Pharmaceutical Executive

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COMMERCIAL INSIGHTS FOR THE C-SUITE
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PRODUCT LAUNCH
BRAND STORIES
Five Paths Forward
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Setting Your Launch Path

WHILE PREPPING FOR OUR TECH TOUR FOR THE C-SUITE ISSUE NEXT MONTH, I spent some time speaking with Bryan O’Malley, head of digital at Fingerpaint in Saratoga Springs, a health and wellness marketing agency, recently named 2019 Agency of the Year by Med Ad News. O’Malley filled me on all things digital affecting pharma marketers, a considerable list for sure, but also extremely relevant to this month’s issue highlighting brand launch. All the factors going into product launch are complex, but the one that remains constant is reaching your target audience: the prescribing physician. The rest of the decisions—reimbursement, access, patient needs, supply chain, etc.—then fall to your therapeutic area. Even in this era of PBMs, payers, and pricing, your targeted physicians’ awareness of your brand is key. Let’s take a look at some of the digital trends that currently affect branding that Bryan shared, and then we’ll get into a brief list of the products we chose to highlight this year.

Mobile phones. OK, you could say we’ve been there, done that. But O’Malley believes this is an area ripe for a better experience. “Mobile may not be sexy anymore, but the reality is that most of pharma still doesn’t do mobile well…they don’t really give it the same priority as the desktop, but that is where your audience is.” To that end, O’Malley says that marketers need to remember the reality that your audience is going to see your campaign on a four-inch phone screen. “If you put the focus on having the best web experience possible, you need to design the experience for the platform. Think about the font sizes you’re using, how easy it is to see and tap on links, how easy it is to discover and consume content—things like that. It’s an area that every brand should focus on to put their best foot forward.”

Apps. Is it a fad that’s passed and something people use for a day and go away? O’Malley says no. “Apps remind me of the early days of the web…everybody put up their website without thinking of the value for the visitor. It took quite a few iterations to figure out what worked well on the web as far as design and content.” He believes it’s the same with the app world. There will be a resurgence of apps but they will be better, faster, and will foster better engagements and provide greater value than what’s been done in the past.

Voice. Based on predictions, O’Malley shared that by the end of next year, 30% of web search will be by voice (think Alexa and Siri). By extension, O’Malley says the time is now for pharma to start ensuring their brands are findable using voice search. “When web search grew, so did the art of SEO. It’s the same for voice,” he says. “There are technical ways to achieve better voice results. Marketers can be doing work to their websites now to ensure their brand will appear in voice search results and make it easier for their target audience to get answers to their questions. There is a huge incentive to make sure you are catering to that, and to make sure you deliver more relevant results.”

THE BRANDS

In alphabetical order by brand, the ones we chose this year and the reasons for including them are:

• Aimovig, Amgen/Novartis. As the first preventative migraine drug available in over a decade, it is entering a crowded fielded, requiring tight market maneuvers.
• Epidiolex, GW Pharmaceuticals. Labeled for use in both Dravet and Lennox-Gastaut syndromes, it is the first drug approved using a cannabinoid.
• Erleada, Janssen/J&J. This drug for non-metastatic castration-resistant prostate cancer (nmCRPC) was acquired through a biotech and was approved ahead of schedule under the FDA’s fast-track designation.
• Mavenclad, Merck KGaA, Darmstadt, Germany. This oral product for multiple sclerosis was recently approved in the US, having been available in Europe for over a year.
• Nuzyra, Paratek Pharma. This is the first once-daily intravenous and oral antibiotic approved to treat both community-acquired bacterial pneumonia (CABP) and acute skin and skin structure infections (ABSSSI) patients in nearly 20 years.

As you read through these brand launch stories (beginning on page 10) and their journeys to market, the decisions made, and the decisions you may soon be facing with your own products, think about their path, but also think about the digital trends. They are simple, yet doable, with the potential for great results. Can you or are you incorporating them into your campaigns?
Product Launch:
Five Paths Forward

Pharm Exec’s annual feature profiling a selection of notable biopharma brands focuses this year on new beginnings and new promise—spotlighting five products with compelling product launch stories that tie strongly with the industry’s broader and evolving market-entry landscape.

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Focus Reports, Sponsored Supplement

A decade into China’s far-reaching healthcare reforms—which began with the implementation of universal, albeit rudimentary, medical insurance—the pace of change and transformation within the country’s life sciences industry shows no signs of abating.

Product Launch

Rep-Prep Overhaul
By Shaun McMahon
Tech-driven changes to training and learning systems—and how brand information is provided and shared—are transforming approaches in sales rep preparation.

First-Year Refresh
By Jon Hesby, Melissa McDevitt, and Esin Izat
Following a new product’s first birthday, there are four key ways companies can refine commercial strategies to maximize product sales.

Other Products to Watch
Elaine Quilici, Senior Editor

18th Annual Industry Audit
Pharma’s ‘Difference’ Makers
Bill Trombetta, St. Joseph’s University, Haub School of Business
Pharm Exec’s latest analysis of financial performance reveals that it’s those drugmakers maximizing the difference between the value and the cost of their capital investments that are delivering the most bang for the buck to shareholders.
Most-read stories online:
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**Pharm Exec Connect**

### Top Stories Online

**2019 Pharm Exec 50**
June issue online
Michael Christel
bit.ly/2Fzzybr

**Creating an ‘Unbossed’ Climate in Workplace**
July issue online
Lisa Henderson
bit.ly/2LFYQkp

**Executive Q&A: Compliance Disruptors**
July issue online
Lisa Henderson
bit.ly/2lstUBA

**2018 Emerging Pharma Leaders**
October issue online
Pharm Exec Staff
bit.ly/2PB6mba

**The Pharma Rep’s Future in Era of AI**
Blog post
David Logue
bit.ly/31viXiH

### Episode 38: Customer-Centric Innovation
Christine Sakdalas, head of franchise strategy and customer solutions at Janssen Pharmaceutical, talks with Pharm Exec editors about how patient centricity fuels innovation—and the difference between patient and customer centricity.

### Episode 37: Standing Out from the Crowd
Pharm Exec editors sit down with Mark Velleca, CEO of G1 Therapeutics, where he details how his company differentiates itself in oncology, and shares his thoughts on North Carolina’s biotech scene.
http://bit.ly/2OVonl0

### Episode 36: Summer Refresh
Catch up on some of the hot topics Pharm Exec covered this summer, with insights from our editors.
http://bit.ly/2GsYXF1

### Episode 35: Communicating Your Narrative
Robert Finkel, CEO of FreshBlood Group, a healthcare consultancy, speaks with Pharm Exec editors about the positives and negatives of pharma’s marketing needs, the founding and evolution of his company, and how emerging pharma and biotech organizations can budget in successful marketing.
bit.ly/2GvTymf

### Episode 34: The Executive of the Future
Cameron Turtle, chief business officer at Eidos Therapeutics; Robin Toft, founder and CEO of The Toft Group Executive Search; and Sabrina Johnson, president and CEO, Daré Bioscience, join Pharm Exec editors to offer their perspectives on the future of the life sciences executive.
bit.ly/2KvlfMa

### Episode 33: Gains in Translation
Pharm Exec editors speak with Jigar Raythatha, CEO of Constellation Pharmaceuticals, about the importance of having a Plan B in biotech and creating a translationally enabled company.
bit.ly/2MGBDeL

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**Patient Adherence: A Hard Pill to Swallow?**

### Pharm Exec Webcasts

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**Managing Global Regulatory Complexity: Clinical Trial Transparency, Reporting**

**AI-powered Biomedical Literature Discovery: Supporting Science-based Business Decisions**

### Reader Feedback

I agree that there is a place for AI in healthcare, but we don’t need to be regarded as too overdependent upon AI. Under AI, one wrong decision will be ported to many, again, with confidence that the AI is correct. Common sense has not yet been placed in AI. The rollout and the sales network for pharma will be met with disdain and skepticism as the generation gaps in medical practice are uncomfortable with the technology.

Anonymous

"Will AI Kill Pharma Rep Jobs?"

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Nancy Giordano, strategic futurist and corporate strategist featured at TEDx and SXSW

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The Murky Outlook for Generic Pharmaceuticals
Market consolidation limits sales, while legal challenges offset regulatory gains

The recent merger proposal involving Pfizer and Mylan reflects continued turmoil in the generic drug industry, as market pressures drive down prices, while “price gouging” charges draw public hostility and erode industry’s credibility. Leading US generics makers face stiffer competition from Indian and other foreign firms, eroding revenues needed to shore up outdated manufacturing facilities. The resulting shortages, particularly for quality sterile injectables, draw sharp criticism from lawmakers and healthcare providers about putting patients at risk.

A main problem for generics firms is that continued consolidation among wholesalers and pharmacies has curbed their ability to negotiate profitable rates. And with fewer blockbuster drugs coming off patent, manufacturers have limited opportunities to boost sales with low-cost versions of widely used medicines. Brands, moreover, look to delay competition through complex patent strategies, curbs on access to supplies for bioequivalence testing, and more “authorized” generics.

The merger of Pfizer’s Upjohn division with Mylan to form a stronger company offers one strategy for generics firms to gain more leverage with suppliers and customers. Only a few years ago, Mylan was looking to take over several competitors, but manufacturing problems and pricing missteps reduced its market value, as is the case with other leading generics firms. Last year, Novartis sold portions of its Sandoz generics arm and indicated that its remaining Sandoz operation would focus more on biosimilars and complex generics. Teva has scaled back operations to cut costs, while also acquiring smaller competitors. It remains to be seen if the new Upjohn-Mylan firm will contend more effectively with stiff competition at home and in volatile foreign markets without its Pfizer link.

Under investigation
Meanwhile, price-fixing charges have hit the generic drug industry hard. In addition to federal actions, more than 40 states have sued 20 generics firms for alleged collusion. State and federal enforcers continue to challenge pay-for-delay deals with brands as designed to postpone generic competition. In July, generics makers Teva, Endo Pharmaceutical, and Teikoku of Japan agreed to pay nearly $70 million to California to resolve anti-comparison charges.

At the same time it announced its merger with Pfizer, Mylan disclosed a $30 million settlement with the Securities and Exchange Commission (SEC) to close an investigation related to EpiPen price hikes. This follows a 2017 settlement with the US Department of Justice (DOJ) over failure to pay appropriate Medicaid rebates on EpiPen sales, just one of a range of legal actions related to controversial price hikes for its anaphylaxis treatment.

Ironically, analysts continue to document how wider prescribing of generics can cut costs for healthcare programs. A recent article in JAMA Internal Medicine found that greater switching to generic versions of widely prescribed drugs for hypertension and heart failure would have saved Medicare almost 90% of the $754 million spent on angiotensin converting enzyme inhibitors (ACEIs) and angiotensin-II-receptor blockers (ARBs) in 2016 and 2017.

Regulatory support
A way for FDA to bolster competition that can help reduce US drug prices involves streamlining and accelerating its process for evaluating and approving abbreviated new drug applications (ANDAs). The Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research (CDER) has utilized revenues from generic drug user fees to expand operations and clarify policies, leading to a record-breaking 1,000 ANDA approvals last year, including a number of first generics. CDER is issuing more guidelines and updating its Orange Book to support generic drug marketing.

A related OGD initiative is to compel manufacturers to file more complete ANDAs that can be processed and approved in one review cycle, avoiding time-consuming discussions on application short-comings. A recent report from the Government Accountability Office (GAO) advises FDA to do more to ensure that initial ANDAs are complete...
Generics makers still struggle to gain market share due to a steady rise in brand companies developing and marketing “authorized” generics of their own drugs due to a steady rise in brand companies developing and marketing “authorized” generics of their own medicines facing a loss in patent protection and new competition. By launching before patent expiration, the innovator firm can maintain sales and profits because these products don’t carry rebates. Analysts count some 1,200 authorized generics in the US that can raise costs over the long run by discouraging competition from outside manufacturers.

Members of Congress have proposed numerous measures designed to enhance competition in the drug market. Generics firms have pressed hard for legislation that prevents brands from blocking access to samples of reference products for required testing, along with measures to improve patent listings in FDA’s Orange Book and Purple Book for biosimilars. But generics makers oppose bills that set time limits for first generics to implement 180-day exclusivities.

Drug importing back on center stage

In a notable about-face, the Trump administration announced last month new policies to facilitate access to cheaper drugs from Canada and other countries for US patients. Democrats in Congress have promoted such action as part of more extensive legislation to limit outlays on medicines, but wider drug importing generally has been opposed by Republicans, as well as HHS and FDA officials even in Democratic administrations.

This time, however, easier access to drugs from other nations was trumpeted by HHS secretary Alex Azar and supported by FDA Acting Commissioner Ned Sharpless. Previously, Azar had termed drug importation a “gimmick” that could not be done safely. Now the reformers consider more advanced drug tracking, labeling, and import oversight systems able to ensure that products marketed outside the US are of similar quality and efficacy as those distributed at home.

However, the path to wider importing remains complex and lengthy, with analysts predicting that few if any drugs would reach US consumers under the new program before the 2020 election.

The administration’s “Safe Importation Action Plan” proposes two pathways for obtaining drugs from foreign markets. Pathway 1 encourages states, wholesalers, or pharmacists to propose demonstration projects for importing drugs approved in Canada that are the same as those marketed in the US. However, the program excludes multiple important therapies, including biological products, infused or injected drugs, controlled substances, certain parenterals, and drugs inhaled during surgery, limiting its potential impact. To authorize such action, FDA would issue a Notice of Proposed Rulemaking (NPRM) to revise current rules governing section 804 of the Food, Drug & Cosmetic Act, a process that usually takes years to accomplish. The new rule would allow applicants to establish demonstration projects that meet requirements for importing compliant therapies.

Under Pathway 2, pharmaceutical companies would be allowed to import approved drugs sold overseas under different national drug codes (NDCs), with assurance that the foreign version is the same as that marketed in the US. Imports could include expensive biologics such as insulin and cancer therapies and theoretically would appeal to manufacturers caught in costly US rebate programs that raise drug prices. FDA guidance is needed to implement the program, another lengthy regulatory process.

The larger issue here is why any pharma marketer would bring cheaper versions of its own products to the US. The Pharmaceutical Research and Manufacturers of America (PhRMA) strongly opposes the plan, maintaining that there’s “no way to guarantee the safety of drugs that come into the country from outside the US supply chain.” Industry noted that Canadians object to wider exporting of their drug supply for fear of wider shortages and higher costs.
Pharm Exec’s annual feature profiling a selection of notable biopharma brands is switching gears in 2019. Instead of recognizing the “Brands of the Year,” the theme is new beginnings and new promise, spotlighting five products with compelling product launch stories. Whether commercial firsts or important franchise expansions, these treatments all share unique paths to market entry—and tie strongly to the industry’s broader product launch landscape. Following our profiles, guest contributors explore today’s most pivotal pre-launch and post-launch strategies for pharma brand teams.

Prevent Defense

Aimovig

Unleashing Novel Migraine Market

By Christen Harm

In May 2018, FDA approved Aimovig (erenumab-aooe), a Novartis and Amgen collaboration for migraine prevention. Rather than treating symptoms once they appear, the subcutaneous injection targets the calcitonin gene-related peptide (CGRP) receptor that is believed to play a role in the inflammatory processes that bring on migraines.

Aimovig was the first drug to be approved in the new class of CGRP monoclonal antibodies. Since then, the market has grown considerably, with the approvals of Lilly’s Emgality and Teva’s Ajovy.

Earlier this year, FDA accepted new drug applications for Alder BioPharmaceuticals’ eptinezumab and Paratek Pharma’s Nuzyra.

Our Selections

Aimovig; Amgen/Novartis
Epidiolex; GW Pharmaceuticals
Erleada; Janssen (J&J)
Mavenclad; Merck KGaA, Darmstadt, Germany
Nuzyra; Paratek Pharma
and Allergan’s ubrogepant. The latter could become the first oral CGRP to hit the market. The drugs in this class have been specifically developed to prevent migraines, in contrast to the antiseizure, antidepressant, and blood-pressure-lowering medications that have been traditionally used for prevention.

Aimovig is self-administered once monthly using the SureClick autoinjector. The recommended dose is typically 70 mg but is also available in 140 mg; it’s injected into the upper arm, thigh, or abdomen. Since its launch, approximately 225,000 patients have been prescribed Aimovig.

Migraine is the sixth-most disabling illness worldwide, according to the Migraine Research Foundation. It affects 39 million men, women, and children in the US (one billion globally) and can be incapacitating. The costs of treating this population have been estimated at $22 billion annually.

