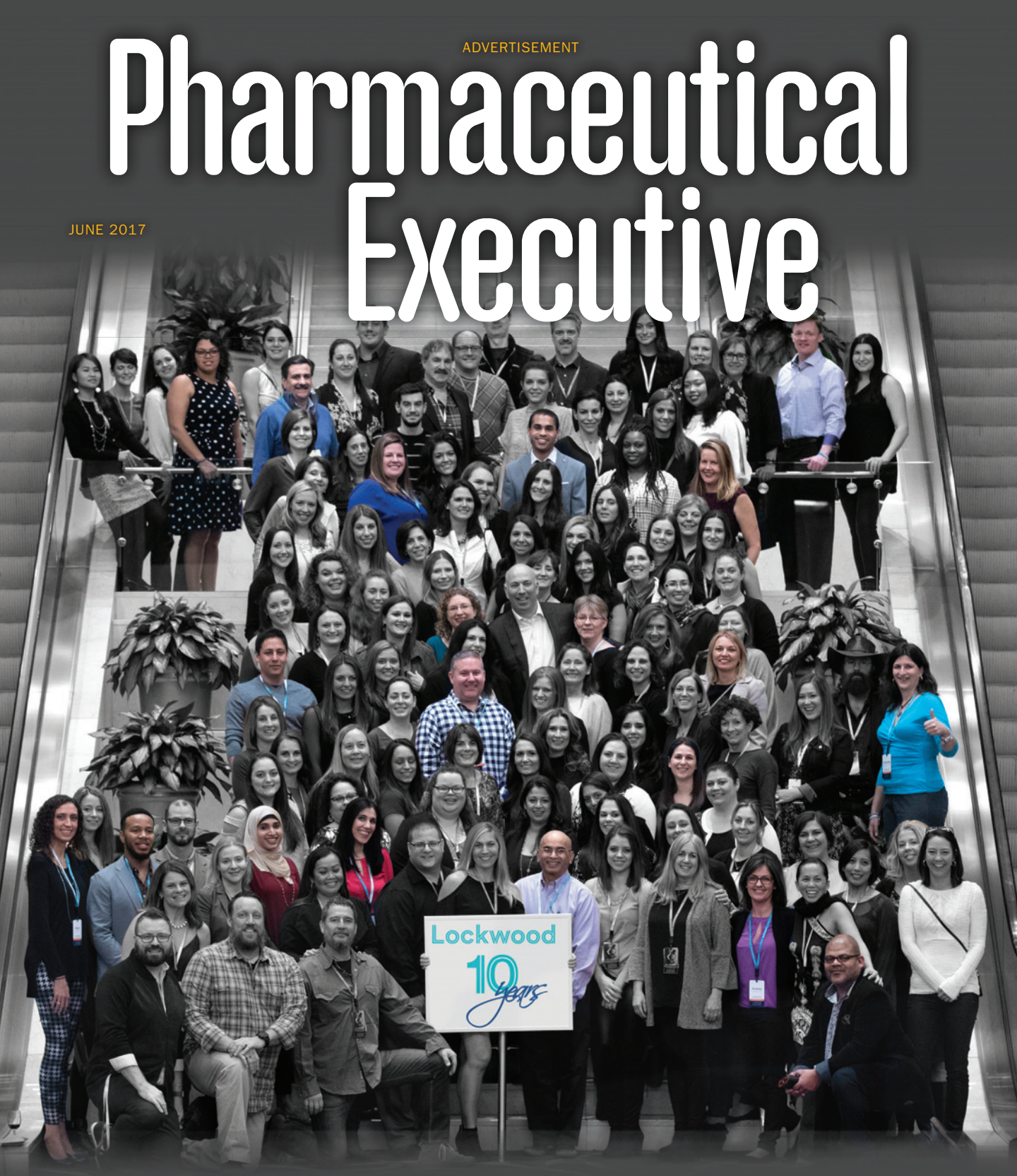
Pharmaceutical Executive

JUNE 2017



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JUNE 2017
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VOLUME 37, NUMBER 6

2017 PHARM EXEC 50

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Talent That Takes You into the Future

WHAT DO YOU WANT TO BE WHEN YOU GROW UP? That's a question we've all heard at some point in our lives, usually when we are in grade school (though for some of us, we may still be wondering). When I asked my sons when they were grade-schoolers that question, the choice was fireman or dog walker. Now in high school, it's much more nuanced, but neither has said "CEO" or definitely not say Chief Digital Officer or Chief External Innovation Officer. But these are the roles noted in our Pharma 50 article from consultants at Russell Reynolds as up-and-coming in the pharma C-suite (see page 18). In fact, there has been much talk about what future pharmaceutical executives face, and the skills they will need, in regard to industry disruption.

LISA HENDERSON
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Recently, Senior Editor Michelle Maskaly attended the FT US Healthcare & Life Sciences Summit and came back with the news that future pharma leaders may not only *not* be from pharma, but will have learned how to fail. If you can't explain how you learned from failure, then you won't be able to address the complexities of the pharma company of the future. (read here: http://bit.ly/2rUYQJ9)

We are currently in the process of accepting nominations for our annual Emerging Pharma Leaders feature, which highlights those up-and-coming individuals that show promise in taking pharma to the next level. What are the qualities that will make them the leaders of tomorrow? We encourage you to submit your nominations at http://bit.ly/2r0yntL by the end of June.

This month also marks the annual meeting of the Drug Information Association, where industry professionals network, engage and collaborate with their colleagues. We recently spoke with Barbara Lopez Kunz, Chief Global Officer of DIA, about the current challenges in our industry. She said, "This is a time of enormous dynamism in the healthcare space. And many of the stakeholder communities have been working hard to optimize within their particular part of the ecosystem. But what we find, is that the opportunities to really make step changes sit at the system level. And that's where DIA plays an really important role. We need to make sure that we address the right problems and think about what people we need to bring forward to make sure we get the regulators integrated with innovators and increasingly, the payers and HTAs, and, of course, the patients have a very strong voice in healthcare product development. We capture the insights that come from these discussions and turn them into action plans, which can be taken up by industry leadership and policymakers and others across the community."

Terese Waldron, Director, Executive MBA Programs, for Saint Joseph's University, and *Pharm Exec* Editorial Advisory Board member, noted some interesting trends in its 2017 Pharmaceutical & Healthcare Marketing MBA graduating class.

"This year, we noticed that many of the titles include 'leads;' so while they have the skills, workload and responsibility of an executive, their titles don't necessarily reflect that," said Waldron. She believes that is because companies are more compressed than ever and the "executive" roles are fewer. "This, of course, leads to increased competition to advance in one's career," noted Waldron.

In addition, also potentially based on the shrinking employee base, many of the graduates are wearing multiple hats. "We see that they are definitely taking on more duties that cover multiple roles," said Waldron.

"In the next two to three years, the pharmaceutical industry is going to become even more dynamic," she explained. "Of course, I'm a big believer in graduate education. SJU's Pharmaceutical & Healthcare Marketing MBA helps high potentials to acquire the skills and strategic strengths necessary to tackle the issues that are coming quickly to the industry. Pharma companies need that strength. I encourage our corporate clients to continuously build their talent. Companies need to invest in their talent now, and not just at the executive level. The middle-managers, directors and leads may be the pivotal employees that need to be leveraged for the future."

Based on a third-party study of SJU's graduating class, nearly 70% have further developed the skills that have already translated into career advancement; compared to 50% averages at nationwide levels. "I look at my Pharmaceutical & Healthcare Marketing MBA graduates, and I know they have the confidence and knowledge to go forward and grow their companies," Waldron concluded.

Whether or not members of this year's MBA graduating class ever imagined themselves to be the next Chief Transformation Executive, or the next Emerging Pharma Leader or the next thought-leader speaker at DIA, there is one thing for sure, there is no lack of talent, expertise and passion in this industry. It is time for the talent to go forth and conquer.

Pharmaceutical Executive

VOLUME 37, NUMBER 6

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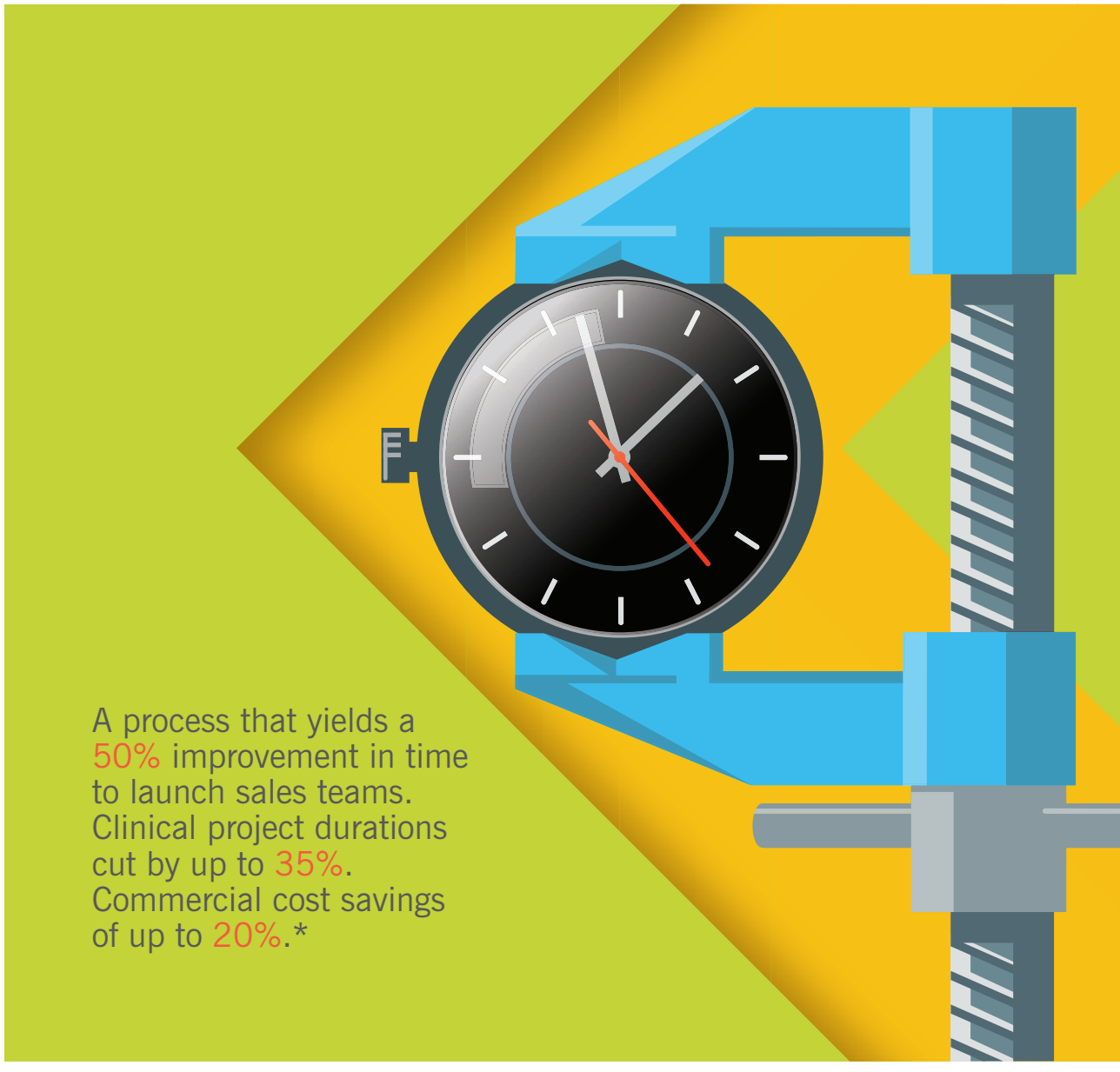

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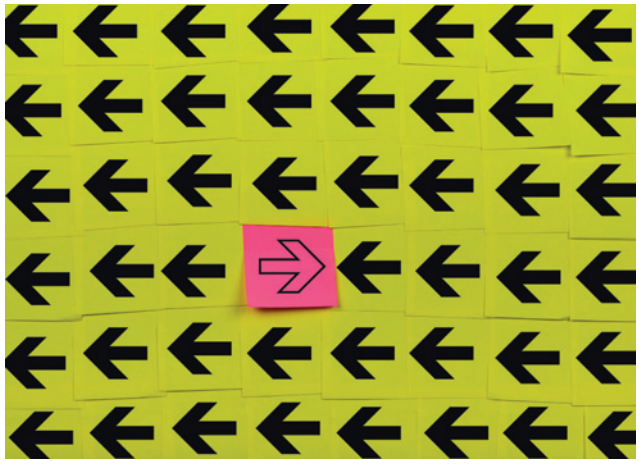

2017 *Pharm Exec* 50

Pharm Exec's 17th annual listing of the top biopharma players paints a stable picture of performance for the usual placeholders, but change and disruption to current business models could upend positioning in the years ahead.

Navigating Through Disruption

By Waseem Noor and Saule Serikova

Outlining the new leadership tactics and C-level specialty roles that Pharma 50 companies will need to steer the industry through the disruptive event on its horizon.

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Patient Engagement

The Pharma-Patient Connection

Julian Upton, European and Online Editor

The patient voice is growing louder in all aspects of the drug development and commercialization journey. *Pharm Exec* examines some of the current industry thinking on the evolving pharma-patient relationship.

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Executive Roundtable

Where is Your Physician?

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A panel of biopharma executives convenes to discuss market access and the changing dynamics in reaching physicians and healthcare professionals.

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NEWS & ANALYSIS

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From the Editor

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Country Report: Taiwan

Although the local pharma and biotech sectors in Taiwan have yet to emulate the success story of its semiconductor industry, companies in the life sciences have reached a solid level of maturity, notably driven by the substantial investments injected by Taiwan's successive governments over the past two decades.

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Readers Weigh In

I'm not so sure every consumer and patient is going to welcome Amazon amassing, leveraging and flogging their medical history.

Anonymous, 5/25/2017
"Amazon and Pharma: Is the Hype Real?"
bit.ly/2qWvMCE

Twitter Talk

■ #PriorAuthorization doesn't have to be a challenge. Independent & objective PA reduces burden for all stakeholders.

HID, @thePAexperts, 5/19/2017
"Tackling the Prior Authorization Challenge: A Critical Task for Pharma"
bit.ly/2rp7VwZ

■ The FDA has no authority over drug prices. In fact, adcomms aren't even supposed to consider price in deliberations.

David Kroll, @davidkroll, 5/5/2017
"Prices, Opioids, and Ethics Dominate FDA Confirmation Hearing"
bit.ly/2r4Dk4K

■ The key for effective social media marketing is in the personalization of content.

Jessica Laurendeau, @jlaurend, 5/23/2017
"Marketing in the Social Media Stream: The Solution is Personal"
bit.ly/2rGTu7m

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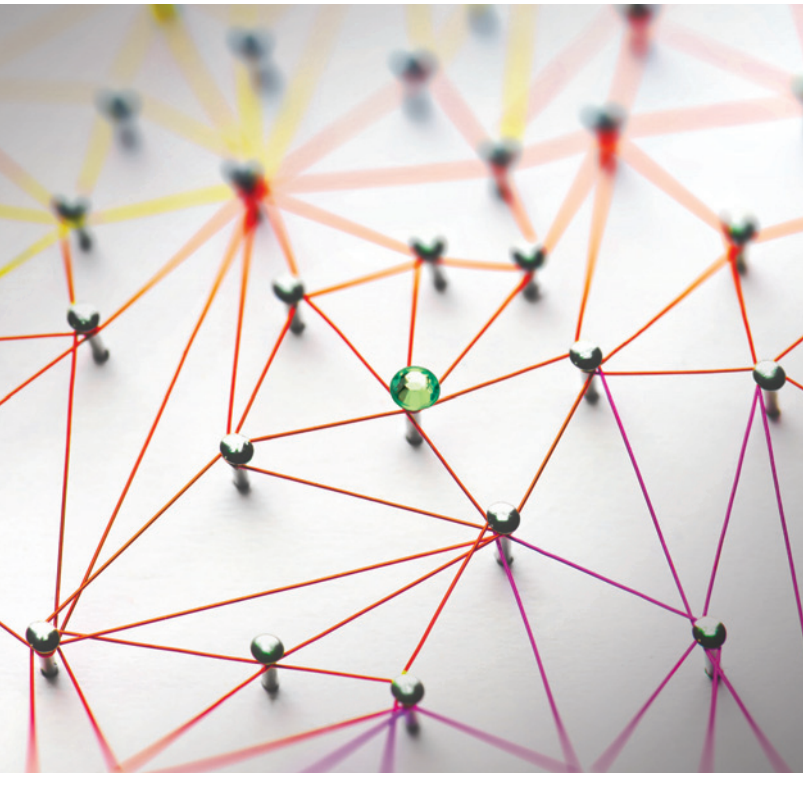

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Gottlieb Takes Reins at FDA, Big Issues Loom

New legislation, administration priorities raise multiple challenges for new commissioner

The Senate confirmed Scott Gottlieb last month as FDA commissioner, encouraged by the nominee's medical credentials and his familiarity with agency policies and programs. An earlier stint as FDA deputy commissioner, personal experience as a cancer patient, and the threat of questionable alternative White House job candidates helped soften the opposition from those concerned about Gottlieb's close ties to industry and potential conflicts of interest.

His first months on the job may be less stressful due to recent Congressional approval of a budget increase for the agency through September. In addition, the legislators are moving to enact a relatively "clean" bill to reauthorize FDA user fee programs for drugs, medical devices, generic drugs and biosimilars before August.

At the same time, FDA continues to face challenges in recruiting the scientists and experts it needs to efficiently evaluate ever-more-complex medical products. And the administration's order for federal agencies to drastically cut regulations raises the prospect of major changes in FDA standards and rules. Funding is uncertain for next year, and a revamped national healthcare system and Medicare budget cuts could reduce coverage and squeeze the broader market for pharmaceuticals and medical products.

Meanwhile, Gottlieb faces a host of policy decisions and administrative issues. During the confirmation process, he backed policies to bring more innovative generic drugs and biosimilars to market and to loosen restrictions on marketer communication of off-label drug information. He earned points by discounting claims of a link between vaccines and autism, signaling some independence from the Trump administration. He also supported greater FDA transparency, possibly through public release of "complete response" letters on nonapproval of drug applications, something long opposed by industry.

Looking at FDA's broader responsibilities, Gottlieb will have to keep a watch on FDA's Program Alignment initiative, which is bringing major changes to the agency's field inspection force after several years of planning. In non-drug areas, FDA faces strong industry opposition to its rules governing food processing and to regulation of cigars and e-cigarettes. The agency is embroiled in a battle over the governance of laboratory-developed tests, and medical device manufacturers seek faster approval of more innovative products.

Combating opioids

It's common for a new commissioner to focus initially on one or two priorities among FDA's vast portfolio of programs affecting public health and medical care, and at the top of the list is stemming the nation's opioid epidemic. Gottlieb cited opioid drug abuse as a "public health emergency on the order of Ebola or Zika" at his confirmation hearing in April; the challenge now is for FDA to ensure access to effective treatment for patients living with pain, while combating public abuse and misuse of these medicines.

FDA has encouraged development of more abuse-resistant formulations, as well as treatments to prevent death from overdose. But such innovative products can be costly, often driving addicts to cheaper, more dangerous medicines. Clinicians and health officials would like to see more effective non-opioid pain treatments and are looking hard at pharma marketing and distribution systems for these products.

On the drug safety front, FDA once again may become embroiled in the battle over secure supply chains and drug counterfeiting, which play a role in the debate to loosen the reins on drug imports to help control outlays for prescription drugs. There's a renewed clamor on Capitol Hill to permit the import of cheaper drugs from Canada and other countries, particularly where shortages and limited competition in the US drive up prices (see sidebar on page 12).

Cures and innovation

The new commissioner comes to FDA as it begins the considerable task of implementing

JILL WECHSLER is *Pharmaceutical Executive*'s Washington Correspondent. She can be reached at jllwechsler7@gmail.com

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References: 1. White House Office of Press Secretary. Fact sheet: Obama administration announces additional actions to address the prescription opioid abuse and heroin epidemic. White House website. https://www.whitehouse.gov/the-press-office/2016/03/29/fact-sheet-obama-administration-announces-additional-actions-address. Accessed December 20, 2016. **2.** Centers for Disease Control and Prevention. Understanding the epidemic. CDC website. https://www.cdc.gov/drugoverdose/epidemic/. Accessed December 20, 2016.

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multiple policy changes authorized by the 21st Century Cures legislation. The day Gottlieb was confirmed, the FDA Science Board approved a detailed work plan for allotting the $500 million (over nine years) provided by Cures to carry out numerous programs intended to advance new therapies and ensure patient access to treatment. FDA faces tight deadlines for issuing new guidances, reports and regulations and for holding public meetings with stakeholders to devise and revise key programs for product development.

Some of the Cures initiatives are familiar, such as qualifying more biomarkers and other drug development tools, expanding the role of patients in vetting the risks of new therapies, and better coordinating the work of FDA Centers, particularly for combination products. A new program involves establishing a framework for approving regenerative therapies, which gained a new designation and review process under Cures.

The legislation also supports more "modern" clinical trial design and greater use of real-world evidence to approve new indications and support post-marketing studies. Critics argued that faster approvals based on modified studies would undermine the FDA gold standard for assuring medical product safety and efficacy. Gottlieb agrees on the importance of maintaining high FDA approval standards, but applauds innovation that permits faster studies as likely to advance medicine and science without compromising safety.

