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SEPTEMBER 2018
COMMERCIAL INSIGHTS FOR THE C-SUITE
VOLUME 38, NUMBER 9

THE GLOBAL CEO

Disruptive Innovation: Managing the New Normal

Paul Perreault, CEO and managing director of Australian-based CSL Limited, a multinational player in the growing plasma protein therapy space.

UBM

URGENT – FY2019 GDUFA Fees Just Announced... Increased by 17%

A New ANDA Holder Program Fee Approach Under GDUFA II

Fees

The ANDA Holder Program fee schedule for Fiscal Year 2019 was just published by FDA and fees increased by 17% from last year. Fees due to the FDA by October 1, 2018 are as follows:

Tier	ANDAS Owned	Fee
Small	1-5	$186,217
Medium	6-19	$744,867
Large	20 or more	$1,862,167

This is a significant expense for many firms. Those with a modest number of ANDAs will again be paying substantial sums for drug products they don't currently market or that are identified as Discontinued in the Orange Book. For a small or medium-tier company this can be a dramatic hurdle to retain the assets they worked so hard to own. And, yes, discontinued ANDAs are still considered approved ANDAs for user fee purposes unless the approval is withdrawn.

In addition, a one-time marketing status report was required to be submitted to the FDA earlier in 2018, identifying the submission as "MARKETING STATUS REPORT / ONE-TIME UPDATE." While there has been **no guidance as to what happens to the ANDAs identified as "not marketed"**, one scenario may be they will be either moved to discontinued status or have their approval withdrawn.

Penalties

What is the **penalty** for not paying the program fee?

1) If the fee is not paid within 20 calendar days after the due date, the parent company will be placed on a **publicly available arrears list**.
2) Any ANDA submitted by the applicant or its affiliates **will not be received**.
3) All drugs marketed pursuant to any abbreviated new drug application held by such applicant or an affiliate of such applicant shall be **deemed misbranded**.

A Solution

For the second year, **ANDA Repository, LLC**. offers significant user fee relief and a solution for companies that have discontinued ANDAs or drug products not currently marketed. Like with a parking lot, car owners need space for their cars, whether in use or not. Only here, in exchange for the space (and a fee) car owners transfers title of the car to the parking lot owner. The former car owners can, with appropriate notice, resume ownership when they choose to use the car again. Since the parking lot owner has enough cars, this venture benefits for all the parties involved, and the cars remain safe and secure.

In the example above, the car owner is an ANDA owner, and the parking lot owner is **ANDA Repository, LLC** which charges ANDA owners an annual fee that is significantly less than the ANDA Holder Fee that the FDA charges small or medium sized firms.

There is NO need to pay excessive fees or be forced to withdraw your valued assets due to short-term market conditions, capacity constraints, API supplier issues, etc.!

Alternatively, if your choice is to WITHDRAW your ANDAs, we may be interested in purchasing them!

The FY2019 GDUFA Generic Drug Applicant Program Fee is due October 1st so please contact us soon!

Phone: +1-570-261-1901 Email: info@andarepository.com

Specialty Supply Chain Decisions

THE DEFINITION OF A SPECIALTY MEDICATION, according to Randy Maloziec, VP of BioPharma Relations for AmerisourceBergen's US Bioservices, is a medication that meets at least five of the following criteria: biotech, injectable, has a mandated FDA REMS requirement, chronic condition, specialist initiated, special handling, a cost in excess of $6,000 a year, and a limited pharmacy or wholesale distribution network. Now, specialty medications and specialty pharmacy are two different things. You don't always need a specialty pharmacy to handle a specialty medication, and specialty medications don't always go through a pharmacy. So what is a specialty pharmacy? Maloziec told a recent audience at CBI's Reimbursement and Access conference that no one really understands it.

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But misunderstandings aside, he said, "It's trendy, it's hot, and everyone wants to get into it." There is a lot of activity in the specialty pharmacy space, which includes expanding entrants from health systems and disrupters; consolidation of existing specialty pharmacies; technology costs; working capital limitations; and new and evolving partnerships, to name a few.

Further, Maloziec outlined the medical-pharmacy vertical integration. The large insurers, Cigna, Aetna, UnitedHealthcare, and Blue Cross Blue Shield, feature their own PBM—Express Scripts, CVS Caremark, OptumRX, and Prime Therapeutics, respectively. Then the specialty pharmacy aspect is also listed respectively with Accredo, CVS Specialty, BriovaRx, and Alliance Rx.

This issue of *Pharm Exec* focuses on specialty pharmaceuticals, not pharmacy. But in today's drug development environment, where orphan designations are on the rise, more complex cell and gene therapies continue through the pipeline, and specialty drug spend grew 9.3% while traditional drug spend fell 4.0% in 2017, the two are linked. How a company decides to distribute its drug through the supply chain requires a discussion that most likely includes a specialty pharmacy.

In an article from Charlie Bell, a senior director at Archbow Consulting (see page 21), he states, "specialty pharmacy brings to mind high-touch therapies supported by hubs, financial assistance, free drug programs, home nursing, and dutifully developed clinical protocols." But, conversely, the specialty pharmacy market is seeing more products on the low-end range of specialty drug prices. And, he continues, "that trend is driving the demand for specialty pharmacy program options that accommodate lower-cost therapies."

There is no doubt that supply chain decisions are paramount in a product launch strategy. At Veeva Systems Commercial Summit earlier this year, CEOs from Otsuka and Spark Therapeutics discussed their launch decisions (see bit.ly/2NnGr2c). Otsuka chose a limited launch for its digital medicine—Abilify MyCite, co-developed with Proteus—to learn as much as it can about data handling implications in a challenging disease state. Spark, with its one-time gene therapy, Luxturna, is opting for a limited centers-of-excellence model, where patients travel to the drug, basically eliminating the need for a complex supply chain or high-touch ancillary services.

Outside of Spark and Otsuka's limited distribution choices, other game-changing therapies require cold distribution in the supply chain, adding to additional complexities.

How a company decides to distribute its drug through the supply chain requires a discussion that most likely includes a specialty pharmacy

Game-changing therapies aside, there continues to be a rough road for what one speaker at the CBI conference termed the "prescription journey map." That is the journey from the prescription to actual medication delivery to the patient. That process should be as seamless as possible, which leads to the many enhanced patient services pharma initiates—including hubs, stopgap plans, rebates, prior authorization service and more.

With the current positioning of HHS Secretary Alex Azar to eliminate rebates, and put more transparency into the drug pricing process, PBMs and health plans appear to be the most against this move. On one hand they want transparency from pharma, but they don't want to provide that same level of transparency themselves.

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Paul Perreault: The Global CEO

Julian Upton, European and Online Editor

Pharm Exec speaks with CSL Limited CEO and Managing Director Paul Perreault about the realities of running the global, Australian-headquartered specialty biotech—and the new normal for multinationals in navigating the fast-encroaching era of disruptive technologies and new priorities in innovation and R&D.

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Cover Photo: Tom Grimes

Specialty Pharma

The Move to Mainstream

Michelle Maskaly, Senior Editor

While definitions for "specialty drug" vary—and distribution and pricing/reimbursement factors remain complicated—this once-niche treatment market may be poised to steer the future of prescription medicine and patient care.

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Specialty Marketing: Beyond Big Data

Julian Upton, European and Online Editor

With specialty companies getting smarter in applying their big data insights to product marketing, the true commercial potential of machine learning and predictive modeling may soon be within reach.

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By Charlie Bell

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17th Annual Industry Audit

Return Performance

Bill Trombetta, St. Joseph's University, Haub School of Business

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Country Report: UK

Faced with looming uncertainties triggered by the upcoming Brexit, the United Kingdom's life sciences sector, which constitutes one of the last big remaining bastions of British industry, is not about to rest on its laurels.

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Learn how life sciences companies are using robotics and artificial intelligence to enhance patient care, what the funding landscape is in this sector, and what C-suite members need to do now to be at the forefront of this emerging technology.
bit.ly/2Pk8MqP

Episode 14: Bright Lights, Big Science
Nancy Thornberry, CEO of biotech startup Kallyope, talks with *Pharm Exec* about the growth of New York City as a hotspot for biotech incubators—and the challenges and opportunities related to space, location, recruitment, and funding. bit.ly/2wx9dan

Episode 13: Helming a Clinical-Stage Startup
Jeffrey Nau, CEO of Oyster Point Pharma, talks about what it's like working on diseases that don't get a lot of press, and offers up best practices in raising startup capital. bit.ly/2LDSYNc

Episode 12: Journey in Regenerative Medicine
Gil Van Bokkelen, CEO and co-founder of Athersys, a regenerative medicine company, discusses the decision to start the firm in Ohio instead of his native Northern California, and shares the secret to staying resilient in the C-suite amid heavy challenges.
bit.ly/2woXYAy

Pharmaceutical Executive PODCAST

Episode 11: Tackling Sports and Science
Former NFL star and current broadcaster, Solomon Wilcots, talks to *Pharm Exec* about the intersection of sports and biopharma, including his work in matching pro athletes who are passionate about a certain disease with biopharma organizations.
bit.ly/2Nubv0f

Episode 10: Mentorship vs. Sponsorship
Michelle and Christen host one of *Pharm Exec*'s Emerging Pharma Leaders, Sabina Ewing, vice president of business technology for Pfizer, who discusses the difference and importance of mentoring and sponsoring in business and pharma.
bit.ly/2wrgebI

Pharm Exec Webcasts

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bit.ly/2yR1Tts

Combination Therapies and Oncology Landscape
bit.ly/2JcY3Pf

Reader Feedback

Acquisitions are more viable than new product developments because of the high cost of developing novel products and the high risk of reimbursement that managed care causes for new products. With the plethora of established in-class products, generics, and biosimilars, acquisitions offer an exceedingly preferable way to hedge-off the high cost of new product R&D and the new drug application, or NDA, process while optimizing managed care reimbursement and return on investment.

Anonymous
"Does the Pfizer Restructuring Make Sense?"
bit.ly/2wqHXdq

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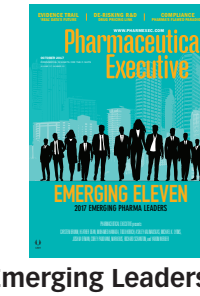
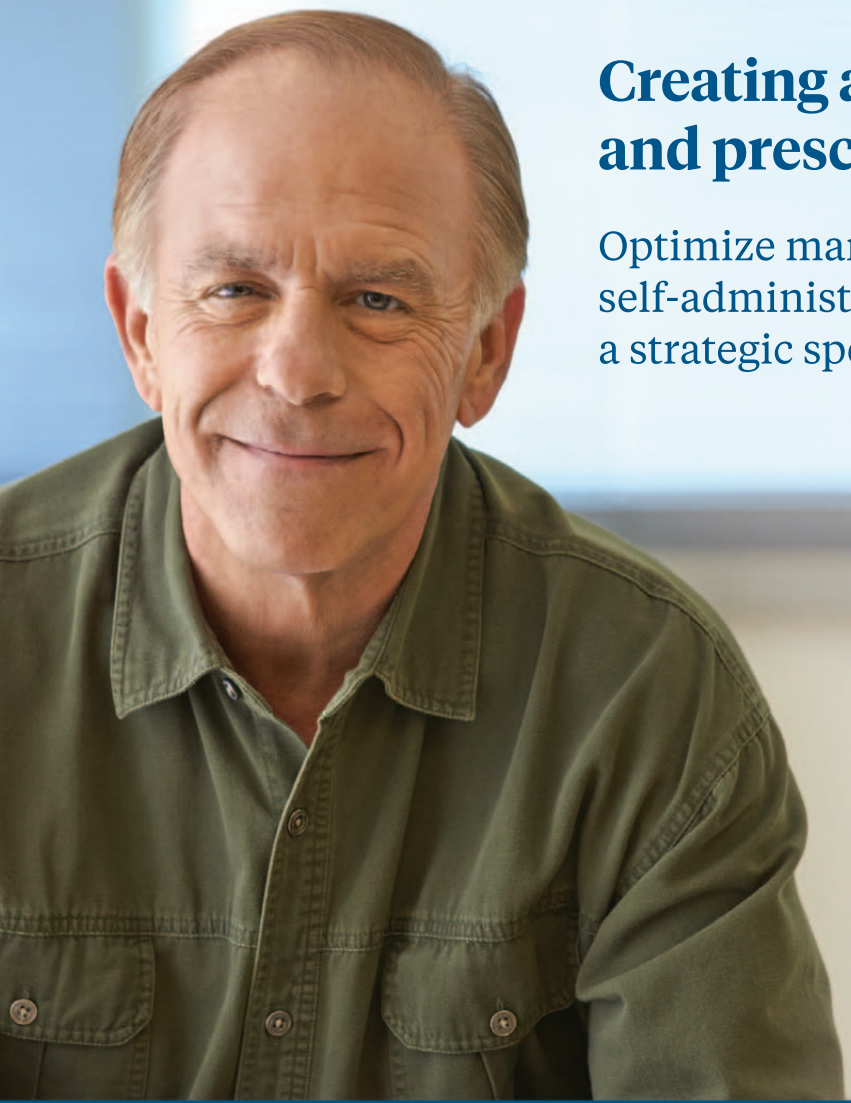


Emerging Leaders
In its annual feature, *Pharm Exec* recognizes a select group of industry executives whose peers and supervisors believe will change the future of pharma. We profile these emerging pharma leaders.



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FDA Struggles to Advance Biosimilars

New Action Plan aims to streamline development, but rebates and reimbursement block market access

A central strategy for enhancing access to more affordable medicines for the Trump administration, Congress, and FDA involves smoothing the pathway for the development and approval of high quality biosimilars and interchangeable biotech therapies. Yet, even though FDA has approved 12 biosimilars, only four have come to market since Congress authorized follow-ons eight years ago. Those delays cost American consumers more than $4.5 billion in 2017, according to a recent FDA analysis.

The main culprits are the lengthy patent challenges and difficult payment policies that stymie biosimilar coverage and prescribing. More complex testing requirements put the cost of developing a biosimilar at $100 million to $250 million per program, much more than the $10 million involved in producing a new generic drug. Consequently, biosimilars come to market at prices only 15% to 20% below the innovator, which often is not enough difference to drive reimbursement. In several speeches over the last six months, most recently in July at the Brookings Institution, FDA Commissioner Scott Gottlieb lamented the "anemic" growth of the US biosimilars market, blaming innovator rebating schemes and contracting practices for blocking less costly therapies from patients (see https://bit.ly/2L6u7kO).

Gottlieb also announced FDA's much-anticipated Biosimilars Action Plan, which lists a range of FDA initiatives for establishing a more efficient review process, including greater scientific and regulatory clarity for sponsors and tools for using modern analytical techniques (see https://bit.ly/2ux50Ct). Most observers found little new in the plan, but acknowledged potential benefits from expanding the Purple Book to make it more useful and from a possible data sharing agreement with European and other regulatory authorities to facilitate increased use of foreign comparators.

FDA also issued final guidance on biosimilar labeling, and more guidance documents are expected on biosimilar data analysis methods, managing post-approval changes, and demonstrating interchangeability with a reference product. To encourage greater uptake of biosimilars, FDA also plans more education of clinicians and patients on biosimilar safety and efficacy to address misconceptions that foster reluctance to prescribe and use these therapies. Biosimilar makers also anticipate that an efficient path for demonstrating product interchangeability with brands will help build prescriber and patient confidence in switching to the new products.

Challenging rebates

Meanwhile, FDA has set biosimilar user fees for 2019 based on an expectation that it will assess and approve 23 biosimilars in the coming year, and that more will come to market as a number of leading biotech therapies lose exclusivity protection. As of July 1, more than 60 biosimilar development programs to 31 different reference products were in the FDA pipeline, prompting the Center for Drug Evaluation and Research (CDER) to establish a new office to better integrate biosimilar policy and review functions to smooth the regulatory process.

But FDA efforts to streamline biosimilar testing and approvals will have limited effect on the market so long as "rebating schemes" or "patent thickets" continue to deter the entry of approved biosimilars, Gottlieb stated in his July speech. Brands "thwart competition by dangling big rebates to lock up payers in multi-year contracts right on the eve of biosimilar entry," he complained. And volume-based rebates further encourage health plans to require prior use of a brand before permitting access to a biosimilar, a requirement that the commissioner said has "no clinical rationale."