The International Headache Society diagnoses migraine based on the pain and frequency of attacks, at least five a month, that last anywhere from four to 72 hours. Symptoms can range from nausea, vomiting, sensitivity to light and/or sound; and can be elicited by stress, anxiety, hormonal changes, bright or flashing lights, lack of food or sleep, and dietary substances. A recent report by the Pharmacy Benefit Management Institute (PBMI) found that direct healthcare costs for patients with migraine were estimated at $2,571 higher than those for similar patients who don’t experience migraine.

In clinical studies, Aimovig proved to decrease the number of migraine days, with a 50% reduction for some patients. “On top of cutting the number of migraine days, patients were able to reduce the use of migraine-specific medication,” Emilie Grand-Perret, VP and head of Aimovig marketing, Novartis, told Pharm Exec, adding that the drug was studied in a variety of patient populations for episodic and chronic migraine. Amgen and Novartis do look at the number of migraines a patient has each month, but the companies say the most critical measure for Aimovig is impact on quality of life and how debilitating migraine days are.

In July, Novartis announced that additional data from a Phase III study confirmed that Aimovig 140 mg decreases the number of monthly migraine days (MMD) as well as migraine-specific medication days (MSMD), supporting the long-term efficacy of Aimovig for patients who have struggled to find effective preventive therapies specifically designed for migraine.

**Pricing and access**

Cost and competing for formulary coverage have been cited as potential obstacles for CGRPs. The list price for Aimovig is $6,900 per year, or $575 a month. The manufacturers have established reimbursement solutions to increase patient access and lower cost burdens, however. “We felt we had an incredible responsibility to make sure that Aimovig would be available to all patients,” says Carly Baron, executive director, head of Aimovig marketing, Amgen.

To ensure quick access, Amgen and Novartis created a bridge program where patients can receive up to 12 free doses while they wait for insurers to process and approve their claims. More than 80% of claims are approved and patients typically pay only a $5 copay, according to the companies. For those unable to secure coverage, there are patient assistance programs available if income requirements are met.

**Outreach and education**

The real hurdle that Aimovig faces is a lack of understanding and acceptance of the disabling impact migraine has on patients’ lives. The disease is regularly stigmatized, with a common opinion that people with migraine are faking it or exaggerating the pain. Family, friends, and even physicians often have misperceptions of migraine, and patients are “up against a tough climb in terms of trying to make sure they’re understood,” says Baron.

To combat this challenge, Amgen and Novartis launched the “I Am Here” campaign to educate the public on migraine and Aimovig. The campaign consists of TV and online commercials, along with substantial engagement with patients on social media. Commercials depict not just the big moments in patients’ lives, such as weddings, graduations, and anniversaries, but moments like going to work, changing a baby’s diaper, or arguing with a significant other.

The campaign’s aim is to show migraine sufferers that Aimovig can help them be more present in their daily lives by potentially delivering better health outcomes. The strategy to use direct-to-patient and social media marketing to reach and motivate “unheard” patients has proven successful so far, the companies say.
A brand is a vessel carrying values and beliefs that consumers associate with a product or service, but it doesn’t start out that way. Deliberate steps must be taken to ascribe meaning to a name that otherwise has no meaning, or to elicit an emotion from a seemingly ambiguous combination of colors and shapes, also known as a logo.

At its core, the role of a brand is to facilitate decision making. It’s a mental shortcut that sparks strategic, purposeful associations. A psychological construct that is significant enough to drive behavior.

To achieve this in today’s world a brand must align with their values and beliefs of its target audience. They want to see themselves in your brand.

Simplicity is key in order for people to understand the “why” behind your brand, or in other words, its purpose. To have an outspoken commitment to a positive impact on society; a meaningful impact on the world. Now that’s something people can connect with.

When done right, a brand’s purpose will ensure meaningful relationships with people are made, while also guiding brand identity creation.

An intimate, comprehensive and objective understanding of your target audience’s psyche is necessary to identify what is meaningful in their eyes. Building this understanding is the first step in developing a brand purpose that is:

- **Distinct.** Standing apart from others in the space, with unique characteristics and an ownable narrative.
- **Authentic.** True to its origin, inspiring curiosity and building trust among audiences.
- **Compelling.** Aligning with closely-held values of your audience to deliver value and drive action.

Various methods, including quantitative research, focus groups and qualitative in-depth interviews, among others, are leveraged to gain insight into the wants, needs and perceptions of target audiences. These methods should be used during the inception of a brand, as well as throughout the brand’s life cycle.

In the beginning of a brand’s life, the reason for this buyer centric research is to understand of the perceptions of the market you plan to inhabit including, the competitive landscape, unmet needs and opportunities. With the understanding of your audience’s perceptions and attitudes toward the current market in place, we can begin to lay the groundwork for building that distinct, authentic and compelling brand purpose.

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Having a framework to synthesize and prioritize these insights will prove to be a valuable companion on the journey to finding your purpose. This framework should highlight the key features and characteristics that are compelling to audience members and distinct within the competitive set.

Next, your foundation should define what those features and characteristics do for your target audience - what problems do they help solve, or how do they help the audience achieve their goals? And finally, how does the brand make the audience feel, and why?

The brand’s purpose is hidden within this framework. Effort and critical thinking are needed to extract the big idea, and define the impact this has on the world. Once you have the answer, creating other aspects of the brand (like a name, a logo, core messages) come easily and interactions are seamless.

To discover a meaningful brand that’s powered with purpose, it’s important to note the old adage: “By trying to be everything to everyone, you run the risk of being nothing to no one.” This may require tough decisions about letting go of things that don’t serve your purpose, but branding is a long-term commitment. Beliefs don’t change overnight. A purpose that is equal parts authentic, compelling and distinct will future proof the brand and facilitate disciplined growth for years to come.

about Addison Whitney

At Addison Whitney, our purpose is to work closely with you to build something that matters. Something that makes a difference. It’s that simple. And it’s that complex.

Whether you need a name that encapsulates and concentrates your brand’s distinctive qualities or a brand identity and story that defines a purpose that sets you apart from everyone else, this is where you begin. With us. For nearly 30 years we’ve been creating brands that have a powerful impact on the world. That’s our passion. Our commitment.
As people have become increasingly aware of the medicinal benefits of marijuana, it was only a matter of time before a prescription cannabidiol (CBD) was approved by FDA. In June 2018, the agency made history by approving GW Pharmaceuticals’ Epidiolex. The twice-daily dose was indicated for seizures caused by two of the most rare, severe, and treatment-resistant forms of childhood-onset epilepsy—Dravet syndrome and Lennox-Gastaut syndrome (LGS)—in patients two years of age and older. It is the first medication to be approved specifically to treat Dravet syndrome, the first drug in a new category of anti-epileptic therapies, and the US’s first FDA-approved prescription formulation of highly purified CBD.

“Throughout the entire process, GW was breaking new ground,” says Steve Schultz, the company’s vice president of investor relations. “This was a completely novel experience, from running clinical trials in very challenging patient populations with essentially a brand-new medicine and mechanisms of action to [being] approved and commercializing the drug.”

Epidiolex originally received fast-track designation for Dravet syndrome and orphan-drug designation for both Dravet syndrome and LGS in the US. The drug’s FDA priority review led to it being approved last June.

A major obstacle for Epidiolex was that all cannabis products were still considered Schedule I at the time. It took strong safety data to get the Drug Enforcement Agency (DEA) to move Epidiolex into its least-restrictive class in September 2018. That paved the way for the drug’s launch two months later.

The next step for Epidiolex is gaining approval from the European Medicines Agency (EMA), which is anticipated around October. After that, GW plans to launch Epidiolex in the EU, starting with France and Germany, followed by the UK, Italy, and Spain.

In addition, GW plans to file a supplemental drug application with FDA later this year for the treatment of seizures associated with tuberous sclerosis complex (TSC) and also is recruiting for Phase III trials to study Epidiolex’s impact on seizures and other symptoms associated with Rett syndrome, a rare non-inherited genetic postnatal neurological disorder that occurs primarily in girls.

“Rett syndrome is an interesting indication for us, because it’s the start of us moving outside of seizures as a primary focal point,” says Schultz. “Our goal with Rett is to not only show that it is effective in reducing seizures in Rett patients, but also to be able to measure and put forward evidence as to the effectiveness of Epidiolex in more cognition and behavioral measurements.”

Access and marketing

To promote patient access, GW set the price of Epidiolex to be in line with other brand-name epilepsy drugs. The average US list price for the drug is $32,500 per year, however, costs are widely covered by insurance. GW’s Epidiolex Engage program also offers copay savings and patient assistance programs.

Since launch, more than 2,500 physicians have prescribed Epidiolex, and more than 12,000 patients have received prescriptions. Though an overwhelming initial demand caused some patients to wait four weeks for their first prescription fills, GW has reduced wait time to two weeks.

A good deal of confusion exists around the various forms of cannabis. To clarify matters and help Epidiolex stand out, GW has concentrated on educating physicians about the drug’s safety and efficacy. In order to cut through the CBD hype and focus on the quality of Epidiolex, the company has a sales force of 60 neurology account managers targeting about 5,000 physicians. It also has placed ads in respected neurology journals and even launched an unbranded website, Cannabinoid
Clinical (cannabinoidclinical.com), full of information, resources, and tools. Because of the small patient population, GW chose digital and social marketing to reach patients and caregivers. The biopharma also has partnered with advocacy groups.

“The focus of our company is to provide a much-missing, and we believe much-needed, facet to the whole CBD discussion, which is scientific evidence that proves that CBD can be effective in some very specific therapeutic targets,” says Schultz. “I think we’re the only company right now that’s been able to provide that type of evidence, and we believe it’s the type of evidence and reassertion that both patients and physicians desire.”

Growing business
The immediate success of Epidiolex has been promising for the future of cannabis-based drugs. The drug posted $33.5 million in Q1 net sales—more than double the market expectations of $16 million. Q2 net sales of Epidiolex more than doubled, coming in at $68.4 million, exceeding the average analyst outlook of about $47 million. Informa Intelligence analysts predict peak annual revenue of $822 million in 2025. With potential EU approval and additional indications, some analysts think Epidiolex could achieve blockbuster status.

Future of CBD medicine
GW is testing a number of additional cannabinoids in its pipeline. It will seek US approval for Sativex, which is currently approved outside the US for the treatment of multiple sclerosis spasticity. Also on the horizon are products in Phase I and II trials for autism spectrum disorders, glioblastoma, and schizophrenia.

“There’s a lot of anecdotal talk about where cannabinoids, and, specifically, CBD, could apply from a medical standpoint. But until you have the science behind it, you don’t have really any evidence,” says Schultz. “Physicians and patients need confidence in the medicine they’re prescribing and taking, and the only way to have that level of confidence is to have a medicine that has been through the FDA process.”

Brand Buildout
Erleada
New Chapter in Survival Story
By Julian Upton

While prostate cancer remains the second leading cause of cancer death in American men, just behind lung cancer, the American Cancer Society (ACS) observes that “most men diagnosed with prostate cancer do not die from it.” In fact, the ACS goes on, “more than 2.9 million men in the United States who have been diagnosed with prostate cancer at some point are still alive today.”

Zytiga (abiraterone acetate) from Janssen (part of Johnson & Johnson) has played a part in the declining number of prostate cancer deaths since its first approval for metastatic castration-resistant prostate cancer (mCRPC) in 2011. As noted by Evaluate Ltd.’s Vantage (Jan. 31, 2019), Zytiga plus androgen deprivation therapy (ADT) “set the bar” in the LATITUDE and STAMPEDE trials in men with high-risk mCRPC. LATITUDE showed that Zytiga plus ADT reduced the risk of death by 38% and radiographic progression by 53%; STAMPEDE showed a 37% benefit with Zytiga on overall survival. By November 2018, the drug had reached nearly $1 billion in quarterly sales, half of which came from the US. At the same time, the doors to generic competition were flung open when the US appeals court turned down J&J’s appeal to block generic sales of Zytiga.

Looking to extend its prostate cancer franchise, Janssen has since pushed Erleada (apalutamide)—an androgen receptor inhibitor indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC)—further into the spotlight. (Around 10–20% of prostate cancer cases are castration-resistant; mCRPC is prostate cancer that keeps growing even when the amount of testosterone in the body is reduced to low levels.) As noted by Evaluate Ltd.’s Vantage (Jan. 31, 2019), Zytiga plus androgen deprivation therapy (ADT) “set the bar” in the LATITUDE and STAMPEDE trials in men with high-risk mCRPC. LATITUDE showed that Zytiga plus ADT reduced the risk of death by 38% and radiographic progression by 53%; STAMPEDE showed a 37% benefit with Zytiga on overall survival. By November 2018, the drug had reached nearly $1 billion in quarterly sales, half of which came from the US. At the same time, the doors to generic competition were flung open when the US appeals court turned down J&J’s appeal to block generic sales of Zytiga.

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Luxturna
FDA’s approval of Spark Therapeutics’ Luxturna (voretigene neparovovec-rzyl) in December 2017 was a milestone. It marked the first FDA-approved gene therapy for a genetic disease—in this case, indicated for children and adults with inherited retinal dystrophy due to RPE65 gene mutations. Luxturna was developed to restore vision and prevent blindness for these patients. The injection delivers a functional copy of the mutated RPE65 gene directly to retinal cells using an adeno-associated virus (AAV). Upon Luxturna’s approval, Spark, currently in an extended takeover bid by Roche, faced supply chain

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New Chapter in Survival Story
By Julian Upton

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Adherence Mission

Mavenclad

Dose, Delivery Gains for MS

By Julian Upton

In March 2019, Mavenclad, from Merck KGaA, Darmstadt, Germany (EMD Serono in the US and Canada), became the first FDA-approved treatment for relapsing-remitting multiple sclerosis (RRMS) and active secondary progressive MS (SPMS) to provide two years of proven efficacy with a maximum of 20 days of oral treatment over a two-year period.

Clinical studies showed that Mavenclad (cladribine) reduced patients’ relapse rate by between 55% and 58%, and that patients taking the drug were 33% less likely to have disease progression than those taking placebo. But it is Mavenclad’s short and convenient treatment course, requiring no injections or infusions, that heralds it as “a new way to treat MS.” Just 10 days of oral tablet therapy are required at the start of the first year of treatment and another 10 days at the beginning of year two, with no treatment in years three and four.
As Chris Round, head of international operations and global core franchises at Merck KGaA, Darmstadt, Germany, told Pharm Exec, the impact of this “relatively small and contained profile is quite extraordinary, and essentially gives patients the opportunity to feel like they’re living a life without the disease, without a daily reminder that they have a medical condition.”

Mavenclad’s FDA approval in March—for the treatment of adults with RRMS and active SPMS—came some 19 months after its European Union approval in August 2017. (It is now approved in over 50 countries.) The drug’s approval journey goes back much further, however. Cladribine was originally approved by FDA in 1993 as an orphan drug to treat hairy cell leukemia. In the mid-1990s, Scripps Laboratories began trials of cladribine for MS. By 2007, a series of rights and business acquisitions saw the drug reach the hands of Merck KGaA, Darmstadt, Germany. But the company’s first submissions of cladribine as a treatment for MS were rejected by the European Medicines Agency (EMA) and FDA in 2010 and 2011, citing a perceived cancer risk and an unclear benefit-to-harm ratio, respectively. With several MS clinical trials still ongoing, Merck KGaA Darmstadt, Germany eventually decided to push forward with the drug with renewed determination. In 2015, the company announced it would again seek approval with data from the completed clinical trials.

**European breakthrough**

For Round, the greatest challenge around launching Mavenclad was to “advance historic perceptions of the product related to the previous filing in the EU and US, and also the large amount of time that elapsed from the end of our Phase III trials and when we re-filed in Europe.” Round and his team maximized their chance of success by “enabling physician and patient access as quickly as possible with a compelling payer value proposition, including novel contracting agreements; initiating a comprehensive Phase IV program to supplement existing data; increasing our field-based medical teams to ensure HCPs questions were answered quickly; and enabling peer-to-peer exchange of early experience with Mavenclad.”

Round says he is particularly proud of the way his team handled the experience. “Our company has been really strong at maintaining successful, mature brands in a competitive environment. However, Mavenclad was our first global launch in a long time, so the team had to adapt and learn,” he says. “We built the right team by putting our best internal talent on the launch and augmenting this with external talent with relevant launch experience. We came at it with the right mindset, with the team recognition that Mavenclad could represent a new standard of care for patients with active relapsing MS (RMS).”

