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VOLUME 38, NUMBER 5

An Investor's Eye

Tim Sullivan
Chief Financial Officer,
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So Much Depends on the Physician

TRANSCELERATE BIOPHARMA RECENTLY ANNOUNCED a grassroots One Person Closer (#OnePersonCloser) social media campaign to inspire more physicians to believe in clinical research and motivate them to have conversations about clinical trials with their patients. Joe Kim, senior advisor, clinical innovation at Eli Lilly, and campaign lead for TransCelerate's Clinical Research Awareness initiative, mentioned that the top reasons physicians don't refer patients to trials are lack of time, lack of financial incentive, lack of trust in the research enterprise, and lack of understanding on how to match patients to relevant trials.

LISA HENDERSON
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After meeting photographer and co-founder of online patient community Smart Patients Gilles Frydman, Kim discovered that they shared a vision: telling the authentic stories of the real people involved in clinical trials—researchers, physicians, and patients—and conveying the essential role each person plays in the development of new medical treatments and breakthroughs. This vision is the inspiration behind the One Person Closer social media campaign, which can be found on Twitter, Facebook, and YouTube (https://www.facebook.com/onepersoncloser and https://twitter.com/onepersoncloser).

As Dalvir Gill, CEO of TransCelerate, told me, "There are many things that are being done. But if we help one person get into a trial, and enough people try to do this, we can move the needle."

A well-intentioned and designed education and awareness campaign to physicians about clinical trials, in general, doesn't seem a bad idea

Beyond the physician, the structure of healthcare and clinical trials in and of itself is a barrier to patient recruitment in these trials. Clinical trials are separated from healthcare because of regulatory and ethical requirements. And while physician investigators are, by definition, physicians, a physician in clinical practice is oriented toward providing patients with individualized care in their patients' best interests. An investigator, on the other hand, makes no treatment decisions, but follows a protocol to further research. Though a patient-participant may benefit from research participation, that benefit or non-benefit is not the investigator's concern.

On the commercial side of pharma, physicians have become an elusive, hard-to-reach stakeholder—a stakeholder that has the trust of his or her patients. The changing healthcare delivery system makes it challenging for pharma to find the prescribers and decision-makers at the larger integrated delivery networks (IDNs). According to an American Medical Association report from 2016 data, 38.7% of physicians in multi-specialty practice reported that their practice included 50 or more physicians, and physicians in multi-specialty practice were also more likely to report hospital ownership, 43.6% compared to 22.8% for physicians in single specialty practice.

Physicians and healthcare professionals (HCPs) have been increasingly burdened over the years with managed care, navigating their own billing issues with health plans, as well as helping patients navigate treatments and care; using electronic health record (EHR) systems; navigating the Affordable Care Act (ACA); and only having, on average, nine minutes to speak with patients in the exam room. Pharma wants to stay close to physicians and goes to great lengths to stay closer through targeted services that help them better inform and educate their patients about prescription costs, adherence, and access.

On one hand, pharma has to be very careful about what it communicates to physicians and patients about prescribed treatments, as well as potential therapies in clinical trials. On the other hand, a well-intentioned and designed education and awareness campaign to physicians about clinical trials, in general, doesn't seem a bad idea to me. Not promoting a specific trial, or even a specific therapeutic area, but maybe utilizing the same medical science liaisons (MSLs) or services that surround commercial physician engagement to reach out and educate them. In the end, until randomized clinical trials are not the standard for human drug trials, more patients having access to clinical trials is beneficial to everyone.

I touch on this topic with our podcast editors in this podcast: http://bit.ly/2Fhfto4

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Science & Strategy: An Investor's Eye

By Michelle Maskaly, Senior Editor

Pharm Exec speaks with Tim Sullivan, a former biology major, biotech investment banker, and venture capitalist, who brings that sought-after melding of business and scientific perspectives to his role as chief financial officer for Apellis, a clinical-stage company hopeful of ushering in novel protein inhibitors for autoimmune disease.

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Cover photo: courtesy of Porter Gifford Photography

Brands of the Year

Brand Stories: Promise and Challenge

In its 12th annual feature, *Pharm Exec* builds on the revamped approach it introduced last year in spotlighting notable biopharma brands, profiling a new round of products that are making waves in five key areas in healthcare and R&D.

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By Michael Joachim

With patient empowerment reaching new heights, what two critical elements will steer pharma's advertising path?

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Readers Weigh In

An excellent analysis of AI. Yes, there is a lot of hype around AI; guess it's more talk than real action. Though pharma stakeholders are hyped up, not sure how many understand the medical relevance of its application. AI might help some super specialties, but a large chunk of contribution in the pharma/life sciences is still from general practitioners/other specialties. AI/digital should give priority to enable this target segment and, in parallel, focus on other segments. As the saying goes, "A bird in the hand is worth two in the bush!"

Anonymous
"AI in the Medical Domain: Not a Quick Fix"
bit.ly/2I3Icjm

Thanks for sharing this blog. It's really very informative. Most businesses and companies are interacting with customers through social media. As explained in the article, in the pharma industry, social media has become a medium of communication between customer and pharma to help gather better insights of customers.

Anonymous
"From Chaos to Calm: Making Sense of Social Media"
bit.ly/2lidQRx

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Hosts, Senior Editor Michelle Maskaly and Associate Editor Christen Harm, take listeners beyond the pages of *Pharm Exec* to gain a deeper understanding of the real issues facing biopharma today—interviewing prominent industry leaders, as well as providing a behind-the-scenes look at what the editors at *Pharm Exec* are working on.

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Devyn Smith, chief strategy officer and head of operations for Sigilon Therapeutics, talks about the pharma industry's reputation struggles in the US and Europe and potential ways to fix them, from a very personal perspective. bit.ly/2ou14OO

Episode 4: Outcomes-Based Contracting
Michelle and Christen take a deep dive into the issue of outcomes-based contracting, with Editor-in-Chief Lisa Henderson and European and Online Editor Julian Upton. bit.ly/2GAh22z

Episode 5: Med Affairs Training
Dr. William Soliman shares the story of how the Accreditation Council for Medical Affairs went from an idea in his head to a training program today that has enrolled more than 3,000 people and is setting new standards for medical affairs professionals. bit.ly/2IUZj6Q

Episode 6: The Pharma vs. Biotech Experience
Michelle and Christen interview Lara Sullivan, founder and president of SpringWorks Therapeutics, about the differences in working for legacy pharma vs. small biotech startups. bit.ly/2EGuvDt

Episode 7: Big-Event Insights
Pharm Exec editors discuss key takeaways from a variety of industry conferences that took place across the globe. bit.ly/2Fhfto4

Gottlieb Tackles Drug Competition & Costs

Pharm Exec interviews the FDA commissioner, who is building support by combating opioid abuse and advancing innovation

Scott Gottlieb has not shied away from tough drug development and access issues since taking the helm of FDA in May 2017. To help mitigate the nation's opioid drug epidemic, he has backed policies to reduce inappropriate prescribing and internet marketing of illegal drugs. And to continue last year's notable gains in bringing important new drugs and gene therapies to market, he has promoted innovative clinical research methods and strategies to make biopharmaceutical testing more efficient.

Gottlieb's overriding goal is for these and other initiatives to achieve "a good balance between innovation and access," he told *Pharm Exec* in a recent interview. The commissioner has loudly challenged high drug prices, blasting brand manufacturer "shenanigans" for blocking generic drug development. While there are more things that FDA can do to create a more competitive drug market place, "there's no one silver bullet," he commented, noting that FDA will continue to promote reforms "that will have an impact" (see sidebar).

In tackling these and other contentious issues, Gottlieb has quieted critics on all sides. Democrats initially feared an industry bias, but have been impressed by his initiatives to advance public health and challenge drug prices. Republicans hoping for a free-market deregulator support his attack on opioid abuse and efforts to speed innovative therapies, devices, and diagnostics to patients.

Gottlieb also has built support in Congress, as seen in the timely enactment of new user fee programs last year and slight modifications in "right-to-try" legislation to lessen its erosion of the FDA approval process and maintain patient protections. Certainly, many of Gottlieb's initiatives are not new and reflect years of hard work by FDA staff. But vocal support from the commissioner has accelerated action on many fronts.

Setting priorities

A clear sign of achievement for Gottlieb is the $400 million boost in FDA's budget plan for 2019, a notable shift from earlier administration proposals to sharply cut agency appropriations. To convince the legislators to approve the requested funds, FDA has outlined how the added resources will advance biomedical innovation (view the agency's budget plan for 2019 here: https://bit.ly/2HqnDj0). There's a prime initiative to develop data and analytical tools to better utilize real-world evidence in accelerating medical product development, plus an expanded "knowledge management system" for evaluating new drugs more rapidly and consistently. Additional funds will support FDA's Oncology Center of Excellence and advance new treatments for rare diseases. And access to generic drugs will gain from further automation of the review process and a proposal for legislation to prevent "first filers" of generic drug applications from blocking subsequent competitors.

Gottlieb also highlights the importance of modernizing the manufacture of drugs and biologics and vaccines to produce needed therapies more reliably and at lower cost. A related initiative is to ensure quality production of safe compounded drugs from outsourcing facilities to provide more reliable sources of needed products, particularly in shortage situations.

"We're now at a tipping point" for advancing drug quality, Gottlieb told *Pharm Exec*. The agency will develop further guidance and standards to reduce uncertainty for industry in adopting high-technology platforms. And more highly trained field investigators will inspect for quality and those aspects of manufacturing that create risks.

This focus on modern manufacturing fits Trump administration efforts to encourage "re-domesticating some of the manufacturing that has moved overseas," Gottlieb explained. He noted that high-quality, small-footprint manufacturing platforms have lower labor costs more suited to US operations. Advances in how FDA oversees medical device production similarly bolsters a "Bring Medtech Manufacturing Home" initiative that encourages firms to retool production operations in the US.

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Challenges ahead

FDA will be hard pressed in the coming months to realize last year's gains in drug development and approvals. But the commissioner shows no sign of sidestepping hot issues, such as nicotine levels in cigarettes, oversight of independent testing labs, and food contamination outbreaks. FDA faces numerous deadlines for implementing the 21st Century Cures legislation, including provisions to support regenerative medicine and to speed the development of new cancer treatments, personalized medicines, and gene therapies. At the other end of the spectrum is a proposal for new user fees to support more efficient oversight and approval of over-the-counter medicines.

Transparency remains a thorny issue, as FDA promotes wider disclosure of data and analyses related to regulatory, safety, and enforcement decisions. Yet complete response letters issued when FDA delays an approval remain under wraps, as industry seeks to keep confidential certain regulatory decisions. And although Gottlieb has supported more liberal FDA regulation of commercial speech in the past, he has said little on this topic as commissioner. Gottlieb expects final guidance on communicating healthcare economic information to payers will encourage "more vigorous discussion" of the economic value of medicines with less FDA oversight, reducing the need for the agency "to police those discussions involving sophisticated parties."

Combating the opioid epidemic remains a prime challenge, as physicians push back on proposals to limit opioid prescribing and mandate provider education. FDA has a key role in developing less addictive pain medicines and new treatments for substance abuse and has gained added resources to detect and block imports of counterfeit or illegal controlled substances at the border. New legislation may strengthen the agency's authority in these areas and in requiring limited-dose packaging.

Other industrial nations pay more for generic drugs than the US and less for innovator therapies—a situation Gottlieb considers a "recipe for destroying innovation."

An intriguing issue for Gottlieb is how current policies and practices encourage global "free riding" on US biopharmaceutical R&D. New FDA data indicates that other industrial nations pay more for generic drugs than the US and less for innovator therapies—"but not a lot less" when adjusted for net price, he points out. The payments should be reversed, Gottlieb says, as the current situation is a "recipe for destroying innovation." PE

De-risking development to lower drug prices

In advocating for less costly medicines, FDA Commissioner Scott Gottlieb has challenged health plan reimbursement and coverage policies for limiting consumer access to drugs and for "rigged payment schemes" that discourage prescribing of biosimilars. To payer complaints about manufacturer co-pay cards, Gottlieb says that good insurance should insulate patients with cancer and other catastrophic events from the high out-of-pocket costs that have led to coupons and co-pay cards in the first place.

He believes that more streamlined clinical research and disease-specific guidance should translate into lower drug costs, along with initiatives to speed more generic drugs and biosimilars to market. While Gottlieb acknowledges that new drugs are priced at what the market will bear, he believes that more predictable R&D pathways can help "de-risk" drug development, which would reduce the cost of capital and permit a lower price to justify initial R&D investment. Such efficiencies may be even more important in bringing a second or third branded product to market, which Gottlieb considers important for achieving a good balance between innovation and access.

The commissioner's concerns about the high cost of medicines reflect his own experience as a physician and seeing ill patients "struggling very hard at the worst moments in their lives" to try to afford drugs that are "absolutely indicated for their disease." He wants to be sure "that in my time here at FDA, I do something to address that."

Gauging the Collaborative Spirit in European Health

Pair of EU meetings, while well-meant, offered little action and beg the question—what's the true merit in working together?

Does working together actually work? Or do the mechanisms devised to promote cooperation merely act as a form of polite camouflage, while everyone is really continuing to pursue their own interests?

Some fascinating opportunities for case studies are presented in the health sector, and particularly in the endless debates about medicines. The latest piece of potential evidence emerged in the wake of the April 23 meeting of European health ministers, convened by the Bulgarian government as a key element in its program, right from the start in January of its six-month presidency of the European Union.

The meeting, in the Bulgarian capital, Sofia, had been prominently billed as an opportunity to get to grips with some of the biggest challenges facing health ministers across the continent. In particular, part of the debate focused on how governments could keep up with patient demand for medicines in the face of the twin evils of growing costs and shortages of supply.

Kiril Ananiev, Bulgaria's health minister, told the European Parliament at the start of the presidency that his aim was to shed light over the coming six months on "the provision of quality treatment based on effective therapies and on the affordability of medicinal products".

He had already made a similar point at an EU Council meeting: "The EU cannot afford to stay caught in the dilemma between commerce and health in the field of drug policy. We must give a clear signal that people's health is a priority."

But the out-turn of the April meeting in this regard was meager, to judge from the official communiqué released at its conclusion. After five paragraphs dealing more extensively with other issues—ranging from nutrition policy to confidence in regulatory systems—all that the Bulgarian presidency had to say on the medicines question was: "Ministers also discussed issues related to the effectiveness and accessibility of medicines, including patients' problems caused by parallel drug exports. In this respect, cooperation among member states is of particular importance."

When a communiqué merely says that a subject was discussed, and offers no conclusions whatsoever, it is reasonable to question whether the discussion led to anything at all. When the non-conclusion is followed by a bland statement that cooperation is important, the distinct impression is that cooperation, for all its importance, was conspicuous by its absence from the discussions. That might be a glib inference to draw if it were not that the discussion of medicines prices and access has already and repeatedly shown itself particularly resistant to cooperation.

Discussion and divide

Notoriously, another well-meant exercise in working together on medicines prices and access fell apart dramatically two months ago, when officials from around a dozen member states walked out of talks with the drug industry on how to construct an agenda for more effective cooperation.

That meeting, in Brussels on March 9, had been planned to build new purpose into an emerging series of meetings between European health ministers and European heads of pharmaceutical companies. But agreement could not be found on working methods and on shared priorities on pricing, competition, and access, and European industry associations accused member states of "walking away from a collective decision." Nonetheless, Dr. Patricia Vella Bonanno, the official in the Maltese health ministry who chairs the process, was simultaneously assuring inquiring media: "There is a strong collaborative spirit within the group and the process is proceeding"—an assurance that inevitably called into question the credibility of that "collaborative spirit."

The attempts at collaboration on these thorny topics stretch back well into the previous century, in a series of European-level processes bringing together drug firms, health authorities, and consumers in semi-official roundtable meetings, multilateral working parties, and reflection groups. As this column suggested last month, many of the same questions being asked now are almost identical to those that were being asked 20, 30, or 40 years ago.

Does this mean that working together is destined by fate to fail, and that persisting in the

REFLECTOR is *Pharmaceutical Executive*'s correspondent in Brussels

face of continued disappointment is a waste of time and an offense against candor?

The answer may depend on defining who the parties are in any attempt at cooperation, and what common interests they really have.

Clearly, for instance, the drug industry has a powerful reason for promoting cooperation among its own disparate membership, as a key to maximizing its chances of influencing policy. The European Federation of Pharmaceutical Industries and Associations (EFPIA), itself the product of an amalgamation of distinct trade groups half a century ago, exists precisely for that purpose, and its possibilities of success depend crucially on maintaining a minimum of shared views among a maximum of diverse individual aspirations. Its US counterpart, the Pharmaceutical Research and Manufacturers of America (PhRMA), is so convinced of the merits of working together that it spent nearly $10 million on lobbying in the first three months of 2018 alone—putting this year on course to beat by a wide margin PhRMA's total of $25.4 million in 2017, which was itself up by more than 25% from 2016.

Consumers—a broad church embracing citizen groups, nongovernmental organizations, patient representatives, and a thousand other shades of public interest activism—have also been seeking new strength in unity in European health debates for the last year. Initially responding to a perceived threat that the EU was going to withdraw totally from health policy, many of these groups have since welded themselves into a coalition that has gained some serious profile under the banner of #EU4Health, and has shown itself capable of establishing a shared agenda on priorities.

The divergence dilemma

It is the third component of this curious triad—Europe's national governments—that has, perhaps, the most difficulty in establishing a common approach to common problems.

Some of the common problems for national authorities responsible for health are evident: more expensive therapies, rising expectations and growing demand for care, and inequalities of access. But while the essence of those problems is common, their manifestation is widely distinct because of the widely divergent nature of the countries of Europe, and their widely differing approaches to tackling them.

At its most obvious, some countries are much richer than others, and can afford to spend more on health and on medicines without wrecking their public finances. But a near-infinite range of more complex distinctions make common views and common actions almost impossible.

The multiple efforts to work together to provide a common front in negotiating on prices with drug companies are testimony to those distinctions. Belgium and the Netherlands, the pioneers in these efforts, are still a world away from finding a common methodology after years of diligent effort.

The wide variations in disease incidence and therapeutic success among European countries reflect other divergences: epidemiology and medical culture can be as richly varied as language across the continent. Varying levels of affluence within society and across regions create different challenges in terms of health and access to care. And the nature of the European market for drugs—with prices fixed at national level but with free circulation of goods across national boundaries—adds a further complication. Bulgaria, as a leading example, suffers lack of access to treatment not only from its limited capacity to pay for expensive therapies, but also from shortages caused in part by parallel trade that quite legally acquires bulk medicines at the low prices that Bulgaria imposes on drug suppliers, and exports them to for resale in other EU countries that allow higher prices.

Broad consensus on medicines policy cannot begin to emerge among all parties, unless and until national governments find more effective ways of working together among themselves

The tentative conclusion that might emerge from this analysis is that working together—clearly a desirable principle, whether on environmental protection, tackling international crime, or defending human rights—will continue to be uphill work in Europe health policy, and that broad consensus on medicines policy cannot begin to emerge among all parties, unless and until national governments find more effective ways of working together among themselves. PE

Bridging Science & Strategy

A former biology major, biotech investment banker, and venture capitalist, Tim Sullivan brings that sought-after melding of business and scientific perspectives to his role as chief financial officer for Apellis, a clinical-stage drug company hopeful of ushering in novel protein inhibitors for autoimmune disease

Tim Sullivan, chief financial officer, Apellis Pharmaceuticals

FAST FOCUS

» Tim Sullivan was named chief financial officer of Apellis Pharmaceuticals in December 2017. In the preceding three years, Sullivan served as partner at AJU IB Investment, a venture capital firm, where he directed its investments in life sciences companies.

» Prior to his career as a venture capitalist, Sullivan was an investment banker and served as managing director, head of life sciences banking at RBS Citizens, senior vice president at Jefferies & Company, and vice president at Bear Stearns. He has also held board positions for companies G1 Therapeutics and Molecular Templates.

» Sullivan received an MBA from the Columbia Business School and a BA in Biology from Harvard University.

By Michelle Maskaly

Ever mindful of the critical investor relations component in moving a promising yet risky experimental drug program forward, biotechnology companies, when filling the role of chief financial officer, often look for individuals who combine a strong grasp of the science with a keen understanding of the biotech investor perspective. One such example is Tim Sullivan, CFO of Apellis Pharmaceuticals—and, himself, a former banker and investor focused in the biotech sector. From those two worlds, Sullivan, before joining Apellis, closely observed the Kentucky-based start-up's evolution to a clinical-stage biopharma, one vying to address unmet treatment needs for serious and debilitating autoimmune diseases.

Pharm Exec recently spoke with the science-educated Sullivan about the unique dynamic for biotech CFOs in steering financing strategy and drug value demonstration in often uncharted waters. Apellis' focus is on developing complement immunotherapies through the inhibition of the complement system at the level of C3, a protein of the immune system. Apellis is the first company to advance chronic therapy with a C3 inhibitor into clinical trials, with its lead product candidate targeting geographic atrophy, wet age-related macular degeneration, life-threatening blood disorders paroxysmal nocturnal hemoglobinuria and autoimmune hemolytic anemia, and kidney disease.

PE: *You have a bachelor's degree in biology and an MBA. How does that scientific background help you in business?*

SULLIVAN: The biotechnology business model is unique. Most biotechnology companies exist for five, seven, 10 years or more with zero revenue while they develop therapeutics that have a high chance of failing and yet represent significant potential value for patients and, as a result, investors.

My dual biology/finance background has been an advantage throughout my career, first as an investment banker focused on financing biotechs, then as a venture capitalist investing in biotechnology companies, and now in my current role as CFO of Apellis. Beyond the typical roles and responsibilities of a CFO, a significant part of my job is to interface with biotech savvy investors and our internal research and development team at Apellis. That means I need to know about what we do as a biotechnology company and how we fit into the landscape of companies focused on treating specific diseases. While my degree in biology is obsolete on its own —1993 science is very old news!—it was foundational for me and was the basis for what has since been an ongoing education in the biology centered on medicines throughout my career in life sciences.

