giving little away about which way they are leaning in this debate. A recent formal document indicated that their evaluation is covering the strengths and weaknesses of the incentive schemes, separately and combined, "focusing on the outputs/results in products catering for a real unmet medical need." It will include cost-benefit analyses of the overall effect and the specific effect on patients, industry, and payers, and will give "an insight on how the various incentives that are related to the legislation have been used, and the financial consequences," while "taking into account changing business models." The Commission says it will then have a better evidence base from a "public health and a socio-economic perspective" on the desirability of any changes.

In the coming weeks, the EU is going to have to decide if the degree of protection it has provided is really in the interests of patients and society—or just gives drug firms an easy ride

Meanwhile, the conflict between patent-holders and generic companies continues unabated at the level of individual firms. Sandoz secured a small victory in January in its bid to break through Johnson & Johnson's SPC on its Prezista HIV treatment so that it can start manufacturing it in advance of a generic launch. Its action in a UK court has led to a referral to the European court for a ruling on the scope of the SPC. The ruling should bring some clarity to a very grey area—and since Prezista's sales worldwide are close to $2 billion, the significance of the outcome will have immediate as well as general implications.

Wide debate

The eddies of the European debates on incentives are reaching the other side of the Atlantic too. The US pharma industry has asked the Trump administration to muscle in to shore up IP protection in Europe. The Washington-based drug industry association, PhRMA, says it is "very troubled by the potential future direction of an ongoing European Commission review of protections and incentives for innovative biopharmaceuticals." It has called on the US Trade Representative for "a focused effort by the US government to promote strong intellectual property protection and enforcement policies throughout the European Union and its member states." The review "could result in proposals to reopen critical parts of Europe's intellectual property framework and potentially weaken existing incentive mechanisms that support biopharmaceutical innovation," it warns, with damaging effects on "American exports and jobs."

The intervention has not gone down well with Europeans seeking radical change in the current EU framework. The Netherlands-based Health Action International group, a vigorous civil society organization, described it as an attempt at "intimidating EU institutions" and "the latest in the string of attacks, originating from the US, on global efforts to improve access to medicines." And Yannis Natsis at EPHA said the PhRMA action "is alarming and equates to bullying on behalf of pharmaceutical companies." He said: "Governments should not be dissuaded by these sort of threats." PE

The Quest to Measure Up

Outcomes-based contracting continues to gain traction as a potential game-changer in linking drug cost with value, boosting healthcare efficiency, and ensuring that appropriate patients benefit from innovative treatments. But several complex strategic and operational challenges remain in the bid to make this model a mainstay

By Michelle Maskaly

There is little argument that the trend toward so-called value-based healthcare is growing—with no signs of letting up. At the center are an increasing number of reimbursement arrangements struck between payers and pharmaceutical manufacturers based on the quality a treatment provides in the hospital/real-world settings rather than simply the volume of care it delivers. Deals established under these frameworks offer potentially promising ways to support patient access to innovative and expensive-to-produce medicines, such as genetic therapy and precision drugs. Outcomes of therapy effect are measured from payer databases using pharmacy and medical claims.

With more value- or outcomes-based contracting agreements springing up between major insurers and big pharma players, a prevailing sentiment is that these arrangements, on a larger scale, will help lower prices of costly drugs, and, in turn, help stem the tide of soaring US healthcare spending. However, there are a number of aspects to this model—and its ability to achieve those results—that people don't always think about when they see a headline relating to the topic.

Examples include the fact that outcomes data are not immediate and take a while to assess, the behind-the-scenes work that goes into collecting the data, and the reality that in many cases, various stakeholders are fundamentally not set up to process these types of analytics.

In short, outcomes-based contracting is still a fairly new concept to those involved, with plenty of kinks still to work out. While it may be the future of healthcare, the move to value-based care is not going to be a quick fix for a number of reasons. "If you look at the healthcare ecosystem, some of the data that is currently available wasn't even available just a few years ago to determine these types of statistics," Ralph Marcello, national biopharmaceutical leader, life sciences, at Deloitte, told *Pharm Exec*.

Slow adoption

Critics argue the industry has been slow to adopt value-based contracts. But experts say that no matter how much industry may want to participate in this type of reimbursement, it fundamentally can't happen overnight, even if it's a high priority on a C-suite executives' agenda.

"There are real hurdles from a strategic to operational standpoint," says Marcello. "It starts with, 'do I have the resources to dedicate…the capabilities to do this?'"

The answer to those questions is causing pharma companies to reallocate resources, build out new departments to manage this, and make a play for top data scientists who would typically be heading over to companies like Facebook, Amazon, or Google.

Value-based care is creating a competitive marketplace for that type of talent, Marcello explains, because to make a reimbursement system based on value successful, pharma companies need people who possess the knowledge to cut through all the data in a meaningful way—to ultimately reveal insights into

FAST FOCUS

» One in four health plans now include at least one outcomes-based contract (OBC) with a drugmaker, according to a survey by Avalere Health. The survey also found that 70% of health plans report they have favorable attitudes toward OBCs.

» According to an October 2017 report by the *Journal of Managed Care & Specialty Pharmacy* (JMCP), in which it surveyed 27 experts, including US payers and EU5 national payers, interviewees generally expected that two to three times more OBCs would be implemented in the next five years than in the previous five years. A key driver in the US included the movement toward accountable care.

» Experts at *Health Affairs*, in a published report last year, cited five fundamental requirements for developing and executing an OBC: Leadership commitment, discernment in drug selection, appropriate use of surrogate endpoints in outcomes measurement, navigating data and operational feasibility issues, and weighing government price-reporting factors.

what tends to be very complicated data.

End-to-end evidence management and building real-world data capabilities are two of the largest potential growth areas Marcello sees within his biopharma clients. By having their own data, it not only gives companies a seat at the table when the value-based conversation comes up, but can also be a vehicle to reduce costs, which is a win-win for everyone involved.

"Our healthcare system structure is traditionally fee for service, and as we move from fee for service to value-based, there needs to be a restructuring, not only in how decisions get made, but where risk is shared in the healthcare system," says Marcello.

Complicating factors

In addition to the internal hurdles that pharma companies face when it comes to value-based care, there are a number of outside factors they have to consider, which can fluctuate dramatically. For example, does the healthcare provider have the capabilities to collect the information? What happens when patients don't adhere to the therapy that is prescribed, and how is that found out and factored in?

Then, there are more complicated questions, which are not exactly new to those focused in this space, but are still debated. Those include how does one define an outcome and who owns, or is responsible for, all this data?

Collaborations are key

Working closely with a trusted partner can be vital to making value-based contracts effective. In May 2017, Optum, the health services business of UnitedHealth Group, and Merck & Co. announced a collaboration to

All in on Outcomes: Sampling of Industry Deals

Outcomes-based contracts are agreements wherein drug manufacturers and health insurers strike monetary reimbursement deals linked to a therapy's real-world performance. This chart presents a sampling of such arrangements currently in effect, grouped predominately by payer.

Biopharma company	Drug	Outcomes measured
Aetna		
Merck & Co.	Januvia and Janumet	If members with type 2 diabetes don't meet certain goals, Merck will pay a rebate to Aetna that increases, dependent on amount of patients who miss the targets. If patients obtain goals—measured by analyzing data from Aetna's claims database, Merck will not make any more payments to Aetna.
Novartis	Entresto	If the rate of heart failure hospitalization of patients on Entresto exceeds a prespecified threshold, Novartis will reduce the price to payers.
Cigna		
Merck & Co.	Januvia and Janumet	Merck pays a higher rebate to Cigna when members report certain blood-glucose levels.
Novartis	Entresto	If the rate of heart failure hospitalization of patients on Entresto exceeds a prespecified threshold, Novartis will reduce the price to payers.
Amgen	Repatha	If Cigna's customers aren't able to reduce their lipoprotein cholesterol (LDL-C) levels at least as well as what was experienced in clinical trials, Amgen will discount the cost of the drug more. If Repatha meets or exceeds expected LDL-C reduction, the original negotiated price remains.
Sanofi/ Regeneron	Praluent	If Cigna's customers aren't able to reduce their LDL-C levels at least as well as what was experienced in clinical trials, Sanofi/Regeneron will discount the cost of the drug further. If the drug meets or exceeds expected LDL-C reduction, the original negotiated price remains in place.
Gilead Sciences	Harvoni	In this deal, Harvoni is the only preferred brand prescription drug treatment for customers with hepatitis C genotype 1. Gilead agrees to pay Cigna additional rebates if Harvoni cures less than 95% of Cigna's patients who take it.
EMD Serono	Rebif	This deal helps patients with multiple sclerosis prevent relapses. Results will be measured in part by the percentage of hospitalization and emergency room visits that are avoided through the use of Rebif.
CVS Health		
Amgen	Repatha	The net price of Repatha is linked to expected LDL cholesterol reductions and anticipated appropriate patient utilization.
Harvard Pilgrim Health Care		
Eli Lilly	Trulicity	If fewer Trulicity patients reach their hemoglobin A1c (HbA1c) target (less than 8%) compared with those using other GLP-1 drugs, Harvard Pilgrim will collect bigger rebates from Lilly. If more Trulicity patients hit their goals, then the drugmaker scores a higher net price for the medicine.
Novartis	Entresto	Harvard Pilgrim will receive a discount from Novartis if Entresto (sacubitril/valsartan) does not demonstrate an agreed-upon level of reduction in hospitalizations for congestive heart failure.
Amgen	Repatha	An "enhanced discount" in the form of an additional rebate if the reduction in LDL-C levels for Harvard Pilgrim members is less than what was observed in clinical trials.
	Enbrel	A two-year contract, where the insurer will pay less for the drug if patients score below certain levels based on six criteria that will be measured and then crunched by "an effectiveness algorithm." The measurements include patient compliance, switching or adding drugs, dose escalation, and steroid interventions.
AstraZeneca	Brilinta	Harvard Pilgrim will be monitoring certain criteria in patients following discharge from hospitalization for acute coronary syndrome. The outcome will focus on measuring the reduction in hospitalizations for repeat acute coronary events for patients on Brilinta as compared to patients on another oral antiplatelet therapy. If the drug fails to meet the agreed-upon outcomes criteria in real patients, Harvard Pilgrim will be charged a lower amount. AstraZeneca and Harvard Pilgrim agree that the health plan will be charged for medicines based on value to the patient, and not solely on volume of medicine sold.
	Bydureon	Harvard Pilgrim will measure HbA1c levels in patients with type 2 diabetes and evaluate the ability of patients who adhere to Bydureon to get to a predetermined HbA1c goal. If the drug fails to meet the agreed upon outcomes criteria in real patients, Harvard Pilgrim will be charged a lower amount. AstraZeneca and Harvard Pilgrim agree that the health plan will be charged for medicines based on value to the patient, and not solely on volume of medicine sold.
Centers for Medicare & Medicaid Services (CMS)		
Novartis	Kymriah	Novartis will only receive reimbursements for Kymriah if patients respond to it after the first month of treatment.
Prime Therapeutics		
Boehringer Ingelheim	Jardiance	As part of its CareCentered Contracting™ program, Prime Therapeutics, a pharmacy benefit manager (PBM), looks at members' experiences holistically. This agreement will focus on the total cost of care for members taking Jardiance and comparing that to the total cost of care for patients taking other diabetic medications. In this manner, Prime can better evaluate the combined cost of pharmacy and medical on select therapies and its impact on overall health costs for the members it serves.

develop and simulate the performance of contractual reimbursement models in which payment for prescription drugs is aligned more closely with patient health outcomes.

Through a multi-year collaboration on a shared "Learning Laboratory," the two companies planned to explore value-based and pay-for-performance models, known as outcomes-based, risk-sharing agreements (OBRSAs), and their potential for broad adoption among payers, pharmacy benefit managers (PBMs), and drug manufacturers. The initiative involves the use of real-world data to co-develop and test advanced predictive models and codesign OBRSAs to reduce clinical and financial uncertainty with respect to payment for prescription drugs.

But, to Marcello's point, these collaborations, and the data they'll measure and the results they'll deliver, will take time. "Companies are investing in capabilities to extract real-world evidence of how a product actually performs in the market," he says. PE

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Pharma: Meet Your New Neighbors

Executives from diagnostics, payer, pharma, and patient care companies converge to share the inside scoop on outcomes-based contracting

(Left to right) Marc O'Connor, of Curant Health; Jerry Conway (moderator), of CDx Diagnostics; and Harry Vargo, of Aetna. Not pictured, but part of the panel discussion, was Sachin Kamal-Bahl, of Pfizer. *Photo/John Halpern*

By Lisa Henderson

The title of a recent panel, held at the CBI Outcomes-Based Contracting conference in Philadelphia late last year, was "Create a Win-Win Scenario—Linking Contracts to Cost-Savings Evidence and Better Patient Outcomes." During the panel, and in additional interviews, the speakers shared their insights and thoughts on the new world of outcomes-based contracting. Jerry Conway, executive VP of managed care at CDx Diagnostics, and formerly VP of payer relations and reimbursement at Foundation Medicine Inc., served as moderator. Harry Vargo, director, trade relations, for Aetna; Sachin Kamal-Bahl, vice president and head, Center for Health Systems Innovation and Leadership, Pfizer; and Marc O'Connor, principal and chief operating officer for Curant Health, a provider of personalized care management and medication management services, participated in the panel discussion.

The following are some insights from the industry neighbors, and key stakeholders in the value-based care equation, on navigating this new terrain.

#1: Dialogue, not dictate: The payer perspective

VARGO: We are trying to change the way we currently partner with pharma. We are looking at a better approach to healthcare—one that provides a better impact for our patients with the best possible outcome for their medications and their overall healthcare.

We are being flexible, we are willing to change. This is different than what we've ever done before. Previously, pharma manufacturers and healthcare

was transactional. "We have your drug, we cover your drug, we pay for your drug." Outcomes contracting is changing that. I like to say when we start talking with manufacturers in these outcomes-based discussions, "We are not trying to prove your drug does not work." We are not trying to prove that. We are just trying to get the best possible outcome for our members and patients.

One thing to keep in mind, there is not a wrong answer, there's not a wrong metric. It's really what you are looking for and the pharma manufacturer. It can be different from one pharma and one health plan. What might be good for Aetna, might not be good for someone else. And what might be good for Pfizer, might not be good for Merck or Lilly.

[It's important to] start to have that dialogue. It may not be the perfect contract in the beginning. But as that dialogue continues and that trust builds, you are going to bridge to something better and better.