Gottlieb cited opioid drug abuse as a "public health emergency on the order of Ebola or Zika;" the challenge now is for FDA to ensure access to effective treatment for patients living with pain, while combating public abuse and misuse

Agency officials anticipate that Gottlieb's prior experience at FDA and his interest in patients and public health will ease the transition. FDA's job of processing reams of data and making hundreds of decisions every day continues despite changes at the top, observed Janet Woodcock, director of the Center for Drug Evaluation and Research (CDER), at a recent conference. "The work goes on," she said, noting that FDA's staff can help insulate the commissioner from difficult individual product regulatory decisions.

Yet, FDA faces "many uncertainties going forward," observed then-acting FDA commissioner Stephen Ostroff at last last month's annual meeting of the Food and Drug Law Institute (FDLI). He expressed concern about the current "charged regulatory environment" and possible threats to agency funding.

FDA plays an important role in developing new vaccines and therapies to combat deadly infectious diseases, a job that requires new research capacity and regulatory flexibility, he noted, adding that an abundance of scientific opportunities related to FDA programs can yield a healthier future for all. PE

FDA and drug prices

During the confirmation process, Scott Gottlieb voiced skepticism about boosting imports to lower drug costs. But he is under pressure now to show the White House how FDA can "do more" to help lower drug prices. His main strategy is to approve more generic drugs and biosimilars to generate market competition. Gottlieb wants to clarify the rules governing the testing and approval of complex generics, such as skin creams and inhalants. He also backs efforts to revise labeling rules and policies that block access to innovator test products, as well as new policies that expand the off-label information that marketers can discuss with payers and formulary committees.

A trickier issue involves added market exclusivity periods for orphan drugs, biologics and other critical therapies, and reform efforts to curb such protections could re-emerge as a way to limit patent "evergreening" that maintains high prices. More streamlined clinical research programs that reduce the cost of developing new therapies or halt studies headed for failure could be framed as strategies for lowering launch prices. And modern manufacturing systems that ensure drug quality, moreover, may gain impetus as investments that can prevent costly shortages and recalls.

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Europe: A Long Summer of Drug Pricing Tension

Several interventions and developments across the continent likely to keep discussions around drug affordability on high burn

I make no apologies for returning to the subject of drug pricing. In the hothouse atmosphere of European governments' anxieties over how they are going to afford ever more expensive medicines, recent weeks have seen perspiration breaking out on the brows of ministers, officials and drug company executives.

EU enters fray

The most sensational intervention came from an unusual quarter—the European Union's competition watchdog. Margrethe Vestager, the commissioner responsible for antitrust, announced a formal investigation into Aspen Pharma's pricing policies. This is the first time the Commission has ventured into this field. Until now, the EU has left drug pricing decisions firmly in the hands of national authorities, since EU law leaves each member state sovereign in how it organizes and pays for its health service.

An Italian court already fined Aspen last year for increasing its prices sharply.

Vestager justified her unprecedented move with "concerns that Aspen Pharma has engaged in excessive pricing concerning five life-saving cancer medicines." Citing allegations of price-gouging backed by blackmailing threats of product withdrawal, she said: "When the price of a drug suddenly goes up by several hundred percent, this is something the Commission may look at."

Vestager's reasoning opens up a whole new territory for European discussion of prices. The implicit rejection of reliance on market forces delights many health officials hard-pressed to stick within budgets, as well as European Parliament members and health campaigners who have long called for a complete re-think of the current logic behind commerce in medicines. But it also raises—at an official level—some questions that until now have been voiced only informally, if loudly and repeatedly over the last few years: notably, the concept of an "excessive" price can exist only if there is a concept of a "fair" price—and that is a subject of perpetual disagreement in European discussions.

What the Commission decides in the course of its investigation will have an impact much wider than the revenues of just one company.

Substitution squabble

Another significant highlight of the last few weeks was the opening of a legal battle at the level of the EU's Court of Justice on whether Roche and Novartis broke EU competition rules by colluding to protect cannibalization of the sales of the Lucentis eye-treatment by the cheaper (and unlicensed for that indication) Avastin. The companies are appealing an Italian ruling that they were operating a cartel, and again the outcome matters more than just whether these two companies can win exemption from the verdict—and the multi-million euro fine—that Italy imposed on them.

Here, the issue is price-related insofar as upholding the Italian ruling would expose many more products and companies to official substitution by cheaper (but unlicensed) alternatives. National authorities keen to make savings in their drug bill could override the need for a medicine to be authorized for a particularly costly indication, and give a free pass to a cheaper product that claimed the same effect. Unsurprisingly, the European research-based industry is strongly opposed to such an approach, and has already asked the Commission to intervene to protect the concept of indication-specific marketing authorizations. But so far, the Commission is keeping out of the battle.

In a related—and equally significant—development, the European consumer organization BEUC, one of the most influential health campaigners in Europe, took advantage of the court hearing to launch a demand for more intrusive Commission action to contain drug prices. It wrote to Vestager urging her to open investigations into Roche and Novartis, as well as into Gilead Sciences' pricing strategy for hepatitis C drug Sovaldi, and Aspen's pricing of its oncologicals.

The BEUC letter was issued before Vestager announced her

REFLECTOR is *Pharmaceutical Executive*'s correspondent in Brussels

Aspen investigation—and although the consumers' intervention was not the trigger for her initiative, the pressure being exerted on the EU institutions by critics of drug pricing should not be underestimated.

Already the health ministers of the member states asked the Commission last June to intensify investigation of "potential cases of market abuse, excessive pricing as well as other market restrictions specifically relevant to the pharmaceutical companies operating within the EU." BEUC naturally cited this invitation in its letter to Vestager—and health campaigners are determined to keep issuing reminders to the Commission that it has been asked by ministers, too, to do more.

Analogously, the Italian ruling on the Avastin/Lucentis case was the consequence of a complaint by the Italian consumers organization. And consumers were also influential in the Aspen case in Italy—a precursor to the action against the firm now taken at the EU level by Vestager. Campaigners are raising their game—and their influence—all the time.

IP, patent influence

Another potentially disruptive development still in the background is that the Commission has also—and again at the urging of health ministers—initiated a study into whether current intellectual property rules governing medicines are operating against public interest and giving drug firms scope to abuse incentive schemes by charging unjustifiably high prices for orphan drugs and other innovations.

And by coincidence, May also saw a date set for the opening of another drug industry case in the European court that bears indirectly on pricing. Servier is appealing a Commission ruling (and heavy fine) for a patent settlement deal—one of a clutch of similar rulings against drug firms for "pay-for-delay" agreements with generic competitors. Drug companies involved say these settlements are often the best way to avoid lengthy and costly court cases, and, thus, are in everyone's interests.

> The implicit rejection of reliance on market forces delights many health officials hard-pressed to stick within budgets, as well as European Parliament members and health campaigners who have long called for a complete re-think of the current logic behind commerce in medicines

But the Commission has taken the view that the public interest is damaged because generic competition can be deferred, with costs to health budgets obliged to continue purchasing higher-priced originator products. Last year Lundbeck, another casualty of a Commission "pay-for-delay" ruling and fine, lost an appeal in the European court's lower chamber, and is now taking that case to the top court.

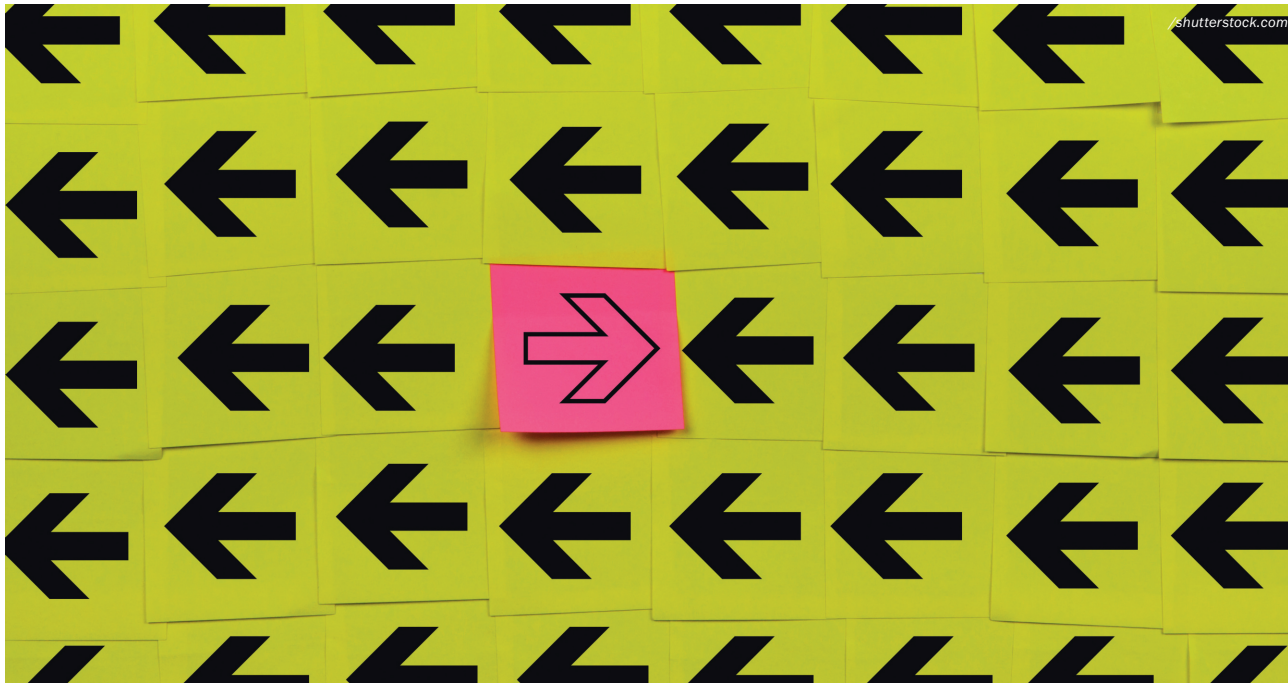
Wide reach

Meanwhile, drug prices continue to feature prominently in the background chatter across many other parts of Europe. In her final address to the World Health Organization in Geneva in mid-May, outgoing Director-General Margaret Chan identified fair drug pricing as a priority for her successor. WHO came out strongly against the research-based drug industry's favorite mantra of "value-based pricing" at a "Fair Pricing Forum" in Amsterdam just days before, which was hosted by the Dutch government.

The Netherlands is the member state that did so much to press for tougher action on drug prices during its turn in the EU's rotating presidency last year, and was one of the prime movers behind the coalition with Belgium, Luxembourg and Austria to present a more united front in negotiating with drug companies on prices.

May also saw the health ministers of Malta, Portugal, Cyprus, Greece, Spain and Italy emulate the so-called Benelux agreement by signing a cooperation agreement of their own in Valletta—hosted by the current EU presidency. This committed them "to cooperate in a fair, supportive and transparent manner" in designing mechanisms for joint negotiation and procurement in accessing medicines.

It is likely to be a long, hot summer in drug pricing. PE



2017 *Pharm Exec* 50

Our latest annual listing of top biopharma players paints a stable picture of performance for the usual placeholders, but change and disruption to current business models could upend positioning in the years ahead

With the exception of a few new bottom-end entrants, and some juggling of positions in the top half, stability remains the name of the game for those biopharmaceutical companies making up this year's list of the industry's top 50 global sales leaders. Of course, the relative calm in the rankings meter doesn't mean that stability necessarily begets profitability for all. Amid growing pricing pressures, key patent losses for some, and a slowdown in M&A activity since the middle of 2016, several mainstays on the Pharma 50 list experienced only modest revenue gains in the latest full-year figures collected, while others suffered slight declines. *Pharm Exec*'s 17th annual listing again features data provided by biopharma market intelligence firm Evaluate Ltd.

Experts attribute the consistent entrenchment of familiar names in the top 10 and 20 to the simple adage of "how business gets done" in this industry—mainly big pharma following a model that continues to prioritize amassing products and innovation through internal R&D, licensing, or acquisition. Pfizer, for example, which repeated as the industry's prescription sales leader, has maintained its hold by applying the latter two. As have companies such as Shire, which spurred by its completed merger of Baxalta in June 2016, shot up from the 30th spot to No. 22 on this year's revenues list. And on the R&D side, Shire's investment increased 45.5% to $1.29 billion.

Merck & Co., despite being ranked fourth in sales, is No. 1 in R&D spend, with a 47.6% spike in investment versus the previous year. The company's newest rising seller, the immunotherapy Keytruda, continues to be studied across numerous tumor types, lines of therapy, and combinations. Others that didn't climb the sales ranks but are investing solidly in R&D include Lilly (15th in sales, eighth in R&D spend) and AstraZeneca (11th in sales, seventh in R&D).

As far as future shifts in sales-figure positioning in the Pharma 50, Jonathan Gardner, EP Vantage News Editor, US, at Evaluate, cites two areas to watch. "The first is pricing, to the extent where payers become more

assertive in areas where they have been reluctant in the past, such as oncology or orphan diseases," Gardner tells *Pharm Exec*. "On the latter, we've seen payers be surprisingly skeptical of new drugs Spinraza and Exondys 51, and there is potential for that to expand. The second issue is disease areas that have become crowded with new agents—autoimmune disorders such as psoriasis and rheumatoid arthritis—that could give payers even more leverage than they've had in the past on franchises such as Humira and Enbrel."

Gardner also notes that until the outlook on US pricing legislation, tax reform, and repeal and replace of the Affordable Care Act becomes clearer, a big rush on M&A is unlikely. "Opportunistic deals will appear, but companies with significant amounts of overseas cash will be reluctant to risk overpaying on taxes to execute major US acquisitions," he says. "Pricing and ACA repeal/replace pose similar, if lower-level risks."

Which leads us to our special Pharma 50 accompanying feature by guest authors at the executive recruitment and talent management firm Russell Reynolds Associates. The authors contend that a significant disruptive event looms on the horizon for the industry, brought on by new US legislation on pricing and new definitions of value. The article points out that traditional sourcing routes for biopharma innovation—in-licensing, M&A, and R&D collaboration—have been expanded by new models of engagement with external innovators, such as open innovation models and corporate ventures. Managing the diversity and complexity of these innovations, and building a more nuanced communication with the external world, will require all those companies in our Pharma 50 to adopt new leadership approaches—and install new types of specialists and C-suite roles to guide the collective industry through the coming disruption and beyond. PE

Rank	Company headquarters [website]	2016 Rx Sales (USD in mln)	2016 R&D spend (USD in mln)	2016 Top-selling Drugs [USD in mln]
1	**Pfizer** **New York, New York** [pfizer.com]	$45,906	$7,841.0	Prevnar 13 [5,718] Lyrica [4,966] Enbrel [2,909]
2	**Novartis** **Basel, Switzerland** [novartis.com]	$41,554	$7,916.0	Gleevec [3,323] Gilenya [3,109] Lucentis [1,835]
3	**Roche** **Basel, Switzerland** [roche.com]	$39,552	$8,717.1	Rituxan [7,410] Avastin [6,885] Herceptin [6,884]
4	**Merck & Co.** **Kenilworth, New Jersey** [merck.com]	$35,563	$9,760.0	Januvia [3,908] Zetia [2,560] Janumet [2,201]
5	**Sanofi** **Paris, France** [sanofi.com]	$34,174	$5,722.0	Lantus [6,322] Lovenox [1,810] Plavix [1,708]
6	**Johnson & Johnson** **New Brunswick, New Jersey** [jnj.com]	$31,671	$6,967.0	Remicade [6,184] Stelara [3,232] Xarelto [2,288]
7	**Gilead Sciences** **Foster City, California** [gilead.com]	$29,992	$3,925.0	Harvoni [9,081] Sovaldi [4,001] Truvada [3,566]
8	**GlaxoSmithKline** **Brentford, England** [gsk.com]	$27,775	$4,696.6	Advair [4,720] Triumeq [2,350] Tivicay [1,291]
9	**AbbVie** **North Chicago, Illinois** [abbvie.com]	$25,299	$4,152.0	Humira [16,078] Imbruvica [1,580] Viekira Pak [1,522]
10	**Amgen** **Thousand Oaks, California** [amgen.com]	$21,892	$3,755.0	Enbrel [5,965] Neulasta [4,648] Aranesp [2,093]

Source: EvaluatePharma® May 2017, Evaluate Ltd, www.evaluate.com

How the listings were compiled: 2016 R&D Spend and 2016 Rx Sales analyses were provided by life science market intelligence firm Evaluate Ltd via its EvaluatePharma® service, www.evaluate.com. *Pharm Exec* would like to thank EvaluatePharma for assisting in the development of this year's Pharma 50 listing. EvaluatePharma takes sales estimates from leading equity analysts to create a consensus sales forecast, currently to 2022. Evaluate's Sales and R&D Spend figures represent the fiscal year that ended in 2016. For most American and European companies, that means the year ending December 31, 2016. For many Japanese companies, the fiscal year ending March 31, 2017, was used. Historic averages were used in the conversion of companies' native currency to USD.

Navigating Through Disruption

Outlining the new leadership and C-level roles of tomorrow needed to take on the disruption event on pharma's horizon

By Waseem Noor and Saule Serikova

The pharma business model is still largely a traditional model characterized by a simple formula: One product. One customer. One price. The model has been viable for decades and has brought high returns to the industry. Since the 2000s, however, the stakeholder map has become more complex, as purchasing power has been shifting from physicians to payers, regulatory bodies and, to some extent, patients. We believe this shift will eventually lead to a significant event in the industry that will disrupt how companies price their products and require a different type of leadership in the industry.

In Earth's history, 66 million years ago, a meteoric disruption—known as the K-T event —led to the extinction of several large species. After the event, dinosaurs became extinct while more nimble and adaptive small reptiles, birds and mammals survived. Is a similar event coming for the pharma industry? We believe a P-E (pharmaco-economic) event will occur, where the US government institutes legislation requiring demonstrated product outcome and prices based on patient value. In this case, the concepts of product, customer, and price are redefined. In the post P-E event era, the indus-

Rank	Company headquarters [website]	2016 Rx Sales (USD in mln)	2016 R&D spend (USD in mln)	2016 Top-selling Drugs [USD in mln]
11	**AstraZeneca** London, England [astrazeneca.com]	$20,967	$5,631.0	Crestor [3,401] Symbicort Turbuhaler [2,989] Nexium [2,032]
12	**Allergan** Irvine, California [allergan.com]	$18,597	$2,845.1	Botox [2,786] Restasis [1,488] Lumigan [688]
13	**Teva Pharmaceutical Industries** Petach Tikva, Israel [tevapharm.com]	$18,462	$2,111.0	Copaxone [4,223] Treanda [661] ProAir HFA [565]
14	**Bristol-Myers Squibb** New York, New York [bms.com]	$18,163	$4,405.0	Opdivo [3,774] Eliquis [3,343] Sprycel [1,824]
15	**Eli Lilly** Indianapolis, Indiana [lilly.com]	$17,173	$4,928.1	Humalog [2,769] Cialis [2,456] Alimta [2,283]
16	**Bayer** Leverkusen, Germany [bayer.com]	$16,886	$3,083.4	Xarelto [2,698] Eylea [1,798] Kogenate [1,290]
17	**Novo Nordisk** Bagsvaerd, Denmark [novonordisk.com]	$16,610	$2,164.1	Victoza [2,979] NovoRapid [2,964] Levemir [2,539]
18	**Boehringer Ingelheim** Ingelheim, Germany [boehringer-ingelheim.com]	$13,316	$3,175.2	Spiriva [3,314] Pradaxa [1,532] Tradjenta [1,248]
19	**Takeda** Osaka, Japan [takeda.com]	$12,773	$2,923.9	Entyvio [1,307] Velcade [1,033] Protonix [680]
20	**Celgene** Summit, New Jersey [celgene.com]	$11,114	$2,761.6	Revlimid [6,974] Pomalyst [1,311] Otezla [1,017]

Source: EvaluatePharma® May 2017, Evaluate Ltd, www.evaluate.com

try will be governed by brand new rules, which will require pharma companies to adapt to avoid going the way of the dinosaur. The old model of single-pill solutions and lifecycle management to drive innovation will give way to more agile companies that are driving whole-patient, or "beyond-the-pill," services and novel therapies.

This changed business environment will also require a new set of leaders that are patient-centric driven, have greater content and scientific expertise, and can understand insights from the vast amount of real-world data generated by products in the market. In order to navigate through this upcoming disruption, we believe pharma companies are already creating new roles and seeking new types of leaders to guide the transformation and adapt to the change.

In our proprietary research, Russell Reynolds Associates (RRA) has examined the new C-level positions (CxO) across the top-50 pharma companies for patterns and trends and developed an outlook for the near future. In this article, we offer a perspective on pharma leadership through two lenses:

- **Changes in pharma leadership to date.** In reaction to stricter regulatory requirements, we observe the emergence of specialist roles and their elevation to the C-level.
- **The next horizon of pharma leadership.** In preparation for a P-E event, we expect an emergence of new leaders, whose goal will be to guide the industry through continued disruption.