Specifically, being a CFO of a biotech company means figuring out the optimal way to finance our long-term investment projects, mainly clinical studies. To do that, one needs to understand biotech valuation, the unique nature of its financing environment, as well as investor expectations. Just like any other business, the financial value of a biotechnology company can be understood through a discounted future cash-flows analysis, with a few nuances. Understanding the potential for those cash flows is highly specialized in biotechnology.

It is important to interpret the impact of biology, drug chemistry and pharmacokinetics, statistics, clinical research, competitive therapeutic landscape, US and global regulatory processes, intellectual property protections, and reimbursement and payment trends that may evolve several or more years in the future when your drug is potentially commercialized.

> If I learned anything in venture capital, it is that people matter more than anything

Understanding how these and other variables fit together is crucial. When a company seeks to develop a therapy that can safely treat unmet disease need, that management team needs to convey that value proposition to investors who will pay for its risky development by articulating the value the drug represents to the end users, including patients who will receive the therapy, doctors who will prescribe it, and the payers that will support reimbursement for that therapy.

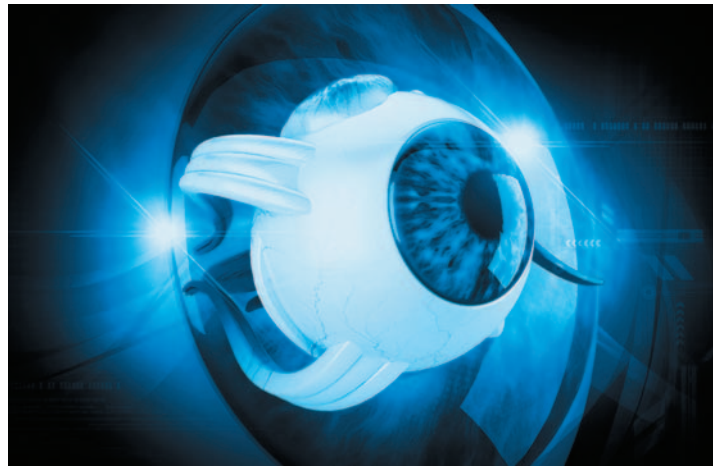
PE: *Was business school and being on the financial side of science always in your career plan? Why/how did you pick the financial side of the business over the science?*

SULLIVAN: There's a part of me that would have liked to have been a doctor, but business was also of great interest—and so like anything, it came down to a life decision after college when I tried to combine my interest in medicine and business. My sister is a general surgeon and she can't imagine doing anything else. I suppose we both believe we are following paths that will hopefully lead to making a few lives better. Our family has a history of social responsibility and interest in medicine. We grew up hearing stories about our grandfather, a physician who pioneered mobile blood banks in WWII, developing processes still used today in the theater and saving countless lives. I think we also inherited a social conscience from our mother, who was a social worker, helping some of the most challenging and heartbreaking cases of pediatric neglect in the Boston area.

PE: *From November 2014 to October 2017, you were an observer on Apellis' board of directors and a partner at AJU IB Investment, where you led the firm's life sciences investments. What made you take the leap from that position to filling the CFO role at Apellis?*

SULLIVAN: Over the three-plus years I was an investor at AJU IB Investment and board observer for Apellis, I came to know the company well from the time it was a preclinical stage company to its transition to a late-stage clinical company with the real potential of treating some very serious unaddressed conditions. Apellis has two special things going for it. It has great science underpinning a promising drug and, perhaps more importantly, it has great people. If I learned anything in venture, it is that people matter more than anything; this is a basic lesson I have relearned several times the hard way.

Apellis' founder and CEO, Cedric Francois, is unlike anyone I've ever met. He's an MD, PhD, and former hand surgeon with a keen social conscience. He also speaks five languages, is an accomplished musician, and he likes to have fun while working



Apellis' lead clinical candidate, APL-2, targets geographic atrophy, a late form of age-related macular degeneration.

hard. Working with someone that dynamic is energizing and inspiring. While I liked very much being a venture capitalist and serving in an advisory role and board member for several portfolio companies, I felt I could only get so close to a company's core mission in this capacity.

When the opportunity arose to become CFO for Apellis, I jumped at the chance to be part of the team. I believe Apellis has the potential to make a difference in the lives of patients with geographic atrophy, a leading cause of blindness with no current treatment, and potentially treat several other severe conditions. And, as a former investor, I believe I can be effective in helping the team in maximizing value for Apellis and its investors.

PE: *One might think a CFO gets less attention in this business because we are usually so focused on the science. But it's such an important role on the leadership team. What are some of the challenges for someone in this role?*

SULLIVAN: I agree completely that the role of CFO seems removed from the business of biotech. However, biotech CFOs are often highly integrated into the investor relations aspect of the business. Since raising capital is vital to the existence of biotech companies, a CFO that offers real experience in the science and investment side of biotech can be far more impactful when a company is pre-commercial, as most are. Since the role requires facility with the science and understanding of biotech investor perspective, it is not uncommon to find CFOs who are former bankers or people with MDs or PhDs. In my case, I was not only a banker but also an investor. I believe having biotech industry experience prior to becoming a CFO helps an individual be a more impactful member of management.

I would say the first challenge is to make sure a CFO understands the unique world of biotech finance and is capable of effectively interacting with investors. Beyond that, challenges may vary depending on the stage of the company. Early companies may find it challenging to secure financing while later-stage companies are faced with managing growth. At Apellis, for example, we will significantly expand operations in 2018, commencing two distinct Phase III clinical programs while our headcount will more than double.

The first challenge is to make sure a CFO understands the unique world of biotech finance and is capable of effectively interacting with investors

PE: *To balance it out, what are some of the positives of the role of CFO?*

SULLIVAN: Being a CFO in biotech is intellectually interesting and tremendously rewarding. I consider myself lucky to be in a position to lead the financing strategy of a company like Apellis and to work with everyone to seek to maximize value for our shareholders. The mission of the company and the team is to develop drugs that help people live healthier and better lives. We believe we have a drug that has the potential to help people suffering from several debilitating diseases with inadequate or no approved treatment options. To work with such a great team toward that goal on operational and strategic initiatives is rewarding. I enjoy it every day.

PE: *When we do talk about the role of CFO, the question of being profitable while still keeping therapies affordable always comes up. How do you balance this?*

SULLIVAN: Everyone in biotech knows well just how many millions of dollars it takes to bring a new therapy to market and how the risk of failure is omnipresent. The updated and oft-cited Tufts study suggests it now costs $2.5 billion to develop a drug. This figure includes all costs, including those of failed drugs, where fewer than one in 10 that enter the costly stages of clinical testing makes it to market. Along with this financial cost, biotech companies, their employees, and the patients they hope to help run the risk of failure every day, where years of hard work can disappear overnight.

At Apellis, we don't yet have a marketed drug nor one where the risk/reward profile is fully elucidated through the final stages of clinical trials, so we haven't had to fully contemplate pricing yet. However, I can tell you that Apellis is committed to pricing therapies, should they be approved, appropriately for the benefit those therapies provide.

PE: *For those on the financial side of a biopharma company who aspire to be CFO one day, what type of career advice do you give them?*

SULLIVAN: I think companies want a CFO that is a partner, a leader, and someone who is committed to the mission of the company. To me, that means developing the skills, relationships, and judgment to provide leadership at a management level. Aside from the basics of understanding the financing, accounting, and operations specific to the industry, I would learn about what makes one company more valuable than another and what factors allow for one company to have greater access to capital and talent than another.

Leadership is continuing one's own learning and development and creating an environment where the learning of others, including occasionally being wrong, is supported

Raising capital is the lifeblood of most biotechnology companies and understanding how to do that well, by finding ways to move the company forward by choosing the right operational path, conveying the value proposition, and approaching the financing markets from the position of greatest strength, are crucial skills. Developing this experience and judgment requires time. Also, being a CFO in biotech is a very people-oriented job. One needs to develop relationships with people in the industry. I would make sure that is something you enjoy.

My career took root in investment banking for nearly a decade before I made the leap into a life science-focused venture profession. In both roles, I felt it was my job to help companies and their teams. My approach was to develop judgment, have an opinion about what is a quality team and quality company, and to help them in any way I could, whether as a board member, strategic advisor, investor, and now CFO.

PE: *When it comes to leadership, can you give us some of your best tips?*

SULLIVAN: Beyond being invested in the mission of the company, I think leadership means being invested in the success of the individual people in the company. Being humble, attentive, a good listener, and creating a collaborative environment where employees can enjoy working together can go a long way. I like to empower positive and collaborative people. Also, I think leadership is continuing one's own learning and development and creating an environment where the learning of others, including occasionally being wrong, is supported.

PE: *Tell us a little about you and your background?*

SULLIVAN: I'm a father of two, married to a PR executive. I love traveling with my family and participating in the kids' activities, such as coaching my son's travel soccer team. I also enjoy a range of hobbies and interests like playing platform tennis, taking hikes with my Boston Terriers, Zoe and Tony, and supporting the New England Conservatory of Music, where my daughter sings in the chamber chorus.

I grew up in Boston with a passion for learning and I am always reading and trying to think critically and creatively about issues that matter to me. I like to express my ideas respectfully and this has always been part of how I operate as an executive and in my personal life. Sometimes it gets me into some very lively debates, but I live for that. PE

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Brand Stories

In its 12th annual feature, *Pharm Exec* builds on the revamped approach it introduced last year in spotlighting notable biopharma brands, profiling a new round of products—selected with the help of our Editorial Advisory Board—that are making waves in five key areas in healthcare and R&D

Our Picks

Brineura; BioMarin
Diagnosis to Advocacy

Kymriah; Novartis
Yescarta; Gilead/Kite
Pricing/Reimbursement

Ocrevus; Roche/Genentech
Administration & Access

Hemlibra; Roche/Genentech
First-in-Class

Eucrisa; Pfizer
Ad Campaign/Outreach

Diagnosis to Advocacy

Brineura

'Precision' Hope Amid the Heartbreak

By Lisa Henderson

"In a world of bad diseases, this one is particularly cruel," Chuck Bucklar, group vice president for commercial in North America for BioMarin Pharmaceutical, told *Pharm Exec*. Children born with the CLN2 form of Batten disease develop normally for the first two to three years of life, with little sign of what is to come. Maybe a speaking delay, but nothing that would alarm a parent or pediatrician. If seizures present, they tend to be treated as epilepsy. The disease progresses rapidly with most affected children losing the ability to walk and talk by six years of age. After that, symptoms are followed by dementia and blindness; feeding and everyday needs become extremely difficult, and then death occurs between the ages of eight and 12.

Margie Frazier, executive director for the Batten Disease Support and Research Association (BDSRA), says, "Parents literally watch their three-year-old disintegrate before their eyes. It is one of the most frightening things to go through as a parent."

This group of lysosomal storage disorders is considered ultra-rare and, therefore, hard to diagnose. Documented reports show pockets of pediatricians and scientists who recognized the disease and worked to advance and share knowledge, but the doctors who finally diagnosed CLN2 Batten in a child had no hope to give families. Then came Brineura.

Articles and videos that have emerged about Brineura form a rich story of how the medicine finally came to be. One trial. Twenty-four patients. A natural history cohort. Four years to approval. First therapy available in its disease class since discovery in 1903. From scientists at Rutgers University in New Jersey who discovered the TPP1 gene and its mutations that resulted in CLN2, which then started the chain to find an enzyme replacement therapy.

Parent advocates Tracy and Jen VanHoutan tracked down researchers and physicians in an attempt to save their son, and kept the fundraising and advocacy momentum going even after he died and his younger sister was diagnosed. When by sheer coincidence a man donated his dachshund suffering from motor deterioration to scientists, they found the same enzyme deficiency. From mice to dogs, researchers were able to find an enzyme replacement that worked, with a difficult but viable delivery system.

BioMarin started trials in 2013. Safety and efficacy data was collected over 96 weeks in a non-randomized, single-arm, dose-escalation clinical study of patients with CLN2 disease compared to untreated patients from a natural history cohort. Of the 22 patients treated with Brineura and evaluated for efficacy at week 96, 21 (95%) did not decline, and only the patient who terminated early was deemed to have a decline in the motor domain of the CLN2 Clinical Rating Scale. On April 27, 2017, the FDA approved the prescription medication used to slow loss of ability to walk or crawl in symptomatic pediatric patients three years of age and older with late infantile neuronal ceroid lipo-

fuscinosis type 2 (CLN2), also known as tripeptidyl peptidase 1 (TPP1) deficiency. The European Commission approved the product about a month later.

When Brineura was approved, Jean-Jacques Bienaimé, BioMarin's chairman and CEO, said in a statement: "Treating children with CLN2 disease requires an extraordinary amount of collaboration between families, hospitals, advocates, and physicians. We are grateful for the partnership of all those involved and look forward to continuing to work together to make Brineura accessible to children who may benefit."

Brineura received the 2017 *Popular Science* "Best of What's New" award in the health category, and the WORLDS*ymposium* 2018 New Treatment Award.

Complex delivery

Children receive Brineura through an intracranial port directly into the brain. The therapy is stored at -20 degrees. Bucklar says this complexity has tested both the hospitals' (mostly large children's centers) abilities and BioMarin's facilitation skills. "It involves different departments in the hospitals, some that don't usually work with each other," he notes. "We have the peds/neuro department, with genetics and neurosurgery (to put in the port), with the ped/hem/onc because they are the ones that in standard operating procedures usually perform ports, the pharmacy for refrigeration and thawing requirements, and the hem/onc nurses, who are used to much shorter infusion periods."

In addition, the therapy is given every two weeks and each infusion is four hours, so the hospitals need to build a system and protocols that are sustainable. Currently, there are just under 20 centers up and running that administer Brineura. These locations also change as parents are moving closer to the centers, or centers are being trained to accommodate local patients.


Courtesy of BioMarin

Physician awareness

As mentioned, CLN2 takes a long time to be diagnosed. Frazier says the diagnosis journey for patients is typically three to five years. In many cases, she notes, they are treating the symptoms of epilepsy or speech therapy, but not the root cause.

Catherine Pajak, senior director of marketing for BioMarin, says the ability to diagnosis early is one of the things that keeps her up at night. To support early testing for children who experience seizures, BioMarin launched "Behind the Seizure," a no-cost genetic testing program. In conjunction with commercial lab Invitae, the 125-gene panel tests for different types of seizures. The testing is leading to more accurate diagnosis of genetic causes of epilepsy, as well as CLN2. A recent paper presented at the American College of Medical Genetics and Genomics (view: https://bit.ly/2qX6KTs) found that patients were diagnosed at age three vs. age five previously, and based on clinician notes on ordering the panel, two of the three children who tested positive for TPP1 were not even suspected to have CLN2.

Pajak sees this as a clear example of the success of precision medicine. "It becomes a domino effect in research," she says. "You identify different types of epilepsy or gene variants more quickly, so they can be diagnosed more quickly; then you learn more about the disease, which goes back to more research."

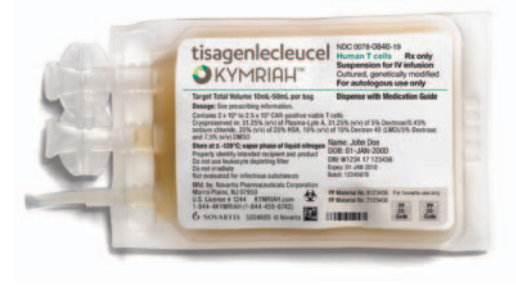
BioMarin representatives and BDSRA's Frazier acknowledge that Brineura would not be here without the efforts of the VanHoutan's. While their own children affected by Batten disease were not able to benefit from a treatment, they recognize that access to Brineura will help other children, and they continue to feel a strong connection to the Batten community. PE

Pricing/Reimbursement

Kymriah and Yescarta

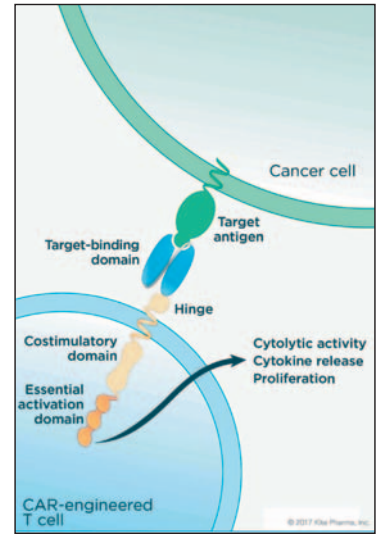
Leading the CAR-T Race

By Julian Upton



Last year's US approvals of Novartis' Kymriah (tisagenlecleucel)—for the treatment of B-cell acute lymphoblastic leukemia (ALL) in children and young adults with limited treatment options—and Kite Pharma's Yescarta (axicabtagene ciloleucel)—for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy—pushed chimeric antigen receptor T cell (CAR-T) therapies into the headlines and ushered in what *MD Magazine*'s Jared Kaltwasser, in a March article, called "a brave new world of gene therapy." Both treatments involve a process of extracting a patient's T cells and genetically reengineering them, using a disarmed virus, to produce on their surface chimeric antigen receptors, which allow the T cells to recognize and attach to an antigen (CD19) found on B cells. The engineered T cells are multiplied in the lab and then reinfused into the patient's body, where they recognize and attack the cancer cells while leaving healthy cells unharmed. After years of discussions and promises about personalized cancer therapies, Cliff Kalb of C. Kalb & Associates says of the CAR-T breakthrough that "finally, the dream has begun to materialize into a commercial reality."

First-in-class Kymriah had its beginnings in 2012 when Novartis began collaborating with the University of Pennsylvania, with the aim of bringing "a paradigm-changing therapy to cancer patients in dire need," as Novartis Oncology's former global CEO, Bruno Strigini, told *Pharm Exec* in a January cover story. The treatment's potential was shown in clinical trials led by Dr. Stephan Grupp of the Children's Hospital of Philadelphia and the University of Pennsylvania's Perelman School of Medicine, in which 82.5% of patients who were given Kymriah achieved either complete remission, or complete remission with incomplete blood count recovery, within three months. Grupp would help guide Kymriah to its FDA approval on August 31, 2017.



Kite Pharma, acquired in October 2017 by Gilead Sciences for $11.9 billion, Gilead's biggest ever deal, was basically a firm focused on bringing Yescarta to market, and its development of the treatment "represented a major shift in the classical paradigm for the development, production, and marketing of a pharmaceutical intervention that could offer a cure," Kalb told *Pharm Exec*. The level of risk was compounded by the need to "not only shepherd a new product through the development and clinical trial process for approval for traditional safety and efficacy." While the process is complicated and not always successful, response rates have been so dramatically improved over the standard of care, FDA designated Yescarta a breakthrough therapy and approved it on October 18, 2017, less than two months after Kymriah was greenlighted.

Both Kymriah and Yescarta need to be administered in specialized treatment centers, and these individualized approaches to modifying a patient's own cells to fight cancer "[bring] all sorts of additional complexities in terms of manufacturing, handling, and logistics," Strigini explained. To address these complexities, Novartis has developed "custom-made patient access programs to support safe and timely delivery," while Kite has invested in facilities around the country to allow patients local access to its procedure.

The price of breakthrough

The introduction of CAR-T therapies brings challenges. "Participating patients face the

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risk of cytokine release syndrome, a potentially life-threatening reaction, and other neurological toxicities, so there is still a long way to go to improve safety," says Kalb. However, he adds, "the bigger challenge may be in the pricing and reimbursement arena, where access may be limited by the healthcare system's ability to cover proposed commercial prices in the hundreds of thousands of dollars."

Kymriah's and Yescarta's price tags are $475,000 and $373,000 per treatment, respectively. Strigini told *Pharm Exec* that "we put a great deal of thought into how to price Kymriah," including taking account of independent evaluations such as those of the UK's National Institute for Health and Care Excellence (NICE), "which estimated a cost-effective price of between $600,000 and $700,000." He emphasized that Kymriah is intended to be delivered to each patient just once as a "one-time, highly effective treatment."

In a March report, the Institute for Clinical and Economic Review (ICER) agreed that CAR T-cell therapies are cost-effective for B-cell cancers. Compared to clofarabine, a standard chemotherapy for patients with B-ALL, for example, Kymriah was said to provide 7.18 more quality-adjusted life years (QALYs), with an incremental cost per QALY of $57,093. ICER calculated that Yescarta would provide 3.59 more QALYs than other chemotherapy regimens, with a cost per QALY of $145,158. Both treatments were deemed to fall within the acceptable cost-effectiveness thresholds.

But while the treatments may be cost-effective overall, the short-term cost may exceed the annual budget threshold. As a result, Kaltwasser notes that insurers have been cautious, "evaluating treatment requests on a case-by-case basis," and some patient advocacy groups have "complained that the high price tags are limiting patient access." A Gilead spokesperson, in a December Bloomberg report, said the company was "confident that Yescarta will be covered by payers," that the "'vast majority' of commercial payers have confirmed coverage," and pledged to "engage actively with Medicare to ensure we are doing all we can to support access."

For Kymriah, Strigini said that Novartis has put in place a "first-of-a-kind arrangement" with the Centers for Medicare and Medicaid Services (CMS), which "includes an outcome-based approach and indication-based pricing," and for which the company will only receive payment for patients who show significant improvement within a month of receiving the treatment.

On April 1, CMS reported that it would pay $395,380 to health providers who use Yescarta; the Medicare payment rate for Kymriah was set at $500,839. Commentators pointed out, however, that the treatments will incur additional costs. Ahead of CAR-T treatment, patients must undergo a process of "lymphodepletion," using high doses of chemotherapy, to make room in the body for the genetically modified cells. In some estimations, the additional hospital fees could push the total cost per patient to over $1 million. Kalb expects both Novartis and Gilead/Kite to address these concerns to make the treatments available to patients who desperately need them, while GlobalData, in a report published last month, predicts that the second half of 2018 will bring "price adjustments in the initial wave of approved CAR-T drugs."