Gottlieb also expects FDA's Action Plan will support market competition by reducing "gaming" of FDA requirements, such as using risk evaluation and mitigation strategies (REMS) to prevent biosimilar makers from obtaining reference products needed for testing. But a main focus is on publicizing how the "rebate trap" permits pharmacy benefit managers (PBMs) and insurers to profit from the spread between list price and the actual rebated price for an innovator therapy, which can amount to hundreds of million dollars in annual revenues for plans. PE

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Paul Perreault: The Global CEO

Pharm Exec talks with CSL Limited's top executive about the realities of running the global, Australian-headquartered specialty biotech company and sustaining a strong focus in a fast-encroaching era of disruptive technologies and new priorities in innovation and R&D

Paul Perreault, CEO and managing director, CSL Limited, at CSL Behring's office in King of Prussia, PA. (Photo by Tom Grimes)

By Julian Upton

After graduating with a psychology degree from the University of Central Florida, Paul Perreault joined Wyeth-Ayerst Laboratories as a sales rep in 1981. At that time, he says, "I really thought I was going to retire as a sales rep. I didn't think about ever being a CEO; I didn't have this grand plan to climb the ladder." But his subsequent career path saw Perreault gain experience in a wide range of industry roles, including training, management, marketing, operations, and finance; he took on additional responsibilities and challenges and pursued opportunities that came his way "even if it did not mean a promotion."

After 16 years at Wyeth, Perreault joined Aventis Behring in 1997, where he held several executive positions before rising to executive vice president, worldwide commercial operations, with responsibility for all commercial and business development activities globally. The Australian-based CSL Limited acquired Aventis Behring in 2004; CSL Behring is now a global leader in the plasma protein biotherapeutics industry. Perreault became president of CSL Behring in 2011, and in 2013 was also appointed CEO and managing director of CSL Limited. Earlier this year, *The Australian Financial Review* named him 2017 CEO of the Year.

Pharm Exec sat down with Perreault to explore his leadership style and gauge the day-to-day realities of running a global specialty biotech company, as well as understand how he sustains a strong focus for CSL as new, disruptive technologies make their presence felt in the industry.

PE: *You studied psychology as an undergraduate. It may be a cliché to say that must have been useful in dealing with people, but how did it feature in your move to industry?*

PERREAULT: First of all, I needed to get a job. I graduated and I had bills to pay, so I started looking for one. I was familiar with the pharmaceutical industry a little and I was fortunate to get a position

in sales with Wyeth. When people think of psychology, they think of putting somebody on the couch, or mind reading or something. But it's really about the way people behave and understanding how organizations operate. So, it was natural for me to want to understand how people are motivated and how they have different desires and goals. And when you're in sales, that's very important because a doctor is not a doctor is not a doctor. They all come from different backgrounds, different schools. Like patients, they're not all homogeneous.

I would say that psychology helps with understanding human behavior and how people operate. Not that I would analyze people. However, working in the pharmaceutical industry also meant that I had to gain a broader understanding of the industry I was in and hone skills outside of psychology. I undertook medical training and courses at University of Florida medical school on a self-study program, which covered pharmacology, biochemistry, anatomy, physiology, medical terminology, etc., and I completed advanced business management training at the Kellogg and Wharton schools of business.

PE: *How does your current role and the culture of CSL continue to motivate you?*

PERREAULT: The main motivation is the ability to impact the lives of patients that we serve. We produce treatments for rare and serious diseases, therapies that are important to patients, of which many may have gone undiagnosed for many years. I know hundreds of patients personally. That gets me going every day because I know that people are depending on CSL and the therapies we deliver.

I don't do that alone, of course. The organization's 22,000 employees have a big impact on what we do, and what I love about our culture is that people are engaged in that process. Obviously, you'll hear the commercial people who engage with patient organizations talking about patients, but you'll also hear people in finance, people in R&D talking about patients. It's a culture that extends to our raw material supply, because a lot of our products are made from human plasma and proteins. Special donors come in every week to donate plasma. We connect them with patients at the very beginning; each of our plasma centers runs an Adopt-a-Patient program. Engaging with patients permeates throughout the entire organization. In fact, we were patient-focused before it was trendy. That's the culture that's maintained here, and it has to start with me. I can't just sit here and tell a department that they should be patient-focused.

CSL was started over 100 years ago by the Australian government as a not-for-profit agency committed to bringing essential medicines to the people of Australia during World War I when the supply chains from Europe were cut off. That patient focus, which was the core and foundation of the company at its inception, still hasn't changed.

> "I know hundreds of patients personally. That gets me going every day."

When CSL privatized from the Australian government and went public in 1994, it was a small company and it took an intense amount of focus to begin the process of globalization. But we leveraged our core competencies, our core adjacencies and synergies to grow the organization. It was about organic growth and doing those things in which we have knowledge and capabilities exceptionally well. We don't engage with M&A just for the sake of M&A. We continue to reinvest in the company—because I haven't found a whole lot better to reinvest in. We have done a couple of acquisitions and some licensing deals, but they are all in our area of focus. I think that's what differentiates us. We don't say we're going to build an area in oncology, for instance, just because 50% of R&D spend these days is in oncology. That doesn't mean it's the right place for CSL. You have to have discipline and focus.

PE: *How do you maintain that strong focus going forward?*

PERREAULT: We focus on the capabilities or the competencies we have. For instance, we just moved into transplantation. But we have current marketed products that have application in transplantation. We understand the products deeply, we understand the mechanisms of action, and we can see the applicability in this new area. Transplant is also an area where you don't need a primary care sales force of 2,000 or 3,000. We can do this within our organization. We already have the resources and the assets, we have the knowledge of the therapies, and we can see how it's applicable to what we do.

We have at least three products that we think are applicable in transplant and can really change the treatment landscape

for these patients. So, when people see us moving into a new area, it's because we already have expertise in that area, in the development and manufacturing, in the product profile, or in our ability to really add value. We've seen other pharma companies go out and spend a lot of money buying another company. They grow it for a year or two, then they have to grow on top of that. Later you see them divest, saying "It's no longer core," which sometimes means, "We couldn't make it work." It disrupts the organization; it doesn't add value over the long term. It's really a matter of maintaining that focus.

PE: *What is the significance of CSL's Australian origins and activities on the way you go about your business now?*

PERREAULT: When CSL privatized from the government, there were a few things that the government required at that time. One was that the chair of the board needs to be an Australian citizen. Also, two-thirds of board members need to be Australian citizens, and the company has to remain listed in Australia. Because of our expertise and our size, we're now the fourth-largest company on the Australian stock exchange by market cap.

Australia is a key part of what we do, but it's also a market like the other markets we serve. We have manufacturing in Australia, which is part of our global supply chain along with other plants in China, Germany, Switzerland, UK, and the US. The way we operate is to make sure that those plants are integrated across the processes and across the product portfolios as much as possible. Australia is a key piece of that.

Australia is also our center of excellence for research and development. Our R&D group operates as a global function, but research in Australia is really the hub. We have hundreds of scientists in Australia doing our initial research and then they work with teams across our other research sites in Germany, Switzerland, and the US. It's kind of a hub-and-spoke model. We have over 30 university collaborations in Australia. If we were in Boston or San Francisco, we'd be competing with many others. But in Australia, we get to have a good look at a lot of the top science that comes around and that's why our research is still based there. What comes out of our research labs in Australia has a big impact on what we do for our future innovation.

PE: *What would you say are the critical skills for your role, and how have these changed over the course of your career?*

PERREAULT: The first is to focus on your strength and synergies and don't get distracted. That can be difficult because you get bombarded with so much stuff these days. Everything is global, everything's immediate, everybody's chasing the next shiny object. That focus is critical and leadership really needs to maintain that.

The second thing is collaboration. As a company, we have to act both locally and globally because we are engaging with global patient communities. Our partnerships with patients and advocacy organizations reach across the globe, so collaborating with and promoting early diagnosis and treatment of the conditions and the diseases are critical.

The third strength is communication. A lot of companies tend to act more *internationally*, I would say. They focus on the US and Europe and then everything else. We actually work *globally*. Whenever we do something in one country, we aim to understand how it impacts everywhere else. So, someone is on the bad end of a phone call every night. It's one thing to be dealing between the US East Coast and Europe, or Europe and Australia, or Australia and China; but if you're dealing with Australia, Asia, Europe, and the US, somebody's going to be up late or up early. That's a skillset that some organizations struggle with.

We do advise people that if you work here and you're on a global team, it's going to take some stamina. Everybody knows the direction of the company and the culture and the expectations. You have to know your priorities and how they align with the core adjacencies and competencies. Then you have to execute. Execution is critical. At CSL, we work every day like somebody's life depends on it, because it does.

The way things have changed

FAST FOCUS

» Before being named CEO and managing director of the parent company, Paul Perreault was president of CSL Behring, where he was responsible for overseeing operations in more than 25 countries, including major manufacturing sites in the US, Switzerland, Germany, and Australia.

» Perreault was previously chairman of the global board for the Plasma Protein Therapeutics Association.

» CSL Limited was founded by the Australian government in 1916 and not privatized until 1994. The company focuses on plasma therapies, recombinant proteins, gene therapy, and vaccines.

is the focus you have to have from an innovation and an R&D perspective. I can remember the 1980s and 1990s; they were very good days in the pharma business. But there were a lot of "me-too" products coming out. In today's market, if you try to do that, you're not going to get reimbursement. You're not going to get access, patients won't get access because governments won't pay. You have to beef up your skills in terms of pharmacoeconomics. You have to look at how the clinical trials are actually organized so that you get the data that you need from a pharmacoeconomic perspective that shows the benefit to the patients and to the healthcare system over time. That's something that we really have to focus on as an industry to make sure that we are making a real difference and that innovation wins the day. If you're not innovating, get out of the business, because you won't be here for the long term.

PE: *Looking to the future, how does your vision for CSL fit into where the industry is heading?*

PERREAULT: I'm focused right now on 2030, and there's a few things that give me confidence that we're in pretty good shape. There are not many companies that have products like ours, which are basically donated from a human and go back into a human. We serve patients now in over 60 countries, and that translates to a lot of people with rare diseases, for instance, hemophilia. We are getting closer to gene therapy for hemophilia, but currently 75% of the world's hemophilia population is either undertreated or not treated. There are still a lot of patients to serve around the globe. There is a strong demand, especially for our largest portfolio of products in the immunoglobulin space. But I don't have my head in the sand, thinking that this is going to go on forever.

> "If you're not innovating, get out of the business, because you won't be here for the long term."

Our organic growth will come from sustaining our ability to invest in new therapies. We're looking at disruption, we're looking at new technologies. Last year, for example, we bought California's Calimmune, which is developing an *ex vivo* hematopoietic stem cell (HSC) gene therapy, CAL-H, for the treatment of sickle cell disease and beta thalassemia. While the first area is sickle cell, it's a platform with potential for treatments for a wide range of other rare diseases that complement CSL's business. So instead of chasing down every new and, as I said, shiny object that comes out of, say, CRISPR technology, or choosing a new gene therapy, this is more of a platform approach, which gives us optionality.

PE: *Does it get easier or harder to look so far ahead?*

PERREAULT: I think it's going to get harder because of the technologies around the delivery of medicines, and the transformation of cells and genes. In 2030, for example, will you still be able to be a researcher, developer, a manufacturer, and seller of pharmaceuticals, or is that chain going to be disrupted somewhere? Is the black box where all this magic happens going to be owned by a GE, for instance, who take the majority of the value in the chain?

In some ways, this industry hasn't progressed as much as I'd like to see. We're not innovating in supply chain operations as much as the consumer sector has already done. I don't necessarily want to be the first cab off the ranks, as we say, but I also don't want to be the last cab off the ranks. I want to be near the front edge of thinking about these things, whether it's AI, whether it's blockchain, you name it. These are things that are happening and we need to pay attention.

PE: *As you mentioned, being a leader at CSL takes stamina. How do your outside interests help keep you focused?*

PERREAULT: I love the outdoors. I love the fresh air, being in nature, hiking, skiing. Those are the things I like to do. You fit these things in as often as you can, but these roles, at least from my experience, are pretty all-consuming. I don't want my job to become who I am, though, because it can all go away in a heartbeat. I try to get to the gym every day. I was at the gym this morning for 45 minutes just to get the blood pumping and get things going, because if you don't, it can be pretty draining. I guess I'm fortunate that I'm used to it and I don't need as much sleep as some other people.

I walk the halls, I do a lot of managing by walking around. I was on the road for more than 200 days last year. People in our company know me. And that's because I feel I need to be *in* the business. I need to understand and see what's happening. I can't just sit in the office and think I know everything. You have to be authentic—in leadership, authenticity is vital. PE

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Specialty Pharma's Move to Mainstream

While definitions and classifications of what constitutes a specialty drug vary—and pricing and reimbursement factors remain thorny—there is little argument that this once-niche treatment market may be poised to steer the future of prescription medicine and patient care

By Michelle Maskaly

Ask three people how they define specialty pharmaceuticals, and you will likely get three similar, but slightly different answers. "A [standard] definition of specialty drug has yet to be adopted," says Sheila M. Arquette, executive director of the National Association of Specialty Pharmacy (NASP). "The FDA, employer groups, health plans, and pharmacy benefit managers (PBMs) all have their own ways of defining this drug category."

The NASP views specialty drugs as more complex than most prescription medications and used to treat patients with serious and often life-threatening conditions. Those include cancer, hepatitis C virus, rheumatoid arthritis, HIV/AIDS, multiple sclerosis, cystic fibrosis, organ transplantation, human growth hormone deficiencies, hemophilia, and other bleeding disorders. These medicines, in some cases can be taken orally, but often must be injected or infused and may have special administration, storage, and delivery requirements. Many of the injectable medications are self-administered in the patient's home. Infused specialty drugs are administered in various treatment settings, such as a patient's home with the support of a home healthcare professional, a doctor's office, or hospital, says Arquette.

At Cardinal Health, a distributor of specialty pharmaceuticals, it classifies this type of therapy in four ways. "Specialty products typically have one or more of the following characteristics: They are prescribed to small patient populations with rare, complex, or chronic conditions; they may be part of a complex treatment regimen or require ongoing patient monitoring; they may have special shipping

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and handling requirements, such as temperature controls; and they are usually more expensive than traditional pharmaceuticals," explains Joe DePinto, president, Cardinal Health Specialty Solutions.

A growing market

If anyone in your C-suite attended a specialty pharma conference 10 years ago, they might have been one of a handful of people in the room. But, as the annual Asembia Specialty Pharmacy Summit in Las Vegas earlier this year showed, this segment has grown exponentially.

Although organizers declined to comment for this article, the growing attendance was the headline of a company press release following the conference, boasting that the 2018 Asembia event set a new attendance record with over 6,500 attendees, and marked the thirteenth consecutive year of growth. It was also one of the most mentioned observations when *Pharm Exec* spoke with attendees, and was brought up during the general session, where one panelist recalled there being just several hundred people on-site in the summit's first year, with specialty pharma a then-niche market.

What factors are behind the surge in this market? Quite simply, it's innovation and money, experts point out. "This has primarily been driven by advancement of the science as well as a shift of capital investment to address patient and market needs," says David Rosner, principal and digital life sciences leader, Deloitte Consulting. "In addition to the increase in the number of specialty-focused pharmaceutical firms, nearly all of the major big pharma manufacturers have added specialty products to their portfolios and consider them key to their growth."

Randy Maloziec, vice president, biopharma relations, at US Bioservices, a part of AmerisourceBergen, echoed those observations.

"Nearly every pharmaceutical manufacturer has specialty therapies in their pipeline and it is universally accepted that the specialty marketplace will continue to see significant growth in revenue and overall pharmaceutical utilization," he says. "This growth—real and anticipated—is driving nearly every stakeholder in the market to develop solutions or capabilities to support these therapies. This could be everything from an integrated delivery network (IDN) opening its own specialty pharmacy to a payer seeking new ways to manage overall spend."

With so many companies entering the specialty pharma space, it begs the question, is what was highly specialized and rare now just becoming the norm?