The dialogue will bring up obstacles and then you can talk through them. We've grown substantially in the last two-and-a-half years. And what the manufacturer ultimately brings to us as a value proposition for the product may not be what the health plan is looking for, not what Aetna is looking for, but in that dialogue, you will find something that you can agree on. So, to me, in that dialogue is the key.

#2: A triple win?

KAMAL-BAHL: Think of it as a funnel, with the patient at the large end. And that the first question one should ask is—does it make sense for the patient? The next question should be whether or not it is good for the system at large. The third question should be how do we create a win/win for other stakeholders? This is a proposed structural and logical way to think of the question at hand. It should start though with the question of whether or not it makes sense for the patient.

#3: Who is best-placed to achieve better outcomes?

O'CONNOR: This may sound like an infomercial for my company, Curant Health, or my industry, but we have a more meaningful way to engage with patients and providers than what a PBM (pharmacy benefit manager), a hub, a specialty pharmacy, or a population health organization can do. Additionally, we can assume risk as part of an outcomes-based contract, along with the manufacturer. Medication management services companies do two things that are very challenging for manufacturers or payers to do. The first is we have those discussions with providers that go outside of the awareness phase. Outside of "here's the label, here's the drug, here's what it does." We provide additional line of sight in the adoption, compliance, and persistence phases, when it's challenging for manufacturers for a variety of reasons, to have those discussions with providers. And then the payers are always challenged in how they engage the provider and the patient. They do engage some patients via support resources, but deep patient support is challenging for them because it's not part of the payers' core focus.

"The first question one should ask is—does it make sense for the patient? The next question should be whether or not it is good for the system at large."

— SACHIN KAMAL-BAHL, PFIZER

Number two—and most importantly—is having an entity that will help determine and deliver improved health outcomes in a way that is meaningful for all stakeholders. When patients are engaged, adherent to their therapy and experiencing improved outcomes, not only do you see improvement in contract metrics between the payer and the manufacturer, but other metrics improve as well. Adoption and compliance numbers go up for the manufacturer. They have a deeper connectivity with the patient. It's all about rebate minimization and it provides a way to have a better relationship with the patient without the manufacturer's legal department having concerns. Most importantly, patient outcomes improve for that disease state.

We are focused on improving the outcomes of the patients—it's a care model to engage the patient and the provider. Outcomes are value that we can sell and that we go at risk on. Our model is based on the alignment of all the healthcare stakeholders. That changes everything.

VARGO: Aetna has an integrated platform; we have both medical and pharmacy, so it's a little bit easier for us because we have both. But with some that have the medical and some that have the pharmacy, it could be a little more difficult because that seamless approach or real-time data isn't going to be there to help point to outcomes.

Marc O'Connor, principal and chief operating officer for Curant Health, comments during the panel discussion at the CBI Outcomes-Based Contracting conference. *Photo/John Halpern*

#4: Diagnostics and genomics as a pragmatic solution

CONWAY: Validated comprehensive genomic profiling (CGP) has emerged in recent years as a pragmatic solution that is central to successful outcomes-based contracting in oncology.

In oncology, the top three most pressing challenges faced by payers are:

- Control of rising cancer specialty drug costs.
- Control of overall cancer care costs.
- Balancing treatment standardization with personalization.

Payers are responding to these challenges by implementing a number of alternative payment models, or APMs (e.g, clinical pathways, medical home, and bundled payments), that are designed to shift from a "pay for volume" to a "pay for value" or "real-world outcomes-based" paradigm.

Precision oncology, or the clinically and financially efficient use of genomically matched, targeted, and immunotherapy treatments and clinical trials, is evolving as a potentially important starting point for cancer care within successful APMs.

CGP drives successful utilization and cost-management strategies to effectively address the top three challenges identified by payers in oncology, and, therefore, should justify the necessity of payer coverage and value-based payment today when used in the appropriate clinical setting.

#5: See the physician, not the prescriber

VARGO: Regarding the physician, none of these value-based contracts should have any influence on what they are prescribing. I don't think that's the idea. We have formularies, we have everything around tiering and status and precertification. I will tell you that value-based contracting should not be any type of an impediment for a physician. The idea of value-based contracting is about making sure that we are seeing agreed-upon, meaningful results for our patients.

We haven't had any need to gather extra data or information from the physician or prescriber about their patient and outcomes. If there came a time when we did, we would go to the manufacturer and talk through it. Certainly, we don't want to put undue onus on physicians or even on our patients.

We have had situations where we didn't meet the targets. For example, it may have been a specific lab value. There have been outcomes where not 100% of lab values have been there, but it was enough that we knew we were getting the result that we wanted. That wasn't a deal breaker because the data was there.

"When patients are engaged, adherent to their therapy and experiencing improved outcomes, not only do you see improvement in contract metrics between the payer and the manufacturer, but other metrics improve as well."

#6: Think long-term, meaningful outcomes

VARGO: If your intention is to do a value-based contract, you have to look at this as multi-year. You are going to put a lot of effort and a lot of discussion into this. Our intention when we start going down these roads is to look at it as a multiple-year [relationship]. And you almost have to. If you go shorter than that, you are not going to get that real, true value of that partnership.

Some drugs have price tags of 400, 500, $600,000 and that's somewhat hard for us to swallow on the pharmacy side; but that is our job as a payer—to pay for product. But that shouldn't be the ultimate reason why we don't pay for a product. We evaluate medicines as they come. We evaluate these contracts on a daily basis, and I'm not exaggerating, we have been fortunate that we have a lot of manufacturers that want to work with us; we have a lot of discussions. And we work internally with our team. We have a health economics person that looks at the contracts and we take them to our clinical team and medical directors to make sure there is meaningfulness in that outcome. That is really the key. That there is meaningfulness to the outcome and value to our members—and, in this day and age, simple to administer. If the administration of these is very in-depth, that can be very difficult.

#7: How do you best provide contracting clarity?

KAMAL-BAHL: All of this hinges on agreement on what it is we are measuring, who measures it, when, who pays for those measurements to be done, who manages the measurement process, and what happens when there is a disagreement on those measurements. The enabling factors underlying this are pretty basic—it's trust and the willingness and desire to further the movement from volume to value.

Maybe there is no disagreement amongst stakeholders on this point, but we can do a better job on providing clarity that can help further the dialogue.

#8: More on data

O'CONNOR: Healthcare stakeholder incentives are going to start aligning. This is the first foray into outcome-based medicine practice. That connectivity with the data must happen, and not just the quantity of the data…big data is okay, but unless you are taking the individual data elements to act on to improve the outcome for the patient, the data isn't meaningful. You need to find the data that is important for the particular drug in question, and its target population, to gauge how it's affecting each stakeholder. To start, though, we must get our heads around what's really needed from big data. Only then will we be able to build on the incentives.

> "That is really the key, that there is meaningfulness to the outcome and value to our members—and, in this day and age, simple to administer."

What manufacturers need to do—or have access to—is the collection of granular outcomes data at the patient level. Manufacturers have a lot of data on physicians and their professional and personal details, but the need for data is going to shift to data that's about the patient.

#9: Unintended consequences

O'CONNOR: It is too soon to tell for sure, but my gut tells me this is very disruptive. There are going to be a lot of impacts on the way complex patients are managed and this is going to step on the toes of a lot of companies and their stakeholders. Again, it may not align with their incentives. So, I don't know what that looks like, but there is no question there are going to be some bumps in the road. We just don't know what they are yet.

VARGO: There's always the opportunity for downsides or risk. But if you focus that it is about the health and outcomes for our patients, and treat our patients to make sure they are getting the best outcomes, medication, etc., then that is the goal.

KAMAL-BAHL: The move from volume to value is real. The risk of not trying to move the system in this direction is larger than any risk of experimenting and innovating in this space. We have to give this a real shot and we have to be smart about how we go about creating this shift. The adjustments in the short-term will have a positive impact in the long-term.

CONWAY: This isn't an unintended consequence, but another area to think about. CGP also has the potential to provide biopharma-sponsored clinical trial alternatives to patients when covered drugs are not an option (i.e., not paid for by payers), as well as accurately identifying clinically relevant mechanisms of resistance or even a complete lack of genomically matched treatment options to help eliminate futile or potentially harmful treatment (cost avoidance). PE

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Risk Sharing, Italian Style

Amid contrasting views on the success of the now well-established system of outcomes-based agreements in Italy, further demands on global healthcare budgets will likely point to their adoption on a wider scale

By Julian Upton

In the US and most of Europe, there is still a tentative approach to outcomes-based (or performance-based) contracts between pharmaceutical companies and payers. In Italy, however, such agreements have been in operation since 2006. Centrally managed through a web-based platform by AIFA (Agenzia Italiana del Farmaco), there are four types of outcomes-based agreements in Italy, defined as:

- **COST SHARING**, for which manufacturers offer a full or partial discount for initial cycles of treatment for eligible patients.
- **RISK SHARING**, for which manufacturers offer partial reimbursement (usually 50%) for patients not responding to treatment.
- **PAYMENT BY RESULTS**, the most widely adopted of the agreement types in Italy, which requires total reimbursement to the payer by the drug manufacturer for non-responding patients (and where the process of "defining the parameters of responsiveness favors manufacturer," according to Fabrizio Gianfrate, Professor of Health Economics at the University of Ferrara).
- **SUCCESS FEE**, the most recently introduced agreement, where payment is due only for patients who respond to treatment.

While the Italian system is well established, Livio Garratini and Alessandro Curto pointed out in 2016 that, even after a decade, no report published by AIFA had "yet included relevant clinical outcomes on drug subject to [outcomes-based agreements]." The authors concluded that "more data are needed to thoroughly assess their effectiveness."[1] With definitive conclusions on the success of the system still out of reach, then, expert opinion varies, with Italian academics such as Garratini and Curto remaining skeptical, while others, such as Gianfrate maintain a positive assessment of the scheme's impact.

Industry perspective

Andrea Landi, consultant and project manager in market access at ICON, told *Pharm Exec* that outcomes-based agreements in Italy have been "quite successful." He explains: "Despite the inherent challenges in administrating and managing these schemes, a lot of high-cost products have been reimbursed under this model. It has helped to create a more collaborative environment for payers and manufacturers and to focus on the real value of products and the collection of real-world outcomes." Gianfrate adds that the majority of pharma companies "welcome the agreements" because they expedite both the price negotiation process and the road to reimbursement. He notes that they have enabled companies to maintain a higher price. "As Italy is a reference-price country for many smaller countries—those in Eastern Europe, for example—maintaining a higher price here translates to achieving a higher price elsewhere."

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In 2015, oncology drugs accounted for 80% of outcomes-based contracting agreements in Italy.

The administrative challenges that Landi highlights, however, remain something of an obstacle to the smooth running of the risk-sharing system. In Italy, hospital consultants are required to complete four online forms for each drug covered by an outcomes-based agreement, in order for the hospital pharmacy to validate prescriptions. The pharmacy then completes another form to release the treatment. If a patient is assessed as a non-responder, the pharmacy applies for reimbursement from the drug manufacturer, who can evaluate the request before accepting or rejecting it and formulating a payback proposal. Landi admits that "doctors are not inclined to spend a lot of time filling in forms after assessing the patient's response," and that there have been delays in requesting refunds from the pharma company. Even Gianfrate concedes that, "if I should find a weakness in the system, it is in the rate of update of data by clinicians at the local level."

Landi also points to cases of "misalignment," stemming from questions about "who is paying for the drug and who benefits from the agreement." He explains: "Some regions are responsible for paying the cost of hospitalization, but AIFA is responsible for the national drug budget. If an agreement hinges on hospitalization savings, then the region should benefit from it, but this is an area where there has been some confusion."

Nevertheless, adds Gianfrate, the scheme is adopted at the national level "and all regions should follow the national decision."

For Landi, the industry has to take its share of responsibility for addressing questions of misalignment. Where Italy has national drug registries for data collection, information regarding hospitalization, for example, is collected at the regional level. "If a company wants to use the hospitalization outcome for its product, it's very important that it is prepared to make a significant effort to unify the two data flows, which requires investment," he says. "This is an important aspect that I don't think companies have been exploring enough."

Companies have also sometimes struggled to communicate the value of their products and these agreements to the relevant stakeholders, experts point out. The industry should be clear on defining the success criteria of a product, says Landi. "Some endpoints are not easy or objective to measure, so it's very important to have a clear endpoint to define success for the product."

Pharma companies should also carefully consider the risks associated when negotiating these types of agreements in Italy. "They can be like a double-edged sword, on the one hand allowing for higher list prices and potentially quicker access, on the

other, carrying inherent risks," says Landi. He notes that all reimbursement contracts in Italy are limited in duration, in the sense that the contract is usually valid for two years and then has to be rediscussed by the parties. If, during these two years, a performance scheme has demonstrated that the real-world performance of the product is poor, Italian payers are likely to leverage that information in the renegotiation, with a subsequent negative impact on the terms of the new contract and relationship with the authorities.


Andrea Landi

"So it is also fundamental for manufacturers to carry out a proper due diligence, and consider the long-term strategy and possible exit routes when planning and executing these agreements," Landi explains.

> "If a company wants to use the hospitalization outcome for its product, it's very important that it is prepared to make a significant effort to unify the two data flows, which requires investment."

Access to cancer treatments

So far, outcomes-based agreements in Italy have focused on high-cost oncology drugs (in 2015 cancer therapies accounted for 80% of such agreements).[2] As Landi points out, these arrangements are easier to manage for oncology indications, as opposed to chronic diseases such as diabetes. For patients, they have allowed for quicker access to treatment, he says; almost all the high-cost oncology drugs are currently available in Italy. For the industry, they offer an opportunity to overcome the clinical uncertainty engendered by "weak-evidence packages," limited patient numbers, and limited observational studies associated with oncology treatments. Importantly, the success for cancer treatments is more clearly measurable than success for products targeting chronic indications such as diabetes.

For payers, says Landi, "the optimal endpoint in oncology is survival, which is easily measurable, objective, clear, and simple. In chronic indications, such as diabetes, this is usually not the case." Levels of hemoglobin A1c (HbA1c), for example, which is the standard endpoint assessed in diabetes trials and also the main criterion considered by clinical guidelines, is not only affected by the drug but also by external factors such as diet and physical activity. Thus, says Landi, "it is very difficult to objectively attribute the therapeutic success to the specific drug, which complicates the application of any performance-based scheme." While quality-of-life considerations in oncology are clinically important, "from a payer perspective, they are very much secondary in Italy to the objective of prolonging overall survival," adds Landi.

Ultimately, he says, outcomes-based agreements have been extensively applied only in oncology, as they may make more financial sense for high-cost indications, "both from the payer side, if the expected savings from the agreement are higher than the cost of supporting the infrastructure to sustain the agreement, and from the manufacturer side, when the expected increase in volume and revenues is higher than any potential contribution that the manufacture has to provide for the implementation and management of the infrastructure."

