2018 OUTLOOK
8 TRENDS TO WATCH

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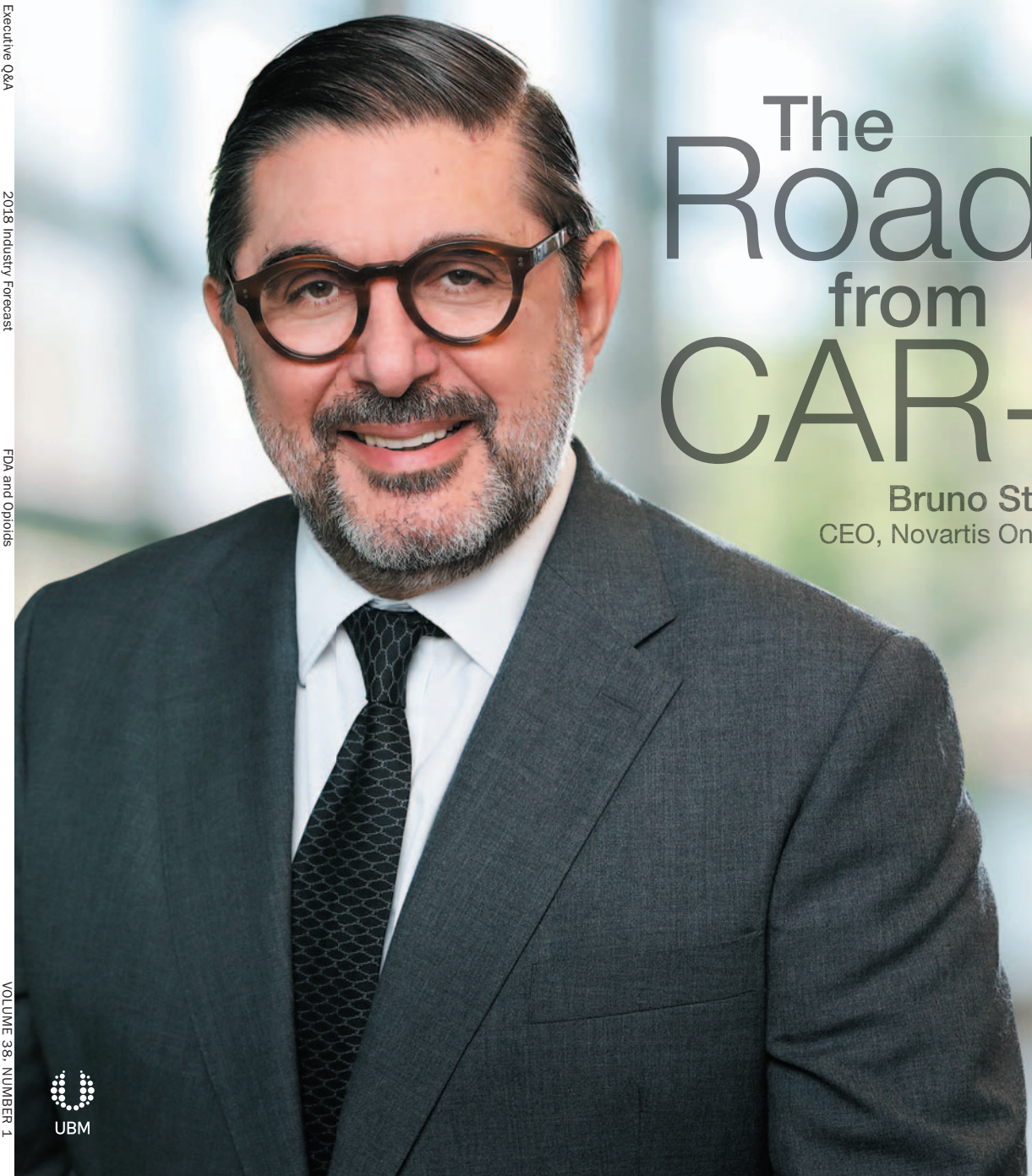

The Road from CAR-T

Bruno Strigini
CEO, Novartis Oncology

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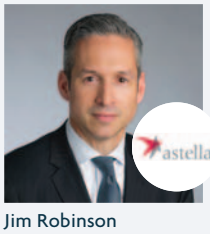

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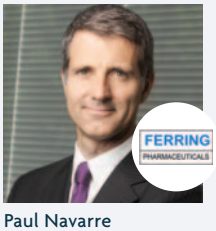

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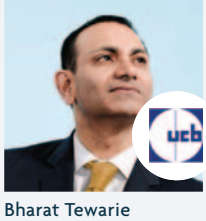

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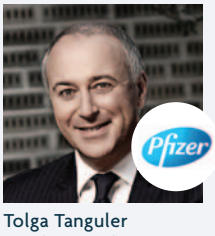

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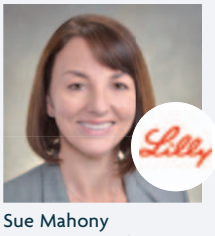

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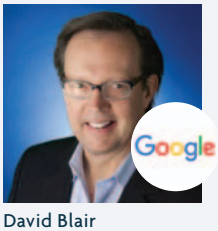

David Blair
Head of Industry
Google

See the full agenda at eyeforpharma.com/philadelphia

CAR-T Concerns for Continued Success

FOR 2018 TRENDS, BOTH EDITORIAL ADVISORY BOARDS (*Pharmaceutical Executive* and *Applied Clinical Trials*) named CAR-T and gene therapy. Ultimately, we chose eight trends to explore in this year's industry outlook, and CAR-T was not on that list. We felt that 2018 is only the beginning of CAR-T therapy development, and the challenges around that will exist for a few years. Those challenges include clinical trials, pricing, and market acceptance. To provide first-hand insight, we were fortunate to have our editorial partner PharmaBoardroom interview Bruno Strigini, the departing CEO of Novartis Oncology, in October. That interview (see page 8) describes the path to bringing the first FDA-approved immunocellular therapy with Kymriah, for B-cell precursor ALL, to market.

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As noted in the annual pipeline report in November, both Kymriah and Kite's Yescarta for NHL were approved by the FDA in 2017. But also that CAR-T is a powerful and risky therapy and drug companies are responding to some of the more worrisome side effects. The FDA recently approved Genentech's tocilizumab (Actemra) to treat severe cytokine release syndrome (CRS), a potentially deadly side effect to CAR-T therapies.

In fact, as Aaron Mitchell, a managing principal at ZS Associates, noted in an email to me, CRS is "the most common adverse event patients are facing in the trials, with 81% of patients in Novartis studies B2202 and B2205J experiencing some form of CRS, with about 45% experiencing Grade 3 or 4." Mitchell said that CRS symptoms can be quite severe and extensive, especially in patients with a high tumor burden. He added that to prevent and manage CRS in CAR-T patients, "companies have implemented rigorous CRS management protocols. For example, Novartis worked with the University of Pennsylvania on its algorithm, which includes multiple lines of treatment to resolve CRS once it appears."

Clinical trial challenges

Because clinical trials are designed to test a completely new treatment paradigm (genetically modified autologous immunocellular therapy), it is significantly different from typical pharmaceutical therapies. For that reason, Mitchell says that many of the standard processes around currently established manufacturing, fulfillment, and treatment have been redesigned to support CAR-T development.

Mitchell said, "The manufacturing process itself is quite complicated in that you are dealing with a highly variable input from each patient and you need to develop a consistent final product. This makes developing a reproducible manufacturing process quite difficult. For Novartis, they have made significant investment in a single site in Morris Plains, NJ, for nearly all their patients in pivotal trials."

Pricing and acceptance

Strigini says in his interview that Novartis put a lot of thought into pricing Kymriah, using standard of care pricing of a bone marrow transplant, as well as independent evaluations, including those from NICE. Kymriah is priced at $475,000 for a one-time treatment, and Novartis is offering value-based pricing, whereby insurers will only pay for patients who go into remission within three months of receiving the therapy. Yescarta is priced at $373,000, offers financial help for patients, but does not offer a value-based pricing scheme.

In December, Cardinal Health released the results of a survey of 200 oncologists conducted to "better understand their perceptions about CAR-T and the potential barriers to adoption (view here: http://bit.ly/2Bh6li2)." The results found that the top three barriers to prescribing CAR-T cell therapy were as follows: logistics of administering and following patients are cumbersome (59%); cost of therapy (44%); and toxicity is too high (35%).

Since CAR-T cell therapies must be administered in the hospital or at an accredited center, gaining community oncologist support is crucial, as illustrated in the Cardinal report, which noted that 31% of oncologists were referring AML patients to academic centers for treatment.

ICON addressed these concerns in an article that appeared in December and provides a list of key factors to help ensure market access. These include continuing to follow patients after the trial closes; engage treatment centers early in the process; develop and share data on the burden of disease; and more.

As these new therapies enter the "traditional" world of pharma, trials, pricing, and acceptance will evolve with time and experience. As Mitchell noted: "Over time, further standardization will happen, allowing these trials to happen more quickly and efficiently and at a global scale. In the meantime, strong partnerships between sponsors, sites/investigators, and regulators is needed to support these trials as well as develop the necessary processes and capabilities."

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Onward in Oncology: From Gleevec to CAR-T

By PharmaBoardroom

Pharm Exec partner PharmaBoardroom speaks with Bruno Strigini, CEO of Novartis Oncology, about the company's pioneering path in cancer—starting with Gleevec and continuing with last year's approval of the first-ever chimeric antigen receptor T-cell (CAR-T) therapy—touching as well on broader industry issues such as pricing and value and the reasons why Strigini believes we are entering a golden age of innovation in cancer science.

8

2018 Industry Forecast

Changing Skies: 8 Trends to Watch

In *Pharm Exec*'s annual temperature check on the life sciences sector and its outlook for the months ahead, we explore eight trends that will shape the biopharma industry landscape in 2018, with input from our Editorial Advisory Board and Washington and Europe correspondents.

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From the Editor

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Country Report: Switzerland

Three pivotal developments that occurred in 2017 illustrate the growing relevance and influence of the Swiss pharmaceutical and life sciences industry on the world stage. Companies in Switzerland are also playing innovative roles in reshaping the pharma value chain and contemporary paradigm of healthcare provision.

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Prices and Competition to Shape the Year Ahead

States will continue to press for price controls, while FDA will tackle opioids and press for innovation

The pharmaceutical industry faces a tumultuous year in Washington, as policymakers continue to press for curbs on too-high drug prices, and tax and budget reforms may threaten resources and initiatives for the FDA, the National Institutes of Health, and public health programs. Inaction by Congress and the White House will prompt more states to propose price transparency and negotiating strategies (see sidebar on facing page), measures that industry fears will dampen investment in innovative research. Federal agencies will strive to rein in the deadly opioid epidemic, in the process generating more investigations and lawsuits citing manufacturers. These issues will shape the November mid-term Congressional elections, which already are heating up as Republicans seek to maintain control of the House and Senate amid continuing debate over government funding for healthcare and drug regulatory policies.

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Coverage and controls

Efforts to scale back the Affordable Care Act (ACA) and state Medicaid and children's health programs will further limit drug coverage and reimbursement. Pharma companies backed the ACA and agreed to pay millions in taxes to expand pharmacy benefits. Now higher out-of-pocket costs for consumers will squeeze drug utilization and ignite further efforts to rein in pharma prices. The Centers for Medicare and Medicaid Services (CMS) recently revised Medicare Part B drug reimbursement policies and has proposed measures to facilitate Medicare coverage of biosimilars and generic drugs. CMS also has floated a proposal for Part D drug plans to share with patients the rebates and discounts negotiated with manufacturers and pharmacy benefit managers (PBMs). A battle over 340B drug discounts pits pharma against certain hospitals, while the push for more transparency in drug prices and discounts could erode revenues for PBMs and further escalate the finger-pointing by manufacturers, insurers, and PBMs over who's most to blame for costly medicines.

These trends will heighten interest in value-based pricing strategies that link drug coverage to patient response to treatment. CMS and insurers also eye arrangements to spread reimbursement over several years for one-time breakthrough therapies. Sponsors will need credible data to convince the Institute for Clinical and Economic Review (ICER) and other third-party analysts that the benefits of a new medicine justify costs.

Innovation and competition

These financial and regulatory pressures will spur pharma companies to seek new partnership and investment arrangements to support the R&D needed to maintain robust development pipelines, particularly involving gene editing and other "disruptive" technologies. The proposed CVS Health purchase of Aetna signals major changes ahead for drug distribution, coverage, and industry organization.

US patent policy and market exclusivity provisions similarly are crucial for maintaining an inviting climate for biotech investment, but current protections face challenges from evidence of innovator firms using patents to block competition. Patent battles are keeping most new biosimilars from the market, and a move to extend protections by transferring patents to a Native American tribe has generated a strong backlash. These actions fuel questions about over-extended exclusivities for new therapies, as seen in Republican efforts to curb the orphan drug tax credit and challenges to FDA priority review vouchers. The Supreme Court will weigh related issues as it considers an important case this year that could revise the current US Patent Office process for reviewing patent challenges.

While FDA generally avoids involvement in pricing issues, Commissioner Scott Gottlieb looks to enhance consumer access to medicines through greater market competition. His main strategy is to speed the development and approval of biosimilars and generic drugs, particularly complex therapies and combination products and drugs in classes dominated by one or two brands. Gottlieb also wants to prevent brands from blocking generics makers from obtaining supplies needed for bioequivalence testing and other tactics to delay market entry.

More pharma competition also derives from more efficient new drug development and timely FDA review and approval of new medicines, especially promising gene and cellular cures. The agency will continue to implement the 21st Century Cures Act and reauthorized user fee programs to encourage more streamlined clinical research, wider use of digital technology, flexibility on evidence standards, and updated information systems.

Combating opioids

Perhaps the top priority for the nation's healthcare system is to halt the deadly opioid epidemic, which is taking thousands of lives and driving up costs on every level. The challenge for health authorities is to ensure access to treatment for patients suffering from pain, while also curbing excessive prescribing and distribution of drugs subject to abuse and misuse. Congress and the White House have rolled out policies and plans to limit opioid use, while looking to expand treatment for addicts and access to opioid overdose rescue drugs, but limited funding may undermine such efforts.

FDA has increased its direct involvement in tackling opioid abuse by encouraging research on new non-opioid pain therapies and more effective medicines to prevent and treat addiction. It also seeks to facilitate development of low-cost generic abuse deterrent formulations (ADFs) and overdose treatments and to devise more secure packaging and distribution strategies for pain medicines.

Meanwhile, federal and state prosecutors are ramping up criminal investigations and lawsuits against opioid producers for deceptive marketing and promotional practices alleged to spur inappropriate opioid prescribing. While settlements are likely for many of these suits, industry's role in fomenting this deadly wave of drug abuse will undermine its stature for promoting public health through biomedical discovery.

