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SCIENCE VISIONARY

AstraZeneca US Head Ruud Dobber

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First Foray into Digital Adherence

IN NOVEMBER, THE FDA APPROVED THE FIRST "DIGITAL MEDICINE SYSTEM" from Ostuka and Proteus in the form of Abilify MyCite, Otsuka's antipychostic medication embedded with an ingestible sensor from Proteus that can show if a medication has been digested. The sensor had been "approved" since 2012 by the FDA to be included in the clinical trials, but in the drug's public debut, interesting opinions emerged. *The New York Times'* "First Digital Pill Approved to Worries About Biomedical Big Brother" (http://nyti.ms/2ipyzQo) is certainly an attention-grabber, and the article did bring up legitimate questions, specifically around ethics, compliance, and trust, as well as some interesting views around the patient population.

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For example, while you can't argue that medication adherence in the schizophrenic population is not stellar—with overall rates roughly at 50% and ranges from 20% to 89%—for the first drug with a sensor that transmits electrical signals outside the body, maybe it wasn't an inspired choice from the standpoint of the population, whose symptoms include "hearing voices, believing other people are reading their minds or controlling their thoughts, and being suspicious or withdrawn."

Said Dr. Paul Abppelbaum, director of law, ethics, and psychiatry at Columbia University's psychiatry department, in the article: "A system that will monitor their behavior and send signals out of their body and notify their doctor? You would think that, whether in psychiatry or general medicine, drugs for almost any other condition would be a better place to start than a drug for schizophrenia."

Leaving that aside for now, the article did profile compliant patients using medications for schizophrenia. One, in the trial for MyCite, didn't like the rash from the patch (which is worn to collect the data), and says he won't take it because he is compliant. Another compliant patient explained that he also wouldn't consider the digital avenue for the medication, but he said those that don't take their pills unsupervised have to get the medication via a shot. For those individuals, he said, the ingestible sensor alternative might be the way to go.

The adherence prism

Adherence for debilitating illnesses such as schizophrenia clearly has benefits for the patient, caregivers, and society. Medication adherence from an overall population health standpoint can be found in the numbers that are most-oft referenced from 2012 data: lack of adherence causes nearly 125,000 deaths, 10% of hospitalizations and costs the US healthcare system between $100 billion to $289 billion a year. The cost of non-adherence to a pharmaceutical company is a loss of $188 billion in potential US sales in 2015, and $637 billion globally.

For the patient, adhering to medicine is a decision around cost and mindset or behavior. For the former, that is one reason pharma invests in access programs for patients, whether in the form of rebates, hubs, or physician education around patient-specific co-pays and tiers because non-adherence is often a decision made around the pocketbook. For the latter, that revolves around patient education and the more trending "patient journey." This means getting to the core of the patient's perceptions around their disease, and recognizing clear goals for adherence, whether it's being able to take a walk with their grandchild without getting winded or preventing future kidney disease and being immobilized by dialysis.

There are quite a number of technologies used to promote adherence. They are as sophisticated as the Proteus IEM technology or AiCure's facial recognition via smartphone, to apps or text messaging systems that send reminders, to blister packs or bottle caps integrated with chips, to wirelessly transfer open data. The more simplistic technologies can't measure actual medication ingestion, further blurring the lines of compliance. In the limitations of use for Abilify MyCite, it states that patient compliance improvement has not been established. At the end of the day, any technology must be endorsed by the user. You can opt-out of text messaging services, or disable an app. And you can decline to share data collected via MyCite sensor.

In a statement, Otuska said that the product launch will be conducted in a limited rollout to select health plans and providers, to identify a group of the most appropriate patients. The hope is to gain feedback and learning for Otuska's broader go-to-market plan.

Some initial learnings may come from the views in *The New York Times* article. Potentially, the use of the digital adherence technology could lead to what Otuska mentions in the release: an opportunity to facilitate a more open dialogue and clarity to better inform medication decision-making for physicians and their patients around benefit, risk, compliance, and behavior.

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Lisa Henderson, Editor-in-Chief

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14

Global Health

Fighting the Good Fight

Julian Upton, European and Online Editor

Pharm Exec details the latest approaches to combating disease and health crises on a global scale—including industry perspectives from those involved on the front lines.

24

Partnerships Hold the Key

Michelle Maskaly, Senior Editor

Amid a widening net of health threats worldwide, alliances forged in research and response may be more critical than ever to stem the tide.

30

Measuring Pharma Social Responsibility

Christen Harm, Associate Editor

28

Market Access

Cell Therapy Access Guide

By Jill Condello, Andrea Favaro, Martin Lachs, and Rebecca Walker

Groundbreaking treatments involving adoptive cell transfer, such as CAR-T drugs, call for innovative access and reimbursement strategies.

20

NEWS & ANALYSIS

Washington Report

Global Report

INSIGHTS

From the Editor

Back Page

Country Report: Canada

Despite having the tenth-largest pharma market in the world and being the birthplace of medical breakthroughs, from insulin to stem cells, Canada seems to be punching below its weight when it comes to health innovation. There are signs, however, that things may be changing as the nation looks to bulk back up.

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Prognos, @prognosAI, 11/14/2017
"Driving Decisions with Data: Sundeep Bhan, CEO, Prognos"
bit.ly/2zGckNv

■ Common ground on #biosimilar coding: "Experts predict that over time, this approach will generate more market competition that lowers prices overall."

Biosimilars Council, @BiosimsCouncil, 11/15/2017
"Common Ground on Biosimilar Coding"
bit.ly/2k9JTDY

■ The more people know about what #HEOR teams do, the more effective HEOR will be.

Taft Communications, @taftcomms, 11/22/2017
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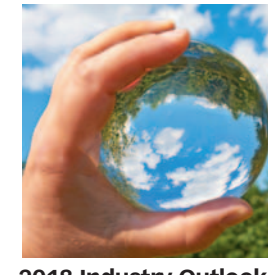

2018 Industry Outlook

Pharm Exec explores the trends that will shape the biopharma industry landscape in 2018, with input from our Editorial Advisory Board experts and Washington and Europe correspondents.

A Year of Transformation for Science & Medicine

In 2017, patients gained access to the first gene therapies and more orphan and breakthrough drugs

In recent months, biopharma companies won FDA approval of several truly breakthrough drugs that modify human cells to treat and potentially cure deadly disorders, and more are on the way. Novartis led with CAR-T therapy Kymriah for patients with relapsed acute lymphoblastic leukemia, followed by Yescarta from Gilead's Kite Pharma for a similar condition. Spark Therapeutics' Luxturna promises to cure a rare genetic eye disorder that causes blindness.

Related discoveries are spurring development of antisense drugs and RNA treatments that can modulate immune pathways, such as Biogen's Spinraza (nusinersen), approved a year ago as the first treatment for spinal muscular atrophy, which is often fatal for infants. And researchers reported success last month in utilizing gene therapy to create healthy skin to treat a life-threatening genetic skin-blistering disorder, raising expectations that genetically modified skin may treat open wounds and related conditions.

FDA reports that some 40 companies are developing CAR-T technologies for multiple indications and that it is monitoring more than 600 active investigational new drug applications (INDs) related to gene and cellular therapies. Scientists also are optimistic about developing vaccines to prevent and treat chronic illnesses as well as infectious diseases such as malaria and AIDS. A new report from the Pharmaceutical Research and Manufacturers of America (PhRMA) cites more than 100 vaccines in development to prevent cancer, HIV, allergies, and other serious conditions.

Regulators encouraging

FDA support for biomedical innovation is a prominent theme in these discussions, and one championed by Commissioner Scott Gottlieb. Since taking the helm of the agency in May, Gottlieb has rolled out multiple initiatives to bolster biomedical R&D, demonstrating in the process that FDA does not impede approval of new life-saving therapies for patients. Priority efforts are to speed up orphan drug designations, spur development of complex generic drugs, streamline clinical trials through expanded modeling and simulation, and help patients gain early access to experimental therapies for serious conditions.

Digital health also is a prime FDA challenge, with Gottlieb unveiling an R&D plan last June to encourage new device and software development. In September, FDA approved the first mobile medical application to help treat substance use disorders, and last month the first digital pill came to market, a version of antipsychotic drug Abilify from Otsuka Pharmaceutical. It contains a tiny chip able to send a signal to an adhesive patch that informs a smart phone when the pill is ingested.

FDA's new Oncology Center of Excellence (OCE), formally established in January 2017, is facilitating approval of dozens of new cancer therapies and additional indications. The latest challenge is developing drugs for patients with certain cancer biomarkers, as opposed to disease affecting specific body organs, as seen in the recent approval of an added indication for Merck & Co.'s Keytruda based on this technology.

The 21st Century Cures legislation approved at the end of 2016 supports many of these initiatives, plus a new program for developing regenerative medicine advanced therapies (RMAT). The new Office of Tissues and Advanced Therapies (OTAT) in the Center for Biologics Evaluation and Research (CBER) has established a process for designating and overseeing RMATs, including gene and cellular therapies that fall under this umbrella. Last month, FDA unveiled a RMAT regulatory framework with guidances for expediting development and review of these promising treatments.

Additional resources provided by the FDA Reauthorization Act (FDARA) fund many of the initiatives for spurring development and efficient oversight of cutting-edge therapies. Of particular note is the expansion of FDA's Office for Combination Products (OCP), which advises sponsors on whether a new combination therapy should be regulated as a drug, biologic, or device. This process increasingly involves gene and other advanced therapies that incorporate pre-

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filled syringes or autoinjectors to deliver treatment. OCP's staff faces a growing volume of queries on combo product development programs, along with commitments to update guidances and prepare additional advisories on labeling issues and bridging studies, among others.

Although the long-term effects of new gene and cellular therapies are unknown, these initial successes have spurred optimism about further development of treatments for both rare and more prevalent serious conditions, particularly neurological diseases such as ALS, Alzheimer's, and Huntington's disease. At the same time, safety issues have sidelined some promising therapies, such as a CAR-T candidate from June Therapeutics that was linked to severe brain toxicity that led to patient deaths in clinical trials.

Policymakers are taking note of these developments, along with related ethical and safety issues raised by the potential to treat serious diseases by editing genes more precisely using CRISPR and cas9 technology

Policymakers are taking note of these developments, along with related ethical and safety issues raised by the potential to treat serious diseases by editing genes more precisely using CRISPR and cas9 technology. A hearing before the Senate Health, Education, Labor and Pensions (HELP) Committee last month addressed the possibilities for preventing conditions such as sickle cell disease and blood disorders and the need for appropriate regulatory oversight of technologies able to change the human genome or to develop biological weapons. Experts agreed that the current FDA regulatory framework, plus oversight by the HHS Recombinant DNA Advisory Committee and institutional review boards (IRBs), can adequately assess the science and ethics of genome editing, and that stricter rules might discourage research or shift it overseas.

Sponsors and researchers also recognize the need to better understand which individuals face higher risks from new gene therapies and the potential for severe side effects. But with R&D pipelines full of innovative drugs, the future looks promising for continuing gains in discovering important new treatments for life-threatening diseases. PE

Partnerships and pricing

Industry sponsors have responded to the surge in new science with a notable increase in investment and dealmaking to support innovative biomedical research. A November report from Deloitte Insights examines the rise in "external innovation" involving biopharma company licensing, mergers, and joint ventures with small innovators to build robust development pipelines. The analysts note a preference for licensing agreements over mergers and acquisitions due to lower upfront costs and evidently higher success rates. There seem to be announcements daily of deals involving new gene editing and other "disruptive" technologies that utilize a range of payment, milestone, and future acquisition and profit-sharing arrangements. Tech companies, in turn, are licensing technology platforms to multiple pharma partners eager for new methods to engineer specific antibodies and cellular functions.

As FDA and industry continue to scope out research and regulatory pathways for these new therapies, they also recognize concerns that high product costs could limit patient access to treatment. Current processes for developing and delivering complex new drugs are expensive, highlighting the need to identify efficiencies and improve methods for testing and producing cutting-edge medical technologies. Also important are innovative strategies to justify coverage and reimbursement of life-saving therapies by both public and private payers.

Unfortunately, public skepticism about R&D costs and pricing decisions has been aggravated by questionable patent strategies and efforts to extend market exclusivities that appear designed to limit competition. Push-back against such actions is generating proposals to change how companies qualify for FDA priority review vouchers for developing treatments for tropical diseases and for rare pediatric disorders. And Republican efforts to reduce corporate taxes on pharma and other industries also propose to limit the value of the orphan drug tax credit, which has been key to spurring development of rare disease remedies.

Front & Center

Accent on Accessibility

Program provides effective, cost-efficient way to help patients overcome affordability barriers and obtain the critical medicines they need.

As drug therapies become increasingly more complex and expensive, there is a need to help patients who cannot afford vital medications. Drug manufacturers have closed this gap through patient assistance programs (PAP) that provide individuals without insurance coverage or the financial means to purchase products access to free medications. As the need for patient support continues to grow, there is a strong focus on the development of new tools to streamline the PAP process and improve patient access to critical medications.

The PAP Evolution

Manufacturer-sponsored PAPs provide subsidies, free or discounted medications to patients who have inadequate means to obtain needed drug products. Eligible patients range from low-income individuals to those who have insurance coverage, but still cannot afford to buy their medication.

"Companies like Triplefin and other patient service providers work with patients to help them to navigate various options to find some form of alternative coverage," explains Tom Doyle, executive vice president, commercial solutions of Triplefin, an H. D. Smith company. "The patient might be eligible for a foundation or a federal program and not even be aware of it. The goal is to provide a high level of service to effectively and cost efficiently enable patients who cannot afford the drugs to obtain access to these products."

Triplefin, headquartered in Cincinnati, OH, has been involved in the PAP market since 1999 through its purchase of RxHope, a central landing point where patients can search for manufacturers' offerings of free medications. Much has changed since then. With the expansion of the biologics and specialty drug markets, drugs are significantly more complex and expensive today than they were in the past. At the same time, the uninsured population has continued to grow, and many patients are falling through the cracks.

Tom Doyle, Triplefin's executive vice president of commercial solutions

PAPs, too, are in transition. The administration of PAPs has historically been a tedious, manual process. As a result, it was expensive and inefficient to screen and qualify patients for programs. Thus, Doyle says Triplefin saw the need to increase efficiency and reduce costs through automation.

Additionally, there has been increased scrutiny by the government to ensure that free goods programs are operated independently of the commercial business. Such challenges have prompted manufacturers to build firewalls between commercial reimbursements for patients and the free goods program. Triplefin is also responding to manufacturers' needs to streamline this experience and to make it as integrated, seamless and efficient as possible.

Automated Solutions

Improving patient access to products through web-based or e-solutions has been a major area of focus for patient-support companies. Most of these efforts have centered on reimbursement programs where patients can enroll in programs through web portals or providers can utilize electronic benefit verification (eBV) or electronic prior authorization (ePA) to navigate reimbursement challenges. Programs that provide access to real-time information and, in some cases, are integrated into the physician workflow are reducing barriers to access for patients with insurance. PAPs are ripe for similar innovations.

Historically, patient assistance programs have relied heavily on fax or paper enrollment and often required W2s or other supporting documents before a patient was granted access to a program. With advances in both real-time benefit and income verification, PAPs are positioned to improve patient access and reduce program cost.

To improve the patient experience, programs need to move beyond web-based portal enrollment to solutions that enable patients to receive real-time eligibility information specific to the drugs they need. With advances in real-time eBV for both pharmacy and medical benefits,

solutions are being created that enable PAPs to determine if the patient has any insurance coverage to support access to critical medicines. Combining this with a real-time soft credit check enables the patient to quickly determine if he or she qualifies for a support program.