A challenging environment

Growth is almost always followed by challenges. "One of the biggest changes is that specialty products continue to become more targeted and patient populations smaller, particularly as more gene-based and cellular therapies come to market," says DePinto. "These products face unique challenges in everything from recruiting patients into clinical trials, to determining how to efficiently distribute the product, to managing payer and reimbursement issues. Not only have the products themselves become more specialized, so has the approach to distributing and commercializing them."

"Not only have the products themselves become more specialized, so has the approach to distributing and commercializing them."

Another key change, according to DePinto, is the increased focus on security and traceability of products. Through advanced technology such as radio-frequency identification (RFID), he says it's now possible to ensure supply chain integrity and to track products at every point from the manufacturing plant to the site of care.

That logistical part of the discussion is critical, especially when it comes to advanced therapies such as gene and cellular therapy.

"Managing the logistics of CAR-T therapies, [for example], is highly complex because of their high value, temperature sensitivity, and the precise timing in which they must be administered to the patient," says DePinto. "It's important to have a scalable distribution network that can compliantly and efficiently transport these products to sites of care nationwide, as well as technology systems to monitor the exact temperature of each dose of medicine the entire time it is in transit. The network also needs clear, standard operating procedures (SOPs) to detail how it would handle any potential logistics risk to the therapy.

"Because of the precise timing requirements, it is critical for the logistics provider to communicate with the pharmaceutical manufacturer, the site of care, and other stakeholders, such as the patient hub, to ensure that all parties are aligned in their efforts to get the therapy to the patient at the right time. Even a minor delay could impact the efficacy

of the product and reduce the patient's chance of experiencing the best outcome."

Another major challenge facing specialty pharma is the shift from fee-for-service reimbursement to a value-based care model where physicians are reimbursed based on the quality of care and overall patient satisfaction.

"Under these new payment models, physicians are rewarded for reducing the costs of care and demonstrating improved patient outcomes," says DePinto. "For specialty diseases, the approach of managing a patient across an 'episode of care' can be very complex because specialty patients are often treated with multiple medications and receive different interventions at multiple sites of care, making it challenging to track results. For manufacturers of specialty medications, it is not enough for therapies to be safe and efficacious, they must also show they can deliver improved outcomes at a better value."

"It is not enough for [these] therapies to be safe and efficacious, they must also show they can deliver improved outcomes at a better value."

Adopting proactive digital health practices in a timely manner; connecting with patients while still staying HIPAA compliant; the volatile political climate that impacts regulations; and perfecting the possibly unachievable balancing act of keeping therapies affordable while also making a profit, were also all reoccurring themes at the 2018 Asembia Specialty Pharmacy Summit.

To hear more about these and other challenges, watch *Pharm Exec*'s video coverage from the event at https://bit.ly/2vJkMLa.

Problem solvers

US Bioservices is not a newcomer when it comes to developing solutions to the challenges of specialty pharma. For example, the company exclusively dispenses a medication for a rare, inherited muscular disorder that typically occurs in boys and causes progressive muscular degeneration. It was a first-to-market treatment for this condition and was approved in other countries prior to its clearance in the US. Initially, patients in North America could try the medicine if caregivers facilitated patient participation in a clinical trial or expanded access program, explains Maloziec.

But, when the drug was approved by FDA, suddenly patients that were already on therapy confronted questions such as if the new product would be covered by their insurance and if there would be medication gaps while going through the prior authorization process. Even with coverage, patients still faced affordability and access questions. Further, the specialists that supported the small patient population indicated for the treatment were specialty-naïve and unfamiliar with manufacturer-limited distribution networks and the prescription referral and prior authorization processes requiring patient and clinical information.

"Working closely with the manufacturer, we designed a program focused on continuity of care as patient prescriptions were transitioned and filled through our pharmacy," says Maloziec. "The program includes physician and practice education and a hub model that is clinically integrated with the pharmacy to ensure high-touch caregiver support and integrated data back to the manufacturer."

According to Maloziec, pharmacy experts help secure prior authorization approvals and letters of agreement, as well as copay and foundation assistance, to expedite the start of therapy. "This is one of many examples of our specialty pharmacy working in close partnership with the manufacturer and other healthcare stakeholders to implement a program that addresses the unique clinical profile of the therapy and the specific needs of the patient population," he says.

Future outlook

The specialty pharma trend in the life sciences doesn't seem like it's slowing down, or getting any easier. As scientists continue to innovate and develop novel therapies, the pricing, reimbursement, and delivery conversations will continue to get more complex.

"Specialty pharmacy will be the new pharmacy," Arquette told *Pharm Exec*. "As more drugs are developed and approved by the FDA as specialty drugs and the focus of these medications is the treatment of diseases that have been historically managed by small molecule therapies, specialty drugs will be the mainstay of prescription drug therapy." PE

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Beyond Big Data: Meeting the Specialty Marketing Challenge

With specialty companies getting smarter in applying their big data insights to product marketing, the true commercial potential of machine learning and predictive modeling may soon be within reach

By Julian Upton

As we advance to an age where almost every new drug entering the market will be a specialty drug, the word "specialty" itself may eventually become redundant. The theory and practice of pharmaceutical marketing, however, is being strongly guided and shaped by the tactical and technological advancements brought about by the challenges of communicating and commercializing specialty treatments.

Connecting with healthcare professionals (HCPs), care providers, and experts in multiple therapeutic areas is facilitating a more delicate balance of technology and human insight, and how marketers think about "traditional" patient populations is changing dramatically. Companies are striving to speak more effectively to individual patients with messages that are more relevant and personalized. In the next few years, predicts Sarah Alwardt, vice president of health and informatics and health and economics outcomes research at McKesson, pharma will move to catch up with the activities of companies like Amazon by providing "ultra-targeted messaging" driven by predictive modeling on big data sets."

The further advancement of specialty pharma marketing depends on the smart use of data. While data has been available and accessible to pharma for a long time, with data sets becoming far more sophisticated, "the hard part," says Paul Shawah, Veeva's senior vice president of commercial strategy, is piecing the data sets together and matching them around an HCP or care provider and, ultimately, a target patient population.

Specialty companies are using a wider volume and variety of data to optimize their route to market. In some specialty treatments, the number of patients that exist for certain diseases is very small, and even in broader patient populations a drug treatment or therapy may only be relevant to a subset of that population. "The trick is identifying where those patients are and intervening at the right point in time," Shawah told *Pharm Exec*. "To do that, you have to stitch lots of different data sets together so that you can identify patterns and then quickly shift your resources based on those patterns."

For orphan diseases with very limited patient and prescriber populations, "there isn't really any room for error," says Remy Sukhija, senior vice president of commercial operations, Otsuka America, Inc. "As an industry, we are not poor when it comes to the amount of data we have. What we need as a next step is to improve our ability to shift from descriptive insights—which tell us what happened yesterday, last week, last month in the market or with a customer—to a diagnostic approach."

Sarah Alwardt

Sukhija believes that data needs to inform not only about "what happened?" but "why did it happen?" as well. "The highest value after that would be using the data at our disposal to arrive at a predictive state, which would allow us to make better judgments about our resources, and to deliver the right information to the right customers at the right time through their preferred channel of communication," he says.

Navigating the data oceans

Bringing data together, making sense of it, and then acting on it quickly has been a process that the industry has struggled with for a long time. But Alwardt sees large pharma companies advancing with their efforts in this area. Many companies are establishing centers for data competence with their own internal groups to focus on the big data sets, she says, making them less dependent on external partners or marketing consultancies. Having the right people on hand to analyze the data is anoth-

er longstanding challenge that Alwardt believes the industry is starting to overcome. "I tend to think that the people who generate the data know the data best," she says. "Bringing in people who really understand particular data sets can accelerate the insight that comes from that."

However, custom-built data warehouses can be costly and time-consuming and outside the reach of smaller companies. Resources such as Veeva Nitro, an industry-specific commercial data warehouse in the cloud, offer an alternative. Nitro is built on Amazon Redshift—a cloud-based, petabyte-scale data warehouse infrastructure—to "ensure the highest levels of scalability and fast-query performance, even on the largest data sets," according to Veeva's publicity. "It makes it easier for the industry to bring together their data sources in a single place in a way that's ready for analytics and for more sophisticated technology like artificial intelligence (AI)," says Shawah, allowing "what took companies one or two years to build previously to be done literally overnight."


Remy Sukhija

"It's now about transitioning from big data to 'the right data'."

Regardless of the route a company takes to process and analyze its masses of data, one thing certain is that the data will continue to grow at an unprecedented scale. "We used to talk about data ponds and data lakes, now we have data oceans," Alwardt told *Pharm Exec*. "We're far beyond even big data. It's now about transitioning from big data to 'the right data'."

Such a transition requires a more informed understanding of the strengths and weaknesses of the data in question. "The data itself used to be enough. You could put it in a PowerPoint slide and it would tell you everything about the market," says Alwardt. "But now you have to think about whether the questions you're asking of the data can be answered in the data sets you're looking at."

And there are concerns such as the velocity of the data. It's not uncommon for a data set to be two or three months old when it's purchased or received. That can make a big difference to the questions that can be asked of it and can have major implications if a product is new to market. "Some data partners, such as McKesson, can give faster data," says Alwardt, "but it's also about asking the right questions upfront and making sure that whoever you're associating with for your data needs understands them."

The role of the rep

In primary care marketing, says Otsuka's Sukhija, "a pharmaceutical product could be considered successful if 50–60% of physicians prescribe it." The orphan disease space, however, requires a different approach. There are fewer prescribers, which makes each one extremely important. Pharma manufacturers in the orphan drug space need to develop a highly targeted approach to determine the unmet needs for each prescriber and their patients.

"Data allows us to understand the unmet medical needs a prescriber is facing beyond what sales reps understand," says Sukhija. "Using data and analytics properly enables the potential to educate more effectively and help them treat their patients with appropriate therapies."

Smarter analysis of the data moves things beyond the sales reps' understanding, but rather than dilute or even remove the human element in sales and marketing interactions, the advance of technology is likely to facilitate a further evolution of the rep's role. "We've been saying for about 5–10 years that the sales rep model in pharma/biotech is going to change, and to some extent it has," says Sukhija.

Data is empowering reps with the understanding of what prescribers need "so that they're more effective and more valued and more relevant," notes Sukhija. As Shawah explains, if a company cannot present the most relevant information or offering for a customer in a way they care about, "it's meaningless." He adds: "Patients are humans, doctors are humans, providers are humans. They like to talk. Customers may have known reps for a long time, particularly in the specialty markets, where they offer both professional and personal value."

The thinking that "all you need to do is to take the data, bring it together, and run a machine learning or intelligence program on it" is misguided, says Shawah. "Data still needs a lot of tuning," he contends. "It will still need a human to help educate others about how it should be used." And there remains a need for human beings to think about things that are not incorporated into the

data, "such as a potential extension to a label or a new indication, or a competitive launch that's about to hit the market place, or a shift in the payer environment that the data isn't smart enough to know even exists yet."

But change is happening in the rep space. Shawah notes that, on the specialist side, reps are increasingly required to display a new set of more specialized and targeted skills. What customers are demanding from a scientific information standpoint is becoming more advanced. "Your data may help you discern what is important to this or that customer, but you need someone to deliver the message who is credible and trusted," says Shawah. "As such, we're certainly seeing a shift toward more scientific engagement."

On the orphan drugs side, for Sukhija, the field roles in pharma/biotech need to continue to evolve with prescribers' needs. "Our customers' needs go beyond just the efficacy and safety messaging," he says. "For example, they are more interested in making sure their patients can access the therapies they've prescribed without unnecessary obstacles." To address these unmet needs, pharma and biotech companies have a variety of field-based roles that interact with the same prescribers, with the goal of answering their questions and delivering a seamless prescribing experience for both the prescriber and the patient.

"As this trend continues, it is difficult to see the traditional 'reach & frequency' sales model remaining the primary way pharmaceutical companies interact with prescribers in the field," says Sukhija.

A new frontier

Where the traditional goals of pharma were around patient adherence and drug utilization, the complexity and cost of specialized drugs has required more of a value- and outcomes-based approach. The shift, says Shawah, is toward "How do I get the patient better?" rather than "How do I get the patient to use my drug?" Again, technology is helping pharma become more precise about how and when a drug should be used, and which candidate patients are likely to have the best outcome. "By going back to the data and understanding the most appropriate and meaningful use of your drug, you can start to achieve value," he says. An organization's data sets were once very siloed—for example, serving either the marketing/commercial or the health economics and outcomes research (HEOR) departments—but they are becoming more connected, and the insights being generated can be compared to effectiveness, efficacy, cost economics, and real-world outcomes.


Paul Shawah

For Shawah, this cross-functional approach—across sales, medical, marketing, market access, etc.—presents "the new frontier" in the commercial application of AI and big data. We will start to see more leading companies apply this approach in the next three to five years, he says. "While AI has been around for some 60 years, we're still in the early stages of its impact on the commercial process." PE

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Banking on Progress in CF

Advancements in the treatment of cystic fibrosis (CF) in recent years have been significant. In fact, a quick scan of the "milestones" page on the Cystic Fibrosis Foundation website will show several approvals of new therapies by the FDA, specifically starting around 2010.

And while that trend is hopeful for individuals like Emily Kramer-Golinkoff, it can get a bit frustrating. Kramer-Golinkoff has the rare nonsense gene mutation of CF, and none of the approved therapies were able to help her. That was the case then, and is still the case now.

"Back in 2011, there were some really exciting new therapies in the pipeline," says Kramer-Golinkoff, who currently has 35% lung function and spends countless hours a day going through breathing treatments. "There were drugs that targeted underlying causes rather than just treating symptoms. All these exciting advancements were wonderful, but because of a specific genetic mutation, I fell into the 10% of the CF community that, unfortunately, they were not poised to treat."


Kramer-Golinkoff

It's the reason why the now-thirty-something, who received a bachelor's degree in communications and a master's in bioethics from the University of Pennsylvania, started Emily's Entourage in December 2011. Emily's Entourage is a nonprofit organization that fast-tracks research for new drugs and a hopeful cure for nonsense mutations of CF.

To date, Emily's Entourage has raised over $3 million and led worldwide efforts to drive high-impact research and collaboration. One example is the sponsorship support from Eloxx Pharmaceuticals, a global biopharma company focused on discovering and developing novel drugs for the treatment of rare and ultra-rare premature stop codon diseases. Premature stop codons are point mutations that disrupt protein synthesis from messenger RNA.

Organoids are created by scraping a patient's intestinal stem cells, and then growing them in a petri dish to figure out which drugs might work in patients with rare mutations.

Eloxx's lead product candidate, ELX-02, is targeting CF and cyctinosis patients with diagnosed nonsense mutations on one or both alleles. In clinical data released in June, ELX-02 demonstrated to restore transmembrane conductance in and promote forskolin-induced swelling of CF patient organoids carrying homozygous and compound heterozygous CFTR nonsense mutations. The early results are not just potentially good news for patients like Kramer-Golinkoff, but on a personal level, also serve as a confirmation that her experience is making a difference in the lives of others, she says.

Eloxx is using organoids, a new frontier of personalized medicine, to predict drug response in CF. Organoids are created by scraping a patient's intestinal stem cells, and then growing them in a petri dish to figure out which drugs might work in patients with rare mutations. New drugs are tested on custom-made organoids in the lab, and if the "mini organs" puff up, it's a sign that the cells are now correctly balancing salt and water, a major issue in CF.

Kramer-Golinkoff has been donating her stem cells to the Organoid Biobank, created by the Netherlands-based HUB foundation, in hopes of helping researchers. In fact, Kramer-Golinkoff says she was the first CF patient from the US to send her organoids to the biobank. She encourages others to donate theirs as well, to help build a "toolbox" of cells for researchers.

"We are very excited about organoids as a platform for testing new drugs," Kramer-Golinkoff told *Pharm Exec*.

Eloxx gets its organoids from the HUB biobank. The donations, which are anonymous, are a critical component to Eloxx's research and a potential game-changer for CF treatment, according to Dr. Pedro Huertas, the company's chief medical officer. "The use of patient organoids from the HUB is rapidly being adopted as a potential surrogate marker likely to predict potential clinical benefit in cystic fibrosis patients by industry, payers, and regulators," he told *Pharm Exec*.