US patent policy and market exclusivity provisions are crucial for maintaining an inviting climate for biotech investment, but current protections face challenges from evidence of innovator firms using patents to block competition

On the international front, FDA is collaborating with other regulatory authorities to combat the import of falsified/substandard medicines, including dangerous pain remedies. The expansion of drug sourcing and production overseas and continued disease outbreaks around the world will raise a range of global regulatory issues. International harmonization of regulatory standards and mutual recognition agreements will advance as authorities look for efficiencies in ensuring drug quality, in managing product lifecycles, and in blocking illegal product trafficking. Brexit will bring further changes to drug oversight and marketing, as the European Medicines Agency moves to Amsterdam. PE

States step up

Months of inaction in Washington on drug and healthcare pricing and payment issues will continue to spur reform proposals in state capitals. California has led the trend with legislation requiring pre-notification of upcoming launch prices and subsequent increases. Maryland enacted a bill to prevent "price gouging" on older generic drugs, while a new policy in Nevada requires price disclosures for diabetes drugs. New York has authorized limits on what its Medicaid program will pay for drugs, and Massachusetts is setting a new trend by seeking authority from the Centers for Medicare and Medicaid Services (CMS) for its state Medicaid program to negotiate discounts on covered drugs, based on a more select drug formulary. Arizona recently requested a similar change, and others will follow.

Several states seek additional curbs on sales reps and expanded reporting requirements and bans on payments and gifts to prescribers, complicating the federal Open Payments program. Most states have enacted "right-to-try" laws that support early access by patients to experimental treatments. State legislatures will consider a host of similar measures in the coming months, further challenging FDA authority and undermining industry efforts to achieve uniform national disclosure and reporting policies.

Bruno Strigini, CEO, Novartis Oncology

From Gleevec to CAR-T

The head of Novartis Oncology talks tradition, new launches, pricing and value—and what he believes is the start of a golden age of innovation in cancer science

Pharm Exec partner PharmaBoardroom, whose "Country Report" series is regularly featured in these pages, spoke recently with Bruno Strigini, CEO of Novartis Oncology. They discussed the drug giant's latest efforts and successes in fighting a disease that remains on the rise globally, and touched on the broader trends and innovation that are propelling new hopes in cancer care.

Please note that this interview was conducted in October 2017. Strigini has subsequently announced that he will retire from Novartis Oncology in early 2018. During his time at the company, Strigini led the integration of GlaxoSmithKline's oncology programs acquired in 2015, navigated Novartis through its Gleevec patent expiration a year later, and, in 2017, helped the organization gain the first regulatory approval of a chimeric antigen receptor T-cell (CAR-T) therapy.

PB: *Novartis is notable for being the first of the big pharma firms to assemble a global business unit dedicated solely to developing and launching innovative oncology medicines. Why was it deemed necessary to adopt this sort of corporate structure of a "firm within a firm?" What advantages does it bring?*

STRIGINI: Novartis' first great foray into oncology dates back to 2001 with the launch of Gleevec, which was a truly revolutionary cancer drug and formed part of a pioneering group of targeted treatments designed to attack a specific cancer-causing genetic mutation. With the advent of Gleevec, the outlook for CML (chronic myeloid leukemia)

patients changed dramatically, and it is great to hear from patients who have the prospect of a normal life 15 years after starting the treatment.

Another critical juncture came in 2015 when we acquired GSK's oncology business, comprising important products such as Revolade, Votrient, Tafinlar, and Mekinist, as part of a broader portfolio swap between the two companies.

Our organizational structure, which right from the beginning was set up as a dedicated business unit focused on treatments for cancer, was key to our success. This organizational set-up underscores Novartis' unwavering commitment to pioneering new generations of oncology therapies, and it also provides a real sense of purpose and focus. The overarching idea was to create a nimble outfit, with speedy decision-making power to accelerate the development and commercialization of our products. One of the aspects that has impressed me the most since I joined Novartis has been the sense of purpose of our associates, and I believe that arises partly from having an organization fully focused on oncology. This is a *modus operandi* that works, and that's why we're now seeing our competitors trying to emulate us in this respect.

Looking at our productivity in 2017 alone, which includes three new therapy approvals, it is clear that the model we established makes good sense. We launched Rydapt in the US and Europe for two rare, life-threatening indications, including a mutated form of acute myeloid leukemia. Also, [last year] we achieved both US and European approval of Kisqali for treatment of postmenopausal women with locally advanced or metastatic breast cancer. Finally, in late summer we were the first company to receive approval for our breakthrough CAR-T cell therapy, Kymriah.

The overarching idea was to create a nimble outfit, with speedy decision-making power to accelerate the development and commercialization of our products

PB: *How, then, is the unit structured? What are the key functions and areas of priority?*

STRIGINI: Novartis Oncology is a global leader in the oncology, hematology, and rare cancer segment, with an unmatched portfolio of products, including more than 20 approved medicines. We also have one of the broadest pipelines in the industry, with over 40 or so new molecular entities in development, including targeted and immuno-oncology compounds.

Our research is driven by a distinctive scientific and clinical strategy, focusing on unmet medical needs. Having initially established ourselves as one of the foremost companies in the development of small molecules against cancer, we have now additionally assembled one of the largest pipelines in immunotherapy, with 18 different compounds. In addition, we are pioneers in CAR-T cell therapies, a new class of immunocellular therapies.

Strategically, we have prioritized five therapeutic areas: breast, blood, and lung cancer as well as melanoma and renal cell carcinoma. This does not mean we are not doing anything in other areas, for example, our R&D groups are active in colon and bladder cancer, but it does help us retain focus in areas where we have depth and breadth of experience. In a highly competitive environment where 40% of the industry's investment is in oncology drug development, we must keep to our core strengths.

In terms of our scope and reach, there are more than 10,000 associates fully dedicated to oncology spread across 85 countries, including eight R&D centers. With this level of experience, knowledge, and investment behind us, we find ourselves equipped and ready to transform cancer care by bringing more breakthrough products to patients and society.

PB: *Tell us about the significance of the CAR-T milestone with Kymriah and how it relates to the positioning of Novartis' oncology business today?*

STRIGINI: We were very proud indeed to see Kymriah, the first immunocellular therapy approved in the US for the treatment of children and young adults up to 25 years of age with B-cell precursor acute lymphoblastic leukemia that is refractory or in second or later relapse. This is a truly game-changing and revolutionary product that responds to an unmet need that is clearly established. Trial results have demonstrated a high level overall remission rate in this patient population with limited treatment options and historically poor outcomes.

The CAR-T journey started five years ago when we began collaborating with the University of


Aerial view of Novartis' Basel, Switzerland, campus

Pennsylvania and invested in bringing—what we believed would be—a paradigm-changing therapy to cancer patients in dire need. Basically, it is a highly personalized therapy in which T cells are drawn from a patient's blood and reprogrammed in our cell processing facility. These genetically coded T cells are infused back into the patient to potentially "hunt" the patient's cancer cells. This represents an entirely new approach for treatment. Our hope is now to be able to progress this "new wave" of CAR-T therapies in a host of hematologic and potentially other cancer types.

Overall, our R&D portfolio is made up of two core segments: "targeted therapy," including our small molecule technology and monoclonal antibodies; and "immunotherapy," comprising our immuno-oncology pipeline. As CAR-T is an immunocellular therapy, it fits perfectly into our overall strategy to attack cancer in a modality-agnostic way.

PB: *Kisqali was approved in Europe one week prior to Kymriah. What were the comparative experiences of the market access teams for the EU and US with regards to these two scientific advances in oncology?*

STRIGINI: The strategies for getting these two different therapies to market had to be thoroughly different. Kymriah needs to be administered in specialized treatment centers and is an individualized approach to modifying a patient's own cells to fight cancer that brings all sorts of additional complexities in terms of manufacturing, handling, and logistics. To address the unique aspects of the therapy, we had to go and develop custom-made patient access programs to support safe and timely delivery. Kisqali, on the other hand, is about a classic small molecule, and our focus was and is to differentiate our offering from competition.

The dynamics of the two markets are also very different. In the US, the market is a mix of private insurance providers, Medicare, and Medicaid. In Europe, you are largely talking about healthcare systems with universal coverage and country-by-country access and pricing negotiations. Our approach in all instances, however, is consistent—and that is to emphasize the principles of value and outcome of our medicines.

PB: *Kymriah comes in at a hefty price tag at $475,000, putting it as one of the most expensive drugs of all time. How did Novartis come to this figure and go about its pricing strategy, especially considering the current cost-cutting climate and potential political and reputational ramifications?*

STRIGINI: We put a great deal of thought into how to price Kymriah. We conducted our own detailed health economics analysis, looked into standard-of-care pricing such as bone marrow transplant, and took into account independent evaluations such as those of NICE (National Institute for Health and Care Excellence), which estimated a cost-effective price of between $600,000 and $700,000.

Let's not forget either, that Kymriah is delivered to each patient just once because this is intended to be a one-time, highly effective treatment. When considering this altogether, the value of what we are proposing becomes more readily apparent.

Importantly, we have also announced a collaboration with the US Centers for Medicare and Medicaid Services (CMS), which represents a first-of-a-kind arrangement in the US. This includes an outcome-based approach and indication-based pricing.

PB: *How do you reply to those who argue that the extent of current public expenditure on oncology drugs is disproportionately high and does not necessarily represent optimum value for money spent vis-à-vis competing claims (such as for antibiotics)?*

STRIGINI: Cancer is clearly on the rise. Right now, cancer causes one in eight deaths globally and, in Europe, it is even outpacing cardiovascular disease in terms of prevalence. The World Health Organization (WHO) is now estimating that global cancer rates will be close to 22 million new cases per annum by 2030.

A recent study involving the EU's five biggest markets demonstrated that cancer affects mostly people in their prime in terms of ability to be productive. The societal cost to those five countries was estimated at €50 billion just in terms of lost productivity.

At the same time, science and medicine are progressing very rapidly, and cancer treatments

are becoming more effective. This allows for the right drug to be employed at the right time for the right patient.

Clearly, industry and the rest of the life sciences community have to work alongside healthcare providers, payers, and policymakers in rendering cutting-edge oncology drugs accessible and affordable to all patients. We believe an outcomes and value-based approach will help in achieving this objective.

PB: *What steps, then, are you taking to make pioneering oncology drugs more accessible to patients in lower-income countries?*

STRIGINI: We have different programs to facilitate access to our cancer drugs. One that I would like to highlight is our collaboration with the Max Foundation, a global, patient-focused, non-governmental organization. In September, Novartis announced a new collaboration with the Max Foundation to support continued access to treatment at no cost for nearly 34,000 current patients with CML, gastrointestinal tumors, and other rare cancers.

We have been longtime collaborators in providing access to care for patients in lower-income countries through the Gleevec International Patient Assistance Program (GIPAP), one of the most innovative patient assistance programs ever implemented on a global scale. The new collaboration, called CML Path to Care, is an evolution from GIPAP. Under the new initiative, the Max Foundation will assume from Novartis the responsibility for delivering our CML treatments to these patients, including supply chain management, and Novartis will provide the funding and drug donation support.

Convergence is occurring across different areas of science, technology, biology, and IT. The onus is on the pharma industry to embrace this change and leverage it

PB: *Novartis has formulated its very own definition of value. Tell us more about this.*

STRIGINI: For us, the value of our products includes four components. First, there is clinical value. Second, there is value to the patient in terms of quality of life. Third, impact on the total healthcare budget; for example, if a new drug avoids expensive hospitalization, then the cost saving being generated needs to be taken into account. Finally, there is the societal value of getting the patient back to being a productive member of the economy.

In short, we look at value holistically. The comparative value of a drug should be calculated against how well it performs with respect to each of these four criteria.

PB: *Do you see the concept of value-based pricing gaining traction with governments?*

STRIGINI: Yes. The arrangement that we struck with CMS in the US demonstrates that healthcare systems are seeing the potential benefits and are prepared to engage. In Europe, we also witness progress being made on health technology assessment and willingness to start the dialogue on outcome-based approaches.

PB: *Where do you see the emerging trends right now?*

STRIGINI: There is a huge amount of innovation in the science of cancer. Digital disruption is also shifting the paradigm; this is clearly the case at Novartis. Big data, predictive modeling, and advanced analytics are changing the way we work in all aspects of our business: research, development, and commercialization. For example, in research, it is helping us to shorten the time between finding a target and proof of concept. Also, the use of real-world evidence could transform the way we approach the development and regulatory processes for a drug.

In short, a golden age of innovation is upon us and convergence is occurring across different areas of science, technology, biology, and IT. The onus is on the pharma industry to embrace this change and leverage it. These are all highly positive steps that bring stakeholders together to the benefit of the patient.

PB: *Do you have a few words to conclude on Switzerland—Novartis' global base—and its role in the life sciences?*

STRIGINI: Switzerland is the home of two of the top global pharmaceuticals players. It possesses a vibrant and flourishing life sciences industry and is also notable for having one of the best functioning healthcare systems. Part of this no doubt derives from a historical tradition of innovation and engineering, and I believe the country's openness and collaborative spirit contributes greatly to this success. PE

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Changing Skies

2018 Trends to Watch

Pharm Exec's Annual Industry Forecast

In this year's *Pharm Exec* Industry Forecast, our annual temperature check on the life sciences sector and its outlook for the months and seasons ahead, we decided to try a slightly different approach. We again are highlighting what we feel are, globally, the most important industry-shaping trends, but have singled out eight specific pulse-setters, in particular, for examination—by our staff and correspondents and with insights from *Pharm Exec* Editorial Advisory Board (EAB) members and other experts. Call it our "8 for '18," if you will. We wanted to make sure the topics and events we explored were diverse—covering areas that impact patients, business, the regulatory climate, and science.

After all, as most would attest, the inevitable change and sway that grips all major industries is afoot. Just look at the flurry of activity at the end of 2017. In the US, major tax reform legislation was passed under the wire. The significantly lowered corporate tax rate and other changes could boost pharma investment and stop the shift of profits by US companies to affiliates in lower-tax countries. At the same time, however, the new law cuts tax benefits for rare disease R&D. In Europe, Amsterdam won the coveted prize as the new home base for the European Medicines Agency (EMA) come March 30, 2019, when Brexit— loose ends and all—is official.

Add to the mix a potential upsurge in M&As, the critical testing period ahead for CAR-T and other novel therapies on the commercial stage, and the pricing debate that rages on (amid new findings that healthcare spending on prescription drugs has almost doubled since the 1990s), and it's clear 2018 is shaping up as must-see viewing. PE

Our 8 for '18

- Patient vs. Consumer
- Pricing
- FDA Commish
- Emerging Markets
- EMA on Move
- Biosimilars
- Diagnostics
- eEnablement

The 'Patient' vs. 'Consumer' Conundrum

Should engagement models consider label change?

During the recent *Financial Times* Digital Health Summit presented by FT Live, one of the speakers asked the audience to do this:

"Raise your hand if you consider yourself a patient."

About five hands went up.

Then, the speaker said this:

"Raise your hand if you consider yourself a consumer."

All hundred or so people in the room raised their hand.

The point the speaker was trying to get across was multileveled, but in general the exercise was to show that unless someone has a specific condition they are being treated for, a majority of people consider themselves a consumer, not a patient. And if pharmaceutical and healthcare companies want to stay ahead of the Apples and Amazons of the world who are threatening to disrupt the industry, they need to start viewing those who use, or "consume," their products as consumers, and not just as patients.

It would signal a fundamental and psychological change in most ways a business functions. In the pharma space, it wouldn't necessarily impact the science behind a drug, but, according to experts, could potentially change the way other aspects of business are done.