Doyle says, "It is cumbersome for the patient to try and track down all of that information and challenging to synchronize it with what the physician's office is sending in with the prescription. The situation is not good for the patient, it is not good for the provider and it is a drain on the resources of the manufacturer and service provider who are trying to provide a good experience and help patients to gain access to much-needed drugs."

Equally important to automating the front-end patient enrollment process is the use of technology to improve the overall management of the patient and provider experience. The same automation of income validation and benefit verification can reduce the time it takes to process and approve patient applications received through traditional fax processes.

Triplefin's propriety platform Rx365®, supports all aspects of patient, provider, and contact center engagement by automating and integrating each step of the patient journey, from program enrolment through delivery of product and ongoing patient support. Doyle notes, "One major key to success is balancing the need for automation while ensuring every patient, caregiver and provider has an exceptional experience with the PAP. Automation that reduces inefficiency and enables the contact center associates to focus on providing each patient with service improves access and helps patients benefit from these often lifesaving therapies."

The Need for Separation

Compliance requirements are driving more separation between historical program structures in which commercial teams also manage giving free product to patients. This is leading to the creation of additional and more distinct separation of manufacturer-supported foundations from the commercial business. This structure has benefitted patients by serving organizations that are laser focused on taking care of the needs of the patients at the most risk of not receiving product.

At the same time, it is important for service providers to focus on providing a similar level of separation, ensuring that reimbursement programs are not comingled with patient assistance programs. This is also driving more interest in creating an environment where both the front-end patient support for program qualification and the physical distribution of PAP product is provided by a service provider that is solely focused in those areas. Service providers go to great lengths to ensure they are fully compliant with these requirements and are continuing to transition to a PAP pharmacy environment where the pharmacy's focus centers on only providing free product and is not comingled with commercial business.

Foundations, often involved with specific disease states, are typically funded by multiple manufacturers and other donors and play a key role in supporting patients unable to afford their medicines. While manufacturers grant funding to them, foundations provide a way to ensure separation to keep the decision to fund patients completely unbiased. The focus is simply on patients who lack affordability options for their medications.

In some cases, patients who do not qualify for the manufacturer's PAP because their income is above the threshold of the government program still qualify for the foundation program. Foundations give patients multiple avenues to exhaust.

Simply put, if foundations receive support, they can help more people. If the PAP model can become more efficient and less expensive to administer, it would free up funds that could potentially help the foundations or other organizations trying to assist patients with access to their medications, Doyle believes.

PAPs in the Future

The next-generation of PAP solutions must consider having a patient-driven website that supports real-time enrollment, provides automation that a supplier can access internally, and initiates outreach to healthcare providers with minimal intervention. Automation will touch every aspect of the process.

"We often hear that everything is going to be electronic and automated and that is a silver bullet. The reality is that, particularly in this space, it often remains a very manual process with patients still wanting to talk with someone," Doyle says. Thus, companies need access to improved tools and systems that are geared to increase efficiencies.

According to Doyle, "The industry is really in flux, and there is a need for improvement. We are all asking the same questions: How can we make this better? What can we do differently? How can we serve patients while controlling costs and making the process as simple and efficient as possible?"

Doyle concludes, "There is a need for an overall smoother, more integrated and consolidated approach. PAP is a space that we, as an industry, we as a society, should embrace to help patients, the people who are truly in need."

Will Europe Turn a Corner in Personalized Medicine?

New action plan urges tighter alignment of public health policy with the development of targeted therapies

A massive improvement in the health of Europe's citizens is within reach, boldly asserted the European Alliance for Personalized Medicine (EAPM) on the eve of its conference in Belfast at the end of November. The ambitious claim is spelled out by EAPM across some 25 pages of a position paper (view: http://bit.ly/2n586Ms) released in advance, and is backed up by extensive arguments about the opportunities that targeted therapies can offer patients, health services, and society.

It is not the first time such a claim has been made in Europe. The rather halting European journey towards personalized medicine dates back more than a decade now, and a plethora of organizations have pitched their approaches to make it work.

Currently, a high-powered inter-governmental effort known as IC-PerMed is laboring toward establishing an action plan. The European Personalized Medicine Association is planning to fund scholarships in education and training of future healthcare professionals with a focus of using diagnostics and patient engagement and empowerment centered on personalized medicine. The private-public partnership of the Innovative Medicines Initiative is running a series of projects related to personalized medicine, including its ADAPT-SMART platform exploring how regulation can be better aligned to the development of targeted therapies. And Europe is still struggling to find ways of putting into effect the conclusions of ministers at the December 2015 health council to "take personalized medicine into account in the broader context of the future framework for sustainable European Union collaboration on patient safety and quality of care."

The coalition mantra

What distinguishes this EAPM approach—as was noted by half-a-dozen members of the European Parliament in the foreword they have penned—is that the alliance is aiming to make a reality of building the frequently-evoked broad coalition among health stakeholders, a familiar slogan in any discussion of making progress in exploiting the wide-ranging scope of personalized medicine. The alliance emphasizes the need for "a clearer understanding among Europe's policymakers and decision-takers that a paradigm change is needed, with new forms of cooperation, collaboration, and awareness across multiple domains and stakeholders."

EAPM has identified many of the barriers that need to be overcome to enable such a "paradigm change." They include a limited evidence base; the absence of personalized healthcare in most cure pathways; a lack of consensus on clinical utility; varying standards and quality of provision; low awareness, particularly among healthcare professionals and patients; and insufficient coordination among policymakers and regulators.

The position paper deals in some detail with many of these challenges. But on one—and that is payment, the one that might be considered the biggest stumbling-block of all at present—it limits itself largely to generalizations: "Radical changes in thinking at the highest policy level in relation to public health generally will enhance the measurement of value for health interventions and adapt payment systems accordingly," it states blithely. But will it, and how will it, and how soon will it?

Value dilemma plays on

In Europe, as in the US, one of the central elements of the personalized medicines debate—the issue of pricing—remains as challenging as ever. Everyone admits that the challenge exists, and particularly for the more expensive innovative products that are most likely to usher in new approaches to therapy. But admitting the challenge is only a first step toward finding solutions—and at the moment Europe is still very much at the first step.

The European Medicines Agency's Guido Rasi warned last month that the speed of advance in the world of therapy is impeding planning. "It is absolutely impossible to predict what new technology will be inserted into the production system for medicines and therapies and the inte-

REFLECTOR is *Pharmaceutical Executive*'s correspondent in Brussels

grated systems that come with them," he said. Italy is introducing a legislative framework for some form of postmarketing appraisal of new drugs in a bid to improve cost-effectiveness, but already there are questions over its criteria and methodology. Portugal has just updated its out-of-date 2006 framework for granting access to new drugs for rare diseases, but with little provision for better funding. Even in prosperous Germany, officials at its G-BA insurance organization recognize that the price of orphan drugs is too high in relation to extent of additional benefit, and are urging tighter controls.

If the authorities in Europe are aware of the problems from their side, drug firms operating here are even more acutely sensitive to deficiencies in the current arrangements. Pfizer complained in mid-November that Ireland is "one of the slowest countries in Europe" to fund the use of innovative medicines. Roche CEO Jens Grueger described to a recent conference the dilemma faced by companies developing multiple potential combinations involving new immunotherapies and personalized drugs. The healthcare systems and health technology assessment (HTA) bodies needed to assess the value of such innovations—and to make sure they are paid for so that patients can receive them—simply do not exist yet, he said.

Shire CEO Flemming Ornskov sees in the not-too-distant future the model shifting to outcomes-based payments, and "not just for rare diseases, but for all diseases." But he told a recent conference in London that his excitement at that prospect was tempered by concerns over current European moves in a contrary direction: "What we are not excited about is an initiative to take some of these incentives away," he warned. A senior official in the UK's National Audit Office fretted in public over the ability of the National Health Service (NHS) to cope with change. Robert White, who is director for health value for money, said the rising costs of expensive, specialist drugs and medical devices are a concern and a worry for NHS sustainability. And Sir Andrew Dillon, head of the UK's HTA body the National Institute for Health and Care Excellence (NICE), said recently that companies with expensive new technologies like CAR-Ts will need to work together with the NHS and think "more creatively" about payment structures.

In the US, pharma is enjoying some sunnier weather under the Trump administration, as more and more pro-industry (and often ex-industry) figures are appointed to senior posts and start to tweak the rules in the interests of drugmakers. Joe Grogan, associate director for health programs in the Office of Management and Budget, pushed back recently on a discount scheme that allows hospitals and health clinics to obtain cheaper medicines. He described it as "incredibly flawed," and said the administration wants to explore new pricing mechanisms that could "create more freedom" for payers to seek creative deals with pharma companies. Otherwise, products like CAR-T drugs "will bankrupt the system and people can't access them," he said.

However, even there, companies are looking over their shoulders apprehensively at potential downsides from current tax reform proposals, which could hit foreign income from intellectual property wherever it is legally held, and threatens to remove or reduce tax credit for conducting clinical trials of rare disease drugs.

> The alliance emphasizes the need for "a clearer understanding among Europe's policymakers and decision-takers that a paradigm change is needed, with new forms of cooperation, collaboration, and awareness across multiple domains"

Answers, not advice

The comprehensive view of an effective strategy for drug innovation is conspicuous by its absence on both sides of the Atlantic. And EAPM, for all its vision, has little to offer in terms of solutions to the central dilemma of pricing. "National authorities, HTA bodies, and pricing and reimbursement agencies should be open to reconsidering how they get best value for patients and society out of public health spending," it says. But "should" is easily said. More than that is needed to start to extricate pharma innovation from its currently closed circuit of frustration among drug developers and recrimination among those who pay for drugs. PE

Fulfilling the VISION of Science

Dr. Ruud Dobber, president of AstraZeneca US and executive vice president of the company's North American business.

Drawing from his research roots and the leadership lessons gained in melding business and culture in geographies across the globe, Ruud Dobber is busy steering AstraZeneca's US course as it navigates the complexities of a fast-evolving therapeutic market

By Lisa Henderson

AstraZeneca was ranked 11th in *Pharmaceutical Executive*'s annual Pharma 50 listing this year, with 2016 worldwide prescription sales of $21 billion and R&D spending of $5.6 billion. Its top-selling drugs globally were Crestor, Symbicort, and Nexium. In 2017, AstraZeneca gained US approval for Imfinzi for bladder cancer and Faslodex for expanded use in breast cancer—and possible approvals for Lynparza, also in breast cancer, and Imfinzi for lung cancer loom in 2018. Dr. Ruud Dobber, president, AstraZeneca US, and executive vice president, North America, is leading his team's efforts to realize the full commercial potential for these important therapies.

Dobber has been heading the region for the big pharma company since August 2016. He is responsible for the activities of close to 6,000 people, leads AstraZeneca's commercial operations in North America, and represents the region as a member of the company's Senior Executive Team. In these capacities, Dobber is accountable for driving growth and maximizing the contribution of North America to AstraZeneca's global business, of which the US represents roughly 40% of

the organization's global product sales.

Most recently, Dobber was executive vice president, Europe, and oversaw business functions in the 28 European Union (EU) member states. Prior to that, he was regional vice president of AstraZeneca's European, Middle East, and African division; regional vice president for the Asia-Pacific region; and interim executive vice president, global product and portfolio strategy. Dobber also was a member of the Board and Executive Committee of the European Federation of Pharmaceutical Industries and Associations (EFPIA) and earlier was chairman of the Asia division of Pharmaceutical Research and Manufacturers of America (PhRMA).

Dobber takes pride in the AstraZeneca pipeline, and credits its CEO Pascal Soriot for its dynamic transformation. "In his five years at the company, he has really transformed it even more toward science," says Dobber. While noting the company was always science-driven, Dobber says Soriot has injected a philosophy of science and innovation throughout every region of AstraZeneca.

"We have the mindset—if you are doing good science, if you think continuously about what science is discovering for patients, and know the value of what we bring to patients, AstraZeneca will be successful," he says. "And you can feel that. I can feel that when I travel to different parts of the US and to various regional AstraZeneca companies around the world."

This science affiliation aligns perfectly with Dobber's passion for research, medicine, and patients. He grew up in the Netherlands, earned a PhD in immunology from the University of Leiden, and eventually became a researcher in the fields of aging and immunology. With his foundation in research, Dobber says, "You learn to be resilient." He explains that research is fraught with failures, "but if you are successful, you have that moment of 'Eureka,' and that's phenomenal."

"I still feel the excitement when I talk to friends working in the area of hardcore science, or our own scientists. … But with that excitement, you still need to be very focused."

Though Dobber has been on the commercial side since 1997, he has never lost his respect or enthusiasm for research.

"I still feel the excitement when I talk to friends working in the area of hardcore science, or our own scientists at AstraZeneca," he says. "For me, it's always very refreshing to hear what they are doing, to hear their enthusiasm and passion. But with that excitement, you still need to be very focused. Science in oncology and other therapeutic areas is evolving so fast, so you need to be clear and dedicated in what you want to achieve and what you want to develop with your colleagues, and I love that."

AstraZeneca's research institutes are located in the US at subsidiary MedImmune in Gaithersburg, MD, and at AstraZeneca in Cambridge, UK, and Sweden.

When Dobber was in research, he didn't imagine he'd work for a pharmaceutical company. He says he was always excited and intrigued about science, but the missing link was how to bring the science to the physicians and the patients.

"I think that was the crucial moment. There was never a doubt that I wanted to stay in healthcare, but when I made the decision to move out of the hardcore science world, it was clear to me that I wanted to go to a pharmaceutical company because they are doing the end-to-end process," says Dobber. "They are discovering new molecules, they are developing new molecules, they try to bring new medicines to patients, and—if registered and approved—

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» Dr. Ruud Dobber began his career as a scientist, researching in the field of immunology and aging. He joined AstraZeneca in 1997 and has held various senior commercial and leadership roles, spanning locations in Europe, Asia, the Middle East, and Africa. He assumed his current role in the US in August 2016.

» Dobber was responsible for the development of AstraZeneca's late-stage, small-molecule antibiotic pipeline as well as its global commercialization.

» Dobber, who grew up in the Netherlands, is married and has two children. He lives in the suburbs of Philadelphia, not far from AstraZeneca's US headquarters in Wilmington, DE.

"As an industry, we need to do a better job of educating, and we need to make sure that governments are understanding the value of medicines."

they're handed over to the medical and commercial departments. I think that is a fascinating value chain; it's fascinating what we try to achieve."

The value of pharma

Dobber acknowledges that the biopharma industry has a profit obligation. "Most of us are listed companies, and we have shareholders, and we need to take care of them," he says. "But the most exciting piece, at the end of the day, is bringing those molecules to the hands of the physician and then ultimately to the patient."

Achieving those results, however, is not always easy, especially in Dobber's latest regional foray in the US.

"When I was offered the job here, [the healthcare environment] turned out to be one of the most complex," he explains. "There are a lot of different players—PBMs (pharmacy benefit managers), Medicare, Medicaid. ... It's highly fragmented. And it's extremely complex."

But the cost discussion is one that Dobber believes will continue for some time—and not just in the US. Overall, healthcare costs increase with evolving treatment pathways, the value of new medical and clinical discoveries, and an aging population. These all increase costs to patients and governments, and require more education and dialogue with those stakeholders.

"Before moving here to the US, I've been privileged to work in every geography in the world, living in Asia and Europe, and frequently traveling to various countries in the Middle East," says Dobber. "Healthcare cost is an issue for governments everywhere. People are living longer and want to live longer in a healthy way and the opportunities and possibilities to do that are massively larger than they were 20-25 years ago. Cancer is a good example. We can't claim to cure cancer, but for some cancer types, it's a chronic disease, which was mission impossible 25 years ago."

"We also know that the last three to five years is the most expensive part of a person's life," adds Dobber. "I have real sympathy for governments that are seeing healthcare costs rising."