In our analysis, we considered the composition of executive management committees and extended senior management teams, including CEOs and

Rank	Company headquarters [website]	2016 Rx Sales (USD in mln)	2016 R&D spend (USD in mln)	2016 Top-selling Drugs [USD in mln]
21	**Astellas Pharma** Tokyo, Japan [astellas.com]	$11,109	$1,985.1	Xtandi [2,332] Prograf [1,421] Vesicare [1,074]
22	**Shire** Dublin, Ireland [shire.com]	$10,886	$1,286.8	Vyvanse [2,014] Advate [1,279] Gammagard Liquid [911]
23	**Mylan** Canonsburg, Pennsylvania [mylan.com]	$10,839	$705.5	EpiPen [1,140] Esomeprazole magnesium [332] Fentanyl Transdermal System [208]
24	**Biogen** Cambridge, Massachusetts [biogenidec.com]	$9,818	$1,973.3	Tecfidera [3,968] Avonex [2,314] Tysabri [1,964]
25	**Daiichi Sankyo** Tokyo, Japan [daiichisankyo.com]	$7,535	$1,857.5	Benicar [1,589] Nexium [787] Memary [456]
26	**CSL** Melbourne, Australia [csl.com.au]	$6,674	$628.3	Privigen [2,712] Human albumin [881] Humate P [546]
27	**Merck KGaA** Darmstadt, Germany [merckgroup.com]	$6,633	$1,655.1	Rebif [1,926] Erbitux [974] Gonal-F [833]
28	**Valeant Pharmaceuticals International** Mississauga, Ontario [valeant.com]	$6,183	$421.0	Xifaxan 550 [932] Provenge [303] Wellbutrin XL [279]
29	**Otsuka Holdings** Tokyo, Japan [otsuka.com]	$5,389	$1,469.6	Abilify [879] Abilify Maintena [527] Samsca [451]
30	**Sun Pharmaceutical Industries** Mumbai, India [sunpharma.com]	$4,804	$401.5	Imatinib Mesylate [307] Atorvastatin [165] Absorica [159]

Source: EvaluatePharma® May 2017, Evaluate Ltd, www.evaluate.com

Front & Center

Patient Support Services—A Model for the Middle

What used to be a very clear line between retail pharmacy and high-end specialty channels is becoming a wide chasm to patient access success.

Thomas Doyle, EVP of Commercial for H. D. Smith Specialty Solutions, is no stranger to understanding the needs of and communicating with patients. As a graduate molecular biology student from Wayne State, Doyle worked in the Medical Genetics and Birth Defect Center at Henry Ford Hospital in Detroit. The center was the only site in the area that offered up-and-coming pre-natal screening programs. What his boss said Doyle lacked in the research scientist role, he more than made up for in his skills working directly with patients. So from lab to patient education Doyle went; running the clinic's MSAFP screening program and explaining results to nervous, expectant parents.

The rest they say, is history. Doyle took his science and communication skills to 3M Pharmaceuticals, where he transitioned into sales and marketing, then upward into director and executive roles, to his current position.

At the recent CBI Patient Assistance and Access Programs conference in Baltimore, Doyle elaborated on issues related to patient access and education that are causing currents in the traditional patient support models. These include:

- Actual emotional and physical impact of diagnosis on an individual.
- Busy lives—47% of adults are in the Sandwich Generation, taking care of both children and aging parents.
- Speed and information at their fingertips.
- Cost matters. Family budgets in peril.
- Managing prescriptions. In some cases only 30% of patients get access to the prescribed medication when a prior authorization is required.

The Hub-Lite® Patient Access strategy provides help for three different stakeholders in the disease treatment process. Patients get the assistance they need to deal with the myriad of challenges that accompany treatment; physicians have a portal through which they can initiate prior authorization and track workflow, and pharma brand managers receive data for both predictive analytics and outcomes.

Combine the changing patient landscape and the overburdened physician landscape with changes in drug therapies and delivery; the stage is set to address a real need in current patient support services.

Mind the Gap

"Around three or four years ago, the types of specialty drugs that were being launched were not all the very high-priced, high-intensive use drugs," explained Doyle. "Instead, we saw an increase in self-administered or oral therapies for products that traditionally required infusion or physician administration. While not traditional specialty products, they do require many of the same services as high touch specialty products; examples can range from newer diabetes drugs to oral oncolytics or self-administered RA drugs that help meet unmet medical needs."

The patients for these middle-ground treatments spread far and wide and often access products through specialty pharmacy models, as they need more attention than traditional retail pharmacies provide. The area between retail and specialty pharmacy–where the channel and the engagements were misaligned–is where Doyle saw a need.

The combination of higher price-tags, along with patients learning to adhere to these newer drug deliveries, shifting

to orals and self-injectables vs. HCP administered (infusions, injections), and the shifting site of care to home or pharmacy, or physician clinic vs. hospital, meant a new service model. "It became clear we needed a service model for these patients in the middle-ground."

That middle-ground solution is called Hub-Lite®. This foundational model from Triplefin, the reimbursement and patient solutions subsidiary of H. D. Smith, builds on Triplefin's existing strengths: the ability to provide a full-range of services that support both high-touch and lower touch products. Their extensive services include co-pay and voucher programs, portal technologies that help patients and HCPs understand coverage and out-of-pocket expenses through electronic benefits verification (e-BV); prior authorization support; case management; health coaching; patient assistance; field reimbursement; direct-to-patient fulfillment; and pharmacy triage, for specialty and products in the middle or "tweener" category.

"The Hub-Lite® patient access strategy is easier from the physician's office standpoint because of the integrated portal and live support services," explained Doyle. "They are registered in the portal and can initiate prior authorization, track workflow, and have a single point of contact for their office."

Doyle and the Triplefin team believe this model will close the gap that currently exists for achieving the best possible adherence and outcomes for these tweener patients. He believes no model—until now—has addressed the myriad of services brand teams need for this transition.

Service Trends

An Accenture analysis of current and future industry-sponsored patient services, which Doyle shared with the audience, indicates that patient services are on the increase, supporting Doyle's theory that a new service model was needed. There are expected to be major increases in the following services between now and 2019: benefit coverage and access support; transportation arrangements; engagement insight development; health coach/counselor; adherence program management; co-pay assistance programs; remote monitoring; affordability and reimbursement support; nursing support; billing and coding assistance; reward and incentive programs, and medication delivery and support. Doyle told the audience that patient models are in transition and brand managers will need to integrate the patient and product journey. "Automation, addressing what can be automated and what can't, will bring these service promises to a reality," explained Doyle.

Brand Team Concerns

Doyle addressed the access struggles for patients and HCPs, but he also shed light on the manufacturer side. Brand teams are well aware of the challenges they face with these newer therapies. Doyle explained that brand teams need speed, predictive analytics, measurable outcomes, patient customer service, and cost conscious solutions. Doyle said, "Brand managers need the patient to have excellent customer service and have all information and access to medication quickly, with little effort on their part."

In addition, brand managers need to receive data for predictive analytics, outcomes and efficacy purposes. At the center of Hub-Lite® is that technology where data is collected and can be used to foresee risks, and also demonstrate the value of a therapy within the healthcare continuum for a patient.

In addition to these challenges, Doyle believes that the technology they choose should be flexible with seamless integration and cost effective. "The flexibility of our model allows for services and business rules that are tailored to meet specific product needs."

Doyle told *Pharmaceutical Executive* after the conference that many manufacturers may not be big fans of any patient services hub model, traditional or innovative like Hub-Lite®. "It's hard for manufacturers to 'give up their baby,'" explained Doyle. However, with the growth of patient services and hub acceptance, brand managers will look closely at what the hub is truly achieving for them.

"They ask themselves, how much will this [program] really help patients? How much can technology help providers and office staff? How much time and effort will it take to connect all the stakeholders? And how much the budget is and how important cost is for the product," said Doyle. While they start this process 18 months prior to drug launch, time quickly evaporates under the pressures of these multiple decisions. "Our goal is to provide the flexible service that they need, with as much automation as possible, with the white glove service they require for their physicians and office staff, in an affordable and cost efficient way," explained Doyle.

Patient access and education is paramount. "Patients can fall through the gaps," said Doyle. He related a story of his own father taking COPD medication recently. "He wanted everything in paper, written out. We have to remember to give patients what they need." And the Hub-Lite® model, while being driven toward digital usage, is customizable for those patient preferences. "There are a lot of avenues for patients to get information, maybe too many. As a service provider, we have to work with manufacturers to coordinate relevant data and education programs."

their direct reports, for top-50 pharma companies. The research was conducted using publicly available information from May 2017, such as company websites, BoardEx, and LinkedIn, and was supported by RRA's ongoing consulting to the pharma industry.

Traditional managers to C-suite specialists

In the 1990s, the executive committees of large pharma companies started to grow in size. Geographic expansion, regulatory complexity in established and emerging markets, and diversification of market portfolio and assets in the R&D pipeline are just some factors that led to the rise of specialists in certain therapeutic areas, geographies, R&D stages, and corporate functions—all with a seat at the C-table. The organizations grew into large and complex matrix organizations.

Today, the average size of the senior leadership team at top-50 pharma companies is 11-12 members, and the range varies widely from four to 28. Among top-50 organizations, 58% have business unit heads in their C-family, on average two to three, and a maximum of eight. Conversely, regional heads have started to disappear from leadership's inner circle, and today only one out of three top-50 pharma firms has regional heads at the very top (see Figure 1 on page 24).

In the 2000s, with regulatory requirements becoming more stringent, a number of specialist position were elevated to the C-suite, replacing traditional managers. Specifically, we see three roles that have extended their remit significantly and have been elevated to the C-level in many pharma organizations.

Chief Medical Officer. Traditionally rooted in the R&D organization, the medical affairs function has evolved dramati-

Rank	Company headquarters [website]	2016 Rx Sales (USD in mln)	2016 R&D spend (USD in mln)	2016 Top-selling Drugs [USD in mln]
31	**Eisai** **Tokyo, Japan** [eisai.com]	$4,301	$1,077.5	Humira [449] Aricept [437] Aloxi [435]
32	**Les Laboratoires Servier** **Neuilly-sur-Seine, France** [servier.com]	$4,167	$1,004.1	Aceon [637] Diamicron [511] Vastarel [464]
33	**Endo International** **Dublin, Ireland** [endo.com]	$4,010	$175.0	Vasostrict [343] Xiaflex [190] Opana ER [159]
34	**UCB** **Brussels, Belgium** [ucb.com]	$4,005	$1,128.5	Cimzia [1,446] Vimpat [895] Keppra [685]
35	**Abbott Laboratories** **Abbott Park, Illinois** [abbott.com]	$3,859	$137.0	Femelle [26] Geptor [20] Cerepro (choline alfoscerate) [13]
36	**Fresenius** **Bad Homburg, Germany** [fresenius-kabi.com]	$3,753	$403.0	Heparin Sodium [74]
37	**Chugai Pharmaceutical** **Toyko, Japan** [chugai-pharm.co.jp]	$3,699	$761.4	Actemra [278] Edirol [246] Neutrogin [112]
38	**Grifols** **Barcelona, Spain** [grifols.com]	$3,572	$218.6	Gamunex IGIV [1,115] Flebogamma [691] Prolastin-C [508]
39	**Regeneron Pharmaceuticals** **Tarrytown, New York** [regeneron.com]	$3,338	$2,052.3	Eylea [3,323] Arcalyst [15]
40	**Sumitomo Dainippon Pharma** **Osaka, Japan** [ds-pharma.com]	$3,197	$748.6	Latuda [1,219] Brovana [299] Meropen [171]

Source: EvaluatePharma® May 2017, Evaluate Ltd, www.evaluate.com

cally in recent years, driven by regulatory scrutiny and operational complexity. Today, medical affairs fulfills a strategic mandate to represent "the voice of the patient" internally vis-à-vis R&D, commercial, and other functions and to drive high value-add activities externally. In 28% of top-50 pharma companies, the Chief Medical Officer reports directly to the CEO and has a prominent external-facing role. For the purpose of this study, we analyzed the background of Chief Medical Officers in pharma C-suites in terms of education and previous professional experience. Our analysis suggests that scientific rigor and previous extensive experience in R&D, medical affairs, and/or regulatory affairs helps increase credibility, independence and authority internally as a patient advocate and externally as the primary medical representative of the company in the market (see Figure 2 on page 24). Additional experience in commercial or project-related activities complements the profile of a Chief Medical Officer and sharpens his/her strategic focus.

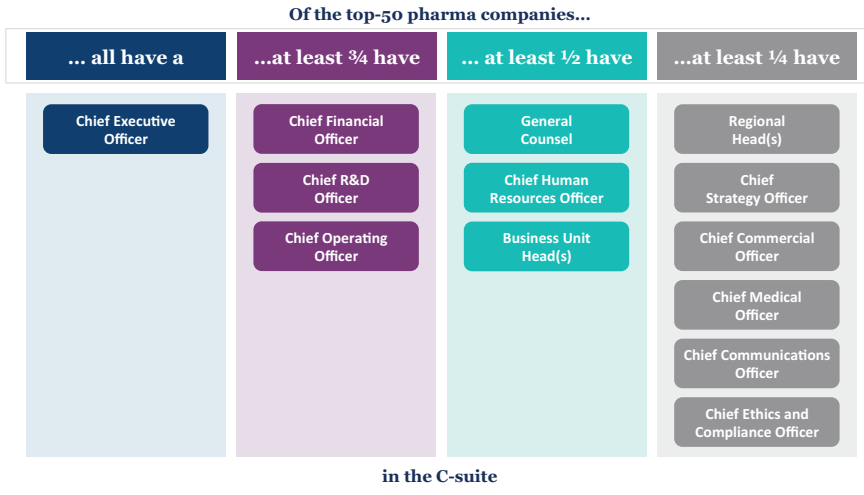
Chief Ethics and Compliance Officer. Recent challenges in the pharma market—sales and marketing malpractice, off-label sales, and data integrity, among others—have led to legal issues and shaped negative public opinion about pharma companies. Going forward, the pharma industry needs to (re-)position itself as a trusted partner in public health. To ensure regulatory and non-regulatory compliance and ethical behavior and find new ways to engage with prescribers, key opinion leaders, and other external stakeholders, pharma organizations are taking an integrated approach to compliance.

Twenty-six percent of top-50 pharma companies have elevated the Chief Ethics and Compliance

Rank	Company headquarters [website]	2016 Rx Sales (USD in mln)	2016 R&D spend (USD in mln)	2016 Top-selling Drugs [USD in mln]
41	**Alexion Pharmaceuticals** **Cheshire, Connecticut** [alxn.com]	$3,082	$747.0	Soliris [2,843] Strensiq [210] Kanuma [29]
42	**Mallinckrodt** **Dublin, Ireland** [mallinckrodt.com]	$2,918	$262.2	H.P. Acthar Gel [1,160] INOmax [474] Ofirmev [284]
43	**Menarini** **Florence, Italy** [menarini.com]	$2,916	N/A	Lobivon/ Nebilet/ Nebilox [290] Enantyum [138] Adenuric [97]
44	**Mitsubishi Tanabe Pharma** **Osaka, Japan** [mt-pharma.co.jp]	$2,696	$613.7	Remicade [606] Tenelia [165] Talion [163]
45	**Lupin** **Mumbai, India** [lupin.com]	$2,490	$327.3	Antara [59] Simvastatin [48] Lisinopril [45]
46	**Actelion** **Allschwil, Switzerland** [actelion.com/en]	$2,448	$537.5	Tracleer [1,035] Opsumit [843] Uptravi [249]
47	**Aspen Pharmacare** **Durban, South Africa** [aspenpharma.com]	$2,403	N/A	Fraxiparine [291] Diprivan [164] Arixtra [115]
48	**Kyowa Hakko Kirin** **Tokyo, Japan** [kyowa-kirin-pharma.com]	$2,228	$495.8	Nesp [519] Regpara [183] Allelock [167]
49	**Ono Pharmaceutical** **Osaka, Japan** [ono.co.jp]	$2,153	$518.7	Opdivo [895] Glactiv [274] Opalmon [162]
50	**Ferring Pharmaceuticals** **Parsippany, New Jersey** [ferringusa.com]	$2,134	$309.4	N/A

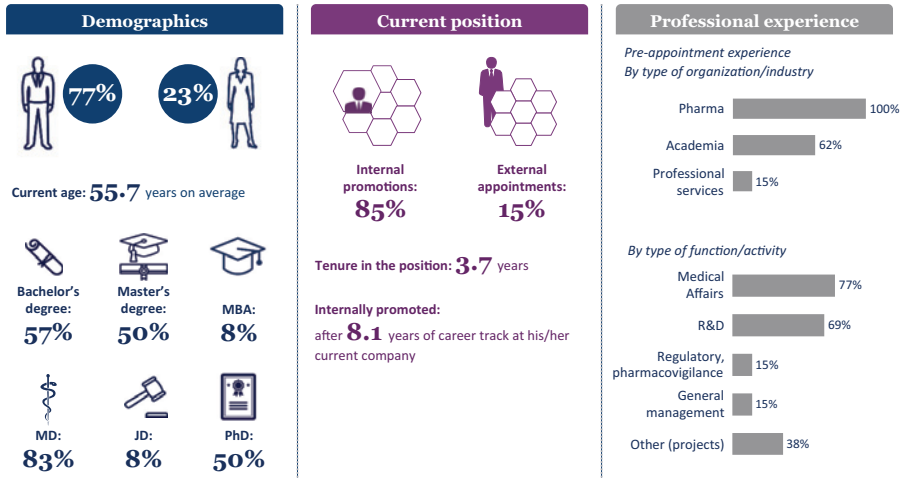
Source: EvaluatePharma® May 2017, Evaluate Ltd, www.evaluate.com

Figure 1: More specialists and fewer "management types" are characterizing the new pharma C-suite



Source: RRA proprietary research on the career paths of members of the executive and senior management teams at top-50 pharmaceutical companies, May 2017.

Figure 2: A solid background in science and R&D grant the Chief Medical Officer necessary authority



Source: RRA proprietary research on the career paths of members of the executive and senior management teams at top-50 pharmaceutical companies, May 2017.

Officer to a direct report to the CEO or the Board. To spot potential issues before they emerge, the Chief Ethics and Compliance Officer assesses the value chain for the possibility of behaviors that violate ethical or regulatory mandates. To set a course of right behavior from the start, the Chief Ethics and Compliance Officer also serves as a key advisor on the adoption of business models and the assessment of transformation risks.

A more detailed look at the profile of Chief Ethics and Compliance Officers leads to the conclusion that a solid legal background and an extensive track record in the pharma industry are prerequisites for the role. A high ratio of internal promotions from deputy General Counsel or divisional legal business partner within the same organization suggests that credibility and trust on the side of business leaders as well as internal connections are essential to get buy-in for this role (see Figure 3 on facing page).

Chief Quality Officer. Over the last decades, the pharma industry has grown tremendously in size and complexity and developed a highly sophisticated system to ensure that patients receive high-quality products. Most pharma companies have been undergoing the transformation process from baseline compliance and delivery on regulatory authority inspections to continuous improvement and a culture of quality, or speaking in their lingo, from quality control to quality assurance. To complete the organizational separation of quality from operations on a corporate level, 24% of companies have elevated the Chief Quality Officer to the level of direct report to the CEO.

A route-to-the-top analysis indicates that this is a narrow field of specialization, as the vast majority comes through internal promotions from within the pharma company's quality function, by having their roots in quality (83%) and/or technical laboratory analysis (50%) (see Figure 4 on facing page). The fact that at the very top, quality is occasionally co-located with other responsibilities, for instance, HSE (health, safety, and environment) explains the broader range of other experiences.

A bolder future of transformation

The roles described have been evolving over time, but companies may decide to shift from this

incremental approach to more aggressive leadership development in preparation for a P-E event. The goal is to provoke and accelerate change bold enough to help the organization adapt to the quickly changing ecosystem while recognizing that the specific type and pace of change should be calibrated to the company's starting point regarding process and cultural maturity.

This change will involve institutionalizing new roles across three categories: transformation leaders, ecosystem leaders, and enabling leaders.

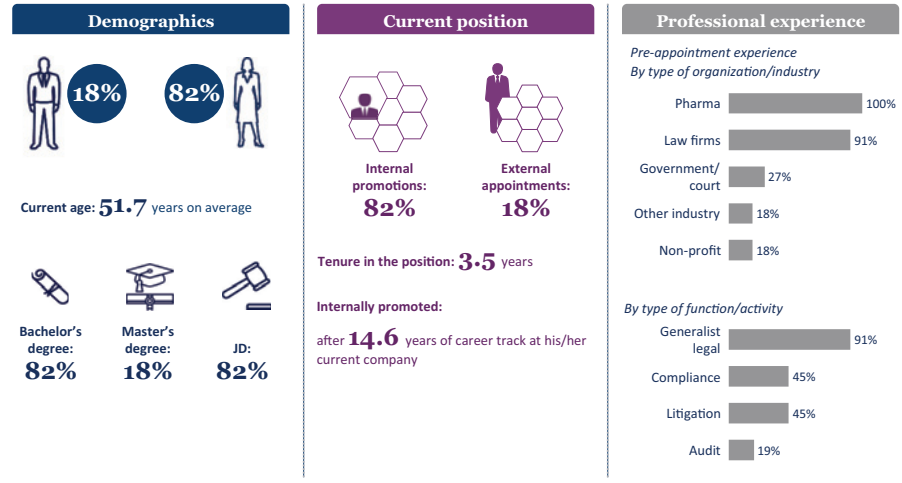
Transformation leaders

The leaders in this first category are the architects, motivators, and catalysts that help pharma companies adapt and grow into organizations that can meet the challenges of a new industry landscape.

Chief Transformation Officer. Chief Transformation Officers have a mandate to lead the organization through momentous times in a company's history. Effective Chief Transformation Officers inspire employees and act as role models for the sort of behavior needed to encourage and embed change. To be able to orchestrate a highly complex process and deliver on results, they need the full support of the Board, the CEO, and the entire executive team. Among the companies in the top-50 pharma ranking, only two have already nominated top executives to lead the transformation—Alexion and Amgen. Given a very limited sample size, we can give only a directional profile of a Chief Transformation Officer: well-regarded senior executive with previous experience in transformational processes at larger organizations outside the pharma sector, excellent problem solving skills, and very strong interpersonal skills.