The gene-therapy future

While Novartis' Kymriah was the first in the new class of cell therapies to be approved, Kalb says that "the initial label was somewhat weaker than Yescarta, which may turn out to be best in class in the longer run." And with Gilead as Kite's new parent firm, it "now has a strong source of financial support to fully take advantage of their position in this emerging new immunotherapy field." But Bloomberg indicated that while Gilead/Kite "currently has the market to itself for hard-to-treat lymphoma … its rivals are drawing closer," pointing out that Novartis has also filed for FDA approval of Kymriah for the same form of blood cancer, with Juno Therapeutics following on its heels. Spark Therapeutics' gene therapy, Luxturna, also "made its own history," wrote Kaltwasser, by becoming the first gene therapy approved (in December) for an inherited disease (inherited retinal disease); he added that Kymriah, Yescarta, and Luxturna "won't be the lone gene therapies for much longer."

It's still early days in the personalized-care quest to harness and strengthen the body's immune system. Kymriah and Yescarta both treat liquid tumors, rather than solid tumors; for the latter, research into CAR-T treatments has yielded less success. But with interest in the gene therapy field now booming, a number of startups are advancing into the solid tumor area. The initial success of Kymriah and Yescarta, Kalb points out, has "stimulated widespread industry interest in joining in and developing even more innovative and non-traditional approaches to care." PE

Administration & Access

Ocrevus

MS Breakthrough, Roadblock?

By Michelle Maskaly

Genentech's Ocrevus has made quite the splash when it comes to novel and highly sought approaches to slowing the progression of multiple sclerosis (MS), for which there is no cure. In March 2017, Ocrevus became the first and only approved disease-modifying therapy for primary progressive MS (PPMS), one of the most disabling forms of the autoimmune disease, when the drug was cleared by the FDA. Ocrevus, a monoclonal antibody, was also approved in the US for relapsing MS (RMS), the most common form of the condition. In January, the drug was cleared in the European Union for both indications.

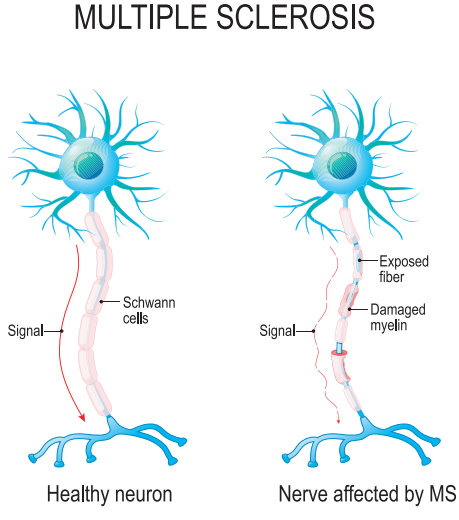
Ocrevus' US approval was based on its demonstrating superior efficacy on the three major markers of disease activity compared with EMD Serono and Pfizer's Rebif. According to Genentech, in two identical RMS Phase III studies (OPERA I and OPERA II), Ocrevus demonstrated superior efficacy by reducing relapses per year by nearly half, slowing the worsening of disability and significantly reducing MRI lesions compared with Rebif (high-dose interferon beta-1a) over the two-year controlled treatment period. A similar proportion of people in the Ocrevus group experienced a low rate of serious adverse events (AEs) and serious infections compared with those in the Rebif arm.

In a separate PPMS Phase III study, Ocrevus was the first treatment to significantly slow disability progression and reduce signs of disease activity in the brain (MRI lesions) compared with placebo with a median follow-up of three years. Again, both arms experienced a similar proportion of AEs and a low rate of serious AEs.

"Until now, no FDA-approved treatment has been available to the primary progressive MS community, and some people with relapsing forms of MS continue to experience disease activity and disability progression despite available therapies," said Dr. Sandra Horning, chief medical officer and head of global product development, Roche (Genentech's parent company), in a press release. "We believe Ocrevus, given every six months, has the potential to change the disease course for people with MS, and we are committed to helping those who can benefit gain access to our medicine."

According to published reports, however, gaining access has been a challenge for some patients, given the fact that Ocrevus must be administered intravenously at a clinic. A December article on *Multiple Sclerosis News Today* reported that some physicians are not prescribing the therapy because the infusion centers are too far away from where patients live.

While patients don't have to travel to infusions center daily, there is a time commitment and multiple visits are required, which could create obstacles depending on a patient's location. The first dose of Ocrevus is a 600 mg dose administered as two separate 300 mg IV infusions given two weeks



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apart over 2.5 hours. Every subsequent dose is administered as a single 600 mg IV infusion every six months given over 3.5 hours.

These potential challenges in drug delivery, coupled with Ocrevus' promise for patients, are what led us to feature the product as part of this year's Brands coverage. Genentech declined to provide *Pharm Exec* with an overview of Ocrevus' delivery challenges, noting, however, that patients, respective of their individual situations, should contact their physicians for much of that information.

"Genentech remains committed to seeking appropriate access to Ocrevus for all patients with relapsing or primary progressive forms of MS," Kimberly Muscara, a company spokesperson, told *Pharm Exec*, also directing patients to call the company's Access Solutions program.

It's unclear the number of US clinics that are approved to administer Ocrevus, or where a majority of them are located. Muscara did confirm that Ocrevus can only be administered in an infusion center and said Genentech trains infusion center teams on how to administer the drug. With limited details available on access, whether reported difficulties in finding infusion centers close to patients is a temporary problem that will lessen as more centers are trained on Ocrevus administration and start to offer the service at their clinics, is also unclear.

One aspect that appears more certain is Ocrevus' pricing structure. "Genentech was recognized by the National MS Society for the leadership we showed with our pricing strategy, and they encouraged other companies to follow suit to create a drug pricing trend that keeps patients first," says Muscara. "The current price for Ocrevus remains at the launch WAC (wholesale acquisition cost) price of $65,000, which is now 31% below the annual price (WAC) of Rebif ($94,641). We believe our unique pricing strategy along with Ocrevus' favorable clinical profile and six-month administration schedule has resulted in positive coverage decisions that have improved access for patients."

According to Muscara, Ocrevus has been "well-received" by the payer community and "we are happy to see the insurance coverage decisions that have been made." Late last month, Roche reported $486 million in first-quarter sales for Ocrevus. The drug's market share has grown to 7% since its launch.

Genentech's Access Solutions program can help those patients prescribed Ocrevus with cost. The program includes Ocrevus "patient navigators" and provides information about coverage, reimbursement, and product distribution. Assistance, Muscara says, is available to patients throughout their treatment, including access, reimbursement, and infusion coordination support. PE

First-in-Class

Hemlibra

Quality-of-Life Boost in Hemophilia

By Christen Harm

Nearly two decades have passed since new medicines for hemophilia A with inhibitors have surfaced. So, when Hemlibra was approved by the FDA late last year for routine prophylaxis to prevent or reduce the amount of bleeding episodes in children and adults with hemophilia A with factor VIII inhibitors, the shift in the treatment process was welcomed.

Hemlibra, made by Genentech, is the only self-administered (subcutaneous injection) hemophilia A with inhibitors treatment, and is only administered once a week. This is a vast improvement over

such therapies that take around 45 minutes to administer every other day, or more involved treatments that last two hours and are required multiple times a week.

Hemlibra has already demonstrated a tangible positive impact in the hemophilia A patient community. According to Dr. Gallia Levy, associate group medical director, Genentech, Hemlibra's outcomes in patients has resulted in children missing less school, adolescents who couldn't play sports for fear of bleeding are able to do so now, and adults who were not able to work are holding down jobs.

Meanwhile, Genentech says it's committed to further advancing Hemlibra and finding new ways to help various segments of the patient population. In April, the FDA granted the drug breakthrough therapy designation for patients with hemophilia A without factor VIII inhibitors. Hemlibra was given similar status last September, with only two months passing before its initial approval in the US.

In clinical studies, Genentech is also pursuing less frequent dosing options for Hemlibra, mindful of patient quality of life and drug adherence factors. Two trials, Levy says, are exploring dosing every two weeks and every four weeks, respectively, potentially allowing for the choice of a dosing option for individual patients. According to Levy, the two-week dosing study showed a statistically significant and clinically meaningful reduction in treated bleeds in patients 12 years of age or older with hemophilia A without inhibitors who received Hemlibra prophylaxis every week or every other week, compared to those receiving no prophylaxis.

Although it's too soon to tell, the significant decrease in the time it takes to administer Hemlibra also has the potential to improve adherence rates among hemophilia A patients.

Safety ripples

Amid Hemlibra's successful approval and status as a breakthrough therapy, concerns have emerged regarding safety. Recently, it was reported that five deaths were recorded among hemophilia patients taking Hemlibra—bringing the risk-to-benefit ratio into question.

"As of the end of March, more than 600 people with hemophilia A with or without factor VIII inhibitors have been treated with Hemlibra globally, including in clinical trials," Levy told *Pharm Exec*. "Since 2016, five adults with hemophilia A with inhibitors who were taking Hemlibra have passed away. For each individual, the treating physician or investigator's assessment was that the cause of death was unrelated to Hemlibra."

Genentech says it has made every attempt to investigate each report thoroughly to ensure continued patient safety. Levy stresses the importance of understanding the reality that people with hemophilia A may face serious health risks and life-threatening complications because of the nature of the disease, regardless of treatment.

"In particular, people who develop inhibitors to factor VIII are at a 70% greater risk for death compared to those without inhibitors," she says. "Three of the adults who passed away were taking Hemlibra through a request from their physician for compassionate use." Compassionate use provides access to investigational medicines for patients with serious or life-threatening conditions who have exhausted all other treatment options.

According to published reports in late April, including one on *Endpoints News*, Roche did acknowledge the first incident where a hemophilia patient developed anti-drug antibodies that resulted in reduced efficacy of Hemlibra. In a statement cited in the report, the company said, "Anti-drug antibodies to Hemlibra may affect whether the medicine works, but they do not change the severity of the underlying disorder."

Levy told *Pharm Exec* that Genentech is developing a dedicated Hemlibra safety website that will update on an ongoing basis. "Patient safety is very important to us, which is why we have systems and processes in place to monitor the safety of all our medicines, including Hemlibra," she says.

Pricing

Despite Hemlibra's hefty list price of $482,000 for the first year of treatment and then about $448,000 per year after that, the totals are reportedly less than half the price of Shire drug FEIBA, the only other approved prophylactic treatment for the indicated hemophilia A population.

In March, Hemlibra was reported as cost-effective by the Institute for Clinical and Economic Review (ICER) after an assessment of adults, adolescents, and children with hemophilia A with inhibitors who will not be treated with immune tolerance induction (ITI) or for whom ITI has been unsuccessful. The report found that Hemlibra offers important improvements in outcomes for people with hemophilia A and inhibitors to factor VIII, while lowering costs associated with the treatment of this condition. PE

Ad Campaign/Outreach

Eucrisa

Insights that Impact

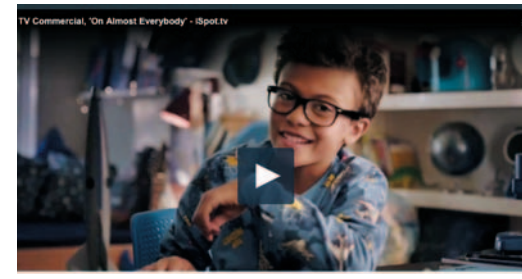
By Michael Christel

Most brand strategists today believe the best outreach efforts in the world of consumer advertising nimbly tap into aspects of everyday life, using identified specific insights to connect and speak with customers on approachable, uniquely "real" levels. Though it may appear an obvious strategy, in the often-complicated and muddled arena of pharmaceutical direct-to-consumer (DTC) advertising, it's a relatively new evolution in tactics, and one that could ultimately help improve coordination along the healthcare treatment path—potentially benefiting manufacturers and patients alike.

"[The ads] are not nearly as clinically looking as they used to be; they're much more about lifestyle and trying to base them on consumer insight," Kimberly Orton, managing director, RedSky Insights, a brand consulting services firm, told *Pharm Exec*. "You're talking to [patients] in the best way possible. All of a sudden they're looking at it saying, 'wow, that makes sense to me.' I think [pharma companies] figured out that's the better way to communicate."

One example from the past year that has leveraged the strategy effectively in Eucrisa, which in December 2016, became the first new FDA-approved drug for eczema, the chronic inflammatory skin disease, in more than a decade. The topical treatment, made by Pfizer (which acquired Eucrisa via its $4.5-billion acquisition of Anacor in June 2016), is the first approved nonsteroidal to block the enzyme phosphodiesterase 4 (PDE4) to treat mild-to-moderate eczema, also known as atopic dermatitis, for people ages two and older. Though corticosteroids are considered first-line therapy in battling eczema—commonly characterized by painful and bothersome breakouts/flare-ups or persistent rash, red skin, and itchiness—many patients are said to be "steroid-phobic." Harmful side effects such as hypopigmentation and skin atrophy can also come with repeated use of a steroid cream. Eucrisa, a natural cream applied twice daily, showed in pivotal clinical trials in 1,522 patients to achieve greater response vs. placebo, with clear or almost clear skin after 28 days of treatment.

In the US, 10% to 20% of young people suffer from eczema, with the condition affecting more than 31 million children and adults overall, according to the National Eczema Association.



Beating to the punch Sanofi and Regeneron's Dupixent, approved last March as the first biologic for eczema (targeting adults only with moderate-to-severe cases), Pfizer launched a national TV ad campaign for Eucrisa last August, spending a reported $2.2 million on its first ad, "Nose to Toes." The 30-second spot opens with a voiceover "[Eucrisa] can be used almost everywhere on almost everybody," and then features children, participating in various activities, asking in response, "the arm of an arm wrestler?" "the back of a quarterback?" and "the face of a fairy?" It follows with a little boy, in pajamas ready for bed, exclaiming, "and it's steroid free." The ad, as of late April, had 3,702 national airings, according to iSpot.tv. To date, Pfizer has done four ads for Eucrisa, and though emphasizing its unique reach in the pediatric space, appealing to parents and caregivers, the company has prominently depicted active adult patients as well, including a 30-something female rancher asking, "the hand of a ranch hand?" and an older woman busily stitching on the couch wondering, "the knee of a needle-pointer?"

"They've done a good job of storytelling and making it catchy and using clever wordplay," says Orton. "A lot of people say, 'oh, if it's mild to moderate, just live with it; it's not that bad.' But the ads are keying into the insight which is, it's about you and there could be something that would make you better. ... When things are approachable, it feels like, 'that's for me, and I'm okay asking my doctor about it.'" Orton believes the insight conveyed meets what she calls the 4Rs: it's relevant to the brand, resonates with the target viewer, invokes a reaction, and shows everyday realities.

Pfizer is hoping to capitalize on being the first to market in a likely new wave of product launches for eczema. Dupixent TV ads began airing in November. EvaluatePharma estimates 2022 sales of Eucrisa at $1.3 billion. The drug's most common side effect is application site pain, including burning or stinging.

"First to market is huge because you get to decide what's differentiated, get to talk to the target first," Orton told *Pharm Exec*. "Someone coming on second has to figure out how to do it now." PE

Patient KOLs: Their Guide to Entering Crowded Markets

Patient influencers look beyond price to help the industry evaluate newly-launched brands

By Jack Barrette

Patient influencers, also referred to as patient key opinion leaders (KOLs), often play an overlooked role in advising the patient communities they lead— combining friends-and-family trust with their own research and the experience of tens of thousands of followers. They can drive awareness by educating their communities, but patient influencers' more critical role is guiding patients from awareness to the doctor's office, and from an initial prescription to the decision to fill.

"People in the patient community know who they can trust, who to turn to," says Anne-Marie Ciccarella, a leading cancer patient influencer. Ciccarella describes a many-sided conversation that speaks to patients in their own terms, and "they seek people they know they can trust to help them frame the questions, and they leave the conversation more confident about what to ask, about what to say to their doctor. That can be the difference between hearing about a drug and actually making the appointment."

Even if that appointment results in a prescription from a credible physician, patients often refer to their trustworthy communities with questions. "After a prescription is where the questions change to cost and insurance—along with the most common question, 'who else is on this?'" says Ciccarella

While patient influencers try to avoid making specific recommendations—"we're not playing doctor," notes Ciccarella—they excel at surfacing the wisdom of the crowd. By probing and asking the right questions, patient influencers uncover the most important decision factors that matter to their community.

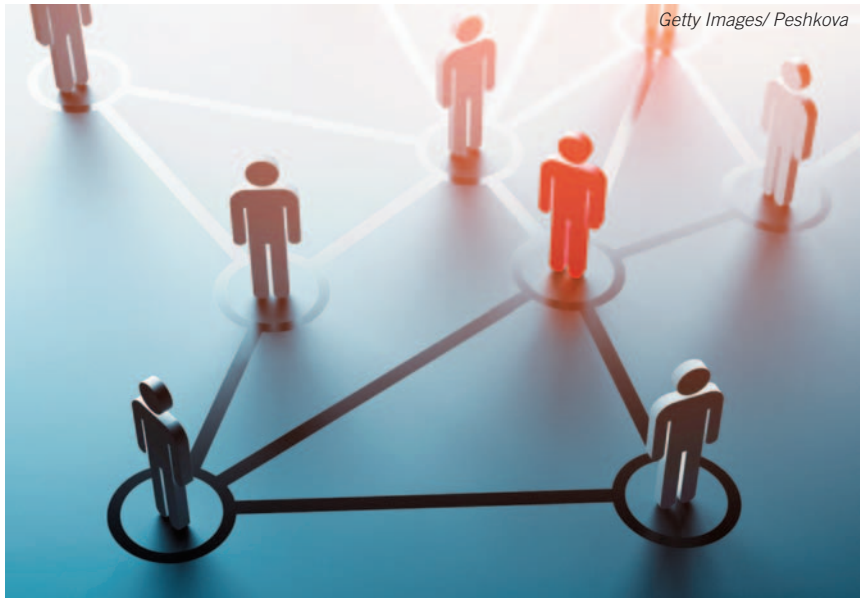
Patient influencers see three dominating issues resulting from thousands of hours of conversation with their communities, exploring every stage of the drug lifecycle, from as early as clinical trial design to loss of exclusivity strategies.

1. Access to empathy, pricing, and patient assistance

Patient communities have become organic support networks, sharing real-life experiences, tips, tricks, contact names, and outright hacks to help each other to pay for their medications. Patient influencers frequently act as navigators and moderators for members wrestling not just confusion, but a range of emotions. "Many cancer drugs are prohibitively expensive. ... Even when insurance companies approve specialty drugs, the co-pays alone can be financially crippling," says Rick Davis of Answer Cancer Foundation, a WEGO Health participant/partner. "Men diagnosed with metastatic prostate cancer are frequently prescribed drugs that run $8,000 to $12,000/month, so co-pays may be as much as $3,000. Knowledgeable patient advocates can reduce patient stress at a time when the immune system is already under siege. Good advocates help navigate the system directing patients to sources of financial and emotional support."

By probing and asking the right questions, patient influencers uncover the most important decision factors that matter to their community

Nowhere are cost-of-care discussions more active than in cancer patient communities, where CAR-T drugs like Novartis' Kymriah and Kite/Gilead's Yescarta offer real hope—and real challenges—for patients who need to know how they'll pay. Davis says, "In cases where expensive FDA-approved drugs are prescribed off-label, we will frequently arm the patient with clinical evidence and specific doctor referrals to pass on to the insurance companies."


Getty Images/ Peshkova

One way that patient influencers help is by learning about, and sharing, pharma companies' patient assistance programs (PAPs). The general perception of PAPs is that they are extremely helpful for low-income patients and the uninsured. "Once Medicare, Medicaid, or commercial insurance enter the mix, it gets really complex," notes Davis. "As advocates, even just explaining the 'donut hole' to Medicare patients can relieve anxiety. We cannot be an expert on every plan, so connecting patients to peers who have already fought the battle can be huge, especially when the same drug is in focus and the pharma has a PAP. Peers will share tips."

Some tips can feel more like hacks—from skipping online forms in favor of live support, to the extreme examples of changing insurance plans or even moving to a new state to find coverage.

Universally, patient influencers feel they can help companies to design better PAPs, and they are ready to collaborate before a PAP causes confusion and even backlash. "Goundbreaking drugs invariably come with a high price that users must address," says Davis. "A good assistance plan shows the patient that pharmas have a heart and they recognize the patient perspective."

2. Efficacy and side effects

Every day, patient influencers and their communities discuss effectiveness of one drug versus another, and it can be a complex topic for patients who don't know exactly what to expect from a treatment. Patient influencers field questions like, "Am I getting the benefit I should?" "Are others feeling better than this after three months?" and, "Should I expect this to keep working?"

Medication side effects run alongside efficacy, and patient communities debate them as equal factors in their decisions to request a new drug. When combined with cost, efficacy and side effects can either drive a prescription fill—or send patients back for an alternative. Patient communities have become sophisticated in their debates, especially in chronic conditions like hemophilia.

"When a new drug comes to market, questions and/or concerns about how it works and if it's safe tend to run amok," says Dakota Rosenfelt, a hemophilia patient influencer. "Connecting patients to others on the same drug is the tried-and-true way of giving someone peace of mind when it comes to switching or starting a new treatment option. When someone is first starting a new therapy, connecting to a patient already taking the therapy can help ease any concerns over safety or efficacy, especially in this age where novel therapies are becoming more and more common."

For launch drugs such as Genentech's Hemlibra for hemophilia A, that lack of shared experiences can slow uptake as patient influencers try to fill the knowledge gap. Pharma companies are often surprised to learn that patient influencers want their help, especially at launch, to provide objective clinical data and "is-this-for-you?" education.

"I use links to studies as well as videos provided by the manufacturers to help inform patients about the therapy they have in question," says Rosenfelt. "It would be more beneficial for manufacturers to provide links to their own studies, and maybe even ones with similar focus, on the websites they develop for the therapies. Some manufactures go above and beyond to provide an educational site about the condition in general."