And, given the environment, there is also pressure on the industry to come up with alternatives, explains Dobber. "What I don't like is the focus seems to be too much on the small part of the healthcare cost—the medicine cost—and not the total cost of care," he says. "As an industry, we need to do a better job of educating, and we need to make sure that governments are understanding the value of medicines. Conversely, we need to understand the ultimate tool and goal is to make sure many patients can afford our medicines."

To uphold the industry's value mission, Dobber says drug manufacturers "need to take those signals seriously" and should do everything they can to educate governments.

"Some may only see the value of what this industry delivers at the moment they are ill, when they are sick," he says. "But the level of innovation and level of sophistication is incredibly high. And there's all the R&D failures that you have on a daily basis as well. But the job of finding medicines—finding something—that will cure patients is a goal of every treatment, or to make a disease acceptable so that you can live a normal life. I find this a noble endeavor and that's the reason I've been in this industry so long."

Leadership experiences

Dobber values medicine, research, and science, and he also values all of the experiences he has had that bring him to where he is to date. He applies all of these views and values to his prism of leadership. Starting when he was offered a position to learn marketing and sales at AstraZeneca, and his visits to Germany, China, Korea, Saudi Arabia, India, and more, Dobber says he has learned from the different cultures and the ways these regions approach problem-solving and consensus.

"I'm a direct person; many Europeans and those in the US have a direct leadership style, but that may not always be the effective one," he says. "There

are more approaches to solve a problem—it forms you as a leader. Cultural diversity is a phenomenal learning for every leader."

Dobber says he has been privileged throughout his career to have managers that were aspiring or pushing him out of his comfort zone. "I didn't always feel comfortable," he notes, "but I'm very grateful for that learning experience. It's good if you have a healthy level of ambition, that you have someone who thinks that you can do more."

This, too, carries into Dobber's philosophy for leading others. "I'm always advising people, if you push yourself you can do so much more and even if it's an area where you have no expertise; if you are curious to learn, and curious to listen to other people, you will have success," he says. "It's incredibly rewarding and refreshing to see that, and it's one of the reasons I like the work I'm doing now. But I'm also grateful for the education that I had in the past."

Dobber advises other leaders—and those aspiring to be—to help their direct reports step out of their comfort zone. "Raise the bar and let them see it as an opportunity. Encourage them to take the challenge," he says. "Give them the mission-impossible challenge and see how they react. You might be surprised, but talented people will have a solution, and rise to the challenge. If you motivate people, they can do so much more."

Other leadership tips? "The moment you are appointed as a leader, you need to think about your successor and have that ready," says Dobber. "Work very active on your succession."

And if you want to be hired by Dobber? Be performance-driven. Show ambition and drive to do the job in an excellent way. Have a level of curiosity to work with other people and be able to work collaboratively. "I look for people with that spark," he says.

Dobber admits, like most in his position, he doesn't have a lot of free time. But, when he can, he does switch off between golfing, dinners out with friends, and learning more about his new home—the US. Since he settled into the Philadelphia area, close to AstraZeneca's Wilmington, DE, headquarters, Dobber's been to several US cities, including San Francisco, Washington DC, and New York. In his new hometown, in the suburbs of Philadelphia, Dobber describes the area as beautiful, green, and warm. Last year, in Philadelphia, the winter was not very cold or snowy, but Dobber disagrees, as he shows me a picture of his dog Ivy in the snow from last year (see photo in online version).

"That's not snow, you can still see the grass," I mention. "You know they are calling for a lot more cold and snow this winter?"

With Dobber navigating AstraZeneca through another critical year in the US, with multiple product launches and continued market challenges, his resilience and leadership will be key in helping the organization to success—and the former scientist and Ivy can enjoy whatever weather the winter brings. PE

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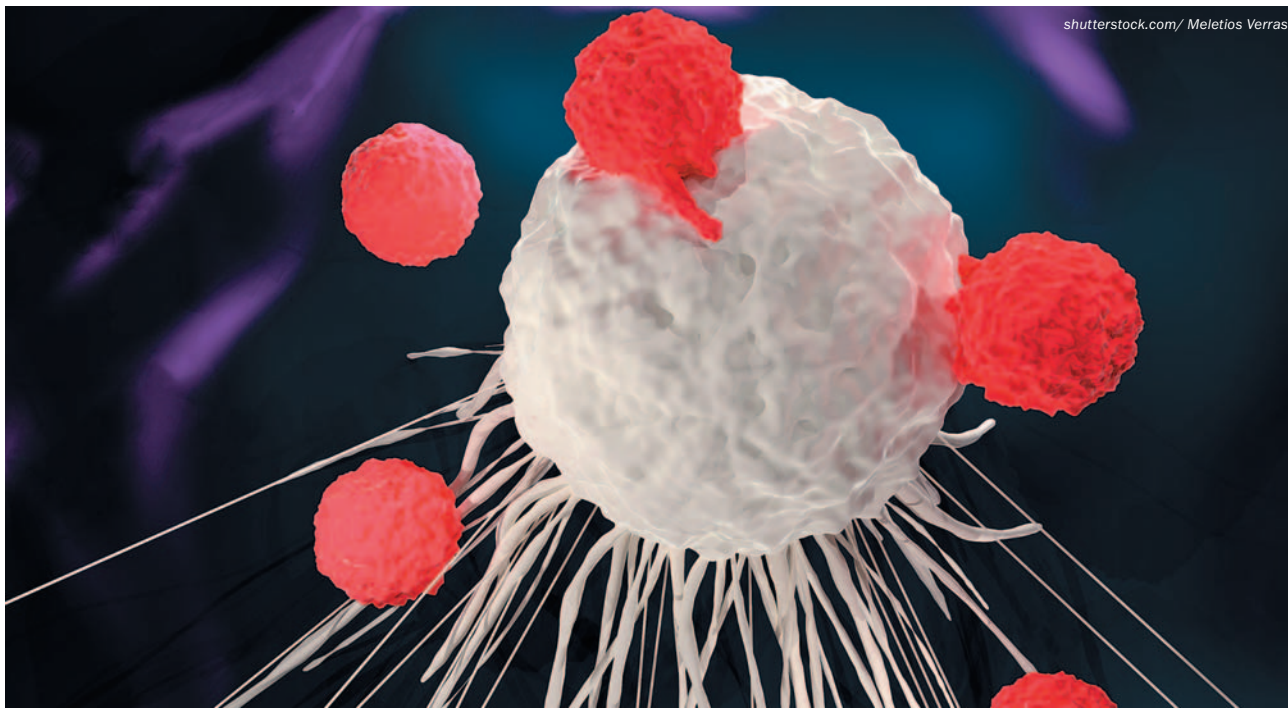
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A 3D illustration of T cells attacking a cancer cell.

Access and Reimbursement for Adoptive T-Cell Transfer Drugs

Groundbreaking treatment approaches call for innovative commercialization strategies

By Jill Condello, Andrea Favaro, Martin Lachs, and Rebecca Walker

FAST FOCUS

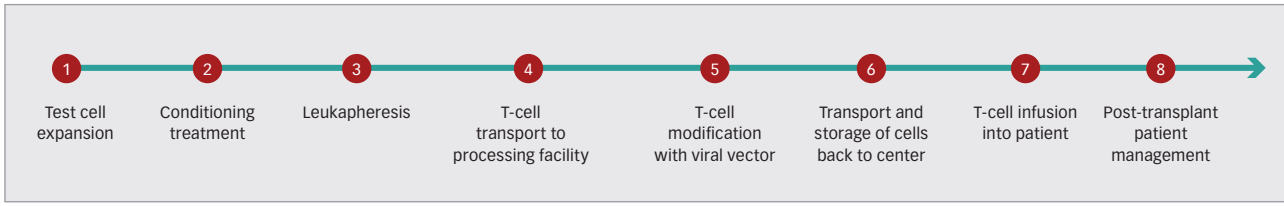
» There are more than 270 clinical trials underway in the CAR-T therapy space. Reports estimate the global CAR-T drug market to grow a CAGR of 46.1% between 2019 and 2028.

» With individualized treatments administered at hospitals, the customer base for manufacturers of CAR-T therapies are the hospital systems/providers and the handful of centers of excellence capable of offering such treatments.

» Pay-for-performance or risk-sharing agreements involving CAR-T drugs will likely become increasingly common in the industry. For example, in the US, Novartis struck an outcomes-based deal with the Centers for Medicare and Medicaid Services (CMS) around the company's leukemia medicine, Kymriah. CMS will only pay for the drug in cases in which patients respond after a month.

The approval of the first genetically modified cell therapy in the US—Kymriah™ by Novartis—made headlines in late August of this year, receiving marketing approval in North America for the treatment of B-cell acute lymphoblastic leukemia (ALL) in children and young adults with limited treatment options. Less than two months later, Kite Pharma received approval for Yescarta™ for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy. Both breakthroughs are chimeric antigen receptor T-cell (CAR-T) therapies that involve adoptive cell transfer (ACT). Over the next decade, we can expect other ACT therapies to change the field of oncology dramatically, particularly in some of the more difficult-to-treat cancers.

CAR-T Cell Therapy Procedure



The production and administration process for CAR-T cell therapies.

In parallel, biopharmaceutical manufacturers of ACT therapies will need to alter their traditional commercial models just as dramatically. First, ACT therapies are not drugs in any traditional sense; rather, they are medical procedures that require individualized, *ex vivo* processing and highly specialized healthcare professionals and facilities. If these first two market entrants are trendsetters, future treatments will be expensive and on a scale well beyond all other oncology treatments to date. ACT therapies will require a very different approach to pricing and market access than anything that has come before.

A wave of innovation

The CAR-T cell therapies Kymriah and Yescarta are produced by deriving cells from the patient, reengineering them in a laboratory to recognize and kill cancer cells, and then multiplying them and infusing them back into the patient (see chart).

Investment in CAR-T drugs is strong, with more than 270 trials underway in this space. Of the approximately 40 companies developing CAR-T cell therapies, the leading players currently include Novartis, Kite Pharma (now part of Gilead Sciences), Juno Therapeutics (in association with Celgene), Bluebird Bio (also in association with Celgene), and Cellectis (in collaboration with Pfizer). According to Coherent Market Insights, the global CAR-T cell therapy market is estimated at $72 million today, with projected growth at a staggering CAGR of 46.1% between 2019 and 2028.

> It is safe to assume that payers will be unwilling to make the leap of faith on long-term benefit without some kind of proof or guarantee

Challenges for payers

Payers will be facing a number of difficulties in evaluating and covering ACT therapies—challenges that biopharma companies must actively address in their commercialization strategies.

Limitations in assessing clinical benefit

At the time of launch, the evidence base for ACT therapies will likely be immature and may not support conclusions on their potential long-term benefits. Indeed, many of these treatments may be approved on the basis of Phase II trials in relatively small patient samples, without long-term, real-world follow-up. It is safe to assume that payers will be unwilling to make the leap of faith on long-term benefit without some kind of proof or guarantee. However, they are unlikely to expect data from ~10-year-long trials. Payers also want to be able to compare the efficacy of a new product with the standard of care, although, in most cases, the data on newly launched ACT therapies will likely not be robust enough for such comparisons.

As with other immuno-oncology treatments, ACT therapies are likely to work well for a portion of patients, providing remission for a number of years. In Kymriah's case, 83% of patients achieved complete remission or incomplete response with blood count recovery within three months of infusion. Payers (along with the entire medical community) will be eager for more insights into which subgroups of patient will benefit from the treatment.

Classification as a medical procedure

As mentioned, ACT therapy is typically developed though an individualized process for each patient, and treatment is provided in the hospital, similar to stem-cell transplants.

This means that in the US, the manufacturer's customer is the hospital system/provider,

In the US, where patients tend to change medical insurers on average every two to three years, how can the cost be borne, and the benefits enjoyed, equitably?

and only a small number (perhaps 10 to 15) of centers of excellence are likely to be capable of offering the treatment. Payers must negotiate contracts with these facilities and be prepared to address policy issues around access and funding, in particular for patients who do not live near one of these centers.

In the major five European markets (France, Germany, Italy, Spain, and the UK), treatment will likely be covered by the hospital funding mechanisms, such as are in place for organ transplants. Funding is typically based on a single, fixed-price per patient to cover costs from the date of admission to a certain number of months post-transplant. There may be no existing mechanism for funding any additional, and costly, services related to ACT treatment.

Cost

Currently, a one-time treatment with Kymriah is priced at $475,000—a price that has pierced prior-cost barriers. (In contrast, a one-year course of treatment with a programmed death cell protein 1 [PD-1] targeted antibody is priced around $180,000). Initially, even at this price, Kymriah will present payers with limited budget impact, as it is indicated only for ALL that is refractory or in second or later relapse in children and young adults (up to 25 years of age). However, the impact on payers will change if/when Kymriah is approved for other more prevalent indications and certainly when other ACT therapies enter the market. Yescarta is priced lower than Kymriah, at $373,000, but it will serve a considerably larger patient population in which the unmet need may not be as high.

While the downstream benefits of ACT therapy are likely to last for many years, the very high cost will be concentrated at the time of treatment. In the US, where patients tend to change medical insurers on average every two to three years, how can the cost be borne, and the benefits enjoyed, equitably? There may be a disincentive to cover such therapy if another entity yields the benefits.

So, how will ACT therapies fit into the existing funding structure? How will payers respond? Their approaches will be different by country and region, but we can expect that they will take a conservative approach when data packages are limited. Particularly in the Euopean Union (EU), payers can prolong their drug listing/formulary decision-making process as approvals work their way through national, regional, and then hospital-level bodies. It is not unusual for this process to take as long as two years. As an example, access decisions on the multiple myeloma drug Farydak® took around two years in both France and Italy. Ultimately, they can restrict or deny access based on the price.

Offsetting uncertainty with innovative contracting options

Experience suggests that some payers will not cover such novel and expensive therapies based on immature evidence without a way to either share the risk or curb or delay the budget impact. They will look for manufacturers to enter into innovative agreements such as:

- **Installment payment plans.** To our knowledge, this has not yet been tried, but such an arrangement would allow payers to stagger their payments, perhaps upon completion of specific steps in the treatment process. One payment might be made, for example, when the therapy was prescribed, another when the patient was infused, and another at a certain point posttreatment when outcomes could be assessed. The final payment could even be spread out over a number of years.
- **Outcomes-based agreements.** Such pay-for-performance or risk-sharing agreements are increasingly common in the EU where the single-payer system results in stable patient populations for payers. Now, the model is coming to the US. In a novel deal, Novartis has entered into an outcomes-based agreement with the US Centers for Medicare and Medicaid Services (CMS) through which the agency need only pay for Kymriah in instances in which the patient responds after a month. CMS,

which has praised the arrangement, plans to publish guidance for other companies interested in exploring innovative contracts.

» **Managed-entry agreements/coverage with evidence.** This is the coverage equivalent to approvals with risk evaluation and mitigation strategies (REMS). Under these agreements, the product is covered upon market entry, albeit conditional on a postmarketing assessment to revisit pricing. Usually, a registry is created to generate evidence that is later evaluated by the payer.

» **New debt instruments.** In the future, it is possible that access will be funded by such means as annuity payments, bonds, credit, mortgages, and risk pooling.

Manufacturers, start your commercial engines

We know that, in general, payers have little appetite to accept uncertainty. A study performed by the UK's National Institute for Health and Care Excellence (NICE) revealed that even when they had a five-year dataset (which is greater than most therapies have at launch), payers were concerned about low subject numbers and the use of a single-arm study. To secure access in this environment, manufacturers of ACT therapies will need to:

» **Develop products with the payer in mind.** In terms of evidence generation, payers should be considered just as important as regulators. Payer-relevant endpoints (e.g., overall survival) for a new cell therapy should be included in early-stage trials; if planned properly, these data can be mature by launch, providing outcomes data over a long period.