— Michelle Maskaly

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The 'Spare-No-Expense' Alternative

How low-cost drugs can succeed in the specialty pharmacy channel

By Charlie Bell

The phrase "specialty pharmacy" brings to mind high-touch therapies supported by HUBs, financial assistance, free drug programs, home nursing, and dutifully developed clinical protocols. As such, it makes sense that manufacturers faced with launching a therapy in the specialty space would consider including many of the above program features in their planning. In fact, most manufacturers begin their launch planning with the directive to build a best-in-class service model that fully supports the providers, patients, and caregivers who use their product. "Spare no expense!" they often say.

But what about therapies where "sparing no expense" is not an option? The market is seeing more products on the low-end range of specialty drug prices. This trend is driving the demand for specialty pharmacy program options that accommodate lower-cost therapies.

At the core of the issue is the payer reimbursement mechanism. Reimbursement to specialty pharmacies is tied to the price of the therapy, which can result in a reimbursement that doesn't cover the costs to fill a prescription. Meeting the challenge of fitting lower-cost therapies into the specialty channel requires a highly organized and cost-conscious approach to program design. Distributors, third-party logistic (3PL) providers, specialty pharmacies, clinical services, and free drug offerings each have their own costs. To find success in these circumstances, manufacturers must:

- Understand the value of offering a specific service for a specific therapy.
- Eliminate overlap and unnecessary features.
- Practice smart contracting with specialty pharmacies and other involved vendors.

Why low-cost medications end up in specialty

There are two main scenarios when a therapy is dispensed primarily through the specialty pharmacy channel:

1. A manufacturer restricts the distribution channel to limit product access to those pharmacies that offer certain capabilities. In practice, this means specialty pharmacies—which do have the needed capabilities—dispense the therapy.

2. Even if a drug is available to any pharmacy willing to dispense, payers mandate the therapy must be filled at specialty pharmacy by only covering prescriptions filled in that manner.

It should be recognized that very few manufacturers set out to develop and market a therapy that would go through the specialty channel at a price below what would reasonably support the economics of the channel. Often, the drug was designed to compete with lower-cost medications in the retail channel but forced into the specialty channel due to product characteristics or unforeseen clinical mandates.

No matter the reason, once a manufacturer is faced with the challenge of launching a low-cost therapy into the specialty channel, a carefully planned approach that considers all financial drivers must be developed and executed.

Smart program design for a low-cost specialty therapy

When planning the distribution channel and support services structure for a low-cost therapy, a manufacturer must be a cost-conscious shopper. There can be no redundant services and each contract needs to be negotiated aggressively.

Of course, negotiating too aggressively can be counter-productive. The incentive for your vendors to work hard on your behalf diminishes when they're not being properly compensated. Deep, direct experience with this type of contracting is critical when walking such a fine line.

Unlike planning for higher-cost specialty therapeutics where discounts and amounts are generously rounded and redundant services between HUB and pharmacy are common, planning for a low-cost therapy requires that services be mapped in great detail. Each contract should be negotiated with a detailed understanding of specialty pharmacy, specialty distribution, and HUB dynamics.

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Launch Strategies For Pair of Treatment "Firsts"

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17th ANNUAL INDUSTRY AUDIT

Return Performance

With less than half of companies in our latest review producing increases in shareholder value, those that did stand out from the pack—particularly the drugmakers who added strong showings in the most critical measure of management performance, return on invested capital, which this year brings a new wrinkle to the prevailing industry question: value vs. cost

By Bill Trombetta

Welcome to *Pharm Exec*'s 17th Annual Industry Audit. We present a unique financial performance analysis of the top 23 publicly traded biopharmaceutical companies based on sales revenue. The Audit focuses on a number of financial performance metrics, particularly critical metrics such as growth in shareholder enterprise value, enterprise value to sales, and return on invested capital. Regarding the latter metric, this year the Audit is introducing a new measure—the impact of weighted average cost of capital (WACC). WACC adjusts return on invested capital (ROIC) by assessing the difference between ROIC and WACC. Another new feature introduces the ratio of executive compensation to median employee worker wages.

Methodology

This year's Audit relies on secondary reported information for the 2016–2017 time period. The metrics are also weighted reflecting their relative importance in assessing a company's performance. Some metrics are more important than others. For example, sales growth is important, but sales growth can occur as a result of mergers and acquisitions and in-licensing. So, it takes a back seat to the crunch metric, ROIC, which measures how well

a company is managed, including margin management (the profit and loss or income statement) and asset management (use of assets on the balance sheet).

Three metrics are included that are not weighted: sales, general and administrative (SGA), or overhead; profit per employee; and, new for this Audit, executive compensation compared to median employee wages.

The higher a company performs on a metric is reflected in a ranking based on the number of points it receives. The highest placing for each metric is 23 based on the number of firms in our Audit, and the lowest is one. For example, if a company places 22 (second highest) on the critical metric enterprise value to sales (EV/S), it receives 66 points on that metric (22 rank × weight of 3 = 66). In another example, if a company comes in at a ranking of five (five places from the bottom) on the metric gross margin (pricing power), its total points would be 10 (5 ranking × weight of 2) on that metric.

Each of the 23 company's points-based placement per metric are totaled to arrive at an overall ranking to determine which of the 23 receives the most points to become this year's winner.

Indices

Basic indices are the growth of the US economy and inflation. A company has to be able to grow faster than the US economy: slightly below 3% in 2016 and higher than inflation as measured by the Consumer Price Index (CPI)—about 2% for 2016. Then there are more specific indices related to economic performance such as the Dow Jones, Standard & Poor's, Nasdaq, and other "macro" benchmarks.

Annual Sales

Company		Sales 2017	Sales 2016	Percent Change
Johnson & Johnson	23	$76.45B	$71.94 B	6.32%
Roche	22	54.15 B	51.34 B	5.38
Pfizer	21	52.55 B	52.82 B	(0.53)
Novartis	20	49.11 B	48.52 B	1.13
Merck & Co.	19	39.98 B	39.50 B	1.23
Sanofi	18	39.54 B	37.41 B	3.65
GlaxoSmithKline	17	38.87 B	37.63 B	8.24
AbbVie	16	28.20 B	25.64 B	10.6
Gilead	15	26.14 B	30.32 B	(13.79)
Lilly	14	22.87 B	21.22 B	7.77
Amgen	13	22.78 B	22.68 B	0.45
AstraZeneca	12	22.46 B	23.00 B	(2.40)
Teva	11	22.38 B	21.90 B	4.24
Bristol-Myers Squibb	10	20.78 B	19.43 B	6.94
Novo Nordisk	9	16.94 B	16.61 B	0.08
Allergan	8	15.94 B	14.57 B	9.41
Shire	7	15.16 B	11.40 B	39.38
Celgene	6	12.82 B	10.92 B	17.40
Mylan	5	11.91 B	11.12 B	7.07
Biogen	4	10.99 B	10.19 B	7.81
Valeant	3	8.72 B	9.67 B	(9.82)
Regeneron	2	5.87 B	4.86 B	20.82
Endo	1	3.47 B	4.01 B	(13.51)
Average		**$26.87 B**	**$25.90 B**	**3.70%**

Table 1

Sales growth

Table 1 above shows sales in US dollars along with sales growth for 2016–2017. It is good to grow, especially organically, compared to just acquiring companies. But that's easier said than done for companies at absolutely high sales levels, such as Johnson & Johnson, Novartis, and Roche. The poster firm for growth is Amazon.

Audit Data Sources & Table Key

( ) Denotes loss
B = Billions of US$
M = Millions of US$

Figures are rounded up where appropriate

Sources: FactSet; EvaluatePharma; New York Times; Wall Street Journal; Business Week; Fortune; Forbes. Financial data are found primarily through FactSet, which was accessed in April 2018 for the 2016-2017 full-year time period.

Enterprise Value

Company		EV 2017	EV 2016	Percent Change
AbbVie	23	$210.0 B	$133.2 B	50.30%
Novo Nordisk	22	122.9 B	104.8 B	17.20
Novartis	21	235.5 B	212.0 B	10.80
Bristol-Myers Squibb	20	108.0 B	97.53 B	10.30
AstraZeneca	19	97.18 B	88.75 B	9.50
Johnson & Johnson	18	358.7 B	327.0 B	9.38
Lilly	17	89.55 B	82.88 B	7.30
Gilead	16	110.2 B	103.96 B	6.00
Pfizer	15	235.5 B	227.2 B	3.50
Amgen	14	125.3 B	128.1 B	(2.3)
Biogen	13	62.5 B	64.80 B	(3.7)
Mylan	12	35.95 B	37.37 B	(3.9)
Valeant	11	30.64 B	33.60 B	(9.1)
GlaxoSmithKline	10	112.33 B	123.72 B	(9.2)
Roche	9	209.20 B	234.50 B	(10.6)
Sanofi	8	107.53 B	121.40 B	(11.5)
Merck & Co.	7	162.30 B	191.60 B	(11.7)
Shire	6	59.26 B	71.85 B	(16.9)
Regeneron	5	33.90 B	40.83 B	(17.5)
Teva	4	55.97 B	72.74 B	(23.6)
Allergan	3	78.0 B	105.0 B	(25.7)
Endo	2	8.42 B	15.40 B	(46.0)
Celgene	1	69.61 B	103.30 B	(47.8)
Average		**$118.1 B**	**105.20 B**	**12.30**

Table 2

Amazon's profits pale in comparison to their competitors, such as Walmart, but its enterprise value (EV), or market cap, is the envy of its peers, less stellar sales growth, notwithstanding.

The average dollar sales for our pharma 23 was $26.87 billion in 2017, vs. $25.90 billion in 2016, a growth rate of 3.7%. That rate outpaced the US economy and inflation and the Fortune 500. Five companies' sales decreased last year.

Assuming Shire is categorized as a biotech, given its thrust toward orphan diseases, biotechs' growth rates exceeded the pack, with Shire, Regeneron, Celgene, and AbbVie at the top. For the so-called big pharma, GlaxoSmithKline, Lilly, Bristol-Myers Squibb, and J&J set the pace.

The sales growth winner for generics was Mylan, followed by Teva, and then with a negative growth rate, Endo.

Enterprise or shareholder value and growth

This is the first of the three crunch metrics. EV/sales and ROIC are the others. There are other worthy performance metrics, e.g., corporate responsibility; sustainability; the best places for women and minorities to work; etc, but our focus is financial performance.

EV is the sum of a company's market capitalization; then add in debt and subtract a firm's debt after adjusting for cash and other current assets. Simply put, EV is the market value of an organization. At present, two firms are fighting it out for the highest company value on earth: Apple and Amazon, with Apple recently eclipsing $1 trillion in market cap and Amazon approaching that milestone.

Table 2 shows that the pharma with the highest EV is J&J at $359 billion, with an average growth for the year of 9.38%. The company that grew its EV the most is AbbVie, with a 50.3% growth rate. To put that in perspective, the average EV for our 23 for the past year was $118 billion, vs. $105 billion for 2016, a growth rate of 12.3%. Only nine firms on our list increased shareholder value, while 14 experienced decreasing EV. Novo Nordisk comes in at number two with an impressive 17% EV growth rate, but AbbVie's rate was three times greater.

Our 23 pharmas' average shareholder value of 12.3% compares to other indices as follows:

» 28.2% Nasdaq Composite
» 25.1% Dow Jones Industrial Average
» 20.0% S&P 500 Healthcare
» 19.0% S&P 500

These indices performed better in 2017 compared to 2016, but the bleak EV showing for the majority of our 23

Enterprise Value to Sales

Company		EV/S 2017	EV/S 2016
Novo Nordisk	23	7.14	5.52
Regeneron	22	6.77	7.89
Celgene	21	6.48	8.8
AbbVie	20	6.43	5.08
Biogen	19	6.33	6.16
Amgen	18	5.23	4.60
Allergan	17	5.18	6.51
Johnson & Johnson	16	5.11	4.13
Bristol-Myers Squibb	15	4.85	5.03
Pfizer	14	4.58	4.20
AstraZeneca	13	4.35	3.90
Novartis	12	4.34	4.02
Lilly	11	4.31	4.02
Merck & Co.	10	4.24	4.37
Shire	9	4.21	7.16
Gilead	8	4.16	5.02
Roche	7	4.13	4.23
Valeant	6	3.95	6.82
Endo	5	3.21	5.32
Mylan	4	3.11	3.11
Sanofi	3	2.73	3.14
GlaxoSmithKline	2	2.69	3.35
Teva	1	2.4	3.49
Average		**4.60**	**5.00**

Table 3

Gross Margin

Company		Gross Margin 2017	Gross Margin 2016
Celgene	23	93.80%	92.50%
Regeneron	22	90.75	91.68
Novo Nordisk	21	83.69	84.17
Gilead	20	82.70	85.50
Amgen	19	82.14	81.70
AstraZeneca	18	81.60	75.80
Biogen	17	78.04	82.28
AbbVie	16	75.90	77.30
Lilly	15	73.50	73.40
Bristol-Myers Squibb	14	72.80	74.61
Valeant	13	70.79	45.38
Roche	12	70.26	70.38
Pfizer	11	69.95	69.80
Merck & Co.	10	68.54	66.17
Johnson & Johnson	9	67.20	69.90
Sanofi	8	66.80	63.07
GlaxoSmithKline	7	65.70	66.10
Novartis	6	65.03	63.89
Shire	5	55.82	55.01
Teva	4	48.36	54.14
Allergan	3	40.43	42.90
Mylan	2	40.17	42.89
Endo	1	36.21	34.30
Average		**73.00%**	**67.09%**

Table 4

pharmas suffered in comparison the past year. Other than Novo Nordisk and Gilead, big pharma performed better than biotech. The three generic companies came in negatively, with Mylan experiencing the least loss.

Enterprise value to sales

EV and EV growth are very important performance metrics. EV to sales supplements that metric by assessing which firms are still climbing, vs. companies whose best performance is behind them, via so-called "value" stocks—those stocks for widow and orphan drugs that, if not growing in value, still pay noteworthy dividends.

Table 3 lists EV to sales. The average EV/S for 2017 is 4.60, a decrease from 2016's 5.00, shadowing the drop in EV growth. Compared to the Fortune 500, our 23 pharmas' EV/S numbers are higher. Plugging in the Fortune 500's market cap to sales, an approximation for EV/S, shows the figure for 2017 at 1.68, vs. 1.55 for 2016; but the Fortune 500 numbers increased over the year, in contrast to our 23 pharmas' decreasing EV/S. At the top is Novo Nordisk, increasing from 2016's 5.52 to 7.14. Similar to Table 2, only nine companies increased their EV/S ratios; the higher the ratio, the more likelihood the firm's performance is going to get better. The top six performers are biotechs, although Regeneron and Celgene went backwards.

Of the big pharmas, J&J, Pfizer, AstraZeneca, Novartis, and Lilly showed respectable numbers. Endo's EV/S was the highest among the generics, followed by Mylan and Teva, respectively.

Operating Income

Company		2017
Gilead	23	54.80%
Novo Nordisk	22	43.20
Amgen	21	42.00
Biogen	20	40.10
AbbVie	19	37.00
Regeneron	18	35.40
Johnson & Johnson	17	33.00
Roche	16	28.30
Pfizer	15	27.50
Bristol-Myers Squibb	14	27.00
Lilly	13	26.60
Celgene	12	24.80
Shire	11	22.40
Merck & Co.	10	20.00
GlaxoSmithKline	9	18.90
Novartis	8	18.70
Teva	7	17.50
Sanofi	6	16.60
Endo	5	14.10
Mylan	4	13.10
Astra Zeneca	3	11.50
Valeant	2	6.20
Allergan	1	(1.8)
Average		**25.10**

Table 5

Sales to Assets

Company		S/A 2017	S/A 2016
Novo Nordisk	23	1.12	1.18
Regeneron	22	0.75	0.77
Roche	21	0.69	0.66
Bristol-Myers Squibb	20	0.62	0.59
Lilly	19	0.55	0.57
GlaxoSmithKline	18	0.52	0.50
Johnson & Johnson	17	0.51	0.52
Biogen	16	0.47	0.48
Merck & Co.	15	0.44	0.40
Celgene	14	0.44	0.44
Gilead	13	0.41	0.56
AbbVie	12	0.41	0.43
Valeant	11	0.4	0.21
Novartis	10	0.37	0.36
AstraZeneca	9	0.36	0.37
Teva	8	0.35	0.30
Mylan	7	0.34	0.39
Sanofi	6	0.34	0.33
Pfizer	5	0.31	0.31
Amgen	4	0.29	0.30
Endo	3	0.27	0.24
Shire	2	0.23	0.26
Allergan	1	0.13	0.11
Average		**0.45**	**0.50**

Table 6

Gross margin

Yes, there is net-net and list price vs. net price, but at the end of the day, there is gross margin, which is tantamount to markup. As Warren Buffet would call it, "the moat around your castle."