Joshua Newman, chief medical officer at Salesforce, explained how consumer-centric companies think about things differently than pure pharma does.

"These organizations appeal to us, they are available to us, and they respond to us," he said at the Summit last fall, adding that there was a time when it was just about the product or just about the customer service. "Now, it's the entire journey," he said.

Using Amazon, Google, and Uber as examples, Newman explained that following this model wasn't the way these companies started out, but they learned to evolve over time.

"Things have changed and the reason is not because we (consumers) have demanded it, but because they were sensitive to it," said Newman. "They were sensitive to what we needed; they realized to compete, they had to give us a beautiful, easy, and frictionless experience. They take care of us not only when we are buying something from them, but from the time before on past the time we have used their product. And they keep reminding us they are around anytime we want to use their products."

In the pharma and healthcare space, some say this is the missing piece of the patient care puzzle—and as patient centricity continues to be a buzzword, and companies dig deeper into what that actually looks like, the consumer aspect is going to come up more and more.

> "Very few people complain about their drugs. But everyone complains about the logistics ... everyone has anxieties, everyone has questions that are unanswered, and that's what the biggest gap is, and it's also the biggest opportunity."

"Very few people complain about their drugs, very few people complain about their devices that have been installed, the surgeries, or the actual mechanics of clinical care; but everyone complains about the logistics," Newman pointed out. "Everyone has a story about the administration, everyone has anxieties, everyone has questions that are unanswered … they don't know what to do, and that's what I think the biggest gap is, and it's also the biggest opportunity."

To think that a patient who is "consuming" drug therapies (e.g., chemotherapy) could one day pick up their mobile phone, open their apps, hop on Amazon, order it, and have it delivered right to their door is far-fetched. But those who believe the pharma industry needs to start thinking of its patients also as consumers will argue that scenario has to be part of the thought process in order to stay relevant, especially as non-traditional companies who excel at the customer experience enter the space.

The driving force amplifying this as an industry trend is technology. As technology evolves in other industries, making them more consumer-friendly, patients are going to expect the same level of cus-

tomer convenience they are getting from other businesses touching their lives.

"How do we establish technological platforms, data connections that lower the activation energy and difficulties that people have right now worrying, learning, and engaging in their health and how this technology more effectively empowers consumers to make decisions about their health?" said Lloyd Minor, dean of Stanford School of Medicine.

But not everyone is behind this shift in wording.

Michael Mittelman, vice president, strategic partnerships and patient advocacy, at the American Living Organ Donor Fund, and a three-time kidney transplant recipient with other chronic conditions, challenges the idea of calling patients consumers.

"Patients referred to consumers bothers me," he said. "Patient-centered programs should be designed for patients. Patients are not consumers."

Although companies like Google or Amazon might be good at what they do when delivering a consumer experience, it doesn't necessarily mean they will be good at translating those skills to pharma, citing Google Health and HealthVault as poor performers.

One thing is certain—the conversation about patients and consumers will continue to gain attention as more non-traditional companies who are consumer-focused enter, or threaten to enter, the pharma and healthcare space.

—Michelle Maskaly

Pricing Fix Elusive

States may take full control

Pricing in the US as a trend for pharma is not new, it just keeps twisting into different forms. Last year, of course, the talk of pricing swirled around President Trump's negative comments around prescription prices. With a lack of any movement on prices on the federal level, individual states took hold of the reins by instituting their own laws around pricing. Will 2018 be the year that states take full control of the drug pricing issue in the US? At least 176 bills on pharma pricing and payment were introduced in 2017 in 36 states, according to the National Conference of State Legislatures.

In early October, California Gov. Jerry Brown signed a law requiring pharma companies to notify the state and health insurers anytime they plan to raise the price of a medication by 16% or more over two years. And companies will have to provide justification for the increase. Health insurers also were instructed to report what percentage of premium increases are due to drug prices.

A new Maryland law takes aims at price hikes on generics of older off-patent drugs after some companies took massive increases on generic drugs not facing competition from other distributors.

In Ohio, a referendum that would have leveled drug prices was defeated and a report said the proposal's complexity may have been its undoing. It would have prohibited state programs, such as Medicaid and state employee health plans, from paying more than what the Veterans Health Administration pays for a medication. But a nonpartisan office concluded it was unclear how much money the proposed change would save, if any.

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And therein lies the rub: "unclear how much money the proposed change would save, if any."

Ed Schoonveld, head of the value and access group for ZS Associates, told *Pharm Exec*, "There is a lot of frustration regarding drug pricing in the US, and much of it is political. Absent of an easy fix, politicians say 'Well, we have to do something' and this is where we are." He added, "It's hard to make sense of list prices. The real concern is where are the rebates going? That's what we should be looking at."

Schoonveld also emphasized that government and payers need to be careful with what they are requiring. For example, what if a company wasn't planning on raising its prices anywhere close to 16% over two years. Now, increasing within the guidelines looks like a great option since no penalties will be enforced.

And in the case of generics, there again needs to be a balanced discussion. At a World Health Organization (WHO) fair pricing meeting last

year, Schoonveld said, "There was a concern over the supply of generics. In effect, they were saying don't make your tender policies so aggressive that companies will exit, leaving you with only few alternatives."

Another trend in pricing is the shift toward value-based or outcomes-based contracting—which is a much larger topic that will be discussed throughout the year. Suffice to say that Schoonveld believes that there needs to be a focus on long-term outcomes and how to fund those. "Many innovations are coming to the market and affordability is becoming a real issue," he says. "We need to have a good conversation about the desired outcomes of new treatments and how we pay for it. It's become a societal issue."

While Schoonveld doesn't suspect the trend with states passing pricing and payment laws will cool off, it also will not resolve anything, he believes. "This is a broader healthcare funding issue. And pharma needs to be a part of the discussion and engage in the dialogue with the insurance industry, medical community, and government."

—Lisa Henderson

FDA Proving Grounds

The agency's man with a plan

"2018 is his year to prove."

"His leadership and vision at FDA is clearly aggressive and ambitious."

"[He is] very proactive, a 21st century thinker."

"[He] believes in adaptive trial design, improving functioning of FDA."

"Will this be the year he makes an impact?"

Albert H. Teich/shutterstock.com

Scott Gottlieb

These were the comments that *Pharm Exec*'s Editorial Advisory Board made regarding FDA Commissioner Scott Gottlieb when discussing this year's industry forecast. Our Washington Correspondent, Jill Wechsler, has covered Gottlieb's appointment and activities since his official nomination in late March. She reported that on the day Gottlieb was confirmed in May, the FDA Science Board approved a detailed work plan for allotting $500 million over nine years provided by the 21st Century Cures Act.

Some of the Cures initiatives include qualifying more biomarkers and other drug development tools; modernizing clinical trial design; using more real-world evidence (RWE) to approve new indications and post-marketing studies; expanding the role of patients in assessing new drug risks; and promoting more coordination among FDA centers, particularly for combination products. FDA, under Gottlieb, has already checked off some of those boxes, and made good on his own promises, signals that Gottlieb is aggressively moving the FDA ball forward.

On June 29, the commissioner told the Senate Appropriations subcommittee that FDA's new Orphan Drug Modernization Plan would eliminate a backlog of 200 pending orphan designation requests by mid-September and establish procedures for vetting such requests within 90 days in the future. The backlog for requests older than 120 days was completed on August 28.

In the area of biomarkers and diagnostics, November saw the FDA approval of FoundationOne CDx (F1CDx), the first breakthrough-designated, next-generation sequencing (NGS)-based *in vitro* diagnostic (IVD). The test can detect genetic mutations in 324 genes and two genomic signatures in any solid tumor type. At the same time, the Centers for Medicare and Medicaid (CMS) proposed coverage of F1CDx. The test is the second IVD to be approved and covered after overlapping review by FDA and CMS under the parallel review program, which facilitates earlier access to innovative medical technologies for Medicare beneficiaries.

In recognition of the importance of postmarketing studies, FDA, in mid-December, reported for its fiscal year 2016 that the number of open postmarketing requirements (PMRs) and postmarketing commitment (PMCs) had decreased from 1,636 to 143. Dr. Peter Stein, deputy director, Office of New Drugs, at the Center for Drug Evaluation and Research (CDER), noted that FDA is committed to making sure industry fulfills its PMRs and PMCs and that the postmarketing studies are transparent to the public. Gottlieb, after the announcement, took to Twitter at @SGottliebFDA: "Post-approval studies enhance patient safety & public health, can lead to safety labeling changes, support expanded use of drug, alleviate risk concerns."

Other comments that Gottlieb has made could come to fruition in 2018 around RWE, biosimilars, and the opioid crisis. Gottlieb has said that clinical trials may not always require randomization, and that faster studies don't necessarily compromise on safety or undermine the FDA gold standard for assuring medical product efficacy. He has said that RWE won't replace traditional clinical trial data in many cases; however, he sees opportunity in the pre- and postmarket context to use this data to modernize development, and that FDA will collaborate with all stakeholders to achieve a "more appropriate adoption of RWE as part of the entire life cycle of medical products."

As noted elsewhere in our Forecast coverage, the topic of biosimilars in the US, in particular, is in a holding position. During Gottlieb's confirmation hearing, he specifically said, "I think Congress didn't envision with Hatch-Waxman that certain drugs would have monopolies in perpetuity, long after their intellectual property has expired, but for the inability of FDA to have a scientific process that can prove interchangeability for those drugs. I think this is an area where we can make a lot of progress. We might need to come back to Congress to talk to them about what additional steps we need to take, but I think there are things FDA could contemplate administratively. This is an area I want to work on. These are literally billions of dollars worth of drugs each year that are sold as branded drugs at high prices, but should be subject to generic competition." However, as noted, much of the biosimilar activity is tied up in the US legal system.

All in all, Gottlieb has started strong and there is no indication he will let up in 2018. In fact, his mid-December blog foreshadowed upcoming activity (view at http://bit.ly/2rm9oAV). Besides his apparent commitment, Gottlieb's Twitter game is spot on.

—Lisa Henderson

Public Health, Private Care

Emerging market perspectives

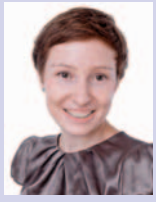
Colombia

The Latin American markets continued to fluctuate in 2017. Recession and public health spending cuts further compromised Brazil's appeal as an attractive region for multinational investors and widened the gulf between the country and its leading BRIC counterpart, China. Venezuela spiraled further into economic collapse, the country's gross domestic product (GDP) shrinking by 19% as the catastrophic effects of steeply falling oil prices and a crumbling political system took hold. The weight of Latin American expectation, then, has since shifted to Colombia, described by *Pharm Exec*'s October 2017 Country Report as "a bastion of peace, stability, and resilience," with GDP growth rates of around 2% for 2017 and "thriving domestic consumption set to propel the value of the local pharma market from $5 billion in 2015 to $7.1 billion by 2020."

Colombia boasts 108 of the 400 free-trade zones in Latin America, with Focus Reports observing that multinationals "tend to be thrilled by the 'level playing field' on offer and the sheer openness of the market." Colombia has implemented trade agreements with a host of countries, including the US, the EU nations, Canada, Japan, and South Korea, while expanding its trade relations with Latin American neighbors such as Mexico. Similarly, Colombia's medical device industry is encouraging international companies to the market in a free-trade zone in the capital, Bogotá. The country's med-tech segment is reaching double-digit growth, with a projected value of $1.8 billon by the end of the decade.

Rachel Howard, director, emerging markets, at Research Partnership, told *Pharm Exec* that "Colombia has been on our radar as an 'up-and-coming' emerging market for some time

now, with the end of armed Farc rebel conflict and decline in organized drug crime facilitating a more favorable business environment, and the proposed healthcare reforms that accompanied President Juan Manuel Santos' successful reelection in 2014." However, Howard explains, "corruption and mismanagement—which have long plagued the country's healthcare system and resulted in costs spiraling out of control—represent broader national issues that have eroded public confidence in political parties to record lows as of late 2017." In a June 2017 survey, 20% of Colombians cited healthcare as the main problem that the next president should address.


Rachel Howard

Colombia heads to the polls in May, with Mexico and Brazil facing elections later in the year. For Howard, "How the policy debates play out over the next 12 months could have far-reaching implications for the prospects for pharma within the region, at least within the public sector." However, she notes, "The regional trend toward privatization of healthcare provision looks set to continue regardless."

Indonesia

GlobalData reported in October that Indonesia's pharmaceutical market—the largest in the Association of Southeast Nations (ASEAN)—is predicted to reach $10.11 billion by 2021, driven by the introduction of 15 economic policy packages to attract foreign investors, growing urban population, and the implementation of the Universal Health Coverage scheme (Jaminan Kesehatan Nasional [JKN]). Despite encountering a number of challenges since its launch in 2014, says Howard, the JKN rollout continues apace, with an additional 117 million Indonesian workers set to be covered from next year (from a total population of 261 million). But, she adds, "as we have seen in other emerging markets that have implemented universal healthcare coverage schemes, increasing the population covered does not proportionately increase the opportunity for multinational pharma companies, as the public market is focused on low-cost generics." (As noted in the GlobalData report, the unbranded generic market in Indonesia was worth $619 million, 10.8% of the pharma market, in 2015, and is expected to rise as more people begin to rely on JKN.)

Instead, for Howard, the private sector will present "far and away the major opportunity for pharma in Indonesia going into 2018, as the growing middle classes demand higher quality care in the context of public hospital capacity becoming even more strained."

Saudi Arabia

Saudi Arabia already has one of the largest pharma markets in the Middle East and North Africa (MENA) region, and accounts for 59% of all pharma purchases within the Gulf. The country's per capita spending on pharmaceuticals is expected to increase from $268 million in 2015 to $400 million by 2020. The government's National Transformation Program, Vision 2030, launched in May 2016, included proposals to spend more than SAR23 billion ($6.1 billion) on new initiatives, including the localization of the pharma industry. Improving healthcare is a key pillar of Vision 2030, with a focus on promoting preventative care and encouraging citizens to make use of primary care, as well as developing the private sector and expanding private medical insurance.

The opportunity in Saudi Arabia "looks bright," says Howard, "especially given its relative political stability when compared with the rest of the region." However, she adds, with the country's "long-term growth outlook overly reliant on potentially unpredictable fluctuations in oil prices, cost containment is a high priority for the government and there is a push to use local generics over patented imports, overcoming consumers' lack of awareness of generics and prescribers' preference for branded products." Gender inequalities in access to healthcare also remain a challenge, with women in Saudi Arabia still lacking equal rights.

China

"No emerging market opportunity assessment would be complete without considering China, given its vast population size," says Howard. Measures implemented in 2017 by the Chinese government to facilitate faster drug approvals and enable more widespread public access to innovative treatments give a "reason to expect rapid growth in China in 2018." This optimism is tempered by the dramatic price cuts that manufacturers are forced to offer to get their drugs onto the National Drug Reimbursement List, and the regulatory and cultural obstacles, such as the struggle for private practices to attract the top doctors, that continue to hold

back the market for private healthcare. But with the number of high net-worth individuals in China surging nearly nine-fold in the last decade, Howard notes that the "explosion" of the private sector healthcare market in China could still be on the horizon. In particular, the April 2017 relaxation of a regulation prohibiting doctors from practicing outside of their primary workplace offers "an important step in paving the way for more rapid private sector expansion through 2018."