» **Continue following patients after trial close.** Trial participants should be followed after the close of the pivotal trial via long-term follow-up to gather data on overall survival. (Novartis's initial Kymriah patient is still alive five years post-treatment).

» **Engage treatment centers early.** In the EU, new funding pathways and contracts will likely be required, and manufacturers can help ensure that they are in place and workable. And in the US, contracts must be in place between treatment centers and payers before treatment can begin. Drug manufacturers can engage with their customers to ensure that they have all that they need to support the contracts.

» **Develop and share data on the burden of disease.** To appreciate fully the economic benefit of ACT therapy, payers should be given data on the costs that are averted. These could include an organ transplant, other associated treatments and costs for families in missed work and stress, etc.

» **Establish launch pricing based on value.** Manufacturers should take into account epidemiology data, the degree of therapeutic unmet need in the market, and the product's clinical value in comparison to that of competitors.

» **Help payers understand which patients are the right candidates for treatment.** Payers may benefit from education on the type of patients who are best suited for treatment (e.g., biomarkers) and from epidemiology data on the prevalence of specific diseases. This will help payers in their budgeting and may allay their concerns, as the number of eligible treatment candidates may be smaller than what they fear.

» **Carve out a unique target.** Competition will increase in this space, and ACT therapy manufacturers should choose their trial populations with care, limiting their focus to those patients for whom the greatest payer-perceived benefit can be demonstrated.

Early manufacturers of ACT therapies need to consider unique strategies toward evidence generation

Think ahead

ACT therapies are so new that most payers have not yet updated their systems, policies, or budgets to accommodate them. Thus, it is impossible to know exactly how to meet their requirements, but manufacturers with ACT therapies in the pipeline should be actively exploring this. It seems clear that early manufacturers of ACT therapies need to consider unique strategies toward evidence generation, working to understand how ACT therapies will require different payer policies, and planning new types of agreements with payers that will afford access to patients. PE

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Fighting the Good Fight

Industry Perspectives on Global Health

Pharma often finds its global commitments to fighting infectious disease outbreaks and chronic health crises attacked or dismissed as inadequate. But the realities of market economics, fiduciary duty, and murky regulatory systems must be factored into the equation

By Julian Upton

Writing for *The Conversation* last year, Nicole Hassoun, a professor of philosophy at Binghamton University-State University of New York, and head of the Global Health Organization, cited a World Health Organization (WHO) report stating that a third of the world's population cannot access important medicines for some of the globe's most devastating diseases. Hassoun wrote, "I believe that [pharmaceutical] companies have a moral and legal obligation to ensure access to essential medicines."

When companies set high prices, lobby to extend patent protections on important medicines, and do not develop enough new drugs for neglected diseases, she went on, they fail to live up to these obligations.[1] While Hassoun expressed her arguments soberly, zealous contingents of activists prefer to use more drastic measures to make their points. In April of last year, seven naked people representing ACT UP London—a "diverse, non-

partisan group of individuals united in anger and committed to creative action to end the HIV pandemic"—stormed the headquarters of Gilead Sciences in London with "#PharmaGreedKills" scrawled on their backs. One of their spokesmen railed that "more than two billion people do not have regular access to the critical medicines they need" and that, "every year, 10 million people die from diseases because drug pricing blocks access to effective treatments."

The merits of these arguments are, of course, arguable, but they stand uneasily with statistics such as those featured in this year's *Pharmaceutical Industry and Global Health: Facts and Figures* report, released by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). According to the report, between 2011 and 2014, drugs and vaccines against malaria saved the lives of 1.14 million African children. Between 2000 and 2014, immunization campaigns helped reduce the number of deaths from measles in Africa by 79%. And in 2014, the pharma industry was the third-largest funder of neglected disease research, investing over $534 million.

As the IPFMA report also points out, the private sector produces nearly all the medicines and vaccines on the market. But the industry is not immune to external or indeed internal pressures; pharma is dealing with rising R&D costs, more stringent testing, stricter reporting requirements, and a volatile wave of political and pricing pressures in its established markets. Similarly, there is always the need to appease stockholders and sustain growth in the face of corporate social responsibility (CSR) obligations and efforts to address health crises in low-income countries.

To maintain its drive, IPFMA observes, the industry has had to adopt new models of innovation, such as joint ventures between pharma companies and partnerships with the public sector, collaborations that "facilitate the sharing of expertise, know-how, and technologies."[2]

One example where collaboration is essential to reach a health-crisis solution is the race to find a vaccine for the Zika virus, which raised worldwide alarm following reports of an outbreak of babies born with microcephaly in Brazil in 2015. Takeda is one of several companies partnering with the US's Biomedical Advanced Research and Development Authority (BARDA) to develop a vaccine to support the Zika response in the US and affected regions around the world.

Rajeev Venkayya, president of Takeda's global vaccine business unit, told *Pharm Exec* that such programs are not sustainable by pharma companies alone. For infectious diseases for which there is an established epidemiology and an established market, he says, companies are more likely to make investments at risk, but the Zika program "is quite different from a program with a competitive dynamic."


Rajeev Venkayya

Venkayya explains: "There is inherent risk in an emerging infectious disease program that you will develop a product and the disease will not be there, or the recommendations will not fit with the profile of the vaccine that you have been developing, or there will be a lot of competition in the market. There are lots of things that make it hard for companies to justify such a program."

Therefore, the financial "de-risking" of the Zika program—in the form of the US government's commitment to fund its R&D

expenses—is essential for such endeavors. With BARDA taking care of much of the financial investment, it is "an easier program to take on, even if the vaccine ultimately has uncertain uptake because of changes in epidemiology or other factors," says Venkayya.

There have to be different mechanisms to support preparedness for unknown or low-probability, high-impact outbreaks of disease, he explains. "It is essential for governments to take on this challenge because it is not something that companies are going to be able to do on their own. That de-risking gives us the ability to go to our governance bodies and to the stockholders of Takeda and say this is a program that represents the right thing to do on behalf of public health."

This does not mean Takeda isn't making substantial investments itself in the program. "We're committing our facilities, our people, our know-how, our technology platforms," says Venkayya. And even government support does not eliminate all risk. Earlier this year, it was reported that Sanofi had pulled out of its Zika vaccine partnership with BARDA, the company citing BARDA's decision to cut its funding. This followed months of increasing tension between Sanofi and its government partners about pricing guarantees.

Takeda's Venkayya admits that when the decision-making on the progression of a program is shared by the partners, it adds a level of complexity. But, for his part, he adds that Takeda's position was well understood from the outset.

"From the time we applied to BARDA, we knew that it was an options-based contract, subject to performance against pre-specified milestones as well as the overall context," he says. "When we entered into this agreement, we agreed on the vaccinology approach that we'd be taking and also agreed on a high-level development strategy."

Venkayya adds: "We are basically in execution mode and we don't really have the time or luxury of adjusting our plan based on what others are doing; the most important goal for us and for BARDA is to get a safe and effective vaccine to people who need it as soon as possible and that is what we're focused on."

> "There is inherent risk in an emerging infectious disease program that you will develop a product and the disease will not be there"

At the moment, the Takeda–BARDA Zika vaccine program has a US focus and is in its early stages. A major near-term milestone is the commencement of Phase I clinical trials, which are expected to begin before the end of the year. Beyond that, Takeda "has an aspiration to make a safe and effective Zika vaccine available to all populations who need it," although Venkayya notes that this will require additional work and investment.

Striking a balance

While outbreaks such as Zika fuel emergency responses, the industry's efforts to combat more widespread and ongoing global health crises continue apace. Despite the claims of the anti-pharma activists, the industry has played a significant part in reducing the number of worldwide AIDS-related deaths from a peak of 2.5 million in 2005 to an estimated 1.1 million in 2015. As IPFMA reports, pharma has developed more that 35 antiretroviral treatments (ARVs) for HIV/AIDS, which have been essential to control the epidemic. Also, industry programs to supply generic drugs, to provide education, and to build capacity are helping to erode the barriers that restrict access to medicines, contraceptives, and sexual health awareness among low-income populations.

FAST FOCUS

» According to the World Health Organization, the global average life expectancy increased by five years between 2000 and 2015, the fastest rise since the 1960s. In turn, global spending on healthcare is expected to increase to $18.28 trillion worldwide by 2040.

» The growing prevalence of chronic diseases is impacting both developed and emerging countries. Deloitte reports that obesity, cardiovascular diseases, hypertension, and dementia are becoming persistent, widespread health problems and are challenging public health systems to meet increasing demand for drugs and treatments.

» An estimated one in 10 medicines circulating in low- and middle-income countries is either substandard or falsified, according to new research from WHO. Since 2013, the agency has received 1,500 reports of cases of substandard or falsified products. Of these, antimalarials and antibiotics are the most commonly reported. Most of the reports (42%) come from the WHO African region, and 21% each from the Americas and Europe.

At the forefront of the fight against HIV/AIDS is Mylan, which currently supplies ARV medicines to 6.4 million people with the disease in more than 100 low-income countries. In its 2015 Social Responsibility report, Mylan nobly announced that "we refuse to allow the thin margins earned in such countries to dissuade us from fighting the good fight. In fact, we continue to invest in additional capacity to expand access." Key to building this capacity was Mylan's 2007 acquisition of India-based Matrix Laboratories, one of the world's largest suppliers of active pharmaceutical ingredients (APIs), including those used for HIV/AIDS drugs. Ten years on, Mylan has a 40% to 45% share of the API market for generic ARVs for the treatment of HIV/AIDS in some low-income countries.

In September, a consortium including the governments of South Africa and Kenya, the Joint United Nations Program on HIV/AIDS (UNAIDS), the Bill & Melinda Gates Foundation, and Unitaid announced a pricing agreement to accelerate the availability of the first affordable, generic, single-pill HIV treatment regimen containing dolutegravir (DTG) to public sector purchasers in these countries. Mylan is one of the program's two suppliers, and has made a further three-year commitment to bringing down the price of the treatment.

"Fighting the good fight," however, cannot be done with corporate abandon. Rajiv Malik, formerly CEO of Matrix and now president of Mylan, has significant experience in running a low-margin, high-volume business model, adept at supplying vital treatments for patients in low-income countries, while also committing to long-term company growth and sustainability. He told *Pharm Exec*: "Sometimes you are forced to think about how far and how deeply you can continue with these commitments. There is always a fear from a business point of view, because there is competing demand for the capital. It's a balancing act."


Rajiv Malik

But while Mylan experienced significant challenges in the US market last year, this did not affect what the company is doing in the developing nations. In fact, it expanded. For example, through its Indian subsidiary, Mylan acquired a women's healthcare business from Famy Care, a specialty company with global leadership in generic oral contraceptive products.

"We are now working with partners like the J&J Foundation to continue to provide access to such products for women in Africa and are part of the UN's Family Planning 2020 commitment," says Malik. "And last year we launched a generic treatment for hepatitis C in India, where roughly 12 million people are infected with the virus. So, we are doubling our efforts. We continue to raise the bar and continue to invest in these critical treatment areas."

India's importance to Mylan's activities is paramount. Mylan's acquisition of Matrix in 2007 was the largest ever takeover in India pharma. More than half of the company's workforce is based in India, making the country its largest product-sourcing base. India is also key to securing future long-term growth and profitability in its low-margin global health activities.

"It is a huge country from an R&D and supply chain perspective," says Malik. "It is also the hub of our business for products we produce for many developing countries; it is where we conduct our selling and marketing operations to reach patients in these underserved areas."

Over the last five years, Mylan has begun to focus on India as a market itself, first with

Measuring Corporate Social Responsibility

How can you measure the resources pharmaceutical companies contribute to global health? It's difficult to calculate the efforts that go into making sure all parts of the world, from big metropolitan areas like Los Angeles to a small developing village in the middle of Africa, have the medications, vaccines, and other therapies they need to treat their people. It can include many factors that are tough to quantify—such as research time, R&D efforts, collaborations, products, and more.

Experts say one of the ways to attempt to measure this is by looking at companies' corporate social responsibility. For example, the Reputation Institute (RI) releases an annual CSR RepTrak report, a study that measures the reputation of the most socially responsible companies globally.

The rankings are based on each company's "pulse." The pulse is an emotional connection that consumers have to brands. Additionally, the results are broken down into performance in citizenship, governance, and workplace dimensions.

The chart below depicts 2017 reputation metrics for the world's most socially responsible pharma companies in eight countries.

— Christen Harm

Most Socially Reputable Pharma Companies

Pharma CSR RepTrak® is a study that Reputation Institute conducts annually to measure the reputation of the world's most socially responsible, highly-regarded and familiar pharma companies in eight countries (Brazil, Canada, France, Germany, Italy, Spain, UK, US).

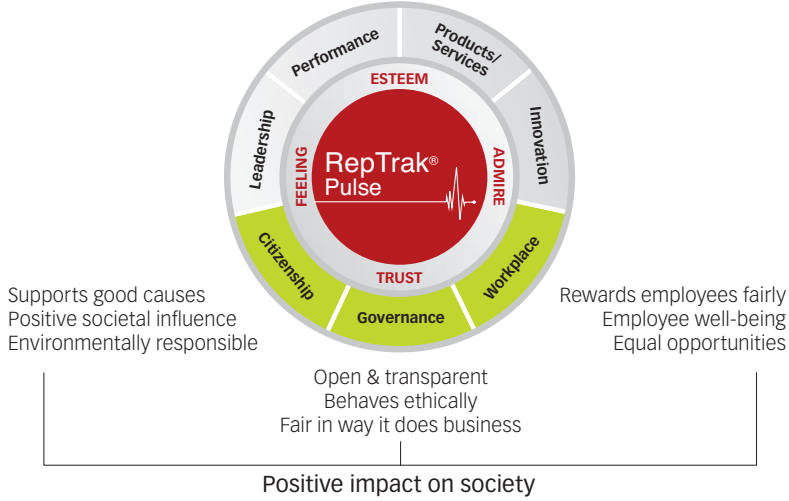
It is the largest Pharma reputation study, with ~6500 ratings collected in Q1 2017.

Rank	Company	2017 CSR RepTrak®
1	AbbVie	73.4
2	Takeda Pharmaceutical	72.6
3	Novo Nordisk	72.4
4	Janssen Pharmaceuticals	71.4
5	Gilead Sciences	71.1
6	MSD (Merck Sharp & Dohme)	71.0
7	Allergan	70.6
8	Eli Lilly	70.5
9	Roche	70.4
10	Merck KGaA	69.8
11	AstraZeneca	69.5
12	Sanofi	69.4
13	Novartis	69.2
14	Bristol-Myers Squibb	69.0
15	Bayer	67.7
16	GlaxoSmithKline	66.4
17	Pfizer	66.3

Source: Reputation Institute

2016 average = 68.2 (18 companies with a strong score); 2017 average = 67.5 (11 companies with a strong score)

CSR RepTrak® reflects performance in Citizenship, Governance and Workplace dimensions



HIV drugs, then oncology (particularly breast cancer, building affordable cancer care through several CSR programs), and latterly in the hep C space. "We have tried to keep the focus on the disease states in India that need a lot of attention," says Malik. "Financially, we just broke even, but we don't invest in India and other rest-of-world (ROW) markets just from the perspective of returns. It is a case of building a base that is going to funnel the growth of our business. These markets may not drive your bottom line in a significant way, but they can definitely give you top-line growth and are a source of durable cash flow."