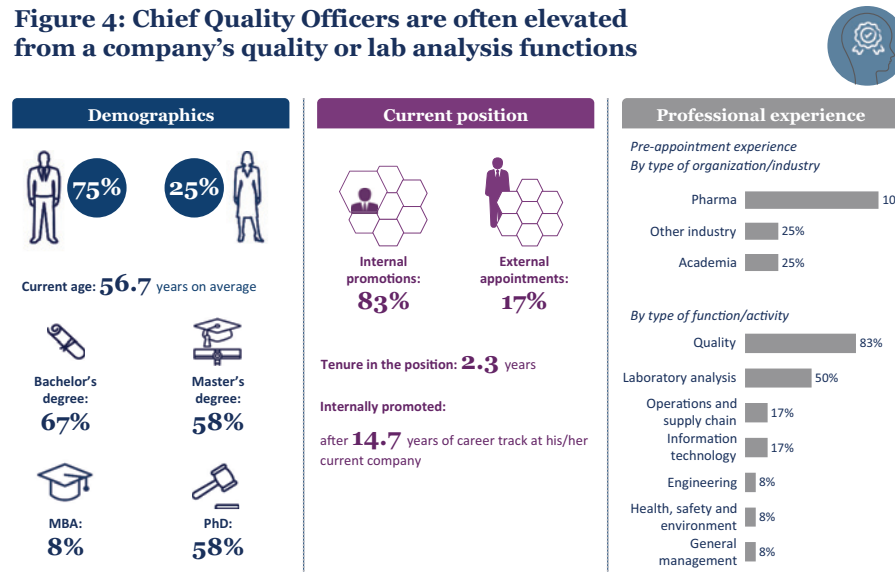
Chief Digital Officer. Digitization of the pharma industry has a strong impact on all functions along the value chain. To reap the benefits of digital, pharma companies must plan for, build, and operationalize their digital capabilities, often into evolving business functions. To accelerate the process, a Chief Digital Officer often acts as a catalyst with a mandate to drive digital transformation, challenge the corporate thinking on digital, and define the digital strategy across all corporate functions. The ultimate goal is, however, to evolve to a digitally

Figure 3: Chief Ethics and Compliance Officers bring legal experience and organizational trust to their roles



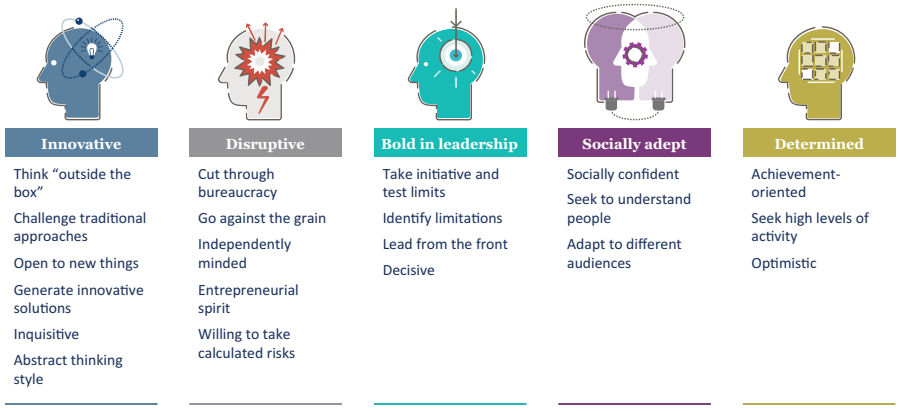
Source: RRA proprietary research on the career paths of members of the executive and senior management teams at top-50 pharmaceutical companies, May 2017.

Figure 4: Chief Quality Officers are often elevated from a company's quality or lab analysis functions



Source: RRA proprietary research on the career paths of members of the executive and senior management teams at top-50 pharmaceutical companies, May 2017.

Figure 5: Five characteristics differentiate transformational leaders from other senior executives



Source: RRA, Productive Disruptors Study, 2015.

integrated organization and develop a generation of digitally savvy business leaders in all functions.

Chief Data Officer. Big data has the potential to revolutionize the industry, though complexity within the regulatory environment and pharma business model are two main reasons why the large pharma companies are still lagging behind in adoption of advanced analytics. In addition to the fact that ownership of post-clinical data is not in the hands of the pharma industry, the key challenge for most companies is how to translate all the innovative ideas into something tangible and "real." The mandate of a Chief Data Officer would be to build the governance process and lifecycle management for big data and define where the most value can be created—i.e., translate the insights from advanced analytics into commercial impact and real financial outcome. Transformation requires the Chief Data Officer to be a change agent with an understanding of relevant data sources, technology and tools, and data science as well as strong business acumen and excellent communication skills.

While each leadership position described so far is distinct in its set of responsibilities, they require a shared set of attributes. In RRA's proprietary analysis conducted in 2015, we distilled the core competencies of effective transformation leaders and found that the most successful leaders embody five specific characteristics (see Figure 5).

First, they are innovative, with a propensity to challenge traditional methods and approach matters in new ways. Second, they are disruptive, willing to take calculated risks and "buck the system" when necessary. Third, they are decisive leaders who boldly carry the torch of change. Fourth, they are socially adept leaders with the ability to understand people and easily adapt to different audiences. Fifth, transformation leaders are determined—a characteristic evident in their high level of optimism and their achievement orientation.

Ecosystem leaders

We are beginning to see many roles emerging with a shared goal—to manage the relationships with the external world—we call them "ecosystem roles." These roles help pharma companies proactively shape their own positioning in the ecosystem vis-à-vis other players, build long-lasting partnerships as well as create and effectively communicate value of pharma products and services. The end goal is improved health outcomes, faster time-to-market for products, and more efficient management of internal and external R&D processes.

The roles that are beginning to emerge to help manage these partnerships are largely situated at the middle-management level and have a mandate to align different (and "siloed") functions within the pharma organization to deliver consistent messages to the external world (see Figure 6 on facing page). In order to break through the organizational barriers and ensure the right level of focus and investment, 30% of companies have introduced one or more ecosystem roles into their C-families, ensuring that their objectives are given high priority, top-level backing, and sufficient resources.

To deal with different players in the healthcare ecosystem, we see several emerging archetypes of positions.

Chief Patient Officer. To reflect the shift to a more patient-centric business model, pharma companies are introducing roles that take a holistic view and think through the entire patient experience. Roles like Head of Patient Journey Excellence,

Head of Patient Experience, and Head of Patient Engagement are seen more in the health services space but have begun to appear in pharma as well. In 2012, UCB was the first top-50 pharma company to appoint a Chief Patient Affairs Officer, followed by Sanofi in 2014. Today, Merck & Co. is the only company among the top 50 with a Chief Patient Officer in the C-suite. The primary goal of the position is to bridge the gap between the patient community and the pharma company—and more broadly, the pharma industry.

Chief Public Affairs Officer. Being traditionally a communications function, this role has evolved over time. Today, it covers strategic communication, government relations, public policy, health policy, investor relations, and more. Among top-50 pharma companies, 25% have a more traditional communications, corporate affairs, and corporate social responsibility seat in the C-suite, and another 25% have extended the role or created an additional one for engagement with external stakeholders (external affairs, public affairs, and global government affairs are the common titles).

Chief External Innovation Officer. Approximately 75% of the most exciting late-stage assets in the collective pharma industry pipeline comes from sources outside of the company that owns them today. The traditional sourcing routes have been in-licensing, corporate acquisition and R&D collaboration. This spectrum has been expanded by new models of engagement with external innovators such as open innovation models, corporate ventures and direct company engagements. In order to effectively manage diversity and the complexity of externally sourced innovations, companies require a more strategic and orchestrated approach. Today, 18% of top-50 pharma companies have a business development leader at their C-table. Other companies have introduced new roles; for instance, Roche has a Head of Partnering in its enlarged corporate executive team, and Abbott has a Head of Ventures in its leadership team. As external innovation and business/corporate development are increasingly becoming synonymous with each other, it is only a matter of time until we see the first Chief External Innovation Officer.

Figure 6: Ecosystem leaders help companies engage with different actors in the healthcare ecosystem

Source: RRA.

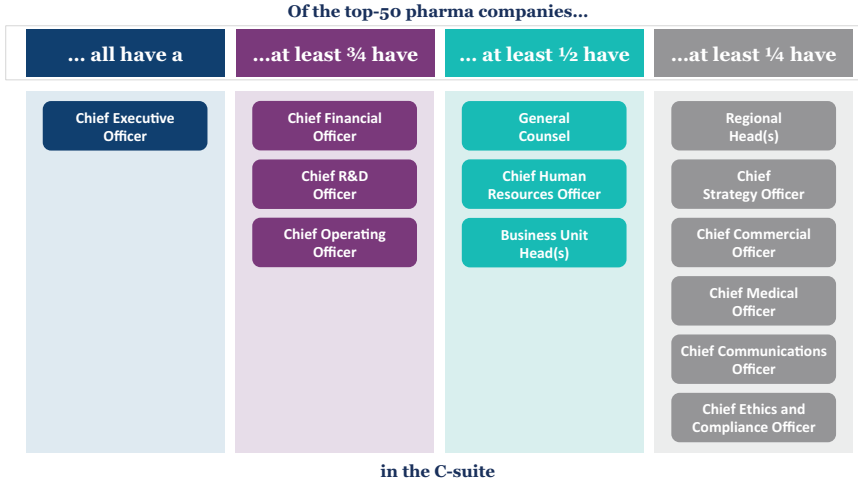
Enabling leaders

In the pharma industry, permanent restructuring, post-acquisition reorganization, cost-cutting initiatives and similar internal disruptions can have two potentially dangerous but highly manageable byproducts: organizational fatigue and burdensome administrative complexity. Two groups of enabling leaders can address these issues, providing the high levels of ongoing support that create an organizational environment that is able to sustain sizable transformation.

People and culture leaders. We can expect new C-suite roles to be created to promote people, culture, well-being, and inclusiveness. In addition to Chief People Officers, we will see more Chief Diversity and Inclusion Officers and Chief Culture Officers at the very top of the leadership ladder—with the mission to actively shape and promote internal company culture and foster employee happiness and satisfaction.

Productivity and efficiency leaders. To address the inevitability of larger leadership teams and more complex organizational structures, we observe the desire to consolidate and even centralize some responsibilities on a corporate level and/or vertically throughout the organization. An example of consolidation is the role of a Chief Administration Officer (6% of

Figure 1: More specialists and fewer "management types" are characterizing the new pharma C-suite



Source: RRA proprietary research on the career paths of members of the executive and senior management teams at top-50 pharmaceutical companies, May 2017.

top-50 companies). This person assumes the administrative back-office accountability and relieves the CEO from his/her day-to-day tasks, allowing him/her to put extra time and effort toward more strategic and critical decisions. An example of centralizing the larger number of administrative responsibilities is placing one person on the senior management team in charge of global business services (6% of top-50 companies). This role is in charge of business support services and can be considered as a "span breaker," i.e., productivity and efficiency gain for the entire global organization.

Considerations and lessons learned

In anticipation of a P-E event, we expect pharmaceutical companies will consider new roles—transformation, ecosystem, or enabling—as a part of their leadership teams. In order to design these roles—and set the leaders in these roles up for success—companies need to think critically and honestly about their unique needs and leadership goals, the full shape of prospective positions and where they are today in the transformation journey (see Figure 7).

While the C-suite changes are just now beginning in pharma, other industries have already progressed in their leadership adjustment. In the consumer goods industry, for example, we have already seen a higher number and an increased diversity of new CxO roles, such as Chief Growth Officer, Chief Customer Officer and Chief Omnichannel Officer. The Chief Design Officer in automotive and the Chief Innovation Officer and Chief Customer Experience Officer in health services are examples of new specialist positions institutionalized at the highest levels of the organization. The pharma industry can learn from these examples and try to break down functional barriers and align the company.

The key learnings from other industries are the following:

The right leader is key. The success of these new roles is dependent on finding someone who embraces the change and confidently leads the transformation. Identifying the best talent either internal or external to the organization, who has transformation competencies, is critical.

Cultural collision is inevitable, so be prepared. As the mandate of a new leader is to challenge the status quo, some degree of conflict is predetermined. In the case of externally appointed leaders, the Board and CEO need to effectively onboard new leaders to minimize cultural conflicts while pushing for the change.

Success must be measurable. A clear set of key performance indicators to measure success of the new roles allows leadership to further refine the role itself and its scope of responsibilities, as well as ensure an appropriate level of dedicated resources.

Monitoring adaptations in organizational structures, both within the industry and outside, will give a clue to how imminent leaders believe this change will happen. Within the healthcare industry, emerging biotech and digital health companies will likely move faster along these future trends, and it may take time for these roles to trickle up to larger more established organizations.

The quickening pace of change in the industry will require a bold reimagining of top-level leadership to adjust and thrive in a new pharma environment that emphasizes demonstrated product outcomes and value to patient. The transformation approach may vary by organization, but all the companies will need to adapt to the change eventually. PE

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Photos/Eric Decker

Where is Your Physician?

A panel of biopharma executives discuss market access and the changing dynamics in reaching physicians and healthcare professionals

The challenge for market access professionals is trying to put the payer, patient, provider, and health system together in a way where they all benefit. Given the complexities of healthcare delivery, which is fragmented, and the increasing costs to patients to purchase their needed medicines, market access executives have a near impossible task. This executive roundtable was underwritten by Zephyr Health and uncovered many themes during the collegial discussion. These issues included physician access and education, patient access, the changing role of the pharmaceutical sales representative, and the role of technology.

PE: *What are the challenges to current market access, as it relates to the physician, and your sales representatives reaching those physicians?*

BRIAN McCARTHY: Access to physicians, with the consolidation occurring in systems as well as physician practices, the

ROUNDTABLE PARTICIPANTS

Mike Staff, Vice President, U.S. Managed Health Care, AbbVie
Nicole Mowad-Nassar, Vice President and Head of US Business Operations and External Partnerships, Takeda
Brian McCarthy, Vice President, Managed Markets, Lundbeck
Andrew Thorrens, Former Head of Reimbursement and Market Access, Allergan
John Jaeger, Partner, DRG Consulting's Life Sciences Practice Group
Lance Scott, CEO, Zephyr Health
Lisa Henderson, moderator and Editor, *Pharmaceutical Executive*

reps are getting squeezed out. They have less opportunity to communicate the value proposition of our medicines. And this is happening at the same time the value proposition has become more complex.

But there is opportunity for pharmaceutical companies to improve how we communicate with physicians. Maybe through electronic health records or e-prescribing, but there is an undercurrent of communication that's taking place that physicians and other decision-makers tap into. So we can get into the communication streams of where physicians, payers and others are consuming information.

"Sales reps have less opportunity to communicate the value proposition of our medicines. This is happening at the same time the value proposition has become more complex."
—BRIAN McCARTHY, LUNDBECK

JOHN JAEGER: To your point, the massive consolidation is changing the dynamics around centralized decision-making. For some regions, there is a large amount of depth and breadth. Think about how heavily penetrated Cleveland Clinic might be in the Cleveland area. Your sales team could be having hundreds of interactions with that system in a given day, but the level of influence that those individuals are having could be very different. Not all visits and interactions and engagement activities are going to be created equal when you have a much more centralized decision-making structure.

McCARTHY: Exactly. That autonomous decision-making of the physician is becoming less and less. We need to move representatives to account managers. Because even at a "rep level," they're dealing with physicians who are part of systems or groups. The reps need to approach that as an account, not solely from a physician-to-physician-to-physician approach.

MIKE STAFF: That's part of the evolution that we've had at AbbVie. But the Cleveland Clinic example is a great one. We recognized about four years ago that there was a consolidation of decision-making at these large health systems. At the same time, the electronic medical record became mandated by ACA. Those events made us start focusing on a relationship with the health systems, not from a promotional perspective but from a business-to-business perspective.

We created health system executives that would dig into their needs and goals, as opposed to a product approach. It's going from a standard-of-care approach to a population health approach. We moved the conversation to, "How do you get more patients diagnosed and ultimately treated?" It's good for the patient, it's good for the system and it's good for lowering the overall cost of healthcare.

NICOLE MOWAD-NASSAR: At Takeda, we too are shifting our approach. We have focused a lot on partnering for access as a priority, and we've been trying to increase our capabilities to do that.

Like AbbVie, we have focused on upscaling our account executives so they're partnering with the healthcare systems but also forging much closer collaborations with our medical affairs associates. So now managed markets and medical are more hand-in-hand than they've ever been before.

It's very important for evidence generation to partner with payers and work within their own system, using their data and addressing obstacles to infrastructure and data analysis. This partnership is necessary to demonstrate real-world evidence in the environment.

ANDREW THORRENS: Which is great because, in doing so, you've now aligned some of the commercial elements with health economics. I see this as a big win for patients and hold out hope that earlier communications between manufacturers and payers may lead to earlier coverage determinations, which, in turn, may improve patient access.

JAEGER: There are tools and resources that can help us take the traditional view we've had of the sales representative role, or the commercial team role, and really help evolve that so it's much more in sync with what's critical to the other stakeholders within the healthcare value chain.

LANCE SCOTT: We released a survey that we did with about 60 leaders across 22 pharmaceutical companies in different roles—market access, sales and marketing leadership. Almost 70% said they're all using some type of market access data on a regular basis. However, 40% said there are still opportunities and gaps in terms of better using that data to align the functions and the go-to-market approach across those functions within any given healthcare company.

MOWAD-NASSAR: In terms of the technology perspective, what is very exciting is the data density that's generated from smartphone devices and other connected devices, and the data from the EHR systems, that's allowing us to drive insights on patients that would have taken us years to uncover before platforms—frankly, like Zephyr's—that allow you to derive insights from algorithms and machine learning.

"Not all visits and interactions and engagement activities are going to be created equal when you have a much more centralized [health system] decision-making structure."
—JOHN JAEGER, DRG CONSULTING

Takeda has recently engaged Zephyr to take our data and make it more patient-insight driven so that the representatives have information that can bring higher utility to their discussions.

We've been really encouraged by the data aggregation and insights we've been able to produce.

THORRENS: You can have a portal that provides sales representatives with a lot of analytics. My prior experiences with rep portals, however, has been varied. Some reps love to mine the data unique to their customers. But many reps don't really use the portal at all. To them, the portal is just another CRM platform that's devoid of real-world experience. They think, "I know my physicians; I have my relationships and know what's going on in their practice." In my opinion, this is part of the struggle in the evolution to create this new kind of specialized business that relies on analytics.

SCOTT: One thing we're doing is based exactly on the rep struggle you described.

Some representatives have a large number of targets or accounts with a lot of data that's changing constantly. We are taking a more consumer-driven approach, serving up information to the field team—be it account managers or representatives—at a time when it could be more useful to them and based on change in that data or information.

It makes their job easier because they can proactively receive information that is being pushed to them programmatically through the software and machine learning. They can then decide what to do with it or how to incorporate it. It could give them guidance in terms of key information, messaging that might be most relevant and/or prioritizing engagement with a given target or account based on something that's changed.

MOWAD-NASSAR: What Takeda likes about Zephyr's platform is the potential to increase pull-through and simplify the representative's job in the very complex ecosystem that they're operating in now.

Imagine, as you're walking into a physician's office, the system gives you a recommendation that's saying, "You can provide this physician, with this information," that takes a lot of the complexity out for the rep. You can use these insights to direct your non-personal promotion as well.

McCARTHY: The better representatives are sophisticated enough to use data to do effective problem-solving or engage the stakeholders necessary to solve a problem. Whereas others just get mired in the ambiguity of the data because it can't be overly specific to a given patient or physician.

JAEGER: I think the biggest barrier is how to build this data infrastructure. Data is a tool, not a strategy. The way you get commercial teams to use it and not

"We are taking a more consumer-driven approach, serving up information to the field team—account managers or reps—at a time when it could be most useful to them and based on change in that data or information."
—LANCE SCOTT, ZEPHYR HEALTH

roll their eyes at it is to build data into the workflow in a way that they're using the data but they may not even be aware that they're using it.

PE: *What else is top of mind in market access that affects reps and physicians downstream?*

THORRENS: It's important to understand the implications of payers to patient co-pay programs as there's not a therapy that has one single payer. You generally have a smattering of payers: 30% Medicare, 40% commercial, the remaining Medicaid, for example. And some commercially insured patients may be subsidized by a State or Federal health plan that may limit their eligibility.

Also, think of all of the changes around Patient Assistance Programs, or PAPs. For these, it's important to consider recent advisory opinions from OIG and seek guidance to develop SOPs or program rules to best navigate their requirements. Given the nuances of these rules, PAPs are not programs that a sales rep can casually discuss with their physician customers despite their best interest for their patients' access.

"We have focused on upscaling our account executives so they're partnering with the health care systems but also forging much closer collaborations with our medical affairs associates."
—NICOLE MOWAD-NASSAR, TAKEDA

JAEGER: We are also starting to see a high level of push back on PBMs as part of the larger pricing dialog. Many different stakeholders are asking questions around how PBMs are encouraging high prices with a heavy focus on rebates. It will be interesting to see if this continues to gain traction, especially as PBMs continue to expand capabilities to include medical benefit drug management capabilities.

PE: *What is happening to shift companies to a more proactive market access strategy?*

JAEGER: Having a harmonized view at an organizational level around what the hypothesis is of that future market environment is critical for a consistent commercial approach. Not having this view creates inconsistency in the commercial evaluation process and diminishes efficiency. While the nature of prediction means it will never be 100% correct, an accurate and harmonized view of the future market access landscape has enhanced the commercialization process for many of my clients.