**The US experience**

Mavenclad’s US team had other challenges to face. Rehan Verjee, president of EMD Serono and global head of the innovative medicine franchises, explains that the RMS treatment environment is different in the US, with far greater use of IV monoclonsals than in Europe. The number of MS and neurology practices in the US—and thus, the distribution of patients across different types of practices—is also different. Patients partner more with their HCPs in their treatment choices, Verjee explains, and, as such, search more frequently for quality information online and through other avenues. Introducing therapies in the US also “allows for an intense focus on data to guide and calibrate launch efforts, given how data rich the environment is,” he says.

Verjee told Pharm Exec: “Our approach accounted for these main factors, for example, by ensuring we appropriately indexed our increases in our field medical and field reimbursement teams to our specific context, and also in terms of the technology and data we put in the hands of the field teams.”

The US team was able to take the commercial, access, and medical learnings from the ex-US launch experience and adjust the US introduction accordingly. There was a “very conscious rotation of talent from the ex-US efforts to directly support the launch in the US,” cont’d, page 20
ARE WE TRANSFORMING IN THE RIGHT WAY?

WHY PRODUCT LAUNCHES CAN’T BE DISTRACTED BY EMPTY PROMISES

We can all agree that innovations in therapeutic development have advanced beyond traditional product launch strategies and service models. In every step of the product lifecycle, we see pockets of transformation. The problem is exactly that – “pockets” of transformation. Consider this:

- Patient populations are getting smaller and clinical trial recruitment has advanced by leaps and bounds. But if you can find the patient, can you engage with them in a meaningful way?
- In phase 3, you can deploy your Medical Science Liaisons to engage key influencers, you can begin planning for the launch of your sales team by analyzing key targets, strategizing on territory mapping, and recruiting and training your sales force faster than ever. But does your field force strategy both describe value AND capture the data to measure value for all patients, payers, and providers?
- Look at the pipeline in regenerative medicine. We focus on the complexity of pricing (which we must), but what about logistics – everything from chain of custody to temperature monitoring – and the risk that comes along the supply chain through patient support.
- Speaking of pricing, payer strategies continue to shift costs to consumers. When hours matter, technology can help you quickly manage benefits verification and find financial assistance. But when you get that patient onboarded in fewer days, did that speed allow for a personalized approach that keeps them continually adherent?
- If you get to launch your product and get that first script to a patient, how will your partners track real-world evidence to pay off the promise of your HEOR strategy?

Pockets of innovation may address these concerns, but to effectively launch a product, I argue that traditional service silos stand in the way of true healthcare transformation. Conflicted partners have conflicted priorities. Do disparate service providers look at the lifecycle in the same way you do? The need for a market access strategy that converts into measurable value. How everything from pricing and payer outreach informs the 3PL, specialty pharmacy, Hub, and PV services. And why these services must integrate into a seamless patient experience that’s strong enough to withstand loss of exclusivity or competing products.

TO EFFECTIVELY LAUNCH A PRODUCT, I ARGUE THAT TRADITIONAL SERVICE SILOS STAND IN THE WAY OF TRUE HEALTHCARE TRANSFORMATION.

We recently helped a client with a first-to-market orphan drug. The therapy was for a complex disease with adherence challenges and our client needed to establish and maintain leading market share in an increasingly competitive segment. With our integrated commercial platform we created a single access point for all onboarding and patient support, established dedicated patient service coordinators and coordinated care for each patient, including wrap-around education and support, and home care.

Our client saw tremendous results, including 95.3% patient compliance, 94.5% patient loyalty and 96% patient satisfaction. We established accountability as a single service provider, shared operational goals, and delivered leading market share (even with three other products in market).

For another client, we jumped in to manage distribution on Day 1. It was a new injectable therapy ready for launch for treatment of a devastating, ultra-rare disease.
This product had extreme requirements for dispensing and delivery which oftentimes prohibits patient access to therapy. While other partners would just map a launch strategy, EVERSANA™ went beyond planning to operations. Our Transportation and Logistics team implemented an Urgent Access Program utilizing our configurable system of storage facilities, cold-chain and non-cold-chain capabilities, safe and secure supply chain, and advanced temperature monitoring and tracking via GPS.

Case studies always get attention, but the fact is every company, every therapy, every patient is unique. Your product launch strategy has to achieve the following:

**Value the voice of the patient.** Listen and collaborate with the patient community (earlier!) for genuine and actionable understanding.

**Protect your revenue.** Research, assess and develop global pricing and market access strategies that propel and preserve revenue during market peaks and valleys.

**Reach all stakeholders now.** You need to deploy sales and clinical field force that’s sharing information from the front line to inform the continued program management and long-term performance.

**Prepare for optimal distribution.** Plan a distribution strategy to address unique patient populations, therapy and channel/network needs, and use a 3PL with one million square feet of cross-country warehouse space with 99.98% unit level accuracy.

**Achieve broad and quality access by reaching all stakeholders.** For one client we achieved 97% of covered lives access within four months of launch.

After decades in this industry, I’m amazed by the “pockets” of innovation, but disappointed that innovation hasn’t converted into more value for patients. That’s why we’ve developed an integrated and independent commercial services platform designed to solve pricing, access, reimbursement, adherence and product delivery challenges across the lifecycle. Because the services are integrated and managed by a single service provider, we’ll contractually guarantee performance and share financial risk.

That’s real accountability…and with it you can finally deliver what your patients deserve – access to efficient, effective and innovative healthcare.

About EVERSANA™

EVERSANA™ is the leading independent provider of global services to the life science industry. The company’s integrated solutions are rooted in the patient experience and span all stages of the product lifecycle to deliver long-term, sustainable value for patients, prescribers, channel partners and payers. The company serves more than 500 organizations, including innovative start-ups and established pharmaceutical companies to advance life science solutions for a healthier world. To learn more about EVERSANA™, visit eversana.com
says Verjee. “This is a leading practice associated with launch success that isn’t often pursued vigorously enough when companies have the opportunity. Some members of the team had nearly two years of launch experience and thus we were able to fully leverage their experiential learnings.”

Post-launch in the US, Mavenclad’s first three months have been “highly encouraging,” says Verjee. Awareness and willingness to prescribe the drug are in line with Merck KGaA Darmstadt, Germany’s goals at this time (above 85%), he explains, “with perception and understanding of the drug profile advancing similar to the evolution we saw ex-US.” Verjee points to “a broad spectrum of early adopters: neurologists from academic centers and from community practices have been able to initiate patients on [the drug], in line with our ambition for Mavenclad to further democratize access to high efficacy therapy,” he says.

The MS landscape has been called crowded; as an area of medicine, it has certainly seen considerable advances in the last 20 years. Verjee notes that significant needs remain, however, and reminds us that, prior to Mavenclad’s approval, “there were only four approved agents considered higher efficacy agents, and only one of them was an oral therapy.” Verjee says that adherence to MS therapies has been poor historically, with many patients discontinuing or switching in less than two years. “So,” he adds, “we have always believed our mission with Mavenclad is important.”

Paratek President and Chief Commercial Officer Adam Woodrow has been with the company for five years, and is in charge of the sales, marketing, and commercialization efforts for Nuzyra. The drug was launched in February and is approved for its two delivery modes—a once-daily oral and an IV formulation.

Woodrow told Pharm Exec two things kept him up at night in regard to the Nuzyra launch: getting the drug to patients quickly and a favorable payer reaction. However, both scenarios were complex because of the target user groups in the hospitals and outpatient clinics. Whether the product was used intravenously or orally also changed the access and reimbursement. Paratek needed a plan for both.

A drug that is used in an institutional setting falls under a diagnosis-related group (DRG) payment, which for branded therapies can cause problems because of the fixed nature of the DRG; it’s a patient classification system that standardizes prospective payment to hospitals and is designed to contain costs.

“We’ve seen this with certain antibiotics in the past where the cost of the antibiotic is more than the DRG and the DRG is supposed to cover...
everything from overnight fees, to testing fees, and everything else," says Woodrow. “So the branded drug cost could negatively impact decisions in what therapy is used.”

On the payer side, where a branded drug can stymie budgets and forecasts, Woodrow noted the high reception for new oral antibiotics. He surmised that patients given oral formulations were less likely to end up in a hospital, where they would invariably cost more money to the plan.

By coordinating the medical, market access, and inside sales before aligning its external field representatives, Paratek ensured that Nuzyra was on many formularies early in the launch—in fact, one-third of commercial lives in the US had access to the product by the end of Q1 this year. For those first eight weeks after launch, awareness with target prescribers increased from 27% to nearly 50% and institutional access was achieved in more than half of its 400 targeted institutions, according to Paratek.

However, the bureaucracy of institutional access is not lost on Woodrow, who explained acceptance by a formulary committee is only the access to the plan. “It’s shocking to me, but it’s a reality that at the beginning of 2018, Olumiant reported $6.7 million in domestic revenue (it launched at the end of Q2) and $195.9 million outside the US. According to analysts, Olumiant could become a $2.4 billion brand by 2022; key factors will be achieving FDA approval for the 4mg dose and continuing to highlight its lower price point. Approval for additional indications may also bolster sales; Olumiant is in Phase III trials for atopic dermatitis.”

Two new JAK inhibitors could refame Olumiant’s position in the RA market. In April, late-stage trials of Gilead/Galapagos’ filgotinib demonstrated a better safety profile than Olumiant and Xeljanz, yet showed similar effectiveness. Rinvoq, AbbVie’s pre-emptive answer to Humira’s expiring patents, is another to watch. Although its safety data wasn’t as strong as filgotinib’s, the drug received FDA priority review and was approved in early August. As the market expands, cheaper biosimilars will provide added competition as well.

— Elaine Quilici
Pre-launch Prep: The Modern Protocol
Tech-driven changes to training and learning systems have overhauled approaches to sales rep preparation

By Shaun McMahon

Whether a pharmaceutical company outsources its sales training programs or develops curriculum in-house, it already knows that thoroughly prepping their brand teams is critical for any successful product launch. But how we access information has changed dramatically in a remarkably short period of time. Not too long ago, training materials were printed, and sales reps would receive stacks of paper to read and review. Today, a large percentage of training is designed for intuitive use, with self-guided movement through curriculum, and accessed via mobile devices (M-learning) or online (E-learning).

With new technologies prompting changes in the ways that we learn and allowing fresh methods for providing information, it’s a good time to review the components of a modern training protocol.

Access on mobile devices
We want instant gratification. A 2012 study by University of Massachusetts professor Ramesh Sitaraman revealed that potential viewers will begin clicking off a YouTube video if they have to wait just two seconds for it to load, and that every second after that results in another 5.8% of viewers moving on. As a culture, we’ve experienced a parallel decline in our ability to pay full attention to almost anything for more than a few seconds. In fact, a 2015 headline-making report from Microsoft determined that goldfish, who’ve shown that they can focus on something exclusively for nine seconds, are now superior to human beings in this ability. (As a species, we can focus our attention without distraction for only an average of eight seconds.)

That same study revealed that almost 80% of young adults reach for their phone as soon as they feel bored. In the four years since then, it’s likely that percentage has grown. So it makes sense that pharmaceutical sales training content is increasingly uploaded onto mobile devices, designed to be accessed immediately, no matter the time or where we are.

EXAMPLE: For a recent client, we introduced a new format of a learning system that did away with audio narration and the traditional screen-to-screen view. Instead, this system was presented in an eMagazine or website style. This format allowed a more responsive design that could be accessed and easily read on laptops, iPads, and mobile phones.

The user experience and reaction was so positive, we have been regularly adding this presentation as an option for all of our clients.

Repetition
Learning isn’t something that happens immediately. Actual retention of information requires consistent review of materials; but “consistent review of materials” can be boring—and then we’re right back to that old problem with attention. So, savvy designers are finding ways to deliver curriculum that is stimulating and spaced out in a way that accommodates shorter bursts of focus.

Microlearning (where materials are broken down into quick-to-review and easy-to-grasp modules) helps quite a bit. Microlearning encourages a boiling down of material to its essence, and once that essence is understood, a platform of knowledge can be built upon. The microlearning format also makes it easier to find and review materials as needed. We’re now seeing microlearning move from “innovation” to standard practice.

Gamification, which applies the competitive structure of games to the learning process, is another longtime—and very successful—component to training, and thanks to inventive new technologies, it’s one that is regularly finessed and improved. Many people are accustomed to playing games on their phones. The trick in training is in repurposing complex information into a gaming format that is attractive and compelling and contains all necessary curriculum.

EXAMPLE: We are using a new technology platform that sends out questions to pharma sales reps on a regular basis in a contest format as a means of sustaining the learning curve and preventing the forgetting curve. Reps compete with each other and against other teams, which motivates them to stay engaged. It also helps them relearn information until it is absorbed.
Personalization
Programs can be designed to match the specific needs of each member of your sales team, with different materials emphasized based upon each individual’s areas of difficulty. Also, if one particular rep does better with interactive platforms while another responds better to video tutorials, each can have a program that responds to their preferences. Curriculum itself can also be adjusted depending on varying levels of understanding. In addition, personalization means that every trainee’s learning track can be supported via chat features that engage with users, answer FAQs, sustain interest in the program, and more.

Methods can also be incorporated into the program to allow assessment of individual learners and the team as a whole. Areas of weakness are identified through regular quizzes inserted into the program, and steps can be taken immediately to strengthen areas of difficulty.

EXAMPLE: We have incorporated personalized learning into many of our programs. Learning gaps can be identified via all sorts of assessments and gamification that then serve up recommendations with microlearning assets. This helps tailor a learning plan to resolve a trainee’s area for development accordingly in a wholistic, not punitive way.

Interaction
Even as technology leads the way in supporting innovative training features, developing face-to-face interaction skills remains essential. However, while getting up and doing a role play in front of the entire team might be fun for some, others prefer to make their mistakes in a more private fashion.

There are new approaches to improving in-person skills that borrow on the concepts mentioned earlier, including the “Selling Village.” Established at pharmaceutical sales meetings, the Selling Village is an area where the trainee is responsible for his or her own success in what is akin to a sales training gym. If they need extra help with verbalization skills, they can camp out at that particular station until they’ve achieved competence. If, on the other hand, they’ve already achieved content retention, they can skip that booth.

EXAMPLE: At a recent company-wide sales meeting for a leading pharma firm, we established a continuous, comprehensive Selling Village that featured several innovative stations where workshop content was extended into live, interactive, and more intimate sessions, allowing immediate application and reinforcement. We also established department stations where sales reps could interact with experts on varied subject matter. Lastly, mini-certification stations were set up to help certified sales reps grow their critical skills in a gradual and organic manner, rather than the traditional checklist approach, which can result in surface learning and poor retention.

Immersion
One of the most transformative elements of today’s training programs that we look forward to introducing soon is virtual and augmented reality. Trainees using VR and AR have the opportunity to practice their presentations and develop their skills in simulated realities.

Virtual reality places trainees in situations that feel realistic and true to the sales experience. This saves on resources and time, and removes the fear of sales call failures. Trainees can be comfortable practicing and trying new approaches in safe environments that mimic reality but are completely simulated and private.

Post-launch training
An 1885 study by researcher Hermann Ebbinghaus established the “Forgetting Curve,” which demonstrates how and why we forget information, and follow-up studies have confirmed that without regular reinforcement, much learned material can be lost. For that reason, you shouldn’t expect the initial training program to be the final chapter in your trainee training process. Keep your product fresh and alive in the marketplace by investing in occasional “refresh” training campaigns to reinvigorate your team members and prevent sales techniques from becoming rusty.

EXAMPLE: As part of a launch for a recent client, we developed a comprehensive sustainment plan which included:

- A multi-faceted, long-term gamification campaign.
- A successful board game provided to sales managers.
- Best practice postcards delivered in the old-fashioned USPS method.
- Videos pulsed out regularly to keep the energy of the launch meeting alive.
- Follow-up meetings with light slides for reinforcement of best practices and to help ensure that lingering questions were answered.

In addition, the sustainment campaign was not static; changes in direction since the product launch were addressed as necessary.
Despite significant investment in pharmaceutical research and development (R&D), productivity is sinking to a new low. A recent report suggested that the costs of developing and securing regulatory approval for a new, innovative drug has grown to $2.18 billion (1). At the same time, return on investment in R&D at the top 12 pharmaceutical companies is the lowest it has been in a decade: just 1.9% (1). This cycle of escalating R&D costs layered onto lackluster output in new drug approvals and falling ROI is unsustainable for the industry.