Strengthening infrastructures

Using the platforms established by low-margin business models and philanthropic/CSR initiatives as a base to secure further growth, reach, and stability across low-income and developing nations is also a long-term objective of Merck & Co.'s Merck for Mothers. A 10-year, $500 million program focused on improving the health and well-being of mothers during pregnancy and childbirth in the US, India, Zambia, Senegal, and Uganda, Merck for Mothers was established in 2011 to address an urgent problem: 800 women a day—one woman every two minutes—were dying from preventable causes and complications from pregnancy and childbirth.

Since its inception, Merck for Mothers has "managed to reach over six-and-a-half-million women and improve their access to both quality maternity care services and quality modern contraception," Dr. Mary-Ann Etiebet, Merck for Mothers' executive director, told *Pharm Exec*. The program's primary purpose, of course, is to improve the health of mothers and to save lives; in the longer term, says Etiebet, it is about "how we use this


Mary-Ann Etiebet

type of investment to strengthen healthcare systems" and how it "can actually benefit, more broadly, countries and other companies working in these areas."

In Senegal, for example, Merck has helped to establish and transition to government ownership a "transformative, well-functioning supply chain system that is already improving access to critical medicines to all people." A major barrier to family planning in Senegal was a lack of availability of contraception. Products were procured, but sat inside central warehouses, often failing to reach the "last mile" primary care facilities where women of reproductive age sought care.

Industry programs to supply generic drugs, provide education, and build capacity are helping erode the barriers that restrict access to medicines and contraceptives among low-income populations

In response, Merck for Mothers partnered with the Gates Foundation, IntraHealth International, and the government of Senegal to scale up a supply chain model adapted from the private sector, which, says Etiebet, has improved the logistics, forecasting, and delivery of contraceptives at health facilities throughout the country.

"The Senegal supply chain project has an impact that is wider than on maternal mortality alone," explains Etiebet. "By improving the performance of the supply chain for contraceptives in Senegal, we were able to extend that model so that the government is now using it to supply over 90 essential medicines. By working on this one issue, we have been able to strengthen the health system in the country. This is the way we like to think about Merck for Mothers—how we can make sure our investments have broader, longer-term impacts."

The supply chain issue faced by Merck for Mothers in Senegal is symptomatic of a litany of challenges facing pharma's activities in global health. Obstacles, ranging from underdeveloped infrastructures and disparate healthcare systems to poor transportation and lack of clean water and sanitation facilities, must be negotiated and overcome to establish effective access to medicines in low-income countries.

Not the least of these problems are the widely varying standards for market entrance and regulation. Malik admits that some companies could do more for global health "if in this part of the world we could have a harmonized framework of sustainable regulations. That would go a long way to motivating industry to come in and make a change."

Dueling commitments

In global health, "fighting the good fight" cannot happen without a number of enabling conditions that involve more than reducing the price of medicines. As the IPFMA report highlights, addressing the issues of regulation, corruption, logistics, poverty, and wealth inequality is a "complex challenge that requires

long-term commitment from government, civil society, and the private sector." Added to that is a pharma company's fiduciary duty to maximize shareholder value and secure its own long-term survival.

The investment banker Lawrence Perkins wrote back in 2001 that "at the end of the day, the company's future existence depends on the bottom line of the income statement. Pharmaceutical companies are no different." While this observation may conveniently sidestep some of the more complex ethical considerations of the global health agenda, it remains an essential truth of the market-driven industry. PE

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Partnerships Hold the Key

Amid a widening net of global health threats, alliances in research and response may be more crucial than ever

By Michelle Maskaly

The right business partnership can be critical to any company's success. Specifically, in the pharmaceutical industry, partnerships between pharma or biotech companies and nonprofit organizations or foundations prove that theory—because by pooling their resources, these entities are working together to combat some of the world's most serious health problems.

Polio, antibiotic resistance, AIDS, and Ebola are just a few of the global problems these partnerships are helping to fight.

Many of the foundations and nonprofits *Pharm Exec* spoke with said pharma companies are key partners, because they specialize in what is needed to create and deliver new solutions to global health challenges. Pharma's essential expertise, such as translating science into products that save lives, safely and effectively testing these treatments, and then manufacturing them in the required quantities, are critical to achieving global health goals.

These types of partnerships are all unique and can make a big difference. Often, the relationships are not just centered around one-off projects. For example, last year, Bayer worked with the CDC Foundation to assist with two critical aspects of the Zika virus response in Puerto Rico. Those included providing women and their partners who want to delay or avoid pregnancy during the Zika outbreak with improved access to a range of contraceptive methods, and giving additional protection to families who want to sleep under mosquito-repelling bed nets. Bayer did this by providing the CDC Foundation with significant product donations of intrauterine devices (IUDs) and oral contraceptives, as well as concentrated mosquito insecticide tablets and insecticide-treated bed nets.

At the time, Dr. Judith A. Monroe, president and CEO of the CDC Foundation, said in a press release, "This is a comprehensive public-private partnership aimed at helping CDC extend its Zika virus response. … To get ahead of this potentially devastating new threat, we must continue harnessing the resources and expertise of private sector partners to boost our national and local response efforts."

According to the CDC Foundation, 138,000 women in Puerto Rico were, at the time, at risk of unintended pregnancy and were not using one of the most effective or moderately effective forms of contraception. Bayer's donation included up to 50,000 IUDs and 40,000 oral contraceptive units. In addition, the company provided 10,000 bed nets for use in Zika prevention kits for pregnant women and more than 700,000 mosquito-control tablets, which can be used to treat bed nets, curtains, and other household items to repel mosquitoes.

Rare diseases

Partnerships span across all diseases and can be especially helpful in the treatment of rare or orphan drug conditions. Take neglected tropical diseases, for example, which are a diverse group of communicable diseases that prevail in tropical and subtropical conditions in 149 countries.

"To get ahead of [the Zika virus] threat, we must continue harnessing the resources and expertise of private sector partners"

Most recently, a three-pronged partnership struck between the World Health Organization (WHO), the Mundo Sano Foundation, and Chemo Research, a division of Insud Pharma, is helping to make an essential antiparasitic medicine for the treatment of Chagas disease widely accessible to children. Treatment with benznidazole in the early stages of infection can cure this potentially life-threatening condition, but, currently, very few people are able to access diagnosis and treatment services, according to WHO.

Benznidazole, manufactured by Chemo Research, is commonly used as a first-line therapy for Chagas disease. Although it has existed for more than 40 years, the drug was not registered by any world regulatory agency until August of this year, when the FDA approved it for the treatment of children aged 2 to 12. It marked the first-ever approval of a therapy for Chagas disease in the US, where, reportedly, at least 300,000 people are estimated to be affected by the illness.

"We are working to enhance access to this medicine to people who need it the most," said Silvia Gold, president of the Mundo Sano Foundation, in a press release. "We are proud to have Insud Pharma as a reliable industrial partner capable of expanding quality-assured affordable benznidazole. Our hope is to transform the dynamic of access to treatment for Chagas disease patients throughout the Americas and beyond."

About six to seven million people worldwide are estimated to be infected with *Trypanosoma cruzi*, the parasite that causes Chagas disease.

With some rare diseases, a medicine donation program is a popular type of partnership. One expert at WHO told *Pharm Exec* that often the product being donated has existed, but the market was very small. So instead of carving out numerous small markets, filled with patients unable to afford the medication, companies agree to work with a foundation or nonprofit who has direct access to the patient populuaton, and create a donation program.

Preventative care

It's great to have partnership programs in place for the treatment of global diseases, but what if more of these international health epidemics were completely preventable? That's the goal of the Coalition for Epidemic Preparedness Innovations (CEPI), a public-private coalition launched at the beginning of

Continued on Page 49

Novartis Pharmaceuticals Canada Inc.

Changing the practice of medicine

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

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HEALTHCARE & LIFE SCIENCES REVIEW

CANADA

INTO THE SPOTLIGHT

Canada celebrates 150 years of independence in 2017 as one of the most prosperous, diverse and stable countries on earth. With one of the highest GDPs per capita in the world at USD 42,158, Canada is also expected to lead the G7 in terms of economic growth in 2017. However, contradictions abound in the country's healthcare and life sciences landscape: the country benefits from a universal healthcare system but lacks universal drug coverage, resulting in Canadians having one of the highest out-of-pocket spending on drugs in the world. At the same time, despite having the tenth largest pharma market in the world with 2.5 percent of global spending, and being the birthplace of medical breakthroughs from insulin to the discovery of stem cells, Canada seems to be punching below its weight when it comes to health innovation.

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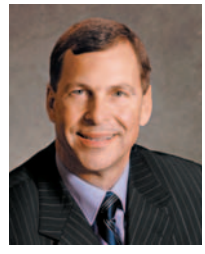
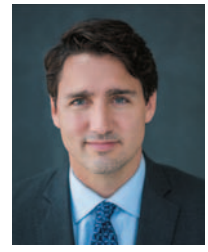
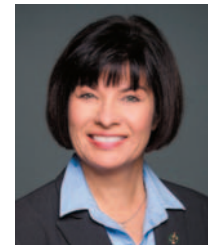
In 1987, Bill C-22 offered industry patent protection in exchange for a commitment to invest ten percent in R&D locally and to offer 'non-excessive' prices, laying the foundation for a stable relationship between industry, government and Canadians for nearly three decades. In recent years however, the national healthcare landscape has seen significant flux, from the renegotiation of the Canada Health Accords, which determine the transfer of federal healthcare funds to provinces and territories, to a slate of proposed regulatory reforms involving Health Canada, the federal regulatory authority, for which Budget 2017 earmarked about CAD 140 million in new funding to advance.

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

Justin Trudeau, prime minister; Ginette Petitpas Taylor, minister of health

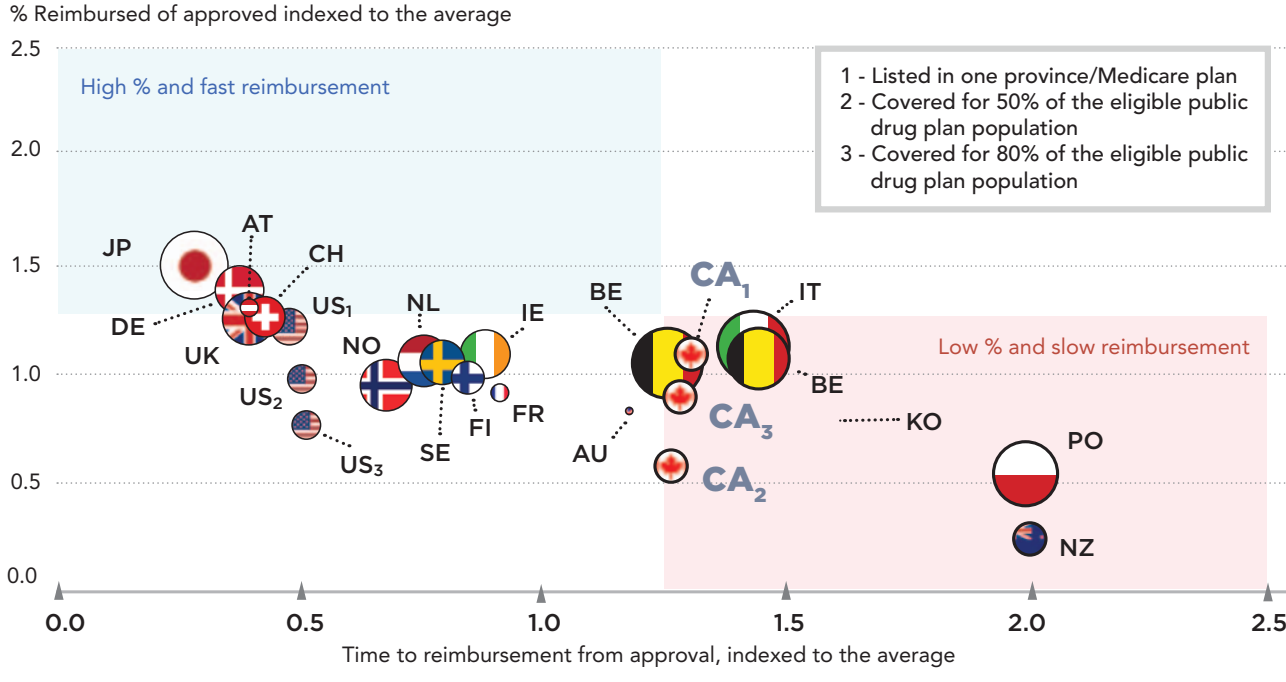
In the words of The Right Honorable Justin Trudeau, Prime Minister of Canada, "we are investing in this sector to ensure the continuous improvement of patient care and to drive economic prosperity. This focus on the future will help position Canada at the forefront of the global health innovation efforts and ensure that our health system is sustainable and responsive to changing needs." Minister of Health The Honorable Ginette Petitpas Taylor adds, "We are proud of Canada's legacy of medical R&D and innovation. Canadian discoveries were created on a foundation of basic science in the public sector. Our Government is committed to supporting our scientific communities to ask the critical questions, identify our R&D gaps, explore solutions, and innovate."

A SHIFTING PARADIGM

Industry experts know that Canada does not have one healthcare system

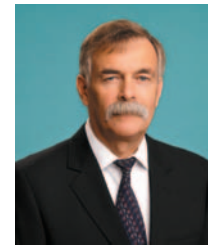
NEW MEDICINES REIMBURSEMENT COUNTRY COMPARISON

Bubble sizes pertain to the percentage of new medicines reimbursed without restrictions (i.e. fully reimbursed) indexed to the average across countries



Source: Innovative Medicines Canada 2016

but 14 health systems. The federal system oversees market approvals while leaving pricing and reimbursement decisions to the 13 provinces and territories, which negotiate their own private deals individually with the industry – resulting not only in higher-than-average prices within the OECD but also inequity of access across the country. Earlier this year, former Minister of Health Jane Philpott brandished the figure that one in ten Canadian patients cannot afford their medicines. As fiscally constrained public payers try to stem rising healthcare costs, the past decade has seen harmonization initiatives like the pan-Canadian Pharmaceutical Alliance (pCPA), as well as a reevaluation of existing structures like the Canadian Agency for Drugs and Technology in Health (CADTH) – the pan-Canadian HTA body – and the Patented Medicine Prices Review Board (PMPRB), the pricing watchdog body guarding against 'excessive' pricing.



Pamela Fralick, president, Innovative Medicines Canada; Jim Keon, president, CGPA

Douglas Clark, executive director at PMPRB, explains, "There is a great deal of internal reflection going on at the federal level about how well a policy balance conceived 30 years ago can address the challenges of the modern-day pharmaceutical marketplace," admitting that "Canada's regulatory landscape for patented pharmaceuticals has been critiqued as a relay race. Our objective is to adopt a more risk-based approach to regulating that builds on the efficiencies in the system, not add a redundant step to the relay race."

AstraZeneca's president and CEO, Ed Dybka stresses, "The [historical] accord between industry, government and Canadian patients worked very well for the ensuing few decades, with good performance across key indicators: market access, pricing, R&D activity, and patient outcomes. In the past five years, many elements of this foundation are being challenged, manifesting primarily in the increasing delays in market access timelines. Where it previously would take only months to get a product reimbursed, now we are looking at a time frame of up to two years." He adds frankly, "I would characterize the overall market access environment as rather chaotic




Ed Dybka, president and CEO, AstraZeneca; Alok Kanti, president and CEO, Bayer; Janice Murray, president, Novartis; Peter Brenders, general manager, Sanofi Genzyme

and difficult to work in." According to the Canadian Institute for Health Information (CIHI), only 37 percent of new medicines received public reimbursement across the country between 2010 to 2015.