Gross margin is total revenue minus cost of goods sold from the income statement. This is quintessential margin management: how price is managed while simultaneously managing operating costs to produce net income. The higher the gross margin is, the more a firm is able to cover operating expenses, including SGA. Table 4 (see page 25) shows Celgene at the top, with a nose-bleed gross margin of 93.80%, increasing from 2016. The biotechs rule pricing as they have ever since the first PE Industry Audit in September 2002. According to *The Wall Street Journal*'s William Galston, between 1980 and 2016, US firms have increased markups by 42%; for biotechs, the markup growth has been 419%.

For the big pharmas, Lilly ranked at the top in gross margin, followed by BMS, Roche, Pfizer, Merck & Co., and J&J. The average gross margin for 2017 was 73%, up from 67.09% the year before. Nine companies grew their gross margins.

For the generics, Teva's margin was highest, followed by Mylan and Endo, but of the three, Endo was the only one to increase its output in this metric. The biggest increase in gross margin goes to Valeant, whose figure went from 45.38% in 2016 to 70.79% a year later, within stalking distance of biotech Biogen's margin of 78.04%.

Return on Invested Capital

Company		ROIC 2017	Weighted average cost of capital (WACC)
Novo Nordisk	23	80.20%	7.54%
Pfizer	22	21.76	4.48
Roche	21	20.76	4.53
Regeneron	20	20.58	11.54
AbbVie	19	13.70	8.22
Biogen	18	13.65	6.87
Celgene	17	13.63	6.71
AstraZeneca	16	12.55	8.05
GlaxoSmithKline	15	10.22	4.74
Gilead	14	9.59	6.66
Shire	13	8.40	7.81
Novartis	12	8.02	5.78
Sanofi	11	5.06	5.42
Bristol-Myers Squibb	10	4.96	4.43
Merck & Co.	9	3.99	6.03
Amgen	8	3.31	8.05
Mylan	7	2.55	6.03
Johnson & Johnson	6	1.42	4.43
Lilly	5	(0.93)	1.96
Allergan	4	(3.62)	4.18
Endo	3	(12.60)	3.38
Teva	2	(37.89)	4.83
Valeant	1	NA	NA
Average		**8.40**	**5.98**

Table 7

Net Profit to Employee

Company	2017
Gilead	$462,800
Novartis	$403,867
Novo Nordisk	$402,530
Celgene	$393,372
Biogen	$347,822
Pfizer	$236,208
Regeneron	$193,308
Shire	$184,582
AbbVie	$182,000
Amgen	$95,140
Roche	$93,574
Bristol-Myers Squibb	$42,489
Merck & Co.	$34,696
Johnson & Johnson	$9,701

Table 8. Note: Only 14 companies had data available.

Operating income

Staying with margin management, Table 5 (see facing page) shows operating income, or profit to sales. Again, the higher gross margin is, the more that contributes to improving operating income. Operating income consists of total revenues minus cost of goods sold and minus operating expenses related to a firm's typical business. It excludes one-time gains and losses, dividend income, and interest income.

At the top in this metric is Gilead at 54.8%, a drop from 60.7% in 2016. Still, most companies would envy that number, which for the majority of firms would be their gross margin, not net income. The average operating income for 2017 was 25.1%, a slight drop from 25.9% in 2016. Only five companies saw their operating incomes increase for the year. Not surprisingly, given their staggering gross margins, the biotechs reside at the top of the operating income pack. The big pharmas are led by J&J at 33%, 30% above average, but no mean feat given its large sales volume from lower-priced, over-the-counter products. The biggest increase goes to Lilly at 20%.

For the generics, Teva ranked the highest in operating income, followed by Endo, which saw its numbers increase by more than 20%, and Mylan.

Sales to assets

Gross margin and operating income have to do with margin management; sales to assets has to with asset management. If a firm is at $70 billion in sales, it won't be doubling revenue anytime soon. If the company has also curtailed SGA and disposed of assets, it won't be cutting operating expenses in half anytime soon either. Then it turns to asset management to do a better job making use of, not necessarily owning, assets. When you multiply profit to sales (operating income) by sales to assets (asset manage-

General & Administrative Expenses to Sales

Company	GA E/S 2017	GA E/S 2016
Endo	22.01%	22.96%
Mylan	27.09	28.79
Gilead	27.93	24.83
Teva	30.53	32.90
Shire	33.47	37.93
Valeant	33.73	33.40
Amgen	37.01	39.50
Biogen	37.95	38.47
AbbVie	38.28	39.12
Novo Nordisk	40.51	41.03
Roche	41.41	40.34
Johnson & Johnson	41.59	41.59
Allergan	42.22	47.46
Pfizer	42.50	42.78
Sanofi	44.30	43.13
Bristol-Myers Squibb	45.77	47.95
GlaxoSmithKline	46.87	41.81
Novartis	48.41	47.17
Merck & Co.	48.53	39.60
Lilly	51.90	55.11
Regeneron	55.35	64.30
Celgene	69.70	65.26
AstraZeneca	70.12	60.29
Average	**42.48**	**42.47**

Table 9

Executive to Employee Wages

Company	CEO Comp/ Employee Salary	EV Growth
Regeneron	529 / 1	12
Johnson & Johnson	452 /1	3
Allergan	393 / 1	13
Mylan	317 / 1	8
Pfizer	313 / 1	6
Merck & Co.	215 / 1	11
Endo	171 / 1	14
Bristol-Myers Squibb	169 /1	2
AbbVie	144 /1	1
Valeant	138 / 1	9
Amgen	127 / 1	10
Lilly	118 / 1	4
Gilead	94 / 1	5
Biogen	92 / 1	7
Celgene	62 / 1	15

Table 10. Note: Data was not available for the eight-non-US-based companies.

ment), you get a far more important measure: return on assets. A firm can have a relatively low profit margin with a relatively high sales-to-assets ratio that will result in a better performance in terms of ROIC. For example, Regeneron's profit margin is lower than J&J's; but its sales to assets is considerably higher, so its ROIC is higher than J&J's.

As seen in Table 6 (see page 26), Novo Nordisk's sales-to-assets ratio is 1.12. For every dollar invested in assets, Novo Nordisk gets back $1.12 in revenue. Conversely, Allergan's ratio is 0.13. For every $1 invested in assets, the company gets back only 13 cents. Novo Nordisk is substantially more productive in managing its assets.

One would expect the generics to lead the pack here, but that is not the case. Teva, Mylan, and Endo's sales-to-assets ratios come in at 0.35, 0.34, and 0.27, respectively.

Return on invested capital

Now we come to the mother of all metrics: ROIC. ROIC is net income left over to shareholders as a percent of debt and common stock. According to longtime organizational consultant Mark Van Clieaf in *The New York Times*, the best measure of business performance is ROIC—how much is a company generating on its capital investments, plant and equipment, minus the cost of that capital, debt, or equity? Combine this with our new Audit addition, weighted average cost of capital (WACC). Management should be providing value that exceeds its cost of capital, Van Clieaf contends. For example, two companies can have an ROIC of 10%; but company 1 has a WACC of 12% while company 2 has a WACC of 7%. The first firm is destroying shareholder value while the second is creating shareholder value.

Prior to the mid-1980s, the conventional wisdom was that debt had a cost (the rate paid for borrowing), but issuing stock was free. But what if the peer groups a company competes with have a higher ROIC? Even though the firm shows a profit, it is

destroying shareholder value if its profit is below its peers' average. What return could an investor get by investing in a company of equal risk? This was the brainstorm of Stern Stewart, a consulting firm based in New York City.

My source for WACC relies on three years of income statements and balance sheets to arrive at a company's WACC percentage.

Table 7 (see page 27) shows Novo Nordisk far out in front with an ROIC of 80%. Second place goes to Pfizer, at 21.76%. For the generics, Mylan is the only one with a positive ROIC, at 2.55%, with negative numbers for both Endo and Teva.

To avoid overstating the impact of ROIC, we use the ROIC number to come up with the rankings on this metric. But the inclusion of WACC in Table 7 tells an interesting story. The greater the difference between ROIC and WACC, the greater the return to shareholders. And, again, Pfizer has an ROIC of 21.76% but a WACC of only 4.48%. With the exception of Pfizer, the biotechs dominate the creation of shareholder value. Ten companies had higher WACCs than ROICs, resulting in loss of shareholder value for those firms.

Net profit per employee

This metric, presented in Table 8 (see page 27), is not weighted in the rankings. But it is interesting to show how profitable the pharma sector is. Of our 23 pharmas, Gilead produces the most profit per employee, at $462,800 per employee. That is quite a drop from 2016's $1.5 million total, but not bad compared to Apple's profit per employee in the same range. Only 14 companies had net profit per employee data available.

And the Winner is…

Company	Score
Novo Nordisk	348
AbbVie	322
Regeneron	309
Biogen	290
Celgene	277
Bristol-Myers Squibb	259
Pfizer	235
Johnson & Johnson	232
Gilead	228
Lilly	225
Roche	223
Amgen	222
AstraZeneca	212
Novartis	199
GlaxoSmithKline	185
Shire	166
Merck & Co.	166
Sanofi	128
Mylan	125
Allergan	120
Valeant	109
Teva	81
Endo	52

Table 11

Selling, general and administrative expenses to sales

SGA is another metric that does not impact the rankings. Nonetheless, it is still important because the expenses in this category are necessary to run an organization and constitute routine spend such as rent, salaries, advertising, marketing, legal, and more. Laying off and firing workers costs money in severance before it begins to pay off. It's also important to keep in mind that this is a one-year comparison. A firm can be making investments in advertising, training its sales force, etc., and that will pay dividends down the road. One swallow does not a season make.

For example, according to a recent article in *Fortune*, Costco's SGA is 10% compared to Walmart's 20%. That partly enables Costco to operate on a markup of 11% to Walmart's 24%. Opportunities exist to cut advertising costs by being more efficient with agencies and revamping supply chains. Also, SGA can increase, but it is the goal for sales growth to grow faster, thereby lowering the SGA-to-sales ratio. Ballooning overhead leaves a firm inefficient and less productive than it otherwise could be.

Table 9 (see facing page) shows the generics are lean and mean on this metric, with Gilead the third lowest of our 23 pharmas. The average SGA for 2017 was 42.48% of sales, vs. 42.47% for 2016. GSK, Merck, and AstraZeneca had the biggest year-to-year increases in SGA to sales. And, again, this may have much to do with new product launches and investment in sales training and education. AstraZeneca's SGA/sales is the highest, at 70.12%. If AstraZeneca were able to lower SGA/sales to the 42.48% average, this would add about $5 billion to retained earnings or to invest in R&D.

Executive compensation to median employee wages

As mentioned, this measure is new for this year's Audit. From a larger societal perspective, we are seeing, globally, an increase in the top 1% of income compared to the average worker. The Gini coefficient measures this increasing wealth distribution disparity. A score of 1.0 reflects high income inequality; a score of zero reflects no inequality. The lower the Gini coefficient,

The Fab 5 vs. the Fearsome 5

Each year at the end of our Audit report, we have some fun by comparing our top five biopharmaceutical performers, or "Fab 5," with *New York Times* columnist Farhad Manjoo's "Fearsome 5." The latter is made up of high-tech stalwarts Alphabet (Google), Apple, Amazon, Microsoft, and Facebook. Here's how the two groups compare across a pair of key metrics.

ENTERPRISE VALUE GROWTH	
Amazon	59.6%
AbbVie	**50.3%**
Microsoft	37%
Facebook	18%
Novo Nordisk	**17.2%**
Apple	10%
Alphabet	(2.1%)
Biogen	**(3.7%)**
Regeneron	**(17.5%)**
Celgene	**(47.8%)**

RETURN ON INVESTED CAPITAL	
Novo Nordisk	**80.2%**
Facebook	23.8%
Apple	22.3%
Regeneron	**20.6%**
Microsoft	18%
AbbVie	**13.70%**
Biogen	**13.65%**
Celgene	**13.63%**
Alphabet	8.4%
Amazon	6.6%

the more equal the distribution of wealth; the higher the score and closer to 1.0, the rich get richer and the middle class and the poor get poorer. The Scandinavian countries tend to hit more equitable distributions of wealth. Mexico and South Africa are among the highest scores, reflecting very unequal differences in wealth, with the US moving more in that direction.

Analogously, there is a similar interest emerging in the difference between executive compensation and the median wages of workers. This year, for the first time, thanks to the Dodd-Frank Wall Street Reform and Consumer Protection Act, companies are disclosing what their CEOs make vs. the median wages of their employees. Recent research from two academics reveals that the average CEO/median worker pay ration has soared from 30 to 1 to more than 300 to 1 over the last 40 years. According to *The Wall Street Journal*'s Patrick Thomas, the median CEO pay in 2017 for 25 biotech, pharma, and life sciences CEOs was $16.08 million, above the overall median of $12.1 million for all S&P 500 companies.

Recently, *The New York Times* published the Equilar 200 Highest-Paid CEO rankings. Equilar is an executive compensation consulting firm. Table 10 (see page 28) shows the rankings for 15 US-based pharma firms; no executive compensation was available for the eight-non-US-based companies. The highest-paid CEOs aren't necessarily associated with outstanding financial performance. The highest ratio was Regeneron, at 529 to 1; the company came in 12th out of the 15 US-based biopharma firms in our Audit in terms of EV growth. Celgene had the lowest ratio, at 62 to 1; the company also generated the lowest growth in EV. The organization with the highest growth in EV was AbbVie, at 50.3%, while its CEO had a compensation/worker ratio of 144 to 1, which ranked 9th.

Final tally

Table 11 (see page 29) reveals the winner of this year's Audit: Novo Nordisk. AbbVie comes in second, followed by Regeneron, Biogen, and Celgene rounding out the top five. We are in good company recognizing Novo Nordisk's performance. EvaluatePharma, in its World Preview 2018, also lauds Novo Nordisk on its investment in R&D and M&As, along with its focused strategy resulting in superior return on investment. BMS, Pfizer, J&J, and Lilly lead the big pharmas in point totals in our Audit. Mylan beats out Teva and Endo for the generics honor. PE

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Continued from Page 21

Distribution channel

There are a number of combinations of 3PL providers, wholesalers, and distributors that a manufacturer could employ to get finished goods into specialty pharmacies. As a general rule, the fewer, the better. The first question to be addressed is whether the drug will be limited to specialty pharmacies or if it will also be available to retail and pharmacy benefit manager (PBM) mail order pharmacies. If the therapy will be limited to just specialty pharmacies, then a combination of a 3PL and one or more specialty distributors will suffice. If it is the latter, a manufacturer will need to consider one or more large wholesalers.

It's an important question because if a manufacturer does not need distribution to retail pharmacies nationwide, there is no reason to pay for that level of service. By using a 3PL, a manufacturer can achieve significant cost savings by selling directly to specialty pharmacies and further utilizing one or more specialty distributors to sell to hospitals and other institutions as needed.

Specialty pharmacy network

When determining the size of a specialty pharmacy network, the primary consideration is the size of the patent population for the therapy. Analysis of specialty pharmacy contracts reveals that the fewer specialty pharmacies in the network, the better the pricing a manufacturer can obtain. Limiting distribution allows specialty pharmacies to have greater volume and also greater negotiating power with payers related to reimbursement. Specialty pharmacies pass these financial benefits along to manufacturers in exchange for inclusion in limited networks.