To spur conversation about these challenges and potential solutions, Pharmaceutical Executive, in collaboration with Parexel, brought together senior leaders in the industry in a roundtable discussion about how innovative approaches to drug development might increase efficiency and boost productivity in R&D. Much of the discussion sprouted from the key findings of a recent report from The Economist Intelligence Unit (EIU), commissioned by Parexel.

In this work, the EIU gathered and interpreted data on the effect of innovation in clinical trials against specific success metrics, including likelihood of launch and market access. It identified inadequate workforce readiness as a major challenge to innovation in the pharmaceutical industry (2). Stemming from this, participants in the Pharm Exec roundtable considered issues such as the current workforce, including gaps in skills and training as well as standardization of clinical trial roles; challenges in data science and how they relate to workforce readiness issues; addressing skill gaps through data standardization and AI; and driving forces to implement change, including making pharma company cultures more appealing.

The following captures the highlights of this roundtable discussion with these leading experts and the solutions they offer to address the current gaps in workforce readiness:

Participants in the roundtable discussion were:

• Julian Upton (Moderator) - Pharmaceutical Executive, European Editor
• Shona Fraser - Johnson & Johnson, UK Clinical R&D Director
• Liam Good - Tecrea Limited, Director
• Alberto Grignolo - Parexel, Corporate Vice President; DIA Global Forum, Editor-in-Chief
• Barbara Lopez Kunz - DIA, Global Chief Executive
• Jim Kremidas - Association of Clinical Research Professionals, Executive Director
• Mishal Patel - AstraZeneca, Senior Director and Head of Health Informatics
• Joseph Scheeren - DIA, Board Chairman; C-Path Institute, CEO
• Paul Simms - eyeforpharma, Chairman
• Albert Siu - Parexel, Corporate Vice President, Learning & Development
• Paul Strouts - Hays Life Sciences, Global MD
• Colin Terry - Deloitte, Partner, Life Sciences R&D
• Michael Thomas - A.T. Kearney, Partner

JULIAN UPTON (Pharmaceutical Executive): Alberto Grignolo will provide a backdrop to our discussions.


Parexel commissioned the report because we were concerned that the cost of drug development continues to increase and is becoming unsustainable. If this pace continues, it will cost more than $20 billion to develop a new drug just 25 years from now. The industry faces several other challenges as well: time to market still takes about 12 years, the failure rate of drug candidates is extremely high, health systems are concerned with the cost of drugs, and companies are hard-pressed to bring affordable drugs to market.

The EIU research objectives were to:

• Look for hard evidence of the role of four specific innovations in drug development (adaptive designs; patient-centric trials; precision medicine trials; RWD trials)
• Identify any barriers that might exist to the adoption of innovation;
• Look for ways to improve efficiency, productivity, sustainability; and
• Seek stakeholders call to action.

Several metrics were used by EIU to assess the impact of these four innovations. Specifically, researchers looked at enrollment time in clinical studies, normalized across the examined trials to be the time it took to recruit 100 participants. Researchers also looked at the likelihood of launch as well as reimbursement and affordability after drugs have gained regulatory approval and are launched.

Let’s look at some key top-level findings.
• All four innovative trial types reduced the time to enroll 100 patients.
• The likelihood of launch was 10–21% higher for drugs that used these innovative trial models than drugs that did not.
• Drugs tested with innovative trial designs were also more likely to be reimbursed.

However, the adoption rates of these types of innovations were very low: 0.6% for adaptive trial designs, 5.2% for patient-centric trials, 13.7% for precision medicine trials, and 0.3% for real-world data trials.

The EIU speculated upon several factors that could enable the adoption of these innovations:
1. **Workforce readiness** to manage health data in a novel and more automated way
2. **Collaborative partnerships** in the global ecosystem of drug development that need to be more diverse and more unconventional, in some cases with competitors working together
3. **Early stakeholder involvement**, including regulators, payers and the patients themselves.
4. **Advanced data analytics**, health data sciences and related activities and disciplines that will only expand and play a far more significant role in drug development. Some believe there is a gap in data analytics skills today and a wide range of competencies in this regard.

In summary, all four clinical trial innovations were shown to benefit drug developers in terms of trial efficiency, likelihood of launch and likelihood of reimbursement. But to be beneficial to developers, the innovation ecosystem needs a talent pipeline and the ability to access and utilize vast amounts of data from diverse sources. So, the question is: who should be involved in creating the workforce of tomorrow?

**CURRENT WORKFORCE READINESS: IDENTIFYING THE SKILLS GAPS**

**UPTON**: With that backdrop from Alberto, let’s get everyone’s perspectives on the kinds of skills gaps or issues that need addressing with regard to the workforce.

**BARBARA LOPEZ KUNZ (DIA)**: The evolution from individual component data to the entire digitization of healthcare creates enormous opportunity. We have an immense amount of information that has driven, and was central to, the development of many current therapies and cures. Assuming that the world continues to develop good data scientists, through advancements in university curricula and ongoing education programs by organizations like DIA and others, it is critical to get a whole system in place so we can harvest the data and use it to develop the next therapies. If we can do this, such a dataset—well-designed and supported by the right workforce capabilities—will create new horizons in healthcare.

**PAUL STROUTS (Hays Life Sciences)**: One problem is a lack of leadership skills in the pharmaceutical sector. A recent LinkedIn report identifies a 40% gap in project management skills in the sector right now. There is definitely a lack of medical technology skills, and a recent Deloitte report lists a 15% gap in product research skills and a 30% gap in product development skills. Lastly, with so much disruption in the life sciences sector at the moment, many smaller biotech companies are emerging and require nimble commercial teams. That’s lacking in the life sciences business.
The skills gap they all mentioned was workforce readiness, but maybe the workforce should break working with robots or advanced automation technologies. They must be trained to qualify, but it doesn’t provide additional their ability to display the competencies required for the role. The model rather than trade on the model.

SHONA FRASER (Johnson & Johnson): We are talking about workforce readiness, but maybe the workforce should break the model rather than trade on the model.

In pharma, we are adding to the amount of data and I’m not sure that analyzing all of it is the way forward. Within J&J, we’ve discussed using BOTS (robotics) to pull data from different systems to prepare clinical research associates (CRAs) to go to site. The CRAs, the data managers, run our studies and need to understand the basics of the science; they are our ambassadors. If you’re not going to change the system, you have to automate it so that when CRAs go to site, they are prepared.

JIM KREMIDAS (Association of Clinical Research Professionals): There is little consistency in performance, particularly at the site level. FDA’s guidance on principal investigators (PIs) says they must be trained to qualify, but it doesn’t provide additional details. So, there is a huge variability in PIs’ ability to conduct clinical research.

Likewise, there are no guidelines or educational requirements for study coordinators. Some coordinators are very good, but others are inadequately prepared for the role. Again, industry faces a lack of consistency and alignment on competencies for individuals implementing protocols at the site level.

Moreover, data shows the competencies of CRAs are diminishing. In our certification programs for CRAs, we are seeing consistently poorer performance over time in terms of their ability to display the competencies required for the role.

MICHAEL THOMAS (A.T. Kearney): Last year, we conducted a review of Alzheimer’s and Parkinson’s research teams in the UK. The skills gap they all mentioned was data sciences. Outside the US, and possibly even in the US, demand for these skills (raw data sciences, data mining algorithm development and data analytics in conjunction with biological knowledge) currently far outweighs supply.

The issue is even more pressing for big pharma. Will a young data scientist want to go to a big pharma research lab or to an academic institute or academic spin-out or start-up? The placement officer for Stanford graduates told us their graduates mainly want to work in start-ups based in London. That’s what excites them in their career. We need to think about big pharma and CRO workforce shortages in Europe, how we invest in building them up, and how we create attractive jobs. Otherwise, young talent will naturally migrate to the more exciting, dynamic and flatter environment offered by start-ups. New company formation in healthcare and biotech is rising at twice the rate of R&D expenditure, so it gives you a sense of just where the jobs are really being created right now.

ALBERT SIU (Parexel): I want to tie up a few points that have been brought to the table. First, do we have a good return on the investment made in workforce development? Most companies cannot tell how much training costs them and unless organizations are clear on their costs of training, investment in areas of skills gaps won’t happen and thus we will continue to compound the issue of inadequacy in workforce development, because we lack accountability in managing training costs.

Second, when we talk about training, we should talk about a framework that can transcend training topics and give us insight into what needs to be trained. The most basic component of a training framework is the “foundational element.” For example, we hire a lot of CRAs with diverse scientific backgrounds. Some may be nurses. Others may be biologists or chemists. For each of those disciplines we look for those that have a strong “foundational knowledge,” as this “foundational” content is taught at universities, and not within a company. Companies like ours must create “context” whereby those foundational elements can be leveraged. “Contextual” content is sometimes called “industry knowledge,” such as by teaching our new hires about drug development, regulatory requirements, clinical monitoring, project management, data management, and real-world data as well as “soft skills” to deal with people issues, through which they can be effective in their role.

The next aspect of training is the “practice” component. Just knowing facts doesn’t mean that one can take care of a real-life situation, so we put a lot of emphasis on the “practice” element. The last part is “credentialing and certification.” Given the needed skills to advance innovations in drug development are multidisciplinary, we need different educational bodies to validate knowledge gained and skills acquired. The credentialing efforts must be multi-disciplinary. The framework described here, the foundational, contextual, practice and credentialing elements are generic in nature, but I believe they can give us commonality to approach addressing the workforce development skill gaps.

KREMIDAS: We pulled together a cross-functional group of sponsors, regulatory, CROs, sites, and developed a framework for CRAs and CRCs. We are also introducing one for PIs.

It’s a starting point, but the industry must agree on a framework for what it means to be a clinical researcher and the skills and competencies needed. Better data and AI may offer amazing solutions for our industry, but if we don’t get the basic building blocks right, it will be very difficult to get into more sophisticated activities.
MISHAL PATEL (AstraZeneca): There were similar efforts in the UK. Within the National Health Service (NHS), the Scientific Training Program is intended to make the workforce ready to understand bioinformatics, informatics and computer science. After proving the competencies in this three-year program, one can gain certification to become a clinical researcher.

The challenge is that we tend to concentrate most on technical competencies and less on the soft skills. Newer data scientists will get a problem and just go with it without asking the what, why and when. We invest a lot of time in building their soft skills.

DEVELOPING JOB SKILLS TO ADDRESS DATA SCIENCE CHALLENGES

JULIAN UPTON: That raises the question of data and what to do about it. Is it about getting people in? Is it about training people earlier? Is it about re-thinking the whole issue of data science?

PAUL SIMMS (eyeforpharma): When you work for a technology company, you have a large responsibility for redefining what that company does. When you work for a pharma company, you’re iterating and, at best, improving an existing process. This is not attractive and must be addressed before we start talking about whether the training is adequate.

LIAM GOOD (Tecrea Limited): Instead of workforce readiness, maybe it’s about employer readiness, about the environment you bring people into.

At Royal Veterinary College, we are involved in training and talk about “day skills.” Before graduation, students need to have a check mark on several skills. This only works if you have an agreed list of what work skills are required. I think that might be something for the industry to work on and agree upon which these skills are needed.

JOSEPH SCHEEREN (DiA, C-Path Institute): I once worked for a company that brought in university students; every two months, they worked in a different department and built an informal network. Today, companies are less willing to do that because it costs money and requires mentoring time. However, such programs could be very beneficial in bringing people on board and giving them a feel of what the industry is about. Image-building for the industry is tremendously important for making it more attractive.

UPTON: If we talk about solutions, is recruiting people from other industries to tackle the problem with data optimization a solution, even short-term?

TERRY: Being competitive—and hunting for talent or people to create solutions—is an industry problem, not a company problem. If we all got to the same standard quicker, it would save everybody cost in trying to repetitiously agree to things that we talked about, whether it is data standards or a utility of different people. There is a risk that key talent simply chooses another industry entirely—like consumer technology—rather than bring their skills to life science challenges and opportunities.

FRASER: It is an employer issue to sort out. They can look at ways to bring in talented individuals using apprenticeships, for instance. These programs are attractive to students who are intelligent, but don’t necessarily want to go to university, or who don’t want to leave universities in debt because all the funding for apprenticeships comes from employers (e.g., big pharma companies). But, finding the framework to create that situation is a joint industry issue; one company approaching one university to start up an apprenticeship program is inefficient and slow.

SIU: In the United States, at the end of the Clinton administration, I was on a government effort called the Al Gore Commission for the 21st Century Skills. That was a public–private partnership effort to identify the needed skills for the 21st Century jobs and examined how the Federal, State and City governments can partner with industries to prepare workers that can thrive in the 21st Century jobs. A series of ideas were proposed, which involved the creation of internships, faculty exchanges with companies and special training programs, with special funding to be channeled from the Federal government to states and municipalities so that universities and, in particular, community colleges can be supported with special programs to augment job skill development. Eventually, this piece of work, together with other public policy debates, culminated in the creation of the “Workforce Development Act” that has since been certified and re-certified for federal funding to be channeled to states and municipalities for job development and job creation purposes. This sort of public-private policy debates and conversations are needed if we are to advance drug development and to take advantage of the innovative approaches to reduce cost while improving productivity in clinical development.

STANDARDIZATION OF DATA AND TRAINING ELEVATES CLINICAL TRIALS

UPTON: The report mentioned data siloes. What are your thoughts about data standardization and what is being done or what can be done?

SCHEEREN: There are two major topics. One is privacy. Patients must provide authorization to use their data. Second, there is general agreement that anonymized data can be pulled together, but there are problems with randomized datasets when they clearly come from different worlds. Even simple differences in date formats can present a challenge. Standards from ISO or another group like CDISC could help.

One of the beauties of having data standardized is that you can more easily pull it together, conduct analysis and uncover

“Instead of workforce readiness, maybe it’s about employer readiness, about the environment you bring people into.”

—Liam Good, Tecrea Limited
information not found in individual datasets. If industry reached a more harmonized way of reporting information, it would help the real-world data and real-world evidence we are trying to gather. KREMIDAS: Yes, industry could do a better job of utilizing data and defining standards. The healthcare industry extends well beyond clinical research, and various electronic medical record systems use different methodologies, compounding the problems.

Also, it’s not just the data that isn’t standardized; again, we really need some standardization among study coordinators and PIs.

FRASER: It is also about knowing what data you want to collect and why you want to collect it. Then, you can standardize it. When a clinical trial protocol is being designed, it generally involves the medical organization and the commercial organization coming together. At that point, the medics may not have much training on adaptive designs or new ways of working, so they tend to pursue traditional ways of running clinical research with head-to-head trials. Training is critical to changing the design of the whole program. I think if you are looking at workforce skills, it is not just the data scientists and the standards. It is the people who are designing programs. Perhaps, medical school doesn’t set them up for the pharmaceutical industry.

HOW LEADERSHIP AFFECTS ORGANIZATIONAL CHANGE

UPTON: In terms of embedding the culture, does it come from the top down? If genuine culture change is needed, is it the CEO? Do we need a chief transformation officer or a chief cultural officer?

SCHEEREN: The CEO can change the culture quite significantly. We have seen that within the Bayer organization with the lead values brought in by the CEO: leadership, integrity, flexibility and efficiency. If a decision was being made that was not in line with one of those values, people were talking about it.

KREMIDAS: While it always takes strong leadership from the top to create an environment, it also takes people at the grass roots. One of the most difficult things is identifying the leaders in lower positions in the organization. They can help drive change within the troops. Finding people who are willing to accept change and developing them into the leaders is a key element for any organizational change in management and culture to be successful.

ARTIFICIAL INTELLIGENCE (AI): A SOLUTION TO WORKFORCE SKILLS GAPS?

UPTON: How might AI help to solve some of these workforce-readiness problems? Is it effecting real change in organizations yet?

FRASER: It has started. We are looking at automating some minor processes so that people don’t have to spend their time doing administrative tasks.

TERRY: I think there’s a couple of things to consider, including educating people about what’s an automation opportunity, what’s a machine-learning opportunity, or what’s a cognitive opportunity. Then, the individuals and teams can quickly identify the opportunities for an enterprise team to drive rather than at the moment, where we have enterprise teams looking for opportunities but not understanding the context of the business needs.

SCHEEREN: It’s a no-brainer that AI and automation will affect the way we operate. For example, operational aspects of the regulatory activities will be automated quite significantly. Will that lead to workforce reduction? I think it will mean a shift in the use of people within the workforce and it will make their work more intelligent and more interesting. Another aspect is regulatory intelligence. If you have a machine that can extract information into a digestible format, it would be a great advantage.