While companies have to adjust to market dynamics in every country, German giant Bayer's president and CEO, Alok Kanti, points out, "other countries like Italy and Spain also have complex regulatory and policy frameworks. Fundamentals cannot be changed, but countries can promote better market dynamics." He suggests, "There could be fewer regulations, more collaborative discussions and more harmonization between the provinces, which would help ameliorate the existing delays in approval, pricing and reimbursement", if not even "increasing regulatory harmonization with US or EU regulatory entities [to] reduce the regulatory burden on industry, especially for smaller companies, as well as reduce friction within the system" – most crucially – "without taking away the independence of Canadian regulators or the provinces' constitutional mandates on healthcare."

Peter Brenders, general manager of Sanofi Genzyme, strikes a stronger note: "I am worried for the future of patient care in Canada. As an industry, we have always tried to work collaboratively with the provinces and territories to help manage the expectations in terms of pricing and to focus on value. The noise and controversy from the US certainly does not help – even though these incidents would never happen in Canada."

He summarizes bluntly, "We cannot be reduced to a commodity supplier. Today's sales pay for tomorrow's cures."

Pointing to the federal government's innovation agenda, he adds, "we have seen new investments in early-stage R&D and science, but innovation is more than just funding early or even applied research. It is walking the talk and adopting innovations when they are developed."

For Janice Murray, president of Novartis Pharmaceuticals, the second-largest pharma company globally, "Every day, we see how difficult it is for patients to access new medications." This is why she hopes to bring Novartis' global expertise to bear locally. "As a global pharma company, we work within a multitude of different healthcare systems around the world, which means we are exposed to what works and what does not. Aside from the policy level, we are also working with individual clinics and hospitals, whether in terms of helping healthcare practitioners better understand the patient journey, identifying areas of costly fragmentation, or simply how to optimize the way patients are treated."

LEADING PHARMACEUTICAL COMPANIES IN CANADA 2016

	LEADING COMPANIES	TOTAL SALES ($ BILLION)	MARKET SHARE (%)
1	JOHNSON & JOHNSON	2.93	11.4
2	NOVARTIS	1.24	4.8
3	TEVA	1.19	4.6
4	APOTEX	1.19	4.6
5	MERCK	1.14	4.4
6	PFIZER	1.06	4.1
7	ASTRAZENECA	0,93	3.6
8	ROCHE	0.88	3.4
9	GILEAD	0.88	3.4
10	ABBVIE	0.86	3.4

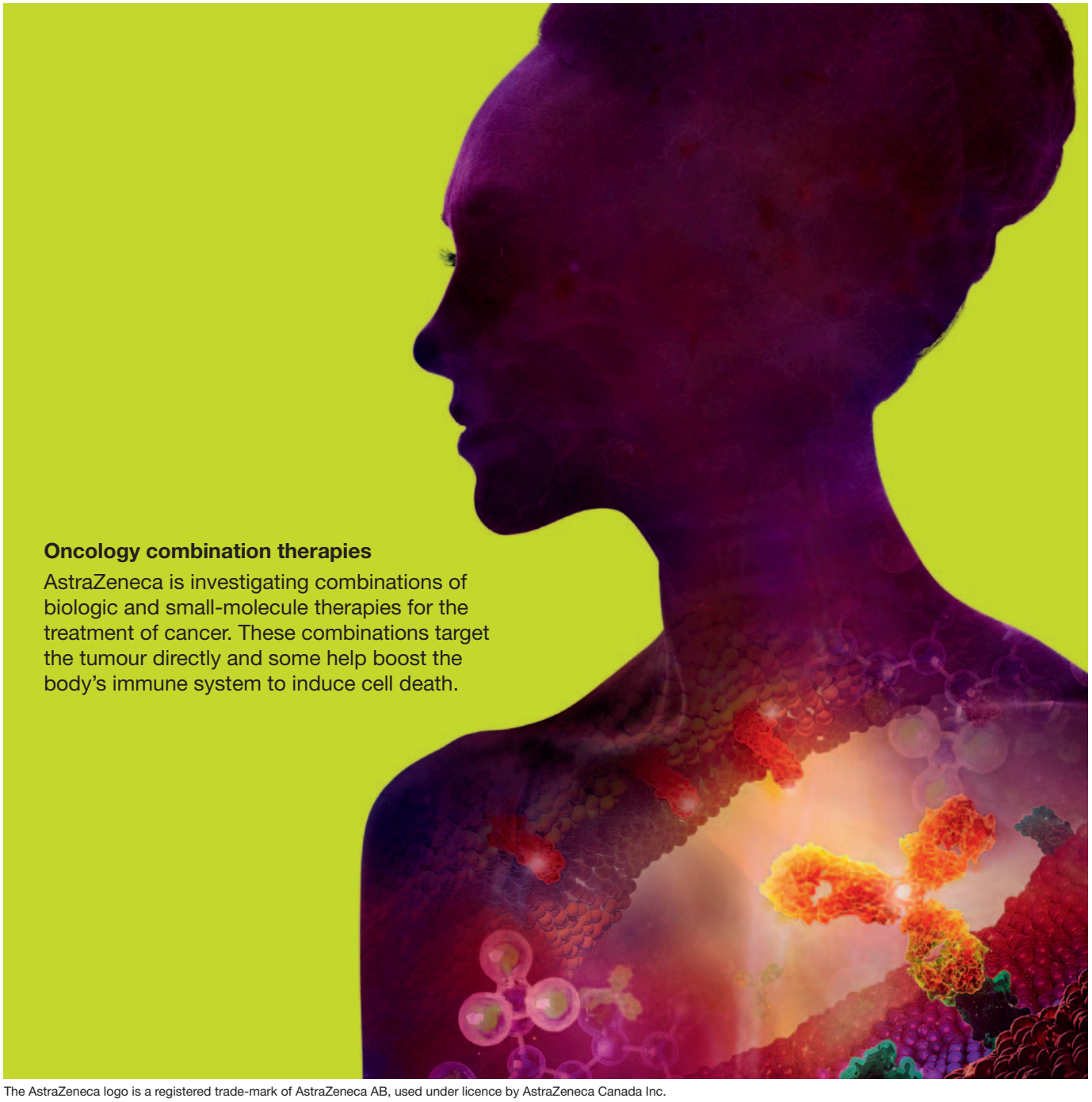
Source: Government of Canada 2016

What Science Can Do

AstraZeneca

At AstraZeneca, we believe in the power of what science can do to transform serious diseases like cancer, heart disease, diabetes, COPD and asthma.

Each and everyone of us is bold in the belief that science should be at the centre of everything we do. It compels us to push the boundaries of what is possible. To trust in the potential of ideas and pursue them, alone and with others, until we have transformed the treatment of disease.



Oncology combination therapies

AstraZeneca is investigating combinations of biologic and small-molecule therapies for the treatment of cancer. These combinations target the tumour directly and some help boost the body's immune system to induce cell death.



Michael Tremblay, president, Astellas; Kennet Brysting, general manager, Gilead Sciences; Ronnie Miller, president, Roche

Industry veteran Michael Tremblay at the helm of Astellas puts some perspective on the numbers. "Drug spend is such a small component of overall health spending: 15 percent in total and around six percent for branded pharmaceuticals. The problem of unsustainable healthcare spending is far larger than the actual or perceived 'cost' of our industry. Eliminating the 'silo' approach will help guide innovation in the right direction because it will ensure that the products we launch generate savings within the larger healthcare system, and that those savings are seen and valued by payers."

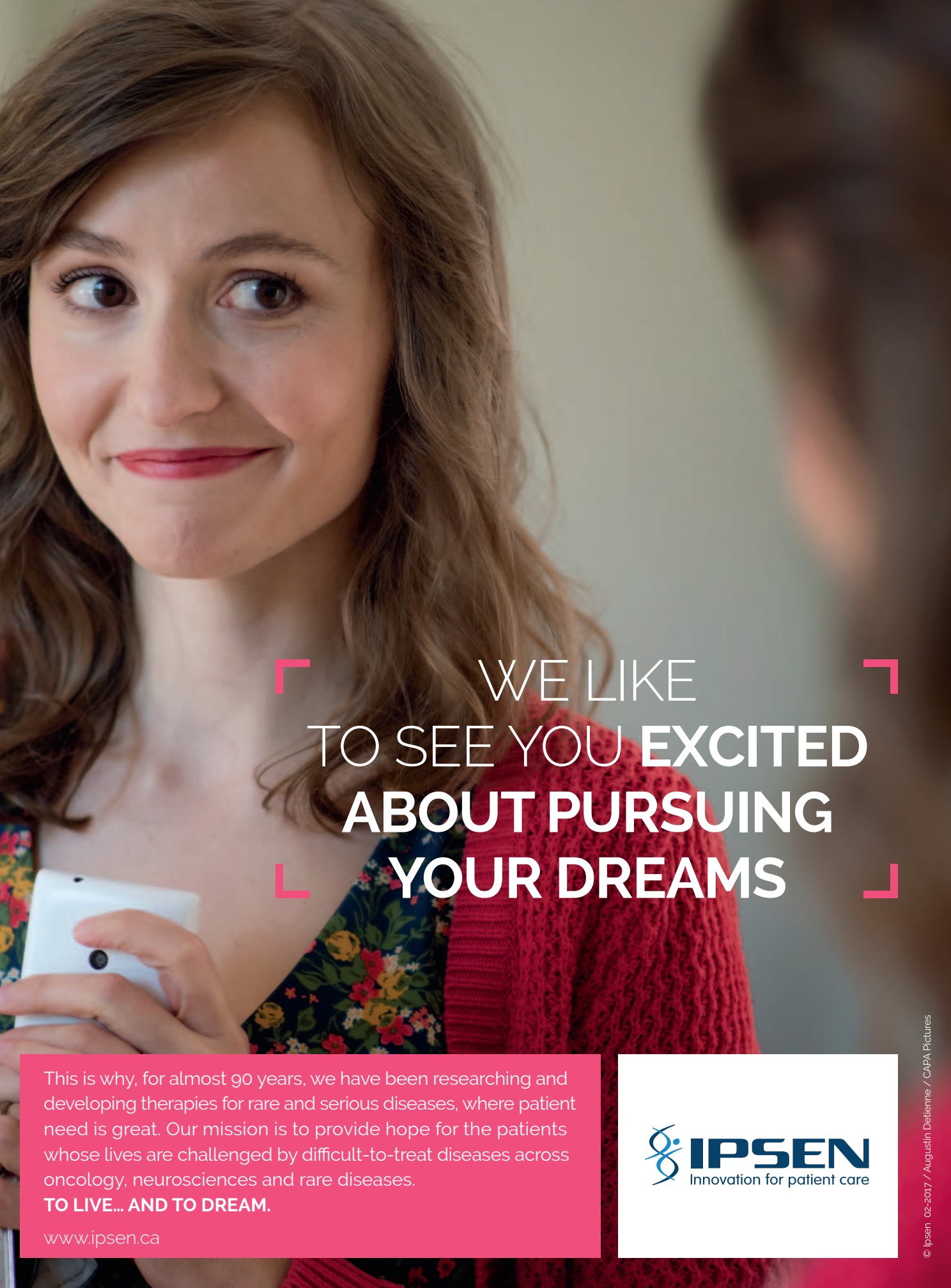
TEARING DOWN THE SILOS

However, market access is not simply an issue of pricing but patient access to innovation. While healthcare spending is usually seen as a cost, healthcare companies drive innovation and economic development – and Canada remains a Tier One market for most international pharma companies because of its market potential. With price pressures intensifying in the wake of proposed regulatory changes, the industry is seeing the need to advocate for increased dialogue between all relevant stakeholders. The long timelines of the industry also complicate matters. Bayer's Kanti outlines, "If a market or society makes the decision today that they do not want to pay for an innovation in a therapy area today, the true impact will only be felt six or eight years down the line and will take a long time to correct."

Novartis' Murray adds, "The pharma sector is highly innovative and should be seen as a valuable partner within Canada's innovation agenda. But there needs to be a process through which we can participate. It is not just about a company investing some money in innovation initiatives." Nevertheless, "Novartis is one of the largest R&D engines in the country [having launched 11 new medications in the past five years and currently conducting over 100 clinical trials]. The Federal government recently announced a proposed CAD 950 million (USD 744 million) 'superclusters' initiative and we would be very keen to participate but, at the same time, we still need to contend with all the uncertainty and lack of visibility surrounding the market access piece."

Kennet Brysting, general manager of Gilead Sciences, a company best-known for its costly breakthrough hepatitis C cure, sees this balance as vitally important. He outlines, "Gilead has had a fascinating journey in HCV. Previous medicines were associated with severe toxicities and could not cure the majority of patients. The subsequent products which we launched have really transformed this therapeutic area, curing 98 percent of all patients." The last one they launched "has been shown to cure 98 percent of the remaining two percent", and therefore, "we can now turn our focus to the next challenge, which is to help eliminate the disease in Canada: screening, diagnosing and linking patients to the appropriate care. We consider ourselves leaders in hepatitis C, so we need to take an active role in supporting initiatives within this space."

Unfortunately, Brysting muses, "It has been a challenge to launch these kinds of curative treatments from a payer's perspective, because of the payer's need to absorb the full cost upfront [even though] the system is relieved of the long-term costs of treating the patient. This needs to be taken into consideration. Chronic dis-



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Québec Pharma Exceptionalism

Gaétan Barrette, Québec minister of health and social services

Québec is one province that has undertaken healthcare reforms while appreciating the need to join hands with industry when it comes to the promotion of health innovation. Outspoken minister of health and social services, Dr. Gaétan Barrette outlines, "Since 2014, Québec has been trying to transform the system significantly." One of his first initiatives was to merge a number of health institutions within the province into a more integrated organizational structure.

In addition, "Québec has the most aggressive approach of any province in this country [for generics pricing]", having pushed through legislation in 2016 allowing for a tendering process for generics procurement". This prompted the industry association to agree to a 40 percent reduction in generics prices, or "an annual cost reduction of over CAD 1.5 billion (USD 1.17 billion) over the next five years."

At the same time, he acknowledges that "there are very complex dynamics at work here. The sustainability of the healthcare system is indirectly linked to the sustainability of industry." Thus, the province announced in May 2017 an ambitious five-year Life Sciences Strategy to propel Montréal into the top five life sciences clusters by 2027, with CAD 205 million (USD 160.6 million) in funding invested over the next five years and the target to attract CAD 4 billion (USD 3.13 billion) in private investments by 2022.

This initiative has been widely lauded by many industry members. AstraZeneca's' president and CEO Dybka praises, "The Québec government has laid out a very progressive plan, with finance, health, and economy, science and innovation ministries coming together to grow and promote the entire life sciences ecosystem in the province. We need more of such initiatives across the country." In the interest to drive this, he adds, "I am presently the co-chair of Life Sciences Ontario and also sit on an expert committee advising the Ontario government on the creation of a provincial life sciences strategy, much like the one Québec just announced in May. Canadian governments could play a much bigger role, firstly in terms of appreciating the value of the existing life sciences ecosystem, and secondly, by investing to make this environment even bigger and better."

Dominique Anglade, Québec deputy premier, minister of economy, science and innovation, and minister responsible for the digital strategy

Supporting this is the provincial HTA body, INESSS (*Institut National d'Excellence en Sante et en Services*), whose president, Luc Boileau, highlights, "the concept of 'added value' is embedded in our mandate. We are piloting POETIS, where we assess the product's efficacy across the entire lifecycle of the disease to understand the overall value it can bring to the healthcare system and patient." Boileau adds, "the distinction between medicines and medical devices is blurring with the advent of innovations like cell therapies, gene therapies and nanotechnology. We need to review our processes to be able to take these ground-breaking developments."

Luc Boileau, president, INESSS

Québec Deputy Premier, minister of economy, science and innovation, and minister responsible for the digital strategy, Dominique Anglade sends a strong final message, "I would like to exhort the private sector to invest more money in R&D. We are here to match any industry contributions and provide a lever to drive economic development – but industry needs to partner with us."

eases are different because the cost of the disease is spread over many years."