Overall success—or failure?

Highlighting the mismanagement and procedural problems deriving from the application of three of Italy's outcomes-based agreements (payment by results, risk sharing, and cost sharing), Andrea Navarria *et al.* concluded in 2015 that "the amount of money that is actually refunded through the application of such schemes is really trifling;" as of 2012, the authors noted, the amount of money refunded through the reimbursement procedures was €121 million ($151 million) out of a total of €3,696 million ($4,612 million), just 3.3%.[3]

Landi agrees that, from the payer perspective, problems in collecting the refunds have hindered the financial success of the agreements. But he points to AIFA's 2013 introduction of the success fee agreement as a move to combat the administrative issues. Success fee differs from payment by results (the most popular agreement in oncology) in that the manufacturer initially provides the

product for free and the National Health Service pays only after the criteria for efficacy have been met. "In this way, the administrative risks are shifted to the manufacturer," says Landi.

Landi continues to stress the positive aspects of outcomes-based agreements, highlighting their flexibility and importance to the value question. "From a theoretical perspective, the model allows to pay for the value of a product in specific indications," says Landi. "In this way, you can have an indication-based pricing approach; at list price, you pay the same amount for a product, but you pay a different net price depending on what indication it is used for, so you pay for the real value of the product in specific indications."

Fabrizio Gianfrate

Gianfrate is more strident in countering the criticisms. "How do you calculate the failures? We don't have the evidence for the other side," he says. "We do know that many drugs have been approved with outcomes-based agreements. And we know that, without them, the price negotiation process would be prolonged and many negotiations would not end in an agreement. They have offered the way to a solution between the manufacturers and the drug agency."

> "How do you calculate the failures? We don't have the evidence for the other side."

Where he likens the traditional method of reimbursement to a payer buying a lottery ticket before the results are drawn (i.e., paying for a probability of success), Gianfrate compares outcome-based agreements with the payer buying the ticket after the results are known (i.e., paying for already-acquired results).

From an industry perspective, as Guy Sherwin, ICON's principal consultant, pricing and market access, points out, there are three underlying objectives for manufacturers when launching a new drug: achieving an optimal price, ensuring broad access to the right patients, and doing so in a timely manner. In this context, these types of agreements are a useful tool to facilitate coverage of a new drug, where reaching a mutual consensus between stakeholders can be challenging. Sherwin explains: "They can mitigate financial risk while maintaining an optimal price point, help address concerns around clinical/performance uncertainty by ensuring linking payment to an outcome, and, lastly, ensure that the treatment reaches patients in a timely manner without significant delays to coverage."

Italy and beyond: The outlook for outcomes-based deals

There has been some pullback from outcomes-based agreements in Italy over recent months, with AIFA opting for more financial-based agreements that function on price/dose discounts, but these decisions have been related to specific cases that have better lent themselves to the financial arrangement, or to products whose value and efficacy have been monitored under previous agreements. Esbriet (pirfenidone), for example, was the first product negotiated under the success fee, but after two years the drug was renegotiated, with the performance-based agreement replaced with a higher net discount. As Landi explains, "Once payers have data supporting the efficacy of products in the real-world population, they may prefer a simpler agreement to improve manageability and budget predictability." Thus, outcomes-based arrangements can pave the way for future financial agreements.

In the future, with the global immuno-oncology pipeline set to deliver more immunotherapies, outcomes-based agreements are likely to feature more prominently, not just in the Italian healthcare system, but far beyond. As Sherwin explains: "There are a number of disruptive forces affecting the industry and we're seeing a number of trends with innovative new therapies, for example, the recent launch of high-cost immunotherapies, which manufacturers are going on to develop in combination." If launched, the combined cost of using two or more high-cost drugs will critically impact payer budgets in Europe, Sherwin says. Eventually, this "will reach an inflection point, where healthcare budgets are not going to be sufficient for these combinations and there will have to be a degree of risk sharing," further opening the door to outcomes-based agreements.

He adds that there is a similar "magnitude of disruption" with the introduction of gene and cell therapies, which potentially provide a lifetime of

benefit and value, but require incredibly high upfront payments for a potentially large number of patients. "Payers' budgets, particularly in Europe, are not set up for this kind of financial requirement," says Sherwin. "Therefore, other types of outcomes-based agreements with novel payment mechanisms will be required."


Guy Sherwin

Improved digital capabilities present another disruptive force, says Sherwin, that will tackle the administrative problems that have surrounded not only the agreements in Italy, but the wider issue of collecting large amounts of data consistently and accurately in heavily fragmented healthcare systems both within and across Europe.

"As our data collection capabilities improve, and as other digital players such as Google and Amazon enter the market, there will be an increased ability to collect and analyze the data and enter into these type of agreements, where companies can more accurately look at the health outcomes that they are improving," says Sherwin.

For this to happen, however, the current focus in Italy, and more recently in the US, on specific endpoints may have to change. "I think the future lies with more focus on the improvement of overall health outcomes," says Sherwin. "It won't be about just monitoring progression-free survival or overall survival, but looking at the patient pathway as a whole and seeing where manufacturers can take greater ownership in delivering improvements. Consequently, pharma companies will need to change their business models, taking greater ownership of the care pathway and improving the overall health of specific patient populations."

Italy continues to journey through its second decade of outcomes-based agreements. As new disruptive forces in healthcare come increasingly to the fore, the world's major markets will be studying the country's progress in this area ever more closely. PE

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Tech Dive in OBC Waters

Dipping your toes into the oncoming wave of outcomes-based contracting (OBC), or value-based contracting, is not for the faint-hearted, but as noted in the previous articles, it is also unavoidable. Managing the tsunami of data necessary for realizing the key markers for contract support is not a barrier, but a definite challenge.

Bhaskar Sambasivan, senior vice president and global markets leader, Cognizant Life Sciences Business Unit, and Prasad Dindigal, senior director, Cognizant Life Sciences Consulting Practice, noted that the data necessary to support these contracts is there, but they are largely disparate and unintegrated. From claims, to the electronic health record (EHR), to clinical and prescription data, each stakeholder holds but one key.

"There is not one data source that will provide what is needed," says Sambasivan. "Different companies are tackling their data in different ways, from in-house systems to end-to-end outsourcing or licensing technology, or using a platform such as our TranZform, that runs over top of the data sources and performs the analytics. It's not a technology limitation. The platform, the technology and the data are already there. But having six or seven data sources, that is the challenge."

And while Cognizant is currently in talks toward using its platform to support value-based care data needs, Dindigal says, "As a third party, we could be the trusted environment for payer and pharmaceutical company data."

It would not be the first time that Cognizant's platform technology was put to use in a shared environment. Last year, the company and TransCelerate BioPharma announced the Shared Investigator Platform (SIP), a multi-tenanted, cloud-based, open architecture collaboration platform with a centralized database of clinical trial investigators that TransCelerate member companies could use to speed up selection and credentialing in the clinical trials start-up phase.

On the OBC front, as pharma and payers work through these contracts, literally on a drug-by-drug and payer-by-payer basis, Dindigal says, "You can't lift one contract to another at this time; the brands are too different. Then it becomes too difficult to put them all in one platform. You need a large platform, and one that will scale." Dindigal also sees in the near future where a need for a common template or common standards will have to be put in place.

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Pricing Turning Point

The Case for Innovating Pharma's Model

Outlining potential strategy shifts that could help evolve the industry's pricing playbook—with a look at implementation lessons from other sectors and the unique hurdles to large-scale adoption in pharma

By Juan F. Rivera and Caitlyn Macdonald

In antiquity, the Romans understood the affinity of price and value. In Latin, the word *Pretium* represented both price and value. In modern times, we speak about the concepts independently. In no other industry has the bifurcation of public perception of price and value been more acute than in the biopharmaceutical industry over the last decade. The perceived imbalance between price and value for drugs has led to negative publicity for the industry in the US, market access delays in Europe and other industrialized countries, and suboptimal penetration in many markets.

Despite the challenging environment, the biopharma industry is poised for tremendous innovation. It is said that as humans we over estimate what can be accomplished in the next 10 years and underestimate what can be accomplished in the next 50. Since Bayer gave birth to the industry back in 1899 with the launch of aspirin, tremendous value has been created for society at large. Lethal infections have been controlled, many killer diseases like heart disease and HIV are now managed, and debilitating conditions like rheumatoid arthritis (RA) have been moderated. Even in cancer, some forms like leukemia are already held at bay with targeted agents, and more forms of cancer will follow this path in the near future.

Progress in medicine is incremental in the short-term but life transforming in the long-term. The genomics revolution that started at the turn of the millennium is finally coming of age as new prod-

ucts developed based on this knowledge, including gene therapy, CRISPR, and CAR-T cell therapy, are making it to market. As the life sciences industry continues to charge ahead with product innovation, its ability to capture value requires it to also innovate in one area where it has largely remained stagnant: its price model.

Challenges under the current price model

A price model consists of two parts: How to charge (the basis)? And how much to charge (the level)? Pricing decisions in the industry have largely focused on the latter for the last 100 years. Since the turn of the millennium, there has been a drastic shift in the industry's product portfolio as biologics (products derived from proteins) have established a presence by capturing market share from small molecules (products derived through chemical synthesis), raising attention on the price level.

When looking at the top selling drugs in 2006 vs. 2016, we can see a large increase in the number of biologics as well as specialty products. As a result of this shift, during this decade-long period, the monthly price of the top 10 drugs in the US has grown by more than 10 times (see Table 1). Back in 2006, the top-selling pharma product globally was Lipitor, priced at around $3.50 per day in the US, according to PharmaCompass.com and Red Book. The layperson could grasp the value Lipitor provided and could rationalize spending $3.50 per day on their health. Nowadays, top-selling biologics, though targeting much smaller populations, can cost more than $50,000 per year. If we consider orphan drugs (products for rare diseases), price levels can be over $500,000 per year, higher than the cost of the median home, the largest purchase for most people. The prices of these new-generation medicines look eye-popping under the current price model paradigm and are harder to communicate, not just in the US but also across global markets.

Bump from Biologics

Top Selling Drugs 2006			Top Selling Drugs 2016		
Name	Revenue in millions (USD)	Monthly WAC	Name	Revenue in millions (USD)	Monthly WAC
Lipitor	$12,886	$105	Humira	$16,499	$4,480
Advair	$6,104	$150	Enbrel	$9,234	$4,480
Plavix	$6,056	$119	Harvoni	$9,081	$34,448
Nexium	$5,182	$128	Rituxan	$8,583	$7,529
Norvasc	$4,866	$60	Remicade	$7,561	$3,215
Zyprexa	$4,364	$447	Avastin	$7,053	$11,657
Diovan/Co-Diovan	$4,223	$105	Herceptin	$7,052	$6,732
Aranesp	$4,121	$1,333	Revlimid	$6,974	$16,931
Rituxan	$3,863	$4,438	Lantus	$6,343	$2,283
Effexor XR	$3,722	$181	Prevnar	$5,718	$174
Average monthly WAC		**$707**	**Average monthly WAC**		**$9,193**

Table 1. Monthly wholesale acquisition cost (WAC) prices in the US of top-selling drugs in 2006 and 2016. **Notes:** Global revenue for top-selling drugs according to PharmaCompass.com and GlobalData.com. 2006 monthly WAC prices calculated based on 20% discount to Red Book-reported average wholesale price (AWP). 2016 monthly WAC prices calculated based on Medi-Span PriceRx-reported WAC prices for the first year of treatment.

> The prices of these new-generation medicines look eye-popping under the current price model paradigm and are harder to communicate across global markets

The model's integral role in pharma's future strategy

The pharma industry is not unique in reaching this turning point. Other industries have faced tremendous price pressure and competition and have effectively implemented shifts in their price models to strategically adjust. Even in heavily commoditized markets, a shift in price model can change the selling dynamics of an industry to align with the customers' needs. The biopharma industry is no exception.

As such, we would like to highlight a few potential shifts that could help biopharma price models evolve concurrently with new product innovation to communicate value more intuitively.

Focus on output vs. input

The seed business in the agriculture industry is largely commod-

Manufacturers have begun to assemble product portfolios that span across the stages of disease progression

itized. Farmers have long made purchases on a per kilogram or per ton of seed basis, with the prices of those seeds fluctuating from year to year. One of the largest players in the industry is Monsanto. The company had historically been able to maintain its market position and technological edge in developing superior genetically modified seeds through patents and contracts with farmers. In order to fully capture the value of its genetically modified seeds, however, Monsanto went a step further and shifted to a royalty type price model, charging a fee after the crops were harvested based on the yield.

This "end-use fee" shifted Monsanto's price model from seed-based to yield-based pricing, i.e., from input- to output-based.[1] The change captures the production of each seed rather than simply the quantity of seeds, more closely aligning price and value. As farmers use more seeds and generate more yield, they pay Monsanto back a share of the excess profits, without impacting their upfront costs to purchase the seeds—a no-risk scenario for the farmers that captures upside for Monsanto.

In the same vein as seed pricing related to yield, a new price model that is recently gaining momentum in healthcare is the payment-by-results model (shift from price per month to price per outcome achieved). The price model shifts the focus of discussion away from purely cost to the goal that is being achieved, though it needs to evolve further as many times it becomes a discounting scheme vs. a truly payment-for-value scheme. Italy is farther along in accepting this type of price model (see related article on page 18), but other countries have been opening up to it (see Table 2 on facing page).

Capture differential value

In the industrial goods industry, Enercon is the third-largest manufacturer of wind turbines in the world. Industrial goods companies like Enercon make the majority of their revenue from the maintenance of their products, generally entering into monthly or annual maintenance contracts. When Enercon introduced a new wind turbine that was gearless and required less maintenance because it broke down much less frequently than competitors, it used the opportunity to introduce a new price model. Enercon has been able to maintain its market position despite charging a premium for this new turbine, however, as a result of the differential value offered by its pricing model.

Under Enercon's Partner Concept, customers sign up for maintenance, services, and repairs at a price dependent on the yield of their turbine. Because Enercon's turbines do not contain gears, they can guarantee more uptime versus competitors.[2] More wind results in a higher yield, which brings more value to the customer, at which point Enercon can charge a higher price. Not only does this capitalize on the efficiency of all turbines, but it also generates differential value depending on the location of the turbines due to its yield-based pricing. If certain turbines are exposed to more wind, they too will generate higher yield and more value to the customer, further supporting Enercon's ability to charge a higher price.

This new price model has resulted in 90% of Enercon customers entering into 12-year service contracts and Enercon's ability to capture differential value based on the design and location of their wind turbines.