Rosenfelt believes this presents a significant "gold mine for patient advocates because it gives us a cumulative central source to send in questions." An example of this type of resource is Bayer's livingwithhemophilia.com. The site provides

comprehensive information about living with and managing hemophilia, presented in an easy-to-understand fashion.

Patient influencers often create their own content to answer frequent questions, from blog posts to podcasts to do-it-yourself (DIY) videos. Supporting this influencer-generated content is another opportunity for pharma companies to work with patient communities. "Having the support of the manufacturers to create these videos and scan them for accuracy would be huge for the patient communities we jointly serve," says Rosenfelt. "Through the help of the company's broad reach and distribution channels, our combined impact seen could be limitless."

3. Lifestyle and convenience

For many patient influencers, helping their communities better understand how treatments will impact their everyday lives is an ongoing effort. Questions such as, "Will I be able to stick to the dosing schedule?" "Do I need to fight for prior authorization with each course?" "Do side effects occur when I'm trying to spend quality family time?" "Will it require a specialty pharmacy?" "Can I carry the injector in my purse?"

Almost unanimously, patient influencers feel that pharma companies and healthcare professionals (HCPs) underplay the real role of daily life in dictating even life-saving treatment decisions. "Patients and even their caregivers are savvy enough to know that even a much more convenient approach may not be a good reason to switch if their current treatment is working," says multiple sclerosis (MS) patient influencer Wendy Booker. "But I also see patients who already feel their illness is impacting their family, or their work, and they weigh a new drug's medical benefits against making their 'non-sick' life harder."

The MS community has been a fast-moving laboratory, testing lifestyle and convenience trade-offs. After decades without many options, MS patient influencers have now become experts at facilitating their communities' many choices. When oral medications in this disease space first launched, there was some skepticism about convenience-over-effectiveness gimmickry, but oral therapies are now well understood and accepted as powerful new options.

For pharma companies, the nuances of the patient community's evaluation can't be understood with only large-scale quantitative studies

Today, products like Genentech's Ocrevus are testing the limits of the lifestyle-versus-efficacy debate for patients. For many forms of MS, the drug is a true breakthrough in disease management, but because it must be administered in special infusion centers, convenience will be a critical issue. "At first, it may look like a step backwards as orals are becoming so common," says Booker. "But Ocrevus is the first disease-modifying therapy for both primary progressive MS and relapsing-remitting MS and it remains to be seen if the community's experience is worth the trade-offs. A lot will have to do with things like transportation and how the infusion experience is perceived."

For pharma companies, the nuances of the patient community's evaluation can't be understood with only large-scale quantitative studies. An MS oral therapy launched a few years ago found this out the hard way. Surveys showed side effects were in line with competition, but the medication had a slightly higher incidence of hair loss. While occurrences were rare, a few stories of rapid hair loss (with pictures) spread fast through the largely female MS community online, and launch expectations had to be reset.

"What companies need to do is listen to us, the patient influencers, early and often," says Shari Berman, another influencer in MS.

True patient centricity means creating a "patient KOL" advisory group, no less important than physician KOLs. Speaking on behalf of their communities' shared experiences, patient influencers are the real-world analysts of the patient journey. Effective groups advise companies on what questions to ask the larger community, then help to translate the findings into a new trial or an assistance program design; they separate the "me-too" from the standout patient marketing and education, and they can help brands build a scorecard that reflects how patients will evaluate their products.

"Pharma companies should know by now that we want to help them get it right," says Berman. PE

JACK BARRETTE is CEO and Founder of WEGO Health

Closing Pharma's Digital Divide

Overcoming the challenges of digital brand management will involve choices in spending and channels

By Peter Houston

By 2020, the US healthcare and pharma industries will spend upwards of $3 billion on digital advertising annually, according to projections by digital market researchers eMarketer. Their forecast represents a compound annual growth rate of more than 13% in pharma's digital marketing spend since 2014. Steadily increasing spending doesn't mean that digital marketing is getting any easier, however.

Even the most tech-connected pharma brand managers can still find it a challenge to navigate the complexities of regulation, patient privacy, and cross-channel promotions in the digital marketing space. And this year more than any other has provided proof positive that digital media's upward trajectory is as vulnerable to real-world pressures as any marketing medium.

Mark Zuckerberg's Congressional *mea culpa* to the many failings of scandal-hit Facebook is only the best-reported reminder that it's not all smooth running on the information superhighway.

New media darlings Buzzfeed and Vice Media both missed their 2017 revenue targets and laid people off. Mashable went from a $250 million valuation to a $50 million fire sale in less than six months. YouTube has had to bring back humans to manage content on its Kids video channel to protect children from obscene content that the algorithm thought was okay.

Never as heavily invested in digital as other industries, pharma marketers can perhaps breathe a little sigh of relief that they're not all-in on digital. Enjoy the moment, then get back to figuring out how to make digital work for pharma brands.

Still need to catch up

If there wasn't before, there's clear evidence now that digital media and marketing is not perfect. But perfect or not, it continues to deliver unprecedented reach, growing engagement, and real potential for building long-term brand awareness.

eMarketer's projections show that healthcare and pharma spend the least on digital advertising among the 10 industries measured. Retail is the biggest and will outspend healthcare and pharma by $20 billion in 2020 if eMarketer's projections hold up.

Research by eConsultancy, in association with Adobe, similarly sees a sector playing catch-up on the digital transformation journey. But their "2017 Digital Trends in Healthcare and Pharma" report goes on to describe prospects for "exponential change," as consumers show increasing interest and participation in their own healthcare. The report says drug companies will be forced to overcome the challenges posed by complex regulation and siloed organizational structures.

While eConsultancy's research shows just 6% of companies ready to describe themselves as "digital first," compared with 11% in other sectors, healthcare and pharma companies are increasingly aware of the opportunities. They are also getting ready to spend more: 71% said they were planning to increase their digital marketing spend last year compared to 60% in other industries.

Pharma futurists see a sector transformed by technology where pills alone are not enough. The US head of Takeda Digital Accelerator, Daniel J. Gandor, told eConsultancy, "It's pills with companion apps, and coaching, diagnostics, and personalized medicine all wrapped into one."

Research from global consulting firm Accenture estimates that digital health funding in the US will grow to $6.5 billion by 2017, with investment sustained by funding for digital health startups.

But French consulting rival CapGemini describes the pharma industry as a "digital beginner" in its "Digital Advantage" report. The reality is, the vast majority of pharma marketers will need to prioritize practical decisions about how to invest their digital budgets today rather than re-imagining the digital healthcare ecosystem for tomorrow.

Multichannel campaign management

A strengthening focus on the customer means that pharma marketers are increasingly having to work across multiple touchpoints. In eConsultancy's 2017 digital trends report, multichannel campaign

management was rated several points higher by pharma marketers than those in other industries—21% versus 16%.

Cross-device targeting driven by data analytics and programmatic advertising is not yet pharma's strong point.

Programmatic advertising—automated media buying that relies on algorithmic bidding—has grown exponentially over the last few years. Forecasts show programmatic buying in the US accounting for more than four of every five ad dollars spent by next year.

Growth has come from the targeting possibilities programmatic ad buys allow marketers to specify, from geographies to detailed audience segments. Done right, it's a dream come true for marketers in a highly regulated market like the life sciences. The problem is, it's not easy for non-technical people to understand rapidly developing technology options or properly control ad placement. This explains estimates showing programmatic advertising accounts for less than 5% of digital ad spend in pharma.

Conversely, longer experience and direct control mean social media was noted as a budget priority for 63% of pharma respondents to eConsultancy's digital trends survey. That compares with an average across other industries of 55%.

Social media maturity

Health communications agency Ogilvy Healthworld recently partnered with social data firm Pulsar to produce its fourth-annual "Social Check-up." The report's conclusion was that pharma's use of social media has "matured" and companies are getting "more and more mileage" out of their efforts on social platforms.

Findings are based on analysis of 11-month's activity on global corporate social channels for 20 leading pharma companies. The data shows that the average number of weekly posts across most of the social channels monitored—Facebook, Twitter, YouTube, and Instagram—has decreased. The one exception is YouTube, which was up but on very limited activity.

This drop in post frequency is in direct contrast with significant increases in both community size and engagement across platforms at half of the top 20 companies. Top brand Novo Nordisk grew its engagement by 13%; Novartis by 77%; Johnson & Johnson by 111%; and Merck & Co./MSD by 122%. None of these brands posted the greatest amount of content.

> The vast majority of pharma marketers will need to prioritize practical decisions about how to invest their digital budgets today rather than re-imagining the digital healthcare ecosystem for tomorrow

The social team at Ogilvy Healthworld came to the conclusion that high-value content, possibly with paid amplification, was key to driving engagement. The definition of high-value content is varied, stretching from the drone footage of Bayer and Eli Lilly's headquarters posted on their respective Instagram accounts, to associations with celebrity influencers.

Celebrities and pharma are not always an easy fit, but Ogilvy Healthworld highlights the spikes in engagement that came from partnerships with Novo Nordisk and Pakistani cricketer Wasim Akram for #ChangingDiabetes and Oprah Winfrey supporting J&J's HIV vaccine announcement.

Highlight the human

According to the Social Check-up report, the underlying message for increasing engagement, at least in terms of content posted, is to highlight the human side of the pharma business. It recommends spotlighting broad initiatives like Novo Nordisk's all diabetes pro-cycling team and unbranded ads around awareness days like Earth Day, World Aids Day, and World Cancer Day.

The report paints the social media space as increasingly "pay to play," with companies looking to paid social promotions as a way to target the right people at the right time. Paid amplification is also compensating for a decline in organic reach, the cash keeping content visible in a crowded space.

As well as posting less and paying more, pharma marketers are also working to leverage the peculiar strengths of a mix of social channels by tailoring content specifically for each channel.

Ogilvy's 2016 Social Check-up showed that the most engaging content for pharma followers was highly visual and, this year, many of the top pharma companies are looking to Instagram as a key channel. The biggest platform for digital marketing, however, is still Facebook.

Facebook's public woes and the hand-wringing over brand-bashing algorithm changes shouldn't fool anyone into believing Facebook is no longer a rele-

vant part of the digital marketing mix. With greater reach that all other channels, 2018's Social Checkup put the average number of engagements per Facebook post at 524, far greater than 190 for Instagram, 61 for Twitter, and just three for YouTube.

There is still a lot of confusion over how changes to Facebook's news feed and likely changes to data usage and advertising practice will impact brand marketing tactics on the platform. But as the President of Condé Nast International, Wolfgang Blau, said when the news feed changes were first announced: "It remains the world's most powerful distributor of that most precious of resources called attention."

Active engagement

The much-discussed algorithm changes to the Facebook newsfeed are a strong indicator of where social media marketing is heading. Facebook's new engagement rules promote comments over "Likes" as a signal of meaningful interaction and social content that inspires active engagement will become ever more important.

Pharma's focus on content marketing illustrates this narrative, with marketers looking to meet increasing demand for reliable healthcare information through content marketing. eConsultancy's data shows 29% of pharma marketers prioritizing content marketing above all other digital-related activities.

Content marketing for consumers is still a challenge in the highly regulated life sciences market and techniques for personalization used successfully in other industries are more difficult for pharma. This means content targeted at healthcare professionals (HCPs) is still a priority.

Social media's appetite for high-quality content is matched by a return to prominence for search marketing. eMarketer's digital advertising forecasts show search and display are equally important formats for healthcare and pharma brands.

Changes to Facebook's algorithm may even bolster the importance of search, as the social network prioritizes content from friends and family over publisher and brand content. According to publisher referral data collected by analytics firm Parse.ly, whose customers include high-traffic sites like *The Wall Street Journal*, Google Search delivered 44% of all traffic to their customers' sites compared to 25% for Facebook.

Traffic from other referral sources is generally very low in comparison; the next biggest social platform, Twitter, sends just 2.6%; and alternative search Bing, just 1.3%.

Declining public trust

Although a priority channel, the developing ROI for social media marketing may also be threatened by falling public trust in digital platforms. The 2018 Edelman Trust Barometer shows trust in social media and search platforms dipping by 11% in the US, the steepest decline anywhere in the world.

Against a background of "Fake News" and amid the backlash against unauthorized data manipulation, brands may be looking back to legacy publishers to deliver the credibility that comes from association with an established media player.

Kantar Media, reporting that total pharma spending on advertising in the US market rose 4.6% to $5.8 billion, noted that the jump includes a 6.4% rise in spending on magazines. That spike explains why consumer publishers from Condé Nast and Time Inc. to newcomers like Vice have all launched health content businesses.

Right message, right place, right time

The right time may be at home on a laptop, or on a social channel on a smartphone. It might also be at the point of care (POC), a channel that allows companies to target specific practices and patients at a point they are more receptive to health information.

Last year, sales and marketing consultancy ZS Associates reported that up to 20% of pharma brands were moving digital media spend to digital POC marketing in doctor's offices or hospitals. Platforms highlighted included exam room tablets and interactive wall boards, waiting room TV, and sponsored apps, some incorporating geo-fencing to target video or text messaging at patients in doctors' offices.

Getting the message right also means compliance. Alongside the age-old worries around FDA compliance, new worries around data protection legislation in Europe are now in play. The General Data Protection Regulation (GDPR), a harmonization of data privacy laws across Europe, is designed to protect EU citizens from privacy and data breaches. The legislation applies to all companies processing the personal data of subjects residing in the EU, regardless of the corporate location. That means that patient data collected in Europe but transferred to the US for processing needs to be complaint. With fines of up to 20 million euros threatened, proper data processing has taken on new gravity. PE

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Patient Empowerment and the Future of Pharma Advertising

In the wake of the recent Facebook scandal and the continued emergence of our existence within a data-driven world, the average consumer for pharmaceutical products are increasingly more aware of how their data is used, and, as a result, more empowered in their expectations as to what advertisements they are exposed to and why.

This balance between data privacy concerns and expectations of a more nuanced ad experience plays perfectly into the capabilities of the pharma industry. First, let's address the privacy concerns. After it was revealed that the personal data of over 70 million Facebook users was shared with several entities for the purposes of hyper-targeted advertising, there was a global gut check. Mark Zuckerberg testified before Congress twice and Facebook made (seemingly) sweeping policy changes in terms of personal data. This is a direct reflection of this growing concern when it comes to the use of personal data for advertising. Where for many industries, this is a hurdle to overcome in regards to establishing consumer trust, for the pharma sector, this is an opportunity.

In many respects, the US is the Wild West when it comes to data privacy; we run on the "opt-out" rather than the "opt-in" approach to granting company access to our data, we do not have anything like the General Data Protection Regulation (GDPR) in place (though it will still impact US companies), and we are one of only two countries in the world where pharma advertising is legal. However, unlike a soda company trying to figure out if someone drinks Coke or Pepsi, for pharma, there is HIPAA in place to protect the consumer and, in turn, protect the brand.

When everyone is questioning which companies have access to their data, what data these companies have, and how it is being used, the pharma industry is the lone wolf. Unlike any other sector, the pharma industry can ensure the proper and private use of user data. With this in mind, pharma should be shouting from the rooftops of its dedication to HIPAA certification in order to put privacy first. There is an opportunity here to quiet the concerns of a now data-phobic public.

By promoting the industry's historical commitment to data and personal privacy, it opens the doors to engaging the empowered consumer in ways they are most likely to respond. Recent privacy concerns aside, what consumers have consistently stated is they hate getting advertisements that don't apply to them. If a person doesn't have diabetes, or fibromyalgia, for example, they're not likely going to want to see ads for those conditions while binge watching the latest new Hulu series. Unfortunately, for many pharma brands, that is the approach taken—mass distribution of a product's message based on generalized demographic data. If one in 10 people in the country has diabetes, and a company runs a national TV campaign in support of an insulin pump product, based solely on the disease prevalence, nine out of every 10 commercials aired will reach someone who is not a potential customer—and potentially annoy a cross section of future customers.

A more empowered patient means they often have a larger voice in their own medical treatments. Again, this presents a prime opportunity for the pharma industry by alleviating customer concerns of privacy with an emphasis on HIPAA certification and what that means for data privacy, and by being aware of the shifting expectations of targeted advertising to be directly relevant to those viewing the ads. There is just one thing missing—technology.

There have been several technological advances over the past few years, which make targeting consumers with ads that they want and need, but without violating HIPAA, possible. These advances include the digital transformation of the industry, wider and faster consumer access to the internet, huge advancements in digital and connected television, and big data analytics and AI. When all of these are combined, brand teams are left with the ability to target customers like never before.

Because of this digitalization, there are more directed channels to reach customers. While HIPAA prevents companies from directly targeting customers individually, it does allow for more targeted focus than a traditional demographic-only approach. Addressable TV is a great example. This broadcast advancement allows for brands to get closer to the individual viewer than ever before. For pharma brands, this means fine tuning the likelihood of reaching that diabetic or fibromyalgia sufferer by applying big data analytics to HIPAA-certified data and folding in the demographic information. This keeps data anonymous but makes the regions targeted go from traditional advertising-designated market areas (DMAs) down to a much smaller geographic division. This changes the efficiency of that diabetic ad campaign from an accuracy of 10% to 25%-40%.

We are at a point in time where the pharma consumer has never been more engaged with their own health experience. We are also at a point where the technology available to us allows the delivery of targeted advertisements to those who would benefit, while leaving those who would not alone. The future of advertising in the pharma industry is a combination of educating the public on data privacy and using the technology available to deliver the results everyone wants by adhering to that data privacy.

— Michael Joachim, Senior Vice President, Growth and Innovation, Medicx

Deploying the Cloud in GxP Environments

Meeting the stringent cloud compliance and regulatory requirements in pharma

By Jaleel Shujath and Stephen Ferrell

The traditional IT infrastructure for most life sciences organizations was not designed to meet the business challenges that companies are faced with today. It can take significant, sustained, and hugely disruptive investment in new technologies and infrastructure to bring internal systems to the required security, performance, and compliance level. At the same time, a life sciences company must do much more than maintain "business as usual." It must reduce costs and increase productivity and innovation against a backdrop of continually changing market pressures and regulatory requirements. This is the reason that we're seeing greater cloud adoption in other parts of the life sciences business. However, good practice quality guidelines (GxP) environments have their own unique requirements. There are very strict guidelines around application and system usage in key business functions, such as research and development, clinical trials, quality, and manufacturing, set by the FDA and other global regulators. This article looks at the cloud deployment models available for GxP environments and how to select the right one for a pharmaceutical company's cost constraints and regulatory profile.

Three types of cloud service

The strengths and weaknesses of internal IT deployments are similar across industries. They are, however, exacerbated in the regulatory environment. A large life sciences company can have thousands of different IT architecture combinations and a large proportion of its overall IT budget is taken up with simply operating, maintaining, and supporting these existing systems. More importantly, the result can often be a lack of agility, if it takes IT too long to respond to changing business requirements. With the additional compliance constraints, it can take many months to deploy a new module or just add extra computing or storage capacity. In addition, users are often faced with slow and inefficient legacy systems and, worse, much of their data remains under-utilized, due to its storage in inaccessible silos throughout the organization.

Cloud services can help overcome many of the drawbacks of existing internal systems. There are infinite combinations of cloud deployments, however; generally, the following delivery types can enable a company to decide which elements of its IT infrastructure to continue to operate internally and which to have executed by a cloud service provider.

- **Infrastructure as a service (IaaS).** IaaS provides a service to establish and run virtualized computer resources over the internet. Virtualization is the creation of virtual—rather than actual—versions of IT infrastructure, such as operating systems, servers, or storage devices. The services provider is responsible for managing and delivering hardware, storage, servers, and data center space that form the foundation of a cloud environment.
- **Platform as a service (PaaS).** PaaS is a cloud computing service that provides all the platform—hardware, middleware, and operating system—components needed for a company to develop, run, and manage applications. The cloud technology provider takes care of all the infrastructure while the pharma company manages its own application portfolio.
- **Application as a service (AaaS).** Also known as software as a service, AaaS provides a completely hosted—and managed if required—IT package. The provider makes applications available to the company over the internet via a thin client PC.

Four types of cloud deployment

Before looking at the four cloud deployment models, it's worth considering the characteristics that all cloud services have in common. Using the internet allows many companies to connect securely to the same service, enabling collaboration and information sharing. Companies using the cloud service have access to shared resources that are continually improving so that they should always have access to the latest and best performing systems. With some cloud service providers, the service is delivered on-demand. Life sciences companies access the service as required and usage can be metered or architected in such a way that they only pay for what they use.

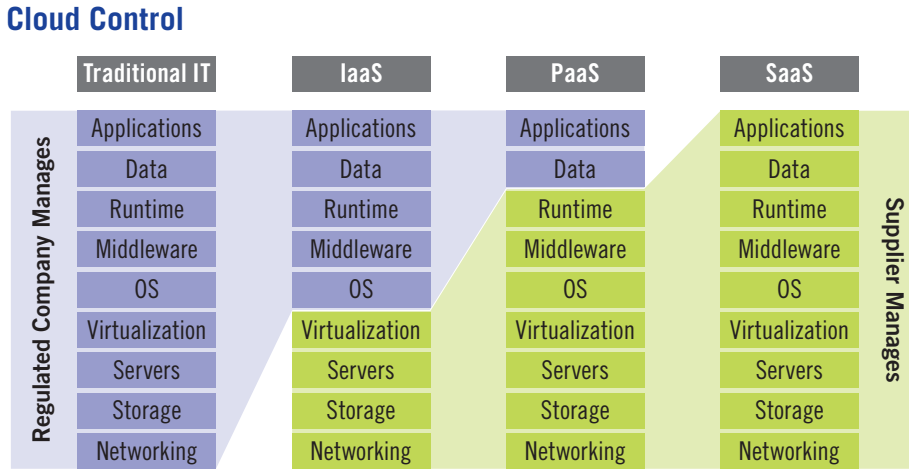


Figure 1. Management comparison of traditional IT vs. the three types of cloud service.