Perhaps in no other area is the need for collaboration as pressing as in personalized medicine, in which treatments are increasingly targeted at smaller patient populations – with greater impact. The rise of 'niche-busters' is creating new challenges not only on the regulatory side but also the reimbursement side. Ronnie Miller, president and CEO of Roche, global leader in personalized medicine, paints a clear picture. "Over the past 17 years, the industry has moved from a 'one-size-fits-all' philosophy of drug treatment to a much more personalized approach involving biomarker-based diagnosis and significant differentiation within a single disease. This will change the dynamics of both drug approval and drug reimbursement. We cannot stay as ostriches with our heads buried in the sand. Companies need to be more flexible when it comes to pricing based on outcomes."

This is an area AstraZeneca is only scrutinizing, because "two-thirds of our portfolio is personalized medicine, where patients must have a corresponding biomarker. Personalized medicine is here to stay. In the future, there will be very few drugs prescribed without an associated biomarker", Dybka explains. "We are focusing on smaller patient populations and greater impact. However, the development cost of innovative medicines remains roughly the same regardless of patient population size. This is taken into account when pricing new medicines."

In this capacity, the innovative pharma association, Innovative Medicines Canada, is positioning itself as a champion of not just the industry but the entire Canadian health ecosystem. President Pamela Fralick affirms, "While acknowledging there can be tensions between health organizations and the private sector, it is key to find areas where both sectors are comfortable with the partnership. My reputation speaks to the fact that first and foremost, I am a collaborator. It may take longer but ultimately, you arrive at better outcomes," she affirms. "As an industry, we are very keen to be able to sit down with the government to have that frank and open conversation, share new ideas and data with them, earn a measure of trust, and work towards better solutions for all, especially patients."

SAFEGUARDING LOCAL GENERICS

Cost pressures – in particular the April 2014 Pan-Canadian Tiered Pricing Framework, as well as pricing agreements with pCPA and Québec's Ministry of Health and Social Services – have also impacted the generics industry. Jim Keon, longstanding president of the Canadian Generic Pharmaceutical Association (CGPA), describes, "We are in a transition period. Lower pricing impacts not only on our manufacturers directly, but also on the entire supply chain."

To exacerbate the issue, Health Canada can only approve a generic drug as long as the patent is cleared – a costly and lengthy legal process. Health Canada also sometimes has additional clinical requirements for a number of products beyond what either the FDA or EMA requires, which increases the regulatory burden. Keon highlights, "Sometimes it seems as if [non-industry members] believe generic products grow on trees. A lot of money goes into developing the active ingredient, doing the testing, developing the clinical trials and submitting it for regulatory approval."

Dr. Jeremy B. Desai, CEO and president, Apotex; Michel Robidoux, president and general manager, Sandoz

Global CEO Dr. Jeremy Desai of Canadian generics champion Apotex,

the largest Canadian pharma MNC, sheds some light on this. "For many types of generics, Health Canada still does not have defined regulatory pathways for market approval. There are many complex products whose patents have by and large expired, but Canadians are missing out on them. Another challenge is that Canada does not have a consistent reference when it comes to regulatory decisions because they sometimes take guidance from the US and sometimes from Europe."

An inevitable result of these market pressures is a steady consolidation of the local generics industry over the past few years, with local players such as Paladin Labs, EuroPharm and Novopharm being gobbled up by MNCs. The top ten players now account for over 90 percent of generics sales. Furthermore, Apotex's Desai laments, "Many companies – branded and generics – have pulled out of manufacturing in Canada due to M&A or strategic reasons. The industry's manufacturing footprint – worth around 10,000 jobs today – is shrinking."

For him, it is a matter of Canadian pride and heritage. He boasts, "Apotex is one of the few companies that can truly claim to be selling products truly made in Canada. Of the 89 million prescriptions we fill yearly, 90 percent are manufactured in Canada – not only as finished products but along the entire manufacturing cycle. Apotex has the largest fine chemical facility in Canada. We even manufacture the plastic bottles that we put our products in!"

Michel Robidoux, president and general manager of global generics giant Sandoz, shares, "within the generics space, Canada is expecting various patent expiries worth a total of around CAD 11 billion (USD 8.6 billion) over the next five years. This means that there are still significant opportunities – as long as we can stabilize the pricing environment." Having been a mainstay of Canadian healthcare – "There is not a single surgery, major or minor, that is conducted in Canadian hospitals without a Sandoz product" – the company is now pushing into new frontiers. Robidoux exults, "we have been transforming the organization by expanding our portfolio into the areas of biosimilars, consumer (OTC), and specialty products – and we believe that these segments will drive growth within Canada as well."

Thinking Out Of The Box

Mark Lachovsky, president, Accel Pharma

Mark Lachovsky, founder and president of Accel Pharma, recounts: "About a decade ago, I saw an opportunity to develop a company with a radically different focus on the generics sector," explaining, "The generics sector in Canada is driven by pharmacies, which make the decision on the particular brand of generic to be used. But the actual payers are the provincial public drug plans as well as private insurance companies. We decided to focus directly on the payers, both public and private … and offered them discounts in exchange for exclusivity on their formularies."

It was not smooth sailing at the start, however. Lachovsky chuckles, "No one likes it when you upset the status quo." Nevertheless, the company established a strong track record as a partner into the Canadian market. "Some companies have chosen to enter the market on their own without fully understanding the complexity of the market, and subsequently faced significant challenges. As a nimble company, we can move and react quickly as changes unfold."

On what continuously drives him, Lachovsky asserts, "The key for us is to find what I call the hidden gems, which are first-to-market generics. We need to do things differently and do things in a smarter way because we are competing against very large companies."

it takes an innovative mindset to change diabetes

Our mission is not only to develop better biological medicines to meet a growing global need, but also to make them accessible to those living with diabetes. With the sharp rise in the prevalence of type 2 diabetes, what was once a rare disease is now considered a global emergency. This highlights the need for action.

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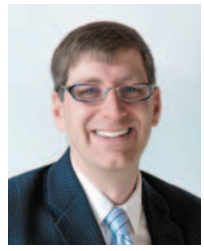



Lyndal Walker, general manager, Ipsen; Patrick Nadeau, vice president business development and marketing, Lupin; Vinod Ramachandran, head, Canada operations, Dr. Reddy's

NEW KIDS ON THE BLOCK

Despite increasing regulatory uncertainty, multinationals have still seen value in entering the market. Success depends on having the right strategy, however. Here, a few managers of new affiliates share theirs.

Ipsen general manager Lyndal Walker shares the story of how the Canadian affiliate started in 2015. "Previously in Canada, Ipsen had an out-licensed product on the market. When we analyzed that product's performance and available market opportunities, in conjunction with Ipsen's upcoming pipeline, we decided that we had to establish a direct presence on the ground in Canada to build face-to-face relationships with healthcare stakeholders here – a top ten pharma market." Two years on, the affiliate lists an impressive number of achievements, from the successful application of a drug establishment license, the approval and reimbursement of a number of products, as well as IMC membership. In addition, a product current under priority review has an active ingredient "fully manufactured and packaged in Canada to supply global markets, so it contributes to Canada medically and economically."

Walker proudly attests, "we are the new kid on the block, but we have made a lot of noise in the past two years. Ipsen Canada has had a great start. We are somewhat of a poster child for the Ontario government now when it comes to attracting more foreign investment in the country."

Global Indian generics powerhouse, Lupin has tailored a strategy to the Canadian market. Patrick Nadeau, vice president business development and marketing, shares: "The company had no presence here before, so it was starting from scratch. Our goal in Canada is to focus on branded specialty products as well as more complex and niche generics that face less competition and see greater medical need as a result of their complexity." For instance, "our first generic is a single-source product and the second is a dual-source product, so these both generate significant savings for governments."

Within the brand space, describing market access in Canada as "a moving target", Nadeau reveals, "the key to success is to bring value." For instance, a core product received strong recommendations from both HTA agencies as there was no alternative. Nadeau boasts, "this pill has been termed 'the miracle pill'" as patients almost 'come back to life'. The strength of this product gave the company a very positive image."

A fellow Indian generics player provides an additional dimension by generating value beyond product innovation. Dr. Vinod Ramachandran, head of Dr. Reddy's, shares, "I am reinforcing Dr. Reddy's brand by ensuring that we continue to be a reliable supplier of affordable and quality generic products to Canadians." He cites, "We have demonstrated that commitment through our 'Infuze' program", providing infusion support for a specific injectable across Canada. Dr. Reddy's pays the cost so there is no out-of-pocket costs for the patients. We are the only company in Canada that is still offering this patient support program for this product."

BACK INTO THE LIMELIGHT

Despite its physical vastness, Canada's population of 36 million represents a meager two percent of the global pharma market, and the challenge of managing 14 individual health systems remains daunting. Nevertheless, buoyed by a robust private sector, Canada has remained a Tier 1 market – but as uncertainty persists in the market access environment, general managers need to be savvier in presenting the right business case for continued, if not increased, investment in Canada.

For Wendy Adams, general manager of Galderma, it boils down to the fundamentals. "We have seen accelerated performance, with double-digit growth across our three business segments, outperforming the Canadian market consistently for the past six years. Our growth is one of the highest among all Galderma affiliates, so we do receive a lot of attention at the global level as an example of a well-managed affiliate." With success comes the responsibility to share best practices globally. Adams highlights, "as the market leader in rosacea here in Canada, we really push ourselves to bring new therapies to market. We also stress executional excellence. There are occasions when companies develop strategies that look good on paper but may not always be available to materialize at market level. Having a strong team and being able to do the local research to adapt strategy to market needs is critical."

Ipsen's stresses the need for proactivity. "I worked it out very quickly that Canada needed to have a profile within the organization." For her, it was helpful that "members of Ipsen's global executive team have had direct experience of the Canadian market [including global CEO David Meek, previously CEO and president of Novartis Canada] – so a conversation about Canada requires very little context." She adds, "When there needs to be context, it becomes a matter of providing the facts on the ground. Once you show the numbers, our growth aspiration and the impact we could have on the global business, people start to understand Canada's potential – and we receive the support we need."

Novo Nordisk's Hilberdink, concurs, drawing upon his stint at HQ. "Through my experience as a former corporate vice president in Global Marketing, I appreciate the constraints that HQ faces when it comes to supporting affiliates. From a pure pharma perspective, the privately reimbursed market helps offset the situation in the public sector, and we are seen as being a good contributor to the global organization. Going beyond sales goals, there are valuable learnings and best practices to be shared globally from this affiliate. Ultimately, it is about framing Canada in a way that makes sense and brings value to the global organization."



Andrew Casey, president, BIOTECanada; Brian Hilberdink, president, Novo Nordisk; Wendy Adams, general manager, Galderma

Lupin Pharma's vice-president (business development and marketing) Patrick Nadeau adds, "As the Canadian affiliate is one of the youngest within the Lupin organization, we really focused on building an organization for the future. We like to see ourselves as the face of the future – where Lupin hopes to be better known as a global specialty pharma player. We can perhaps be a showcase example for other affiliates. For this reason, Lupin's global management team is very supportive of the Canadian affiliate."

CAN CANADA'S BIOTECH INDUSTRY TAKE OFF?

Despite a stellar tradition of innovative medical breakthroughs like insulin, the discovery of stem cells, and critical vaccines, as well as strong Canadian representation on the boards of global pharma companies and heading global clinical trials, Canada is glaringly lacking a homegrown innovative pharma MNC, languishing in the shadow of the world's largest life sciences hotspot to its south. The debate as to whether Canada needs to have its pharma Bombardier – or if the plane has left the tarmac, so to speak – has raged on for decades.

Danish Novo Nordisk's story offers a very interesting perspective on this situation. Hilberdink notes, "One of the top exports from Denmark is insulin, as a result of our activities – and insulin was discovered in Canada in 1921! Sir Frederick Banting, the Canadian Nobel Prize winner that discovered insulin, was actually nominated for the award by Dr. August Krogh, Novo Nordisk's founder." He warns, "Without an anchor biotech pharma company, the great biotechnology discovered in Canada often heads down south."

Custodian of the Canadian biotech industry, Andrew Casey, president and CEO of BIOTECanada, the biotech association, admits. "The first [challenge] is access to investment capital. Canada has a very vibrant life sciences ecosystem, but we have to compete globally to attract and retain promising biotech start-ups because unlike resource-based industries like mining or oil and gas, ideas are very mobile. With 125 pre-commercial biotech companies in the association and probably hundreds more outside, Casey adds, "it would be ideal if we can boost this sector into one of the top three in the world."

In this regard industrial development entity, the National Research Council, investing - and strategically - in the life sciences. Dr. Roman Szumski, vice president for life sciences, reveals, "look[ing] at the track record of drug development in Canada, for small molecule development, the pathway to the US or Europe is very quick because such technology is very easy to patent and these products can be manufactured everywhere. Our sense is that biologics and vaccines are a little harder to shift; there is an art as well as a science to master, so it is more likely that whatever is discovered in Canada will be commercialized in Canada."

While the government has injected significant amounts into various elements along the entire value chain, including, most recently, CAD 515 million (USD 403.2 million) for fundamental research announced by Federal Minister of Science Kirsty Duncan in September 2017, still more seems necessary.

Dr. Fernand Labrie, founder and CEO of Endoceutics, a Canadian biotech success story with huge ambitions to develop into a global leader in women's health, shares, "I had made calculations on the difference between Canadian and American per capita spending on medical research: it was a fivefold difference in favor of the US."

Endoceutics is today "a truly complete Canadian pharmaceutical company with operations along the entire value chain of drug development with in-house R&D in Quebec, manufacturing in Montréal, as well as our first product on the market in the US," their product having obtained FDA approval in November 2016 without a black box. But, he stresses, "the total cost of bringing this product to market was CAD 265 million" (USD 207.5 million) – the price of success. This has paid off, as Dr. Labrie charts: "we have also begun the market approval process for Europe. We hold patents until 2031 in the US and around 2028 in the rest of the world, which puts us in excellent position moving forward." Surely a potential contender for the first ever innovative Canadian pharma multinational company!

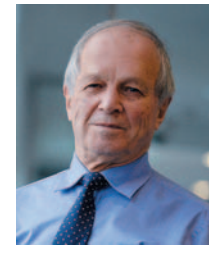
Given the vibrancy of Canada as a top ten market and the presence of MNCs, a recurring concern centers on the impact of international pharma companies on the local biotech ecosystem. Certainly, industry has a role to play in boosting the local biotech sector. Bayer's Kanti reasons, "After CAD 100 million, (USD 78.3 million) investment in life sciences here seems to have hit a block. For this reason, multi-stakeholder collaboration is important. In December 2016, Bayer, along with investment firm Versant Ventures, invested CAD 275 million (USD 225 million) in BlueRock Therapeutics, a global stem cell therapy commercialization venture to develop best-in-class therapies."

Novo Nordisk's Hilberdink chimes in, "Novo Nordisk has Canadians heading our research facilities in obesity and type II diabetes outside of Canada and strong collaboration with world renowned researchers like Dr. Daniel Drucker at the Lunenfeld-Tanenbaum Research Institute at the University of Toronto. As a company, we are making great strides in discovering the cure for type I diabetes, and I certainly hope that part of the IP of that discovery will be Canadian in origin."

Genzyme's Brenders exhorts, "We tend to worry excessively about local companies being bought out by international companies. Canada should not be trying to build a global MNC life sciences company like a Sanofi or a Pfizer; in today's interconnected world, that is not necessary. Canada should be fostering more and more biotech companies to feed into the global life sciences engine, much like a giant incubator."