Connecting with (middle-class) customers

The opportunity offered by emerging markets, says Howard, "is becoming too big to ignore, with pharma and life sciences companies including them at earlier stages of their global clinical R&D programs and placing them at the heart of their future strategic vision."

The issue of cost, however, remains a critical one. The immediate opportunity for pharma continues to be driven by urban middle classes who can afford to pay out of pocket. These patients, and the healthcare professionals who treat them, are increasingly digitally connected and health-literate. As such, "the content delivered to them by pharmaceutical companies in 2018 will need to reflect that."

— Julian Upton

EMA in Transition

Praise, concern surround relocation, future

The November announcement that the European Medicines Agency (EMA) will relocate from London to Amsterdam in 2019 brought an injection of clarity to the ongoing debate around how Brexit will affect both the European and UK life sciences sectors. The decision was widely welcomed by those who have to deal with EMA's core activities, notes *Pharm Exec*'s Brussels correspondent, Reflector, "not so much because they are keen on Amsterdam in particular, but because they are keen to be able to plan for business moving ahead." He adds: "The same concerns applies for drug developers, patients, and health professionals—the uncertainty has been a handicap for the last 18 months."

The EMA head office in Canary Wharf, London.

European industry associations issued congratulatory statements on the EMA announcement, although they sounded an inevitable note of caution. European Federation of Pharmaceutical Industries and Associations (EFPIA) Director General Nathalie Moll emphasized that "[s]ecuring transitional arrangements and long-term cooperation on medicines regulation between the UK and EU is the best way of ensuring that patients across Europe continue to have access to safe and effective medicines," while John Brennan, secretary general of EuropaBio, commented: "Now that we have more clarity, it is vital that the relocation of the EMA will be carried out in such a way as to minimize as much as possible any disruptions that could negatively affect access to medicines for patients."

Reactions from the UK were, not surprisingly, less equivocal. BioIndustry Industry Association CEO Steve Bates noted that "London's loss is Amsterdam's gain. Today's decision on the location of EMA means 1,000 high quality jobs leaving the UK, disrupting 1,000 families as a direct result of Brexit, with implications for thousands more. Businesses now need certainty." The UK writer and campaigner Ben Goldacre warned that the move "will cause upheaval and delays."

As Reflector observes, the relocation will certainly present a range of practical problems that were foreseen, and a wider range of challenges that did not receive much attention in the run-up to the decision. "The known challenges relate largely to the physical transfer of staff to Amsterdam and the likely lead for recruiting replacements for the staff who choose not to move, which the EMA estimates as perhaps 200 out of the total 900 full-time employees," he says.

Hurdles include the need for temporary office accommodation, as the Amsterdam building will

not be ready in time, and the need to find housing in Amsterdam's already overheated accommodation market for the staff who move there. "The time that will be taken up with these administrative tasks will inevitably have a negative impact on the running of the agency's normal business," Reflector says.

And "London's loss" will continue to be a bugbear for the UK. The impending exit of EMA from London and the lack of clarity around the Brexit negotiations in general had already begun to affect the UK's life sciences recruitment sector in 2017, with recruiters speculating on the further level of impact with concern. Karl Simpson, founder and CEO of executive recruitment firm Liftstream, told *Pharm Exec* last year that he was already seeing "a reluctance on the part of people based in continental Europe to look at the UK as a legitimate destination."

While such staffing concerns were largely driven by the confusion surrounding the negotiations at the time, Simpson also noted that US companies preparing to make the move into Europe, for example, had become more decisive in choosing destinations other than the UK to move to. "I've had conversations with organizations coming over to Europe from the US who have explicitly chosen to move to Switzerland when their preference originally was for the UK," he said.

Richard Acton, vice chair of the REC's (Recruitment & Employment Federation) life science sector group, told *Pharm Exec* that he had seen the same pattern with European firms and staff—"something I've noticed a lot more since Article 50 was triggered." James Chaplin, CEO of recruitment industry data publishers, Vacancysoft, said that what Brexit "seems to be doing is accelerating the Belgian R&D triangle," while also observing "a lot of activity now in the French pharma industry."

Such observations stemmed from the general climate of uncertainty that dogged the Brexit process for most of 2017, but when the EMA relocation was finally announced, Christopher Stirling, partner and global chair of life sciences at KPMG, could declare more firmly that "for Amsterdam, it's a windfall beyond just the regulatory jobs."

Stirling also offered a positive spin, however, adding that the relocation will "open doors for the creation of a single UK agency for medicines, medical devices, and veterinary medical products… [and] could provide an opportunity to streamline and enhance the abundance of regulation in this area, to find better and cheaper ways of preventing, treating, and curing disease."

From a staffing and recruitment perspective, tensions were further eased by the Brexit negotiation "breakthrough" of December 8, when, alongside a number of key commitments, it was established that EU citizens living in the UK (and vice versa) will have their rights to live, work, and study protected. The Academy of Medical Sciences President, Professor Sir Robert Lechler, welcomed this development as "much-needed assurance" for the EU nationals who make up almost 25% of medical research staff working in UK universities.

As Reflector reminds us, however, the impact of the EMA relocation decision is not limited to the UK; it affects countries across Europe: "The earnest bid for transparency that inspired the open competition to host the agency had the unintended consequence of leaving as many as 26 disappointed candidates." He points out that "resentment triggered among administrations that had invested heavily in time, energy, and resources started to bubble over even before the voting had finished," noting that the reaction from Italy was "virulent" when Milan "lost on the toss of a coin."

As the smooth running of the agency depends entirely on the corporation of all European member states, he adds, the EMA relocation process will be "a difficult transition."

— Julian Upton

Biosimilars Boom Soon?

Trajectory uncertain amid legal wranglings

Could 2018 finally be the year of the biosimilar? Maybe. Or, maybe not.

"There are a number of cases [involving biosimilars] moving through the courts whose decision will have a significant effect on the US market," says Art Cook, principle, ZS Associates.

The results of those legal battles will impact a number of areas—everything from launch dates to how much regulation the FDA will have when it comes to biosimilars. Until those are resolved, the US biosimilar market is in an uncomfortable holding pattern, with lots of turbulence and possible

Crowded Field

In the US, intense competition is on the horizon – will it cause a race to the bottom?

Graphic provided by ZS Associates

Source: Citeline as accessed in November 2016. Highest phase of development worldwide has been considered. Biosimilars in preclinical stage of development have not been considered.PsA- Psoriatic Arthritis, AS- Ankylosing Spondilytis, JIA- Juvenile Idiopathic Arthritis, PsO- Psoriasis, HS- Hidradenitis suppurativa, CD- Chron's disease, UC- Ulcerative Colitis, NHL- Non Hodgkin's Lymphoma, CLL- Chronic Lymphocytic Leukemia, GPA- Granulomatosis with Polyangiitis and MPA- Microscopic Polyangiitis

scenarios. This makes it difficult for experts and pharmaceutical companies to predict how the biosimilars arena will all shake out.

Experts across the pharm industry think that 2018 could be the year that these legal issues get resolved, and biosimilars could finally start to make a splash in the US. But they also were quick to point out that no one can be 100% certain. Even if the current cases do get resolved, new legal challenges can always be filed, as companies try to protect their patents and block biosimilar entry into the US market.

For example, innovator biotech companies are defending their products by, among other things, filing additional patents related to manufacturing processes and uses, licensing deals that require royalty payments for IP use, encouraging the FDA to impose naming and labeling regulations that clearly differentiate biosimilars from originators, and presenting data that calls into question the safety of switching patients.

All of this uncertainty makes the situation very uncomfortable for the whole industry, but specifically for those creating and developing the biosimilars. It's forcing companies to prepare the groundwork for a variety of outcomes, hopefully enabling them to move quickly once the federal court system does make a ruling.

For instance, in general, biosimilars manufacturers are trying to drive the conversation through pricing and contracting agreements, partnering with large pharma companies that have sales and marketing expertise, partnering to decrease time to market, building larger bioreactors to achieve economies of scale, and leveraging broader R&D expertise related to Chinese hamster ovary (CHO) cells and monoclonal antibodies (mAbs).

So, let's pretend the courts rule in favor of the biosimilar companies, there are no additional legal challenges, and a host of biosimilars begin to enter the market. What will that scenario look like?

Experts believe biosimilar companies are going to take an immediate three-pronged approach, starting with simultaneously talking to providers and educating physicians on the safety and efficacy of these products, launching and providing a host of patient support services, and negotiating with payers. On the flip side, those companies whose drugs are at risk for competition from biosimilars will also be looking to payers and trying to extend contracts into the three- to five-year range as a way to derail a biosimilar surge.

Should this happen, the much-ballyhooed hype around biosimilars making a significant impact on the prices of expensive innovator biologics could be

delayed, and it will take longer to see that shift than expected. But experts say it will happen, eventually.

A small group of experts believe even if long-term contracts with originator companies are not in place when biosimilars get approval, the skepticism from physicians who worry that biosimilars may react differently than their reference products will lead to a hesitation in prescribing them. Conversely, experts argue that companies will be able to point to the successful use of biosimilars in Europe without many adverse side effects as a way of minimizing this type of pushback. The biosimilars that have entered the US market in the past year have shown positive outcomes and have been well received, and Cook expects that to continue for other follow-on biologics that may hit the market in 2018.

Experts can make predictions, companies can prepare for various scenarios, but the future outlook for biosimilars in the US commercial space, in particular, ultimately hinges on the legal system.

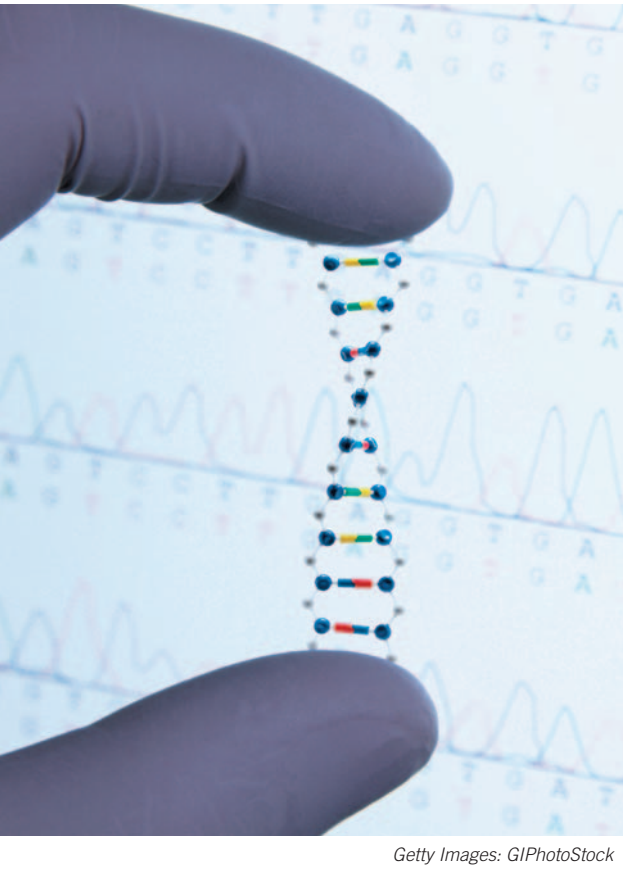
— *Michelle Maskaly*

Dissecting Diagnostics

Experts gauge direction of evolving market

The diagnostics space is heating up, but companies will need to address the impact of regulatory uncertainty, ongoing cost-containment pressures, and the practical challenges of working with big data with new, collaborative strategies. That's the message from diagnostics expert Harry Glorikian—author of *Commercializing Novel IVDs: A Comprehensive Manual for Success*—who recently spoke to *Pharm Exec* about the developments set to affect the diagnostics landscape in 2018 and beyond.

Harry Glorikian



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As treatments become more individualized and based on variant-level genomic alterations, the market for companion diagnostics will continue to expand, says Glorikian. Next-generation sequencing (NGS)-based diagnostics are taking on a greater role in healthcare, with oncology taking the lead, particularly with companion diagnostics. It's not just oncology that will see growth in this area, however. "Treatments based on genetic variants are already a reality for some chronic diseases, like cystic fibrosis," he says.

Other technological advancements such as CRISPR, with the ability to potentially correct genetic mutations, will also fuel the demand for accurate diagnostics. And while it's a few more years down the line, liquid biopsy is a technology with "incredible potential for use as part of an annual physical exam, catching cancers before the patient exhibits any symptoms," says Glorikian.

According to the author, the biggest impact on the diagnostics industry in the next few years will be centered around data. He explains: "There are some labs that have built up massive data repositories. That data is incredibly valuable to the company, but patients, providers, and researchers have made the point that the data needs to be shared with others to drive innovation and scientific breakthroughs and to ensure patients are treated appropriately."

In the future, the value of holding on to the data

itself will be secondary to what companies do with the data. "This presents a unique opportunity for the diagnostics industry to establish working relationships with other companies," says Glorikian.

He points to Google's recently launched artificial intelligence (AI) product, Deep Variant, to help researchers make sense of the genome. "*In vitro* diagnostics (IVD) manufacturers that partner with companies using AI, machine learning, or cognitive computing are going to be at the leading edge of the industry in a few years," he says.

Regulatory concerns

Despite the tangible potential of the technology, the regulatory space for diagnostics continues to be in "a state of flux." FDA has released draft guidance on the Clinical Laboratory Improvement Amendments (CLIA) waiver applications and 510(k) dual submissions, but Glorikian notes that it is "unclear if the agency will finalize these documents in the next 12 to 18 months." More certain will be the impact of the Protecting Access to Medicare Act (PAMA).

The Road Ahead

ZS Associates' Jim Adelizzi, principal, and Maria Whitman, managing principal and head of specialty therapeutics and oncology, offer their perspectives on the key issues dominating diagnostics in the year ahead.

Regulatory

Adelizzi: Historically, there have been two big focus areas for the regulatory bodies with respect to diagnostics. The first is in clarifying the regulatory path for a companion diagnostic and associated therapeutic, and the second has been dealing with newer technologies that have the ability to provide insight on multiple markers in one test that also cover multiple diseases or tumors. On these fronts, there has been significant progress over the last few years and, in 2017, there were approvals in the next-generation sequencing (NGS) space, e.g., Thermo Fisher and Foundation Medicine, that cover multiple biomarkers for multiple tumors simultaneously.

One remaining step is greater clarity with respect to the regulatory path for kits and laboratory developed tests (LDTs). Clarity on this issue will eliminate uncertainty and help with investment in the space.

Technology

Adelizzi notes there will be:

» An increase in less invasive technologies for sample extraction, collection, and processing (e.g., liquid biopsies).

» Technologies that through artificial intelligence better integrate biological and non-biological data.

» Continued reduction in cost for sequencing and increased ability to use proteomic and RNA information for personalized medicine.

Key challenges

Adelizzi identifies:

» Reimbursement

» Disruptive technologies—many of the traditional technology platforms will need to deal with the democratization of technologies that previously were only able to be afforded by academic centers.