STROUTS: It seems that it’s about willingness to change. Some companies are so slow in getting to the next point of the process internally. We’re talking about AI here and you have to foster that; you have to really want to make the change.

GRIGNOLO: Many of you have mentioned a lack of sense of urgency within the pharmaceutical industry, especially large companies. What will make the pharmaceutical industry engage in transformative change?

TERRY: It will be something that hits hard in the wallet. For instance, if European drug pricing was implemented in America. In our report a couple of years ago, we looked at what NICE pricing would do to our numbers and essentially it gives everybody a haircut of 15% because a lot of sales projections are US-based. That would give everybody a wake-up call that we need to engage in transformative change.

Second, if a FAANG (Facebook, Amazon, Apple, Netflix or Google) company entered the market at scale, it would definitely light a fire under the industry. If the data locked up in American payers suddenly became available to the world, that would represent a very different place and challenge the incumbents.

THOMAS: When 60% of your new filings are by companies that have never filed before, that’s no longer a wake-up call; it’s several wake-up calls [for large pharma]. We are reaching a point where 70% of industry-driven R&D expenditure accounted is accounted for big pharma, basically driving only a quarter of the portfolio.

INCREASING THE ADOPTION OF INNOVATIVE CLINICAL TRIAL DESIGN

GRIGNOLO: Why are the four innovative designs or approaches adopted so infrequently, as I mentioned earlier? And, in relation to workforce readiness, what solutions can this group think about that could be captured as a call to action to increase the adoption of innovations?

THOMAS: The straightforward answer is incentives. As long as the primary measure of R&D reward is time-to-regulatory filing, clinical trial methods won’t change. There is still an overwhelming culture of “get this product through its first regulatory approval” and the whole reward model largely hinges on that. In addition to personal incentives, it’s also about how the capital markets will view you.
SIMMS: I agree. Opportunity cost is important and there is far too much romanticization in R&D of trying to hold on to what could be a big project when the signs are it is anything but. I call it being more comfortable with failure. Biotech companies certainly are; they’ll pull through a lot more projects than pharma does.

FRASER: Going back to the four points on design, I disagree with the metrics that were represented. If I look at my portfolio, these innovations are in most of the studies. What you have to imagine is that patient-centricity should be in all of our trials. Adaptive design and patient-centric trials are life. Why are they not employed? In J&J, we do employ them. We work with patient groups. That’s part of our normal business. In the UK alone, we have contracts with different patient participation groups. We contact them, speak to them, and involved them in our discussions. Patients are central to everything we do.

Moving into precision medicine is important. If you are looking for particular molecular screenings or for a patient with a genetic mutation, it is very difficult to find those patients within the systems we have in the UK. Every doctor owns their patient’s data. Pharma has pockets of information on patients that they screen. There’s no joint way of doing precision-genetic testing across the world. There’s not a large biobank with all that information that we can readily use, so every patient must be screened and that takes a long time. There is a very good chance the patient will relapse during that period and is no longer available for that trial. If you had a biobank that worked, you would simply pull and use the patient data.

PATEL: I agree. Regarding real-world trials, most of our trials have elements of most of the innovations you mentioned, but we don’t tend to just back one of them. When you look at real-world data, having a visual comparator arm would be one of the biggest breakthroughs we could probably push and that is what we are trying to do. At the moment, we use real-world data to select patients, physicians, and sites. What needs to happen is to understand where the gaps are and apply data science, AI, to help us bridge those gaps, and that’s challenging.

THE PATHWAY FORWARD

A clear message coming out of this roundtable discussion is that cutting-edge drug development strategies must rekindle R&D productivity in the industry. Getting to this point, however, is impossible if the existing and future workforce is unprepared for such innovation. Thus, companies must focus on closing gaps in workforce readiness such as by removing cultural barriers (including making the company culture more appealing to young, talented workers interested in pharma), addressing preconceived notions about innovation, and breaking down organizational and data silos.

The need for trained data scientists who understand drug development, for instance, becomes especially critical as data management becomes more unconventional with the evolution of clinical trial strategies. “People who understand a little bit more about the end-to-end drug process, through mentoring and other internal activities, are actually some of the most valuable people in the industry. They don’t happen by accident. We have to grow them,” said Terry, noting that there is a shortage of these individuals going into the industry today.

Closing this gap in workforce preparedness is vital to the future of the industry and requires, as Fraser suggested, collaborative efforts (such as with apprenticeships through universities) and face-to-face hands-on training as opposed to web-based, virtual training.

Overall, collaborative partnerships in the global ecosystem of drug development likely need to become more diverse and less conventional. As Grignolo stated, “This may make for strange bedfellows, as we look at it today, but 10 years from now, we may find that these bedfellows absolutely belong together.” Such collaboration may even take the form of data-sharing, data prioritization, alternative data sources, and predictive analytics, though industry needs to first come together for data standardization.

Meanwhile, Kremidas stated, “The most urgent issue is alignment on competencies for clinical research.” He explained that while some work must be done to define clinical roles, industry is missing a huge opportunity to increase efficiency by jointly agreeing on some common functions and definitions for these roles.

Another call to action from panelists was to continue to focus on patient centricity during clinical research as innovation advances this area. “Of the three main stakeholders (regulators, payers, and patients), only one has been top of mind for the last years: the regulators. The payers and the patients are now absolutely top of mind and will become even more so in the coming years,” Grignolo pointed out.

“You won’t have clinical research if you don’t have patients,” Fraser agreed. “The pharmaceutical industry needs to change how it’s perceived based on bringing the patient voice along with it.”

The workforce size and capabilities will become a critical bottleneck if the issues raised in this roundtable are not addressed and the workforce is not ready to leverage these innovations in development and clinical trials. Siu concluded that the way to bring the pharma industry forward is to reconsider how it develops its workforce and cultivate its talent pipeline of future employees. “The innovations and the unique skills required to drive it must come from a broader network of partnership efforts than what exists today,” he stated.

References
18th ANNUAL INDUSTRY AUDIT

Pharma’s ‘Difference’ Makers

In our latest examination of financial performance—this year assessing the top 20 companies—metrics such as sales growth and enterprise value saw solid spikes on average, but it’s those drugmakers that are maximizing the difference between the value and the cost of their capital investments that are delivering the most bang for the buck to shareholders.

By Bill Trombetta

Welcome to Pharm Exec’s 18th Annual Pharmaceutical Industry Audit. We present a unique financial performance analysis of the top 20 publicly traded biopharmaceutical companies based on sales revenue. That total has been reduced to 20 to this year due to mergers and acquisitions during the 2017–2018 time period.

The Audit focused on a number of financial performance metrics, particularly critical metrics such as growth in shareholder enterprise value, enterprise value to sales, and return on invested capital. Regarding the last metric, this year’s Audit repeats the impact of weighted average cost of capital (WACC). WACC adjusts return on invested capital (ROIC) by assessing the difference between ROIC and WACC. Another continuing feature introduced in our last Audit is the ratio of executive compensation to average employee worker wages; then the rankings of the average ratio of executive compensation are tracked against which organization performed the best on increasing enterprise or shareholder value. Did the highest paid executives generate superior shareholder value?

Methodology

This year’s Audit relies on secondary reported information for the 2017–2018 time period. The metrics are also weighted reflecting their relative importance in assessing a company’s performance. Some metrics are more important than others. For
example, sales growth is important, but sales growth can occur as a result of M&As and in-licensing. So, it takes a back seat to the crunch metric, ROIC, which measures how well a company is managed, including margin management (the profit and loss or income statement) and asset management (use of assets on the balance sheet). Then ROIC is adjusted for WACC, illustrating which companies did the best on maximizing the spread or difference between ROIC and the cost of capital: cost of debt plus cost of equity.

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

The higher a company performs on a metric is reflected in a ranking based on the number of points it receives per metric. The highest placing for each metric is 20 based on the number of firms in our Audit, and the lowest is one. For example, if a company places 19th (second highest) on the critical metric enterprise value to sales (EV/S), it receives 57 points on that metric (19 rank x weight of 3 = 57). In another example, if a company comes in at a ranking of five (five places from the bottom) on the metric gross margin (pricing power), its total points would be 10 (5 rank x weight of 2).

### Indices

Basic indices are the growth of the US economy and inflation. A company has to be able to grow faster than the US economy: about 3–4% in 2017 and higher than inflation as measured by the Consumer Price Index (CPI)—about 2% for 2017. Our 20 companies handily outpaced that growth on every metric.

### Annual Sales

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<tr>
<th>Company</th>
<th>Sales 2018</th>
<th>Sales 2017</th>
<th>Percent Change</th>
</tr>
</thead>
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<tr>
<td>Johnson &amp; Johnson</td>
<td>$81.53B</td>
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<td>Average</td>
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Table 1

### Other benchmarks include:

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<tr>
<td>S&amp;P 500</td>
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<td>DJIA</td>
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### Sales growth

Table 1 above shows sales in US dollars along with sales growth for 2017–2018. It is good to grow, especially organically, compared to just acquiring companies. But that’s easier said than done for organizations at absolutely high sales levels such as Johnson & Johnson, Novartis, and Roche. The poster firm
for growth is Amazon. Amazon’s profits pale in comparison to their competitors such as Walmart, but its enterprise value (EV), or market cap, is the envy of its peers, less stellar profit growth, notwithstanding.

The average dollar sales for our 20 pharma was $30.5 billion in 2018, vs. $26.9 billion in 2017, a growth rate increase of 13.7%, outpacing the US economy and inflation and the Fortune 500. The top pharma by total revenues last year was J&J at $81.5 billion. Celgene posted the highest growth rate at 18.9%.

Enterprise or shareholder value and growth

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

EV is the sum of a company’s market capitalization; then add in debt and subtract a firm’s debt after adjusting for cash and other current assets. Simply put, EV is the market value of an organization.

EV is the sum of a company’s market capitalization; then add in debt and subtract a firm’s debt after adjusting for cash and other current assets. Simply put, EV is the market value of an organization.

Table 2 on facing page lists EV to sales. The average EV/S for 2018 is 4.20, a decrease from 2017’s 4.60. At the top is Novo Nordisk at 6.23, but a drop from the drugmaker’s 7.14 EV/S in 2017. Eight companies increased their EV/S ratios: the higher the ratio, the more likelihood the firm’s performance is going to get better.

Gross margin

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

Gross margin is total revenue minus cost of goods sold from the income statement. This is quintessential margin management: how price is managed while simultaneously managing operating costs to produce net

Enterprise value to sales

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

Table 3 on facing page lists EV to sales. The average EV/S for 2018 is 4.20, a decrease from 2017’s 4.60. At the top is Novo Nordisk at 6.23, but a drop from the drugmaker’s 7.14 EV/S in 2017. Eight companies increased their EV/S ratios: the higher the ratio, the more likelihood the firm’s performance is going to get better.

Table 2

<table>
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<tr>
<th>Company</th>
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</tr>
<tr>
<td>Novartis</td>
<td>6</td>
<td>$205.2B</td>
<td>$235.5B</td>
</tr>
<tr>
<td>Mylan</td>
<td>5</td>
<td>$27.78B</td>
<td>$35.9B</td>
</tr>
<tr>
<td>Biogen</td>
<td>4</td>
<td>$46.9B</td>
<td>$62.5B</td>
</tr>
<tr>
<td>Teva</td>
<td>3</td>
<td>$44.76B</td>
<td>$55.97B</td>
</tr>
<tr>
<td>Gilead</td>
<td>2</td>
<td>$79.64B</td>
<td>$110.2B</td>
</tr>
<tr>
<td>AbbVie</td>
<td>1</td>
<td>$150.9B</td>
<td>$210.0B</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>$131.6B</td>
<td>$118.1B</td>
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</table>
Enterprise Value to Sales

<table>
<thead>
<tr>
<th>Company</th>
<th>EV/S 2018</th>
<th>EV/S 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novo Nordisk</td>
<td>6.23</td>
<td>7.14</td>
</tr>
<tr>
<td>Amgen</td>
<td>5.35</td>
<td>5.23</td>
</tr>
<tr>
<td>Lilly</td>
<td>5.22</td>
<td>4.31</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>5.20</td>
<td>4.35</td>
</tr>
<tr>
<td>AbbVie</td>
<td>5.15</td>
<td>6.43</td>
</tr>
<tr>
<td>Biogen</td>
<td>5.12</td>
<td>6.33</td>
</tr>
<tr>
<td>Pfizer</td>
<td>5.09</td>
<td>4.55</td>
</tr>
<tr>
<td>Merck &amp; Co.</td>
<td>5.05</td>
<td>4.24</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>4.35</td>
<td>5.11</td>
</tr>
<tr>
<td>Allergan</td>
<td>4.20</td>
<td>5.18</td>
</tr>
<tr>
<td>Novartis</td>
<td>4.15</td>
<td>4.34</td>
</tr>
<tr>
<td>Roche</td>
<td>3.91</td>
<td>4.13</td>
</tr>
<tr>
<td>Celgene</td>
<td>3.87</td>
<td>6.48</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>3.68</td>
<td>4.85</td>
</tr>
<tr>
<td>Gilead</td>
<td>3.45</td>
<td>4.16</td>
</tr>
<tr>
<td>Sanofi</td>
<td>3.25</td>
<td>2.73</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>3.08</td>
<td>2.69</td>
</tr>
<tr>
<td>Endo</td>
<td>2.86</td>
<td>3.21</td>
</tr>
<tr>
<td>Teva</td>
<td>2.50</td>
<td>2.40</td>
</tr>
<tr>
<td>Mylan</td>
<td>2.41</td>
<td>3.11</td>
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<tr>
<td><strong>Average</strong></td>
<td><strong>4.20</strong></td>
<td><strong>4.60</strong></td>
</tr>
</tbody>
</table>

Table 3

Gross Margin

<table>
<thead>
<tr>
<th>Company</th>
<th>Gross Margin 2018</th>
<th>Gross Margin 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celgene</td>
<td>93.10%</td>
<td>93.80%</td>
</tr>
<tr>
<td>Novo Nordisk</td>
<td>88.09%</td>
<td>83.69%</td>
</tr>
<tr>
<td>Amgen</td>
<td>82.75%</td>
<td>82.14%</td>
</tr>
<tr>
<td>Biogen</td>
<td>81.77%</td>
<td>78.04%</td>
</tr>
<tr>
<td>Gilead</td>
<td>78.15%</td>
<td>82.70%</td>
</tr>
<tr>
<td>AbbVie</td>
<td>76.93%</td>
<td>75.90%</td>
</tr>
<tr>
<td>Lilly</td>
<td>73.81%</td>
<td>73.50%</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>71.78%</td>
<td>81.60%</td>
</tr>
<tr>
<td>Bristol Myers Squibb</td>
<td>71.25%</td>
<td>72.80%</td>
</tr>
<tr>
<td>Roche</td>
<td>70.73%</td>
<td>70.26%</td>
</tr>
<tr>
<td>Pfizer</td>
<td>70.16%</td>
<td>69.95%</td>
</tr>
<tr>
<td>Merck</td>
<td>69.22%</td>
<td>68.54%</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>67.89%</td>
<td>65.70%</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>66.66%</td>
<td>67.20%</td>
</tr>
<tr>
<td>Novartis</td>
<td>64.53%</td>
<td>65.03%</td>
</tr>
<tr>
<td>Sanofi</td>
<td>60.18%</td>
<td>66.80%</td>
</tr>
<tr>
<td>Endo</td>
<td>45.83%</td>
<td>36.21%</td>
</tr>
<tr>
<td>Allergan</td>
<td>44.18%</td>
<td>40.43%</td>
</tr>
<tr>
<td>Teva</td>
<td>44.00%</td>
<td>48.36%</td>
</tr>
<tr>
<td>Mylan</td>
<td>37.98%</td>
<td>40.17%</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>77.69%</strong></td>
<td><strong>73.00%</strong></td>
</tr>
</tbody>
</table>

Table 4

income. The higher the gross margin is, the more a firm is able to cover operating expenses, including SGA. Table 4 shows Celgene holding fast at the top with a nose-bleed gross margin of 93.10%. The biotechs rule pricing as they have ever since the first Pharm Exec Industry Audit in September 2002. According to The Wall Street Journal’s William Galston, between 1980 and 2016, US firms have increased markups by 42%; for biotechs, the markup growth has been 419%.