A major benefit of the cloud is its virtually limitless scalability and geographic agnosticism—that can be applied extremely quickly to meet demand. One life sciences company found that it would require 250 internal servers to meet peak processing times during certain phases of global clinical trials. This meant waiting for internal resource to be freed up, and as the project was estimated to cost $150 per second, that was a very costly delay.[1] Switching to a cloud service meant that the company not only could meet its computing requirements quickly, but it could scale up for peak processing and scale down afterwards—only paying for the resource they used.

Further qualifying the virtualization tools themselves can greatly reduce qualification time, especially in the scenario where the underlying specifications of the servers are identical, allowing the rapid deployment of pre-qualified server packages.

The cloud deployment models available allow a company to access the benefits of cloud computing while ensuring that its working within the performance, security, and risk levels of the organization's requirements.

HOSTED PUBLIC INTERNET

A public cloud is a publicly accessible cloud environment owned by a third-party cloud service provider (CSP). Services are provisioned in a multitenant environment where many customers are using the same service. The infrastructure may be hosted on the premises of the service provider, a third-party data center, or, possibly, multiple third-party facilities and, further, may reside on equipment owned or leased by the CSP. It is vital before engaging with such a provider that a pharma company fully understands its provider's architecture, the layers of service-level agreements (SLAs), and the relationships between all of the delivery partners. Ultimately, though, the environment will be operated by whoever is making use of it, be it life sciences companies, government organizations, or academic institutions.

The service is delivered across the public internet and accessed via thin clients at the customer site. The main features of hosted public cloud include:

- Fast and easy deployment of standardized solutions.
- Easy to connect and collaborate with external customers, partners, and suppliers.
- Complete management and support of IT infrastructure.
- System performance and continuity guaranteed under SLA.
- Reasonable levels of security.
- Lack of auditability—while most public cloud providers will offer standard third-party audited accreditations, such as ISO27001 or SOC 2, they will not generally permit traditional GxP audits.

While companies have access to the latest web security standards, the hosted public cloud will not deliver the highest levels of security possible and is likely not to be up to the companies' requirements if this is a foremost concern.

The Four Core

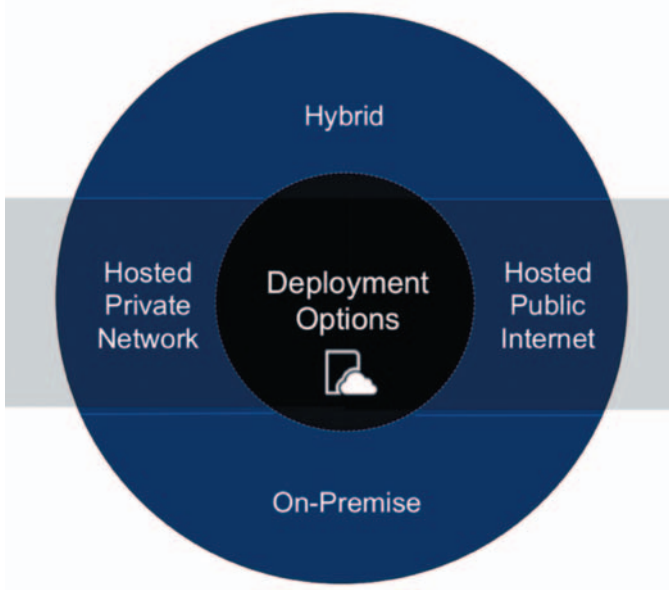


Figure 2. The four deployment models for cloud computing.

In addition, the cloud provider is responsible for the creation and ongoing maintenance of the public cloud and its IT resources. It is more difficult to control patching and upgrade frequency and it is likely that the user will have little-to-no transparency over what happens below the operating system.

Where application and infrastructure qualification and validation assurance is essential, a pharma company will need to find ways of working with the cloud provider to gain all the information it needs to meet the organization's compliance requirements. Appendix 11 of the ISPE GAMP Good Practice Guide for IT Infrastructure Control and Compliance[2] provides strategies for qualifying the suppliers for each of the different engagement types.

HOSTED PRIVATE NETWORK

A private cloud, as the name suggests, is solely owned by the cloud service provider. Deployed internally or externally, a hosted private network offers high levels of security using the provider's private cloud and delivers data management and business continuity services. It is the ideal choice for organizations that need to manage their host applications and other applications used by their customers. The main features of a hosted private network are:

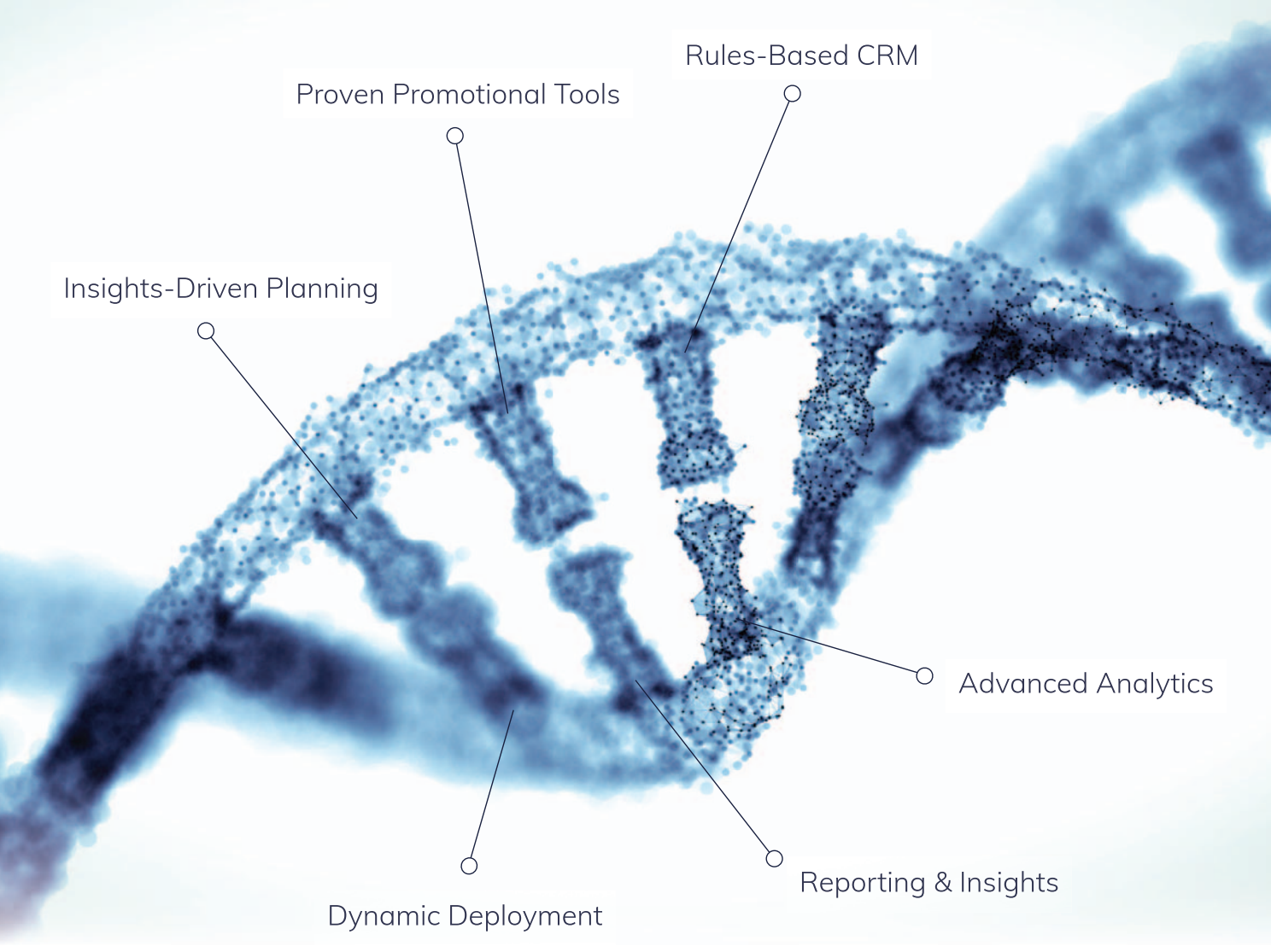
- Ability to retain existing IT system customizations.
- Flexibility to modify systems as required.
- Flexibility on the control of upgrade and patch frequency.
- Maximum levels of reliability and scalability.
- Maximum levels of security.
- Greater control over cloud infrastructure.
- Typically running on dedicated hardware (though private clouds can be virtualized).

There isn't a great deal of difference in the design structure between hosted public cloud and hosted private network. The biggest difference for the latter is that the provider is, effectively, delivering a single tenant service over a multi-tenant architecture. It is essential that the provider can prove complete customer and data isolation—that a company's applications and data are completely isolated from that of any other customer using the provider's services. As such, the security, performance, and compliance benefits of the private model will come at an increased cost.

HYBRID CLOUD

A hybrid cloud contains the best parts of the hosted public cloud and hosted private network models. In a hybrid cloud deployment, the cloud environment is comprised of two or more different cloud deployment models. For example, one may choose to deploy cloud services processing sensitive data to a private cloud and other, less-sensitive cloud services to a public cloud. A hybrid cloud delivers superior data management, security, scalability, and performance, but adds complexity in terms of management and reliability due to the diverse configurations that this model can create. The hybrid model potentially provides the best opportunity of balance for a GxP-regulated entity; higher-risk GxP applications and services can reside in a qualified cloistered environment, while non-GxP applications can exist outside of the more constrictive GxP control set. The main features of hybrid cloud are:

- Ability to deploy primary solution on premise.
- Ability to retain existing IT system customizations.
- Flexibility to modify systems as required.
- Flexibility on the control of upgrade and patch frequency.
- Flexibility to deploy business continuity and disaster recovery capabilities externally.
- High levels of reliability and scalability.



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» High levels of security.
» Greater control over cloud infrastructure.

Hybrid cloud deployments can be complex and challenging to create and maintain due to the potential disparity in cloud environments. Life sciences companies need to work closely with the cloud service provider to know exactly who is responsible for managing every element of the IT infrastructure. Where qualification and validation is important, the cloud service provider must be able to demonstrate and record that all its activities meet a company's GxP compliance requirements.

ON-PREMISE CLOUD

Where security and control are paramount concerns, on-premise cloud deployments are preferred. In this model, all IT infrastructure remains within the organization. With on-premise cloud, a company uses cloud computing technology as a means of centralizing access to IT resources by different parts, locations, or departments of the organization.

Even though the cloud infrastructure physically resides on the company's premises, the IT resources it hosts are still considered "cloud-based," as they are made remotely accessible via the cloud to both internal and external users. The service provider delivers the level of management and maintenance skills the pharma customer requires to operate the system. The main features of on-premise cloud are:

» Ability to qualify the data center infrastructure, cloud stack, and virtualized architectures.
» Ability to remain using existing hardware.
» Ability to maintain system on-premise.
» Ability to retain existing IT system customizations.
» Flexibility to modify systems as required.
» Flexibility on the control of upgrade and patch frequency.
» Ability to use provider to flexibly resource IT infrastructure.
» Maximum levels of security.
» Maximum control over cloud infrastructure.

From the standpoints of data integrity, security, and software validation, on-premise cloud represents an attractive option. However, it does have drawbacks. Unsurprisingly, this cloud type suffers from some of the key weaknesses of internal IT systems. Key among these is the potential lack of scalability. A company is still bounded by the capabilities of its existing servers and can't take advantage of the unlimited potential to quickly and securely scale computing capacity as business requires.

Further, with a hardware refresh rate of three to five years, and the internal costs of managing the solution and any associated regulated expectations, this deployment type can soon exceed the perceived value of an on-premise architecture.

The regulatory paradox

To meet the criteria for computing in a GxP environment, software applications have to be carefully validated and other IT infrastructure components—data center facilities, network components, and infrastructure software and tools—needed to be properly qualified. The life sciences industry had become very comfortable with using the GAMP 5 for the validation of applications. Until recently, similar guidance for cloud deployments was in short supply, but the International Society for Pharmaceutical Engineering (IPSE), the creator of GAMP 5, has addressed this with the publication of the *GAMP Good Practice Guide: IT Infrastructure Control and Compliance rev 2*.[2] The guide directly addresses the vastly increased risk profile for cloud computing and provides a roadmap for transitioning from an internal self-managed relationship to a model for working with a qualified supplier, such as a CSP.

The IPSE guidance for achieving compliance now places new emphasis on:

» Supplier assessment and management.
» Installation and operational qualification of infrastructure components (including facilities).
» Configuration management and change control of infrastructure components and settings in a highly dynamic environment.
» Management of risks to IT Infrastructure.
» Involvement of service providers in critical IT Infrastructure processes.
» SLAs with XaaS (i.e., IaaS, PaaS, SaaS) providers and third-party data center providers.
» Security management in relation to access controls, availability of services, and data integrity.
» Data storage, and in relation to this, security, confidentiality, and privacy.
» Backup, restore, and disaster recovery.
» Archiving.

This new guidance comes at a critical time, as regulatory pressure elsewhere in the business are

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It is essential that companies are sure that the change control and documentation processes of the provider meet their requirements

likely to encourage life sciences companies to investigate cloud services. A slew of recent and forthcoming regulations across the European Union (EU) place an emphasis on information sharing and improved data management. The EU General Data Protection Regulation (GDPR), which deals with the management of personal information; the ISO Identification of Medicinal Products (IDMP), which involves improving information sharing and reporting of medicinal products; and the EU Clinical Trials Regulation (CTR) will affect every company that sells, markets, or works in Europe.

In all three cases, the regulations require enterprise-level of control and visibility of data within an organization—and, in some cases, its suppliers, partners, and customers. It involves bringing together different data in different formats from different parts of the business. In many cases, existing legacy systems will labor to meet performance, security, and transparency requirements to comply with these regulations. The scalability, reliability, and proven security capabilities of the cloud make it an increasingly attractive option.

What to expect from a cloud provider

Delivering cloud services into a regulated environment places extra responsibility on service providers. Often, as the GAMP Cloud Special Interest Group has pointed out, this will involve them being willing to adapt their business model, as "it involves even greater movement of control toward the supplier, but still leaves the responsibility for the data and process within the regulated company. …The compliance concerns are just as valid, on infrastructure, platform, and application level, with little or nothing that we as life sciences companies can influence with regard to the provider's management processes."[3]

While true, many service providers have made significant efforts to tailor their service to meet GxP requirements. In addition to meeting all the latest cloud standards, such as SSAE and ISO 27001, some deliver against qualification standards and include validation packages that let a company take a risk-based approach to application development, delivery, and amendment. They will all provide the most stringent security, access, and change controls to meet the needs of regulated environments.

Where some providers differ is in their willingness or ability to deliver the level of audit rights and documented processes that life sciences companies require to meet their GxP compliance responsibilities. It is essential that companies are sure that the change control and documentation processes of the provider meet their requirements, especially within their qualification documentation practices.

Ready to go

The cloud is not an immature technology. Properly architected, built, and managed, it is a highly resilient, scalable, and secure platform that has been proven to successfully host mission-critical applications. More and more industries—even the US government—are quickly moving to adopt a "cloud-first" strategy. The GxP environment, like other regulated environments, has very stringent requirements and that has certainly slowed adoption.

The lack of clear implementation guidance has been an issue. However, with the new IPSE guidance and a risk-based approach to cloud deployment backed by a cloud service provider whose services are designed for regulated environments, companies can now begin to benefit more fully from the cloud. Today, the cloud is better suited to deliver GxP-compliant services that will help life sciences organizations meet their key business challenges. As the GAMP Special Interest Group says: "We all know it's the way to go."[3] PE

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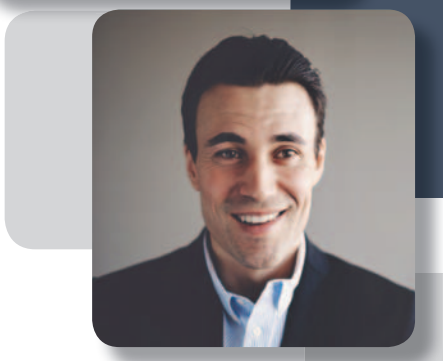

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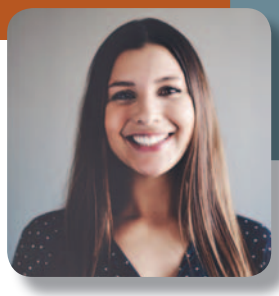

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The Total Care Package

Charting the course that has led to payer vertical integration and what it may mean for pharma manufacturers

With the emerging and now well-chronicled shift in healthcare from one based on rewarding volume of services to one focused on the value of services provided, the pharmaceutical industry is searching for varying methods and formulas it can leverage to best adapt to the changes. One solution many are finding is vertical integration, which is built on the premise that in order to win in the value marketplace, a player needs to offer comprehensive services, have comprehensive data, and exert comprehensive control in the market.

Payers aligning vertically

Vertical integration has been increasing in the hospital system/provider space over the last several years. According to a recent physician survey conducted by the American Medical Association, 2016 marked the first year that less than 50% (47.1%) of practicing physicians owned their own clinical practice.[1] The need for greater alignment, less variation, improved outcomes, risk diversification, and cost containment were clear driving factors.

Larger health systems create even more leverage and higher pricing. As a counterweight, payers are integrating as well. There has been a flurry of acquisitions recently, notably CVS announcing the purchase of Aetna and Cigna's acquisition of Express Scripts—which itself recently purchased medical management company eviCore. Not all integration has been via acquisition. Anthem's decision to break with Express Scripts and go its own way in the pharmacy benefit manager (PBM) space with the creation of IngenioRx represents another significant move in vertical integration.

The drivers for payers seeking to integrate are not all that different from those driving systems and providers. Payers are looking to expand business, diversify risk, have greater insight/control on both sides of the business (pharmacy and medical), and reduce costs while improving patient care.

For payers seeking to manage the total cost of care, drug management is a natural place to focus. When used appropriately, drugs can reduce medical complications and enhance patient health; uncontrolled drug use raises costs and can potentially cause harm. The increasing focus on drug costs, particularly specialty drugs, also motivates payers to be seen as part of the solution in order to stay relevant and competitive.

The challenge for payers is knowing what the true value of a medication is in the overall cost of care. The ongoing shift from volume to value has given rise to an increasing number and utilization of value tools to assess what value pharmaceuticals bring to the market. Each of these frameworks assess value differently and are intended for different uses and audiences. What is clear is that payers are increasingly accessing these tools as an input in their review of drugs.[2,3] The Institute for Clinical and Economic Review (ICER), in an announcement last June, has even been tapped by the Department of Veterans Affairs (VA) to have ICER's cost-effectiveness assessments used in the VA's formulary decision-making.

What can we expect once the dust settles and the landscape shifts to predominantly integrated players? The purchase of Aetna by CVS will expand medical care access in clinics by potentially bringing direct patient care to thousands of retail CVS stores throughout the country. These community-based sites of care are intended to reduce patient cost. An expanded community-based care site footprint could also mean expanded sites of care for infusions and a resultant shift away from higher-cost hospital outpatient facilities.

These and other advantages will make CVS a leader in pharmacy/clinic access, pharmacy benefit services, and health plan benefits. Cigna's purchase of Express Scripts would allow better, more efficient management of patients' medical and pharmacy histories to reduce costs and improve patient outcomes.

If these acquisitions are approved by the Federal Trade Commission (FTC), the traditional carve-out PBM will become increasingly scarce. Anthem's IngenioRx seemingly embraces a PBM model focused more on total cost of care and avoiding medical spend versus the more drug-focused, rebate-

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JEREMY SCHAFER is Senior Vice President, Payer Access Solutions at Precision for Value.

centric model that PBMs serving Anthem followed in the past.

Where do drugmakers fit in?

What does this all mean for pharmaceutical manufacturers? At a minimum, the realignment brings an obvious increase in the leverage these powerhouses have in drug pricing negotiations. The sheer size of covered lives in these organizations will put significant pressure on manufacturers to propose rebate deals and contracting strategies above what is seen today. The combined data-gathering and -reporting resources may also make unique contracting opportunities available. The greatest change, however, will be entities with a myopic focus on either the pharmacy benefit or medical benefit disappearing in favor of organizations whose goal is to reduce the total cost of care. For manufacturers, that means presenting value propositions that take into account how the drug impacts all the costs—medical and pharmacy—related to treating the condition.

What will these integrated payers be seeking from manufacturers? Chiefly, a trifecta of information: the drug's impact on pharmaceutical costs (its own and utilization of other drugs), how the drug impacts medical costs including procedures or utilization avoided, and the impact on total patient health. Telling this story will require manufacturers to use tools both old and new. Manufacturers will need to be prepared with robust budget impact modeling by segment (commercial, Medicare, and Medicaid) that takes into account impact on total cost of care. Pharma organizations need to develop partnership strategies that are more aligned to the capabilities and information these combined entities find meaningful. Large integrated payers may seem similar to each other on the surface, but each will have its own ideas and strategies on how to reduce cost of care as well as differentiate in the market.

A manufacturer that can develop strategies to align with these payers' primary objectives will have an advantage. For CVS/Aetna, a value partnership that furthers the entity's clinic expansion goals may resonate. For Anthem, aiding in showcasing the value of its PBM integration may be key. Account understanding and segmentation will be just as important in the new world as in the old. For manufacturers of medical benefit products, there will likely be an increase in traditional PBM tactics being applied to the medical drug management.

As claims processing systems become more aligned and integrated, there will be greater data collection and real-time management of medical drug claims. Pharma will need to have a good understanding of the claims processing and utilization management process. The ability of manufacturers to understand the process and the criteria requirements will help in negotiating proper coverage based on product labeling and clinical data. Most importantly, manufacturers must be prepared to show a payer value proposition that tells a complete story in cost, healthcare utilization, and patient outcome across the episode of care.