» Finding growth in a marketplace that is going through disruption and has significant cost pressures.

Keeping up with the competition

Whitman says:

» Worry less about the competition and more about customers and patients.

» NGS will become more common but the industry is likely to be divided into two segments—academics with their own NGS test and internal Dx expertise and communities with limited diagnostic infrastructure that will continue to depend on outsourced laboratories. In either case, pharma needs to consider how NGS will affect testing, particularly where CDx exists.

» For pharma, there is a reality that development time and pace of technology does not match. What may seem like a competitive advantage from a Dx perspective in clinical trial design today may not be tomorrow, and so it is more important than ever that organizations are projecting forward and considering these new technologies in their approach (e.g., by the time we launch, will RNA be more relevant?)

» Dx companies will likely look to collaborate with pharma to offer both multi-marker and single-marker tests for a given product, which may also cover multiple diagnostic technology platforms.

"We can expect to see the pace of mergers and acquisitions pick up after PAMA, as smaller labs and those with significant Medicare business bear the brunt of lower reimbursement for certain tests," says Glorikian. "But it's important to recognize that not all companies will be impacted to the same extent. Molecular diagnostics and highly technical genomic tests are seeing smaller payment reductions and in some cases, higher reimbursement levels than before, compared to routine chemical assays. Companies will need to consider diversifying their test portfolio so that they are better able to withstand lower and fluctuating reimbursement levels."

Glorikian sees diagnostics companies having a major role in lowering overall healthcare spending. He points specifically to precision medicine for oncology. "It's becoming more important to identify the underlying genomic mutations before starting a patient on chemotherapy, so that you get the right treatment for the patient the first time." Not only is this better for the patient, but it can reduce costs associated with failed treatments and adverse events.

If diagnostics are leveraged in the right way, says Glorikian, "healthcare can become more streamlined, more precise. Capturing the data around the use of IVDs in clinical care is the essential component to making this happen. If you aren't collecting the data, it's going to be increasingly difficult to remain competitive."

Competition and value

So how do pharma and medical device companies remain competitive? Glorikian believes they must plan for commercial success from the very beginning. "Clinical studies to assess the analytical and clinical validity of an IVD shouldn't be an afterthought for companies that intend to seek reimbursement from CMS (Centers for Medicare & Medicaid Services) or private payers." He says the recent FDA and CMS decisions for Oncomine DX and Foundation1CDx demonstrate that NGS-based panel tests have a role in clinical care.

"That presents a substantial opportunity for companies in the space, but the key is having the data to back it up," says Glorikian. "Is there clinical validity for the variants on the panel? What is the clinical utility of those test results? Is it changing treatment decisions?"

Ultimately, what pharma and medical device companies need to do is show the value of their products. It's not going to be sufficient in the future to focus only on price and number of variants that are assessed, says Glorikian, if the assay doesn't improve patient outcomes or change patient management in any way.

Companies that have that data available or plan to capture it during development will be ahead of the competitors when it comes to seeking reimbursement, Glorikian believes.

"Genetic/genomic testing is a key example. There are tens of thousands of tests on the market today and more launching every month. Companies need to consider how they can make their product stand out," he says. "Does their test have more variants? Is it more accurate? Is it an improvement over existing technology? Does it change how the patient is treated? These are essential questions that companies need to ask themselves early in development, and convey that information to providers and payers—no matter what the reimbursement business model looks like."

— Julian Upton

Next Step: eEnablement

Innovating at the point of prescribing

When it comes to market access for pharmaceutical companies, access to the physician and the ability to help physicians guide patients through the hazy prescription supply chain has become a value-add. If pharma can help healthcare professionals (HCPs) get through life a little easier, the hope is that more patient prescriptions will get filled and potential problems addressed at the point of prescribing—the physician's office.

The first bit of "e" that physicians adopted was the eRx. Many of us have sat in the office while the doctor sends our prescriptions electronically to the pharmacy. According to Ron Lacy, senior director of products and services for United BioSource Corp. (UBC), adoption of eRx took years for the industry to achieve. Following eRx came ePA (prior authorization), which is now becoming much more prevalent. Lacy believes that close to 50% of all PAs on the pharmacy benefit are happening through the ePA standard, and it will continue to increase.

"The physician is aware of benefit information at the time of writing the prescription, allowing for proactive decisions such as seeking additional patient-support services."

For the next wave of physician eEnablement, look for 2018 to be the dawn of electronic benefit verification, or eBV. "Adoption will start this year," says Lacy, "But it will take a couple of years to get all PBMs (pharmacy benefit managers) and prescribers to use prospective electronic benefit verification. We expect adoption rates to go faster, as the eBV solutions will be tied directly in with prescribers' eRx capabilities."

The adoption starts with broad deployment by PBMs and healthcare organizations. At the same time, pharma companies will also look for their patient-support programs to leverage eBV solutions.

So what does eBV bring to the table? Like eRx, the eBV standard can be embedded in the electronic medical record (EMR) system or stand alone. Historical solutions that were associated with eRx products were file-based and only provided formulary information at the plan level. These solutions were often times out of date and did not provide patient-specific benefit information. With the next generation of eBV solutions, the physician can see if a patient is covered for the

Industry Rewind: Evolution of Outlook Trends

Pulling from various topics examined in *Pharm Exec*'s annual Industry Forecast reports, we highlight ahead the evolution of certain continuous trends from the past five years, focusing on the Affordable Care Act (ACA), M&A activity, and the uncertainty in the EU from Brexit.

Affordable Care Act

In 2013, the pharma industry still had some time to consider how the US healthcare system would be restructured, as plans for the ACA came to fruition. The beginning of 2014 displayed continued uncertainties as to what provisions would or would not be in effect as the year unfolded.

Pharm Exec reported in early 2015 that the individual mandate requiring all Americans to have minimum essential healthcare coverage on their IRS filing meant that, come April 15 of that year, for the first time, "all individuals must pay up, one way or the other, lest they face penalties on their 2015 IRS return." Considering millions of lower income, younger, and healthier ACA patients swept into the program, "the likelihood of the success for American innovator Rx's in Obamacare for 2015 will only get more difficult," said Tom Norton, principal at NHD Smart Communications.

Returning in 2016's trends coverage, penalties attributed to not purchasing health insurance expected to be the greater of $695 in fees or 2.5% of an individual's modified adjusted gross income, according to Norton. He added, "…to get health insurance at these levels, Rx options in these basic plans will continue to be reduced, and pressure to lower Obamacare Rx drug prices will only increase."

With the onset of the Trump administration, the US pharma industry had been expecting the demise or reform of the ACA, repatriation of overseas profits, and reduced regulation and taxes, freeing up cash. It achieved some of that with the passage of US tax reform last month (which also repealed ACA's individual mandate), but it remains uncertain what lies ahead for US healthcare legislation and further attempts to modify or overhaul the law.

M&A

The pharma and biotech M&A transition started slow in 2013, with a gradual increase that peaked at the end of 2014. Less than a year later, the number of deals rose from 58 to 77; however, they dropped in value by 71.5%, according to a report from EvaluatePharma. Since then, industry dealmaking activity has remained steady, wavering slightly between

drug, by pharmacy. The provider can also determine which pharmacies may have better prices, which tiers and options the patient has, and can communicate that to the patient. The hope is that the patient will then be prepared for what comes their way in the pharmacy; unexpected high prices and PA forms often leave patients frustrated and walking out of pharmacies without prescriptions.

The prescribing HCP can even let the patient know if they have a pharmacy benefit that limits the number of times that the individual can fill their prescription at retail before having to move to mail order.

"The benefit is that the physician is aware of benefit information at the time of writing the prescription, allowing for proactive decisions such as seeking additional patient-support services," says Lacy. So, while it makes the physician and patient more informed, the need for patient-access services to help patients with the most difficult cases does not go away.

"The PBMs are changing—CVS/Caremark purchasing Aetna, for example, signaling the continued focus to drive efficiency in the pharmacy chain," says Nicole Hebbert, vice president, patient access and engagement, UBC, and a member of *Pharm Exec*'s Editorial Advisory Board. This e-Enabled investment by patient-access program vendors and specialty hubs creates solutions to seamlessly move patients/physicians to vendors and PBMs quickly so that they can get access to medicines faster and without calls and faxes, explains Hebbert.

"And as part of that efficiency, we can save on pharmacists' overload from being on the phone," she says. "It's a motivated movement."

— Lisa Henderson

quarters in 2016, before rising by 19 deals in the last quarter.

Despite an increase—no doubt due to J&J's acquisition of Actelion, completed in June—the deal count plummeted significantly (-35 deals) at the start of 2017 compared to the same period the previous year. According to Evaluate, the drop was attributed in part to lack of clarity on tax reform at the time (as mentioned, the GOP tax bill was passed in December).

Last year's decrease in volume of deals, experts point out, was by no means consistent, which may hint that underlying demand and activity remains healthy. While some of the challenges in recent quarters may linger, dealmaking is poised to increase in the near future, experts believe. PwC predicts that pharma companies will continue to turn to inorganic methods to supplement growth and innovate their business models.

Glenn Hunzinger, PwC's US pharma and life sciences deals leader, said in a recent PwC *Deals Insights* report, "While we saw a decline in deal values during Q3 2017, we continue to be encouraged by the discipline employed across the sector, most notably in the pharmaceuticals and biotech subsectors. As we look forward, pent-up demand and available firepower indicate M&A will likely be the tool used to achieve the industry's growth agenda."

EU/UK

In 2014, the greatest uncertainty for Europe involved the impending EU Parliament elections. A year later, *Pharm Exec*'s Brussels correspondent, Reflector, noted "stirrings of hope" regarding the appointment of the new team. Yet, Reflector also hinted at a dissension within and among the EU institutions and between member states. The UK vote in June 2016 to leave the EU has left the pharma industry with uncertainty, creating contention surrounding Brexit and, until recently, the relocation of the European Medicines Agency (EMA). It was decided in November to move the EMA to Amsterdam.

Before the Brexit vote, *Pharm Exec* noted that the biggest questions for the industry in the UK—should it indeed decide to leave—would be the impact on regulatory processes and market authorization of drugs. The prospect and then reality of Brexit left many wondering if the drug approval process in the UK would still fall under EMA post-secession.

An article in the *Financial Times* last year reported that the UK's health secretary, Jeremy Hunt, and business secretary, Greg Clark, said "the UK would like to find a way to continue to collaborate with the EU, in the interests of public health and safety."

— Christen Harm

New Year, Next Steps in Digital Transformation

Five predictions on evolution of data and predictive insights that could be critical for pharma go-to-market strategies

With 2018 off to a roaring start, now is the time to reflect on the journey the life sciences industry has taken over the last 12 months and chart the trends we see on the horizon for 2018—especially those on big data and predictive insights.

1. Data is still the belle of the ball

The healthcare data landscape is more complex than ever, with exponential growth in the sources and types of data available. Extracting insights—the right insights, at the right time—from the available data is crucial to the kind of personalization that is now required for commercial success. At the heart of these insights, however, is the data—as is the ability to connect, link, and interrogate big data, little data, and disparate data, ensuring that the insights are multifaceted and multidimensional.

Historically, the task of connecting and analyzing data fell on humans such as analysts and consultants. Now, the body and diversity of the data is so significant that it's necessary to utilize computed analytics and machine learning to manage and link the data for timely and actionable insights. Artificial intelligence, and in particular machine learning, will be a core underpinning of any winning big data or digital transformation strategy in 2018.

Another important step in the digital transformation journey is breaking through the data silos that exist between business units and technology teams, and gain efficiencies from the data being created and purchased.

2. The customer journey gets 'digitized'

Life sciences companies are increasingly looking at ways to build value "beyond the medicine" and offer complementary services and value-added, integrated care solutions. Frequently these include service centers, where patient-reported outcomes and other feedback create insights into the care continuum and all that it entails, from pricing to delivery.

These data points—patient experience, disease progression, treatment, disease management, preventive measures, and beyond—are crucial to commercial initiatives, as a growing number of payers are asking for the comprehensive impact of medicines on patients or mandating that companies track the patient journey. Capturing this data, and integrating it back into the company's strategic go-to-market approach, however, is not so simple. Each point of engagement creates "digital exhaust." Just as a wisp of exhaust trails a car's tailpipe, new data elements generate an important digital trail that can be used to create a more personalized approach to commercialization and customer engagement.

3. Predictive insights become programmatic

Our personal consumer experience with technology is setting the standard for technology with ease of use and intuitive, relevant delivery of information and insights. Companies like Google, Facebook, and Amazon collect enormous amounts of data to analyze our historic activity and predict our future preferences. They position recommendations, in the form of products or advertisements, in a highly targeted way, wrapped in a seamless user experience. We are served with what we need next, before we even know we need it.

This is the north star for life sciences companies; as they implement more comprehensive go-to-market strategies to address pressures in the healthcare ecosystem, they also need to reexamine the technology platforms and applications their commercial organizations are using, and provide a powerful, "programmatic" delivery of the customer journey to sales and marketing teams.

It is now critical to engage with, and influence, a broader group of decision-makers to successfully create access to, and adoption of, a medicine or therapy therapeutic. Additionally, it's important to understand where "customers"—providers, payers, patients—are within the buying cycle and treatment journey. This extensive and complex go-to-market approach demands that life sciences companies make better use of a broader body of data and use predictive, programmatic insights from this data to guide their strategy. For 2018, it will be a business imperative to connect more disparate data sources, process and analyze them, and operationalize these with programmatic

WILLIAM KING is Founder and Executive Chairman of Zephyr Health

recommendations to deliver an experience akin to Amazon's product recommendations.

4. Customer relationship networks gain influence

Leading life sciences companies are taking steps to analyze and leverage networks within the healthcare landscape to maximize the impact of their commercial efforts and ensure improved returns on their investment in go-to-market initiatives.

The number of stakeholders shaping the decision-making for appropriate treatment and intervention continues to grow, and the relationship between these players—prescribers, physicians, payers, organizations—influences these decisions, positioning network-based decision-making as the new normal.

Whether with structured networks, like integrated systems of hospitals, physician practices, health clinics, and provider networks, or unstructured networks, it has been difficult for life sciences companies to develop a commercial approach that can successfully navigate these networks. In fact, these relationship networks can be defined and connected by subtle factors, such as physicians being co-authors on publications or guidelines, co-investigators on key clinical trials, common education or residency at medical schools, or shared patient management due to referral or management of multiple comorbidities.

Effectively understanding these networks of influence requires a sophisticated approach that goes beyond information captured from field personnel and taps into the multiple, external data sources that can collectively populate any gaps. In a recent survey of more than 110 biopharma leaders in sales and marketing roles, 71% said they believe that the behavior of a healthcare provider (HCP) or organization (HCO) is heavily influenced by their relationships with other HCPs/HCOs, but less than 30% of them are using, or are even able to analyze these relationships. In 2018, organizations that leverage technology to identify and analyze these relationship networks, and integrate the resulting insights in their go-to-market approach, will see their competitive advantage accelerate.