In the Enercon example, the same turbine in a different location could yield a different value. In oncology, indication expansion acts in a similar way. Each new indication may have varying

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» Even in heavily commoditized markets such as agriculture and energy, a shift in price model can alter the selling dynamics of an industry to align with customer needs. The biopharma industry should be no exception.

» The concept of indication-based pricing provides an opportunity for drug manufacturers to capture differential value as their product labels expand and payers determine whether more nuanced coverage is warranted for products by indication. In some regions, separate risk-sharing agreements have been applied to certain treatments on an indication-by-indication basis.

» An annuity price model could potentially address pricing concerns in cases of curative therapies that require only one-time treatments, where manufacturers would typically need to capture the value of the drug upfront.

safety and efficacy profiles vis-à-vis different competitors and in absolute terms, e.g., higher overall survival (OS) or progression free survival (PFS) as compared to prior indications, introducing different price potential. Some manufacturers have provided indication-based pricing solutions in order to achieve the optimal pricing for each indication, e.g., Genentech's Avastin. In Italy, for example, separate risk-sharing agreements apply on an indication-by-indication basis for Avastin, and a specific additional 7% discount applies to the product when used in advanced colorectal cancer.[3]

This indication-based pricing concept poses an opportunity for manufacturers to capture differential value as their products' labels continue to expand and payers discern whether they believe more nuanced coverage is warranted for treatments by indication.

Offer total solution vs. components

Medical technology products have often been sold *à la carte*. The capital equipment component is used in a hospital or outpatient setting and the technology component may include additional services. The manufacturer largely makes a return on the initial purchase and the maintenance of the equipment.

Fresenius Medical Care historically operated like any other medical technology manufacturer. In the 1960s and '70s, Fresenius sold dialysis machines and dialyzers built by other companies until producing its A2008 dialysis machine in a newly acquired factory in 1979. From 1979 until the early 21st century, Fresenius continued to advance its dialysis offerings, with the merger of Fresenius Worldwide Dialysis and National Medicare, resulting in the listing of Fresenius Medical Care at the stock exchanges in Frankfurt and New York. Despite various advances, it wasn't until 2006 that the current Fresenius Medical Care model was created with the acquisition of Renal Care Group. This acquisition introduced a network of 2,000 dialysis clinics around the world through which Fresenius could provide dialysis treatments. Not only did Fresenius continue to produce dialysis machines and dialyzers, but it incorporated settings of care to sell and utilize that equipment. The company shifted from individual product selling to solution selling, opening the door to providing patients with a one-stop shop.

In integrating forward from a supplier to a full-service provider, Fresenius Medical Care is now the world's leading provider of products and services for people with chronic kidney failure.

In several indications, manufacturers have begun to understand the advantage of being able to provide a suite of solutions. In oncology, for example, patients may advance beyond a certain therapy, requiring physicians to prescribe multiple lines or a stack of treatments. Manufacturers have begun to assemble product portfolios that span across the stages of disease progression.

With this portfolio of products, a manufacturer could provide a predictable cost for the payer in exchange for customer retention over time if the patient remains within their product family for treatment. For instance, in multiple sclerosis (MS), RA, hemophilia, or oncology, manufacturers could offer a price per month regardless of which product or how many are needed, as long as they are from the same manufacturer and the patient initiates the necessary treatment without any delays. As a full-service provider of therapies, a manufacturer could consider treatment on a per-patient basis rather than per drug and payers could more easily forecast and track the costs associated with each patient.

Align payments with customer buying cycle

Tire selling, like drugs, was historically based on a simple price

Ruled by Results

Product	Country	Mfgr.	Est.	Details
Imnovid (pomalidomide)	France	Celgene	2014	Payment for patients that meet certain treatment criteria.
Afinitor – BC (everolimus)	Italy	Novartis	2013	Payment for responders.
Bosulif (bosutinib)	Italy	Pfizer	2014	Payment for responders at week 12.
Victrelis (boceprevir)	Spain	MSD	2014	Payment for patients that have reached a specific level of viral response.
Velcade (bortezomib)	UK	Millennium	2007	Payment for patients that do not experience a 50% reduction in tumor size after the first 4 cycles of treatment.
Kymriah (tisagenlecleucel)	USA (CMS)	Novartis	2017	Payment for responders by the end of the first month of treatment.
Trulicity (bevacizumab)	USA (Harvard Pilgrim)	Eli Lilly	2016	Manufacturer provides additional discount if patients do not meet A1c level targets.

Table 2. Selected performance-based agreements.

Alternative Approaches

Model	Industry example	Application to pharma	Challenges to overcome
Per outcome (of product)	Monsanto	Outcomes-based contracting	Patient registry and monitoring, Medicaid Best Price
Per differential value	Enercon	Indication-based contracting	Enhanced dispensing tracking
Per total solution (of a bundle of products / services)	Fresenius	Multi-line solution selling	Perceived lack of choice
Per customer's buying / payment	Michelin	Annuity payment for curative therapies	Patient insurance switching

Table 3. Alternative pricing models for biopharma that have been implemented in other industries.

model—price per tire. With the entry of competition from developing countries, particularly from the Far East, tire manufacturers started to feel the pinch. When Michelin developed a new tire that lasted 25% longer than existing tires, the company found it difficult for customers to accept a premium.[2] Rather than giving away the innovation, Michelin changed its price model. Truck fleets, a key customer segment, track cost per mile for each truck as their revenue model is also based on charging its customers per mile.

Michelin decided to adapt its price model and to offer the new tires on a price per mile rather than per-tire basis.[2] The company then offered a contract to replace the tires after they wore down. Under this new price model, customers perceived a parity price as they were not asked to pay more, while the longer-lasting tire from Michelin was able to capture a premium for its innovation.

Payers currently operate on annual budget cycles. This poses a particular challenge for upcoming therapies that require a one-time treatment but have a benefit that lasts for many years (e.g., gene therapy, CRISPR). Based on the current price model, a patient would pay for their CRISPR therapy at the time of treatment. Unlike other courses of treatment, however, there would not be any refills or additional treatments because it is curative. The manufacturer would, therefore, need to capture the value of that curative treatment upfront, a price that—depending on the indication and level of medical need—could be staggering.

An annuity price model could address this concern. Much like a mortgage on a house, under the annuity model, payers would pay for the product over time vs. having an upfront payment. The annuity could simply spread the payment over a number of years (e.g., 10 or 15), or could be a lifetime model. If the patient were to pass away shortly after taking the medication in the lifetime model, the total revenue on the medication is low. If, however, the patient lives longer due to the efficacy of the treatment, the payment is high. The risk is, therefore, fully aligned with the status of the patient. Departing slightly from the mortgage example, the payment for a one-time treatment could also be variable and tied to specific other outcomes.

Paving the way for new price models

Though not exhaustive, the four price model shifts we highlighted could help the biopharma industry adapt to ever innovative product offerings (see Table 3). In order to support these shifts in larger scale, some hurdles would need to be overcome. In particular, patient and dispensation monitoring; mitigating concerns of portfolio offerings; Medicaid "Best Price" implications in the US; and collaboration across insurers in fragmented markets like the US would need to be addressed.

Patient registry and monitoring

Indication-based pricing and performance-based price models would require enhanced moni-

toring. Privacy laws and the interconnectivity of devices have laid the groundwork for monitoring enhancements. In many cases, pharmacies and practices would need to further augment their dispensation tracking in order to differentiate not only between the drugs they prescribe but also for which indications they are being prescribed. Performance-based price models would also require patient registries in order to more centrally track specific outcomes. Policymakers and insurers could streamline the implementation of such tracking enhancements with alignment on common or compatible tracking standards.

Medicaid Best Price

The Medicaid Best Price policy requires drug manufacturers to offer state Medicaid programs the lowest of 23.1% off the list price or the best price offered to any other private or public purchaser if such a purchaser receives more than the minimum discount.[4] Under this law, offering performance-based agreements or indication-based pricing could trigger additional rebates to Medicaid resulting from the method used to calculate best price. Policymakers would need to amend the Medicaid Best Price policy to revise the method of calculating best price.

Portfolio-based contracting perception

In some cases, physicians and insurers are hesitant to enter into portfolio-based contracts because they are concerned with losing autonomy/choice. Manufacturers could alter this perception with an emphasis on patient-support programs and other added benefits patients and insurers could gain from receiving multiple therapies for a patient from the same manufacturer.

Inter-insurance agreements

In healthcare systems such as the US, with fragmented payers, where patients tend to switch insurers regularly, spreading out treatment cost across several years to match the annual budget cycle of payers can be challenging. In order to alleviate this, there would need to be an inter-insurer agreement to deal with the outstanding payments. Similar agreements already exist in other industries, such as the inter-bank credit agreements established for syndicating loans.

Education and alignment

While new price models can facilitate the communication of value, no price model will be successful in a world where the industry has a bull's-eye on its back as a key target for cost containment. As an industry, the biopharma sector needs to help educate not just physicians, but also policymakers and the public on the benefits brought by innovation to society at large. As societies get wealthier, they are likely to spend a larger proportion of income on healthcare. The discussion around drug spending should, therefore, revolve more around the concept of effective spending versus the percentage of the budget it represents. In a recent industry study conducted by Simon-Kucher and Partners, the number one limitation for future revenue growth according to industry executives and managers was price.

The price models we highlighted are newer to the biopharma industry but time-tested in other sectors. With buy-in from policymakers and the correct enhancements to pave the way for implementation, these new price models could help right the biopharma sector's price perception and better align with the value created to help unleash the newest wave of innovation. PE

With buy-in from policymakers and the correct enhancements to pave the way for implementation, these new price models could help right the biopharma sector's price perception

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A Bold Path Etched in DNA

Forever rooted in drug discovery—with successes and new hills to climb—Markus Warmuth, CEO of cancer genomics company H3 Biomedicine, fits the profile of today's new breed of biotech business leaders, who let the science chart the course, where knowledge is currency

Markus Warmuth, president and CEO, H3 Biomedicine.

By Michael Christel

Though it may sound cliché, Dr. Markus Warmuth, a trained scientist in internal medicine and oncology, is used to the long journeys—the twists and turns and uphill battles—that come with drug discovery and forging paths for promising biomedical ideas to advance. In fact, he's lived them in many ways. When the native German and former academic oncologist and investigator supplanted his family from Munich to San Diego, Calif., in 2002, moving into their new house the day before Halloween, "we were all confused," Warmuth recalls, "because there were a ton of people knocking on our door asking for sweets and we had no idea what was going on!"

But like drug discovery itself, adapting to change and uncertainty is a must in his profession, Warmuth says, the 2002 move specifically bringing the cancer researcher to the Genomics Institute of the Novartis Research Foundation (GNF), where he headed up its kinase platform and oncology pharmacology program. Warmuth has lived in the US ever since, eventually switching coasts, where today he is a combination business leader and scientist. Perhaps it's no surprise that Warmuth is also an avid cyclist, enjoying the thrill of challenging mountain paths—even venturing to the Alps and taking on the same tough climbs as those in the Tour de France.

Whether in a figurative or practical context, having traversed such diverse trails in his career and life has many pointing to Warmuth, now the CEO of H3 Biomedicine, an early clinical-stage cancer genomics company, as being part of a new wave of biotech leaders. They are those that let the science lead the way while marrying that knowledge with an astute understanding of business. The science, in this case, is H3's precision oncology approach to drug discovery. It focuses on identifying therapeutic targets and biomarkers based on genetic aberrations identified in patient

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» Dr. Markus Warmuth received his doctorate in medicine from the Ludwig-Maximilians-University of Munich, Germany, where he trained in internal medicine and oncology.

» In April 2017, Warmuth joined the board of directors of Relay Therapeutics as an independent board member. Relay, a biotech company, is focused on developing medicines centered on protein motion.

» Warmuth began his career in 1998, when he was appointed as a principal scientist with the "Clinical Cooperation Group Signaling" at the German National Research Center of Environment and Health. There, he studied the mechanism of action of and resistance to multiple small molecule kinase inhibitors in leukemia and lymphoma.

samples catalogued in the company's data science platform, which consists of cancer genomic data from greater than 100,000 patients. The Cambridge, Mass.-based company, which formed in 2011 as a wholly owned subsidiary of Eisai, the Japanese big pharma organization, specializes in tracking the role of changes in DNA that contribute to cancer and influence various hallmarks of the disease. Although H3 works on a diverse set of targets, a particular strategic focus area is on alterations in the RNA splicing machinery, which are critical to translate genes to functional proteins.

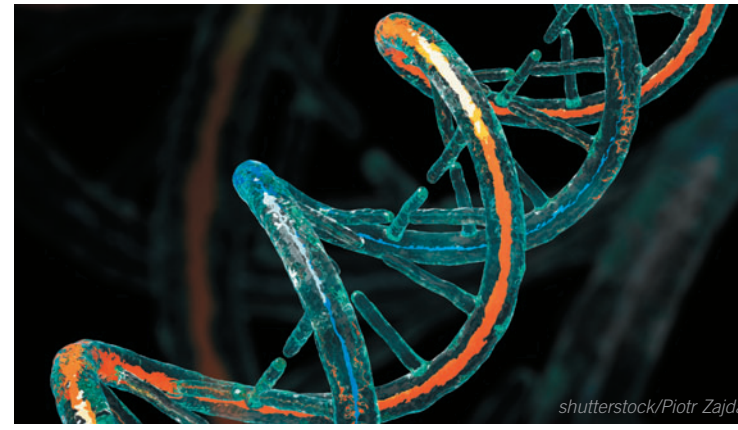
Warmuth joined H3 a few months after its launch as chief scientific officer and was named president and CEO that same year. Under his leadership, H3 has built an integrated discovery/development platform that identifies genetic targets that define specific patient populations, and validates those targets with the hopes of delivering genomics-based small molecule drugs or antibody drug conjugates.

The company has advanced three projects into early-phase clinical trials, including H3B-8800, a splice modulator that received orphan drug designation from the FDA last year for the treatment of acute myelogenous leukemia and chronic myelomonocytic leukemia. H3 also has multiple discovery programs in the works.

When you come to work in a small biotech, every minute counts

On the business end, Warmuth has helped strike research partnerships with Horizon Discovery, Selvita, Sage Bionetworks, and, most recently, Foundation Medicine, the cancer diagnostics company. Before joining H3, Warmuth was head of oncology drug discovery for the Novartis Institutes for Biomedical Research (NIBR), where he oversaw a significant portion of NIBR's oncology R&D portfolio, including novel therapies that have since won commercial approval.