For manufacturers of medical benefit products, there will likely be an increase in traditional PBM tactics being applied to the medical drug management

Mind adjustment

The US healthcare landscape is changing rapidly to meet the challenges of an aging population and growing costs. Stakeholders all along the continuum are looking to address risk, cost, and outcomes. Multiple levers to address these issues are being used by the industry from value assessments to acquisitions and integration. The result will ideally be a different healthcare marketplace with increased focus on value, additional resources, and a priority on outcomes that reduce total cost of care. As payers and providers shift their mindset, so too must the pharmaceutical industry. PE

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COMING OF AGE

The tenth largest economy on the planet by GDP ranking, Canada clearly deserves its status at the international high table of the G7. However, despite the country repeatedly bringing forward world-class innovations and great minds, the nagging perception lingers that Canada's brand image remains understated. Perhaps nowhere is this more evident than in its thriving life sciences sector, all too often overshadowed by the bigger, more overbearing neighbor next door.

With universal healthcare solidly anchored in its system, Canada is already firmly cemented as a top ten pharmaceutical market. Moreover the local dynamics and growth trajectory are overwhelmingly positive: "Over the 2015-2016 period, we have witnessed the overall value of the Canadian pharmaceutical market rise by 3.5 percent to USD 22.6 billion," assures Rami El-Cheikh, national pharma and life sciences leader at PwC. Yet, despite these rosy figures, a complex, sprawling and splintered regulatory landscape has all too often proved overwhelming for new entrants. Equally challenging has been to stand out as an attractive investment destination with the world's largest pharmaceutical market, the United States, looming on the doorstep.

Finally, though, matters look set to change. Away from the glare of publicity, a tranche of bold reforms, aimed at harmonizing the national health system and delivering value for money, are fast nearing completion. Meanwhile, against this radical backdrop of price cuts, unified procurement and anchored budgets for priority areas like palliative care, Canada's life sciences pioneers have been busy trailblazing in entirely new market niches such as cannabinoids. Canadian life sciences may well be coming of age.

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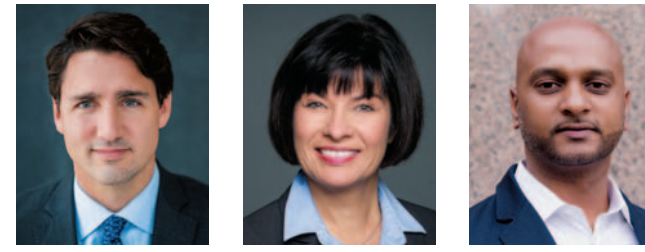
REPACKING THE BASKET

Discussion around pharma pricing models and their impact on the financial sustainability of the public healthcare apparatus tends to animate debate in most mature life sciences markets around the world and Canada is certainly no exception in this respect. Locally, discussion has intensified, as a serious reform package is in the works, much of which is already in the process of being enacted. Douglas Clark, executive director at the Patented Medicines Prices Review Board (PMPRB) acknowledges that Canada's "regulatory framework has traditionally failed to keep pace with important shifts in the operating environment," underlining that the board is now belatedly "in the midst of reworking and modernizing both its regulations and guidelines."

Brian Lewis, president and CEO of MEDEC, Canada's medtech association, adds "It is a well-known fact that the Canadian healthcare system is stressed, due to the expense of our public system as well as an aging population that is consistently growing. While the focus has predominantly been on cost control, we need to shift this focus and ask ourselves how we extract value that adds to system sustainability and limits the total cost."

The PMPRB was originally created by the state, back in 1987, primarily with a view to helping keep innovative drug prices in check by leveraging a reference basket of seven countries: namely France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the US. As one of the core pillars of Bill C-22, the body was mandated to harness that mechanism to calculate patented drug price tags and to insulate consumers from skyrocketing medicine expenses.

One critical element that is now set to change is the makeup of this basket of countries that Canada deploys as the reference for pricing referral. Precisely because the current selection of reference nations comprises some profligate, high roller mature economies where the average price of medicines can be considered somewhat exorbitant, former federal minister of health, The Honorable Jane Philpott, had in 2017, expressed her firm intent to remove high spending Switzerland and the United States from the basket. Consequently, the average price of reference would plummet: a longstanding objective of payers who have long been complaining that they are being squeezed by a relentless burden of escalating drug costs.

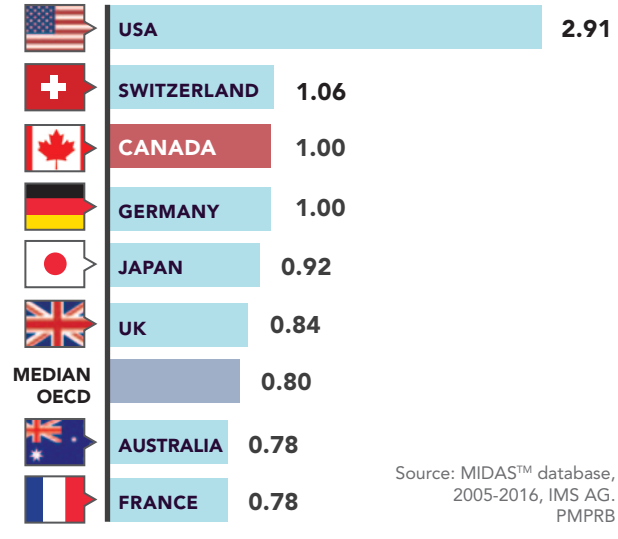


Justin Trudeau, prime minister; Ginette Petitpas Taylor, federal minister of health; Imran Ali, senior manager, pCPA

Philpott persuasively argues that the original rationale behind incorporating free-spenders such as the US and Switzerland within the basket was that it would "likely generate a positive ripple effect whereby companies from those nations would find it worthwhile to invest heavily in R&D within Canada." However, not only do "the fruits of this aspirational choice appear not to have materialized," but the Canadian tax payer and individual patients have been left to pick up the tab for "the third highest drug prices and second highest per capita pharmaceutical spending in the OECD."

With the Canadian state struggling to contain drug spending that has increased by an eye-watering 184 percent as a share of GDP since 2000, it is perhaps unsurprising that the freshly installed, new federal minister of health, The Honorable Ginette Petitpas Taylor, remains staunchly committed to enacting her predecessor's intended reforms.

AVERAGE FOREIGN TO CANADIAN PRICE RATIOS, PATENTED DRUGS, OECD (2016)



Source: MIDAS™ database, 2005-2016, IMS AG. PMPRB

READY FOR HARMONIZATION

Meanwhile, the current negotiation process for drug prices is also undergoing considerable overhaul. While full control over the pricing negotiations previously used to reside with the individual 13 provinces and territories, in 2010, a landmark decision to harmonize the process was taken. A full eight years later, the initiative is finally up and running.

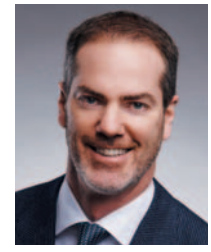
Nowadays a freshly created public body, the pan-Canadian Pharmaceutical Alliance (pCPA), wields the power to negotiate prices on a federal level on behalf of public drug plans from all 13 provinces and territories. Its senior manager, Imran Ali, describes the process. "Once a drug receives the final recommendation from the Canadian Agency for Drugs and Technology in Health (CADTH), that is the agency for all provinces except autonomous Quebec, and/or Quebec's own HTA agency, called the Institut National d'Excellence en Santé et en Services Sociaux

(INESSS), then that recommendation is passed on to the pCPA so that the various jurisdictions can discuss evidence and comparators in greater detail," he explains.

What appears to be relatively straightforward in theory, however, actually poses significant challenges in practice, as many provinces are proving reluctant to yield power while the pCPA, itself, appears somewhat overloaded and under-resourced for the enormity of the task at hand. "I'm afraid to say that, up until last year, the pCPA's activities were conducted in the absence of federal leadership; on a shoestring budget; with a tiny office staff endeavoring to manage its hugely important work, so we've obviously been taking concrete remedial steps to improve upon this situation, but there's still much to do," attests Philpott.

Ali describes the pCPA's mission thusly: "to enhance access to clinically- and cost-effective drugs; to increase the consistency of decision making; to promote fair and stable drug prices over a sustained period; as well as to reduce duplication and improve resource allocation when it comes to price negotiations." Initial signs are certainly encouraging. According to Philpott, the pCPA is "already saving taxpayers over CAD 700 million (USD 741.9 million) through its collective buying power to negotiate better prices, despite only officially entering negotiations last year."

Despite the fact that the pCPA's mission is clearly defined, actually adapting to the new rules of the game has been challenging for some stakeholders. The PMPRB, CADTH, INESSS, and the industry players have all had to accommodate their role to the pCPA's new sphere of activity. "I think it's fair to say that necessarily there's been a bit of an adjustment period. While we would ideally be able to accomplish everything at once, resource constraints dictate otherwise and we always have found ourselves having to prioritize. You will encounter these sorts of trade offs and lag times occurring right across the pharma landscape, especially when fresh rules are in the process of coming into effect," admits Brian O'Rourke, president and CEO of CADTH.



Douglas Clark, executive director, PMPRB; Brian O'Rourke, president and CEO, CADTH; Brian Lewis, president and CEO, MEDEC

"We are aware of the vital role played by the pCPA in leveraging the collective purchasing power of public payers to negotiate deep discounts for their respective drug plans," explains Clark.

"We seek to complement that role by providing regulatory relief in instances where the monopsony power of the pCPA is an insufficient countervailing force to the monopoly power of the patentee."

OVERCOMING THE JITTERS

While not all drug developers necessarily share the payers' perspective about what constitutes optimum pricing reform, there is industry-wide appreciation about the fact that the current system is financially unsustainable and unnecessarily complex, and thus mass recognition of the need to harmonize pricing and reimbursement discussions on a federal level and to simplify the overall processes.

Chirfi Guindo, former president and managing director, Merck

According to Merck's former president and managing director, Chirfi Guindo, the "sheer time taken to adopt new products is way too sluggish" and is a "direct consequence of an overbearing bureaucracy comprised of a tangled web of different agencies involved in product approval, HTA, pricing and reimbursement," he bemoans. "Unfortunately an additional repercussion of this messy state of affairs is that it is virtually impossible to reach a single overarching agreement for product listing so we need to take active steps to rectify these points."

Yet while there is general consensus that the time is ripe for overhauling the process, many CEOs are quick to warn against vigorous price slashing. Allison Rosenthal, general manager of Otsuka, says she "personally believes in the pCPA, but some price requests for innovative branded products are neither realistic nor sustainable in the long run."

Many say that a race to the bottom on price would also harm patients. "Our biggest challenge is always to bring our products to the market, and if we are now going to be facing additional pressures around reimbursement listings and pricing, then that's going to be bad news for the patients," warns Lee Ferreira, general manager at Ferring Pharmaceuticals.

Moreover, high price pressure can quickly degenerate into negative decisions on investment in innovation and discourage research activities being brought to Canada. "The last thing we want to see is a reduced range of medicines in the pharmacies because some companies have felt compelled to vacate their products from the marketplace or not launch them in the first place…such a scenario prevents both physicians and patients from making an

Test Bed Canada

The fragmentation of the Canadian healthcare landscape is frequently the subject of complaints, from sources as wide-ranging as regulatory bodies, foreign companies wishing to enter the Canadian market, as well as Canadian company heads, physicians and patients.

Nevertheless, there are always two sides to a story, and some players have identified beneficial reverberations of this fragmentation. Merck's former president and managing director Chirfi Guindo sums up: "The positive side of fragmentation is the diversity that Canada offers. You have single-payer European-style health systems, combined with a well-developed private sector similar to the US; and you have access issues in parts of Canada that remind me of emerging markets. Add to that immigration, with people from all over the world entering Canada, it makes for a very interesting market that functions essentially as a microcosm of the world."

Brian Canestraro, general manager of Intercept Pharma, describes the Canadian landscape as "a global petri-dish." Merck's Guindo agrees, pointing out that, "The advantage of that is that you can experiment with different models of care. We have a global program called Merck for Mothers that promotes initiatives to reduce maternal mortality and improve child health outcomes in aboriginal communities. What is fascinating is that we are applying models we have used in parts of Africa and Asia."

Hence, there seems to lie in Canada an opportunity to consider the other side of the coin: a unique system in which companies can launch products in one province at a time, testing out adoption and responses from the medical communities in very differently structured systems.

Richard Lajoie, president of Valeant Canada, reprises: "Canada might not be a big country and the perspectives for overall sales can certainly not match those of the US. Nevertheless, Canada has a stable economy, it is very structured and regulated. Exactly because of its size however, it can actually become an innovation test bed for many companies."

MERCK

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WHY WE INVENT

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Merck is inventing because the world still needs cures for cancer, Alzheimer's disease, HIV, and so many other causes of widespread suffering in people and animals.

We are taking on the world's most challenging diseases to help people go on, unburdened, to experience, create and live their best lives.

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Allison Rosenthal, general manager, Otsuka

Gaby Murphy, managing director, EMD Serono

informed choice, especially when there is only one product available on the market. Not all patients react the same to a treatment for a specific condition, which is why diversity in offering is so incredibly important," argues Ferreira.

"Price should certainly not be the sole decision making criterion. When it comes to determining whether a product should remain on the market or not, the value to the patient and to the healthcare system needs to always be the primary consideration," she advocates.

Some also fret about the unpredictability that radical reforms might engender. Gaby Murphy, managing director of EMD Serono (Merck KGaA), describes the up-coming changes as disruptive in the sense that they loom over the heads of those endeavoring to formulate their business plans. "The big issue we are currently facing as an industry is to predict the impact these changes will have … Historically, Canada has always been a Tier One market for product launches, but right now between 60 and 65 percent of all innovative drugs launched are being evaluated by the PMPRB and this is creating a degree of uncertainty."

Lee Ferreira, general manager, Ferring

Many even take issue with the general premise of significant price reductions. "There is a strong misperception that Canadians are paying too much for their drugs and this has been driven by recent price controversies, especially those in the US, but the reality of the price-listing agreement (PLA) model used within the public healthcare system in Canada is that the list prices are not the actual prices paid, which are a lot lower," highlights Merck's Guindo. "So we should really be looking at these plans with an objective eye and determining whether they are actually fair," he suggests.

EMD Serono's Murphy, likewise doubts "whether payers properly appreciate the importance of the life sciences industry in terms of employment and economic contribution to Canada" and calls for "reasonable pricing that takes into account this value generation." After all, the Ministry's own statistics demonstrate that the local life sciences segment accounts for more than 90,000 jobs in about 850 pharmaceutical and medical device firms, and represents CAD 7.8 billion (USD 6.1 billion) in GDP and CAD 13.2 billion (USD 10.3 billion) in merchandise exports.

"This is comparable in scale to other R&D-intensive sectors, such as the aerospace and automotive industry. Overall, Canada's life sciences manufacturing sector stands as Canada's third-largest R&D spender, fifth-largest manufacturing exporter, and sixth-largest employer of R&D professionals," confirms The Honorable Ginette Petitpas Taylor.

On balance, however, the general mood is collaborative and constructive. So far, there seems to have been little let up in foreign investment flows. The PMPRB calculated the total R&D expenditures of patentees in Canada as reaching CAD 918.2 million (USD 710.8 million) in 2016, and those figures remain pretty much constant today. Likewise, the ten largest global pharmaceutical players present on the local market all maintain an active in-country clinical trials footprint and some have even been betting big on heavyweight infrastructure projects such as Johnson & Johnson's opening of the first international JLAB in Toronto.

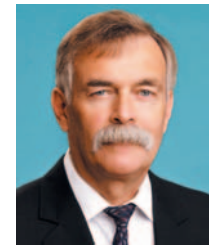
Moreover, despite the aforementioned concerns raised, the industry appears ready and willing to join forces proactively with the authorities in bringing about harmonious reform, "As members of the industry, we need to provide the required data when engaging in negotiations. Vice versa, payers have a responsibility to listen and consider thoroughly all data collected that demonstrates the cost savings of a more expensive treatment versus the expenses born out of a more affordable treatment that has to be prolonged in order to be efficient," asserts Ferreira.

TOWARDS AN OUTCOME-BASED MODEL?

The circle may well be squared by reverting to an outcome-based pricing model. Ferring's Ferreira sees such a model as a possible "solution, providing it includes a listing on time and a monitoring of compliance, efficacy and safety criteria. Under such a model both parties, the industry and the payer, take a risk. As industry, we promise a specific outcome to which we will be held accountable." Guindo ingeminates this, reassuring that Merck—and the industry as a whole—is "prepared to work with the federal and provincial governments on a longer-term solution, which would provide certainty for their budgets as well as our business operations and ensure that Canadians gain more rapid access to the innovative medicines and vaccines that they deserve."

However, not all regulatory bodies seem on board for such an evolution. Brian O'Rourke of CADTH is skeptical about the validity of such a system: "very few countries have true outcomes-based performance agreements in the pure sense of the term. Most are financial-based agreements, and we have those in Canada as well," he says, further stressing the multiple challenges and questions such a model would create: "how do you develop it, who monitors and reports on the outcomes, and who determines whether outcomes have been reached?" Nonetheless, he identifies reassessments as being an axis CADTH will likely be pursuing in the future. Under such a logic, a listed drug's value could be reexamined after a certain period, in order to determine if its price and reimbursement are still illustrative of the outcomes it provides for patients.

Moreover, O'Rourke promises that, in 2018, CADTH will review its logic of operating on a "first in, first out" basis when assessing submitted drugs. The simple, but inflexible logic can be ameliorated in order to "get promising new therapies to patients faster," by assessing them first and "perhaps working towards delivering regulatory approval, our reimbursement recommendation, and maybe even the price negotiation in a similar window of time." This would potentially revolutionize the approval and reimbursement process in Canada, as another major complaint of industry players has been the multitude of layers and lack of predictability a submission has to go through before return on investment is eventually secured.



Jim Keon, president, CGPA

Tarik Henein, president, Generic Medical Partners

TOUGH TIMES FOR GENERICS PLAYERS

For generics players the future looks potentially less promising. Many are struggling under on-going reforms to pricing and fretting over future evolutions in their market space, where price cuts are also a recurrent challenge. Today, generic penetration stands at 70 percent in Canada, while the US for instance boasts 89 percent penetration. Yet, in terms of sales, generic drug revenues account for only 22.4 percent of the value of the overall pharmaceutical market in Canada in 2016.

Despite this, there have been continued efforts on the part of provincial governments to increase pressure on generic prices. Jim Keon, president of the Canadian Generic Pharmaceutical Association (CGPA) candidly admits that, "In the past, our products at retail level were higher than the international average," but says that current initiatives to correct that discrepancy risk going too far. "The general public and the private payers do not understand the generic pharmaceutical business. Sometimes it seems as if they believe generic products grow on trees. We have tried to educate them on this matter by explaining that a lot of money goes into developing the active ingredient,

Michel Charbonneau, executive vice president, Accord Healthcare

Madhusudhan Venkatachari, CEO, Natco Pharma Canada

doing the testing, developing the clinical trials and submitting it for regulatory approval," he exclaims.

"In terms of the generics space, I think that we are in a transition period which has affected the entire supply chain," he continues "There's been a lot of discounting and rebating going on which is requiring an alteration of the business model all around."

Entry prices have been constantly dropping over the past years and many generic companies do not possess the financial backing of large innovators so the going is especially tough. "Entering the Canadian market with certain molecules is not worth the return on investment anymore given their large infrastructure and very high cost of doing business," regrets Tarik Henein, president of Generic Medical Partners, a local distributor of generic medicine.

Unfortunately, he has witnessed many producers, "repatriating operations to cheaper producer countries despite the problems in business control and management this can entail." "In the long run, this will eventually cause shortages of drugs in Canada," he predicts.

BACKORDERS: PRACTICAL SOLUTIONS

Looming shortages are also pointed out as a potential risk by Accord Healthcare's executive vice-president Michel Charbonneau, even citing backorder situations as one of the reasons the Indian company decided to set up shop in Canada in the first place. "As several generic companies in Canada faced the challenge of backorders, we were repeatedly approached to bring products to Canada that were not available to hospitals on the local market, and subsequently introduced those to Canada," he recalls.

Competition is always fierce in the generic market, especially when it comes to retail in Canada. "Margins can be small for the industry when there are only five big chains of retail pharmacies. Therefore, whereas the breadth of available drugs may be rich, there are only five pharmacies to approach, which results in tough price competition." Hence, "cost-effective retail cannot be guaranteed in Canada," leading some generic players to think twice before even venturing into the marketplace.

Accord Healthcare, nonetheless, remains committed to maintaining and ensuring not only quality and cost, but also supply over the coming years. Charbonneau highlights the importance for collaboration between various generic players: "The failure to supply is a recurring problem in Canada. By being proactive and collaborating with other generic companies, we can assist each other in case of a backorder, minimizing or at least better planning for such situations of supply failures. The prerequisite for this is of course the will to help without taking advantage of the situation."

Madhusudhan Venkatachari, CEO of Natco Pharma Canada, another Indian generic manufacturer, recognizes that "pricing can be challenging in Canada," but that the series of backorders Canada has gone through are just as aggravating. He considers that, "as a supplier one must ensure consistent supplies. At Natco we have been able to avoid backorder issues due to our strong manufacturing integration." The company's vertical integration is its competitive advantage and has allowed it to be successful right from the beginning in its Canadian adventure.

Venkatachari sums up: "Every stakeholder pursues his or her own interest, this is true in case of the governments. As industry players we need to adapt." He considers that, with the right strategic approach, every market is manageable just so long as you are aware of its specificities. "In the end, challenges

can even become opportunities if you navigate them well. Competition eliminates fringe players, and under the logic of the 'survival of the fittest', we try to ensure Natco Pharma is the fittest and survives. Many price pressures are created by the fact that there are too many players competing for too small a market. This is why our niche-focused portfolio is suited to the price-sensitive Canadian market. We avoid overcrowded therapeutic areas by focusing on products where the API is difficult to source and requires sophisticated manufacturing."

As is so often the case, the ability to adapt and engage in dialogue is crucial to addressing disagreements between industry and regulatory bodies and minimizing fear on both sides. Those companies that are actively pursuing conversations with payers and able to rely on consulting forces in market access that are specialized on the Canadian market have repeatedly been able to turn Canada into a success story.

TOP DRAWER

Especially for some multinational pharmaceutical companies, Canada has developed into an important market for their global operations. The country has proven to be a stage where dedication pays off, and those companies that have elevated Canada to figure amongst their top affiliates have generally not been disappointed in the return generated on their initial investment.