> For 2018, it will be a business imperative to connect more disparate data sources, process and analyze them, and operationalize these with programmatic recommendations to deliver an experience akin to Amazon's product recommendations

5. Multichannel marketing goes 'artificial'

The life sciences industry is highly skilled at understanding the return on investment for discrete engagement initiatives targeted at a specific stakeholder group, such as non-personal promotion to physicians or direct-to-consumer campaigns focused on specific geographies and demographics. Today, marketing leaders must optimize the channel mix, investment, and messaging across multiple stakeholders and networks.

A data-driven go-to-market strategy requires broader use of derived insights to determine the best multichannel strategy, spanning both sales and marketing. For 2018, improved personalization of both content and delivery channels will be top of mind for biopharma marketing leaders. This means they need more dynamic, real-time feedback data from these same channels—field force and non-personal.

Additionally, companies need to coordinate, measure, and enhance activities across multiple internal customer engagement teams. This includes market access teams targeting pharmacy benefit managers or health insurance companies, national account teams interacting with integrated delivery networks, sales representatives detailing physicians, and all the complex interactions that span across these networks. At the campaign or product level, this translates to additional complexity for sales and marketing programs that span field activity and multichannel marketing.

Just as machine learning is paramount to connecting the multitude of data sources that underpin these efforts, augmented (or artificial) intelligence will support the increasingly dynamic, data-driven evolution in multichannel go-to-market.

While 2017 gave us a glimpse of the potential for technology to integrate broader data and extract deeper insights, 2018 will be the year when leading life sciences companies take the next, most crucial step in digital transformation, and put data and predictive analytics at the forefront of their go-to-market strategies. PE

Novartis Oncology

Changing the practice of medicine

At Novartis, we harness the innovation power of science to address some of society's most challenging healthcare issues. Our researchers work to push the boundaries of science, broaden our understanding of diseases and develop novel products in areas of great unmet medical need. We are passionate about discovering new ways to extend and improve people's lives.

NOVARTIS

HEALTHCARE & LIFE SCIENCES REVIEW

SWITZERLAND

The Great Pioneer

Three momentous events defined the Swiss pharmaceuticals and life sciences industry in 2017. Firstly, the emerging field of modifying and deploying a patient's own cells to fight cancer received a massive boost when Novartis secured FDA approval for the first-ever chimeric antigen receptor T cell (CAR-T) cancer therapy. Secondly, the highly acclaimed Swiss biotech, Actelion, was acquired in an unprecedented USD 30 billion all-cash deal. Thirdly, Swiss pharma exports surpassed a value of CHF 80 billion (USD 80.9 billion) bringing a net trade balance in at around CHF 47.9 billion (USD 48.5 billion), by far the highest of any country in the world. Each of these developments, in their own way, point to the growing relevance and influence of Swiss pharma and life sciences on the world stage. What is less publicized is the highly innovative and inspirational role that Swiss firms are also currently playing in reshaping the pharma value chain and contemporary paradigm of healthcare provision.

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FRESH TACTICS FOR THE WAR ON CANCER

Switzerland has long positioned itself at the vanguard of countering cancer; a disease which the WHO predicts will reach an incidence rate of 22 million new cases per annum by 2030. Pertinently though, Switzerland's trailblazing spirit in facing down this major public health threat never ceases to impress.

First came Novartis' unprecedented decision to assemble a global business unit (or 'firm within a firm') dedicated solely to developing and launching innovative oncology medicines, thus enabling the company to deploy a nimble outfit, with speedy decision-making power especially suited to accelerating the development and commercialization of new generations of cutting edge cancer therapies.

Then, this year the Swiss giant unveiled 'Kymriah,' the first CAR-T immunocellular therapy, approved in the United States for the treatment of individuals with B-cell precursor acute lymphoblastic leukaemia. "Basically, this constitutes a highly personalized and game-changing therapy in which T-cells are drawn from a patient's blood and reprogrammed in our cell processing facility. These genetically coded T-cells are subsequently infused back into the patient to potentially hunt down the patient's cancer cells," describes Bruno Strigini, CEO of Novartis Oncology.

However, beyond Novartis, a multitude of Swiss life science firms are furiously busy reconsidering how to go about treating and managing a disease that is no longer necessarily a death sentence. "There is a whole new market segment materializing that pertains to cancer supportive care," points out Saad Harti, president and founder of Legacy Healthcare. "If you think about it, cancer can increasingly be regarded as a chronic illness because many people are today surviving the acute stage of the disease, but ending up with a substantially reduced quality of life following the affliction," he reasons.

"Because cancer hits you everywhere, synthetic chemical medicines with onerous side effects often have to be utilized to counter the initial impact, but it makes little sense, however, to be prescribing additional drugs carrying yet more side-effects. Far better, wherever possible, to instead resort to reaction-free botanicals at this particular stage when the patient is already highly medicated," he argues. Legacy's lead candidate, CG428, a botanical hair lotion that helps re-establish the natural balance of the hair cycle when disturbed by chemotherapy and hormonal cancer treatments, strives to do exactly that.



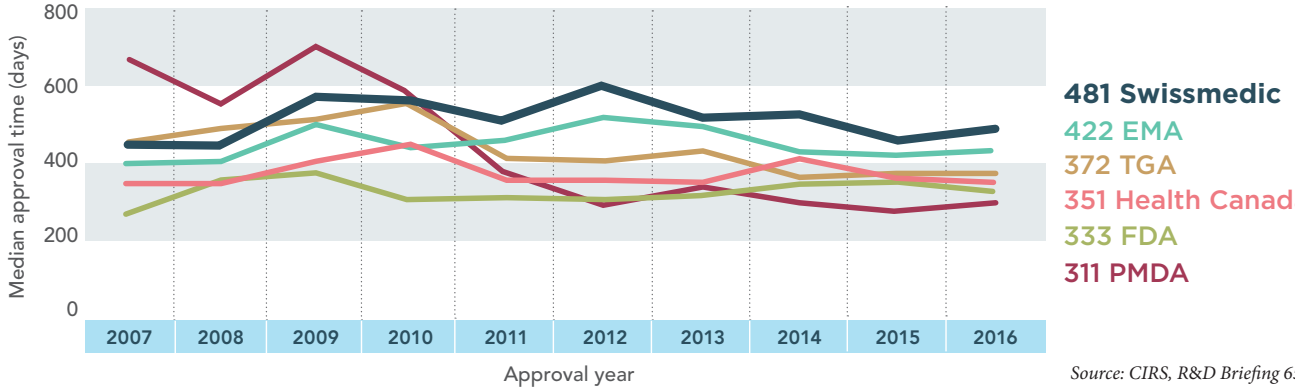
Petra Doerr, head of sector Communication & Networking, deputy executive director, Swissmedic; Bruno Strigini, CEO, Novartis Oncology*; Jean-Paul Clozel, CEO, Idorsia

Nor is this an isolated example. Other local entities like the medical device firm, Stratpharma, have been arriving at much the same conclusions. "Right now, we are moving towards oncology, specifically radiation oncology… One of our products - StrataXRT - is for the prevention and treatment of radiation dermatitis. We take the management and treatment of radiation dermatitis and do it in a completely different way, by changing the way the symptoms are handled," explains CEO and founder, Darren Kerr.

"Eight of the top ten cancer drugs today are biologics or biosimilars. You have TKInhibitors, EGFR and PDGFR inhibitors, for example, each of which targets cell parts and molecules which are also involved in the functioning of the skin. Patients treated with these new therapies can therefore develop rashes and radio-sensitization. While we have new radiation machines that have skin-sparing technology, these

*** Please note that the interview with Bruno Strigini was conducted in October 2017. Bruno Strigini has subsequently announced that he will retire from Novartis Oncology in early 2018.**

NEW ACTIVE SUBSTANCE (NAS) MEDIAN APPROVAL TIME FOR SIX REGULATORY AUTHORITIES IN 2007-2016



Source: CIRS, R&D Briefing 65

biological targeted therapies are running in the other direction. There is greater efficacy, but you get drug rashes as a side effect. Our products work to significantly reduce these drug rashes in a non-pharmacological way, and they constitute a fantastic medical breakthrough," he affirms.

A NEW COHORT OF ADVENTURERS

Switzerland's pioneering contribution to going beyond the boundaries of medicinal science is not confined to the urgent matter of oncology. Even the most cursory glance across the nation's bio-valleys and life sciences hubs uncovers a myriad of SMEs active at the sharp end of new discovery.

Neovii's flagship product, Grafalon for example, has attained great acclaim for its potential to prevent chronic GVHD after stem cell transplantations. "Historically, the product was used to prevent acute rejection of the organ during transplantation. It has been developed into a stem cell transplantation setting; a development that has been well documented in relevant medical journals," recalls CEO, Juergen Pohle.

"We have seen opportunities to develop the product further. For example, we can transfer the product into allogenic paediatric stem cell transplantation and hub flow haploidentical stem cell transplantation. We are also looking at opportunities to enter autologous stem cell transplantation as well. This aspect of pharmaceutical study has been brought to our attention through recent scientific publications. So essentially, we are looking at expanding Grafalon's value both from a patient's and a physicist's perspective. Specifically, we are interested in cells that are transplanted into the patient. The potential is huge," he assesses.

Another homegrown innovator, Polyphor, has invented an entire new class of antibiotics called Outer Membrane Protein Targeting Antibiotics (OMPTA). "A new class for Gram-negative pathogens of this ilk had not been witnessed for over 40 years. This is an area where there is an increasing and enormous medical need, and Murepavadin, the frontrunner of this new category is looking extremely active against resistant strains, which will be major news if it successfully passes phase III trials," exclaims CEO, Giacomo Di Nepi.

Darren Kerr, CEO, Stratpharma

Juergen Pohle, CEO (as from January 2018), Neovii Pharmaceuticals

Geistlich, meanwhile, a family firm that dates back to the 1850s, has been innovating bone graft technologies and collagen based-products for regeneration in the dentistry and orthopedic sectors. "We started early on with tissue and bone as a main focus before branching out into underserved areas where we can make a real difference to patient lives," remarks the company's CEO, Paul Note. "We work hand in hand with universities and some of the best specialists in the field in other institutions worldwide and are incredibly proud to rank as one of only a handful of companies that holds in-house research and development resources in these areas."

Yet others are engaged in defining entirely novel fields of therapeutic enquiry. Biognosys's main focus is the decoding of the proteome, an activity that its founder, Oliver Rinner, claims "will impact the life sciences more than the genome revolution." Proteins constitute the most significant functional elements in the body. The human physiology is almost entirely run by proteins in regards to cellular structure, enzymes, and receptors. The purpose behind the creation of Biognosys has been to better understand the mode of action of various drugs and biological processes by understanding the changes in the protein levels and activation," he proclaims.

Paul Note, CEO, Geistlich

Oliver Rinner, CEO and founder, Biognosys

What then nourishes this abundance of locally implanted pioneers? Some would say an incredibly supportive ecosystem and a talent catchment pool encompassing some of the sharpest scientific minds. "We are fortunate to be able to bank upon a highly efficient local infrastructure with easy access to exactly the caliber of scientists that we require," laughs Note. "The highly-skilled talent available here is immense. The country also has a very positive attitude towards innovation and business as well as a reputation for being extremely stable politically. This backdrop allows independent companies to put reliable long-term plans into action," agrees Pohle.

Another driver could well be the dramatic success story of biotechs like Actelion that stand as role models and reference points. J&J acquired Actelion earlier this year for a mighty USD 30bn. The deal was unique in that nobody was laid off, Actelion's project pipeline was not disrupted, and the development capabilities were spun off to form a new independent entity called Idorsia. "There was no value destruction. We have to be the only start-up that sets out with 650 people! … That pretty much sums it up. I sincerely hope that we can act as a model for others to follow in how to conduct M&As intelligently and non-destructively," urges Jean-Paul Clozel, Actelion's former owner and now CEO of Idorsia.

He does sound a cautionary note for anyone striving to copy his achievements, however. "Past success is the biggest enemy of future success. Just because you have succeeded in the past does not mean you will necessarily succeed in the future. This has been true with the creation of Idorsia … You need to be constantly reinventing yourself. Idorsia's story should be viewed as a reinvention. I do not want Idorsia to turn out as an Actelion clone. If anything, it has to be an improved Actelion, an 'Actelion-plus' if you like," he counsels.

OUTSOURCED MANUFACTURING: AT THE ELITE END OF THE SPECTRUM

Switzerland remains both influential and relevant in global pharma circles not just for the obvious core activities of research, discovery and marketing, but also for its prowess in outsourced manufacturing. This might seem surprising considering the comparatively high cost of Swiss labor relative to the rest of Europe, let alone further afield. "There's no denying that Swiss manpower is expensive, but when you measure us in terms of quality at source, you'll find Switzerland located right at the top of the leaderboard," counters Marc Funk, COO of Lonza Pharma & Biotech. "This country ranks very highly for doing things right first time and for established trust so it is clear that manufacturing, where these sorts of attributes are highly prized and valued, has an important role to play within the local economy. This is something that is readily understood and appreciated by our partners and clients," he continues.

Indeed, those seeking to manufacture high grade, complex pharmaceuticals are increasingly drawn to reliable, high performance and efficient environments like Switzerland. "You just have to look at the direction of outsourcing trend horizons and the abundance of companies that, having initially relocated to places with a meager cost of labor, subsequently reverted back to host countries that are quality-at-source friendly … Ultimately there's a great deal of truth to the saying: 'That which is cheap is always too expensive!'" laughs Funk.

The same rings true for active pharmaceutical ingredient (API) producers. Synbias Pharma, which took a strategic decision to relocate to Switzerland back in 2011, is a case in point. "We secured our first credit line from the European Bank for Reconstruction and Development which was a very important milestone for the company's development because it enabled us to invest in our own fermentation plant and rely on our own raw materials ... before long we found ourselves dominating

the world market for anthracycline antibiotics," recalls Marina Lugova, executive VP for business development.

She considers their unique selling points as quality, process innovation and efficiency. "The foremost challenge in our segment constitutes the regulatory requirements, which are becoming ever more stringent, so the most sought-after criteria tend to be quality and safety. Our clients have been working with us for over a decade and will continue to do so because of our track record and dependability on the quality front and the trustful relationships that we have managed to forge. Our most eye-catching feature is the purity of our APIs, and the fact that our products are truly best in class, matching the very highest European and American standards," she affirms.

Lugova also agrees that the sorts of efficiency savings, productivity levels and intelligent processes that they are able to leverage in an advanced ecosystem like Switzerland more than outweigh any labor cost drawbacks. "We are renowned for the extent of our process innovation which is reflected in our portfolio of different patents and our cost structure… Our capabilities started from API production and we integrated backwards into fermentation building new competencies and expertise all the while. Being in Switzerland and utilizing Swiss talent has enabled us both to outsmart some of our competitors and create our own intellectual property," she confides. "Switzerland also provides us with unparalleled opportunities for fundraising so as to further develop the business," she adds.

Naturally, Swiss API providers tend to concentrate on the most sophisticated categories where the value additions are most pronounced. "We hone in on the more complex molecules that would be most difficult to emulate," says Peter Kaufmann, CEO of Selectchemie. Their flagship product, Caspofungin takes a time-consuming 34 fermentation steps for the API to take form. Consequently, few companies around the world possess the necessary capabilities to fabricate it. "Caspofungin must be stored at minus 70 degrees Celsius, shipped at minus 20 degrees and is kept in a vial form. Initially we had expected clients to buy the dossiers through a down payment and a finished dosage form, but interestingly, this was not the case. The process is actually so complicated that buyers would prefer to purchase the finished product than look to assemble it themselves, so we now have to oversee that step as well," he admits.