The average gross margin for our 20 pharmas in 2018 was 77.69%, up from 73% in 2017. So pricing power for the pharma industry seems to be holding its own. Eleven companies were able to increase gross margin in 2018.

Operating income

Staying with margin management, Table 5 (see page 36) shows operating income, or profit to sales. Again, the higher the gross margin is, the more that contributes to improving operating income. Operating income consists of total revenues minus cost of goods sold and minus operating expenses related to a firm’s typical business. It excludes one-time gains and losses, dividend income, and interest income.

At the top in this metric is Celgene at 44.38%. Coming in second with an operating margin of 43.44% is Amgen. Most companies would envy these numbers, which for the majority of firms would be their gross margin, not net income. The average operating income for 2018 was 26.3%, an increase from 25.1% in 2017. Twelve companies saw their operating incomes increase for the year.

Sales to assets

Gross margin and operating income have to do with margin management; sales to assets has to do with asset management. If a firm is at $70 billion in sales, it won’t be doubling revenue anytime soon. If the company has also curtailed SGA and disposed of assets, it won’t be cutting operating expenses in half anytime soon either. Then it turns to asset management to do
Tackling patient access to offset the challenge of declining ROI in drug development

Protocol complexity — impacting the speed and cost of clinical development
Assessing burden on the patient and site to stress test the impact on patient recruitment

Discussion around the increasing cost of drug development has dominated industry forums for many years, largely because of the challenge that the biopharmaceutical sector has had with many of the blockbuster drugs going off patent. However, it is only in the last few years that commentators have started to reflect on whether the reaction to this challenge has actually increased the complexity (and consequently the cost) of drug development rather than improve the situation. Protocol development has historically been in the hands of the scientists and therapeutic experts at Biopharma with high sensitivity to input from external sources, but could there be an alternative approach? Biopharma organisations are looking for innovative solutions to improve efficiency in clinical development, are they looking in the right place for a solution? Could additional insight support a better way to increase predictability in therapeutic testing and reduce costs? Research shows that protocols are becoming increasingly more complex. This increases time and cost and also importantly, burden on patient and investigators alike without necessarily gaining improvement in outcomes. By analysing data collated across multiple studies and a wide spectrum of therapeutic areas and indications, it is possible to gain insight that can be used to vary the protocol and positively enhance patient access and decision making.

Patient power and dynamics
Focusing on unmet needs

The patient has always been at the centre of drug development, but the patient journey has changed and is still actively evolving with increasing access to more information online and the support of patient advocacy groups. Industry research has shown patients still largely prefer to hear about clinical trials from their healthcare professionals; however, that doesn’t stop them researching their condition on the web and being able to have more informed conversations with their doctors. The appointment of senior roles in biopharma with a focus on patient interactions is hardly unexpected as organisations address this changing dynamic and the need to get closer to this important stakeholder, to give patients what they need rather than what pharma thinks they want. Developing drugs for unmet need that will really make a difference to patient lives seems like an obvious objective but the best intentions may not always deliver on this and sceptics suggest that pharma companies are not focusing enough on therapeutic areas and indications that are most acute. For example we are all too aware of the challenges of an ageing population and the increase in Alzheimer’s disease where there is an acute need for therapies. The question is whether pharma is investing enough to tackle challenging areas of research such as CNS, where if there were successful outcomes it would be beneficial to patients, society and to Pharma in the long run.

Virtual trials — extending the reach of clinical trials
Democratising trials for greater access

Having to conduct a clinical study exclusively through investigator sites limits a sponsor’s access to patients, as patients need to take into account the proximity to the nearest site for visits. Increasingly, sponsors are looking at ways to decrease patient burden and the frequency of visits to site through virtual trials. This is especially true for non-interventional studies but is also possible for pre-approval studies. Virtual studies can make use of a combination of devices, sensors, and home nursing services, all of which contribute to making them more convenient for the patient and truly patient centric. This is not a totally new phenomenon with many organisations arguing that they have been bringing studies to the patient in various forms or hybrid trials for many years. What is new and improving all the time is the emerging technology that will enable a more holistic approach from the outset, such as enabling sites to conduct telehealth sessions with patients, new forms of sensors and wearables to capture data and all of which have the potential to make it easier for the patient. These trials will extend the geographical radius, extending the outreach for patient recruitment and also improving the options of clinical trials as a care option for the patient.

The above is an extract from a special report based on a panel discussion chaired by Dr Nuala Murphy, President Clinical Research Services, ICON, with three leading experts: Dr Tero Laulajainen, Vice President, Head of Global Clinical Science and Operations, UCB Biosciences, a clinical scientist with specific expertise in diagnostics and a keen interest in creating unique, positive experiences for patients; Dr Tushar Shah, Senior Vice President, Global Specialty Clinical Development, Teva Pharmaceuticals, who is renowned for development of many respiratory medicines and has recently been involved in the approval of a new innovative digital inhaler and Prof. George Demetri, an eminent medical oncology clinical and translational researcher from Harvard Dana-Farber Cancer Institute and Harvard Medical School, who is helping pioneer new treatments in the field of oncology.

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If you would like to receive a full copy of the report, “Addressing the challenges of increasing complexity and declining ROI in drug development,” contact us at ICONplc.com/contact
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Site and Patient Solutions
ICON’s focus on understanding and engaging with patients throughout the journey of a clinical trial improves patient recruitment and retention.

- Leveraging patient insight based on health information collaboration, patient surveys and forums to gain better understanding of patient motivation and engagement
- Highly targeted recruitment and retention strategies that improve patient communication and compliance

Increasing predictability in patient recruitment.

ICONplc.com/patients
a better job making use of, not necessarily owning, assets. When you multiply profit to sales (operating income) by sales to assets (asset management), you get a far more important measure: return on assets. An organization can have a relatively low profit margin with a relatively high sales-to-assets ratio that will result in a better performance in terms of ROIC.

As seen in Table 6, Novo Nordisk’s sales-to-assets ratio is 1.05. For every dollar invested in assets, Novo Nordisk gets back $1.05 in revenue. Second-place Roche’s sales-to-assets ratio is 0.73; for every $1 invested in assets, Roche gets back 73 cents. Novo Nordisk is substantially more productive in managing its assets than the rest of the Audit field.

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

In a recent *Business Week*, Peter Coy authored an article describing NYU Stern Business School Prof. Aswath Damodaran’s use of the spread between ROIC and WACC. A spread of five points, according to Damodaran, signifies a very good performance; a spread of minus five points is poor performance.

Prior to the mid-1980s, the conventional wisdom was that debt had a cost (the rate paid for...
borrowing), but issuing stock was free. But what if the peer groups a company competes with have a higher ROIC than that company? Even though the firm shows a profit, it is destroying shareholder value if its profit is below its peers’ average. What return could an investor get by investing in a company of equal risk? This was the brainstorm of Stern Stewart, a consulting firm based in New York City.

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

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

To avoid overstating the impact of ROIC, we use the ROIC number to come up with the rankings on this metric. But the inclusion of WACC in Table 7 tells an interesting story. The greater the difference between ROIC and WACC, the greater the return to shareholders.

Net profit per employee
This metric, presented in Table 8, is not weighted in the rankings. But it is interesting to show how profitable the pharma sector is. Of our 20 pharmas, Biogen produces the most profit per employee, at $568,038 each; not a bad number compared to Apple’s profit per employee in the same range.

Selling, general and administrative expenses to sales
SGA is another metric that does not impact the rankings. Nonetheless, it is still important because the expenses in this category are necessary to run an organization and constitute routine spend such as rent, salaries, advertising, marketing, legal, and more. Laying off and firing workers costs money in severance before it begins to pay off. It’s also important to keep in mind that this is a one-year comparison. A firm can be

### Table 7: Return on Invested Capital

<table>
<thead>
<tr>
<th>Company</th>
<th>ROIC 2018</th>
<th>WACC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novo Nordisk</td>
<td>76.00%</td>
<td>5.03%</td>
</tr>
<tr>
<td>Roche</td>
<td>24.43%</td>
<td>2.50%</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>25.63%</td>
<td>7.30%</td>
</tr>
<tr>
<td>Biogen</td>
<td>23.62%</td>
<td>9.80%</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>18.66%</td>
<td>4.10%</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>17.16%</td>
<td>7.00%</td>
</tr>
<tr>
<td>AbbVie</td>
<td>18.07%</td>
<td>8.20%</td>
</tr>
<tr>
<td>Novartis</td>
<td>12.69%</td>
<td>3.60%</td>
</tr>
<tr>
<td>Amgen</td>
<td>16.55%</td>
<td>8.10%</td>
</tr>
<tr>
<td>Celgene</td>
<td>16.62%</td>
<td>8.60%</td>
</tr>
<tr>
<td>Lilly</td>
<td>15.03%</td>
<td>7.10%</td>
</tr>
<tr>
<td>Merck &amp; Co.</td>
<td>12.17%</td>
<td>6.80%</td>
</tr>
<tr>
<td>Pfizer</td>
<td>11.08%</td>
<td>7.60%</td>
</tr>
<tr>
<td>Gilead</td>
<td>11.22%</td>
<td>7.60%</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>7.03%</td>
<td>4.10%</td>
</tr>
<tr>
<td>Sanofi</td>
<td>5.63%</td>
<td>2.60%</td>
</tr>
<tr>
<td>Mylan</td>
<td>1.37%</td>
<td>6.60%</td>
</tr>
<tr>
<td>Teva</td>
<td>(4.91)%</td>
<td>6.36%</td>
</tr>
<tr>
<td>Allergan</td>
<td>(5.43)%</td>
<td>7.03%</td>
</tr>
<tr>
<td>Endo</td>
<td>(11.69)%</td>
<td>7.02%</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>14.54%</strong></td>
<td><strong>6.35%</strong></td>
</tr>
</tbody>
</table>

### Table 8: Net Profit to Employee

<table>
<thead>
<tr>
<th>Company</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biogen</td>
<td>$568,038</td>
</tr>
<tr>
<td>Gilead</td>
<td>$495,909</td>
</tr>
<tr>
<td>Celgene</td>
<td>$457,072</td>
</tr>
<tr>
<td>Amgen</td>
<td>$390,419</td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td>$211,159</td>
</tr>
<tr>
<td>AbbVie</td>
<td>$188,567</td>
</tr>
<tr>
<td>Novo Nordisk</td>
<td>$141,525</td>
</tr>
<tr>
<td>Pfizer</td>
<td>$120,595</td>
</tr>
<tr>
<td>Roche</td>
<td>$113,603</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>$113,227</td>
</tr>
<tr>
<td>Novartis</td>
<td>$100,758</td>
</tr>
<tr>
<td>Merck &amp; Co.</td>
<td>$90,145</td>
</tr>
<tr>
<td>Lilly</td>
<td>$83,557</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>$50,951</td>
</tr>
<tr>
<td>Sanofi</td>
<td>$48,807</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>$33,463</td>
</tr>
<tr>
<td>Mylan</td>
<td>$10,071</td>
</tr>
<tr>
<td>Teva</td>
<td>($50,547)</td>
</tr>
<tr>
<td>Allergan</td>
<td>($301,562)</td>
</tr>
<tr>
<td>Endo</td>
<td>($330,504)</td>
</tr>
</tbody>
</table>

Table 7

Table 8
making investments in advertising, training its sales force, etc., and that will pay dividends down the road.

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

Table 9 shows that generics makers are lean and mean on this metric. The average SGA for 2018 was 42.38% of sales, vs. 42.48% for 2017.

The best measure of business performance is ROIC—how much is a company generating on its capital investments, plant, and equipment, minus the cost of that capital, debt, or equity?

Executive compensation to median employee wages
From a larger societal perspective, we are seeing, globally, an increase in the top 1% of income compared to the average worker. The Gini coefficient measures this increasing wealth distribution disparity. A score of 1.0 reflects high income inequality; a score of zero reflects no inequality. The lower the Gini coefficient, the more equal the distribution of wealth; the higher the score and closer to 1.0, the rich get richer and the middle class and the poor get poorer. The Scandinavian countries tend to hit more equitable distributions of wealth.
Mexico and South Africa are among the highest scores, reflecting very unequal differences in wealth, with the US moving more in that direction.

Analogously, there is a similar interest emerging in the difference between executive compensation and the average wages of workers. Thanks to the Dodd-Frank Wall Street Reform and Consumer Protection Act, companies are disclosing what their CEOs make vs. the median wages of their employees.

Recent research from two academics reveals that the average CEO/median worker pay ratio has soared from 30 to 1 to more than 300 to 1 over the last 40 years. According to The Wall Street Journal’s Patrick Thomas, the median CEO pay in 2017 for 25 biotech, pharma, and life sciences CEOs was $16.08 million, above the overall median of $12.1 million for all S&P 500 companies.

Recently The New York Times’ Peter Eavis wrote that the median executive received compensation of $18.6 million, an increase of $1.1 million for 2018. CEO pay reportedly increased at almost twice the rate of ordinary wages; the average American private sector worker got a 3.2% raise, or an extra 84 cents an hour. According to the Economic Policy Institute in Washington, German executives earn 97 times the average worker wages, vs. 312 times as much for the biggest US companies.

Top scorers
Table 11 reveals the winner of this year’s Audit: Novo Nordisk, with 277 total points, according to our scoring system explained on page 31. The Danish-based drugmaker also topped last year’s list. Lilly comes in second with 259 points, followed by Celgene (250), Biogen (238), and Amgen (229) rounding out the top five.

Table 10 on facing page shows the rankings of CEO compensation compared to average worker compensation. The highest-paid CEOs aren’t necessarily associated with outstanding financial performance. The highest ratio was for Teva at 363 to 1; however, the company came in 18th out of the 20 firms in our Audit in terms of EV growth. GlaxoSmithKline had the lowest ratio, at 81 to 1, but comes in with the 15th highest increase in shareholder value. And note how much lower the executive compensation ratio to average worker salary is for foreign-based pharams compared to those headquartered in the US.

Table 11

<table>
<thead>
<tr>
<th>Company</th>
<th>Enterprise Value to Sales</th>
<th>Return on Invested Capital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microsoft</td>
<td>6.45</td>
<td>Novo Nordisk 76.00%</td>
</tr>
<tr>
<td>Novo Nordisk</td>
<td>6.23</td>
<td>Facebook 27.89%</td>
</tr>
<tr>
<td>Amgen</td>
<td>5.97</td>
<td>Apple 27.55%</td>
</tr>
<tr>
<td>Lilly</td>
<td>5.35</td>
<td>Biogen 23.62%</td>
</tr>
<tr>
<td>Biogen</td>
<td>5.12</td>
<td>Alphabet 18.18%</td>
</tr>
<tr>
<td>Celgene</td>
<td>3.87</td>
<td>Celgene 16.62%</td>
</tr>
<tr>
<td>Amazon</td>
<td>3.20</td>
<td>Amgen 16.55%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lilly 15.03%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amazon 13.52%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Microsoft 10.50%</td>
</tr>
</tbody>
</table>

Bill Trombetta, PhD is Professor of Healthcare Strategy & Marketing at St. Joseph’s University Haub School of Business in Philadelphia. He can be reached at trombett@sju.edu
WHAT

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China’s meteoric rise as an economic and political power on the global stage dominates discourse today. While the ‘Middle Kingdom’ is reclaiming global attention, an equally remarkable story of transformation is coalescing within the country’s healthcare and life sciences industry. A decade into China’s far-reaching healthcare reforms, which began in 2009 with the implementation of a universal, albeit rudimentary, medical insurance, the furious pace of change shows no sign of abating.

Since the State Council issued the Healthy China 2030 blueprint in October 2016, China has forged its own path towards the Holy Trinity of access, affordability and innovation. A cascade of reforms and policies aimed at aligning China with the best practices of the global industry while accommodating the exceptional needs of the Chinese market is steadily shaping a new healthcare system with Chinese characteristics.

Witnessing the birth of an industry is a rare occurrence, and how this will play out for stakeholders still remains to be seen. One thing is clear; in this high-octane environment, only the fittest will survive — and thrive.

"THINK BIG, START SMALL, LEARN FAST"

This start-up mantra might well by the rallying cry of Chinese society. Faced with managing a vast country with nearly 1.4 billion inhabitants spread across 34 provincial-level administrative units and despite the centralized system of governance, Chinese leaders instinctively understand the need to ‘ground’ grand ambitions with small, concrete actions. In a country where the ripple effect of any single policy could become a tsunami hitting hundreds of millions of citizens, the government’s caution is understandable.