Based on this financial dynamic, a specialty pharmacy network should include as few specialty pharmacies as reasonable based on the patient population. The argument against limiting the number of specialty pharmacies in a manufacturer network is based on payer coverage. A health insurer will have its own specialty pharmacy network—sometimes with just one specialty pharmacy. If a referral for a specialty therapy goes to a pharmacy that is not in the health insurer's network, there will be some delay for that patient to receive their drug.

Generally, the more patients a specialty pharmacy can serve without any out-of-network hurdles, the more efficiently and cost-effectively they can serve the providers and patients using a manufacturer's therapy.

There are hidden financial forces that can subvert the commercial success of these products

When negotiating a contract for a low-cost specialty therapy, it is critical to have a detailed understanding of the core services offered by each specialty pharmacy being considered. Knowing what the specialty pharmacy will provide as a core service informs the contracting process and eliminates the mistake of paying for a service that might be offered for free and guides the smart design of any additional services required. Additional services need to be carefully considered; if they are not necessary, then a manufacturer should avoid them for low-cost therapies.

HUB services

Many traditional specialty therapies employ what are commonly referred to as HUB services. These are financial, clinical, and other support services provided to patients and caregivers by a third party that is separate from the specialty pharmacy—though some HUB service providers share common ownership with specialty pharmacies. No matter the ownership structure, these services should always be operationally and contractually separated from the services a specialty pharmacy or distributor will provide.

HUBs typically charge manufacturers on either a full-time equivalent (FTE) or a transactional basis. Either way, each service the HUB provides will end up costing the manufacturer. Because many of the core services at specialty pharmacies are performed at no additional expense to the manufacturer, with lower-cost specialty products it is especially important to ensure that the HUB does not duplicate these services. In general, a HUB is a luxury for low-cost specialty therapies and the services provided by the HUB should be minimal or potentially even eliminated in the interest of managing costs.

Low-cost therapies can be successfully dispensed in the specialty pharmacy channel. However, there are hidden financial forces that can subvert the commercial success of these products. It is vitally important to understand the fundamental complexities that need to be overcome in order to not only facilitate the availability of a therapy in the specialty channel but also ensure financial success. PE

CHARLIE BELL is a Senior Director at Archbow Consulting

AstraZeneca

What science can do

Circulating tumour DNA

AstraZeneca has pioneered the use of circulating tumour DNA (ctDNA) in the diagnosis of cancer. Pieces of DNA break off from a tumour and circulate in the bloodstream where they can be analysed to give genetic information about a patient's tumour. This allows healthcare professionals to determine the right treatment for the patient using a minimally invasive blood test.

VVPM ID: GB-12846 Date of Preparation: July 2018

UK

A VOTE OF CONFIDENCE

Britain's GBP 64 billion (USD 83 billion) life science market has long ranked proudly as one of the most alluring pharma prospects within Europe not just courtesy of a very decent 3.3 percent growth rate, but also because of the country's heavyweight medical science infrastructure and a well-honed reputation for elite innovation.

"I think one of the tremendous advantages we enjoy here in Britain is that we possess three world-leading assets: our iconic National Health Service (NHS), a thriving life sciences ecosystem, and a formidable academic research base. Each one is recognized as a world-beater in its own right," resolutely declares parliamentary under secretary of state for health Lord O'Shaughnessy. "And, so long as we can bring this triad of actors together in concert, we can establish a truly extraordinary and highly-optimized public health scenario," he adds.

Meanwhile the sector's value to the national economy stands uncontested. "I consider it absolutely no exaggeration to say that the life sciences sector constitutes one of the last big remaining bastions of British industry. Many of the other traditional heavyweight industries have been gradually hollowed out and relocated to other parts of the globe, but with life sciences, the hub remains staunchly implanted within the UK," remarks Terry O'Regan, Biogen vice president and managing director of the UK and Irish affiliates.

Yet the overarching vibe is hardly one of a local industry content to rest on its laurels. "With the NHS celebrating its 70th anniversary, a fiercely ambitious and forward-looking Life Sciences Industrial Strategy (LSIS) entering into force; and a historic opportunity to take our sector global with the advent of Brexit, these are profoundly exciting times for anyone involved in the British pharmaceutical or biotech community," muses Mike Thompson, CEO of the Association of the British Pharmaceutical Industry (ABPI).

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ENDURING APPEAL

The UK's perpetual attraction for multinational pharma thus transcends matters of market dynamics, notwithstanding resilient consumer demand and the country's 66.5 million-strong population, and also reflects its defining characteristics as a fertile ground for drug discovery and trendsetting. "The UK is an important country for Gilead, not just because of its size as an attractive pharmaceutical market, but because of the power of the UK to shape and influence trends across the world. The UK has a tremendous science base and a thorough understanding of how to value healthcare innovation. This makes us uniquely positioned from a global perspective," concedes Hilary Hutton-Squire the company's general manager covering the British Isles.

Lord O'Shaughnessy, parliamentary under secretary of state for health

Simon Stevens, CEO, NHS

Indeed, a number of acclaimed institutions stand out for their pioneering and ground-breaking spirit. For instance, Britain's national genome apparatus is busy sequencing some 100,000 whole genomes from NHS patients with rare diseases, and their families, as well as from patients with common cancers. "My expectation is that we will ultimately be credited with creating a dataset of de-identified whole genome sequences matched with clinical data at a scale absolutely unprecedented in the entire world…. simply no-one other than the British is operating at scale in a real health system yet," reveals Sir John Chisholm, executive chair of Genomics England.

Then there are certain therapeutic niches in which the UK is blazing new trails, while the uniquely centralized structure of the NHS helps to secure sufficient critical mass to build up hubs of expertise. "For conditions like neurodegenerative disease, Britain's Institute of Neurology is generally regarded as a global pioneer and this stems partly from the clinical structure of our country. Due to the way our NHS is organized, anyone afflicted with a rare neurological disease in the southern half of the country is referred to this particular hospital which has been invaluable in enabling us to ramp up our knowledge base," points out John Hardy, professor of neuroscience at University College London.

Nor can one overlook the UK's distinctive enabling ecosystem for biotechs. Not only does Britain possess the so-called 'Golden Triangle' – the third largest technology cluster in the world outside Silicon Valley and Boston – but no less than three of the world's top ten leading universities. "All in all, Britain offers a pretty compelling proposition for life sciences entrepreneurs and researchers wanting to operate at the bleeding edge of new drug discovery. If we consider funding, the UK has consistently ranked as the most active country for biotech capitalization in Europe," ventures Steve Bates, CEO of the BioIndustry Association (BIA).

PUTTING DOWN DEEP ROOTS

Given this context, it is perhaps little wonder that many multinationals have developed extensive R&D footprints on the ground. "Amongst J&J's 5,000 UK employees, approximately 1,000 are dedicated to Janssen, with some 500 active in R&D-related functions rendering us the largest single foreign investor in life sciences in the UK. Moreover, the J&J Innovation Centre based in London constitutes our European hub and is one of only four global research centres responsible for identifying and accelerating early stage external innovation by establishing unique collaborations," details Janssen's Mark Hicken.

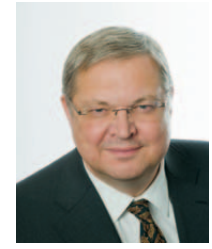
Amgen meanwhile maintains a 300-strong local R&D team, which coordinates clinical trials across Europe that account for over 60 percent of the company's total world volume. "This work plays a significant role in advancing our innovation and

securing European approvals for our medicines. Many of our UK R&D team hold global and international roles and contribute to Amgen's global R&D strategy. I know that Amgen has always recognized the value of the UK in providing access to world class science talent and now that I have had a chance to work alongside them, I can see why," exclaims newly appointed vice president and general manager, Chris Fox.

Then there is Roche, which invests more than half a billion pounds in early R&D in the UK annually. "I think there are two reasons why Roche has been committed to the UK. Firstly, there is great talent here, we are able to attract and retain the best staff. Our people are ultimately what make us a great company. Secondly, the UK has some of the world's greatest institutions across science and clinical medicine and it is great to be able to access that expertise," explains its country manager, Richard Erwin.

What's more, the investments continue to flood in. Ipsen, an ambitious French mid-cap player that has globally been converting a classic business model into a commercial powerhouse and efficient launch machine in oncology, has been deepening its UK R&D presence. "Our British operations nowadays constitute one of three strategic focal points for the company globally, and encompass an R&D facility on the outskirts of Oxford, commercial capabilities in Slough and a manufacturing site in Wales that generates our neuroscience drug Dysport® for global distribution… All in all, this is a pretty substantial commitment with about 600 employees, and 200 patents filed from our R&D site," recounts Ewan McDowall, general manager of Ipsen UK & Ireland from July 2014 to June 2018.

"Our strategy is consciously to leverage the UK's status as a global life sciences epicentre looked up to by the rest of the world, by mobilizing great partnerships with academia and thought leaders and through making full use of the opportunity to attract top talent," he adds.



Mike Thompson, chief executive, ABPI; Steve Bates, CEO, BIA; Sir John Chisholm, executive chair, Genomics England

LSIS: BLUEPRINT FOR THE FUTURE?

Ever-attentive to the need to preserve and extend the UK's competitive leadership, in August 2017, the British government unveiled its Life Sciences Industrial Strategy (LSIS) – the product of a comprehensive, independent cross-sector review into the long-term future of the industry led by Sir John Bell – the recommendations of which were subsequently codified with a far-reaching "Sector Deal" between industry and the state.

Ewan McDowall, general manager, Ipsen UK & Ireland (July 2014-June 2018)

Alongside calls for an increase in conventional research funding, initiatives to boost home-grown pharma manufacturing and a target of importing an additional 2,000 discovery scientists from around the globe to work in domestic laboratories, the LSIS has raised eyebrows for proposing to set up a Health Advanced Research Programme (HARP) to invest many hundreds of millions of pounds in high-risk, high-reward "moonshot" projects. The aim would be to "create two to three entirely novel industries over the

The Golden Triangle: World Class Academia Meets Industry

Most of the activity and productivity in the UK's life science sector emanates from the so-called 'Golden Triangle' of cities known for their elite academic and research institutions – Oxford, Cambridge and London. 600 life science companies operate in the region, ranging from multinationals to start-ups and with a combined market capitalization of GBP 5.7 billion (USD 7.5 billion).

AstraZeneca moved its global headquarters to Cambridge in 2016 to be closer to this scientific base. Country President Laurent Abuaf explains that, "having our corporate headquarters in Cambridge allows us to create and access an ecosystem of science, innovation and academia. We are also re-joining our roots as a company, with our MedImmune R&D arm already being located in Cambridge. We know that collaboration within a buzzing environment where we can meet intellectual capital is what triggers great innovation and science."

Industry-academia synergies are well established in Oxford, as Richard Barker, former director general of the ABPI and a leading voice in British life sciences, details. "We now have the Oxford Sciences Innovation (OSI) fund of GBP 550 million (USD 720 million), that will support spinning out technologies from the University of Oxford into companies," he proclaims.

London is a global innovation hub and financial center, allowing biotechnology start-ups access to new ideas and technologies as well as investment capital. The BIA's Steve Bates declares that, "London is the largest city in Europe, and the flexibility and opportunity it represents are impressive. I often joke that platform nine and three quarters is where the magical journey starts – not just for Harry Potter – because on one side of King's Cross Station we find the Francis Crick Institute, the most significant biomedical organization in Europe, and on the other side we find Google Deep Mind's campus; they combine to form a magical setting!"

The Japanese Connection

Gary Hendler, chairman & CEO EMEA, Eisai

Stewart Pearce, managing director UK and Ireland, Otsuka

Japanese firms have tended to penetrate European markets late in the day, having traditionally focused on their home nation and the more lucrative US market. However, those that have taken the plunge into Europe have frequently selected the UK as their regional headquarters and launchpad for operations across the continent.

Stewart Pearce, managing director of Otsuka UK and Ireland, posits, "to Otsuka, Europe is in many ways a test bed for success in Asia. Europe has some of the toughest markets globally and within that mix, the UK holds the undisputed position of the toughest single market. Our way to look at this as a group is that, if you can make it in the UK, you can make it anywhere!"

Jon Neal, Pearce's counterpart at Takeda – which has its European Center of Development in the UK – agrees, noting that, "the UK is a very strategic market for Takeda, not just for the quality of the infrastructure available, but also because of institutions like NICE, the UK's health technology assessment (HTA) vehicle. NICE is a thought leader globally and serves as a reference for many HTA bodies. Once we achieve a positive NICE approval, this step holds importance not just for the UK but Takeda globally, just as a negative response from NICE can have important ramifications for all our affiliates."

Jon Neal, managing director UK and Ireland, Takeda

Gary Hendler of Eisai, another Japanese firm with regional management functions in the UK, explains that, despite Brexit-based uncertainties, "We do not have any intention to relocate our EMEA headquarters out of the UK. As an investing Japanese company, we do not simply have a commercial hub here in the UK, we possess a research hub and a manufacturing facility. Although this makes us unique, it also presents assets we cannot simply move around on a whim."

next ten years" around emerging disciplines such as the deployment of artificial intelligence (AI) and virtual reality to transform pathology and imaging.

"Essentially we are seeking to emulate the Americans who have proven to be very good at this… They perform the research and deploy that as a way to then dominate an entire sector. They have already done it very effectively with satellites and GPS and managed to generate many multiples of what was initially invested," reasons Bell.

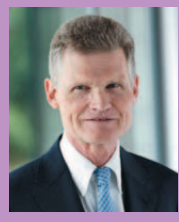
"I really believe in the LSIS. I think it is something the UK is capable of delivering and should be a clear priority for the industry and government. We have long been strong advocates of seeing accelerated strategies implemented in the British approach to the life sciences," declares Bryan Morton, executive chairman and founder of EUSA Pharma, a specialty drug developer focused on oncology and rare diseases.

He believes that the LSIS can go a long way towards helping Britain realize its full life sciences potential. "Firstly, I hope these initiatives will inspire a public market that is more receptive to, and understanding of health technologies, and secondly that they will improve its speed of translating great ideas from the academic field into robust commercial opportunities. Previously, British industry has created dynamic companies only to subsequently sell them on to big American corporations. This is something I believe can change so long as we can construct several British healthcare companies with significant size and value. In order to do that, we have to do a better job not only at mentoring British entrepreneurs to be more global, but also to improve funding with experienced, focused investors," he muses.

Laurent Abuaf, country president UK marketing company, Astra Zeneca; Terry O'Regan, vice president and managing director UK and Ireland, Biogen; Hilary Hutton-Squire, general manager UK and Ireland, Gilead

Some actors have voiced concern, however, about the proper financing and implementation of the proposals and will not have been reassured by a House of Lords Science and Technology

Core Take-Aways from the Life Sciences Industrial Strategy (LSIS)



Sir John Bell

- Moonshot Programs: Fashioning two to three entirely new industries over the next decade, by investing in "high risk/high reward" initiatives and funding pioneering research.
- Fundamental Research: Working with industry to increase spending on R&D to 2.4 percent of GDP by 2027, and then to three percent over the longer term with a view to attracting 2,000 new discovery scientists to the UK.
- Translational Science: Supporting a 50 percent increase in the number of clinical trials over the next five years.
- Capability Engineering: Creating four UK companies valued at over GBP 20 billion market capital within a decade.

Richard Erwin, general manager, Roche Products Ltd

Select Committee hearing in April which judged the government's execution of the LSIS to so far be "both incoherent and inadequate."

Roche's Richard Erwin is forthright about tempering expectations. "We are moving in the right direction. I am convinced it is hugely important that government listens when British business points out what has to be improved. We are in need of a committed plan, and the LSIS was a start, but it is just a start." Gilead's Hilary Hutton-Squire agrees, noting that "The government has done a lot of work to understand how to position the UK as a hub for the life sciences industry, and the LSIS is a great output of this. It now needs to be implemented."

THE NHS: PRIDE OF THE NATION

Many commentators are quick to point out the linkages between Britain's enduring leadership in life sciences and the existence of as remarkable and exclusive an institution as the National Health Service (NHS). "Within the UK, the NHS is a source of immense national pride and for a very good reason… unlike equivalent apparatuses in Germany or France, genuinely free healthcare is administered to all citizens from cradle to grave without anyone ever receiving a doctor's bill in the post," enthuses AstraZeneca's Laurent Abuaf.