A Novel Format of Partnership

Marc Funk, COO, Lonza Pharma & Biotech

A joint venture between Lonza and Sanofi for a combined facility in the southern Swiss district of Visp has raised eyebrows for disrupting traditional Pharma-CMO dynamics. The initiative, with an initial investment of roughly CHF 290 million (USD 294 million) shared equally between both parties, puts Lonza's Ibex™ manufacturing concept to the test, and essentially couples flexibility in facility-build-out with fully tailored business models.

"By joining forces in this way we realized that we could reduce our individual requirement to build assets whilst remaining responsive to future needs and uncertainty in a more efficient and effective manner. When you have a joint plant that can cater to both Sanofi's and Lonza's manufacturing capacities, you end up with a very different type of facility than if we had both gone ahead and built our own separate factories. Ultimately, we can better plan capacity usage and anticipate production cycles as well as ensure better usage of the entire possible output," affirms Lonza's Pharma & Biotech COO, Marc Funk.

"Often, when a large pharma player possesses an important commercial molecule, the tendency is to build a large-scale asset that is then not maximally used because the numbers of units required is not necessarily clear in advance. By making this facility versatile enough to cover the type of loads that we will need to produce alongside those of Sanofi, we can ensure that, at all times, the plant will be operating at maximal capacity irrespective of fluctuations in market demand," he reasons.

Still Room for the Family & Friends-style Firm

Marina Lugova, executive VP for business development, Synbias Pharma

Many of Switzerland's most avant-garde, pioneering life sciences outfits constitute family and friends-run small and medium sized businesses. Laboratoires Diepharmex, which two decades ago disrupted the ear-hygiene market with what was then a groundbreaking product to remove earwax, Audispray, serves as a good example. The family-run firm has today lost none of its original pioneering spirit and recently set about launching a brand new high-end OTC product line called "Micro H" for the treatment of haemorrhoids, which notably is presented in a single dose form, in contrast to conventional cream-based therapies.

Benjamin Rousselot, the company's VP for strategy and corporate development, believes Laboratoires Diepharmex's nimble organizational setup, family ownership, entrepreneurial mindset and flat reporting structure have all been key ingredients in the sustained success of a firm that today manages to punch far above its weight.

"I think our major strength is our very fast decision-making process. Our management model is collaborative, and it is my duty to make sure that everyone has the opportunity to bring new ideas to the table. Usually, it does not take long for our management team to decide whether to work on a new idea or not. Most of our competitors are Big Pharma companies. In France for instance, we go head-to-head with heavyweights such as Sanofi, Bayer and Pfizer. Typically, these companies tend to require a rather longer decision-making process. Being a first mover and making the right decisions first time round can be challenging, but we also know that being able to outstep the competition in this way can also deliver a decisive market advantage."

A similar dynamic can be witnessed with some of the more creative service sector firms. Synbias Pharma, a contract manufacturer that produces highly potent APIs used in cancer therapies, started out in 1995 as a small entrepreneurial venture between a doctor, an oncologist and several chemists. The firm subsequently gone on to achieve worldwide renown and success in the niche of anthracycline antibiotics, but still retains the original start-up mindset.

"We place great emphasis on the makeup of our team and make a point of not accepting status-quo people," confides Marina Lugova, executive vice president for business development. "We remain a small company with 80 employees in total spread across Germany, the Czech Republic and Switzerland and firmly believe that being small confers an important advantage… As you know, many Big Pharma companies are suffering from a lack of innovation. Even companies such as Pfizer and GSK are currently spinning off parts of their business into start-up companies, because they emphasize the value of start-up culture. I am immensely proud to be able to say we possess this culture."

ADVENT OF THE FLEXIBLE SERVICE PROVIDER (FSP)

With both the pharmaceutical and biotech industries increasingly looking to outsource critical functions from manufacturing to clinical research, Swiss service companies and multinationals operating locally have been quick off the mark to embrace fresh business models more aligned with evolving needs. "One trend that we perceive is that the nature of our interactions with our clients is undergoing a profound shift and we now find ourselves serving a whole range of different types of actors often displaying distinctive requirements," reflects Lonza's Marc Funk.

"Looking back, the mainstay of our work used to be about supplying manufacturing batches and conducting development work across modalities for small molecules and biologics. That offering alone is no longer sufficient for the present-day context. The sheer number and type of actors populating the biopharma landscape today has radically evolved. Moreover, the kind of therapies being developed these days is also quite different. The rise of complex biologics and the sensitivities around their handling imply a great deal more risk," he notes.

The ramifications of all of this has been a surge in demand for bespoke, custom-made solutions. "Current clients require greater flexibility in terms of how to address future volumes and commitment to reserving manufacturing capacity in the light of the uncertainty and unknowns inherent in the prevailing drug development process. Furthermore, there is also a real desire on the part of our customers to reduce the costs and increase the efficiency of the manufacturing part of the value chain," he reveals.

Switzerland's contract manufacturers have therefore been responding by repositioning themselves as 'flexible service providers.' Thomas Huber, CEO of Skan Group gives an example from his niche segment of pharmaceutical conditioning. "Quite frankly the new world of medicinal science has been revolutionizing the filling manufacturing business. Small batches and personalized medicines are now very much the name of the game… Today, customers require the production of as many as four different products on the

Peter Kaufmann, CEO, Selectchemie

Stefan Frefel, CEO, Bilfinger Industrial Services



Jonathan Koch, group president, R&D Laboratories, Covance; Vicky Levy, head of life sciences and healthcare, Deloitte; Thierry Mauvernay, president and delegate of the board, Debiopharm

same machine in the same shift. The challenge is thus not so much the filling process itself anymore, but rather how to clean the machinery between batches to ensure there is no cross-contaminations between products," he explains.

German entity, Bilfinger Industrial Services, which undertakes not just pharma manufacturing but a suite of industrial service solutions including assembly, maintenance and process technologies, equally finds itself being compelled to be more versatile. "Things are changing quite a lot, even for our big clients. One year, they could have full production, the next they could have lower production, and we have to adapt to such fluctuations," recounts Stefan Frefel, the company's CEO for Switzerland.

The business logic underlying the contract manufacturing process has therefore matured to better reflect the trajectory of demand. "A decade ago, everybody was talking about scaling up. The aim was basically to acquire a small production line and then, providing everything went well, to purchase a large one so as to mass-produce products for the global market. Today we are instead speaking about scaling out. You buy one small line, then a second, a third and so on. Rather than having one mega line housed in a single production center in a choice country, you'd nowadays prefer to have four small lines distributed around the world and be able to produce much more locally," elaborates Huber.

Service firms also need to be much more internally agile so as to be able to simultaneously cater to the demands of differentiated client groups. "Lonza has many Big Pharma customers on its books that already possess in-house capabilities. The nature of our relationship with them is very much one of true partnership. They require a partner to manage their overall manufacturing strategy and we view ourselves, in many respects, almost as an extension of their assets. The style of relationship we have with them is much more entwined than that of a traditional outsourcing service provider," explains Funk.

When it comes to servicing biotechs, however, the nature of the relationship is rather different. "Generally, they do not possess in-house capabilities or any kind of know-how about the manufacturing process. In many cases, they are seeking not just the use of our facilities, but also the expertise on identifying optimum manufacturing and development solutions for molecules where the destiny of the end product is often still fraught with uncertainty. In this case we serve as a one-stop-shop CDMO and partner of choice that can fulfill their full range of needs, whilst helping them buffer volatility," he says.

A similar pattern of disruption exists in the clinical research domain, where leading CROs have been jockeying to inject more flexibility into their service offering. "There are many more types of organizations participating in pharmaceutical development today, from small biotechs to mid-size biopharma, to large multinationals … These clients have a wide range of different needs and as a top-tier CRO you have to be versatile and flexible enough to respond to these forces. The one-size-fits-all template of yesterday is no longer fit for purpose," concurs Jonathan Koch, group president for R&D Laboratories at Covance, a leading US

clinical research specialist whose state-of-the-art Global Central Lab in Meyrin, in the canton of Geneva, stands as the largest of its kind in Europe.

"Some clients come looking for a partner that can be highly and truly full-service in nature. Others may be conducting the trial predominantly in-house, but nonetheless require an element of support maybe in the data resources or monitoring or programming or oversight. Flexible service providers are agile enough to conform functionally to whatever is required at a particular moment and that is precisely why we have been making some strategic acquisitions that can bolster our capabilities and help us deliver the precise breadth and depth of service that each and every one of our clients are seeking. Our recent purchase of Chiltern, for instance, allowed us to round out those FSP solutions by bringing us added strength in areas such as clinical analytics," he recounts.

Karen Huebscher, CEO of Solvias, a world leader in contract research, development and manufacturing (CRO/CDMO) very much mirrors these assertions. "The complexity of drug development today is driving a tendency towards outsourcing to the point where the pharma companies of the future might well be holding the platform, with significant activities actually in the hands of third parties. Meanwhile, the service industry is transitioning from a pure transactional model towards much more of a partnering, full project scope interaction," she observes.

"As a Swiss entity with a staunchly scientific, perfectionist, precision technology mindset, we have to show ourselves flexible enough to adapt to customers' real needs… sometimes they will require speed and functionality, rather than the gold-plated, luxury version and we have to be versatile enough to deliver that. If what a client really needs is a Citroën 2CV, then we can't be insisting that they take a Ferrari," she warns. "Developing a drug is a massive undertaking and our mission at the end of the day is to understand our customers and help them bring products to the market faster, efficiently and more cost effectively."

The nature of the work conducted has also been changing. "We've overseen a re-balancing of our service portfolio over the last four years between small and large molecule development. Our business line dedicated to large molecule development has been registering strong growth of in excess of 20 percent and biologics are constituting an ever greater share of our workload," she concedes.

Karen Huebscher, CEO, Solvias

ACTIVELY SHAPING THE FUTURE OF PUBLIC HEALTHCARE

It is not merely in client relations that locally implanted firms have been reconsidering their way of doing things, but also in their engagement with payers, healthcare providers and the public health system. "While US companies are innovating through partnerships with biotechs and health technology specialists and can often claim to be at the forefront of a lot of the scientific advancement, I see the European companies, generally speaking and especially the Swiss, leading the charge in endeavoring to tackle the main challenge associated with contemporary healthcare: how to manage the health of populations that are getting older and sicker and in need of affordable treatments, but simultaneously innovative ones that can counter the disease profile of today," analyses Vicky Levy, head of life sciences and healthcare at Deloitte.

She perceives many Swiss pharma companies "reaching out to health systems and paving the way for new financial arrangements that reduce costs to the health systems, whilst still rewarding the industry for the patient outcomes they achieve with their medicines."

The Botanical Pathway to Patient-Centricity

Saad Harti, president and founder, Legacy Healthcare

Today, the vast majority of medicines that patients ingest in mature markets tend to be chemically synthesized, potent compounds with unique mechanisms of action, often carrying adverse side-effects, untested long-term toxicities and unknown drug-drug interactions. Saad Harti, of Legacy Healthcare, believes that such a treatment paradigm is "far from desirable in a world in which fewer people are dying from acute illnesses, but more patients find themselves needing to live with and manage prolonged chronic disorders that are non-life threatening, but still, requiring day-to-day treatment."

Pointing to FDA studies that suggest that adverse drug reaction has become the fourth biggest cause of mortality in the United States and spending on unhelpful drug combinations is an unnecessary and counterproductive drag on health expenditure, he is advocating the widespread use of botanical therapies to manage the symptoms of chronic disease. "Current treatment pathways, in many cases, no longer fit with what patients truly expect from a treatment for their chronic disorders: improve quality of life, without triggering other issues so we are suggesting the use of botanics as a complementary therapy to address these shortcomings," he posits.

Legacy Healthcare, therefore takes botanical ingredients that people consume on a regular basis and turns them into drugs. "Our drugs exhibit fewer, and considerably less severe side-effects than synthetic drugs. They inherently register much better tolerance profiles because rather than extracting a single molecule, we take everything so what is being consumed is as close as possible to what people would be ingesting naturally on a regular basis. Incidentally this also means that we can collect data from the public domain, which you obviously cannot do with a brand new, untested chemical entity, so there is even an acknowledgement of a priori safety," he maintains.

Raising the necessary capital to bring a rich pipeline through to fruition is complicated, however, with many venture capitalist funds wary of gambling on such a young and fresh sectoral niche. "It's only a matter of time before we reach a tipping point, though, where botanics go mainstream as an important part of the therapeutic mix... Legacy Healthcare views itself very much as one of the first movers that will trigger this effect," he confidently predicts.

First among them is probably Novartis, which has shown itself open to negotiating entirely new performance-related payment mechanisms for some of its latest-generation therapies. "We put a great deal of thought into how to price Kymriah, which is delivered to each patient just once because this is intended to be a one-time, highly effective treatment. Our approach was to collaborate with the United States Centers for Medicare and Medicaid Services (CMS) and come up with an outcome-centered arrangement whereby they only pay if the patient proves responsive to the therapy and also indication-based pricing, which together represent a first-of-a kind arrangement for the United States," details Bruno Strigini.

Debiopharm's president Thierry Mauvernay meanwhile is appealing to health authorities to rethink the pricing of antibiotics, especially given that recent KPMG studies demonstrate that this important category of medicines adds, on average, some ten to 15 years to human life expectancy, compared to only five or fewer for many oncology products.

"In our view, the prices of many antibiotics are set far too low and not sufficiently appealing enough for industry because it's difficult to cover the costs of developing new antibiotic compounds. Changing the business model is therefore an urgent necessity. Considering that new targeted compounds are only being deployed by physicians when absolutely necessary so as to minimize the spread of antibiotic resistance, we believe a smarter way of doing

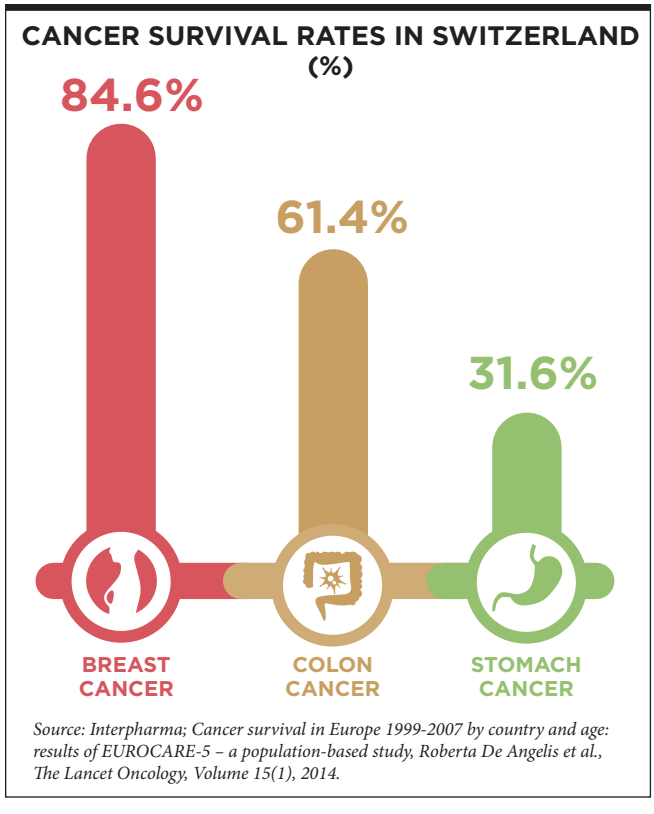
things would be to have antibiotic price policy mirroring that of the insurance industry," he advocates. "For instance, for a hospital with 100 beds, you could end up paying a fee each year for the right to use a targeted antibiotic. With 200 beds the amount would be doubled regardless of whether they actually end up being filled or not," he elaborates.