Nevertheless, the pace of progress is relentless. Promises to accelerate regulatory processes for clinical trials and drug approvals have been successfully met, including China joining the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) in 2017, while updates to the National Reimbursement Drug List (NRDL) started conservatively with one round each in 2017 and 2018, which focused first on priority areas like cancer.
The generics quality consistency evaluation (GQCE) process was started to raise quality standards within the local pharma industry. Pilot programs designed to test the waters have been unveiled successively, such as a national reimbursement price negotiation mechanism in 2015; the ‘4+7’ volume-based procurement policy mandating centralized tendering of selected genericized products, intended to drive down prices; and the Marketing Authorization Holder (MAH) system launched in ten provinces enabling pharma companies to outsource production to contract manufacturing organizations (CMOs).

Against this hectic backdrop, industry players must cultivate agility to navigate the changing environment successfully: From Big Pharma companies re-orienting their global infrastructure to integrate China better to aspiring Chinese biotechs seeking their time in the sun, or shrewd service providers looking to capitalize on the market boom. Song Ruilin, executive director of PhIRDA – which represents a broad cross-section of local innovator organizations – exclaims, “the Chinese market is China’s but it is also the world’s market. I hope that CEOs of pharmaceutical enterprises globally see China as a platform for future growth and international cooperation. We are full of hope for the future.” RDPAC’s managing director Kang Wei, who represents innovative pharma MNCS in China, echoes this optimism, “this is a critically important industry for China. We need to be able to bring in innovative products as well as innovative chronic care treatment models. I hope we can reach a win-win solution for all parties: industry, patients, government and physicians.” The golden age of the Chinese pharma industry is well underway.

US, CHINA ... AND THE REST

From a commercial standpoint, the sheer market size and needs of China, bolstered by an increasingly welcoming regulatory environment and a burgeoning middle class, translates into a clear-cut case for the importance of the China market. Nevertheless, for many China GMs, the case for China is no longer just extrinsic but fundamentally intrinsic.

Pius Hornstein, appointed chair of Sanofi China in March 2019 following a long career with the company, including most recently four successful years at the helm of Sanofi Brazil, enumerates, “China is not only Sanofi’s largest Emerging Market, it is the second-largest affiliate for the Group globally after the US, representing eight percent of global sales. In terms of growth, we represent an even greater proportion.” This is despite Sanofi facing the same headwinds as MNCs with significant legacy portfolios in China. He emphasizes, “a couple of years of changes or challenges linked to ongoing policy changes do not alter the fundamental potential of Sanofi China. In any possible future, China will maintain a fundamental role within our global strategy.”

He highlights, “today, our peer companies are no longer talking about US and the Top Five markets but about US, China, and the others. The fact that Sanofi created a new Global Business Unit called ‘China and Emerging Markets’ [demonstrates our] fundamental commitment to the country and the Chinese people we serve. This was a very deliberate and very smart decision.”

With the size of a mature market but the characteristics of an emerging one, the Chinese pharma industry is still in the awkward adolescent phase. Boehringer Ingelheim country president Felix Gutsche articulates, “China is a very dynamic environment, whether we are talking about regulations, workforce or other aspects. This sometimes conflicts with internal processes [and] usual timelines [when] we need to make overnight decisions here.” Bridging global and China was therefore precisely the mandate he was tasked with. He continues, “if our business here is growing 25 percent year on year, our organization needs to develop at the same pace. We have reached a size where we need to re-evaluate the way we operate. It is a fine line to tread: we need to be good corporate citizens and fulfil corporate expectations while retaining some local flavor [to] excel in the local market.”
To support this balancing act, he adds, “after 24 years at BI, I possess a significant network within the global organization [and] experience in many functions across different businesses in different countries. I [also] have the privilege of being one of the four free-standing country managers within BI – alongside my peers managing the US, Germany and Japan” whereas in other markets, country managers also oversee a business unit directly.

In these critical periods of transition, HQs tend to prefer a steady, known pair of hands at the wheel. 24-year Lundbeck veteran Lorena Di Carlo, appointed in October 2018 as GM of Lundbeck China, certainly fit the bill. It is important to have, she stresses, “strong cross-functional collaboration with HQ to put in perspective and translate the opportunities that are present in China. We have increased our footprint and clearly identified China as a key strategic market for future growth. There is so much news coming out of China that it can become overwhelming, particularly compared to mature markets. It is important for us to contextualize the news and also provide reassurance.” To support this weighty task, she also sits on the Global Commercial Leadership Team. She lists, “my first objective is to bring my learnings and experiences from global to China, and my second is to take the learnings from the China market back to Lundbeck HQ – to ensure that we continue to allocate the appropriate resources to China.”

Perhaps the company most acutely aware of the importance of the China market is Servier, for whom China is already the top sales affiliate. GM Stéphane Mascarau enthuses, “I could share tonight many figures, numbers and milestones to review these last 40 years, but for me, the success of Servier China is based on the quality of the people who have been associated with the company over this time. The celebration of our 40th anniversary is an important moment to reinforce, on behalf of our team, our commitment to contribute to therapeutic progress and to serve patient needs.” With the importance of the China affiliate comes the importance of the China organization. This is why, for
him, “the most important [factor] is the mindset of the team: the willingness to embrace new ways of working, to build a strong sense of teamwork – within and across departments – and the desire to succeed, sharing together a common vocation, common vision and common values.”

He exhorts, “a fundamental success factor in China is agility: agility to adapt quickly, to adapt locally. It is not enough to be fast, you have to be faster than others. The winning company in China in the future will not necessarily be the biggest company but rather, the company with the ability to foster agility and teamwork within this very dynamic market.

His message to HQ is clear: “within our industry, to be successful in the future, China has to be considered, if not as a center of attention and strategic focus, then together with the US as dual priorities for the organization. Today, there is a race – not just between multinationals but also with local companies, who are attracting talent, money and attention. Servier must capitalize on our strengths to position ourselves. A sense of urgency is so critical in China. It is not enough to be fast; you have to be faster than others. Today’s decisions shape tomorrow’s Servier.”

Gaobo Zhou, partner of McKinsey China, has worked closely with the Chinese healthcare industry for nearly a decade, and he agrees that the China market is still not well-understood by the global industry. He warns, “there still remains a mentality that business in China is predictable – as it has been for the past couple of decades – and sometimes HQs try to impose a five-year forecast or strategy. In reality, things are changing extremely quickly. Companies need to have some level of flexibility built into internal KPIs and projections. Despite its size and value, China still does not resemble a mature market. Whether we look at ways of working, culture, process design and interactions with global functions, there remain a lot of inefficiencies.” Even as HQs has elevated China in importance, the question is “how to give China the independence and the decision-making power that it demands whilst still maintaining the affiliate’s ability to collaborate and coordinate across the global organization.”

A very concrete and necessary action he proposes is that “current CEOs and executive teams gain China experience and exposure by visiting China … not coming once a year to conduct an annual business review but thoughtfully and strategically planning a series of meetings with relevant stakeholders at provincial, municipal and local levels; identifying relevant conferences to attend; identifying the messages that need to be delivered on each platform – all very micro decisions [essential for] orchestrating high-level China visits and having productive dialogues.”

BUILDING THE ECOSYSTEM

With the scale and depth of complexity the China healthcare ecosystem entails, Big Pharma MNCs – who still represent a far lower proportion of the market compared to mature markets – are unequivocal on the need and responsibility to plug more fully into the overall environment.

Pharma giant Janssen encapsulates the sentiment of ‘patient-centricity’ in their phrase ‘beyond the pill’. How does that translate to a country of 1.4 billion? President Asgar Rangoonwala asserts, “the fundamentals do not change, only the scale. Being patient-centric is about the individual patient.” Their work in schizophrenia in China exemplifies this. “If you visit a patient with schizophrenia, you see the same unmet medical need across the world. Our value lies not only in selling our three-month long-acting injectable but also in our work with different doctors and local governments to
establish community care centers to act as a bridge for patients’ transition from hospital to home.”

He articulates, “the healthcare problems have to be solved over generations. We cannot expect to solve them alone or in one shot. This is why we form collaborations with key players.”

While approvals and reimbursement of new and innovative products have ramped up, industry generally agrees that much more is needed. Despite Novartis having launched 15 drugs between 2018 and 2019, Ingrid Zhang, GM of Novartis Pharmaceuticals opines, “we also need to work with the relevant stakeholders to further accelerate accessibility. We have to make sure patients can obtain the medicines, their out-of-pocket drug expenses are reasonable, and that they are taking their medicines properly.” To illustrate, she cites their holistic commitment to ophthalmology in China, where they are the largest player, “in addition to bringing various innovations to China, we are also working with ophthalmologists, associations and medical societies … to provide better education and training. Not only have we invested in working with leading centers of excellence, e.g. helping to set standards for physician training, we have also gone to counties and more remote areas to work with general ophthalmologists and build their skill sets.”

Conservative German healthcare titan Boehringer Ingelheim has gone one step further by deciding to expand their stroke franchise in China through a ground-breaking pilot initiative: establishing a stroke rehabilitation center in Shanghai – the first such center for BI globally. President Felix Gutsche shares, “from a purely pharmaceutical perspective, we are not seeing much innovation in the industry. [However], we can reach the next level of innovation [by] focusing on patient-centricity and meeting the overall needs of the patients rather than treating a specific
condition or symptom.” He explains, “in China every year, there are around three million strokes. Many of these patients, even if they have received treatment, do not receive decent rehabilitation after treatment. We have aligned with a German hospital partner and are testing the pilot at the Shanghai International Medical Center (SIMC). We hope to build a case for extending this pilot to more hospitals.”

While China may be catching up in many areas of pharmaceutical R&D, in one aspect she is certainly at the vanguard of development: digitalization. For this reason, when Servier envisions their part in supporting China’s healthcare ecosystem, digital looms large. GM Mascarau emphasizes, “today and in the future, digital technology, will play a large role in supporting our mission to transform lives of patients suffering chronic diseases [including through] innovative, large-scale, patient-centric projects such as disease awareness programs, patient education programs, and medication guidance programs. Recently, we are providing innovative solutions for doctors and patients, by working with technology companies, digital service providers and internet hospitals and pharmacies.”

He adds, “through WeHealth by SERVIER, we are closely following and working with Chinese start-ups, seeking innovative solutions to assist doctors in their clinical diagnosis through the use of Artificial Intelligence as well as to develop new devices and systems to improve disease control and management.” It is clear that in China, digital technology is another language pharma companies must master to be successful within the market and truly reach patients.

**A NEW MODEL OF CHINESE BIOTECH**

As the Chinese pharmaceutical landscape transforms, talent, capital and policy have come together to form a perfect storm for biotech innovation. With this new wave of biotech CEOs typically boasting decades of distinguished career experience at global pharma and biotech behemoths, they are no longer content with establishing run-of-the-mill product companies nursing a handful of clinical candidates. With burgeoning confidence and intimate knowledge of the arduous drug R&D process, they are setting their sights on building long-lasting platform companies with strong and productive pipelines anchored on proprietary technology.

Its speed and ambitions notwithstanding, China still stands decades behind more developed markets when it comes to biotech innovation. For Chinese companies set on innovative drug development for the global markets, they face an international minefield of IP and patent rights. Xue-ming Qian, CEO of Transcenta Group elucidates, “for an antibody to be valuable, it needs to be efficacious, specific and safe; it needs to be manufacturable at low cost; and there needs to exist good freedom to operate using this antibody, meaning that the antibody does not infringe on any existing patent rights held by other companies.” However, “Western companies started working with biologics two to three decades ago so they have a lot more experience and history in this field. Many have learnt not only to patent their own therapeutic antibodies but also the epitopes these antibodies bind to.”

Their Immune Tolerance Breaking Technology was developed to generate antibodies with diverse epitopes to circumvent this issue and has already been validated by the discovery of their flagship drug candidate, MSB2311. Qian raves, “MSB2311 is probably the only pH-dependent PD-L1 antibody globally. We have demonstrated in the pre-clinical setting that this antibody can be recycled after it binds to a tumor cell. This means that drug can work for a longer time. We see excellent activity, but much lower toxicity compared to other first-generation PD-L1 molecules.”
What is EPS
A Company for Life Science Solutions
Bridging Japan with China and Beyond

https://www.eps-holdings.co.jp/en/
These biotechs also see the global industry as potential collaborators, not competitors, aiming ultimately to contribute to the industry’s R&D productivity. In the words of Adagene co-founder and CEO Peter Luo, their broader objective is “to be a source of constant supply of innovative medicines ... [and] to help other pharma companies in the industry solve problems as partners.”

Through his time with MSD, Luo realized that, “even at Big Pharma companies, the path from molecule to market is not always clear. Many programs start and stop.” This led him to question: “how can we undertake drug development more systematically? [How can we have] differentiated molecules that genuinely address unmet patient needs? [How can we] move antibodies from pre-clinical in vitro and in vivo studies into clinical trials with higher translatability fidelity?” This was the driving force behind the company’s development of their Dynamic Precision Library (DPL) platform, which aims to solve issues at the core of translational medicine. The company initially raised USD 8 million to show POC of their platform and to start building a global company in China. The five years it took Adagene to take the platform from conception to implementation has paid off: in March 2019, biotech powerhouse Celgene signed an agreement with Adagene to use the platform for antibody discovery.

It was his background in basic science, especially protein folding, that led him to approach fundamental topics such as the origin of antibody diversity from first principles. In addition to the DPL platform, they have also developed the SAFEbody™ platform, a dynamic precision masking technology designed to enhance the safety profile of therapeutic antibodies. Today, Adagene is capable of generating unique antibodies able to cross-react with evolutionarily conserved epitopes against a range of challenging targets where other technology has failed. Many of these differentiated products against both validated and novel targets have been approved to enter clinical trials in the US and China.

Due to their open and international worldview, these biotechs are also aggressively open to leveraging their technology into fruitful collaborations. With their unique

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small-molecule drug discovery and development platform targeting DNA damage response, Impact Therapeutics is focusing on the synthetic lethality approach to target cancer. CEO Bao Jun highlights, “Impact has been very successful in its in-house R&D efforts, having discovered some very innovative and interesting molecules [including their Phase I PARP inhibitor, IMP4297 with the potential to become ‘best-in-class’], but now the company is entering the drug development phase with products in the POC testing stage. My previous experience in commercial operations can bring value. BD and licensing are in my blood. I can help Impact generate and explore potential opportunities to collaborate with other companies, whether through combination therapies or in-licensing other companies’ programs into Impact.”

He reveals, “we are looking for assets that fit our focus on the platform of synthetic lethality, either on their own or in combination with our current assets. For instance, we currently have a collaboration with another Chinese biotech company, CStone Pharmaceuticals, and their flagship candidate CS1001, which is a PD-L1 antibody. For biotechs like us, we have to be very proactive and cast a very wide net so that we can snap up the good projects. We want to be the first to spot the next big thing!”

**LONG MARCH TO MARKET**

With the new wave of Chinese biotechs generally boasting a productive multi-asset pipeline through a combination of strategic in-licensing and internal R&D activities focused mainly on validated targets, they tend to advance assets into the clinic at a quicker pace. As a result, the Chinese industry is now facing a clogged clinical pipeline. With speed to market being increasingly important for commercial success within such a crowded space, the role of service providers is more important than ever.

As veteran industry leader Luo Shun assesses, “Chemistry, manufacturing and controls (CMC) is the bottleneck for most biotechs in China. Most of the overseas returnees have worked in research, but fewer in commercial processes, and even fewer in manufacturing. Small and new biotech companies may believe that their focus should be to develop...
Chinese Commercial Champions

While many Chinese biotechs are still close to the starting line with their product portfolio, Junshi Biosciences and Ascletis Pharma have crossed an important finish line by launching their own products on the Chinese market.

Champions of the Chinese PD-L1 race, Junshi launched their PD-L1 checkpoint inhibitor for melanoma in February 2019. CEO Li Ning shares, “our revenues were USD 11 million [in Q1 2019]. To put this into perspective, most products in China take between two and three years to make USD 14 million. Our projection is to reach between USD 80 and 90 million this year” – an exceptional level of sales.” To achieve this, Junshi undertook a very strategic approach to pricing, sales and marketing. Li shares, “pricing has a tremendous impact on the rate of market penetration, so we determined the price point for our PD-L1 through both price comparison and patient surveys,” eventually arriving at a figure that is a third of rival MSD’s Keytruda’s price in China. In addition, “around 90 percent of all cancer patients in China are treated by around 500 hospitals. In October 2018, we set up our sales team to specifically cover those 500 hospitals. We also implemented a system to train our salesforce in carrying out scientific promotions based on scientific data.”