MOWAD-NASSAR: Takeda's been moving, over the last few years, from a primary care company to a diversified company with primary care and specialty products. We recognize we need different capabilities.

For the last 18 months, we've been investing to win in specialty, which means building upon our hub, creating different patient services, understanding different reimbursement dynamics and helping patients understand how to get access to our medications.

Now we're comfortable that we've built those capabilities—we've transitioned from what's needed in primary care to what's needed in specialty, and focus on leading in those areas. But it is really a capability shift.

THORRENS: Looking at that primary care mold another way, reps used to call on physicians by knocking on doors. I'm oversimplifying, but for a specialty drug, where the calling point might be an urban hospital setting—trying to get access or the level of complexity associated with the decision-making processes in that hospital can be daunting. Especially when it comes to deciding the patient's care in a post-acute care setting. Will it be the physician, the discharge planner, or case management?

MOWAD-NASSAR: We see the challenges of cost containment, cost shifting, and consolidation at all levels across the system. That's what's really leading to higher rebates and a more thoughtful approach to how we're helping that patient in the cost shift.

From a policy perspective, Takeda has been trying to get involved in the conversation and make people think about medicines not as an expense but as an investment in a chronic care solution.

PE: *Medicine as an investment. Doesn't that start to get into a value, outcomes or HEOR (health economics and outcomes research) discussion?*

McCARTHY: Historically, in drug development, it used to be, "Just study it enough to get it FDA-

approved." You'd look for HEOR after the fact, which is hard to do.

At Lundbeck, we've set up our drug development steering committee to include not just medical but commercial, HEOR, the cross-functional management team, in order to instill technology-based elements that can pick up nuances. So when you do get to the product approval, those nuances or potential benefits have been studied and can show a meaningful difference—one that has been studied from Day One, rather than in the sequential fashion of the past.

STAFF: I think that becomes a base or a core competency we all have to build. Can you show not just differentiation, but an economic improvement into the standard of care? In the future, if you're not doing that, you're just going to be swinging and missing constantly.

JAEGER: Providing that context around,"What is the value that it brings to the market and what can it ultimately mean from a commercial standpoint?" is absolutely imperative.

"It's incumbent for innovators to be able to effectively convey the value of their product in the context in which it's reimbursed."
—ANDREW THORRENS, ALLERGAN

STAFF: We say, "What does the future look like three and five years out?" What do we have to be doing now to get there? Because, as we know, any kind of research, or clinical development, or paradigm shift with a payer, is going to take that long. That guides our principles on how we work together cross-functionally.

We don't even think about how are we going to commercialize a medicine that has been submitted for approval without having a completely locked strategy with our medical affairs and health economics teams.

MOWAD-NASSAR: I think we're getting very close to where big data analytics is going to allow us to bring payers, providers and industry together to look at a common set of data that's very unifying around what is the patient outcome and what is the real-world evidence we can generate.

"Can you show not just differentiation, but an economic improvement into the standard of care?"
—MIKE STAFF, ABBVIE

PE: *Could you give one piece of advice for your colleagues in the industry on the topics we've discussed today?*

STAFF: Never stop learning in the healthcare reimbursement space. Just when you think you've figured it out, you're going to understand that there's a lot that you don't know. More than ever, every patient—based on their employer, their health plan, their benefit, the medicine that they're taking, the geography they live in—is a unique situation.

Once you stop asking questions and trying to innovate, it's going to pass by you so fast; it's moving exponentially.

McCARTHY: Ensure the integration of marketing, managed markets, sales, HEOR, and medical affairs. That integration is so important because healthcare is an interdependent relationship.

THORRENS: It's incumbent on every innovator to be able to effectively convey the value of their product in the context in which it's reimbursed. Just because it fulfills an unmet need is not nearly enough. Understanding all of the elements around their product's coverage by a payer, the necessary coding and setting of care implications leading to adequate payment for the healthcare provider is critical, especially in a buy-and-bill environment.

MOWAD-NASSAR: Takeda has a relatively new CEO (Christophe Weber, appointed CEO in 2015). And he said pretty simply how we're going to refocus the business and our priorities and I think it's true. He said, "Patient, trust, reputation, business. If you put the patient at the center of everything you do, you will build trust with society." PE

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The Human Factor

The Quest for Meaningful Pharma-Patient Dialogue

With the patient voice growing louder in all aspects of the drug development and commercialization journey, we outline some of the current industry thinking on the evolving pharma-patient relationship

By Julian Upton

Over the last decade or so, patient groups have become better organized, more professional, and, not least, more vocal. As the pharmaceutical industry and regulators have acknowledged this strengthening of influence and resources, the patient has begun to have more impact on the way pharma works, particularly in health technology assessment markets. Consequently, the move to involve patients across the drug development and commercialization process—from R&D and clinical trials to promotional campaigns—is becoming an increasingly important consideration for companies committed to pursuing transformational medical innovation.

There are, of course, remaining barriers to the smooth cooperation of pharma and patient groups. A pharma company is a commercial organization, bound by regulatory restrictions and the expectations of all its stakeholders. The relationships pharma companies have with patient organizations can only advance if the right balance is struck and clearly defined boundaries are established. Historically, as Steve Wooding, head of Janssen's global commercial and market access strategy organization, points out, there have been issues resulting from the potential of both pharma and patient organizations to use their influence inappropriately.

"The patient voice has to come through, but there needs to be a clear separation between responsibility and accountability," Wooding told *Pharm Exec*. "We do need to make sure that the relationship is on an equal footing and is based around appropriate exchange of information."

Ipsos MORI's head of ethnography, Victoria Guyatt, notes the operational barriers to shifting further toward patient centricity. "There's still the thinking among pharma companies that, 'if we talk to patients, does that mean we can't deliver for our stakeholders?'" she says. "One of the things that pharma is getting good at is the gathering of patient insights—listening on social media, for example—but embedding and pushing these insights out to the rest of the organization, the R&D teams, is still difficult. And there's a lot of anxiety about doing the wrong thing."

For Abeona Therapeutics' vice president for patient advocacy, Michelle Berg, "harmonizing language and terminology" is a challenge. "It can be difficult for some individuals, or families or community members to understand the drug development practice, gene therapy and clinical trials," she says.

The digital dilemma

Developments in digital communication have radically altered the position of patients, and there is broad consensus that the resulting empowerment has brought major improvements to the pharma-patient dialogue. From a rare disease perspective, in particular, social media and online forums have proved to be vital tools that can engage patient communities that were hitherto almost invisible.

Abeona Therapeutics focuses on developing products for severe and life-threatening rare genetic diseases, such as mucopolysaccharidosis (MPS) IIIA and IIIB, a progressive neuromuscular disease with profound CNS involvement, which manifests in young children. Berg told *Pharm Exec*: "I am grateful that we have such communication tools available for families, because knowing that these are such rare diseases, there are not clusters of families in a region who can find each other and share experiences. With the advent of digital communications, families and healthcare providers have the opportunity to locate and support one another."

A patient diagnosed with acanthamoeba keratitis, a rare amoebic infection of the cornea, told *The BMJ*'s Stephen Armstrong ("Social Networking for Patients," August 10, 2016) that when she was first diagnosed, "most of the information I could find was either inaccurate or terrifying. But I found a Facebook group, with only 38 members at the time, and the relief was enormous. I was so happy to connect with someone, to share the same emotions and experiences, the same anxiety and frustration and shock in a normal, accessible way."

"There's still the thinking among pharma companies that, 'if we talk to patients, does that mean we can't deliver for our stakeholders?'"

Armstrong adds that online groups don't just enable patients to share experiences and support each other. He points to research from the University of Toronto conducted in 2011 that found that the 620 groups on Facebook for breast cancer had purposes including fundraising (44.7%), raising awareness (38.1%), promoting products or services (9%), and exclusively offering support to patients or caregivers (7%).

However, Armstrong also highlights the risk of social media disseminating misleading, superfluous, or incorrect information, or being used for the promotion of dangerous or unsuitable remedies. Berg adds that "communication tools are only going to be as good as the information that is perpetuated, and a problem can be that false or inaccurate information can be perpetuated quite quickly, which can have a negative impact. That's why it's important for organizations to have resources available and that are committed to supporting individuals and families with rare diseases, offering resources that can serve as a

FAST FOCUS

» Regulatory restrictions and operational barriers continue to challenge the transition to more industry-wide adoption of true patient-centricity. However, experts say, pharma companies are getting better at gathering patient insights through social media and other channels.

» Advancements in digital communication have also shown to empower patients, particularly rare disease groups, resulting in improvements to the pharma-patient dialogue.

» This shift has forced pharma to reevaluate how it incorporates the patient view in its processes. It's also led to a rethinking of how the patient voice should fit into discussions with payers and regulators around treatment outcome improvements vs. symptomatic relief.

» A recent survey of 3,000 US patients and caregivers found that the majority of them are in favor of patient advocacy groups partnering with biopharma companies to develop drugs for medical conditions.

fact-check against any information that might not be right."

Marc Princen, EVP and president, international business, Allergan, reminds us that pharma is a very regulated industry. "We are talking about decision-making where trained healthcare professionals must make the right decisions," he says. "It shouldn't be just a free-for-all. We need to respect the regulations. It is helpful that the technology exists and people can get better informed, but professional advice and decision-making is still needed."

Armstrong observes that "few physicians are currently using social media to talk to patients." Indeed, for some patients, "the idea of any healthcare professionals taking part in patient groups is an anathema; many see them as private patient spaces where people can vent frustrations about treatment," he says. If clinicians are to engage, they need to keep up to date. Armstrong spoke to one parent who explained that her daughter, who has type 1 diabetes, only uses the photo and picture-based platforms Instagram and Snapchat rather than Facebook or Twitter. She added she had "no idea" how clinicians could use these platforms even if they can understand them.

Patient-driven results

Nevertheless, the pharma-patient dialogue continues to advance, and pharma is faced with re-evaluating how to incorporate the patient view in its processes, not just to facilitate a better relationship but effectively to translate innovation into the market.

"In the old days, you had your product and you put it out there. But to bring meaningful innovation to people today, for instance, with clinical trials, we have to ask ourselves: are we designing trials that are great for the scientists but impossible for the patients?" says Wooding. "The latter will ultimately delay access and commercialization of your medicine. And what endpoints do we need? Whether a treatment shrinks a tumor, for example, is a useful endpoint from a regulatory standpoint; but it may not be enough from a patient standpoint, if they don't feel better or their quality of life is not improved along with the medical benefit."

These are the criteria, says Wooding, that payers are starting to look at, "so we have an opportunity now to build those metrics into the process in a meaningful way."

In many cases, symptomatic relief is more important to patients than outcome improvements in the long run. With payers in the past having valued

"To bring meaningful innovation to people today, we have to ask ourselves: are we designing trials that are great for the scientists but impossible for the patients?"

outcome improvements higher than symptomatic improvements, it has become clear that the patient voice needs to be drawn further into the debate. As *Pharm Exec*'s Jill Wechsler noted in her April column, FDA is now looking to improve communications with patients by forming an Office of Patient Affairs in the Office of the Commissioner. "This would provide a single, central entity to handle inquiries from the patient community, and would expand the current patient team in FDA's Office of Health and Constituent Affairs," she wrote.

From the industry side, building meaningful relationships with patient groups is less a case of responding to patient lobbying and more a case of encouraging them "to share with us what is important to them so that we can actually make those developments," says Wooding.

Princen, who was formerly Takeda's president of Europe and Canada, notes that it is about finding out "how you can institutionalize working with the patient." He says that Takeda worked with an outside think tank, which put together criteria for inflammatory bowel disease, Crohn's disease and ulcerative colitis. "We developed an app that included these criteria, allowing for collection of data on symptoms, triggers and aggravating factors, and provided it to patient organizations," he says. "This type of objective criteria-setting is really useful, and it is where the patient organizations are very helpful. The next step was to work with the payers, measuring the real patient outcomes and then work out how the funding could be shared."

So, what does pharma look for from a patient group to facilitate an effective collaboration? Ideally, according to Wooding, it's the ability to connect with a large unifying group.

"But that isn't always possible," he says. "It is certainly an advantage if they have a depth of

scientific knowledge. They should be informed and have a clear structure that we can interact with; they need to have the right charter in place and to be professionally operated."

Wooding adds that, in specialty areas, particularly in diseases with increasingly complex treatments and where the side effects need to be managed effectively, "effective partnering is easier with a better informed, better aligned patient."

For Berg, "it's very important to collaborate and partner with those specific communities that we are aiming to serve, in order to step into their shoes and understand the impact of what that disease might be, not only for the individuals afflicted but, in the case of much of what we're working on, in the pediatric population." She believes that understanding what's important to the parents and caregivers is critical and, in some cases, may be more important than understanding the priorities of the children themselves. "Because with these diseases, their voices are not really able to be heard," says Berg.

The voice of the patient is not only going to become more influential, but will have a significant impact from a business point of view

A measure of how important patient input is perceived in the rare disease area is highlighted by results of a survey of over 3,000 US patients and caregivers across several hundred diseases and conditions, conducted this year by Rare Patient Voice. The survey found that the majority of respondents (55%) were in favor of patient advocacy groups partnering with pharma or biotechnology companies to develop drugs for medical conditions. Some of those who support partnerships stressed that they can enable drug development to take patient perspectives into account; that they are the best way to obtain funding; that they can accelerate the development of treatments; and that, ultimately, "anything that might help obtain a cure or improvement should be tried."

Writing on the Clinical Trials Arena website, Horizon Pharma's Dr. Jeffrey Sherman, in an article published late last year, emphasizes that "engaging with patient groups to understand the patient voice from the beginning of research can greatly benefit overall drug development." Sherman outlines how, for a clinical trial evaluating a medicine for the treatment of Friedreich's ataxia (FA), a rare neuromuscular disorder, Horizon collaborated from the outset with the patient organization Friedreich's Ataxia Research Alliance (FARA).

"FARA offered crucial input on trial design to ensure that travel requirements, medicine administration and study eligibility criteria were realistic within the FA community," he notes. "Moreover, FARA provided full access to its comprehensive patient registry, the only collection of demographic and clinical information for 2,000-plus FA patients around the world."

The result was that the FA study completed enrollment in less than one year, "an unusually fast pace for a rare disease trial."

An expanding opportunity

While Wooding acknowledges that, in terms of involving patients, "there are only so many things that you can choose to do within an R&D setting," he points out that Janssen's move in this direction has begun to deliver results for the company in the last couple of years.

"We are now starting to see patient-reported outcomes become acceptable in terms of registration and licensing and labeling," says Wooding. "For example, for a prostate cancer medicine, we now have within the indication the fact that the drug can have an impact on pain. For most patients, that is their most relevant day-to-day symptom. Those kinds of things are working their way through into labels. The only way for a company to anticipate what's important to patients is to have their input. With the availability of more data, to link to the genotype and phenotype, this will become even more of an opportunity."

Wooding concludes: "We have always been a patient-oriented company, highly aware that patients are waiting. We realize, however, that not only are patients waiting, they are engaging and wanting to take more control of their own destinies."

It is very clear, he says, that the voice of the patient is not only going to become more influential, but will have a significant impact from a business point of view. "At Janssen, we heard it," says Wooding. "Now we needed to do something about it. Some of that is about best practice sharing; some is about spreading the message within our organization. In other cases, it's about trying out new approaches and seeing what works. It's about continuing the patient dialogue—and learning from it." PE

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HEALTHCARE & LIFE SCIENCES REVIEW

TAIWAN

In the Global League

"Fostering the development of the pharmaceutical and biomedical industries holds a central importance within President Tsai's strategic vision to build Taiwan's new economic model", firmly announces Tsung-Tsong Wu, minister without portfolio of the Republic of China (Taiwan) who supervises and coordinates the country's interministerial program for the development of the biomedical industry. "As a matter of fact, these two sectors were included in Taiwan's '5+2 Industrial Innovation Program', which aims to prioritize resource allocation to five innovation-centered industries that are set to nurture the long-term growth of our country's economy," he continues, before stressing that "the commitment of Taiwan's government toward the development of the pharmaceutical, biotech, and biomedical industries is probably unrivalled in the world".

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A SENSE OF PRIORITIES

Since May 2016, the 23-million inhabitant island, whose remarkable economic development over the past three decades has been essentially propelled by the tremendous growth of its semi-conductor industry, is headed by an executive duet that displays eye-catching experience in the pharmaceutical and healthcare fields: President Tsai Ing-wen, who was the former chair of one of Taiwan's most successful biotech companies, TaiMed Biologics, and Vice-President Chen Chien-jen, a famed epidemiologist, former minister of health and vice president of Academia Sinica, Taiwan's premier research institution. "From the very beginning of her campaign, President Tsai has been closely working with industry leaders, researchers and investors to further build up Taiwan's medical sector," adds Chih-Kung Lee, Taiwan's minister of economic affairs, while Carol Cheng, COO of TRPMA, the association gathering 28 local, R&D-driven companies, confirms that "even before President Tsai's election, TRPMA and her campaign team were already discussing crucial reforms that could be implemented under her tenure, especially with regards to labor and corporate regulations – and this privileged and preserved flow of communication now stands as a great asset towards our common objective to boost Taiwan's biotech capacity."

Tsung-Tsong Wu, minister without portfolio of the Executive Yuan, Republic of China (Taiwan); Chih-Kung Lee, minister of economic affairs, Republic of China (Taiwan); Carol Cheng, chief operating officer, TRPMA

Although the local pharma and biotech sectors have yet to display the type of success story of Taiwan's semiconductor industry, these companies have already reached a particularly interesting level of maturity, notably driven by the substantial investments injected by Taiwan's successive governments over the past two decades. "The total market capitalization of local, publicly listed biotech companies has increased 700 percent since 2008", recalls Johnsee Lee, chairman of the Taiwan Bio Industry Organization, which notably organizes the annual BioTaiwan conference – one of the largest biotech-related events in Asia. "The market capitalization of Taiwan's healthcare-related industry amounted to around NTD 200 billion [around USD 6.5 billion] in 2016. If we continue to sharpen the

IPO MARKET IN LIFE SCIENCES SECTOR

LSHC IPO IN 2016 (MILLION US$)

COMPANY	SECTOR	IPO DATE	RAISING CAPITAL
Excelsior	Medical device	2016/1/7	11
Great Tree Pharmacy	BioPharma	2016/3/30	4
Pharmaessentia	BioPharma	2016/7/19	100
Medeon Biodesign	Medical device	2016/7/27	27
Dyaco International	Medical device	2016/9/20	15
Lumosa Therapeutics	BioPharma	2016/9/26	165
Syngen Biotech	BioPharma	2016/9/26	4
Crown Bioscience	CRO	2016/12/12	21
Onyx Healthcare	Medical device	2016/12/21	14

Source: Deloitte Taiwan(2017.02)

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Development of a safe and long-acting interferon has been an elusive goal until the discovery of Ropeginterferon alfa-2b, a novel mono-pegylated interferon developed based on PharmaEssentia's PEGylation platform.

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Hong-Jen Chang, chairman & CEO, YFY Biotech Management Company; Johnsee Lee, chairman, Taiwan Bio Industry Organization; president & CEO, Personal Genomics

attractiveness of our biomedical ecosystem and adapt the government's support to the evolving needs of our pioneering companies, reaching a capitalization of NTD 1000 billion [around USD 32 billon] within the next decade clearly stands as a reachable objective," states Minister Wu.

In light with this vision, Taiwan's government has already triggered a comprehensive effort to upgrade the country's regulatory framework. The first aspect relates to further deregulating the country's capital and investment sectors, one of Taiwan's main strengths from an international standpoint. "Over the past decade, many countries have been trying to build a viable and vibrant biotech stock market. In this regard, Taiwan has truly managed to establish the hottest viable biotech financial market for small biotech and medtech companies – outside of the US, the unsurpassable leader," highlights Hong-Jen Chang, current CEO and chairman of YFY Biotech Management Company, a Taiwan-based VC fund that has been playing an instrumental role in the development of the local biotech industry. While being able to go public before registering profits has encouraged biotech startups to list early, PwC estimated in 2015 that biotech accounted for 19 percent of the listed companies in Taiwan, compared to respectively seven and six percent of China's and Hong Kong's listed companies. Still on the regulatory side, the Legislative Yuan also recently underwent the revision of Taiwan's Biotech and New Drug Development Act. "Previously, only new drugs and advanced medical devices were being fiscally incentivized through tools such as tax rebates. Now, a third category has been added to the Act - new biomedical technology, which covers precision medicine and cell and gene therapy technologies," explains Taiwan Bio's Johnsee Lee.

Aligned with the international ambitions of a local industry that cannot content itself with a limited domestic market, the government is also embracing the evolving needs of Taiwan's most advanced companies. "By adapting our tax incentives and immigration processes, we want to encourage international professionals and experts to

The Challenges of a Rapidly Aging Population

Tzou-yien Lin, former minister of health and welfare, Republic of China (Taiwan); Hui-Ting Huan, president, Taiwan Adventist Hospital

"Taiwan's National Health Insurance (NHI) system was implemented in 1995 to ensure that our entire population could access quality and comprehensive healthcare services – and, in many regards, it has already achieved this fundamental mission," explains former Minister of Health and Welfare Lin Tzou-yien. The NHI now covers more than 99 percent of the population and is proudly regarded as a frontrunner in Asia, while latest annual polls revealed that 83 percent of its beneficiaries are satisfied with its delivery. "Nevertheless, the share of our population above 65-years old is set to increase from 13 percent now to more than 25 percent in 2030," reveals former Minister Lin, "which has been critically altering the historically sound balance between NHI's revenues and expenditures," he adds.