Moreover, "when you consider that the UK boasts quite a unique ecosystem – a NHS that is universal and free at the point of delivery, thus one of the most advanced and comprehensive health data sets –it is hardly surprising that the UK has achieved worldwide acclaim for its innovation in early phase drug discovery," points out Biogen's Terry O'Regan.

Indeed, according to Sir John Chisholm, it is absolutely no coincidence that the UK ranks as the only market worldwide to date with a working genomics structure. "The initial premise behind establishing Genomics England was that we possess something in this country that frankly does not exist anywhere else: a single payer market and a nationwide, fully publicly-funded healthcare system that attends to citizens' health needs over the entirety of their lifespan… The strong advantage of working in this country is the extraordinarily strong coherence emanating from the commanding heights and pervading the entire apparatus," he exclaims.

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Roche

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Chris Fox, vice president and general manager UK and Ireland, Amgen

Chris Stirling, chairman and partner of global life sciences practice, KPMG

making care better for patients, but just as importantly making life better for staff," agrees newly appointed secretary of state for health and social care, Matthew Hancock.

The advent of AI-based diagnostics is perhaps a case in point. "NHS patient records can be seen to be especially suited for driving the development of powerful algorithms that could transform healthcare," muses Sir John Bell. "Considerable value lies in the datasets used to train algorithms on tasks ranging from speech recognition to diagnosing disease. As the world's largest publicly funded health service, the NHS finds itself blessed with one of the most comprehensive health datasets in existence. Akin to what Google is doing in other sectors, Britain actually possesses an equivalent unique position in the health space," he exclaims.

CHAMPION OR IMPEDIMENT?

The LSIS, of course, assigns the NHS a role as lead protagonist and primary vehicle for materializing the UK's ambition as a world leader in life sciences. "We require the NHS to be embracing new technologies that come through the R&D base here; not just adopting innovation initially, but actually harnessing it in full and mainstreaming it," posits under-secretary of state, Lord O'Shaughnessy. However, many analysts remain sceptical that the institution can ever really become a proper agent of change.

A longstanding and commonly voiced refrain has been that Britain's healthcare apparatus is too underfunded and stressed to shoulder such an onerous task. "The NHS appears to be very fatigued. When you talk to people who work there and sit across from healthcare professionals at any level, you get a sense that it is very labour-intensive for them to deliver care to patients. The cost constraints and what they need to spend their time on makes daily business very tricky. They are working for a good cause but finding it rather difficult to bring that value to fruition. We try to be sensitive to that and offer solutions which will ease some of that strain where possible," candidly observes Amgen's Chris Fox.

Fortuitously, the recent announcement of the British government that the NHS will be receiving an extra GBP 20 billion (USD

26 billion) a year in real-terms funding (once inflation is taken into account) by 2024, representing an average increase of 3.4 percent every year on the GBP 114 billion (USD 148 billion) budget for the next five years, goes a long way to alleviating the worries relating to the institution being too undercapitalized to deliver on its objectives. In the words of Simon Stevens, the institution's CEO: "As the NHS turns 70, we can now face the next five years with renewed certainty. This multi-year settlement provides the funding we need to shape a long-term plan for key improvements in critical services and the execution of our vital function."

Nonetheless structural hurdles still abound and there are many indicators that an organization that was conceived in the post-war, welfare state period is struggling to keep up with the times. While many of contemporary society's daily activities are now conducted online - from shopping to socialising - the NHS remains heavily reliant on older, often obsolete, technologies with the service infamous for its status as the biggest purchaser of pagers, fax machines and stamps in the world!

"The UK is in a truly amazing position and second only to the US in terms of science and technology; however, we are still waiting to see whether the NHS is serious about championing innovation… in order for companies to continue to see incentive to invest, I think there has to be a vision of sorts. The NHS has to visualise that healthcare will look very different in five years' time and act accordingly. We can already see that younger generations are eager to adopt new ways of accessing care, and many initiatives are under way, but the NHS is a 70-year old structure and henceforth intrinsically resistant to change," shrewdly concludes Chris Stirling, chairman and partner of KPMG's global life sciences practice.

NHS-INDUSTRY COLLABORATION

This is, however, precisely an area in which industry can assist. Already, medtech companies are working hand in hand with the NHS to introduce state-of-the-art diagnostic devices and reconceptualise care pathways with a view to rendering healthcare provision more effective and sustainable. "J&J has established a partnership with Bart's Hospital to run their orthopaedic department. Medtronic, meanwhile, have managed to strike a similar deal in cardiology at Hammersmith Hospital, while Leica and Philips have been participating in the establishment of a centre for digital pathology harnessing AI capabilities. The state's ambition is to apply the same sort of methodologies to the relationship with pharma companies at a moment when drug developers are demanding a deeper level of interaction than hitherto the case," notes Lord O'Shaughnessy.

Indeed, examples of this nature are also becoming increasingly widespread. Santen, for instance, has been collaborating to rationalize eyecare. "In some parts of the UK, we are already working in tandem with the NHS to modify treatment pathways. We aim to avoid referring to hospitals people with mild conditions, but require GPs, optometrists and pharmacists to be more confident in assessing conditions," recounts general manager, Craig Wallace.

Mylan, meanwhile, has been delivering up compelling value propositions from its generics portfolio which help free up sufficient finances for the NHS to afford cutting-edge, latest generation treatments such as costly, but effective CAR-T cancer therapies. "We strongly believe that Mylan is well positioned to be a solution provider and partner to the NHS. The launch of our generic version of Seretide® for asthma patients three years ago is an example of savings generated to the system. Today, it is generating between

Eyeing Up Success

Craig Wallace, general manager UK and Ireland, Santen

Philip Lewis Williams, managing director, Théa Pharmaceuticals

The UK ophthalmology market – the third largest in Europe – is a different beast to those of its European counterparts; prompting affiliates of enterprising international mid-caps Santen and Théa to adopt disruptive strategies in what can be an awkward and unorthodox business environment.

Théa's Philip Lewis Williams explains that, "the British marketplace in eyecare differs markedly from that of France in that the functions of optometry and ophthalmology are split … If you experience a minor problem with your eyes in France, you will likely visit one of the country's 8,000 ophthalmologists and it is relatively easy to secure an appointment. In Britain, however, there are only 1,250 ophthalmologists who will be busy dealing with more serious issues and the waiting times will be considerable." Craig Wallace of Santen concurs, noting that, "In the UK, if you have an ophthalmologic condition, your first port of call will either be the GP, or you might go to an optician or a pharmacist. A patient will only see a specialist ophthalmologist if he or she is referred to one."

The successful navigation of a market so unlike others in Europe has required Théa to enact a root-to-branch shake-up of its operations. Lewis Williams exclaims: "We had to try to be superior in every task that we undertook. That started with our sales representatives and ensuring that they properly understood the subject matter and were not overly pushy. We also placed a lot of early emphasis on getting ourselves known in local academic circles." Lewis Williams also recalls that, "we embraced a rather disruptive business model in which we targeted high street opticians and independent optometry outlets in much the same way that cosmetic companies like Chanel sell their beauty products."

The UK strategy of Santen has prioritized inter-stakeholder collaboration to help redesign a healthcare system more conducive to eye health and create a patient population more receptive to ophthalmological products. Wallace stresses that, "in some parts of the UK, we are already collaborating with the NHS to begin the process of redesigning the system, striving to find ways to modify pathways." He continues, "we aim to avoid referring people with mild conditions to hospitals, but therefore need GPs, optometrists and pharmacists to be more confident in assessing conditions. In the case of a severe dry eye conditions, however, we need to work towards an accelerated pathway to the specialised ophthalmologist. This is exciting as these projects are transformative and clearly demonstrate our commitment to improving eye health in the UK."

GBP ten and 12 million (USD 12.7 and 15.3 million) in savings to the NHS, just by providing patients with another treatment option with the same molecule," explains the company's managing director, Jean-Yves Brault. "Every generic we introduce in the market provides healthcare professionals with a new option and creates more access for patients while taking off pressure on NHS' budget management. That is how we believe we can be perceived as a solution provider to the challenge of healthcare… The recent introduction of our Glatiramer Acetate 40mg/ml is yet another example of Mylan's contribution to improving access for patients, providing more treatment options for healthcare professionals and helping the NHS optimise the available funds," he adds.

INNOVATION: SLOW ON THE UPTAKE

While the UK has firmly established itself as a global power in basic science and research, when it comes to actually bringing state of the art technologies to the domestic market, the path is strewn with hurdles.

As AstraZeneca's Laurent Abuaf points out, "the UK has what it takes to be a global life sciences leader, from a scientific capital perspective, from an infrastructure perspective and, more recently, from a political intention perspective – but this political intention needs to transform into real decision-making." Lord Philip Hunt of the Labour opposition describes improving uptake of innovation as "the one issue above all else that I would tackle as a Health Minister … We know that we are a little bit slow to adopt new ideas, despite the fact we are brilliant at developing them."

Making an international comparison, Roche's Richard Erwin laments that, "for many, the UK market is seen as one of the most challenging in healthcare. Not in terms of sheer size, such as the US or China, but in terms of market access and uptake of innovative new products. In Germany, for example, access is often rapidly granted, and uptake of innovative breakthrough products guaranteed; however, the UK ranks low in international comparisons for access to new medicines. Sometimes, even when access is granted, uptake can be slow."

Terry O'Regan of Biogen – the manufacturers of Spinraza, an innovative treatment for spinal muscular atrophy – points out that despite an expanded access program for the drug being implemented, patients still struggled to receive it. He recalls how "despite the provision of free drugs; infrastructure and capacity challenges still needed to be overcome before patients could receive them. It was, quite frankly, seriously heart-breaking to hear that a breakthrough therapy with the potential to fundamentally change the course of disease was not immediately available, but, resolution was found, and many children are now being treated through this program."

Louise Houson, managing director UK and Ireland, MSD

Haseeb Ahmad, country president, Novartis

MSD's managing director, Louise Houson, believes that industry needs to partner more with authorities to counter this slow uptake of innovation. She posits that, "for the UK to remain a very attractive market in post-Brexit times, we have to ensure rapid uptake. I believe the solution lies in partnerships. The aforementioned challenges concern the industry, as well as the NHS, NICE and the Department of Health and Social Care (DH). We have a responsibility to partner to overcome the current affordability challenge faced by the NHS to work towards a more flexible system with rapid uptake at its core."

AstraZeneca's Abuaf strikes a similar chord: "we have to figure out, as an industry and together with academia and officials, how we can strike the perfect balance between ensuring that the best innovation reaches patients in an affordable manner and encouraging innovation on the other side. There is no easy answer, but I see that the foundation for discussion is here in the UK and that ultimately, everybody has the health of patients on their mind. This will lead all of us to make the right decisions moving forward."

PRICING: AT THE LIMIT!

The main obstacle facing pharmaceutical companies operating in the UK is, however, the country's pricing structures. Neil Dugdale, vice president and general manager of UK and Ireland at Sobi, opines, "prices in the UK market have been driven down significantly over recent years. While this is a good thing for taxpayers and should mean greater access to innovative medicines for patients, it has a sum of negative repercussions. First and foremost, we have to ask ourselves, how long is such a system with constant price cuts sustainable? The looming threat is that, at some point, companies will have to make the decision not to launch highly innovative products in the UK, because it does not make sense financially."

Otsuka's Stewart Pearce agrees on the difficulties of navigating the UK's pricing structures. "It is hard to get through NICE without drafting out confidential discount schemes," he notes. "As a reference market, we display a gross price, visible to other markets, in addition to the net price required for NICE negotiations. To us, the barriers we have to surmount to bring a product to the UK are hence twofold as we need to consider reimbursement just as much as the impacts our pricing in the UK will have on other markets we want to launch in."

Roche's Richard Erwin is even more pessimistic. He asks, "we do ask how a country like the UK can justify having some of the lowest thresholds for ICER (incremental cost-effectiveness ratio) amongst developed nations. As a British citizen, I find this unacceptable; the value the UK places on a year of life gained is one of the lowest in the developed world." Erwin continues, "the current ICER thresholds are challenging to navigate. In some cases, we have offered free access to our medicines, but this just is not a sustainable business model." AstraZeneca's Abuaf adds that, "NICE cost-effectiveness thresholds are some of the lowest in Europe and have not changed since 1999, despite inflation, which can be challenging when trying to bring innovative medicines in the UK."

Gilead's Hilary Hutton-Squire pinpoints the main discrepancy in pricing thusly: "Today, I see an issue arise because there should be a difference between the areas where it is easiest for procurement bodies to drive down costs, and the areas where we value innovation the most," she moots. "However, we often see that the areas where it is easiest to drive down costs are the areas where we value innovation the most, in new medicines and innovations. As opposed to medicines that have been around for

a long time, they are medicines in highly specialized areas and often one-off treatments as opposed to chronic treatments."

PRICING WOES FOR RARE DISEASES

For rare disease specialists, the situation is particularly difficult. Biogen's Terry O'Regan outlines the alarming figures: "Of the 143 rare disease therapies approved within the EU, a mere 68 were available on the NHS in 2016. Equally concerning is the fact that it takes on average two and a half years for approvals to be attained." Sobi's Neil Dugdale adds, "within NICE, there is a 'one-size-fits-all' approach to treatment appraisal, as it was designed to analyse the cost-effectiveness of products treating thousands of patients. In rare diseases, however, we see patients gaining access to treatments – treatments that could either cure or extend their life substantially with a good quality of life – significantly later than in most other developed economies."

Dugdale elucidates that, "in rare diseases, patients have to wait an average of five years to get a diagnosis and many of these patients are children. These families with sick children have been stressed and traumatised for an average of five years. Some are then told that there is either no diagnosis or that there is a diagnosis but that no treatment exists. The best case is a diagnosis and a treatment. However, with the current appraisal process, the treatment might be delayed significantly compared to other developed economies; my fear is that some may never reach the market if an agreement cannot be reached with the NHS. Furthermore, a company may decide to prioritise supply to countries that do not insist on the low prices demanded by the NHS. The situation where a family has to go through the extreme stress of non-diagnosis, to the relief of a diagnosis and a suitable existing treatment, to then learn that it is not yet available in the UK, is just not acceptable for a top five global economy, considering its science base and global leadership."

O'Regan does, however, see signs of positive change in terms of the authorities' attitudes to rare diseases. "NICE and NHS England responded favorably to our request to sit around the table and decide on a workable solution in the interests of patients," he notes. "The fruit of these discussions was a common agreement on how to move forward. The critical issue now is to prevent any clock stoppages along the way. I am, however, genuinely optimistic about how everything is panning out. We are witnessing an unprecedented degree of flexibility being shown by the authorities and that, in itself, appears to herald a new dawn."

Neil Dugdale, vice president and general manager UK and Ireland, Sobi

Bryan Morton CBE, executive chairman & founder, EUSA Pharma

Dugdale is, though, less optimistic, gloomily opining that "the challenge we encounter in the UK is that often the focus is on cost reduction and not innovation and not a free choice for healthcare professionals to utilise all treatments for the benefit of their patients. Recently, in Ireland's assessment of haemophilia treatments, a large proportion of the criteria considered for reimbursement were clinical outcomes. In the UK, 85 percent of criteria for the haemophilia A tender process were based on cost alone with no weighting at all for innovation or patient outcomes. Therefore, the majority of the people in the UK living with haemophilia A continue to be treated with conventional factor replacement products that have not changed significantly for 20 years."

GENERICS: RACE TO THE BOTTOM?

The UK has the highest percentage of generics penetration in Europe, at 86 percent. However, this does not naturally make the British market a playground for generics companies; indeed,

as Tim de Gavre, country head of Sandoz, sums up, the UK market can be categorized as, "highest penetration, lowest prices, lots of competition." Otsuka's Stewart Pearce is even blunter: "Sometimes, the UK really feels like it is a race to the bottom once generics come in," he sighs.