SHIFTING REGULATORY GEARS

Interestingly, the Swiss authorities themselves recognize the importance of proactively working hand in hand with the industry to lower the costs of drug development so that innovative therapies can become more affordable again. Certainly, the regulator appears attuned to industry concerns and proposals. "It is undeniable that the regulatory burden today is more onerous that in the past and therefore we are sympathetic to the [drug companies'] predicament and the effect that this has on end pricing. I would point out, though, that a more stringent regulatory regime is the natural consequence of enhanced patient safety. The solution is to work together to optimize the regulatory process without any reduction in standards. I think that a more pragmatic flexible approach to clinical trial design is the direction in which we are all headed. Already you see the FDA taking a lead in rethinking and reevaluating the parts of the clinical trial process to make it more fit for purpose under certain specific circumstances. Swissmedic can be expected to follow suit," declares Swissmedic executive VP, Petra Doerr.

Benjamin Rousselot, vice president, strategy and corporate development, Laboratoires Diepharmex

She notices a rising tension between a demand for faster access to innovation from patients on the one side, and a call for enhanced regulatory stringency and oversight on the other, but is confident that competing interests of safety and innovation, flexibility and regulation, and price can be balanced through deep collaboration involving all stakeholders. "We have established a working group with representatives from different patient consumer organizations that meets four or five times a year to discuss precisely this sort of conundrum. Right now, we are at the stage of exchanging insights and information so that all stakeholders around the table understand each other and the different motivations in play. There are ways to square the circle, but the starting point has to be common understanding. Pharma companies obviously seek



Source: Interpharma; Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE-5 – a population-based study, Roberta De Angelis et al., The Lancet Oncology, Volume 15(1), 2014.

faster approval timelines and payers demand affordability, but this cannot come at the expense of safety and no one really wants us to degenerate into a soft-touch regulator," she explains.

Equally forward-looking on the part of the Swiss regulator is their overt acknowledgement that, in an era of upheaval in drug development characterized by post-market access clinical studies, predictive modeling and the fast emergence of personalized therapies for which the genetic variances make clinical evidence impossible, the regulatory framework itself is in need of modification so as to adapt to the times. "The way that drugs are being developed is being rethought as new technologies become available and scientific awareness in areas like genetics increases. We do therefore feel a need to update and mature some of our legacy processes to make them more fit for purpose and aligned with the current environment. To ensure that we are proactive in doing this we have implemented a system for horizon scanning that seeks to identify trends and developments likely to affect us in the future. It is clear that we have to move with science and be flexible and versatile enough to react in time to unfolding developments," admits Doerr.

AGENTS OF DIGITAL DISRUPTION

Yet another way in which the Swiss are managing to shift the paradigm across drug discovery, targeted medicine and healthcare provision is in facilitating the big data revolution. "The incorporation of disruptive technologies in the medical world is definitely ten years late, not due to a lack of interest, but because of regulatory difficulties" opines Debiotech's CEO, Laurent-Dominique Piveteau. "The political environment of Switzerland is crucial for this type of development."

He continues, "Switzerland boasts a strong image for respecting privacy of data thanks to its heritage stemming from the banking sector. Despite the current negative connotations surrounding the financial sector, it must be outlined that from a personal data and legal perspective, alongside a stable political context, Switzerland ranks highly. If you have a private, semi-public or public institution keeping your data, you want to make sure as a patient that over time this will remain the same and that things won't change. You don't want a change in the political environment tomorrow which will make digital data available to everyone. That is why stability is a crucial aspect."

Petra Exner, regional director for the DACH countries, INSIGHT Health; Tobias Haber, managing director for Switzerland, INSIGHT Health

Already, locally active firms have been quick in mastering the arts of secure life science data. For instance, INSIGHT Health, which acts as a data provider and consultancy, is proud of the scope of its capabilities. "We have assembled an experienced team of 25 professionals dedicated to taking care of data quality processes and so forth. This way we can minimize the risk of mistakes and have full control over the data. Our secure solutions begin with the data we receive: it is already anonymized. Not even a malevolent person could retrieve personal information from our data," enthuses Petra Exner, regional director for Germany, Austria and Switzerland.

"Moreover, if we zoom into micro regions, we never look at a single data source like an individual pharmacy. We combine several pharmacies in one 'brick.' Our bricks never fail to

contain more single sources than the data protection law requires. This way we can work with very detailed data but simultaneously can ensure the highest level of confidentiality. We therefore demonstrate that market transparency and data security are both simultaneously possible," adds Tobias Haber, the company's managing director for Switzerland.

Nor should the extent of these achievements be underestimated. "With fast and transparent supply of data analyses we can create value additions for the pharmaceutical developers, health insurance, scientific institutions as well as decision makers in healthcare provision," claims Exner. "Today we see ourselves as a solution provider for the entire marketplace supporting our customers individually and efficiently in all manner of ways – from product launches and optimization of sales force to portfolio management and patient-know how – while at the same time affording them access to a DACH-wide database that provides an overview on the performance of brands and products across Germany, Austria and Switzerland simultaneously."

Another entity, Appriver, which is regionally headquartered in Switzerland has been making headway in securing medical records so that they

Bringing Responsible Access Global

Jaron Spigel, CEO, Farmamondo

With two billion people globally, predominantly in low and middle-income countries, having little or no access to medicine, a select group of service providers have emerged to try and further dialogue between pharmaceutical companies, regulators, healthcare professionals and patients on the issue of expanding access to medicines. At the forefront of this group is the Swiss-based Farmamondo, which draws on over 100 years of history to help provide access to medicines to patients with unmet medical needs around the world.

As Jaron Spigel, Farmamondo's French-born CEO notes, "The whole world is moving toward patient-centricity and our efforts to facilitate patient access to medicines are at the center of this." Farmamondo operates through two distinct lines of business: Named Patient programs within Switzerland, whereby certain patients can access products prior to their approval and Global Early Access, helping provide fast-tracked access to medicine in over 65 countries worldwide, across all continents.

A key tenet of Farmamondo's business model is that the access to medicine that it helps facilitate must be 'Responsible' and 'Ethical.' The 2013 case of Josh Hardy in the USA - where social and traditional media launched a campaign to pressure Chimerix to allow access to a novel, yet unapproved therapy, despite the patient not fitting the drug maker's access requirements - further highlighted the need for more 'Responsible' and 'Ethical' access. Manufacturers, biotech companies, regulators and healthcare professionals alike called for more stringent guidelines for providing access in a responsible manner, separate from societal or media pressure; an area in which Farmamondo specializes.

In terms of the advantages of being based in Switzerland, as well as privileged access to Swiss pharmaceutical giants such as Novartis and Roche and the country's thriving ecosystem of innovative biotechs, Spigel highlights that "Providing responsible access to medicine is a concept that indisputably fits the Swiss DNA – a combination of being compassionate towards other people, exporting product and services, strict regulatory compliance and international scope."

First Impressions and Immediate Priorities

Jeff Dufour, country manager, Pfizer

Having previously focused his career on the US market and with a stellar reputation at Pfizer HQ in New York - including in his most recent role as vice president global marketing Inflammation & Immunology - Jeff Dufour took on his first country manager position at Pfizer Switzerland in July 2017.

In terms of first impressions, Dufour feels that Switzerland "is a country that punches well above its weight class and has a level of sophistication that is genuinely surprising for a country of only eight million people. Almost everything about Switzerland is incredibly advanced and the country is at the cutting-edge in a number of different aspects." Swiss healthcare also stands out to Dufour as "particularly interesting from an American perspective because if you take the logical conclusion of President Obama's healthcare reforms in the US; it's Switzerland… When you look at that level of sophistication here, it shows that the dream of Obamacare can work!"

During his first half year in the role as head of an already successful affiliate, Dufour has prioritized bringing more clinical trials to Switzerland, noting that "We do a lot of clinical trials in oncology here, but there is probably room for us to do more in paediatrics and rare diseases for example. Switzerland is an ideal place to do clinical trials for any of the more sophisticated therapeutic areas because the levels of being able to find patients and treat them effectively is very high here." Due to the Swiss healthcare system's similarities with the US, Dufour sees the potential for Pfizer Switzerland to play a bigger role at the cutting-edge of the global organization as something of a test market, noting that "we may be in a place to look at new models for areas such as gene therapy."

Looking towards the future, Dufour foregrounds the importance of increased stakeholder dialogue and closer relationships in Switzerland; foreseeing "a fundamentally different relationship with the insurance providers and the Federal Office of Public Health (FOPH)." In terms of Pfizer Switzerland's role in the global organization, Dufour hopes "that we can establish ourselves as the pilot launch country in Europe."

can be digitally handled by the appropriate practitioners and patients. "All our services are cloud-based; therefore, our customers' mission-critical information never leaves Switzerland. In the healthcare industry, email encryption has been an extremely strong area for us. For example, when a doctor sends an x-ray file to a patient via email, it is like sending a postcard at the post office. The perception is that nobody can view this information, but the reality is that administrators can see this confidential file at any time. Therefore, we have developed an end-to-end encrypted technology, so the file can be sent privately by the doctor and the patient can encrypt the message," expounds Rocco Donnino, executive vice president of corporate development. Tellingly, moves are already afoot within Switzerland to incentivize life sciences-related start-ups to get on the digital bandwagon. Debiopharm, for example, has set up a special 'Innovation Fund' that invests in smart data companies to acquire know-how. "Our industry badly needs strong data management competencies to progress … we look for companies developing solutions in precision medicine – digital therapeutics, digital markers, clinical decision support systems, patient monitoring tools and smart drug discovery and development tools – areas where utilization of big data and AI can create tremendous improvements for patient care. The goal of this CHF 150 million (USD 151 million) fund is to build a portfolio of smart data companies and build the future together," envisions Mauvernay.

This is vitally important because often life sciences entities are ill-equipped to fully utilize and exploit the data that they are collecting. "A crucial aspect is the relationship between data generation and data interpretation. The latest technological developments have enabled the acquisition of huge data sets but ultimately researchers want to test their hypotheses and answer their research questions. Converting data into knowledge is often the hardest step in this process as few biologists come from a statistical or data analysis focused background," observes Biognosys founder, Oliver Rinner. "Moving forward, I think data interpretation can become a main value driver. By using reference data sets, for instance, we can offer contextualized information that has been built up over many years," he points out.

Already some prominent actors along the pharma value chain have been making headway. Novartis has been astute in leveraging Big Data, predictive modeling and advanced analytics to shorten the time between finding a target and proof of concept, leading Bruno Strigini to speak of the "dawning of a golden age of innovation brought by a gathering convergence of the worlds of science, technology, biology and IT."

Covance, for its part, has earned the epithet of 'the Google of Blood' for its amalgamation of LabCorp's proprietary lab data with Covance's operational data to better inform drug discovery. "The skill is to identify which specific disruptive technologies are going to be the most productive and effective tools, because there usually is a lot of attrition involved so you can't pursue them all simultaneously," admits Jonathan Koch.

Food for Thought in Cancer

Program puts a new—and very real—spin on patient nutrition

When Susan Bratton, founder and CEO of Savor Health, started approaching pharmaceutical companies four years ago with the idea that nutrition and customized recipes should play a part in disease treatment, she did not immediately receive a warm welcome.

But Bratton was persistent. She had seen firsthand how difficult getting the correct nutrition was for patients, particularly after a life-altering diagnosis—and especially if the disease or its side effects impacted the patient's ability to eat, drink, or cook.

Fast forward to 2017. That's when Bratton's company struck a partnership with Merck & Co. around its new program, *Your Cancer Game Plan*, an awareness campaign focused on helping people with cancer and their loved ones tackle their emotional, nutritional, and communication needs.

How it started

In the past, the pharma industry generally didn't consider this type of nutritional intervention a priority, Bratton says. Yet, as she explains to *Pharm Exec*, a secondary problem to arise after a cancer diagnosis can often be malnutrition. In that context, it makes total sense.

Take head and neck cancer, for example, which was the first disease that Merck focused on when it launched *Game Plan* with the help of NFL Hall of Fame quarterback Jim Kelly, a head and neck cancer survivor. This condition describes a number of different tumors that develop in or around the throat, larynx, nose, sinuses, and mouth. According to Merck, many people with head and neck cancer face unique challenges as a result of surgeries and/or treatments that impact a person's appearance, speech, smell, taste, ability to swallow, and sight.

This is where Savor Health comes in. The company not only creates recipes with balanced nutrition so that a patient's body has the nutrients it needs to fight disease, but Savor Health also takes into consideration disease-specific problems that might arise for the patient. For instance, an individual who has head and neck cancer may have a hard time swallowing. Savor Health offers recipes that provide the specific nutrition required, but can also be prepared in a way that makes it easier for the patient to eat.

"Making sure your body gets the nutritional support it needs may help to keep your strength up through a treatment course," says Bratton. "Adapting and managing meals is important for people living with head and neck cancer, and we've developed helpful tips and recipes that are designed with this in mind."

Close to home

Besides medical research to back up Bratton's nutritional claims, the executive has also witnessed the toll of cancer on a personal level. Her friend, Eric, was diagnosed and later passed away from glioblastoma, a rapidly spreading cancer that begins in the brain. His experience was her inspiration for starting Savor Health.

"He was just a lovely human being," recalls Bratton. "All of his friends adored him. He had a personality that was bigger than life. [After his diagnosis] he lost so much weight, because he was unable to eat."

Bratton praised Merck for creating *Game Plan* and recognizing that there are many factors besides the drug itself that can influence a patient's success when it comes to their treatment. And, although this program is not specifically attached to any value-based reimbursement, it doesn't mean that it couldn't be in the future.

According to Merck, many people living with head and neck cancer may experience different physical and emotional hurdles than those with other forms of cancer. To help address these challenges, *Game Plan* provides support and resources, including tips from Kelly, the former Buffalo Bill, on how to remain positive, and healthy recipes for those with the disease.

In addition to Savor Health, Merck also partners with the Head and Neck Cancer Alliance (HNCA) and Support for People with Oral and Head and Neck Cancer (SPOHNC). The organizations have supported the head and neck cancer community for nearly six decades combined. HNCA provides patients with resources that can help them manage their emotional needs at every stage of their journey, while SPOHNC offers guidance for patients in communicating with family and friends and expressing themselves in an effective way.

As Bratton points out, *Game Plan* takes a holistic approach to the treatment of head and neck cancers by truly going "beyond the pill" to support those afflicted in all areas of their life. PE

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