To guarantee its financial sustainability, NHI's reimbursement system is "evolving from its historical fee-for-service approach into a pay-for-performance basis, especially for chronic, non-communicable conditions such as hypertension, asthma, diabetes or chronic kidney diseases, among others", explains Lin, while the government also aims to foster a greater resource allocation between hospitals and primary care centers through the enhancement of the NHI's patient referral system.

In the meantime, President Tsai has established the strengthening of long-term care as a priority. "In this regard, we just released a new ten-year strategic plan through which we will invest USD 1 billion every year," announces Lin, allowing to double the number of related products and services reimbursed (and notably cover the treatment of dementia) and significantly increasing the number of beneficiaries. Finally, innovative primary-care-based initiatives aim at better detecting and preventing the progression of life-altering disabilities, such as neurodegenerative diseases, thanks to the implementation of a new community care model, inspired by the US Program of All-Inclusive Care for the Elderly (PACE) and Japan's Integrated Community Care System.

In line with that, Taiwan Adventist Hospital, a unique regional hospital that focuses on quality and facility security, is supporting long-term care by introducing a different approach to health. Dr. Hui-Ting Huang, Taiwan Adventist Hospital's president emphasizes the importance of prevention: "making the elderly more active can extend their life span. Conceptualizing and communicating this message to the elderly can ease the burden of budgets and long-term care. Therefore, we are pushing the concept of health literacy as part of our health promotion program. This concept focuses on empowering the patients to manage their health, to acknowledge the importance of communication with health professionals, and to make treatment decisions in a proper way." In addition to promoting preventive medicine, the hospital prides itself on building an efficient patient-centered system through introducing a lean hospital. "This year we started to apply the strategy of building the lean hospital. This means we want to provide the highest quality products and deliver them in the shortest period of time. Incorporating this type of concept will eliminate eliminating the waste of time, transportation, overproduction or unnecessary surgeries… It can reduce patient waiting times, and raise the efficiency of the hospital."

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#4 ASIA

*WEF 2016-2017 Global Competitiveness Report

#1 ASIA

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*Taiwan Biotechnology and Pharmaceutical Industries Promotion Office (BPIPO) 2016

TAIWAN'S MEDICAL TECHNOLOGY IS THE FIRST IN ASIA, AND THIRD IN THE WORLD, AFTER THE UNITED STATES AND GERMANY

14 14 TAIWANESE HOSPITALS ARE IN THE **WORLD'S TOP 200 HOSPITALS LIST**

#3 IN **IPOs**

*Genetic Engineering & Biotechnology News (GEN's) 2016

#3 GLOBALLY / **#2** ASIA

BEST INVESTMENT ENVIRONMENT IN THE WORLD

*2017 Global Entrepreneurship Index (GEI)

*Business Environment Risk Intelligence (BERI) 2016-I

BIOMEDICAL CLUSTERS

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  - Nankang Biotech Plaza
  - The National Biotechnology Research Park
- Hsinchu Science Park
  - Hsinchu Science Park
  - Hsinchu Biomedical Science Park
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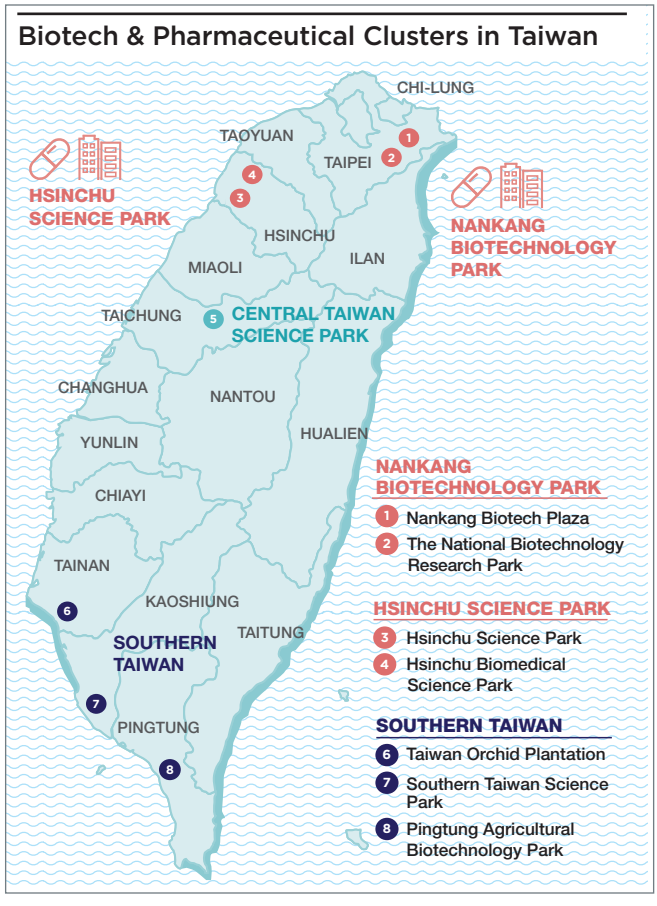
come to Taiwan and help our innovative companies to get the human resources they need to compete on the global stage," explains Minister of Economic Affairs Lee. While government also put in place closer monitoring and stronger support towards all significant investments coming into Taiwan, direct government funding for innovative companies is far from running out. "Around 13 percent of this year's budget is specifically allocated to support flagship projects from these 5+2 innovative industries that are set to drive our country to new heights. Precision medicines, including companion diagnostic devices, are for example eligible to be supported by this exceptional fund," details Lawrence Gan, president and CEO of Taiwan's Development Center for Biotechnology (DCB) and its 260 R&D scientists, an organization that truly operates as the R&D branch of Taiwan's biotech capacity, focused on new drug discovery and the pre-clinical development of pharmaceuticals, biologics, and botanical drugs.

Nevertheless, in Taiwan, the development of the local industry now clearly stands as a shared responsibility that is not solely weighing on the shoulders of the economic arm of the Taiwanese government. "We recently decided to follow the example of the US and establish the promotion of the local industry as one of the key missions of the Ministry of Health and Welfare, in addition to their historical responsibilities for the evaluation of product safety and efficacy," explains Minister Wu. "In this regard, our renewed ambition to speed up market approval and reimbursement timelines will contribute to sustain the development of local, R&D-driven companies, as most of them look at bringing their products to the Taiwanese market in parallel to other key international markets," highlights former minister of health and welfare, Lin Tzou-yien. "Nevertheless, heightened regulatory support should be provided at the very early stage of the drug development process, by following the way of the US FDA and its "breakthrough therapy designation," complements TRPMA's Carol Cheng.

Lawrence L. Gan, president, Development Center for Biotechnology

"Propelled by the excellence of our physicians and scientists, combined with the quality of our medical infrastructure, Taiwan's overall research capacity has been progressing fairly rapidly over the past few years," adds Minister of Economic Affairs Lee, and "as such, Taiwan can truly stand the comparison with some of the most developed countries in the world, including Japan." While biopharmaceutical





Albert Liou, vice chairman, Asia Pacific, PAREXEL International; Guo-Liang Yu, executive chairman, Crown Bioscience International; Grace Yeh, president & CEO, PharmaEngine

companies can already leverage the sheer amount of data accumulated by the National Health Insurance (NHI) for the development of personalized medicines, the country's efforts to ensure its regulations are perfectly aligned with the most stringent international standards also create a particularly favorable context for local companies. "Thanks to its strong regulatory system and well-developed clinical research environment, local companies can conduct early and mid-phase trials in Taiwan and use this data for a Phase III study in the US or in the EU," explains Albert Liou, vice chairman, Asia Pacific, at PAREXEL, whose APAC headquarter is located in Taiwan. "For agencies like the Center for Drug Evaluation (CDE) and Taiwan FDA (TFDA), international collaboration is now a priority, and this remarkable openness also contributes to propelling our local industry onto the global stage," he concludes.

INTO THE GLOBAL INNOVATION RACE

"In Asia in general and in Taiwan in particular, the current innovation drive has been nurtured by the increasing number of returnees, who – after having studied in the most prestigious universities and worked for some of the most advanced biopharmaceutical companies globally – come back to their home country and leverage easily-accessible private equity or government-backed funding to launch their own biotech companies," analyses PAREXEL's Albert Liou. This experience, honed in the EU and US naturally contributes to accelerating the development of Taiwan's biopharmaceutical companies. "My perception is that, initially, Taiwan's biotech industry followed the path of the very successful domestic electronics and IT sectors, which first gained international momentum by copying American products and manufacturing them at Asian costs – before eventually following a true innovation-driven strategy. In the biotech sector too, the mentality has been changing recently and the country has been rapidly catching up in terms of innovation capacity," documents Guo-Liang Yu, executive chairman of Crown Bioscience International, a world leading company in drug efficacy testing that has been building an unrivalled capacity in patient-derived xenograft (PDX) cancer models.

This innovation focus, initially triggered by some pioneering companies in the early 2000s, has already started to bear its fruits. In this vein, PharmaEngine's innovative oncology product received US FDA approval in October 2015 and was moreover included in the guidelines of the National Comprehensive Cancer Network® (NCCN®), an alliance of 27 of the world's leading cancer centers, as a category 1 treatment option for pancreatic cancer in May 2016. "Looking at our return on investment, we licensed-in this product in 2003 for USD three million and licensed it out for USD 220 million of milestone payments as well as tiered royalty payment based on the net sales in Europe and Asia," explains PharmaEngine's CEO, Grace Yeh, while the company now holds Ipsen (US market) and Shire (worldwide without US and Taiwan) as commercial partners for the product.

Considering that 225 drugs developed by Taiwan-based companies are currently undergoing clinical trials, including more than 115 products that already received an IND approval from

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Amy Huang, general manager, OBI Pharma

Du- Shieng Chien, president & CEO, TaiRx

the US FDA, new groundbreaking treatments should soon reach the global stage. OBI Pharma, for example, is competing against world's leading biopharmaceutical companies in the development of active immunotherapies in oncology. Although the Phase II/III trial of its investigational vaccine in patients with metastatic breast cancer did not meet its originally designed primary endpoint, "patients who demonstrated an immune response (IgG or IgM) showed a highly significant improvement in progression-free survival – and this represented around 50 percent of the patients involved in the trial," explains OBI Pharma's general manager Amy Huang, prompting the company to strongly believe that this product can benefit certain types of cancer patients, who can actually produce enough antibodies to fight the progression of the disease. "KOLs we met at the 2016 annual meetings of the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO) truly encouraged us to move forward on the development of our product and start global phase III trials," she continues, while the company is now collaborating with international regulatory agencies to design the protocol of this global phase III study.

Other ambitious Taiwan-based companies are also targeting frontier mechanisms to tackle tumor development: TaiRx's CVM 1118, for example, is a New Chemical Entity (NCE) which "looks at halting vasculogenic mimicry, a tumor development process that used to be a moot point among oncology researchers before being now widely accepted by the scientific community", explains Du-Shieng Chien, president & CEO of TaiRx. "Vasculogenic mimicry relates to the now-proven capacity of highly invasive and genetically deregulated tumor cells to create their own blood-delivering tubes, independently from classical angiogenesis. The tubes that these smart tumor cells build are dangerous not just because they allow them to receive needed blood: they also foster the migration of tumor cells to new parts of the patient body (metastasis), which is responsible for most cancer deaths," he continues, while TaiRx's CMV 1118 became in 2015 the first drug in the world targeting vasculogenic mimicry to enter phase-I trials in the US and in Taiwan. "Looking forward, we now plan to start phase-II trials in the US in 2017", adds TaiRx's Chien.

In the meantime, Senhwa is advancing the clinical development of CX-5461, a novel molecular targeted agent

The Virtue of Persistence

"Within the next decade, our objective is to generate revenues of between USD five and ten billion and establish PharmaEssentia as one of top 50 biopharmaceutical companies in the world," firmly states Ko-Chung Lin, founder and CEO of PharmaEssentia, a Taipei-headquartered biotech company founded in 2003 whose philosophy, both in terms of drug development or marketing approach, is very similar to those implemented by the most innovative companies in Boston or San Francisco. "Actually, I decided to set up the company in Taiwan and not in the US because Taiwan probably stands as the best country in the world to raise funding for biotech companies, which has proven being particularly true for us too", he continues, as PharmaEssentia, with a market capitalization of over one billion US dollars, now clearly belongs in the top half of biotech companies globally.

If Ko-Chung Lin's growth vision is plausible, it is essentially because the company (successfully) dared to concentrate its efforts on improving interferons, an ambition that the global industry seemed to have completely given up on. "In 2009, we started developing our own interferon, deeply convinced that we could bring a better product onto the market than those already available. The results of our phase I study quickly confirmed that our product could display outcomes that the industry as a whole has considered unreachable for a new interferon: a substantially heightened tolerability, safety, and a significant improvement in dosing schedule," explains Lin.

Eight years later, the company is now on the verge of bringing its once-every-two-week interferon to worldwide patients with polycythemia vera (PV), a myeloproliferative neoplasm (MPN) characterized by an increase in red blood cells. "Patients with PV have heightened risks of hemorrhage and thrombosis as well as of long-term development of mylefibrosis (MF), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML). PV has unfortunately been a devastating disease for more than 25 years, while prevalence in the US (57 per 100,000) is higher than for any other MPN and appears to be increasing," he highlights. PharmaEssentia is currently expanding its footprint in Japan and the US and Lin reveals that, "beside PV, our objective will be to maximize the value of our lead compound: we plan to use half of the USD 135 million we raised with our IPO to move our three on-going phase III trials in Hepatitis C forward, while the phase II data we got was absolutely mind-blowing."

Ko-Chung Lin, founder & CEO, PharmaEssentia

The second main aspect of the company' R&D approach relates to cancer treatments, while existing interferons' dramatic side effects and limited dosage forms did not fit within the global ambition of the research community to turn cancer into a chronic, manageable disease. "Albert Xiao Qin, our recently appointed CMO, is one of the world's experts in the interferon field. Thanks to his expertise, the increased safety and tolerability of our product and our company's technology platform, we want to develop longer-acting protein drugs, with the objective of decreasing the number of injections needed over the course of a year – and therefore open a new era of cancer treatment for interferon products," he concludes.

which induces tumor cell death without impacting normal cells, as it can activate pathways of both the Pol I inhibitor and G-quadruplexes to target cancer development. "G-quadruplexes (G4s) sequences are highly prevalent in the human genome and are involved in DNA replication, gene expression and regulation, telomere/chromosome maintenance and genomic instability. When the G4 structure is stabilized by drug-like molecules, it may cause replication fork stalling, DNA breaks, and transcription–replication collisions, resulting in tumor cell death. Therefore, the development of novel stabilizers of G4 stands as an exciting anticancer approach in the potentially broad clinical applicability," details Senhwa's president & CEO, Tai-Sen Soong. While ongoing clinical studies of CX-5461 for breast cancer (phase II), and hematologic malignancies (phase I) respectively won sponsorships from Canada's Stand Up To Cancer (SU2C) and Australia's Peter MacCallum Cancer Centre (PMCC), Senhwa's other product CX-4945, a selective, small molecule inhibitor of Casein kinase 2 (CK2), was granted US FDA Orphan Drug Designation in December 2016 for the treatment of advanced cholangiocarcinoma. "Phase I/II clinical trials have been underway globally, with CX-4945 used in combination with first-line chemotherapies — gemcitabine and cisplatin — in an attempt to block DNA repair of tumor cells and enhance the sensitivity of cancer cells to

Benny T. Hu, chairman, Senhwa Biosciences; Tai-Sen T. Soong, president & CEO, Senhwa Biosciences



Guochuan Emil Tsai, founder & CEO, SyneuRx; Chih-Yi Weng, chairperson and CEO, Charsire Biotechnology; Tzu-Ling Karen Tseng, CEO, Bio Preventive Medicine

these anticancer therapies," says Senhwa's chairman Benny Hu.

Taiwan's utmost innovation capacity is not limited to the oncology field, as two of SyneuRx's schizophrenia products under development have already been granted breakthrough designations by the US FDA, in December 2014 and November 2015, a recognition that is particularly rare for CNS products. In this field, Charsire Biotechnology however chose to leverage the country's talent pool and expertise in botanical new drugs and the increasing recognition of these products' therapeutic potential in the West. "BAC, our botanical new product for vascular dementia and Alzheimer's disease, received approval by the US FDA for a phase II clinical trial," reveals Chih-Yi Weng, Charsire's chairperson and CEO. One of the key specificities of this product lies in its dosage form: "BAC is a topical application drug, while most other pharmaceutical companies active in the CNS field are concentrating their efforts on oral drugs. As a topical product, it will then hold the great advantage to be easily combined with other oral products taken by patients," she adds.

Taiwan's biotech market is also transforming the delivery of health by embracing innovation for diabetic kidney disease. Bio Preventive Medicine (BPM), a leading company in the renal biomarker area, helps in the development of new drugs in the renal area and renal safety. "The diagnostics of DKD are important as around half of the population with end-stage renal disease (ESRD) have their kidney diseases derive from diabetes. Around 30 percent of patients with diabetes develop DKD... Therefore, it is very important to use a new test to identify the development of DKD as early as possible," states Karen Tseng, BPM's CEO. "Due to a lack of evaluation tools for the renal efficacy of DKD drug development, BPM's technology provides the solution; this is our market opportunity," she adds, while addressing their recent partnership success: "We have entered into a partnership with Boehringer Ingelheim (BI) where DNlite technology is used

Bringing a New Class of Drugs to the World

To anybody who has been following the development of the global biotech industry over the past three decades, the name of Tse-Wen Chang should sound familiar. This Harvard University PhD holder co-founded the biopharmaceutical company Tanox in 1986, where he headed the development of anti-IgE therapies leading to the commercialization of Xolair (Omalizumab). In August 2007, Genentech acquired Tanox for USD 919 million. Since his return to Taiwan in 1996, Chang has notably served as president of Taiwan's Development Center for Biotechnology (DCB) and as a Science and Technology Advisor to Taiwan's Executive Yuan – but he is now back in the innovation race with "T-E™ pharmaceuticals", the technology platform at the core of his new company Immunwork, founded in Taipei in 2014.

"Most oncology drugs currently available unfortunately display low response rates (usually below 50 percent) and severe side effects. The thinking behind Immunwork's technology platform is then to increase the efficacy of these drugs and lower their side effects," explains Chang. Immunwork's new drug molecules contain both targeting (T) and effector (E) moieties, which are expected to achieve increased efficacy and safety while broadening the scope of applications of existing products. "We have already designed more than 20 new products, in oncology, auto-immune diseases, infectious diseases, CNS diseases, pathological clots, and organ transplantation," he reveals. "Our technology can be used to prepare ADCs and bispecific antibodies as well as various products in versatile configurations which have improved product homogeneity, drug payloads, target-binding valency, and consistency in the manufacturing process. Our platform is very suitable for personalized/precision medicine," he adds.

Tse Wen Chang, founder, president and CEO, Immunwork

Although Chang is considering bringing a few of his prototypes to early phase clinical trials before seeking development alliances, some international biopharmaceutical companies have already been attracted by the potentially increased efficacy and safety profiles of Immunwork's T-E™ pharmaceuticals. "Building strategic partnerships with major pharmaceutical companies will be critical in our overall development strategy, and these leading companies' interest in our technology – after less than three years in activity – is extremely promising," he concludes.

to evaluate renal effect in a phase IIIb global clinical trial in T2DM patients."

Ben Chien, chairman, president and CEO, Foresee Pharmaceuticals

For another Taiwanese success story, Foresee Pharmaceuticals, global partnerships have been key. These partnerships include a recent deal with Ferring and joint ventures with ScinoPharm and Pierre Fabre. This fully integrated pharmaceutical company is driven by the need to help patients through its innovative technologies - Drug Delivery Technology (stabilized injectable formulation (SIF)) and Rational Drug Design (novel new drug development (NCE)). Their injectable drug FP001 for Prostate Cancer successfully achieved its primary efficacy endpoint in the Phase III clinical trial this year. Foresee CEO Ben Chien describes how "phase III trials clearly indicated that with FP-001, testosterone concentration in advanced prostate cancer patients is suppressed, proving that treatment's efficacy data is similar to the existing products." Chien also highlights the convenience of their product: "Foresee's product is in a pre-filled syringe and ready to use, meaning Foresee's formulation has a more stable and user friendly profile." In terms of FP-025, Foresee's MMP-12 inhibitor for the treatment of asthma and Global Chronic obstructive pulmonary disease (COPD), Chien plans on leveraging the technology platform to ensure future growth: "Over the next 20 years, medical costs related to COPD will total

Jonas Wang, chairman & CEO, StemCyte

approximately $800 billion in the United States, according to a study presented at the American Thoracic Society International Conference on May 2006, and there is no treatment available. MMP-12 is an enzyme that plays a key role in the recruitment of inflammatory cells, which consequently cause physical reactions and symptoms experienced with COPD… The favorable characteristics of the compound were mainly determined by the core MMP-12 mechanism, which as predicted showed greater direct action via inhibition and selectivity of the MMP-12 enzyme. The Phase II study of FP-025 is set to start by the end of the year."