The Boston-area resident spoke recently with *Pharm Exec* about, among other things, his career journey, the biotech culture differentiator, and the revolution and continued cautions in cancer genomics.



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PE: *What drove you to follow the arc from science and research to the business side of medicine and the life sciences?*

WARMUTH: Honestly, I'm not a person who spent a lot of time planning out a career. I'm not doing things because they look great on the CV. For me, having worked at Novartis for nine years, I felt that was great training grounds, but I also saw a lot of the other side. Huge organizations, lots of stakeholders; it can take a long time to get to decisions. So, after a while, naturally I was interested to take on a position beyond just sort of owning and driving the science; I could really impact the entire business.

When you come to work in a small biotech, every minute counts. One small mistake, one bad decision really impacts the value of the company. I was interested in being at the helm of a company and implementing some of my philosophy around how to drive drug discovery, how to grow a business, and how to have impact on patients in the future.

PE: *While you were with Novartis, the field of cancer genomics was starting to make significant strides. How unique was it to have that vantage point and watch the field emerge almost in sync with your career progression?*

WARMUTH: That really influenced me and my thinking. That's not to say that there aren't other areas. Obviously, in immuno-oncology, we see it having revolutionized over the last four or five years. I believe in a strong connection between cancer genetics and immuno-oncology. We do work on some of these aspects here at H3.

Clearly, we have now seen how rational drug development around genomic aberrations can really drive impact on patients and also value for a company. There's been a lot of learnings over the past seven years around changes to the cancer genome.

Before we started H3, my belief then was it's mostly around making cancer cells grow faster and survive longer. Now, I realize that changes to the cancer genome really do impact all aspects of cancer. One of these aspects is escape from the immune system. We recently published a story in *Nature Communications* around a series of mutations in bladder cancer that are clearly linked to modulating the level of T-cell infiltrates in tumors of bladder cancer patients. For us, that's really been the big grind.

The scientists, the teams need to own the programs. … [Leaders] can't be successful if we're not finding the next talent and empowering these individuals

PE: *Given that honed-in focus, what is distinctive about the culture of H3?*

WARMUTH: My philosophy is clear and it's really that the scientists, the teams need to own the programs. The culture we've established here is around what we like to call "empowered teams." There's no leadership committee. We have leadership teams, but project teams usually don't come to a leadership team at H3 to ask for approval to do an experiment or to move a project to the next stage. That's something we try to drive in a very dynamic way, by being confident in the actions of the project teams and project team scientists.

That's the underlying philosophy that has allowed us to build what we have in the past seven years. In recognizable speed, we've brought three assets into clinical trials. And none of these were in-licensed—this was all science we had built from the ground up. It goes back to the empowerment of your project teams. The larger the organization, the harder it is to stay true to that philosophy. It really requires you to remind yourself every day when you come to work that this company is about empowered teams and not to deviate from that philosophy.

PE: *How have personal connections or mentors from your past contributed to your ability to instill that mindset today?*

WARMUTH: I was fortunate enough to work with great bosses and mentors who were never afraid of what I would be doing next. At GNF, I had a lot of support from Pete Shultz, who, back then, was the Institute's director. What I truly learned from him was to be open-minded and really support young, dynamic investigators with sometimes crazy ideas. When I came to GNF, I had very little experience in drug discovery. Within a few months, Pete essentially gave me responsibility to build and drive the ALK [oncogene] program [in non–small cell lung cancer].

The same is true with my boss later at Novartis, Bill Sellers (former VP/global head of oncology, NIBR). He brought me over from GNF, really stepping aside and giving me the room to grow and build a group that was able to shape the future portfolio of his group. That's really important for us as leaders. As much as we would like to drive and dominate, we can't be successful if we're not finding the next talent and empowering these individuals to own certain areas.

PE: *What's one way the industry has changed since you entered the pharma space?*

WARMUTH: The one thing to mention—and it's probably partly due to a lot more success stories—is the industry's become very competitive. And that's not to say competition is meant to be negative. It's great to see how much more is going on, especially in oncology drug discovery—how much more impact there has been on patients and their lives and how much more there is to come. Of course, it makes it harder and harder for companies to differentiate themselves and find their own space. And it also bears risk, because we are seeing, in my eyes, some of it around immuno-oncology and combination treatments. I do think [the heavy competition] runs the risk of companies prematurely entering into development programs because they feel practical, without really having solid underlying data to support them.

PE: *Is there, in a sense, too much volume, as far as projects and clinical assets in some areas?*

WARMUTH: Yes. In a way, it crosses a "me-too" [drug] kind of behavior, where you're starting to see a lot of the same assets being developed—and it's hard to understand the difference that you can still make if you're the fifth or sixth entrant in a particular class.

I am concerned that with some of the increased spend—exciting as it is in this area—if the success

stories are not holding up the dollars spent, then it can impact future investments. You really have to carefully monitor all of this. That's every CEO's responsibility. As much as we obviously want to deliver back return on investment to our investors, we also need to be careful and thorough and not push too much into an area or a registration or program just because we feel we need to justify valuations and investments. It really is important to stay true to data-driven decision-making.

PE: *How do those factors influence the way your company operates?*

WARMUTH: For us, it's trying to be unique and differentiate what we're doing. Sometimes it's the uniqueness of the target, sometimes it's the uniqueness of a mechanism of action. One of the best examples for that is our program targeting estrogen receptor, which is a very well-known target. When we started this, it was really driven by the discovery of hot-spot mutations in the estrogen receptor in a subset of breast cancer patients. We had a long debate about whether we should even enter into that space, because it's very crowded. A few years back, there was a lot of hype around the next generation estrogen receptor degraders. After quite some debate and scientific discussions, we realized we had another potential mode of action that hasn't been explored yet, which is covalent antagonist of the estrogen receptor. While crowded, we felt that would probably be a way to differentiate, and some of our early data supported that.

That program (H3B-6545) is in a Phase I trial. It's too early to talk about any of the data, but all the preclinical data we have in hand very nicely distinguishes that molecule from standard of care molecules and that class of next-generation estrogen receptor degraders.

I'd rather be in a niche and different versus being the fifth in class in a broader indication. For small companies, that's extremely important.

PE: *What in your career to date has made you most proud?*

WARMUTH: Obviously, with everyone who works in drug discovery—and it doesn't matter if that's on the biology side, chemistry, in management, finances, legal, whatever—whenever you are involved in a drug that eventually makes it to the market and you see how it impacts patients, it makes you feel very proud. And it almost doesn't matter how much you contributed. For me, the moment when ceritinib (Zykadia) got approved (in 2014 for patients with Crizotinib-resistant ALK-positive NSCLC)—I was no longer with Novartis at the point—six, seven, eight years of really hard work all of a sudden made a ton of sense.

One of the molecules I was involved in when I came over to join Novartis in Cambridge was ribociclib (Kisqali). Seeing that approved now in breast cancer (cleared in the US and Europe last year) makes me feel really proud too. There were hundreds of people involved to eventually make that happen. One of the big learnings for anyone in this industry is it takes a huge team and tremendous effort from a lot of people to get the job done.

The other thing that makes me proud is really to see—and even where I'm still relatively young in my career—how some of the folks and scientists that have worked for me have grown and are now CSOs and COOs on their own. For me, as a manager, that's really important. Because, again, everyone wants to have a career and be successful. But it's really also about growing up the next generation of leaders.

PE: *What are some challenges in your focus area of cancer genomics that keep you up at night?*

WARMUTH: When we started H3 around this paradigm of cancer genetics, when the Cancer Genome Atlas released its first data set, very quickly it became clear that it was different from what we expected. There wasn't really this next super obvious oncogenic driver. We knew PI3 kinase mutations and Ras mutations from before. I think there was a clear expectation that we would find many more of these in large-scale genomic efforts, but we really didn't. As a matter of fact, what we found was mutations in the splicing machinery, and no one really understood what that meant and what these mutations would be doing. We found mutations in metabolic pathways that before were worked on for diabetes and other areas.

So, it was really sort of grappling with the fact that that quick path that everyone had expected to novel therapies might not be so quick after all. We had to react to that by building an infrastructure that could give us deeper and broader insights into how the cancer genome changes, but then also to interpret what these changes actually mean, not just for proliferation and survival of the cancer cells but for differentiation, migration, escape of the immune system, and almost any hallmark of cancer.

PE: *What would be your advice to new professionals entering this industry—particularly your specialty field?*

WARMUTH: For me, what's really worked is don't plan too much, don't be too plotting, and as a matter of fact, be ready to change dramatically if you need to. About a year before I moved my family from Germany to San Diego, I didn't think I'd ever move to the US. Then a year later, I did. Because I realized this is where innovation lives.

> We need to be careful and thorough and not push too much into an area or program just because we feel we need to justify valuations and investments. It really is important to stay true to data-driven decision-making

I think sometimes you just need to follow the flow of your life instead of trying to influence it too much. I think the same is actually true for how you grow a company. We started out seven years ago in a fairly unique setup, where instead of being formed out of an academic group and with venture capital, we started up as a spinout from Eisai. We are still organized as a wholly owned subsidiary. While some might still think that's not such a good idea, I would say we probably wouldn't be where we are right now if it wasn't for Eisai and their bold investment.

Looking at the future, I do think there's opportunities to change the business model and certainly my goal is to continue to grow H3 Biomedicine into a brand that's really recognized for the innovative science it's doing and innovative drugs it's generating, and potentially also at some point into a standalone company.

PE: *Can you elaborate more on H3's relationship with Eisai and what makes your funding model unique?*

WARMUTH: One of the main advantages of that setup was our ability to access key resources from Eisai. There's something to be said about the experience of big pharma companies. When we started H3, it was on a bold investment thesis that Eisai, instead of spending money internally, wanted to fund and build a biotech-like company—high energy, entrepreneurial spirit, and in the premier biotech hub in the world. And give it its own identity, its own culture, but allow it to collaborate and benefit from the decades of experience that Eisai has in its own organization.

When we started, to support us, Eisai did commit to $200 million in startup funding and then additional funds coming in as we improve ourselves and hit certain milestones. Up until now, Eisai has continued to fund us, but there's certainly also recognition that if we, as H3, wanted to continue to grow and really leverage the platform that we have built, that we should actually go more outside and have collaborations with other companies and also maybe transition into a model that would allow us to accept outside funding.

PE: *One of your collaborations is with Foundation Medicine. How has that progressed?*

WARMUTH: It's been extremely fruitful. It's an agreement that allows us to access Foundation's genomic data, which has now grown to over 100,000 patients, and some of its scientific expertise. It's really interesting, there's been a lot of debate around how many genomes you need to sequence at what depth in order to have enough information. The information we can derive from accessing Foundation's data is quite stunning and has led to new projects, but really also greatly informed the clinical path for some of the existing assets, and seeing genomic changes with a lot more granularity and at bigger depths and more longitudinal clearly helps.

PE: *You're a pretty hardcore cyclist in your spare time. How much does your professional life define your personal identity and your drive to achieve?*

WARMUTH: [Cycling] is a bit like drug discovery. You're in there, and it depends on where you ride. I do like to ride in the Alps. When you start at the bottom, you know you're in there for at least an hour, sometimes two and a half hours—and you're still just getting into it. I think it's like drug discovery. You know when you start a project, you're probably in there for 10 years-plus, if it's successful. You know you'll have a lot more gray hair by the time you come out at the top. But if it's successful and you do see that it impacts patients' lives, it's absolutely worth it. And just to be able to go up these mountains, because the view from the top is really spectacular. PE

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The Personalized Genetic Profile: It's Time to Align

Innovations in consumer genetic health are rapidly advancing—and pharma commercial thinking needs to catch up

We are on the verge of a massive industry change in the world of pharma: individuals are starting to own their own genomes. The trend of innovation in consumer genetic health is blurring the lines between patient and customer. The introduction of relatively inexpensive biological assays, especially around known genetic biomarkers and mutations, is both creating a new industry and evolving the behavior of "consumer-patients."

Although pharmaceutical companies are investing in R&D to capitalize on this new world, they are lagging in the innovation of their commercial models. The industry will need to step up to maximize value creation for their customers and themselves.

There is already significant innovation in treatments specific to genotypes or biomarkers. There are reportedly roughly 130,000 known biomarkers associated with about 2,500 diseases. Genetic testing is being prioritized, as underscored by the FDA, which has approved about 200 drugs for identified, actionable biomarkers, and there are another ~5,000 clinical trials in progress for drugs associated with those biomarkers. For example, in June 2017, the FDA approved Thermo Fisher Scientific's Oncomine, which finds 23 genetic alterations. In addition, in November 2017, the FDA approved Memorial-Sloan Kettering Cancer Center's profiling test, MSK-IMPACT, which looks for alterations in 468 genes.

People suffering from diseases and those who want to manage potential life-threatening illnesses can now achieve a better understanding of their own genetic risk profiles. As a result, they are more engaged with treatment profiles and are seeking an increase in personal genetic health services such as those offered by 23andMe. We expect this to be a $50 billion market by 2026, and part of an emerging industry that provides personal access to genetic profiling, disease biomarkers, and mutations.

There is an opportunity and an imperative to link the science to the commercial relationship between innovators and their patients. We need to create not just personalized medicines, but a personalized interaction between drug company, healthcare professional, and patient.

Pharma is already tackling R&D innovation

As the volume of innovation specific to a biomarker or phenotype increases, pharma companies are speeding the pace of development of supporting diagnostic strategies. The growth of genetic testing companies like 23andMe means the amount of data that can be used to help R&D has also grown exponentially. Investments need to be made to understand how to use

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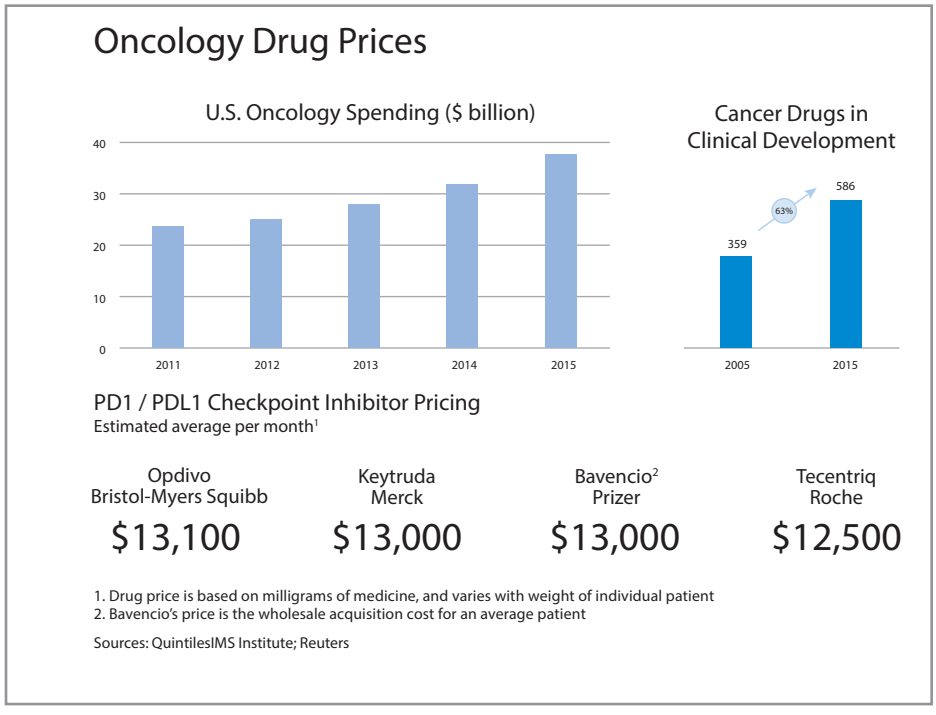

A look at the rise in oncology activity in recent years. The costs of new cancer immunotherapies may quadruple by 2022, according to research firm GlobalData.

this data and make drug development more targeted, thus saving money in the long run.