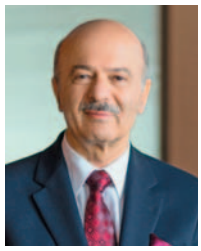
The pharma industry clearly sees potential in Canada, with Johnson & Johnson, for instance, having established its first JLABS – a 40,000-square-foot life sciences incubator – outside the US in Toronto in 2016. Not only can industry provide resources and capabilities, they are often a gold mine of potential products for Canadian entrepreneurs, as in the case of

Dr. Roman Szumski, vice president, life sciences, National Research Council



Dr. Fernand Labrie, president and CEO, Endoceutics

Canadian biotech darling, Clementia Pharmaceuticals, whose August 2017 IPO raised USD 138 million in an upsized deal due to significant investor interest. CEO Clarissa Desjardins shares, "I was working at a think-tank collaborating with Roche on public-private partnerships. A senior Roche executive pointed out a Nature medicine paper to me, which showed that a new class of molecules … were potent inhibitors of new bone formation in animal models of this devastating disease, FOP," FOP, or fibrodysplasia ossificans progressive, is an extremely rare disease characterized by abnormal bone growth in muscles, tendons and ligaments, resulting in increasing mobility and function loss, with sufferers having a median lifespan of 40 years. Desjardins details, the "Roche executive agreed to help facilitate the out-licensing of this molecule if I created a biotech company for it!"



Reza Moridi, Ontario Minister of Research, Innovation and Science; Clarissa Desjardins, CEO, Clementia Pharma; Stefan Larson, CEO, Northern Biologics

Another Canadian biotech success has found both US venture capital and Big Pharma vital partners. Three-year-old Northern Biologics is about to file their IND for their lead oncology candidate, a first-in-class monoclonal antibody that expects to enter clinical trials January 2018. CEO Stefan Larson shares, "Incubating and launching an early-stage drug discovery biotech in Canada with the backing of a [US-based] venture capital firm like Versant Ventures and a strong pharma partner like Celgene allowed us to set up Northern Biologics for success right from day one."

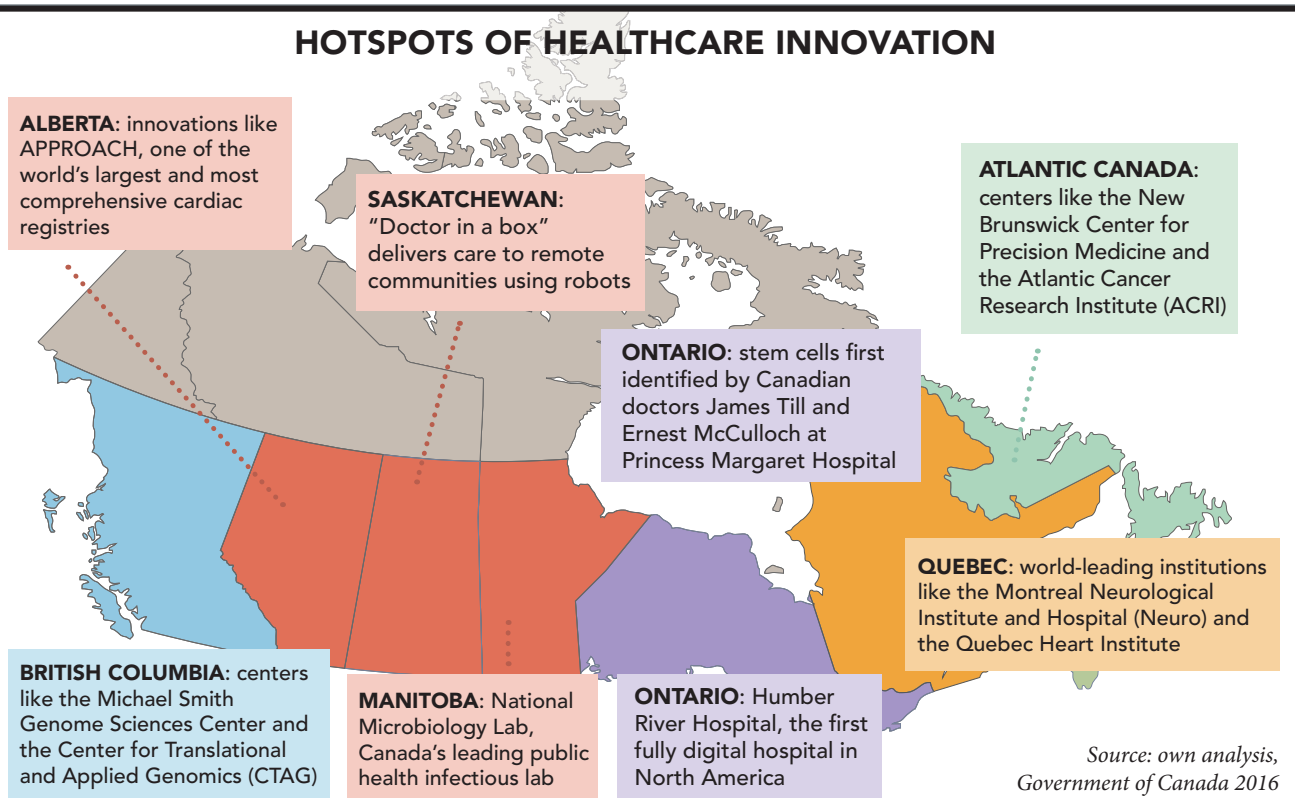
On the question, he opines, "Being sold to Big Pharma is already a stunning success story, because it means that Canadians have created something of real value that the global market is interested in!" He predicts, "Eventually, there will be a Canadian company that will refuse to sell and grow to be an anchor tenant of the biotech industry. Until then, we should be realistic and celebrate the success stories we do have."

STEPPING UP TO THE PLATE

In any case, Ontario minister of research, innovation and science, Dr. Reza Moridi counsels, "it is essential to remind ourselves as well as the global public that in North America, there are not simply two countries. Rather, there are 63 autonomous or semi-autonomous jurisdictions. If you compare those 63 jurisdictions, Ontario will be in the top three or five in a multitude of sectors, representing an economy with a GDP of CAD 800 billion (USD 625 billion) – nearly half Canada's total GDP. Toronto is the second largest financial city in Northern America, second only to New York. Toronto should not be underestimated."

Québec Deputy Premier, minister of economy, science and innovation, and minister responsible for the digital strategy, Dominique Anglade chides, "Many Canadians seem to view modesty as a quality. I think it is a big flaw! We need to bring our scientists and entrepreneurs into the public eye and talk about the pride of being Canadians, especially in this day and age."

HOTSPOTS OF HEALTHCARE INNOVATION



Source: own analysis, Government of Canada 2016

Continued from Page 31

the year whose goal is to stop future epidemics by speeding the development of new vaccines.

According to CEPI, vaccine development needs to start long before an epidemic so that final clinical trials or emergency deployment can begin swiftly in an outbreak. However, needed vaccines in many such cases aren't being developed often enough or quickly enough. And contributing to matters are the traditional difficulties in designing vaccines that work and are safe.

CEPI was founded by the Bill & Melinda Gates Foundation, the governments of India and Norway, the medical research charity Wellcome, and the World Economic Forum. It's an alliance between governments, industry, academia, philanthropy, intergovernmental institutions such as WHO, and civil society.

"We exist to finance and coordinate the development of new vaccines to prevent and contain infectious disease epidemics," CEPI states on its website. "As epidemics disproportionately affect low-income countries, CEPI will ensure that the vaccines we help to develop are affordable, so that price is never a barrier to access, and they are available to populations with the most need."

The vaccine race

Efforts around vaccine development are strong examples of how pharma companies, governments, and nonprofits are partnering together for a common cause. This is something Rajeev Venkayya, president of the vaccine business unit at Takeda, knows a lot about. Prior to joining the company in 2012 to launch its global vaccine business, building upon a longstanding business in Japan, Venkayya served as director of vaccine delivery for the Global Health Program at the Gates Foundation. There, he was responsible for the foundation's efforts in polio eradication and new vaccine introduction, and a grant portfolio of $500 million a year. While at the foundation, Venkayya served on the Board of the Global Alliance for Vaccines and Immunization.

Venkayya explains that when it comes to vaccines, public and private entities need each other. In general, nonprofits or governments that have tried to launch their own vaccine have been unsuccessful. By leveraging knowledge from the pharma industry, it could help vaccine R&D advance at a faster pace, Venkayya believes.

Vaccines are pretty well-established, straightforward investments for companies, but that doesn't mean there aren't challenges involved. This is especially true with emerging infectious diseases. Developing a vaccine can take eight to 12 years, or more, and the associated costs are steep. Partnering with a group like CEPI, or a foundation, can help eliminate that burden.

It's that knowledge piece of the puzzle that drives Mei Mei Hu, co-founder and CEO of United Neuroscience. Hu is passionate about developing vaccines that treat and prevent neurological disorders. Her company has built a translational platform to rapidly design and develop targeted immunotherapeutics, leveraging the organization's endobody vaccine technology. United Neuroscience's proprietary technologies have successfully commercialized over three billion doses to date in multiple indications and launched one of only a handful of licensed vaccines against an endogenous host protein in the world.

This, Hu told *Pharm Exec*, could not have been accomplished without partnerships, having enlisted what she says are some of the smartest researchers across the globe.

"Those collaborations are important, because you don't want to miss out on the expertise of people outside your immediate ecosystem," says Hu.

That knowledge network could encompass everything from strategic partnerships with academic institutions to informal informational meetings with groups like the Michael J. Fox Foundation about the latest advancements in Parkinson's disease. Hu is a big proponent of open sourcing and sharing information, acknowledging, like many in her field, that most of the major health issues facing the world today, such as Alzheimer's, cannot be solved by one person, or a company alone.

A united front

Those from both the public and private sectors that *Pharm Exec* spoke with about the value of forming relationships between nonprofits and industry all stressed that such efforts can make a significant difference in global health. They point to pursuits to almost eradicate polio worldwide as an example of how true global partnerships between governments, nonprofits, foundations, and pharma companies can make an impact. And how those paths paved by global coalitions such as CEPI will be critical to ensuring a worthy battle against future health threats. PE

MICHELLE MASKALY is *Pharm Exec*'s Senior Editor. She can be reached at michelle.maskaly@ubm.com and on Twitter at @mmaskaly

Messages of Hope

Figuring out the right formula to address global health—for the better

There are numerous examples of the impact the pharmaceutical industry has had on improving global health, as evidenced by our feature coverage in this month's issue. However, one example seemed to stick out the most at New York Pharma Forum's 28th Annual General Assembly early this month: "We have taken AIDS from a death sentence to a chronic disease."

That sentiment could have resonated with the hundreds of pharma professionals who gathered from across the world simply because the event, "Pharma's Commitment to Global Health," was held on World AIDS Day, Dec. 1. But it was much more than that. It marked an example of public, private, and government groups coming together to conquer a public health problem, one that not only created a lethal threat to people's lives, but also instilled a sense of fear that affected wealthy communities in Beverly Hills to remote villages in the middle of Africa.

"Everything that has happened in [healthcare] in recent times has created a better place—not a perfect one, but a better one," said Dr. Andrin Oswald, director of life sciences partnerships for the Bill & Melinda Gates Foundation. "And we are working to make it an even better place 20 years from now."

Accomplishing this, forum speakers noted, will take commitment, partnership, and the ability of various entities to work in unison on multiple fronts.

"It requires a lot of different stakeholders coming together," said Oswald.

For the Gates Foundation, the potential of such efforts go well beyond just the funding aspect. As a trusted nonprofit, the Foundation sits in a unique position to bring a variety of healthcare influencers to the table.

"We have the ability to convene a bridge between government and other partners," said Oswald. "The barriers that shouldn't be there in the first place are broken down. The Foundation believes that the private sector has an important role to play in global health. Making a profit while doing good should be supported."

This is why partnerships are so vital when it comes to protecting global health. Take the Ebola virus, for example. Michael Nally, president of global vaccines at Merck & Co., and a 2016 *Pharm Exec* Emerging Pharma Leader, explained that the company knew Ebola was never going to be a significant commercial opportunity, but, at the same time, it was aware that only a handful of organizations could translate the science to make the vaccine.

"Without collaborations around the world, we would have never gotten far enough with a vaccine," he said. "[The pharma industry] has a broader obligation to global health. Shame on us if we are not working together with the global health community to find innovations. We are a science-based company. We cannot rest on just new innovation, and we have to work with the broader healthcare community to make our industry a more reputable public health partnership."

While foundations or government agencies can provide as much funding as possible, it's that science from pharma and biotech companies that they lean on the most.

"Those in the nonprofit sector are not going back to the stockrooms and creating miracles in a test tube," said Ambassador Sally G. Cowal, senior vice president, global cancer control, at the American Cancer Society. "We need your industry."

And, in turn, the industry should depend on nonprofits. However, there needs to be a better short-versus-long-term balance in these relationships, those in industry expressed at the event. "Organizations struggle with what that model is that allows a fair return, but also can have maximum global impact," said Nally.

Advocates pointed to noncommunicable diseases as the next area of global health that must be addressed. Doing more in cancer was especially brought up as an example.

"The tsunami of cancer threatens lives and livelihoods around the globe," Cowal said. "Cancer is undermining people's abilities to support their families."

She pointed out that, on average, cancer strikes people at the prime of their work life, ages 40-60. The disease's economic impact—from premature deaths to disability costs—can hurt the bottom lines of all companies.

Such realities, however callous in comparison, illustrate that global health is not just about the health of people, but the health of economies, businesses, resources, and ecosystems across the world. PE

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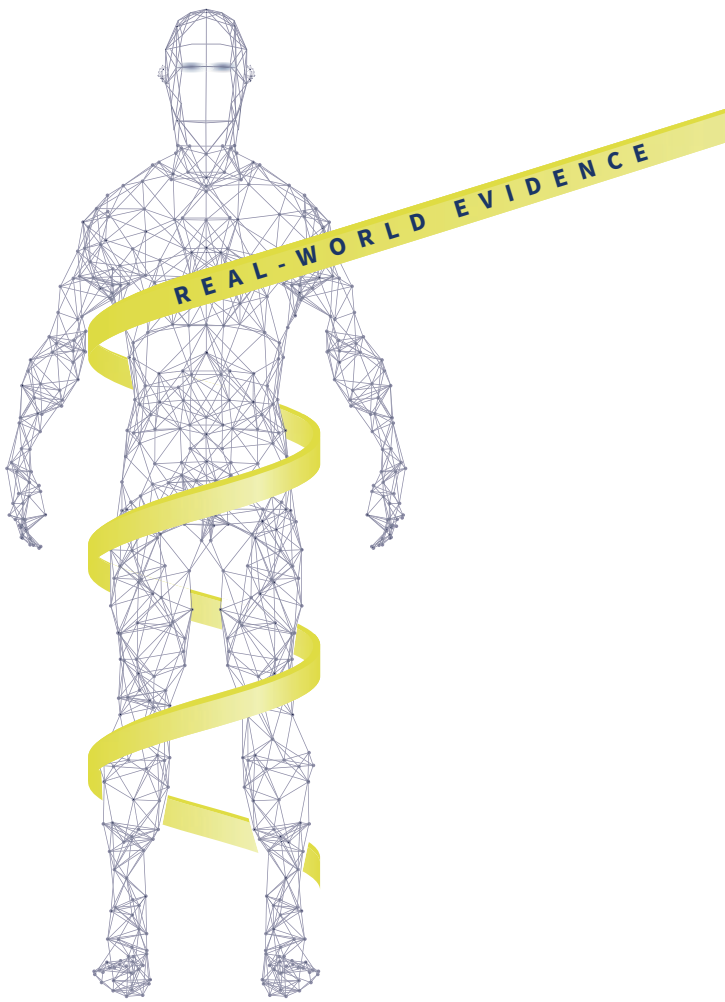

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