Because of this, many generics companies are attempting to diversify into higher margin areas in order to remain profitable. Ben Ellis of Lupin explains that, "we have about 30 products in our UK portfolio, implying that we have reduced our product range significantly as we are trying to get away from 'vanilla generics,' where there is very little margin at all in the UK." Mylan's Jean-Yves Brault documents how, "several generic companies remain pure generic players, others, like Mylan have ventured into diversification, and some have walked down the path even further. I see biosimilars as being tomorrow's big game changer and those companies that will count biosimilars within their portfolio will most likely benefit from it."

As a counterpoint, Thomas Broeer of Indian generics specialist Aurobindo, does not feel that pricing pressures for pure generics are too severe in the UK. He proffers, "the high rate of genericization in the UK market means that brand loyalty in the generic sector is less impactful; the importance is, therefore, competitiveness and ensuring the possibility of supplying the market sustainably. For Aurobindo, the UK operates as a level-playing field in which our cost-leadership and vertically integrated structure are given the opportunity to shine. Pricing is not necessarily aggressive if you take into consideration all aspects of a market structure before entry."

SURVIVAL STRATEGIES

This backdrop of slow uptake of innovation and difficult pricing structures has pushed companies to develop a wide mix of country-specific strategies. As Haseeb Ahmad of Novartis astutely notes, "this is a market where you need to be able to transform and perform at the same time. It takes individuals that can master agility and organizations with the ability to pivot rapidly to succeed here."

For Otsuka, this means sagacious product selection. "Otsuka has a smart strategy: it will never bring to market a 'me too' product," explains Stewart Pearce. "Aligned with our global mission of truly improving healthcare, we focus on complex products in areas of high unmet medical needs. By bringing products through our pipeline that are truly innovative and very specific, you have of course better chances of success."

Jean-Yves Brault, country manager, Mylan

Lundbeck has chosen to focus on second and third-line treatments, rather than the crowded first-line treatment market. Thomas Bo Bjorn Klee, managing director UK and Ireland, clarifies: "I looked at our market potential and the challenges we faced. For example, in depression, first line treatments are now mostly generic and so we are looking at entering the market with either second and third line treatments. Similarly, generics are dominating the first line treatment of schizophrenia. Our biggest challenge was to translate our global strategy – showing the essence of the new Lundbeck – into a local strategy; one that focuses on offering second and third line options that make a difference to patients while responding to the financial pressures within the NHS."

Other companies have adopted even more unconventional business models. Clinigen, in the words of its CEO Shaun Chilton, "expands and extends the true value of a pharma or biotech partner's product's lifecycle. Our uniqueness stems from our ability to manage different commercial and access situations for our partners. Whether these companies want to retain rights but improve access, divest or license their products to us, we find a solution nonetheless.

CDMOs on the Rise

Kevin Cook, CEO, Sterling Pharmaceutical Solutions

Ian Shott, CEO and executive chairman, Arcinova

The UK's contract development and manufacturing market has seen healthy growth in recent years, with Big Pharma increasingly outsourcing all but its core functions and looking more to reliable, well-regulated markets such as the UK.

As Kevin Cook, CEO of Sterling Pharmaceutical Solutions, an API manufacturer based in England's North-East, explains, "roughly ten years ago there was a shift to Asia to solve financial problems and resolve API manufacturing issues. We now observe a reverse trend of manufacturing returning to the West." Cook continues, "certain projects will never return to the West, nonetheless, where there is a degree of complexity and hazard, Sterling in particular is well placed to add value… We now see strong growth in the CDMO space, particularly within emerging pharma."

Ian Shott of Arcinova articulates the enduring value of companies which focus on small-molecule development in an environment where advanced therapies dominate the headlines. "Today, advanced therapies are in a way more 'sexy' than small molecule medicines," he notes. "However, many so-called biotech and emerging pharmaceutical companies focus on the development of small molecule treatments and small molecules still dominate the sales portfolios of all the major global pharmaceutical companies."

In terms of what British-based CDMOs can offer, Cook points to "assurance of supply and reliability." He continues, "from a compliance point of view, we operate a simple approach: safety, quality, and quantity. If we cannot perform the operation safely, we will not accept the project, and there is an excellent framework within the UK to do things safely."

We see it as our responsibility to ethically manage access to difficult to procure medicines, mitigating the risk of counterfeit medicines entering a company's supply chain and thus ensuring that the health and safety of patients are not compromised."

Bristol Labs, which has grown into one of the UK's leading generics manufacturers since its foundation in the late 1990s, has focused on bolstering its productivity to ensure success. Tembalath Ramachandran, the firm's founder and chairman notes that "when you are going head-to-head with low labor cost countries such as China or India, and wages in the UK market are on average ten times more expensive, it is essential to absorb that difference in operating costs through much higher productivity. That comes about partly through doing our research and coming up with an optimum selection of products. We have to be very attentive in our initial identification of which molecules to run with. Beyond that, our great track record on productivity hinges upon the excellence of our manufacturing equipment and our streamlined, rationalized operating procedures."

Ramachandran continues, "we have invested substantially in developing our Luton site into a state-of-the-art, MHRA-approved facility that is highly automatized. This has entailed installing the best possible machinery for pharma manufacturing which in turn enables us to produce a great many types of tablets, capsules, and sachets. Moreover, our high-speed packaging machines markedly reduce turnaround time and generate greater efficiency in the working style of the staff. Much emphasis is also given over to the training of the personnel and to automation. You have to make sure the operator or technician has effectively understood the process and has the wherewithal and resourcefulness

TOP 15 PHARMA COMPANIES IN THE UK

TOTAL MARKET (INCLUDING OTC), MOVING ANNUAL TOTAL (MARCH 2018)

	COMPANY	MARKET SHARE
1	PFIZER	8.2%
2	NOVARTIS	6%
3	GLAXOSMITHKLINE	5.3%
4	MERCK & CO	5.2%
5	BAYER	4.6%
6	ROCHE	4.5%
7	ABBVIE	4.5%
8	JOHNSON & JOHNSON	4.3%
9	SANOFI	3.9%
10	GILEAD SCIENCES	3.1%
11	ASTRAZENECA	3%
12	BRISTOL-MYERS SQUIBB	2.6%
13	BOEHRINGER INGELHEIM	2.3%
14	MUNDIPHARMA INTERNATIONAL	2.3%
15	BIOGEN	2.2%

Source: IQVIA



Thomas Bo Bjorn Klee, managing director UK & Ireland, Lundbeck; Shaun Chilton, CEO, Clinigen Group; Tembalath Ramachandran, chairman and managing director, Bristol Laboratories

Jeremy Thorpe, managing director, Tillotts Pharma

to be able to optimize it even more when the opportunity arises."

Swiss-headquartered gastroenterology specialist, Tillotts Pharma, has built its success in the UK on a perspicacious in-licensing strategy. Jeremy Thorpe, the company's managing director points out that "the UK is full of such opportunities, and Tillotts is very interested in products that other companies might look to divest whether this is on national, regional or global scale. A big pharma company may lose interest in a legacy product as it approaches the end of its patent life even though it may continue to address patient need or may simply find that a gastrointestinal product does not fit in their broader portfolio anymore, so they lose interest and ignore the brand. We are, as a globally-acting company, interested in taking on these products particularly those with projected annual UK sales in excess of GBP four million (USD five million)."

Thorpe also highlights that not only is Tillotts offering products at a lower price than its Big Pharma competitors, but also outdoing them in terms of added support. He says, "the NHS was already cash-strapped in 2012, and we aligned ourselves with the new NHS strategic requirements, providing Octasa 400mg tablets as a high-quality lower-priced alternative to Asacol 400mg tablets. From total annual sales of GBP 230,000 (USD 293,161) in our first year in 2012, we took Octasa 400mg tablets to GBP 4.75 million (USD six million) in 2013. I believe this was because we had the most interesting value proposition to the system both in terms of financial savings and through a real passion for supporting patients with IBD."

THE BREXIT EFFECT

Naturally, the UK's impending withdrawal from the European Union is the topic on everyone's lips; especially in terms of how Brexit might impact both existing local market dynamics and the country's lofty ambitions to consolidate its position as one of the world's great life sciences powerhouses.

Many MNCs are concerned about the implications of regulatory de-alignment with EU norms and what this might mean for product launch timelines and approval frameworks.

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BRISTOL LABORATORIES

Sanofi's chairman of the Brexit committee and UK market managing director, Hugo Fry, for example, bemoans that, "were the UK to end up requiring a separate regulatory submission, the market will automatically sequence behind America and the EU for product launches in much the same way as we see for other mature markets that possess their own distinctive regulatory frameworks such as Canada, Australia and Switzerland… this means market entry for new products will likely occur later than in the past with the result that patients will have to wait longer."

Tim de Gavre of Sandoz very much concurs. "Even in a robust and professional market like Switzerland, for example, just having an additional layer of bureaucracy slows down the process and delays how products launch. For some of our biosimilars, they are now close to six to 12 months behind the UK," he warns.

Others are uncertain about the possible logistical complexities around having two parallel jurisdictions. "Many people do not appreciate that so many products come through the EU regulatory process and products manufactured outside the EU are tested and quality released in EU laboratories. It is not clear what is going to happen going forward and whether these activities need to happen in the UK specifically or in any EU member state which is currently the case. This leaves companies like ours having to try and second guess a hard or soft Brexit and put in contingency plans to cover a broad range of eventualities," asserts Lupin's Ben Ellis.

"If we have a 'Hard Brexit' I anticipate that changes will be necessary as the regulatory status of products in the UK will change. Marketing authorisations held in Europe will have to be transferred to the UK, and visa-versa, batch release will have to be conducted in the UK and there will be VAT implications as the customs status will change, there may also be delays at customs clearance and disincentives to supply the UK," confides Tillotts' Jeremy Thorpe.

In most cases, however, insiders are tending to downplay the risk of widespread disruption. Bristol Labs' Ramachandran reflects that, "companies like ours will not be any weaker after Brexit, but clearly we will have to adapt to certain changes. For example, we used to employ a lot of East European workmen in our factories but are witnessing that particular talent pool drying up in the wake of the Brexit decision so we will have to source affordable staff from elsewhere in the future."

Roche's Richard Erwin is equally serene. "The impact on Roche is likely to be limited. We manufacture in Switzerland and the US exclusively, so we are already importing our products from a third country with very high-quality standards. Our role in the UK consists of ensuring we have continuous supply and we are confident that, by working closely with government, this can be achieved," he laughs.

Clinigen's Shaun Clinton is also sanguine on the country's future prospects, noting that, "irrespective of what is going on around Brexit, the UK is still a fantastic source of innovation and talent and a great base for building successful international companies."

Nor do British-based biotechs appear particularly flummoxed. "It is possible for biotech companies to be pragmatic about upheavals such as Brexit, by our very nature we are constantly going through change. In order to survive, we have to embrace such change.," confesses TC BioPharm's Michael Leek.

Erik Nordkamp, managing director, Pfizer

Meanwhile the government has been at pains to reassure industry that any disturbance will be kept to a minimum and that stability will be maintained. "In terms of our relationship with Europe, our intention is to secure an associate membership of the EMA, which would mean a continuity of the kind of relationships that we have now, albeit on a slightly different legal basis," declares Lord O'Shaughnessy. "I am confident that the reasons that companies will want to come to the UK in the future will be the same: namely that we possess a terrific, high-performance life sciences ecosystem, and world-leading academic institutions combined with an ingrained attitude of wanting to drive uptake, plus the recognition that that is something that really does need to happen," he opines. Any member of the scientific community fretting about being cut off from EU research funding can also rest easy from the news that the UK government will match or better any available grants.

Equally confidence building is the reality that Europeans and Brits alike have strong motives to continue to align closely. "Quite frankly, fracturing the European life sciences industry as a result of Brexit would be damaging to the industry across Europe. That's why it is in the interests of the EU to ensure the UK remains integrated as far as possible to the European life sciences eco-system, which would also be in the best interest of European patients," reasons the ABPI's Mike Thompson.

SPYING THE OPPORTUNITIES

Moreover, an increasing number of actors are now starting to identify likely opportunities for the post-Brexit period. "As a nimble and agile player with rapid reaction speeds, we calculate that Brexit can help us create a better commercial environment for inward investment from the government and for commercial return," reveals Eisai's Gary Hendler.

Others speak of Brexit as injecting a certain level of momentum and energy into the industry. "What is making the UK particularly relevant right now is the pressure it is under to really think about its future. This reality combined with the need for the NHS to transform generates an impetus that forces creativity and prepares the ground for innovation to thrive," enthusiastically asserts Pfizer's Erik Nordkamp.

Haseeb Ahmad of Novartis also feels that opportunities are there for the taking. "Juan Manuel Fangio, one of the best racing drivers of all time, once explained his superior win ratio with the words: when I see an incident up ahead, while all the other drivers take their foot off the gas, I put the foot to the floor because I view that as my opportunity to lead. Well, I tend to look at Brexit in a similar way," he recounts. "This could be an excellent chance to take British life sciences global!"

Design Thinking in Pharma

How industry can benefit from this new view on innovation

Everybody's doing it. Hiring Chief Innovation Officers. Looking for ways to "disrupt." Trying to reinvent or reimagine their business though they're not sure what that means or where to start. Are these initiatives just passing fads or actually a smart investment for companies, particularly those in the pharmaceutical industry?

The short answer: it depends. When design thinking is incorporated into the business model, and when innovation itself is not the singular goal but a measurable benefit of a pursuit, pharma businesses can truly differentiate themselves and recognize a valuable impact. Design thinking is an emerging practice that helps organizations take a fresh and honest look at innovation and improves how companies identify and meet their clients' needs. Design thinking can revolutionize an innovation agenda and, in turn, a company.

Rather than traditional methods of product and solution development that begin with an end state already in mind, design thinking centers on empathy and achieving a true understanding of the target audience. A design thinking-led approach acknowledges and addresses existing pain points and works from those to improve user experiences. Design thinking brings forward breakthrough frameworks, tools, and processes that start with a client's needs, not just the needs of the business. It challenges companies to put themselves in the shoes of their clients/patients to understand their perspective, rather than only what a business feels it needs to stay competitive. For example, companies rush to build flashy apps—but is that really what the customers want to improve their user experience? Design thinking challenges companies to start with the why instead of the how or what, to not just jump to innovation for the sake of innovation.

Pharma stands to benefit from design thinking in a number of different ways as illustrated by the following applications:

» Onboarding a new pharmacy for the pick-up and distribution of a new drug traditionally entails mountains of paperwork. How can manufacturers and distributors make this process easier for those purchasing their products and encourage them to remain a long-term client? Through observation of the onboarding process from the client's perspective, a clear and thoughtful understanding of needs could significantly improve a user's experience.

» With the constant pressures of R&D costs, demanding shareholders, and watchful Wall Street analysts, pharma executives are challenged to cover costs and move product. Taking a design thinking lens requires leaders to see skyrocketing drug costs from the perspective of a newly diagnosed patient facing what seem like insurmountable medical expenses.

Might your company consider alternate ways for patients to pay to help alleviate financial anxiety while facing a serious illness? This is clearly not a simple problem to solve, particularly with drug theft making its own negative impact, but a more empathy-driven, human-centered approach changes the dynamic of the issues at hand and helps break down silos through a common cause. It may be possible to streamline access to critical treatments while still meeting business and shareholder objectives.

» Serialization is typically seen solely as a cost by pharma executives who must now devote time, resources, and budget to track-and-trace compliance requirements. Viewing this process as an opportunity rather than a regulatory exercise opens the doors to multiple ways to improve business operations. Once implemented, drugmakers will have access to a tremendous amount of data, including the status of each sellable unit, how long a product remains at each supply chain node, and how quickly it moves from manufacturing to packaging to third-party logistics (3PL) to distributor. By using the outputs of serialization, emerging data, and feedback from supply chain employees, companies can help to identify areas for operational improvement and even help to optimize the entire supply chain network.

When people hear the words innovation, disruption, and design thinking, they often think of the Apples and Ubers—new generation, consumer-facing giants that are changing how we live our lives. But real success comes not only from sleek new products or apps but from an understanding of a customer's needs and preferences across a wide range of client-facing ways. That's why a challenge-based, empathy-led business approach applies just as much to Bridgewater, NJ, and Raleigh-Durham, NC, as it does to Silicon Valley. In fact, no industry is riper to benefit from instilling a design thinking mindset than pharma, and many have already embraced the shift in perspective. PE

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