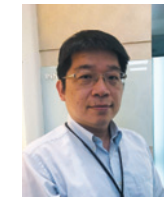
Finally, StemCyte, a global leader in the regenerative therapy field located in the US, Taiwan, and India, just released among the most impressive results in the history of spinal cord injury (SCI) treatments for a phase II clinical trial which aimed to prove the efficacy of the company's technology platform. "We have developed a patented process to extract mononuclear cells from cord blood units, as well as a patented storage technology and a unique transportation system to ship these cells all around the world," documents Jonas Wang, chairman and CEO of StemCyte and former vice president of research and technology at Johnson & Johnson. "Thanks to this in-house technology platform, mononuclear cells can be used up to five days after their extraction, during which we can guarantee a similar level of therapeutic efficacy, which stands as a real breakthrough: previously, transplants had to be used within 24 hours." StemCyte also plans to start the clinical development of its second R&D project in 2017, "for which we want to leverage the same technology platform to treat patients affected by chronic strokes – a market that is ten times larger than for SCI therapies" continues Wang. "We want to conduct the phase I clinical trial in Taiwan, the perfect country to conduct high-quality, cost effective clinical trials, where we will be able to easily access a large patient population," explains StemCyte's CEO and chairman Jonas Wang, while he plans that "StemCyte can easily become a billion dollar company if we manage to develop the aforementioned treatments for SCI and strokes."

THE POWER OF TECHNOLOGY

Leveraging Taiwan's remarkable talent pool in chemistry, some of the country's fastest-growing companies have been concentrating their efforts on technology platforms that allow them to develop a plethora of potentially game-changing medicines, rather than focusing all their resources on the risky development of a single, potentially groundbreaking product. "The true core of our company is our in-house developed technology platform, OralPAS®, a self-microemulsifying drug delivery system which allows the transformation of an existing, non-oral product (for example an injectable) into an oral dosage. In this regard, we clearly position ourselves as a technology-based biotech company rather than being focused on a specific therapeutic area," confirms CS Hsu, president of Innopharmax, which was ranked seventh fastest growing high-technology company in Taiwan by Deloitte's "2015 Technology Fast 500 Asia Pacific" ranking. "Our teams have developed our technology platform from scratch, an effort that has clearly paid off as we now hold many patents in various international markets, covering not only the commercial rights of our products but also their APIs," he says when analyzing Innopharmax' impressive year-on-year growth rate of 519 percent that made it one of the fastest-growing life sciences companies in the region in 2015. "The potential of our technology platform has been drawing the interest of a rapidly-growing number of international pharmaceutical companies over the past years, essentially from China or India but also from North America and Europe, and we are now involved in several commercial partnerships all around the world, " reveals Hsu.

InnoPharmax's focus on developing products complying with the requirements of the US FDA's 505(b)(2) NDA, an appealing drug approval pathway that avoids unnecessary duplication of studies already performed on a previously

approved drug, is actually far from unusual in the Taiwanese biotech landscape. "By fully leveraging our proprietary technology platforms, 505(b)(2) products should bring great growth prospects to the company, as many crucial treatments are still only available through injectable and/or oral dosage forms around the world," confirms Howard Lee, chairman and CEO of Easywell Biomedicals, which was recently ranked the tenth fastest-growing high-tech company in Taiwan by the same Deloitte ranking, thanks to an eye-catching 367 percent growth rate in 2016. In this regard, Lee also highlights the importance of holding the global rights of all the company's products under development, "in comparison to some Taiwan-based companies that rely on in-licensed products for which they only own local rights". Besides being extremely rewarding, the process innovation developed by these companies' technology platforms also reveals itself as truly life changing. "In the US, there is so far no approved medicine for the treatment of cholangiocarcinoma, beside an injectable available under NCCN® guidelines. Nevertheless, after a 6-month chemotherapy, it is physically difficult for patients to handle the frequent injections as prescribed, while oral treatment are more convenient and lightly dosed than injectable products", explains Innopharmax's Hsu, as the company received in January 2016 US FDA Orphan Drug Designation for an in-house developed gemcitabine oral, which is about to enter a phase II trial. In the same vein, Easywell Biomedicals' transdermal Parkinson patch, for which the company started a Pivotal PK Clinical Trial in Malaysia, also holds mind-blowing market potential, as the global sales of the current oral treatment already amount to over USD 600 million. "By bringing a transdermal patch to the market, we expect to both ease treatment usage and increase patient adherence, meaning that market size should increase too. In other product categories, we already saw that the market entry of transdermal treatment form increased market size up to fivefold. In the past, most of the patches brought to the market were also more highly priced than oral dosages – usually around twice the price of the pill – as soon as the heightened efficacy and therapeutic advantages of the patches are clearly proven," anticipates Easywell's Lee.



Howard Lee, chairman, Easywell Biomedicals & partner, The CID Group; C.S. Hsu, president, Innopharmax

Min-Che Chen, managing director, Asclepiumm

Finally, this focus on in-house developed, proprietary platforms also comes with the broader ambition to develop a novel class of drugs holding greater targeting power and lower side effects than existing drugs. "In this regard, my long-term vision is to establish our company as a world-class design center for smart protein and peptide drugs, where scientists can leverage our Antibody Switch-on Cytotoxicity (ASC) platform to combine their research and turn it into marketable products, envisions Chen Min-Che, founder and managing director of Asclepiumm, whose ASC platform comprises a very innovative way to block or control intracellular signals. "To put it bluntly, this technology operates as an ASC shuttle that brings antibodies and peptides directly to targeted cells. As most existing effector molecules are cell-penetrating peptides, they are integrated with cell signaling regulation peptide functions after reaching their targets, while we found out during our animal studies that our technology platform enhanced effectors to reach the cells' nucleus and operate at the gene level," explains Chen. "As this ASC technology could allow us to control gene expression and protein interaction, we now want to develop our research capacity with the ambitions to develop ASC bio-drugs in areas such as oncology, anti-aging therapies, and tissue-specific hormones therapies, " he adds.

Nevertheless, Taiwan's world-class scientific and technology capacities should not overshadow the importance of implementing the right commercial strategy. "In Taiwan, there is a popular saying which states that "it is easier to train a good scholar than a good businessman." This is precisely the challenge that our biotech sector is currently facing: Taiwan needs to be a pioneer in a way that goes beyond technology, which requires developing and implementing new business models that will allow our companies to rapidly stand out from the international competition," warns Minister of Economic Affairs Lee.

THE TRUE SUCCESS FACTOR

Industry reviews spanning the last 15 years show that development timelines have been increasing, while the number of new drugs actually reaching the global market has been decreasing, prompting more and more companies to implement innovative business models and novel drug development approaches, notably based on a broader use of CROs, CRAs and other drug development partners and third parties. "The generalization of this new R&D pipeline approach, where drug development is licensed-in, then licensed-out, and simultaneously advanced by various partners and service providers in different countries, has strengthened the competitiveness of Taiwan's pharmaceutical and biopharmaceutical companies," considers Minister of Economic Affairs Lee, while PharmaEngine's recent success, based on a "No Research, Development Only" approach combined with a Networked Pharma structure, proves him right. "As part of this two-fold model, we do not hold a laboratory or a manufacturing facility, which further allowed the ramping up the development of the company and crucially reducing its cost structure. Looking at the drug development process, we license-in interesting compounds at the preclinical stage and license them out again when we receive positive results for phase II trials," documents PharmaEngine's Grace Yeh. First and foremost, this approach requires very strong competences in project evaluation. "With a business model essentially based on the in-licensing of early

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Building on API Leadership to Reach New Heights

Fred Y. Chen, president & CEO, ScinoPharm

How would you summarize the transformation that ScinoPharm - an indisputable API leader for complex, difficult-to-make products - has been experiencing over the past two years?

We have been vertically expanding our offering to now encompass the manufacturing of finished injectable products, a field where there is a high demand. Our new, upcoming injectable plant – focused on high potency drugs requiring flexibility in batch sizes - is being positioned to prepare its first registration batch this year, and we expect an USFDA on-site inspection in 2019. In the meantime, we have been tremendously improving the competitiveness of our organization, favoring a product mix with a heavier weighting of more profitable oncology products combined with tighter cost control and enhanced management efficiency.

What will be the importance of international partnerships in this new strategic vision?

A crucial aspect of our new growth approach relates to our "double A" strategy (API+ANDA), as we are teaming up with pharmaceutical companies to jointly apply for ANDA in US/EU and export final drug products globally. Currently two ANDA submissions have already been filed, while we have formed partnerships based on co-development and profit sharing models for eleven products overall. Furthermore, ScinoPharm is currently negotiating with major international companies exclusive distribution rights in Europe and the U.S for developing drug products indicated for cancer, multiple sclerosis, osteoporosis, diabetes mellitus, etc.

We also want to grow our contract manufacturing business, especially in partnership with new drug development companies, while six of our current partners' products are currently undergoing phase III clinical trials. As we are already the leader in providing oncology APIs to the most advanced markets worldwide, we want to extend our service portfolio to provide contract manufacturing of finished dosage form of injectable products.

How does ScinoPharm's leadership in the API field make you an attractive partner for providing such services?

Let me give you an example: we have recently developed a complex, peptide-based API for an innovative oncology product, which is now undergoing a phase III clinical trial. Given the problems they faced when finding a qualified producer for the manufacturing of such a sophisticated product, this customer decided to leverage our upcoming injectable plant and contracted us as the manufacturer of the finished product too.

Muh-Hwan Su, chief technology officer, Sinphar Group & general manager, SynCore Biotechnology

stage compounds, our enduring ability to identify the best compounds that we could integrate in our R&D pipeline – with regards to our technology capacity – is absolutely critical to nurture the long term growth of our company", explains Muh-Hwan Su, the general manager of SynCore Bio, the innovation-driven, oncology & dry AMD focused subsidiary of the Sinphar Group. "Such a business model also requires holding a deep and extensive knowledge of the global market, assessing the needs of patients and the healthcare community in all strategic geographies as well as anticipating their evolution for the next ten years," adds PharmaEngine's Yeh. "We indeed see that many emerging biotech companies out-license the development and marketing rights of their products once they get interesting phase II trials. However, they have limited resources and cannot take risk repeat clinical studies. In this regard, we are helping them better targeting and integrating the requirements of the reimbursement phase in the early design of the trials, so they can display more appealing clinical data, and, as a result, negotiate better deals," highlights PAREXEL's Albert Liou.

Although this innovative business approach is particularly appealing to investors, who are sometimes reluctant to wait for an entire R&D drug development program to end before receiving their return on investment, other Taiwan-based companies are however implementing a more end-to-end business model. "Bringing our in-house developed products onto international markets has been integrated into the core of our overall strategy from day one," explains Ko-Chung Lin, founder & CEO, of PharmaEssentia, which stands as one of the very first Taiwan-based, R&D-driven companies to develop its own marketing and sales capacity in the US and Japan, while the company also holds a manufacturing facility to produce its in-house developed interferon.

Nevertheless, be it through licensing agreements or the development of an integrated business model, most Taiwanese biotech companies embrace a global strategy – with a strong focus on the US market – at the notable exception of Taigen, one of the pioneers among the local R&D-driven industry. "My overarching goal has always been to secure market share in the rapidly growing Chinese pharmaceutical market, and we have now proven that TaiGen holds the experience and expertise needed to bring innovative products into this rather challenging ecosystem," documents Ming-Chu Hsu, chairman & CEO of TaiGen, which recently announced a joint-venture with Hong Kong–listed

YiChang HEC ChangJiang for developing a treatment for chronic hepatitis C in the Greater China region, which is home to 25 percent of all HCV patients worldwide.

Overall, the vast majority of these investor-backed, ex-nihilo biotech companies follow an organic growth approach, in a local industry context marked by a very low level of M&A activities. In this regard, Easywell's development approach truly emerges as an exception, as, under the leadership of its CEO Howard Lee - who is also a partner at the CID Group, one of the largest private equity firms in the region – and after several strategic acquisitions in Taiwan and in the US, Easywell now truly stands as an integrated healthcare company in the making, encompassing drug development, regenerative medicines, medtech products and also manufacturing facilities located in China (medtech products) and in the US (pharmaceuticals). "By holding the global rights of our promising 505 (b)(2) products, bringing to the market our innovative regenerative therapy for advanced wound care, and further enhancing synergies between our different business units, Easywell now displays a very limited risk exposure while targeting huge market niches which should deliver very promising growth rates for the upcoming years," expects its CEO.

In the meantime some industry players are reinventing themselves by starting new companies operating in complementary fields. For example, Formosa Laboratories Inc., an established API and UV-filters manufacturer, announced the set up of a new drug development company called Formosa Pharmaceuticals. "Formosa Pharmaceuticals will be an internationally focused company developing large and small companies. In terms of compounds, we have one oncology drug in Phase I trial; an IND (Investigational New Drug) approved by US FDA, as well as modified antibiotic drug and antibody drug conjugate under development" details Formosa's president, C.Y. Cheng. Formosa Laboratories, continuously focusing on the improvement of its core business and investments into new capabilities, will leverage years of experience to support the business of Formosa Pharmaceuticals. "Formosa Laboratories will remain the main shareholder in Formosa Pharma. I have to keep the business of Formosa Laboratories strong and stable to support the development of Formosa Pharma. One of our advantages is the fact that Formosa Laboratories is well established; not only can we provide the funding but also the support needed in drug development pathways; we can be a good API supplier and help with documentation. Formosa

Ming-Chu Hsu, chairman & CEO, Taigen Biotechnology

Partnering at All Levels

Peter Tsai, chairman and CEO, Orient EuroPharma

Founded in 1982 as a distribution business by its current CEO and chairman, Peter Tsai, Orient EuroPharma notably counts among its partners Italy's Chiesi and Recordati, Spain's Almirall, Pfizer as well as France's Pierre Fabre, for whom OEP is the regional distributor, serving Singapore, Malaysia, Hong Kong, and Taiwan. "In addition to our existing subsidiaries in Singapore, Malaysia, Hong Kong, the Philippines, and China (in Shanghai and Guangdong), we plan to enter Thailand and Vietnam in 2017 and to increasing our activities in Indonesia," documents Tsai, who also wants to further strengthen the company's diversified portfolio built on a specialty product approach. "For example, in 2016, we became the first Asia-based company to sign an exclusive distribution agreement with US-headquartered Second Sight Medical Products for their breakthrough implantable bionic eye technology, and, on April 13 2017, this product has been implanted in the first patient in Asia", explains Tsai.

Nevertheless, "distribution is a tricky job", as Tsai puts it, and he has made moves to diversify the company's activities over the past decade. In this regard, he expects to complete the construction of a new injectable plant in 2017, before aiming for US FDA certification to complement OEP's current US FDA and Japan MHLW certified production facility for oral dosage forms. "Our world-class manufacturing arm stands as a particularly attractive asset for international companies that have strong R&D capacities but less developed manufacturing capabilities, allowing us to develop comprehensive partnerships encompassing CMO services," highlights Tsai.

In the meantime, OEP's manufacturing and drug development subsidiary, OrientPHARMA, is focused on CNS products, leveraging the company's three unique technology platforms. "I perceive the development of high-quality 505(b)(2) products as the future of our company, as we hold the financial means, the technology platforms, and the manufacturing capacity to efficiently bring such products onto the global market," states Tsai. In terms of new product development, the company is moreover increasingly collaborating with US, EU, and Japan-based companies. "For example, in 2012, we signed an agreement with Japan's NanoCarrier for the development of an anti-pancreatic drug, on which we have been working since its phase I trial," explains Tsai, before adding that OEP currently holds five products undergoing phase III clinical trials overall.

While strategic partnerships will remain absolutely critical to the company's ambitions to climb up the value chain, OEP's second key differentiator relates to its commercial flexibility. "We would for instance be ready to leave to our partner the commercial rights for key markets, including the EU, China, or Japan; the most important aspect to us being to leverage our marketing and sales network in Southeast Asia," concludes Tsai.

Laboratories will be the initial investor in the company; early next year we will also introduce our drug development arm as an investment opportunity for venture capital firms and private investors." The future success of Formosa Pharmaceuticals lies in its ability to distinguish individuals that can indeed perform in an efficient manner. "I am able to assemble people with the right experience, people that have been in this industry long enough; they know how to act in a systematic and prudent way and will not stick to failure for long. Thus, eventually, Formosa Pharmaceuticals will succeed and have a higher success rate than some of the younger companies just starting and learning their way through drug development."

In Taiwan, the easy access to funding through institutional investors and/or stock markets usually avoid drug development companies to set up parallel commercial activities to fuel their R&D ambitions – a development approach that can however reveal itself being rewarding in the long-term. "We have indeed developed three main technology platforms in the areas of regeneration, circulatory disturbance, and anti-inflammation - and accordingly derived a premium portfolio of botanical skin & personal care products, whose rapidly increasing revenues have been nurturing our new drug development ambitions," explains Chih-Yi Weng, chairperson and CEO of the botanical new drug focused Charsire Biotechnology. "This allowed us to remain an independent, privately-owned company, while developing our in-house capacity throughout the entire value chain, from R&D to marketing and sales. More importantly, this commercial footprint now provides us with a direct access to users' feedbacks and a better understanding of their needs – which we can leverage when designing the specificities of our botanical new drugs," she adds.

C.Y. Cheng, chairman & president, Formosa

Nevertheless, one should not think that Taiwan's R&D driven industry is exclusively composed of ex nihilo companies. "Many historical, well-established pharmaceutical companies are leveraging the important resources generated by their generics businesses to bolster new drug development activities, whether as the result of a fundamental strategic shift in these companies' R&D strategies or through the establishment of research-oriented subsidiaries," analyzes PAREXEL's Albert Liou. For some historical players, such as Sinphar, a top ten domestic pharmaceutical group with a footprint in China and North America, R&D ambitions actually go back to the beginning of the millennium. "In 2001, Tim Lee, Sinphar Group's chairman, decided to set up a cutting-edge R&D center comprising nano-technique


Yita Lee, deputy chairman, Sinphar Group; P.H. Huang, chairman and CEO, Johnson Chemical Pharmaceutical Works (JCP)

development, microbiology and molecular biochemistry laboratories, as well as a dedicated R&D-driven subsidiary focused on innovative botanical drugs", explains Yita Lee, deputy chairman of Sinphar. "Leveraging this R&D experience honed with the successful development of innovative botanical drugs, we then moved to the NCE field and set up SynCore Bio in 2008, which now stands as the R&D-driven entity of the Sinphar Group," adds Muh-Hwan Su, chief technology officer of the Sinphar Group and SynCore Bio's general manager, while the latter is now focused on advancing its four drugs currently under clinical development (three in oncology, one in dry AMD). "We want to continue to integrate new projects into our pipeline, whether they would be developed internally, through our historical partnership with the National Healthcare Research Institution (NHRI), or any other licensing agreements," says Yita Lee, while SynCore holds the competitive advantage to be integrated within a well-established pharmaceutical group with international operations. "When it comes to dosage development, CMC, or product manufacturing, SynCore Bio can now fully benefit from the expertise that the Sinphar Group has been accumulating for forty years," confirms Yita Lee.

There is however no obvious route for historical players holding NCE ambitions, and Synphar's decision to directly integrate an R&D-driven subsidiary remains particularly rare to date. "We recently formed a joint-venture company with one of Taiwan's leading oncologists and spearheaded the CMC of a new class II oncology therapy," explains PH Huang, chairman and CEO of JCP, a cornerstone household brand for numerous products in Taiwan's domestic market, most notably with CNS medications, which is now reinventing itself. "We chose this model because if you invest in new drug development as a public company, earnings per share will automatically be diluted, validating spin-offs as a much better alternative. Our JV partner is currently in charge of taking this candidate through phase II clinical studies, some of which will likely take place in the United States, " PH Huang says to illustrate the trial and error approach this five-decade old generic company has been implementing in the oncology segment.

From Promising Spinoff to Global Takeoff

Lee-Cheng Liu, president & CEO, EirGenix

Only four years ago, EirGenix' history started with the acquisition of the pilot plant facility of Taiwan's Development Center for Biotechnology (DCB) and the vision to tackle the country's lack of biomanufacturing capacity. "From 2013 to 2016, our company's revenues have increased 4100 percent," explains Lee-Cheng Liu, president & CEO of EirGenix, while the company has moreover managed to make a name for itself on both domestic and international markets. "Overseas customers already make up around 40 percent of our total revenues and we are now in contact with some Big Pharma companies," reveals Liu.

Far from resting on its laurels, EirGenix is now further expanding its market positioning. "From our CD&M business to the on-going development of our own biosimilars, we aim to become the new hub in Asia for biologic product development and manufacturing," he highlights. This vision translates into a two-fold action plan, whose first arm relates to the set up of the company's commercial-size biomanufacturing plant. "We want to ensure that this very flexible, world-class facility, which will become Taiwan's largest biomanufacturing plant, would be up and running by the third quarter of 2018. Although it will also hold extra capacity for the commercial or late stage production of our partners' products, it will first and foremost focus on manufacturing our upcoming biosimilars", he adds, as EirGenix's most advanced product, EG12014 (trastuzumab biosimilar), is set to complete its phase III trial over the second half of 2019.

Liu indeed expects that CD&M service activities will make up only 30 percent of the company's revenues in ten years. In this regard, forming strategic alliances with ambitious commercial partners is now "EirGenix' second key priority" according to Liu, as he wants to implement a smart portfolio positioning to truly differentiate the company's offering. "For example, we will be able to provide our partners with the combination of both trastuzumab and pertuzumab, which has proven providing greater outcomes than the single use of either of these products", while Liu also considers forming co-development partnerships with some customers to further enriching EirGenix product pipeline, which currently holds seven biosimilars in development.