For some pharma organizations, this has meant drug discovery through **new strategic relationships**, for example:

» Pfizer has entered into an agreement with 23andMe, thereby gaining access to DNA data on about 650,000 individuals. As a result, Pfizer is considering genetic loci linked to the risk of major depression, and has identified 15 regions of interest. The study will enable Pfizer to find new targets for treating the disease and design new clinical trials.

» In April 2016, Human Longevity Inc. (HLI) signed a 10-year contract with AstraZeneca, in which HLI will sequence 500,000 genomes from the clinical trial population of AstraZeneca. This data is being used to identify novel drug targets.

We need to create not just personalized medicines, but a personalized interaction between drug company, healthcare professional, and patient

Other pharma companies have focused R&D innovation on **companion diagnostic tests** that enable screening and diagnosis. With more accurate diagnoses, companies can provide targeted therapy and create greater value for patients.

» Illumina and Amgen have collaborated on the development of a next-generation sequencing-based companion diagnostic test that screens patients with colorectal cancer. Patients with the mutated RAS gene do not respond well to Vectibix, therefore only those patients with the non-mutated form of the gene are eligible for treatment.

Time to tackle commercial innovation

Commercial models as currently configured will not sustainably support this new class of product and, if left unchanged, will harm both patients and pharma companies.

Expensive drugs based around molecular genetics and biomarkers and the understanding of disease-causing mutations, such as Bristol-Myers Squibb's Opdivo and Gilead Science's portfolio against hepatitis C virus, have seen success in the market. In October 2017, BMS highlighted the strong sales of key immuno-oncology products Opdivo and Eliquis. In addition, while BMS is benefiting from these sales today, $250,000 to $300,000 per patient is not sustainable for the healthcare system to absorb as more of these drugs are introduced to the market. The system must evolve for targeted treatments to flourish.

Novartis is responding by testing an innovative commercial model, and its effect thus far is startling. The company's CAR-T therapy Kymriah carries a price tag for pediatric patients of $475,000 per treatment cycle. Yet Novartis' commercial features are leading to more public acceptance of that high cost. First, if the treatment does not work, then patients do not pay for any aspect of the therapy,

and, second, Novartis has introduced a call center to smooth the path for the patient and the healthcare provider. Gilead, in releasing its CAR-T-based treatment, Yescarta (approved for patients over age 65), has struggled to get reimbursement from Medicare/Medicaid, leading to a growing waiting list and lower-than-hoped-for revenue, according to published reports.

What could an innovative commercial model look like?

More companies need to think seriously about their future commercial models. We believe pharma companies should consider either adapting their payment model or their sales model.

The payment model

Payment models can become performance-based and flexible. **Contingent payment models** are in keeping with the growing need for outcomes-based payment. Novartis has taken the lead with the aforementioned pediatric CAR-T treatment for acute lymphoblastic leukemia: payment is required only if the patient shows improvement within 30 days. Also, by pricing the product at less than the equivalent bone marrow transplant, the company is demonstrating both commercial awareness and sensitivity to the high costs inherent in treating these indications.

Deferred or distributed payment models may encourage patients/payers who would otherwise refuse treatments due to the expensive, one-time, upfront payment. Amortization of the cost over months or years may challenge the industry in the short term but will provide longer-term income. This will smooth the cost, allow more patients to get treatment, and provide a respite from the boom and bust of new product introduction and patent expiry. It may be that pharma companies will use their significant financial muscle and comfort with long-term investment models to create new payment schemes that reduce the initial impact.

The sales model

The increased use of a **scientifically qualified sales force** by pharma companies in the last few years is an indication of the sales model changes that are required. The complexity of new therapies has already changed the ratio of sales representatives to scientifically qualified staff from the typical 10:1 to ~7:1. This trend will likely continue as treatments become more personalized. Scientifically qualified sales teams are supporting expensive treatments, working with healthcare professionals on reimbursement, helping patients get onto treatment plans, and supporting patients through the process.

Personalized wellness programs will also change. One of the big challenges for wellness has always been the uncertainty of disease progression and treatment effectiveness. If you indicate, for example, that there is a one in 10,000 probability of falling ill, most people cross their fingers and hope that they are safe. The REVEAL study on Alzheimer's disease, conducted several years ago, showed that those patients who understood they had a genetic predisposition to develop the disease put more effort into educating themselves and working to remain healthy, according to a report in *NEJM*. Drug manufacturers could play a role that goes beyond their current patient-support programs.

Innovation around commercial models must match the innovation going into the science and promote engagement with patients around a new common understanding of genetic profiles

Synergy with science

Personalized medicine will bring the pharma industry closer to the patient than ever before. Innovation around commercial models must match the innovation going into the science and promote engagement with patients around a new common understanding of genetic profiles. Patients are looking for ways to prepare for risks that they can now understand, and the pharma industry must support that.

Contingent payments recognize that, with greater certainty around disease causation, there needs to be a shared commitment to treatment success. Extended payment models can recognize that these treatments are highly expensive and often rationed. The use of a scientifically trained sales force can engage not only with patients, but also with potential patients who want to understand their options. PE


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HEALTHCARE & LIFE SCIENCES REVIEW

INDIA

PHARMACY TO THE WORLD?

In 2018, the global importance of the Indian pharmaceutical industry and the affordable generic drugs it produces is indisputable. As Daara B. Patel, president of the Indian Drug Manufacturing Association (IDMA) astutely asserts, "There is pretty much no country on earth that can manage without Indian medicines. Almost every developed country has an aging population and, as their budgets continue to shrink, affordable quality generics from India become increasingly appealing."

Dilip G Shah, secretary general of the Indian Pharmaceutical Association (IPA), strikes a similarly confident tone in proclaiming that "The relative affordability of India-made generic drugs compared to their patented counterparts elsewhere has not only enabled India to provide quality drugs at a low cost for its own people but has also rendered the country a de facto pharmacy to the world." He continues, "In many markets, including the US, there is a large section of society which does not have the means to pay for the treatments it requires. The Indian industry is providing low-cost medicines around the globe and the beauty of its model is serving a social cause through financially viable enterprise."

Moreover, Indian pharma's international role is gradually evolving not only to encompass low-cost generics, but also more complex and greater value-added products. At the forefront of this phenomenon is the recent US FDA approval of Ogivri™, the biosimilar to trastuzumab, developed by US-based Mylan and the Indian entity Biocon. Ogivri™ ranks as the first biosimilar to be approved for stomach and breast cancer in the US. Biocon's chairperson and managing director Kiran Mazumdar-Shaw proudly notes that, "Getting the approval of Ogivri™ is a significant endorsement of the quality of this product and to our capabilities to develop these complex drugs for global markets."

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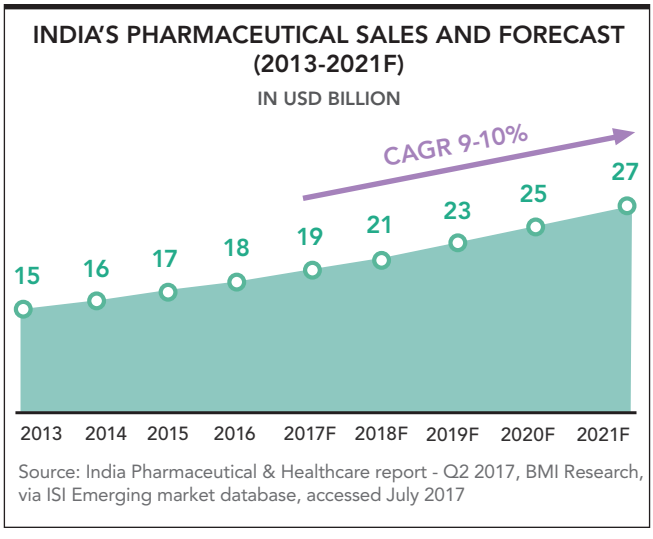
HEALTHCARE WOES: UNDERPERFORMANCE AND NCDS

As a backdrop to these international successes, however, India's domestic healthcare system remains underperforming, undercapitalized and generally unfit for purpose. Kanchana TK, director general of the Organization of Pharmaceutical Producers of India (OPPI), paints a rather gloomy picture: "India continues to be one of the poorest performers in its region in terms of quality and accessibility of healthcare, ranking at 154, far below China, Sri Lanka and even Bangladesh, according to the Global Burden of Disease study published in The Lancet in 2017... In fact, the total expenditure on healthcare in our country as a percentage of GDP is a mere four percent, while in the US it is 17 percent," she bemoans. The comparative statistics certainly make for unhappy reading: according to World Health Organization (WHO) data, for countries performing best in the healthcare sector, the US ranks 37, while India lags behind at a lowly 112.

Despite a decrease in the burden of infectious diseases in India, the country's already dire healthcare situation is being compounded by an increase in Non-Communicable Diseases (NCDs) such as heart disease, stroke and diabetes. As Jawed Zia, country president of Novartis explains, "India is facing a dual public health burden. The pressure from communicable, maternal, neonatal and nutritional (CMMND) diseases has somewhat reduced, but still remains uncomfortably high. Indeed, according to The Lancet, deaths from CMMND diseases – largely preventable and mostly due to poor sanitation and public health – decreased from 53.6 percent in 1990 to a nonetheless sizeable 27.5 percent in 2016." "At the same time, deaths from NCDs accounted for 61.8 percent of all dealths in 2016 versus 37.9 percent in 1990," notes Zia. The impact that a rise in NCDs places on the wider economy can be severe, as



Source: India Pharmaceutical & Healthcare report - Q2 2017, BMI Research, via ISI Emerging market database, accessed July 2017



Daara B. Patel, secretary-general, IDMA; Kanchana TK, director general, OPPI; Jawed Zia, country president, Novartis

Melvin Oscar D'Souza, CVP and general manger, Novo Nordisk

Zia elaborates, "NCDs not only affect health, but also productivity and economic growth."

Novo Nordisk's Melvin D'Souza has, however, seen a change in attitudes for the better on the NCD front. "I believe that the situation positively changed over the past five years as the government has slowly started to give special focus to chronic care. That is why they established a fund for NCDs. However, we believe the focus that they currently give is not sufficient and they should allocate more funds. On the one hand, we cannot entirely blame the government because they are still caught up with the communicable disease burden, but on the other hand it is fundamental that we play a key role". D'Souza continues, "To this purpose, we are trying to work closely with healthcare experts in the government setting and build an understanding of the disease. At the moment, for instance, we are involved in a project in which we cooperate with more than 100 healthcare centers in Bihar where we train doctors."

A NEW NATIONAL HEALTH POLICY: TURNING THE CORNER?

To combat India's myriad health issues, the government of Prime Minister Narendra Modi put forward a new National Health Policy in 2017 (NHP 2017), which advocates providing a larger package of insured comprehensive primary healthcare. This is to be achieved by establishing 'Health and Wellness Centers' throughout the country, allocating a greater proportion of resources to primary care with two beds per 1,000 population distributed to enable access, and ensuring the availability of free, comprehensive primary healthcare services for all aspects of reproductive, maternal, child and adolescent health. Also included in the package is free at the point of delivery treatment for the most prevalent communicable, non-communicable and occupational diseases. The Indian government clearly sees this step as a

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- Caripill was awarded Silver Award under the 'Acute' Category for 'New Introduction of the Year 2016 and Tenepride was awarded Bronze AWARD under the 'Chronic' Category for 'New Introduction of the Year 2016' by AWACS Marketing Excellence Awards 2016
- Dolo-650 awarded as 'Asia's Greatest Brands 2016' by Asia One Magazine and PwC India
- Brand Dolo was awarded India's Most Admired Brand 2015 by White Page International
- Micro Labs Sikkim manufacturing unit bagged the prestigious Silver Award at 'India Manufacturing Excellence Awards (IMEA)' 2015 & 2016, held by Frost & Sullivan in association with The Economic Times
- Micro Labs is a regular recipient of IDMA Quality Excellence Awards - Gold Award 2017 for Sikkim Plant and Silver Award 2017 for API Unit, Bommasandra

The other milestones:

- Ranked amongst top 19 pharmaceutical companies in India with a market share of 1.95% as per AIOCD-AWACS December 2017
- 19 specialty divisions, widest product range with over 5600 dedicated field force
- 13 World class manufacturing facilities approved by USFDA, UK-MHRA, Health Canada, WHO, TGA Australia & Medsafe - New Zealand, with 2000 qualified technical personnel
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Vinod K. Paul, member, NITI Aayog; Shravan Subramanyam, managing director India and Neighboring Countries, Roche Diagnostics; Bhupendra Singh, chairman, National Pharmaceutical Pricing Authority (NPPA)

departure from previous policies, with Modi tweeting immediately after having secured Union Cabinet approval that, "This National Health Policy marks a historic juncture in our endeavor to create a healthy India where everyone has access to quality healthcare."

Vinod K. Paul from the National Institute for Transforming India (NITI), the government think tank involved in drafting the policy, describes the shift in approach that it embodies thusly: "An important pillar of the policy is to build a very strong primary healthcare sector as a way to build a new India, on which individual health priorities will be addressed." "At the moment, healthcare is very much focused on maternal and reproductive health issues," he notes. "As we move towards a comprehensive aspirational comprehensive primary healthcare, we will have to include care for major NCDs, geriatric healthcare, mental health, palliative care and rehabilitative care services."