One such company is the medical device outfit, Baxter. "Canada remains extremely important for Baxter's footprint, and the legacy behind the 80 years that we have been present is absolutely tremendous. The Canadian affiliate was the first one established outside of the USA, and within the first couple of decades we even took the decision to establish an in-country manufacturing facility… Many of the innovations within our organization subsequently came from this affiliate, such as the first flexible IV fluid bag, and the first mini bag products to name, but a few," proudly declares company president, Stephen Thompson.

An affiliate's ability to export best practices as a record of its achievements is another way to highlight the relevance it holds for the global operations. Linda Tibbits, general manager of Pierre Fabre Dermo-Cosmétique explains that, "Our Canadian affiliate has proven a pronounced capacity in pioneering when it comes to internal initiatives and positioned itself as an exporter of best practices. We might be small, but very experienced and still very agile, both qualities highly appreciated by global management." John Simmons, vice-president sales and marketing (health systems) at Philips Healthcare equally describes the Canadian affiliate as generating "learnings and best practices that are subsequently shared and applied across other markets."

None of these successes have come about by chance, however. Each are the products of carefully nurtured business strategies. Marina Vasiliou, managing director of Biogen—for which Canada ranks a top five or six affiliate globally—recognizes that there are clear in-country challenges that have to be surmounted, but that this is the case in every healthcare market around the world. "If there is one thing a global career has taught me is that the primary subjects in each country are very common, but stakeholders and their diversity differ markedly from country to country. Thus, adaptability is key. You need to embrace each system, understand the interest of all stakeholders involved and build true partnerships with them to be successful. Adaptability certainly gives you the edge in those conversations."

Marina Vasiliou, managing director, Biogen

Vasiliou is convinced that by adapting strategies, as a manager but also a company, there is no such thing as the impossible market. She firmly believes that "it is a very exciting time for Biogen to be in Canada" as demonstrated by the heavy R&D investments that her company is making. She claims that Biogen presents a "unique value proposition" in being "the only company that is 100 percent invested in neuroscience."

"We have seen big pharma players investing in the field, but given that neuroscience remains a very difficult turf, it is challenging to be a relevant and persistent player if not all of your efforts are devoted to this particular field. Therefore, I can proudly say that Biogen is the undisputed leader in neuroscience," she explains. To her, Biogen's very focused strategy is precisely what

Caring Deeply. Working Fearlessly. Changing Lives.™

At Biogen, our mission is clear: We are pioneers in neuroscience.

Since our founding in 1978 as one of the world's first global biotechnology companies by Charles Weissman, Heinz Schaller, Kenneth Murray and Nobel Prize winners Walter Gilbert and Phillip Sharp, Biogen has led innovative scientific research with the goal over the last decade to defeat devastating neurological diseases.

Millions of people around the world are affected by Multiple Sclerosis, Alzheimer's Disease, Parkinson's Disease, and Amyotrophic Lateral Sclerosis (ALS). Many people also suffer from less common diseases such as Spinal Muscular Atrophy (SMA) and Progressive Supranuclear Palsy (PSP).

We believe that no other disease area holds as much need or as much promise for medical breakthroughs as neuroscience.

Biogen has some of the world's best neurologists and neuroscientists. We engage with physicians and scientific leaders around the world with the aim to further medical research. Our focus on neuroscience, our deep scientific expertise, and our courage to take risks make us **leaders in the research and development of medicines to transform neuroscience to benefit society.**

Our technology and engineering capabilities create novel ways to seamlessly transition products from development to manufacturing with the intent of bringing our high-quality medicines to market faster.

We respect the contributions of health care providers caring for people living with neurological diseases.
We honor the important role of caregivers, families, and friends who care about them.
Biogen is **committed to working with advocacy and patient organizations** as they serve the communities they represent.

Recognizing the challenges facing health care systems today, we collaborate with regulatory authorities and customers such as health care providers and payers, so that those in need can **access our medicines.**

Professional, ethical, and compliant, we hold ourselves accountable to **deliver value to our shareholders.**

Biogen contributes to the communities where we live.
We are committed to our employees, diversity and inclusion, and environmental sustainability.

We care deeply about making a difference.

We work fearlessly.
We do not give up even when challenged, pursuing innovation in all that we do.

We are humbled by the opportunity to change lives.

Biogen

Jamming with JAMP Pharma

Louis Pilon, president and CEO, Jamp Pharma

Originally based in British Columbia, Canada, JAMP Pharma was a small contract manufacturing organization (CMO) eking out CAD six million (USD 4.65 million) in revenues, before now-owner, president and CEO Louis Pilon saw its potential, bought it and relocated to Montreal. After a spate of strategic acquisitions, the company now boasts sales to the tune of CAD 150 million (USD 116.32 million), propelling JAMP Pharma into the top 50 companies in Canada.

Today, Pilon divulges proudly that, "we are the fastest-growing generics company in Canada, not only launching the largest number of new products every year but also achieving a cumulative growth of 40 percent year-on-year for the past few years"—music to any business owner's ears!

One of the keys to success has been a finely-tuned strategy. Pilon outlines: "While we produce generic versions of most products within the Top 50, we also focus a lot on niche and complex products. This means, products for which there are either no or few available generics alternatives and/or products that are expensive and highly complex to develop and obtain approval for."

Jamp Pharma Head Office, *Credit: Jamp Pharma*

Careful orchestration of one of the largest sales forces across Canada has also been a forte of JAMP Pharma. Pilon articulates, "A large portion of the Canadian market is still composed of independent pharmacies. We are one of the few generics companies to have a sales force that covers every single pharmacy in Canada. It all comes down to our people, and we have a very competent team." He concludes, "We want to build an elite team here at JAMP Pharma, and we focus on hiring entrepreneurial people."

has allowed the affiliate to perform so well: "The most important thing is to develop and make accessible breakthrough therapies that provide significant value. We are not speaking about 'me too' therapies but on the contrary areas of real innovation in difficult neurological conditions."

SMALL ENTRANTS WITH BIG PLANS

In a new wave of investment, several smaller pharmaceutical companies have chosen to set up first-time operations in Canada recently, recognizing the potential for product launches and development or taking back their out-licensed portfolio. Japan's Taiho are a case in point. Having only opened operations in 2017, the company's flagship oncology drug Lonsurf® received fast-track review and approval from Health Canada and plans to become an important player in oncology on the local market. Ross Glover, the company's general manager, reveals that, "the establishment of the Canadian affiliate had always been part of our global expansion plan, whereby the intention was to establish a strong presence in the US first, before venturing across the border." Glover admits that the company's venture has paid off: "we have been very successful in hitting objectives in the first year."

The Canadian affiliate of Valneva, a vaccine-specialized French company started out in 2015, but "already contributes 20 percent to global revenues," according to its general manager Greig Estabrooks. "For a new and emerging company, we are punching above our weight and will continue to do so in the years to come," posits Estabrooks. Like many CEOs of newly founded operations, he follows a clear path to ensure the successful development of the subsidiary. Estabrooks confides: "I have a mantra: 'Practice like you have never won and perform like you have never lost.' For a relatively new company, this is very important across our entire in-country organization and something I try to instill in all employees."

As many new entrants do not set-up full functions immediately, they leverage shared services from their companies' US operations. Taiho and Mallinckrodt, for example, both profit from the close proximity to the US and have been able to drive efficiency as a result. Glover notes that there is a "complementary aspect in the collaboration" and highlights how the Canadian affiliate "was able to refer to the US team's experience with the launch of their flagship oncology product Lonsurf® three years prior to its introduction to Canada."

Ross Glover, general manager, Taiho

Greig Estabrooks, general manager, Valneva

Mallinckrodt's general manager Robin Hunter, though, emphasizes that one of the "most difficult aspects lies in correcting the assumption that a product launch in Canada can be successfully executed by a US-based brand team." Canada is not just the 51st state to replicate a schema in the expansion of a company but requires a targeted strategy. He adds, "Mallinckrodt Canada today is not yet the company we aspire to become. I think people should keep their eyes on us through our transitional period, and in 2020, those who did not will say 'I wish I had known that company before. I would have liked to work there.'"

The French ophthalmic company Théa, by contrast, chose to enter Canada in the form of a joint venture with local Labtician. The new company, Labtician Théa, launched in November 2017 is "a very natural fit" and the collaboration of "two pretty amazing companies that are very well aligned culturally and both have a rich history in innovation," in the words of its president Mark Smithyes. He sees "Théa's rich pipeline of preservative-free treatments, which are already the standard of care in Europe, [combined] with Labtician's proven sales, distribution and service expertise truly representing a major win for Canadian eye care



Robin Hunter, general manager, Mallinckrodt; Brian Canestraro, general manager, Intercept Pharma; Mark Smithyes, president, Labtician Théa

professionals and their patients. We have set out to leverage the strengths of both organizations to be the leader and essential partner for optometrists and ophthalmologists locally."

Not only does Smithyes aim for leadership with Labtician Théa, he considers Canada itself to have enormous potential "to be a leader. All the building blocks for a robust life sciences sector are here: an innovation mindset, great science and scientists, world class universities and research, entrepreneurs and a growing investment community. What is there not to like?"

Other new entrants are including a research dimension in their activities from the start. Indeed several affiliates of the latest wave of entrants were established precisely because of the potential for conducting research in decisive therapeutic areas in Canada. Intercept Pharma came to Canada in 2015, and immediately started heavily relying on research conducted locally in its efforts to bring its drug for PBC (primary biliary cholangitis, a non-viral liver disease and the number one reason for liver transplants among women in Canada) to the market.

Intercept's Brian Canestraro recalls that, "I was actually impressed by the number of Canadian sites that are part of our clinical programs. We had number of sites participating in early PBC research as well as a significant number of sites in long-term extension studies as part of our post approval commitments. We also have a number of sites participating in our NASH (nonalcoholic steatohepatitis) registration studies and are very optimistic that this will continue to be the case as we explore potential further research in PSC (primary sclerosing cholangitis)."

"Overall," he continues, "I have found that there are sometimes limitations in relying solely on translating data from abroad into the Canadian environment in a way that is meaningful. This underscores the importance of incorporating Canadian-specific epidemiology and disease outcomes data into planning, which ultimately supports stakeholders and healthcare professionals to make better decisions."

Taiho also has an already operational R&D site in Canada and "intends to further capitalize on the rich R&D landscape here," according to Glover. "When I first came on board, I noticed that we lacked research activity in Canada, and there was tremendous scope to ramp up and expand operations. I am immensely excited that we have started a new level of colorectal research and cholangiocarcinoma research in Canada. Indeed, the country should certainly not be overlooked for R&D operations as it enjoys excellent global connectivity. We offer a more affordable environment than other major countries like Germany, the US or the UK. We have excellent facilities and the best academic minds in the world," he enthuses.

Many of the new entrants that have yet to start R&D activity in Canada identify great potential to do so at a future date and have been lobbying their global management boards appealing for precisely that opportunity. "Advocating for additional research investment to come to Canada is one of my key priorities right now because we are very keen to take advantage of the exceptional quality of research centers Canada offers," discloses Hunter of Mallinckrodt.

He is echoed by Valneva's Estabrooks who is a strong proponent "for clinical trials to be conducted in Canada for the company's pipeline vaccine candidates—given the available talent and abundant

The Canadian MNC?

Richard Lajoie, president, Valeant Canada

Echoing the question whether Canada affiliates of MNCs can be successful, there is the eternally looming question whether there can be such a thing as the Canadian pharmaceutical MNC. Valeant, headquartered in Laval near Montreal, is probably the closest thing Canada has to a home-grown MNC and the perfect example of a Canada-born pharmaceutical company that has successfully expanded beyond national borders. Richard Lajoie, president of Valeant Canada, states: "We take pride in our Canadian heritage, especially as we have significant manufacturing activity, which is very strategic for Valeant globally. Canada produces CAD four billion (USD 3.11 billion) worth of sales, destined not only for the Canadian market but also for export. Over 30 percent of worldwide sales are produced here, further underlining that our operations here are key for the global group … While we may not be the first in terms of sales in Canada, we are certainly the largest innovative Canadian healthcare company. I believe that our successes have been somewhat understated, but to Canadians there is a fine line between taking humble pride and being overly boisterous."

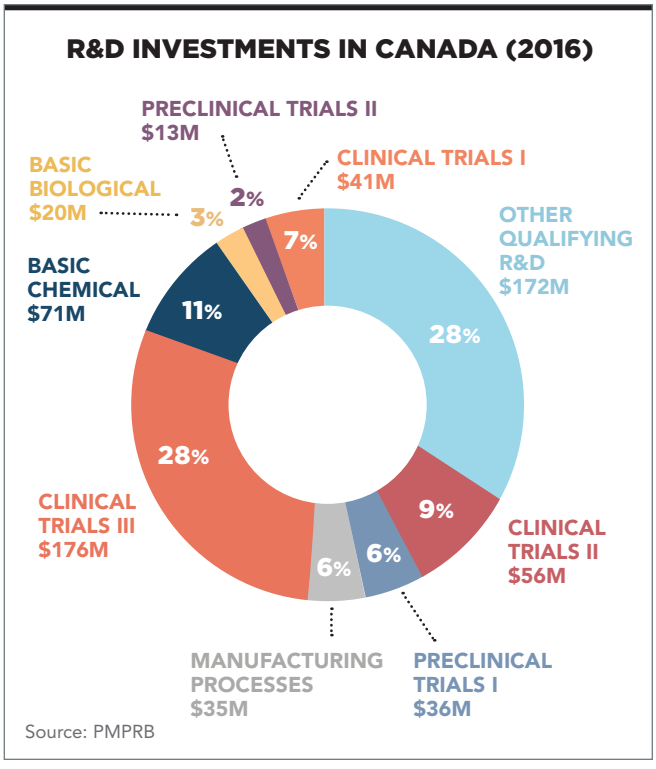
Credit: ***The Orange Country Register, May 19, 2014***

resources for vaccine research locally, especially in areas such as Lyme disease, which is becoming especially prominent in the country."

Evidently, it would seem, ramping up R&D investment is no longer just the prerogative of big pharma and that the smaller mid-cap players, many of whom are recent entrants, are busy rendering this area a priority as well.

INVESTMENT BY STEALTH

When trying to ascertain the overall tempo of research in Canada, the picture is mixed. Following the agreement of Bill C-22 in 1987, patentees in Canada committed to invest ten percent of their revenues in local R&D in exchange for enhanced patent protection. Over recent years, the PMPRB has not been shy in pointing out that the industry is falling short of fulfilling this commitment. The PMPRB annual report of 2016 states that total local investment in R&D was below five percent for all patentees and for IMC (Innovative Medicines Canada) members likewise, 4.4 and 4.9 percent respectively.



It is to be noted however, that those figures do not tell the whole story. Investment in R&D follows new patterns these days, with substantial resources being allocated to academic laboratories or disseminated in the form of outsourcing with CROs, or even the acquisition of smaller biotechnology players. The bottom line is that investment, in itself, is not decreasing in Canada as sometimes erroneously perceived, but rather tends to take radically different forms.

Canada's excellence in research is world-renowned. The country displays a series of characteristics underlining this, from excellent research infrastructure and academia to breakthrough research results, from ebola vaccines to stem cell discovery. It holds the first rank among the OECD countries in terms of share of university graduates within its working-age population and contributes over four percent of global knowledge, despite accounting for just 0.5 percent of the world's population.

Furthermore, in Ontario alone, there are 3,200 clinical trials on-going at any given time, and the 44 universities in the province produce 40,000 graduates in science, engineering, mathematics and related technologies every year. Tapping into the Canadian potential means not only leveraging on the incredible talent pool in research available in the country, but also taking advantage of Canada's unique features in terms of diversity (Toronto is the most diverse city in the world) paired with stability of its population in Quebec for instance, whose people do not move often.

CONVERTING RESEARCH INTO RESULTS

Canada's proximity to the US combined with its unique culture ensures that the country acts as somewhat of a bridge between Europe and the US, something Biogen's Vasiliou considers to be "a unique value proposition [of Canada] in the R&D landscape." Canada's proximity to the largest pharmaceutical market in the world and the location of its life sciences hubs (around Toronto and Montreal) just across the border from the Boston pharmaceutical cluster, allow it to leverage on potential collaborations, but also put it in the shadow of its neighbor.

David Main, CEO and president of Aquinox Pharmaceuticals, a biotechnology company from British Columbia developing novel drugs to treat inflammation, inflammatory pain and blood cancers, addresses the issue that all in all, there is a very strong commitment from government to drive innovation and fund basic research, but that because "the coordination is poor and the investment landscape highly fragmented, it is composed of a multitude of individual initiatives rather than a concerted focus which would encourage efficiency."

David Main, CEO and president, Aquinox Pharmaceuticals

The result, according to Main, is that "nothing translates truly into action. For instance, having a life sciences dimension in the recent super cluster initiative that identified industries of focus, would have been very beneficial and an important sign that things were moving in the right direction. Yet, when the government announced the industries part of its Innovation Superclusters Initiative, life sciences were left out! What is lacking in Canada is the focus on moving research from the early stages all the way through to commercialization, to capture the value of the full ecosystem," he cautions.

This failure to translate excellent science into commercial success is very visible for some executives in the Canadian SME segment, where biotechnology companies rarely make it beyond the stage of commercialization on their own. Some companies hence feel that what is missing is the adequate framework to see the next biotechnology company rise and develop to become tomorrow's Canadian pharmaceutical MNC. Optimism remains nonetheless, and Lajoie of Valeant sees the government undertaking some supportive measures as in the "recent government innovation strategy announcements" that will hopefully contribute to displaying Canada "as a country [...] in a better position to attract R&D projects, which countries around the world are vying for."

A Medtech Trailblazer

With a medical device market projected to grow to 8.6 billion by 2020, conditions are ripe for medtech success in Canada. As Brian Lewis, president and CEO of MEDEC, the country's medtech association, notes, "There is ample potential to build a strong medical device ecosystem within Canada. Canada is a highly sophisticated marketplace."

Dave O'Neil, vice president and general manager, Zimmer Biomet

Against this backdrop, the Canadian affiliate of Zimmer Biomet – a global leader in muscoskeletal repair created from the merger of Zimmer and Biomet in June 2015 – has been thriving and, as vice president and general manager Dave O'Neil points out, "the global group looks at Canada as a trailblazer in many ways." He continues, "the timing of the Zimmer-Biomet merger was ideal as the Canadian musculoskeletal market is growing tremendously and we were able to take full advantage of this in 2017."

O'Neil elaborates on this 'trailblazer' status by asserting that "after the official merger, the Canadian affiliate was the first to be fully integrated last year." Furthermore, he posits that, "Canada has been identified by the global group as a test-bed that can export best practices. The Sidus® Stem-Free Shoulder System [a minimally invasive bone-sparing shoulder implant system] for example was first launched in Canada before being introduced to the US market."

Zimmer Biomet Canada is also heavily involved in the group's global innovation push. O'Neil asserts, "we have a development center for personalized solutions in Montréal. At this center, patient-specific instruments and implants are developed, while the group is also leading our entry into the robotic space. We inherited a robot for neuro and spinal surgery from an acquisition a few years back, and the team in Montréal is developing a robot for knee surgery. This global effort driven out of Canada is a prime example of how Canada is a perfect spot to foster innovation."

HOTSPOTS: RARE DISEASES

The research areas in which Canada has the potential to excel are numerous, one being the world of genomics. The stem cell itself having been discovered in Canada, Marc LePage, president and CEO of Genome Canada, identifies great potential to attract more fundamental research into that domain. He himself has massively contributed to establishing the genome program in Canada and has big plans for the future: "In less than five years we aim at having in every hospital in Canada—not just the large university hospitals—genomic diagnostics available for rare diseases."

For a developed country with high healthcare standards such as Canada, it is to be expected that rare diseases would be well incorporated in the system. However, Canada stands out as the only country within the G7 to not possess a rare disease framework. Thus, access to lifesaving drugs for those among the 35 million Canadians living with a rare disease is difficult, even more so when diagnostics are challenging. Moreover, as Shire's general manager Eric Tse contributes: "Rare diseases are individually quite rare, but collectively, there are around 7,000 rare diseases in total, so they are quite a prevalent issue. Around one in 20 Canadians suffer from a rare disease, which puts it into perspective."

LePage is excited to drive forward human genome programs, as he believes "This will entail much better patient outcomes by providing a meaningful test to establish the right diagnosis for the one million Canadians with a rare disease. In the process, we will also be driving forward our data sharing, so that the collected sequences may be available in each province. The rare disease program is thus the foundation on which we will build a broader precision health program for Canada. We have been dedicated to implementing precision health in Canada for some time and now we are excited to help usher it into the implementation phase," he reasons.

MADE IN CANADA

Canada could, both in research and manufacturing, clearly do much better when it comes to promoting local opportunities and attracting investment into those areas. Not only is the cost of production much lower than in the US for instance, those companies that decide to produce in Canada could not speak more highly of the workforce they are able to hire also underlining to the reputation 'Made in Canada' holds on an international stage.

Dwight Gorham, CEO, Pillar5 Pharma

Stephen Thompson, president, Baxter

Pillar5 Pharma is a Canadian CDMO established in a former Pfizer facility. A true Canadian success story, its president and CEO Dwight Gorham exults: "The beauty of Canada is not only the geographic proximity to the US but due to the regulatory landscape it can also act as an attractive partner to European companies." This double positioning speaks for Canada as a destination for companies wishing to service both markets, Europe and the US. The dual expertise of Canadians is valued, but as with everything in an increasingly competitive environment, the secret lies in one's niche.

Gorham comments that, "'Made in Canada' has certain heft in other markets, especially from a sales and marketing perspective. I believe that if Canada wanted to attract more investment, companies should seriously consider finding areas of specialization. Specialization tends to drive barriers to entry and has connotations of being higher on the technology scale, which is why we work so hard in an attempt to predict market trends. We respect preservative free formulations, we are observing what is happening in Europe to see where they are going next because it will ultimately also transform the US market, and we want to be at the forefront of this transformation. We are already trying to identify the next trend that we can leverage to grow our company tomorrow!" And, as Gorham sums up: "Just because it is a regulated industry does not mean that it has to regulate your thinking."