HISTORICAL (COMPANIES') MOMENTUM

Entering the NCE field only stands as one growth strategy among many others for historical, generics-focused companies that want to overcome the limitations of their domestic market. "Through our distribution arm CYH, we already work with various international companies, including US and Japan-based players, which are eager to leverage the market knowledge of our sales force to launch and build their brands in Taiwan - without having to locally establish their own marketing and sales network," details Derek Wang, chairman of the board of the China Chemical & Pharmaceutical Group (CCPG), one of the leading pharmaceutical groups in Taiwan, which notably encompasses an API branch (CCSB), a generic focused company (CCCP), and then an autonomous distribution platform (CYH), which plays an active role in bringing in more innovative products to Taiwan.

In parallel to in-licensing opportunities, domestic generics companies look at leveraging their utmost drug development expertise and manufacturing capacities to enter new markets. "Taiwan undoubtedly holds a very experienced generics industry that has already reached international standards, including the research and manufacturing capacity required to compete on the global stage," assesses Samuel Wang, honorary president of Taiwan Generic Pharmaceutical Association (TGPA). "JCP's new facility, which will ultimately triple our production capacity within the next two years, will have three focus areas: the first is extending our CNS drug pipeline; the second is targeting diseases related to aging populations, and the last is oncology", explains JCP's chairman and CEO PH Huang, while he overall plans to "leverage these added manufacturing capabilities to increase JCP's international presence and introduce the company's products into more overseas markets."

Samuel Wang, honorary president, Taiwan Generics Pharmaceutical Association (TGPA)

In this regard, the internationalization strategy of generics-focused companies diverges substantially from the global market approach favored by biotech startups, as historical players' emphasis is undoubtedly regional, with the huge but challenging Chinese market in the crosshairs. "We actually entered the Chinese market at a pretty early stage in comparison to many of our competitors, which has allowed us to rapidly raise awareness around the quality of products and the excellence of our manufacturing capacity. In this regard, we have already bounded several promising distribution partnerships in the region with Chinese companies, which helps us to get a better grasp of the local market trends and needs, but also to better tailor our commercial approach to the specificities of this



Derek S. Wang, chairman of the board, CCPG; Kao Su-Chin Chang, chairman, Weidar Pharmaceuticals; Fangchen Lee, chairman, YungShin Global Holding

challenging market," details Kao Su-Chin Chang, founder and chairman of Weidar Chemical and Pharmaceutical. "As a Taiwanese company, we are undoubtedly in a privileged position to increase our market share in China, thanks to our culture and geographical proximity but also to the various regulatory agreements binding Taiwan and China's pharmaceutical sectors, although some of China's regulations still render market penetration more difficult than in other countries," she considers. In terms of new market entry, Weidar also wants "to accompany President Tsai's "New Southbound Policy" and strengthen its business operation in other ASEAN countries," adds Chang, before stressing that direct sales are not Weidar's only tool for increasing international revenues. "CMO activities represent up to 50 percent of our total sales, and ten percent of these activities are already conducted on behalf of international customers. Looking forward, we notably identify a strong interest from Japanese pharmaceutical companies in benefiting from the utmost quality and effectiveness of our manufacturing facility," she adds.

In this vein, industry-wide regional focus does not prevent some of the largest domestic generics companies from holding commercial ambitions in advanced markets. "Over recent years, one of our main objectives has been to increase our presence in the US and Japanese markets, where we have already started to successfully export high-potency drug products," details CCPG's Derek Wang. "We received our first US FDA ANDA in 2014 for an in-house developed osmotic controlled-release oral delivery system for an anti-hypertensive. In the mid term, we want to deepen our collaboration with both our US and Japan-based commercial partners and get more largely involved in the marketing and sales of our products," he adds, before stressing CCPG is also actively looking for acquisition opportunities to strengthening its vertical integration in these strategic markets.

Nevertheless, when it comes to finished dosage forms, being truly competitive in the US market still stands as a particularly challenging endeavor. "None of Taiwan's leading domestic companies currently holds the critical portfolio size needed to be competitive in the US market, while we see that the those Taiwanese generics companies that have developed their marketing and sales network in the US have not yet been able to earn the returns on investment they had expected," analyses CCPG's Wang. "I have had the chance to meet with the heads of other leading domestic pharmaceutical groups to discuss a potential collaboration and jointly enter the US market. So far, we have however not been able to design a strategy that would be fully satisfactory to everyone," he reveals, while Fangchen Lee, chairman of YungShin Global Holding, another leading pharmaceutical group of companies in Taiwan, states that "if Taiwan's government could allocate just a share of the tremendous resources exclusively invested in our biotech industry to bring our domestic generics companies together, our country would have greater chances to give birth to a real pharma success-story within the next decade".

Is Taiwan's government too focused on nurturing the growth of biotech startups, to the detriment of historical, generics players? "Actually, this has been a recurring issue, as - even under the administration of former President Ma Ying-jeou - the government has directed the majority of their attention to pharmaceutical companies focused on innovative drug

The Right Mindset for a Win-Win Relationship

Mike Exton, managing director & country president, Novartis

"Without any doubt, international pharmaceutical companies can greatly enhance Taiwan's innovative eco-system through a variety of different partnerships that go beyond our companies' own products", states Mike Exton, managing director & country president of Novartis Taiwan. "Nevertheless, our industry's game changing commitment to Taiwan is also subject to some crucial conditions, which notably encompass the strengthening of satisfactory access to innovative medicines, mostly by displaying greater speed and transparency throughout NHIA's reimbursement process," he adds, while total healthcare spending in Taiwan in 2016 only amounts to 6.6 percent of GDP, which is particularly low, even by Asian standards.

"In a local context moreover marked by a rapidly aging society, perpetuating Taiwan's tremendous successes in providing its population with universal health coverage will require either increasing NHI funding through new taxes or increasing co-payments. Nevertheless, both options seem politically unpalatable," Exton adds, which prompts him to call for a true mindset change, as the current reimbursement process does not really allow innovators to prove the heightened cost-effectiveness generated by their treatments. "The NHIA's annual budget being fixed, a few

Po-Chang Lee, director general, National Health Insurance Administration (NHIA)

members of the [reimbursement committees] may sometimes be hesitant to include new, innovative drugs or technologies within NHI's reimbursement lists due to their substantial financial impact," acknowledges Lee Po-Chang, a transplant surgeon by training who became the first healthcare practitioner to head the National Health Insurance Administration (NHIA). "Through my 37 years of practice, I know how much difference it makes for patients to be able to access needed treatments", stresses Lee. "In this regard, I considered a relative mindset change was also needed and partially reshuffled these committees, bringing on board new experts and healthcare practitioners to add another perspective to our approval process," he adds.

"On the other hand, innovative pharmaceutical companies need to acknowledge that the NHIA does not hold unlimited financial resources and our focus should be on showcasing the value that our treatments can bring to Taiwan", complements Exton, "while the industry and the government need to continue working together to provide Taiwanese patients with better health outcomes. In this regard, we have to praise the openness of the new government to jointly discussing the changes we need to implement," he concludes.

development," regrets JCP's Huang. "From a practical standpoint, increasing funding to the generics sector would subsequently increase R&D, notably for the development of new dosages and combinations, and, in turn, production output, while ultimately augmenting revenue streams to Taiwan," he continues, before adding that "compared to her predecessor, President Tsai Ing-wen has however been more receptive of generics players' concerns and has begun undertaking new initiatives that favor the domestic, generics industry. In this vein, TGPA's Samuel Wang highlights that "according to the numerous meetings our association already held with key members of President Tsai's government and administration, I am particularly confident generics companies will receive more support to develop our industry's capacity with regards to new formulations and new drug delivery systems".

In this regard, the current government seems to favor a collaborative approach between emerging biotech companies and historical manufacturers, be it through contract manufacturing partnerships, joint investments or joint ventures. "The overall expertise and capabilities of our manufacturing companies are absolutely world-class, and a great share of them already hold GMP, US FDA, EU EMA, or Japan CPMDA approved facilities – even for the manufacturing of complex products such as injectables. After the full implementation of the PIC/S GMP in 2015, we now want to help these manufacturers to further upgrade and develop their capabilities, in order to ensure they can become the manufacturing partner of choice of our biotech companies but also bolster their regional and international expansion," reveals Minister Wu.

THE DAWN OF A WORLD-CLASS ECOSYSTEM

As satisfactory as this collaborative approach may sound to the ears of generics players, it however perfectly illustrates the broader industry vision that the government strives to implement. "We want to accelerate the development of a comprehensive innovation ecosystem to sharpen the global competitiveness of our local companies, by strengthening the integration of our different innovation clusters and bolster the improvement of this industry's value chain," highlights Minister Wu. This objective notably targets the country's world-class biomedical located in Nangang [in the Taipei area, mostly focused on new drug development, e.d.], Hsinchu [commonly referred to as Taiwan's Silicon Valley, e.d.] and in Central and Southern Taiwan, which form the country's "biotech corridor". "Hsinchu Science Park was the first in Taiwan to establish a cluster exclusively

Chuan-Der Huang, president & CEO, Krisan Biotech

dedicated to the life sciences industry, and the cumulated revenues generated by the companies established in our Biomedical Science Park increased by 140 percent from 2015 to 2016," explains its director general, Wayne Wang, while a new 12-storey building is about to see the light, ready to welcome new pharmaceutical, biotech, and medtech companies. Furthermore, as Hsinchu already stands as the heart of Taiwan's ICT industry, the further development of this biotech and biomedical cluster could foster an extremely promising interplay between these two pioneering industries, while cross-sector investments, research projects, and other partnerships could truly propel the development of Taiwan's "bio-ICT" sector, following the global convergence trend happening between the pharmaceutical and medtech sectors.

"Nevertheless, to the contrary of other advanced biotech eco-systems around the world, Taiwan still lacks of comprehensive, fully-fletched hubs, gathering within a close perimeter the entire biotech value chain, from emerging drug development companies to world-class service providers and cutting-edge medical and research capacities," considers Chuan-Der Huang, president & CEO of KriSan Biotech, a recently established service provider focused on new drug process and analytical R&D for small molecules and peptides from Preclinical (IND) to Phase II clinical trial. "As a result, these well-funded, publicly-traded biotech companies still struggle to find service providers aligned with their own standards, highlighting that besides the undeniable quality of our biotech companies, Taiwan's innovation value chain still needs to be substantially strengthened," he explains. "If Taiwan holds at least five API-focused companies; most of them are concentrating their efforts on large-scale API production," hence creating substantial market opportunities for local, specialized service providers in this field, which can leverage Taiwan's market needs to foster their own international development. "Only a few months after we started our operations, we are already working with 16 different customers, including two US and EU based companies, which truly proves that our unique positioning – combining Asian cost-efficiency with Western know-how – can also be extremely appealing on the international stage," explains KriSan's Chuan-Der Huang.

In the meantime, biotech companies' focus on partnering with the best service providers globally sharpens the opportunity for the latter to establish a local footprint and benefit from the growing partnership opportunities that the

Taiwanese ecosystem holds. "At the moment, our interactions with Taiwan's innovative companies are still emerging, but they will undeniably gain in intensity as the local R&D-driven industry continues to climb up the innovation chain and look at developing more and more innovative treatments in oncology," predicts Guo-Liang Yu, the executive chairman of the efficacy testing focused Crown Bioscience International. "In this regard, Crown can contribute to bringing international expertise and make the local industry benefit from our pioneering technologies and PDX models – this is exactly why we decided to set up an affiliate in Taiwan! If any company in Taiwan is developing innovative oncology drugs based on novel mechanisms of action, we can help them identify for which specific gene mutations and patients their compound will be the most efficient," he stresses.

The Taiwanese government's ambition to attract more international talents and companies to undertake innovation-oriented projects in the country is palpable in this aspect, with the idea of building Taiwan's reputation as a world leader in some specific areas and become the partner of choice of international companies for their global R&D projects. "Attracting international investments is a global competition and we need to continuously sharpen our competitive advantages, which means further harmonizing our regulations, better positioning our country's offering vis-à-vis international healthcare demand, and generating new market opportunities for international companies," recognizes Minister Wu.

In the meantime, there is a crucial need to develop Taiwan's open innovation culture, as such a collaborative approach encompassing both academia and the industry hasn't yet been embedded deep enough in the roots of the local ecosystem. "Taiwan undeniably holds world-class research and cutting-edge innovation capacities, while our biopharmaceutical eco-system has been accumulating a sheer amount of expertise over the past decade. Nevertheless, the impact of these twenty years of intensive R&D efforts could be further enhanced if local research institutions and international companies were partnering more comprehensively and at an earlier stage of the drug development process," explains Carol Cheng, COO of TRPMA, which just released bioIPSeeds, a groundbreaking, utterly safe digital platform based on the blockchain technology that aims to foster a greater collaboration between Taiwan's individual researchers and research institutes and the global industry (biopharmaceutical, medical devices, and all healthcare-related companies as well as venture capital companies).

In the country's ambition to truly play in the big league, Taiwan's last room for improvement probably relates to fostering greater consolidation among the local industry. "Our industry's next stage will be to expand more into the international arena and gain the critical size needed to truly fulfill our global ambitions. In this regard, one strategy that government and industry have been considering is to trigger a phase of mergers and acquisitions - to make smaller companies bigger and help them merge with international companies," highlights Taiwan Bio's Johnsee Lee. As a matter of fact, the government is currently revising the Business Merger and Acquisition Act, and in July 2016, a public-private fund worth NTD100 billion (around USD 3.15 billion) was set up to support M&A activities, notably in the life sciences field. "In the grand scheme of things, I am confident Taiwan's biotech and pharmaceutical ecosystem will further strengthen its regional leadership and global attractiveness over the upcoming years, while Taiwan-based success stories in the most advanced markets globally will continue to accumulate," concludes Johnsee Lee.

Health Supplement Innovation, Drug Development Exigency

George J. Lee, chairman, SunWay Biotech

Tzu-Ming Pan, vice chairman and chief technology and science officer, SunWay Biotech

It is particularly rare for a health food-focused company to release more than 120 scientific publications and conduct two clinical trials to test the safety and efficacy of its product. Why did Sunway Biotech do so?

• Tzu-Ming Pan: As the result of more than ten years of tremendous research efforts, we have indeed developed a red yeast extract that is free of all statins, while all products available contain monacolin K, whose long-term consumption may cause cumulative side effects such as liver damage, rhabdomyolysis, and acute kidney diseases.

• George Lee: Our product's combination of two new active compounds, monascin (MS) and ankaflavin (AK), moreover received US FDA's New Dietary Ingredient (NDI) status in January 2015. As we are now bringing our product onto all international markets (EU, South America, Japan, and China) and want to increase our market share in the US, this science-based, evidence-backed product development approach stands as a great differentiator.

Furthermore, in the long term, our R&D focus will be on leveraging the therapeutic effects of the combination of MS and AK beyond the health food area. As our combination displays similar efficacy to statin-based products without generating these products' side effects, I have no doubt that pharmaceutical companies would be interested in jointly developing it as a pharmaceutical product.

Tips for Success from a Big Pharma Leader

An honoree at last month's HBA's Women of the Year awards luncheon, Bahija Jallal's story is one of courage and resilience

Inspiring and passionate.

Those were the two most common ways Bahija Jallal, executive vice president of AstraZeneca and head of MedImmune, was described by her colleagues, employees, and friends during the Healthcare Businesswomen's Association's Women of the Year awards last month in New York City.

"She is smart and hard-working," said Pascal Soriot, executive director and CEO of AstraZeneca. "Bahija is a true citizen of the world. She came to the US to change the world."

Jallal, who grew up in Morocco, studied in Paris, worked in Germany and then in the US, was honored as the 2017 HBA Woman of the Year during a luncheon that drew 2,200 in-person attendees and many more watching via live feed at more than a dozen viewing parties across the world. We chronicled Jallal's career journey for our April issue cover story.

"Bahija is courageous and resilient," said Soriot, before inviting Jallal to the stage. "She fights for what she believes in."

Soriot went on to relay examples of how Jallal did this, noting that when AstraZeneca brought MedImmune into its portfolio in 2007, the translational sciences leader was faced with harsh critics, but she never let them get the best of her.


Bahija Jallal

Many times Jallal was faced with people calling MedImmune a "money drain," and as a result she would "put her job on the line many times," Soriot added.

And every time, Jallal would prevail.

Success rooted in humility

"In my heart of hearts, I am a scientist," Jallal told the ballroom filled with seasoned pharma executives as well as those aspiring to become the healthcare leaders of the future. "It has been an incredible journey of curiosity. Every answer leads to a new question.

"My dream was to figure out the answers to all my questions. I always followed my heart in my career decisions. I've never done a development plan or chased titles."

Those questions, as Jallal told *Pharm Exec* for the April cover story, started when she was nine years old and her father went to a clinic in pain with a suspected kidney stone and never came home.

She shared several tips that have helped guide her success. First, don't be afraid to fail.

"If you don't fail, it means you're not pushing innovation and science far enough," said Jallal. "And, when you do [fail], be resilient. Dust yourself off, figure out what went wrong, and try again."

Second, dream big.

"We can turn science fiction into science fact," she said.

Third, get back to your roots.

"Remember, amidst all the ups and downs, and highs and lows, why we come to work every day," said Jallal. "I followed science and followed my heart. Do not apologize for being smart, or following your passion."

Her last bit of advice centered around what she likes to call the, "what will people think of me" syndrome.

"All too often we get stopped in our tracks in search of perfection," she said. "By [doing this], we hold ourselves back. We don't have to be perfect. No one is perfect."

Unfinished business

Despite all of her accomplishments, Jallal said there is a lot more work to do. She explained that science has never been better when it comes to innovation and breakthroughs. "But too many patients still suffer from cancer, diabetes, asthma, and other diseases," she added.

Other winners

In all, more than 30 women were honored as 2017 HBA Luminaries, and more than 60 were named 2017 HBA Rising Stars.

In addition, Joaquin Duato, worldwide chairman, pharmaceuticals, at Johnson & Johnson, received the Honorable Mentor award, and Ceci Zak, principal and COO of Batten & Co (a strategic consulting firm within the Omnicom Group) received the STAR award. PE

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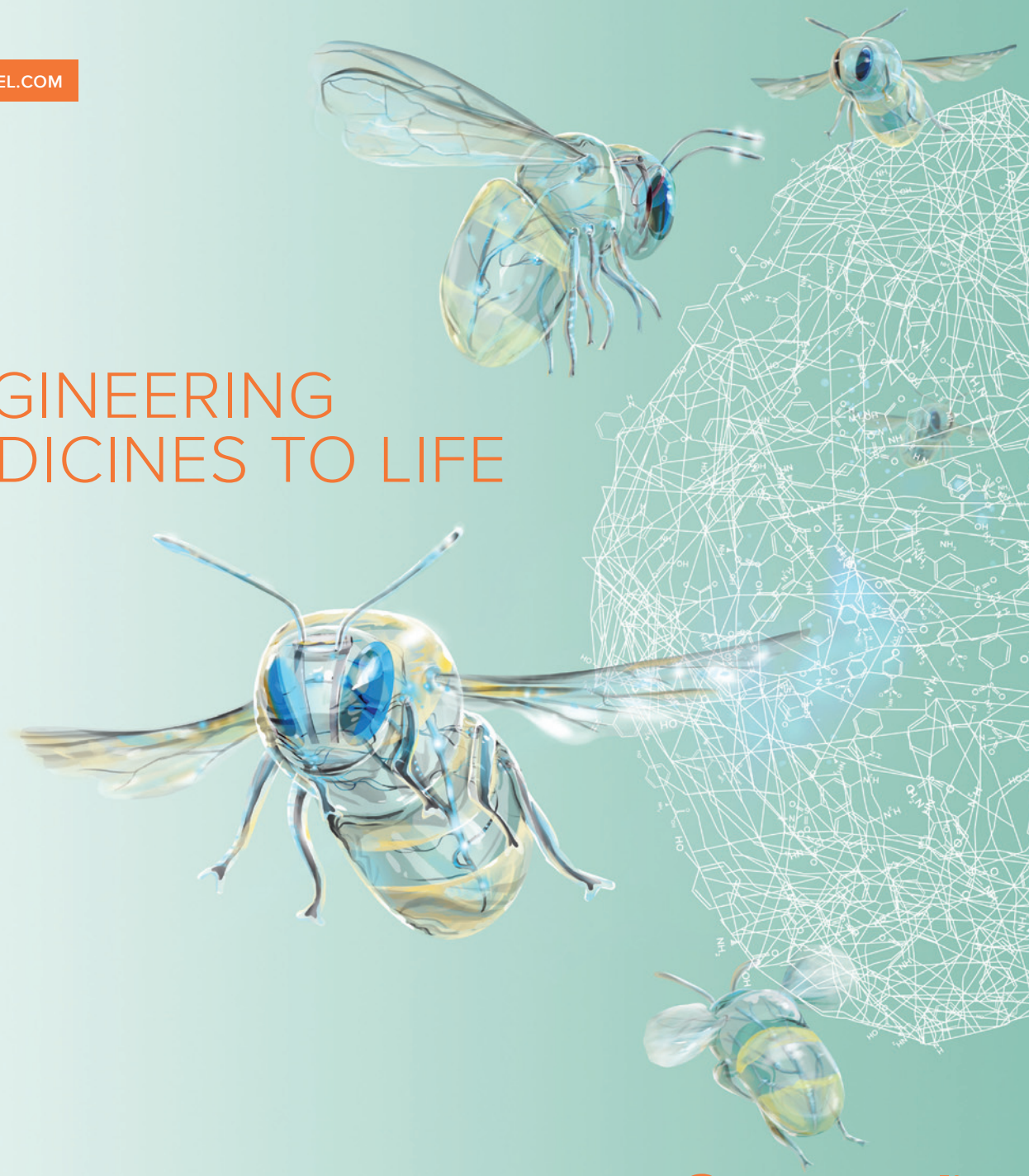

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