PRICES ON THE SLIDE

Such a comprehensive stepping up of healthcare investment will not, however, come cheap. One method of securing the necessary funds to implement NHP 2017 is shifting the responsibility from government to the pharmaceutical industry by forcing companies to reduce the prices of their drugs, a solution that the industry is unsurprising disgruntled with. "India is only taking baby steps towards the concept of 'value over cost.' In many Western countries, you see value attributed to say a diagnostic test based on how much hospitalization or public spending it might save. In India, unfortunately there is still the tendency to correlate price with cost rather than value," warns Shravan Subramanyam, managing director of Roche Diagnostics.

"About 20 percent of the drugs manufactured in or imported to India are under price control based on the National List of Essential Medicines prepared by the Ministry of Health and Family Welfare," confides Bhupendra Singh, chairman of the National Pharmaceutical Pricing Authority (NPPA). "Our responsibility is to ensure that these drugs are available at affordable costs as per the government's guidelines, which we have implemented accordingly. Furthermore, under exceptional circumstances NPPA can cap the price of any other drug which is not part of the National Stockist of Field Medicines," he confirms.

"The biggest challenge is to convince the industry that our pricing is helping them instead of harming them. At the end of the day, we create affordability in a marketplace in which out of pocket expenditure accounts for between 60 and 70 percent of spending on medicines," argues Singh. Indeed, the most recent

Keeping it in the Family

Dilip Surana, chairman and managing director, Micro Labs Limited

Any visitor to India is immediately struck by the proliferation of family-run, family-owned firms and the local pharmaceuticals market is no exception to this trend. According to PwC, Indian family businesses are extremely optimistic about their growth, with 84 percent expecting to grow either steadily or quickly and aggressively over the next five years. An emblematic example of a second-generation entrepreneurial success is Micro Labs. "We have been active players in the market for the past 40 years and we have always positioned ourselves as a premium brand with quality at the forefront of our philosophy", muses Dilip Surana, chairman and managing director of the company.

Surana took over the reins of Micro Labs from his father in 1983, but was attentive to maintaining the company's traditional internal spirit and business philosophy. "We have started looking at in-licensing locally, whereas internationally we have more of a joint venture approach", explains Surana regarding his growth strategies. "For instance, in France we are tied with Biogran through which we market our products in France – you share your profits, but you also get the volumes immediately. In short, we are doing a lot of molecule-to-molecule as well as country-to-country business," he continues.

Under his leadership, "Micro Labs and its associate companies has become a multi-faceted organization with an annual turnover of approximately USD 25 billion, including global business and exports that contribute to 40 percent of revenues. While Indian family businesses are facing the challenges posed by government pricing policies and regulations, for some of them, moving up the value chain and producing branded generics seems still to be the overarching priority. "We want to be associated with quality. Our focus will be on niche generics and retroviral drugs in which we are doing a lot of work. In order to grow and develop specialty generics, quality is crucial," underlines Surana.

Ministry of Health figures suggest as many as 18 percent of Indian households face what are known as "catastrophic healthcare costs," defined as "health expenditure exceeding 10 percent of total monthly consumption expenditure."

Some companies have managed to de-risk their operations and are proving successful in bringing a steady stream of new, quality products to market despite prevailing constraints on prices. "The challenge is very much about identifying optimum ways to launch efficacious products at affordable price tags," acknowledge Satish Kumar Singh and Shashi Shekhar Kumar, managing director and vice president international business of Alkem's fully owned subsidiary Cachet. This might mean reworking the business model to hedge risks and reduce exposure to state mandated pricing policies. "The way we do it is for Cachet Pharmaceuticals Pvt. Ltd. to focus on the non-regulated market segments while Alkem Laboratories Ltd., our parent company, has its hold in regulated markets and, as such, we complement each other," he explains. "The end result is that we maintain a good tempo of product launches and patients periodically see new medicines coming in," they enthuse? .

"Recent changes in pricing ensure that the market remains dynamic and the pressures on industry are running high, but ultimately it is the patient that matters and that is why we have made 'going beyond the pill' a strategic priority for the future," recounts Venu Ambati, managing director of Abbott India. He believes that the industry should no longer content itself just with pushing pills and medical devices but needs to "play a proactive role in "building an interactive and affordable approach to public healthcare."

However, he is quick to point out that 'affordability' should not be dealt with in isolation, but rather as part of a comprehensive, holistic strategy. "We also need to focus on improving the other 'A's of the system – that is 'accessibility' and 'availability,' he muses. "There are multiple pathways to affordable medicine, but what is for sure is that we strive to be a proactive and involved partner in ensuring quality, trusted, affordable healthcare for the Indian people," he stresses. "Over the next five years, we want to create an innovative healthcare ecosystem that improves access and is based on technology and insights, for both 'now' and 'next' therapies."

THE INDIAN DOMESTIC MARKET: ENDURINGLY IMPORTANT

Despite the aforementioned pricing problems among other issues, there remains great cause for optimism in the Indian domestic pharmaceutical market. India's enormous population of around 1.35 billion; a national economy beginning to purr with 7.4 percent GDP growth projected for 2018; and a growing middle class with greater purchasing power – the number of households with a disposable income of more than USD 10,000 leaping from around 2.5 million in 1990 to nearly 50 million in 2015 – has led to market growth in both the innovative and generics segments.

Satish Kumar Singh Singh, managing director, Cachet Pharmaceuticals; Shashi Shekhar Kumar, vice president - international business, Cachet Pharmaceuticals; Venu Ambati, managing director, Abbott India Ltd

Amit Mookim, managing director South Asia at IQVIA, feels that the USD 36 billion Indian market is now entering a new époque. He explains that, "There are three phases in the development of the Indian pharmaceutical market. The first phase, which lasted from 1990 to the early 2000s, was the period of building up of the industry and the product mindset, where the plants came up, the portfolio came up and the TRIPS landscape was defined. The next stage was hardcore commercialization where individual companies started to



Amit Mookim, managing director South Asia, IQVIA; Umang Vohra, managing director & global CEO, Cipla; Suresh Pattathil, CEO, Ferring Pharmaceuticals

possess more than 150 brands. Today, large pharma companies typically preside over something in the region of 700 to 800 brands. Now, we are entering the third era, which is oriented towards patients and will likely transform the way that pharmaceutical companies operate in India."

Within this context – and despite the rapid internationalization of many Indian pharma companies – the Indian market remains the bread and butter of most domestic firms' operations. Umang Vohra, managing director and global CEO of Cipla, asserts his organization's commitment to India and the enticing opportunities still present there: "There is a lot of energy being spent in trying to make sure that Indian market lives up to its full promise. We are talking about a USD 36 billion market and Cipla is aiming to reach USD two billion in terms of sales in the country. The chance to service such a vast patient population is huge and we made this our main mission."

"We believe that the Indian market will ultimately consolidate as the number of manufacturers rises," Vohra continues, "I think what is driving India is, first and foremost, purchasing power. More and more Indians can afford medicines which, in turn, increases market penetration. Hospitals have attained a certain standard of caregiving and we see patients increasingly using hospitals to get treated. The second trend that we observe is a more conspicuous amount of consumption that goes into tier two, three and four cities. Last but not least, there is a favourable environment in terms of the policy context that generates access – price controls are one way to generate greater coverage. As such, India is largely a volume growth story."

TOP 15 PHARMA COMPANIES IN INDIA (2017)

#	COMPANY	MARKET SHARE (%)	GROWTH RATE (%)
	INDIAN PHARMA MARKET (TOTAL)	100	5.5
1	SUN PHARMA	5.5	7.0
2	CIPLA	4.6	3.2
3	ZYDUS CADILA	3.9	9.8
4	MANKIND	3.6	5.4
5	LUPIN	3.3	7.9
6	TORRENT	3.2	5.9
7	ALKEM	3.1	3.9
8	ABBOTT	3.1	4.7
9	RANBAXY	3.1	4.1
10	GLAXO	3.0	7.6
11	MACLEODS	2.8	6.1
12	INTAS	2.8	5.9
13	GLENMARK	2.4	9.3
14	ARISTO	2.4	3.5
15	PFIZER	2.4	-3.5

Source: IQVIA

STILL A LAND OF OPPORTUNITY FOR MNCS

For multinational companies, despite 'pharmerging markets' not holding the hype and allure they once did, India still stands as a land of opportunity for a variety of reasons. Novartis's Zia points out that "India, in terms of demographics, is the youngest nation in the world. The median age today is under 27 years. At the same time, it has a large aging population and lifestyle diseases together with a growing middle class will lead to a rise in demand for healthcare and hence pharmaceuticals."

Suresh Pattathil, CEO of Ferring in India, sees opportunities for MNCs in market shaping, positing that, "An area where foreign multinationals can truly make a difference is market definition. If the market is not formed yet for diagnostic treatment choice or even origination, then you have real rewards to reap from being the first mover." However, Pattathil is keen to caution that "If the market is already shaped and has become a commodity market, then foreign multinationals find it very difficult to enter certain segments. One has to judge how one wants to build and expand the business model in India and with a specialized portfolio and differentiated products then there is generally a higher chance of success."

If pricing remains a bit of a sore point, there are improvements with other aspects of the regulatory landscape. In May 2016, the government issued a National Intellectual Property Rights Policy with the aim of strengthening the country's somewhat precarious IP regime and fostering new tranches of inward investment. As might be expected, such a move was roundly applauded by innovative drug developers. "Brands are there for a reason: they denote quality, the years or how much a company has invested in R&D globally, and how much you care about the patient and whether you have pharmacovigilance and sometimes continued medical education in place…I do not think that it is in the best interest of the

patient for brands to disappear completely so this step is welcome news," opines OPPI's Kanchana TK.

Sanjiv Navangul, managing director, Janssen

Many of the multinationals invested in India not only to see the opportunities inherent in the country, but also the ethical importance of contributing to the economic health of the nation, bringing their treatments to the country and meeting unmet need. Roche's Shravan Subramanyam, for example, sees his affiliate as, "not just a multinational organization operating in the diagnostics space. What we are doing in terms of enabling health is actually nation-building and contributing to the economy. India is a very labor- and people-intensive market. Not without reason is the country is known for its skilled labor and technology. If our people fall sick we lose an economic driver, which is the reason why the discussion around preventive healthcare and keeping people healthy is so vitally important to running the economy."

Sanjiv Navangul, managing director of Janssen, is clear that "Big Pharma companies should be interested in the health of the Indian population as we are 18 percent of the global population and nearly 20 percent of the global disease burden – it is an ethical responsibility for Janssen to be present in India." Furthermore, Navangul feels that traditional pharma business models are not appropriate in India, suggesting that, "Simply providing medicines to patients, especially in a country with limited resources like India, does not solve the problem. We take an integrated disease management approach to supporting patients, which includes partnering on campaigns aimed at driving disease awareness and treatment adherence, undertaking medical innovation and R&D, and empowering a new generation of healthcare workers through training on clinical management of diseases."

For Novo Nordisk's Melvin D'Souza, it is the sheer numbers of patients affected by diabetes that drives the company's activities in India. He notes that, "Novo Nordisk estimates that 46 million people in rural areas are affected by diabetes and that the number of patients will significantly grow to 73.5 million in 2030." To combat this situation, D'Souza explains that, "In partnership with local health authorities and other stakeholders, Novo Nordisk in India helps more than 4,000 children through 21 'centers of excellence' across the country where they provide free insulin, free consultation and free blood sugar check-ups twice a day to children under 18 with no income."

Novartis has also been working to fill the gaps and improve access to medicine via infrastructure development through it Aroga Parivar ("healthy family" in Hindi) initiative, first launched in 2007. This program, Novartis's first social business model, is "organized into cells that currently total 239. Each cell – covering 35-40 km – includes 60 to 75 villages and small towns with around 200,000 inhabitants.

Today, the program operates across 11 Indian states, covering some 14,000 villages and small towns that are home to more than 32 million people," notes Jawed Zia. Arogya Parivar broke even in less than three years and has been sustainable ever since, meeting both its commercial and social targets. It is expected to reach 44 million people through health education meetings and health camps by 2022."

'MAKE IN INDIA': A BOON FOR MULTINATIONAL MANUFACTURERS

Ranjit Madan, CEO, LSSSDC

In addition to policy updates in the healthcare, pharmaceutical pricing and IP fields, India has also looked to improve the state of its manufacturing industry. On this track, Prime Minister Modi's 'Make in India' campaign, first launched in 2014, aims to attract even more MNCs by allowing 100 percent FDI in 22 sectors of the economy and emphasizing the country's manufacturing appeal and cost/value ratio.

Ranjit Madan, CEO of the Life Sciences Sector Skill Development Council (LSSSDC), explains that, "the 'Make in India' campaign encourages companies to set up shop in India and leverage the advantages that the country has to offer in terms of demography and domestic demand." "The country's potential as a competitive place to set up operations and the ease of doing business are definitely getting better," he assures. Within this cross-industry scheme, "the government is fully cognizant of the opportunity and potential that pharmaceuticals has to offer and has therefore designated it one of the five or six priority sectors for the 'Make in India' initiative," notes Madan.

India's attractiveness as a manufacturing hub is based on a number of attributes. Suresh Pattathil of Ferring identifies three: "Firstly, to put up any facility in India is about 40 percent cheaper compared to other global sites. Secondly, here you have trained manpower available which, again, is cheaper than in the US or in the EU. Last but not least, India has a big domestic market which will continue to grow over the next five to ten years." Not only does India fare well cost-wise in comparison to the US and EU as a manufacturing destination, but Pattathil also posits that his nation punches above its weight even compared to China, adding that "when it comes to manufacturing basic medical products and drugs, India is far superior to developing countries in the Far East due to resources including manpower, a talented and technically educated workforce, along with its many WHO GMP (Good Manufacturing Practices) and US FDA approved facilities."

Dishman manufacturing plant

Sanjit Singh Lamba, managing director, Eisai Pharmaceuticals

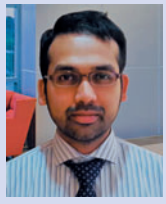
Dilip G Shah, secretary general, IPA

Sanjit Singh Lamba of the Japanese firm Eisai – which exports Indian manufactured drugs to Japan as well as supplying the Indian market – outlines his company's impressive manufacturing footprint in India: "We spent around USD 50 million on the current manufacturing facility in 2009. In 2012 we filed this on an international level to receive accreditations, in the same year we were awarded the title 'facility of the year' and in August 2011 we started the first exports to Japan. I think this has been a sort of case study and we created the best-in-class quality systems." Singh Lamba is adamant that in-country manufacturing no longer means compromising on quality standards, confiding that "What we invested most in was perhaps the training of the Indian personnel at the site because we needed to create an excellence in understanding the real needs of the Japanese patients who, of course, expect exemplary standards. And we were, quite frankly, very successful in doing so: our facility has exported 1.5 billion tablets to Japan in the last three years and we never had quality complaints by patients or authorities."