Some medical device companies have also maintained manufacturing activities in Canada over the years. BD has acquired a local producer and continued to leverage on its facilities and Baxter is celebrating 60 years of manufacturing in Canada in 2018. "For Baxter, manufacturing in Canada has been highly beneficial, as the environment is that of a very stable economy, with many advantages from a business point of view," says its president, Stephen Thompson. He further highlights the key benefits Baxter sees in its production in Canada: "First and foremost, we are the only large-scale IV fluid and dialysis solution manufacturer in the country. Hence, we contribute in large part to ensuring product supply and pandemic preparedness for the Canadian healthcare system. Secondly, through our direct presence, we are able to tailor our products to the unique needs of the Canadian market," he reminds.

The contribution of manufacturing to the local economy cannot go unmentioned either. Lajoie of Valeant identifies "several benefits to manufacturing in Canada. We are contributing to the local economy, something we are proud of as Canadian citizens." BioVectra, another Canadian CDMO, manufactures historically on Prince Edward Island. President Oliver Technow puts forward the immense opportunities in pharmaceutical manufacturing and innovation laying in Canada: "Firstly, it has an underrated yet over-delivering education system, with top-ranking schools in many areas, including Atlantic Canada. The talent base is tremendous and there is a university network that embraces the idea of innovation and science to its fullest extent. The overall cost structure in Canada is highly competitive. On a comparable level of quality, and taking into account tax, cost of labor, cost of doing business etc., Canada ranks number two worldwide. We outscore and outpace by far in quality those countries that focus only on price."

Now the task to get the word about Canadian excellence out to the world remains, and, as Lajoie points out, the quality is undisputed, what is lacking, is a promotional effort made on behalf of Canadian manufacturing: "While 'Made in Canada' is a sign of quality, Canadians, as part of their mind-set, are often too humble to promote themselves and their achievements on the international scene."

CANNABIS: IN POLE POSITION

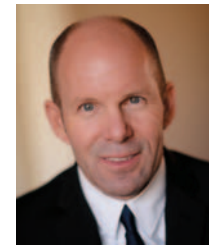
Thousands of years old, the treatment of ailments with cannabis is now for the first time taking form as an organized industry, and Canada seems in pole position to lead the way and be a trendsetter in the field. All stars seem aligned for the medical cannabis sector to take off and propel the industry in the position of a new showcase of Canadian excellence in innovation and research.

The figures illustrate an industry that responds to a high demand with a total number of patients in Canada at 250,000 already and ten percent more patients receiving prescriptions every month. Economic figures surrounding medical cannabis are equally impressive: licensed producers raise amounts of CAD 100 million (USD 77 million) on what seems a regular basis, and one is hard pressed to keep up with news surrounding facility expansions, research collaborations or performed IPOs.

In Canada, the moment seems opportune for the medical cannabis segment to takeoff. Not only is a liberal administration in power led by the youthful and unconventionally forward-looking Justin Trudeau, but society is inching towards greater tolerance for cannabis usage, while an ongoing opioid addiction epidemic discredits and taints many orthodox pain management medications. In the words of Federal Minister of Health, The Honorable Petitpas Taylor, "our government is deeply concerned by the opioid crisis and its devastating impacts. Opioid-related overdoses have claimed the lives of thousands of Canadians, affecting families and communities across the country and we are thus stridently committed to exploring ways to promote new and innovative ideas to help overcome this crisis. We are supporting research to provide new tools and treatment options and medical cannabis has its place amongst those treatment pathways under consideration."

Ironically it was actually a previous conservative administration that enacted the Marijuana Medical Access Regulations (MMAR) allowing for patients with a prescription for medical cannabis to grow their own supply, which indicates the extent of openness within Canadian society for incorporating cannabis-based treatments within the overall healthcare paradigm. Nowadays medical cannabis is becoming even more mainstream. Since 2013, new regulations permitted licensed producers with an authorization by Health Canada to grow and sell cannabis directly to patients. Justin Trudeau's liberal regime subsequently replaced MMAR with the more progressive Access to Cannabis for Medical Purposes Regulation (ACMPR), which came into force in August 2016, paving the way for the sector to increasingly decriminalize cannabis for medical purposes and enhance patient access to medical marijuana.

The legalization of cannabis for recreational use is the next step through Bills C-45 and C-46, initially planned for July 2018 and now postponed to fall of the same year. This would render Canada the first country amongst the G7 to legalize cannabis for recreational use. In the words of The Honorable Petitpas Taylor, "We know that the current approach to cannabis does not work and has allowed organized crime to profit, while failing to keep cannabis out of the hands of our kids. We are pinning our hopes on a regulated framework to annihilate the black market and ensure a controlled distribution of cannabis, which would be taxed and submitted to controls like the beverages or tobacco industry."



Greg Engel, CEO, Organigram

Barry Fishman, CEO, ABcann

STEPPING INTO THE UNKNOWN

Unlike the tobacco and beverages industry however, every new undertaking in the field of medical cannabis is a step in the dark. All elements surrounding regulatory aspects remain to be concretized. On the one side, this fosters opportunities, excitement and a sheer endless stock of opportunities in innovation, collaboration and treatment. Greg Engel, CEO of Organigram, a New Brunswick producer, happily reflects that, "It is not every day that you get to participate in building an entire industry. In this space, nothing is set in stone

John Fowler, CEO, The Supreme Cannabis Company

yet; everything is new and has to be developed. Times are exiting and being part of it is thoroughly thrilling!"

On the other side, business insecurity and uncertainty are rampant. In product forms for instance, many producers have a pipeline bustling with ideas, but are awaiting decisions from Health Canada surrounding which ones they will be allowed to bring to the market. Terry Lake, vice president corporate social responsibility at Quebec-based producer Hydropothecary describes the current situation as such: "The first challenge is knowing what products will be allowed by the regulatory system. People often ask me about my work in the cannabis industry, given the dramatic policy shift. To give you an analogy, it is like running in the forest at night—we do not know where the trees are! Following complete legalization, we assume that Health Canada will announce regulation on a series of different products like edibles. However, for the time being, all manner of aspects are still up in the air."

As legalization of cannabis for recreational use is literally just around the corner and demand for medical cannabis is skyrocketing, many of the producers are scaling up their production accordingly. The monthly increase in patients of ten percent and the onrush expected to be triggered by legalization (11 million people are expected to try cannabis for the first time after legalization in Canada) have to be considered. Engel of Organigram details: "Our expansion rhythm has been tremendous, and we are today considered to stand amongst the leading indoor growers in Canada. One year ago, we were employing 58 people; today we have 150 staff and plan to hire another 100 employees by June 2018. We are currently in the middle of a 36-month period of ongoing expansion. We raised capital of CAD 54 million (USD 41.8 million) in December 2017 and added another CAD 115 million (USD 89 million) in January of this year. In terms of production capacity, we have recently tripled our capacity with Health Canada approval of Phase 2 of our facility and will be increasing it by 20-fold over the next 24 months."

These are no exceptional numbers in the cannabis industry. Barry Fishman, CEO of ABcann, also leads a company in the midst of expanding its production notes that, "firstly, we are in the process of expanding our capacity by integrating a new plant to our flagship cultivation facility in Nappanee, Ontario. By the end of 2019, we will reach a total production capacity of over 30,000 kilos of output annually over the next two years, and plan to supplement our internal capability by purchasing from strategic partners."

Fishman aims to see his company become a top five player and reach CAD 500 million (USD 385.5 million) in revenue in five years. Expansion is one step on the ladder to achieve this. The others being branding and product development. "Coming from the pharma world, I have been involved in product development for over two decades," Fishman relates, "and I think that the cannabis industry certainly has room for the innovators to spend time and money to create new novel delivery devices, formulations and strains. The cannabis industry in Canada is at the brink of ground-breaking developments and exponential growth. The opportunity to be innovative is also one of the most exciting features of the cannabis industry to me personally."

GROWING UP QUICK

Indeed, it is to be noted that the medical cannabis industry—as young as it is—already presents some of the characteristics of the much more mature pharmaceutical industry. There is consolidation as well as first moves towards differentiating business models. One company moving away from the usual producer model of production and direct to client retail is The Supreme Cannabis Company. It has decided to focus on production and become a wholesaler to other producers directly interacting with patients. CEO John Fowler believes the optimum way forward is to take a step back from the current hype and strategize. "It is essential for us to learn managing ourselves along the axes of a competitive mix and maybe even more importantly, learning to say 'no'. In the still very virgin cannabis field I detect the risk of an overload of opportunities.

We have to be self-conscious as to where we allocate our resources, especially our human resources."

He also sees cannabis as potentially disrupting conventional treatment pathways, by presenting itself as an alternative, more enjoyable treatment option for many patients. "I think that with medical cannabis, there is a chance to re-evaluate entirely the way we look at medicines. For the last hundred years we have been convincing patients medicine should not be enjoyable and that something must be wrong with it if it is," he posits. "Ironically, there have been tremendous efforts made on rendering medicine more enjoyable nonetheless, with sugar coating on pills, easier to swallow capsules, taste-enhanced cough syrups. With medical cannabis, we are at the core of this discussion. I reckon there is nothing wrong with enjoying cannabis-based treatments, and on the contrary, believe it is essential that patients do. As treatment evolves into something more agreeable, patients are likelier to stick to their treatment plan and actually consume the prescribed amounts."

Producers are still fighting stereotypes, however, and focusing on demonstrating that medical cannabis is a serious business despite all prejudices and misconceptions many clinicians and patients might hold. One way to counter this is by complying with the stringent regulations Health Canada has put in place around medical cannabis. As with pharmaceutical companies, medical cannabis companies have been complaining about slow movement at the regulatory level and Warren Bravo, CEO of Green Relief—a highly original producer growing cannabis with an aquaponics method—bluntly states: "Quite frankly, we are light-years away from where we should be—and where we need to be in the space."

While the wish for Health Canada to move faster on approval of licenses and regulations for new product forms is universal amongst the industry players, most recognize that given the absence of global benchmarking opportunities, authorities are doing as good a job as one can expect them to. Bruce Scully, CEO of WeedMD, a producer specializing in the care of elderly and long-term patients is positive towards what the future still has to offer in terms of regulatory reform: "I am not concerned. Actually, I am very confident we will be moving forward and I am thrilled by the will being displayed by our government to do so. Like everybody, we would like to see things move a little quicker; so that we can help more patients have access to our medicine. However, the endeavor that Health Canada has undertaken is monumental and highly pioneering and it is easy to overlook the fact that the framework from a regulatory perspective is still in the making."

Bravo qualifies such optimism, though by drawing to attention the fact that, "We are missing out on the opportunity to deploy cannabis in combination with different medical devices or produce different treatment forms, such as capsules or creams." "However, while Health Canada is moving slow, I do not necessarily believe that it is bad as such, as they are making well thought-out decisions and because they want to ensure that we are manufacturing at very high standards, always having the best interest of Canadians health and safety at heart," he acknowledges.

SURPASSING THE STIGMA

The stigma that still clings to cannabis—as a drug or not—is important: only three percent of practitioners prescribe it in Canada, and in the vast majority of mature economies it is still criminalized. Education is the name of the game to surpass this stigma, as Bravo explains: "Canadian health practitioners require peer-reviewed papers and double-blind studies, just as they do with traditional primary care medication. They need the science behind the properties of the plant in order to make informed choices for their patients. Up until this day, doctors take all liability and we, as an industry, have to come forward with studies how different cannabinoids profiles target different medical issues."

Bruce Scully, CEO, WeedMD

Warren Bravo, CEO, Green Relief

Marc Wayne, CEO of Canopy Health, the R&D arm of Canopy Growth, one of the largest growers in Canada, also points

out that "the current slate of published research consists of small studies, which are limited in scope, which has always been the main criticism of the industry." "We are hopeful to see investment into bigger studies like we are working on at Canopy Health. Eventually, we will, as an industry, have to disseminate this data to physicians and healthcare professionals, so they can become more educated and more comfortable prescribing cannabinoids," he notes. By taking the cannabis plant through clinical trials Wayne hopes "to elevate the image of cannabis to be a true medicine, which is prescribed as a proper pharmaceutical or natural health product," as this would enhance patient access. "This is what I call Medical Cannabis 2.0," he exclaims.

Beyond the Flower

Bernard Fortier, CEO, Tetra Bio-Pharma

Brendan Kennedy, CEO, Tilray

Tilray and Tetra Bio-Pharma are two medical companies that want to offer patients a solution beyond the dried cannabis flower: a real drug. Two different methods are employed to attain this goal.

Tetra Bio-Pharma operates as a biotech company and promises not only landmark results from its clinical trial program but wants to be the first company to see a dried cannabis drug become a real prescription drug, achieving a drug identification number (DIN).

Its CEO, Bernard Fortier, sees Tetra Bio-Pharma on the fastest track to realize this. Its PPP001 drug for cancer-related pain was granted orphan drug designation for the treatment of complex regional pain syndrome by the FDA in March 2018, and the phase III trial has just been approved by Health Canada.

Fortier considers this to be a cornerstone in the reduction of stigma attached to medical cannabis as only three percent of physicians are prescribing medical cannabis today. Indeed, "the physicians do not recognize the provided data to be comparable to that of controlled trials for traditional pharmaceutical drugs." Fortier thus argues: "The surest way to overcome the stigma attached to cannabis is to produce scientific data that will be recognized as tangible proof for the efficacy and safety of cannabis-based drugs."

As he points, out: "Today, we are still missing the big scale, peer-reviewed studies, double blind, placebo controlled, randomized trials. Without data of this scale and scientific backup, the medical cannabis industry does not match the entry criteria for pharmaceuticals and will never be recognized as bringing comparable therapeutic value."

He also expects more breakthroughs to occur once big pharma and medical cannabis companies engage into more dialogue. "The biggest leaps happen—as it is the case everywhere—when there is collaboration." This is the path Tilray has taken in its efforts to achieve the next step in cannabis-based drug development. It has just announced the first ever agreement between a medical cannabis company and a major pharmaceutical player, Sandoz Canada.

Tilray's founder and CEO Brendan Kennedy explains the terms of the collaboration: "Tilray has formed an alliance with Sandoz, the generic division of Novartis, to be an exclusive partner to them in Canada. In this partnership, both companies have seized an opportunity to forge an alliance between likeminded companies that are interested in providing patients with access to new medicines. We will produce co-branded products before the end of this year and are both very excited about the tremendous potential this partnership holds."

He further expands: "We bring expertise in medical cannabis; we know how to cultivate and process the plant, but we are lacking the complex knowledge to build a sufficient sales force to master a market such as Canada. Sandoz is an expert in manufacturing, supply and distribution and has the know-how necessary to ensure availability of products throughout Canada. […] Furthermore, our collaboration will involve the development of new product formulations. Sandoz already has the expertise to develop sprays, patches and many other form factors, and we have started thinking about what will be possible to develop for the Canadian and global market."

As medical cannabis becomes a field increasingly attracting interest from all around the world – with several countries such as Germany and Australia and even some US-American states having legalized its use – big pharma players are also becoming aware of this industry disruptor. The next question is: is there room for collaboration between both sides? Or do pharmaceutical companies perceive the new and fast-growing cousin as a threat, especially in the field of pain management?

Rami El-Cheikh, national pharma & life sciences leader at PwC comments that, "The evolution of medical cannabis as an alternative to opioid-based products is now becoming very real in the pain management segment. As medical cannabis research advances, the threat of disruption may increase in other therapeutic areas. In the future, partnerships between medical cannabis players and pharmaceutical companies will be crucial to revolutionizing and strengthening the legitimacy of medical cannabis." While competition seems unavoidable, the general attitude is one of consensus and excitement towards the upcoming opportunities in collaboration.

Scully of WeedMD for instance is excited about the potential collaboration on research medical cannabis companies could conduct with pharmaceutical players: "I see great potential in collaboration with big pharma as we consider the next steps together as an entirely new industry. The scale to conduct the large and deep research needed at the next level is something we could never hope to master as well as the large pharmaceutical corporations. They reign over resources and knowledge and have an ability to translate data on a level that will allow us to move research much farther than the stage it is at now."

In order to reach this level of collaboration, Canopy Health is getting ready to meet big pharma requirements. Its CEO, Wayne, strategizes: "Similar to traditional biotech, Canopy Health, as a specialty pharma type play, aims to take away some of the risk associated with early stage clinical testing for these larger pharma companies. We are dedicated to carrying out the Phase I and robust regulatory scale Phase II clinical work. We believe that pharma companies will become much more receptive to taking a Phase III ready asset through final development and would be open to discussing potential partnerships with larger companies on later stage projects." He finishes on a bullish note: "I believe that across the board, pharma players should be looking into the field of cannabinoids and if they are not, they are missing a huge opportunity."

A HIGH FOR CANADA!

Medical cannabis seems to be the niche Canada has found for itself to excel in as it is gradually pioneering its way through regulatory processes, clinical trials, cannabinoid research and collaborations. It is building up an industry that will be able to export. Engel perceives that, "the cannabis industry provides Canada with a unique opportunity for global leadership. We are still in the process of establishing a framework for the industry but have already built up a functioning industry and gathered the experience needed to now be able to export knowledge globally. Several countries are looking at Canada as a model market and reference country. Canada is already the pioneer in this field, but it should also continue to take advantage of this clear leadership position." Scully also shares his excitement: "I think it is wonderful that Canada has the opportunity to lead and create an entire industry from scratch."

The opportunity to lead is regularly put forward in talks with players in the sector. Wayne is even more direct: "The cannabis industry is a good example where Canada is able to take a lead over the US and the world." For once, it would seem, Canada has not only found its niche but will take it to the next step. "I think it is time for everyone to realize that the medicinal cannabis industry is here to stay," concludes Engel.

Marc Wayne, CEO, Canopy Health

Rami El-Cheikh, national pharma and life sciences leader, PwC

Doctors Are People Too

It's just as hard to make treatment look good to physicians as it is patients—but communicating through entertainment can be done

Pharmaceuticals is a big business. Industry spend on digital marketing is predicted to hit $3.1 billion by 2020, as brands continue to battle for market dominance. On average, a third of revenue is set aside for ever-more elaborate drug advertising, while only a twelfth is invested into R&D.

This in itself is not overtly shocking. Competition is the lifeblood of an efficient market, offering more choice and lowering drug prices to the benefit of customers' health. But who holds the real power in this mad scramble between brands?

Doctors.

The reason for this marketing outlay is simple. As prescribers of a treatment, healthcare professionals are the catalysts behind a huge portion of sales. Their opinion matters. It's no wonder that doctors are the targets of constant messaging, bombarded with imagery and persuasive wordplay to promote a drug or procedure of choice.

SCOTT FREEMAN is Integrated Director at The Operators Creative

Visual metaphor

Note that doctors are people before they are professionals—a vital consideration when creating visual content. Medical jargon and photoreal diagrams of anatomy won't cut it anymore. Instead, creatively envisioned visual metaphor is becoming the popular approach for pharma companies.

Case in point: a recent campaign for Abbott to promote its nutritious, organic brand image. Here, we helped model a countryside set entirely from fiber-based ingredients like broccoli, berries, and satsumas, before bringing it to life via photography and stop motion animation (see image at left). This was used as a sweeping metaphor for diarrhea medication with relaxing after effects. Doctor or not, viewers will understand the message at a glance—and in a much more memorable format to boot. Essentially, the use of visual metaphor leads to greater message engagement in an industry bogged down with scientific jargon. Doctors can enjoy a brief respite from intensive workloads and academic research.

Mixed media

Digital advances have led to multiple methods of capturing a doctor's attention—leveraging film, CGI, retouching, photography, animation, VR, and beyond. In short, pharma marketing has become a mixed media beast.

This convergence of media can even inspire huge cultural shifts, which ripple across the pharma industry for professionals and patients alike. McCann Health helped create the most-awarded digital campaign in Asia, dramatically altering the public attitude toward giving blood through a simple app. Patients can post a message on Facebook saying that a friend needs blood. Via the associated app, a map shows the nearest clinic for anyone who replies that they want to give blood.

Digital engagement technology has prompted a rewrite of the pharma playbook. This free exchange of information is open to everyone. Don't disregard it in an age when the world's first digital natives are entering med school.

Embrace digital entertainment

Pharma companies are thinking about different mediums and how they resonate with the treatment in question, all to present something that jumps off a screen, demanding the viewer's attention. A key challenge here is to balance budget with creative prowess—especially in a world where every organization is a publisher, all outreach is personalized, and content is constantly in demand. Integrated approaches to production are taking over.

There are ways to be smart about production costs by sourcing photographers, directors, and app developers through a single service provider. When dealing with multiple digital channels and platforms, it is critical we find cheaper ways to do business and economize the production process—without compromising on creativity quality.

From creation to delivery, we can no longer rely on traditional production methods in the modern pharma landscape. PE

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Senior Therapeutic Strategy Director, Drug Development Lead, IQVIA

Bruce Basson
Senior Scientific Advisor, IQVIA

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As a senior leader in emerging biopharma, you know that examining your product development program through the lens of all stakeholders, in particular your investors, is critical for success.

In this webinar, IQVIA strategic drug development experts Tara Rheault and Bruce Basson discuss key strategic considerations that emerging biopharma companies should tackle early in drug development in order to tell a clear and compelling story to investors. Specific points will include:

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- Anchoring your clinical and commercial product goals in a target product profile
- Mapping clinical and/or regulatory plans required for approval
- Understanding the trade-offs related to development cost, time and risk for robust decision-making
- Articulating asset value through a clear and differentiated value story

Key take-aways:

- How to articulate your product vision early in development so you can focus your resources for efficient planning
- Why and how robust design practices can inform and help you defend key investment decisions
- Gain a clearer understanding of design-related trade-offs related to development cost, time and risk as they impact product value at key decision points

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