TENTATIVELY SCALING THE VALUE CHAIN

India may have raised its performance when it comes to manufacturing standards and the quality of medicines being produced, but the jury remains out about the country's ability to properly master cutting-edge technology at a time when drug development is undergoing great transformation and biologics are increasingly the name of the game. Unquestionably more in-country R&D is being conducted than in yesteryear, but that, of itself, only paints part of the picture. "Back in 2000, when the IPA was founded,

Reconsidering Ophthalmologic Innovation



Nikhil Masurkar, executive director, Entod Pharmaceuticals

Entod Pharmaceuticals is a specialty pharmaceutical company and, while its main focus has always been ophthalmology, the company has the ambition to invest in stem cell research and become market leaders in the field of ophthalmology in ten years' time by adding more cost-effective and highly effective dosage forms to their strong product portfolio.

"As part of this, we have always been competing with the multinationals, and all this time has been quite difficult, but the last ten years we have seen exponential growth in our company. This has been purely because of our business model, which is quite unique compared to other ophthalmic players", stresses Nikhil Masurkar, the Entod's executive director.

With its two formulation laboratories in Glasgow and Mumbai, Entod has historically been focused on formulation R&D, which is aimed at improving the formulations of the existing molecules that they have. "Our take, given that we operate in ophthalmology, has always been that we do not need newer molecules but better dosage forms. If you take for instance other therapeutic areas, medical advancements have been impressive whereas in ophthalmology we have been using eye drops since the 1920s – our very research objective is to have better dosage forms that last longer and improve patients' compliance", affirms Masurkar.

Kiran Mazumdar Shaw, chairperson and managing director, Biocon

companies were spending between one and two percent of turnover on R&D, whereas now our members' research-related spending ranges between two and 13 percent, with an average of eight percent," exclaims the IPA's Dilip G Shah.

At the forefront of this new era of Indian R&D is Biocon, which Kiran Mazumdar-Shaw asserts, "today stands apart as a very different kind of biopharmaceutical company in India as we have strong leadership due to our strong global perspective of what we do. The fact that our product Ogivri™ is the first biosimilar to trastuzumab approved by the US FDA is a testimony to that focus." Mazumdar-Shaw continues, "We realized that biopharmaceuticals required huge investments both in terms of R&D and creating manufacturing facilities – and this is what I decided to do as an entrepreneur as I felt there was a big need as well as an opportunity to differentiate ourselves from the rest of the biopharmaceutical companies in India."

Another investor in R&D is Cachet Pharmaceuticals, as Satish Kumar Singh and Shashi Shekhar Kumar explain: "major R&D activities are carried out at Alkem Laboratories Ltd (Cachet's parent company). They have a dedicated R&D center. At Cachet Pharmaceuticals Pvt. Ltd. we have a small R&D department which operates at our Baddi manufacturing location. We are committed to developing world class medicines to benefit the patients at affordable prices. For products to be marketed in international markets, we carry out additional studies like bio equivalence studies, stability studies as per the country requirement. Our scientists ensure the safety and efficacy of our products at par with the innovator."

"Our country has long been renowned as a manufacturing powerhouse and today we see many leading companies investing big in R&D: the top five indigenous drug makers together spent a record of USD 1.2 billion in 2017," posits Sharvil Patel, managing director of Zydus Cadila. "However, I firmly believe that it is not a matter of how much money you spend, but rather a question of where you are focusing your energies on and how successful you are in those areas that will determine whether you actually advance up the value chain," he tempers. "Most of what I see around here is players investing more in incremental innovation by coming up with new formulations and product enhancements or filling outstanding gaps in already existing therapies."

Entod would be a good example of this type of phenomenon about 'innovating around the molecule.' "We do not, as such, research newer molecules, but rather try to improve the formulations of what we already have in our portfolio and our research is thus more focused on innovative drug delivery which is an area where we identify immense potential to make therapies more patient-centric," explains executive director, Nikhil Masurkar.

Indeed, examples abound of Indian firms bolstering their value offering, but in many cases this is still within the context of generics. "We have stopped the production of vanilla generics and now dedicate ourselves towards producing specialty ones. This is a logical next focus in any market in which we identify the potential for branded promotion," recounts Micro Labs chairman, Dilip Surana.

Other firms seeking to buck the trend include Zydus Cadila, which has even gone as far as to purchase a Western company in a bid to break out of the innovation silos experienced back home in India. "We started the year with the acquisition of US-based Sentyln Therapeutics. Basically, we had always been strong in the generics segment



J.R. Vyas, Chairman and managing director, Dishman Group; Ashok K. Bhattacharya, executive director, Takeda; Sharvil Patel, managing director, Zydus Cadila

and we felt that the time was ripe to build a specialty care franchise alongside. Through this acquisition we are looking to enhance our commercial presence in terms of how to tailor products and place them on the market but, more importantly, to learn a lot and move our business offering to the next level through exposure to new thinking and work styles," says Sharvil Patel.

J.R. Vyas, chairman of Dishman Group, tells a not altogether different story of looking abroad to secure the kind of R&D impetus and blue sky thinking that he identified as lacking within the domestic market. "When I went to Switzerland to close the operations for the purchase of Carbogen Amcis, I saw that more than 400 Swiss German PhDs were working in their R&D lab. This ultimately spurred me to go ahead with the acquisition," he recalls. "Historically, R&D centers were concentrated within the developed world as companies restricted high-end R&D activities to their home country and within the physical boundaries of the corporate firm. Little by little, certain multinationals are belatedly deciding to look into more emerging markets and establish local R&D centers, but, while the market size renders India an attractive location for large foreign companies seeking to expand operations, I believe that the lack of standardization of training across the country plays an important role in preventing companies to do so. For instance, in the Carbogen Amcis offices everyone is PhD educated, commercially savvy, but you would be hard pressed to seamlessly source that same base of talent out here in India," he reasons.

Some argue that the real impediment to transformative innovation is not just the local resource base or amounts expended on R&D, but the ingrained mentality of scoping in on 'affordability' and 'volume.' "Currently, India holds the distinction of being the pharmacy of the world, but the ultimate vision of becoming an internationally renowned innovation hub is still some way off. In order to accomplish this ambition, there needs to be an overhaul of the country's pricing policy and a certain shift of mentality," posits Takeda's executive director, Ashok K. Bhattacharya.

"We are cautiously scaling the value chain, but it is slow and gradual process... the basic reality today is India is excellent at re-engineering; however, we still have much to do to refine our skills at innovation. This is very much a nationwide predicament…even looking outside of medicine, I cannot recollect the last great car, device, or phone we created," laments OPPI's Kanchana TK.

Others take a more optimistic view and believe it is only a matter of time before India starts to realize its full innovation potential. "Low-cost manufacturing capabilities augmented with a strong R&D is very much how I see Indian pharma's future," predicts Abbott managing director, Venu Ambati. "As we gradually shift from generic to innovative, 'bigger is better' models are also slowly caving in. I am sure India will some day shift to being recognized for its innovation capabilities, rather than being just a frugal innovation location, which incidentally is something the country does very well indeed," he forecasts.

LOOKING WESTWARDS

On the back of a strong domestic manufacturing base and the aforementioned prowess in frugal innovation and affordable medicine, homegrown Indian pharma brands like Lupin and Glenmark have successfully made it into the top 50 companies globally in terms of sales by taking a larger role in the export of generic drugs and vaccines. With Indian companies

Yogesh Agrawal, managing director, Ajanta Pharma

now covering more than a quarter of the overall US generics market, it goes without saying that the main export target is the new continent.

After a few initial hiccups, Indian ability to penetrate the American market has been a resounding success. "In 2015, when some of our members received warning letters from the US FDA, it came as quite a surprise. We did not, however, take the view that India and Indian companies were being targeted as we had already established a fairly positive relationship with the US FDA," reflects the IPA's Dilip G Shah. "In fact we have entered into a biannual direct dialogue with the FDA that will benefit both sides and the strong results of these kind of initiatives are there for all to see: right now approximately 1,400 manufacturing units in India are WHO GMP certified, 573 facilities are FDA approved and over 800 are UK MHRA approved. India has the highest number of US FDA-registered manufacturing facilities outside the US and we will work toward becoming a quality benchmark globally," he emphasizes.

"I believe the lesson now is well learnt and that there is the willingness to understand the seriousness of complying with US standards, not only at GMP level but also in terms of data integrity," perceives Yogesh Agrawal, managing director of Ajanta Pharma, of which a full ten percent of annual revenues of USD 308 million derive directly from the US. "Some 35 percent of US generics volume is supplied by Indian companies, hence Indian companies play a massively important role in the US generic space, so I am very optimistic," he adds.

Certainly, the American market's reliance on Indian affordable medicine continues to deepen. The US FDA has recently granted approval for Tesaro's cancer drug which will generate revenues of two billion over the course of three to four years and which Dishman will produce at Unit Nine of its Bavla facility. "When the clinical trials of this drug were happening, Dishman was the API supplier alongside being a key supplier to Tesaro. Now that this cancer drug has been approved the volume will jump significantly. Given the relationship and the trust that we have established over the years with the US FDA they allowed us to start the supply of APIs to Tesaro already," remarks chairman J.R. Vyas.

THE SOUTH-SOUTH DIMENSION

While Indian companies' forays into the American pharma market are widely recounted, less publicized has been the manner in which many Indian entities are establishing a strong foothold in underdeveloped or dysfunctional markets in Africa and Asia. "As part of our internationalization strategy, we picked some unique emerging markets like Iraq for instance where we invested during the UN sanctions. In Iraq we participated in the Oil-for-Food Program, which was a UN resolution established to allow Iraq to sell oil on the world market in exchange for food and medicines. When the market opened up, we saw that there were many opportunities and, as a matter of fact, we are today the sixth largest private pharma company in the country," narrates Ajanta Pharma's Yogesh Agrawal. "In Africa, we have established wide-ranging footprint and this is actually where 40 percent of the global revenues come from… Furthermore, we supply antimalarial products to initiatives like the Global Fund and stand proud as the first generic company to secure WHO prequalification approval," he adds.

Entod's development story is not dissimilar. "Our main focus is in Africa right now and within Africa we have certain markets that we are penetrating quite well such as Nigeria and Kenya and South-East Asia is also very much on the radar with the Philippines counting as one of our biggest export markets… Our aim as a company is to provide medicines in countries where those medicines do not exist so we find it much more exciting to go to a small country in Africa where we can make a tangible impact," reasons Nikhil Masurkar.

Part of the reason why Indian companies are able to thrive in such markets may well be to do with their first-hand experience of India's own developmental trajectory. "When you look at India three years back, places like Morocco, Algeria or some other African countries are easily associable to what our own country used to be like. Accordingly, we tend to replicate the Indian business model in some countries," observes Cipla's Umang Vohra.

"2017 has been the year during which we evaluated how to gain a bigger share in emerging markets. South Africa is a great example of this as we rank as the fourth biggest pharmaceutical company in the country. We see this as a great opportunity because, while the time for Africa may not be this or next year, there are billions of people living there and some of these places are ignored by companies because they are not the most exciting locations to set up shop, compete and grow, but you do have opportunities to gain a great first-mover advantage," he expounds.

On top of that, there is the Indian tendency to not equivocate, but rather to race in and seize opportunities in advance of them becoming completely prospective. "Wherever we see potential, we conduct studies and surveys. Sometimes it is just very fortunate. For instance, I once read an article about blood products being carried by drones from one city to the other in Rwanda. We did primary research in India and then decided to travel there with my team for survey and to check the possibility to start a pharmaceutical business and nowadays we operate pretty successfully there," recall Cachet Pharma's Satish Kumar Singh and Shashi Shekhar Kumar.

Setting the Standard

How one pharma vet helped create the first industry-wide training standards for aspiring medical affairs professionals

When it comes to medical affairs, Dr. William Soliman is no newbie. He has held a number of key positions where he was instrumental in launching a variety of innovative platforms expanding the role of medical affairs across the pharmaceutical industry.

That experience, at companies such as Retrophin, Veeva Systems, Eisai, Gilead Sciences, Abbott Laboratories, Boehringer Ingelheim, and Merck & Co., has led Soliman to what could arguably be his most influential role to date—the developer and chief advocate for the Accreditation Council for Medical Affairs (ACMA).

Although, technically, his official title with the organization is founder and chair, the mission of the ACMA—to establish, certify, and maintain the competencies of qualified medical and scientific professionals who have a focus in medical affairs within the pharmaceutical and biotechnology industries—is uniquely the result of Soliman's personal experiences and keen observations of the industry.

During his 20 years working in medical affairs, Soliman observed a number of situations that all led back to one basic concept: there was a lack of universal medical affairs standards when it came to training people for these roles. While each company Soliman worked for had its own internal training, there was no industry-wide standard.

William Soliman, executive chair of the Accreditation Council for Medical Affairs (ACMA).

Toward the end of 2013, Soliman gathered a mix of medical and pharmaceutical school deans, medical affairs professionals, and others to pursue the spark that had been burning inside his head for a while.

"'Wow, that's going to be a lot of work,'" says Soliman, with a laugh, as he recalled what the most common initial reaction was to his idea to create a set of standards. But, Soliman points out, such reactions were always quickly followed by unanimous support and agreement that this was a missing key to the medical affairs training puzzle.

It took about two years to design the program, which includes a board-certified medical affairs specialist program that consists of 20 different modules, progress quizzes, and case studies.

The program has been translated into over 10 languages, and since its inception, has had approximately 3,000 people go through it.

"I never thought it would get to this large of a scope this quickly, especially from an international perspective," says Soliman.

A component to the ACMA's success and something especially important to Soliman is the partnerships they have built with academic institutions to help provide training in a subject area traditional medical or pharma schooling doesn't typically offer. Some of these institutions include Rutgers Graduate School of Biomedical Sciences and NYU's School of Medicine.

But, it doesn't stop there.

Most recently, Soliman says, the city of Chicago has approved the ACMA as the provider of continuing education to support license renewal for the mandatory pharmaceutical representative credentialing program.

To be an effective medical affairs professional in this day and age, one must understand compliance and regulations, have a broad knowledge that includes genomics and diagnostics, and have a comprehensive understanding of the ever-changing healthcare system, among other things. ACMA's program is updated regularly to keep up with those changes.

For pharma companies, Soliman stresses that an essential takeaway from this program is that it is a way to mitigate risk, especially in such a highly regulated environment.

"This is a way to empower the industry, and empower us as professionals," says Soliman. PE

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