Ascletis can certainly lay claim to many firsts in China: first home-grown biotech to launch their own product in China, first to receive reimbursement, and first to IPO on the Hong Kong biotech board. GANOVO®, their first Hepatitis C virus (HCV) drug with a 97 percent cure rate, has been marketed since June 2018. Working in chronic diseases, Ascletis chose to go broad. CEO Jason Wu sketches, “we cover Tier One cities all the way to Tier Four. This widespread coverage is very important. Not all the patients are in Tier One cities. We are also investing a lot in medical education with doctors and physicians.” To further supplement that reach, they have also taken advantage of a relatively new channel, ‘Direct-to-Patient’ (DTP), working with over 200 DTP pharmacies. Wu emphasizes, “we really have to differentiate ourselves in terms of our understanding of the market and patient needs.”

Both CEOs concur that the current environment in China is highly conducive to launching their products. Junshi’s Li recounts, “We recruited everyone for our commercial team within three months, without the use of recruiters or headhunters. Around 90 percent either come from MNCs or have MNC experience.” Ascletis’ Wu agrees, “we were lucky to have recruited what I believe to be the best team within the hepatitis area [with] a lot of Big Pharma experience. For instance, our National Medical Director was the national medical affairs director for Gilead China.”

Innovative products to generate commercial value. However, if you cannot manufacture your products, they cannot reach the market. Global biotech leaders like Genentech and Amgen actually invested a lot of resources into process manufacturing from a very early stage. Largely because of that strategic decision, [they] grew into global industry players.”

Having worked in biologics for over 25 years with heavyweights as such as Serono, Genentech and Amgen, he
Putting the ‘Nova’ in Innovation

Another company with dreams of optimizing drug discovery and development is EnnovaBio, which has developed their own bio-informatics platform as a key technical differentiator. As co-founder and CSO Shou Jianyang frames, “we wanted to differentiate ourselves from MNCs [with] the resources we do not have [and] from local companies that also have many talented people with rich expertise. The attrition rate for biotech projects is so high. As a small biotech, we are not equipped to discover new targets ourselves but if we manage to develop strong data-mining capabilities to extract useful information from publicly available data, that would give us the competitive edge.”

He philosophizes further, “we do not see drug discovery linearly. We view complex diseases as a network. We perform sophisticated network analysis to identify key nodes in disease pathology, which may not only produce higher success rates [for] target selection but also means these targets have increased opportunities to extend into multiple indications, which would de-risk our overall pipeline.

As a result, they have not only been able to build their own pipeline, led by their flagship asset, an oral medication for diabetic retinopathy (DR) currently in preclinical development, but also form partnerships with other biotechs for combination studies in immuno-oncology. At the ASCO 2019 conference, CSO Shou recalls, “a key message was that combination therapy is the future of cancer treatment but so far the industry has met limited success.” CEO Jiang Lei echoes, “drug discovery is fundamentally risky and uncertain, so to mitigate that we focus on rational design as much as possible. The same applies to combination studies. While there are many combination studies ongoing, many lack strong theoretical support. Since there are almost an infinite number of ways to combine different compounds, without a rational basis, it is challenging to have clinical success with limited resources.”

Impact Therapeutics is dedicated to the discovery, development and commercialization of novel targeted therapeutics to treat cancer and other life-threatening diseases with its focus on synthetic lethality as a mechanism to kill cancer cells.

Among global biotech companies, we have built the broadest and the most competitive DDR product pipeline spanning early discovery to late clinical stage. Targets related to DDR (DNA damaging response) are the most clinically- and scientifically-validated synthetic lethality therapeutic targets.
GM TJ Deng adds, “BioDuro 4.0 is really about explosive growth. In three years, we are looking to double our current size in China and the US. In China, we are looking to add a third site to our existing network in Beijing and Shanghai, which will be able to accommodate over 1,000 scientists and researchers.”

A niche provider in a sector where strong M&A activity has bred giants like IQVIA and Syneos Health, BioDuro understands the need to differentiate themselves from the giants. CFO Ian Wisenberg asserts, “we are not looking to be the biggest necessarily but certainly to be the best … offering very differentiated solutions. BioDuro is focused on helping [our clients] bring their discoveries into Phase II.” To support this, they have already made a few strategic acquisitions including Molecular Response in 2018, which possesses the world’s largest living tumor bank. Wisenberg shares, “[this has] allowed us to position our oncology business as a separate business unit offering highly differentiated technology.” They also look to add capabilities in API manufacturing from IND enabling to Phase II stages, and in biologics.

MEDICINES FOR THE MASSES

Despite China’s rising economic might, the country faces a dramatic urban-rural divide. 43 percent of China’s population is still rural, compared to 18 percent in the US, and the rural income deficit averages 63 percent nationwide (against four percent in the US). Newer and more innovative medicines, usually imported and pricey, do not usually penetrate the hinterlands, particularly if they do not receive national or provincial reimbursement. Despite the Chinese government’s measures to promote the establishment and use of community hospitals and clinics, there remain severe challenges to overcome.

For respiratory diseases, for instance, OMNI Pharmaceutica founder Kai Zhang contextualizes, “China has nearly 100 million patients with chronic obstructive pulmonary disorder (COPD) and 60 million patients with asthma. The prevalence in rural areas is higher than in urban cities but the treatment rate is disproportionally low. 80 percent of national sales within the respiratory category come from only 25 cities in China.” Part of the reason, he suggest, is that the majority – 95 percent – of inhalation products for COPD and asthma were being imported by pharma MNCs. This inspired him to establish OMNI in 2011. He reminisces, “I believed that I could make a change. If I could bring superior technology combined with local manufacturing capability, it would be very helpful to people in China.”

While local companies were previously impeded by high technical barriers in both device and dosage forms, Omni can leverage on its founder’s decades of R&D and manufacturing experience, and as of October 2019, the commercial capabilities of newly appointed CEO – ex-Eli Lilly veteran, Sonia Wang. She announces proudly, “I believed that I could make a change. If I could bring superior technology combined with local manufacturing capability, it would be very helpful to people in China.”

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Our mission: to provide patients with treatment options that work better and cost less.
Setting their sights beyond the Chinese market is Ronnsi, which stands out amidst the sea of cancer biotechs in China for their unorthodox focus on heparin-related products. CEO Yiming Yao recounts, “heparin is a natural product discovered in 1916. It has been used within the clinical setting for over 70 years [and] is listed on the World Health Organization (WHO)’s List of Essential Medicines, used mainly as an anticoagulant in surgery and dialysis.”

Conventional production of pharmaceutical-grade heparin relies on the use of pig intestines, which causes a problem for Muslim patients. Yao explains, “the Muslim-majority countries are severely undermedicated in terms of heparin when compared to their requirement. The maximum price is CNY 400,000 (USD 60,000).”

In addition, another pressing problem is the lengthy ‘vein to vein’ time, (time from when cells are extracted to when they are infused back into the patient) For products approved in the US, cell manufacturing takes two weeks and the total procedure could take as long as 30 days. He laments, “We are treating very late-stage patients. Some patients would lose the opportunity to get clinical benefit during long wait.” This is why Gracell, he enthuses, has developed “FasT CAR technology, [which] allows for manufacture to be completed overnight – the shortest in the industry so far. This achievement was made not through increased labor hours or cutting corners, but simply by ‘working faster’. We benefited from our strong interdisciplinary teams [and] also made a number of other technical adjustments.” As a result, T-cells cultured with FasT CAR technology possess higher potency, better proliferation, better memory/stemness, less exhaustion, better migration to bone marrow and spleen and higher manufacturing success. “The findings of FasT CAR preclinical and clinical studies were released at CAR-TCR-T Summit Asia, June 20 this year in Shanghai.”

FasT CAR technology is just the tip of the iceberg, however. Cao exults, “Beyond FasT CAR, Gracell is also evaluating Dual CAR, UCAR3, (off-the-shelf CAR-T) and Enhanced CAR T cell therapies in investigator initiated trials to get first hand clinical data, followed by IND filing. We may be based in China, but our vision is to contribute novel therapies worldwide. Gracell is built to expedite cellular immunotherapy from lab to bedside. After all, he adds, “there are so many diseases and unmet medical needs, one company cannot cater to all of them. We hope to have wide-spectrum partnerships with other pharma companies – in order to benefit the most patients, in China and globally.”
Product Versus Platform

China and Japan are the two largest economies in Asia and jostling for position as the second-largest pharmaceutical market in the world – discounting the Traditional Chinese Medicine segment of the market, as some analysts do. The two countries have always had a complex relationship. Economically, their ties are intricate, with China being Japan’s most important trade partner and Japan being China’s third-largest. Nevertheless, EPS Group Chairman Yan Hao laments, “despite the geographic proximity and cultural similarities, Sino-Japanese relationships and collaborations have never run as deep or as broadly or as fruitfully as Sino-US partnerships.” Established in 1991, EPS Group is today the largest clinical contract research organization (CRO), the largest site management organization (SMO) and leading clinical services organization (CSO) in Japan.

Born in Suzhou, China but having emigrated to Japan at 18, he is well-placed to theorize the reason for this disconnect: “both the US and China’s industrial development culture is more focused on platform development. Companies like Google, Amazon [in the US and] Alibaba, Tencent and Baidu [in China] ... are platform companies. [This] facilitates cross-border discussions and partnerships between the US and China [and also] helps US-educated overseas Chinese returnees pitch their ideas to Chinese government officials for funding and support.” On the contrary, “Japan is almost the opposite, they focus on individual products, on concrete details – what I call ‘craftsmanship’. Therefore, when they try to pitch their projects or companies in the Chinese market, their ideas do not resonate with the Chinese market.”

Nevertheless, there is much to learn from each other. Yan points out, “Japanese companies have a longer history and track record of expertise in new drug development. Japan is still ahead when it comes to pharmaceutical innovation. Having a good product is important, but [so] is having the right commercial and business model. Therefore, Japan is a very complementary partner to China.”

In 2008, Yan decided to return to China to establish EPS China as a local CRO with a significant investment of USD 45 million. His vision? “I like to use a Chinese proverb: ‘building a nest to attract phoenixes’. This means leveraging our positioning, excellent track record and an extensive network within the Japanese pharmaceutical and medical device industry to offer them our business development platform in China.” He expresses, “we hope that will not only attract many Japanese ‘phoenixes’ – innovative pharma and medtech companies – but also American and European ones. As our name suggests – ‘EPS’ stands for ‘Ever Progressing System’ – we are very open to collaboration and new ideas, and we welcome all potential partners and clients. We hope to be your partner in China!”

Innovate to Excel

Founded in 2019, Transcenta is a global biotherapeutic company that fully integrates antibody-based discovery, R&D and manufacturing to help patients globally. We focus on developing innovative biologics in oncology, bone disorders and nephrology at affordable prices.

Our proprietary Immune Tolerance Breaking Technology is capable of generating antibodies with diverse epitopes. With T-BLOC, our flexible manufacturing facility, we can accelerate product development and improve quality control while significantly reducing production costs.

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to the US and Europe. With a total 1.7 billion Muslims globally, the market potential is huge.”

In addition, Yao supplements, “80 percent of porcine heparin is produced in China. This creates an immediate supply chain risk as a single incident of widespread Africa swine fever in the country [currently occurring in China] will jeopardize the continuous supply of this life-saving medicine.”

Ronnsi has developed a new product: heparin from sheep (ovine) intestines. He suggests, “currently, we might be the only company in the world to work in the area of ovine heparin!” Already in the process of regulatory filing in Indonesia, they hope to receive approval by end-2019, and are also in discussion with the FDAs in the US, Pakistan and Iran.

**CHINA AND THE WORLD**

The emergence of the modern European and US pharma companies in the 20th century has shaped the global industry as it stands today, setting standards and conventions across the value chain as well as contributing the vast majority of innovations. Merck KGaA, Darmstadt, Germany GM Rogier Janssens ponders, “today, when we can expect new biopharma innovations to reach the Chinese market in the same year as the North American and European markets, I think the revenue model will change drastically.” In this context, Merck has high ambitions in China. He reflects, “Our 2025 horizon is quite clear for China: we want to transform the lives of 40 million patients. A good part will be from off-patent products for NCDs, but at the same time, we are looking to launch major innovations in the Chinese market.” At the same time, he emphasizes, it is not just about products: “we want to build a patient-centric platform in the ways we engage with patients and the public, develop innovative business models, and forge new and interesting partnerships with stakeholders here.”

As the global pharma industry’s center of gravity shifts east, all eyes are on the mercurial Chinese market. With a kaleidoscope of players jostling for new opportunities and growth in the high-risk, high-reward market, China is certainly not for the faint-hearted. Nevertheless, the excitement is palpable and industry leaders in China seem imbued with an adventurer’s courage and optimism. Eli Lilly GM Julio Gay-Ger describes, “all emerging markets have instability and risks. The Chinese pharmaceutical market is advancing very quickly in terms of accelerated market approvals, reimbursement, policies promoting innovation and so on – all very positive developments, [which nonetheless] create dynamics of uncertainty and risk.” This is why when Gay-Ger arrived in China, his mandate was clear: to set up the organization for future success. He enthuses, “Lilly China is at an absolutely critical point where we can serve a lot of patients and bring a lot of innovation here in a very short period of time.” As a result, he continues, “I feel incredibly honored to be here. We have a long-term vision for the country. Lilly has always been ‘in China for China’ but in a few years, we would like to say we are ‘in China for the world’.”

Today China is pouring substantial resources into its healthcare industry and a veritable army of overseas returnees has been mobilized to join the cause to transform the country into a biopharma innovation powerhouse. With talent, capital and a supportive regulatory environment, China’s rise seems inevitable. What this might mean for the global pharma industry remains the landmark question of the century.
The Time to Refine

Celebrate a new product’s first birthday by examining post-launch commercial issues

Life sciences companies can spend years creating a commercial strategy that brings a new product to market. But once that therapy gains a foothold with physicians, how can the company continue to improve the product’s commercial performance and grow the number of prescribers and prescriptions? The product’s first birthday serves as an ideal time to analyze sales and optimize commercial operations.

Now armed with a year’s worth of sales data and proper computing power, the commercial team can take a hard look at sales and marketing tactics to see what’s working and what’s not—and then take appropriate action. Analysis should include sales force feedback on physician accessibility, desire for additional product-related materials, and response to future marketing efforts.

The commercial team can deploy a mix of advanced and traditional analytical techniques to glean from data insights that improve the post-launch commercialization strategy and enhance sales force effectiveness. To do so, the team will reevaluate assumptions and address shortcomings, then make changes. One common change is to switch the incentive compensation payout structure from commission-based to quota-based. But there are four other ways life sciences companies can refine commercial strategies to maximize product sales, post-launch.

1. Enhance targeting. One year after launch, the commercial operations team further understands customer behavior and their interactions with the product. That means the company is better equipped to fully account for the customer perspective in its marketing strategies. First, the commercial team can review sales data to identify which physicians—known as “early adopters”—prescribe the drug as compared to its competitors. Second, using primary and secondary data, the company can analyze indicator behaviors and attitudes prior to product sales. Finally, the commercial team can use these insights to enhance targeting and optimize its customer base.

If data shows that early adopters share certain attributes, including demographics, geography, prescribing behavior, or accessibility, the commercial team can identify physicians with those same attributes who may see value in the product as well. The company would then update any field-facing tools to communicate new targets to the sales force.

2. Refine messaging. Commercial teams should also revisit product messaging one year after launch. They can survey physicians on the product and its competitors, and measure message recall and attribute importance. Sales force feedback can help analyze messaging effectiveness. The commercial team then combines all these insights to update the product’s communications strategy.

3. Follow the patient journey. One year in, the commercial team should merge various data sources and examine the patient journey for any opportunities or obstacles in the treatment plan. For example, if a product experiences an unusually high number of unfilled prescriptions, the company should investigate any barriers and work toward a solution. Perhaps physicians prescribed the product, but high copays or other issues with payers discouraged patients from filling it. The commercial team could then consider working with payers on strategies to increase product sales.

As another example, we surveyed physicians and patients and reviewed claims data to map a patient journey for a product that the commercial team positioned as a second-line therapy. The map indicated, however, that physicians began prescribing it as a first-line therapy due to its superior safety profile. This insight allowed the company to update its marketing and messaging strategies.

4. Prepare for the lifecycle ahead. Data collection and analysis are essential and continuous components of lifecycle management. A product’s first birthday is the perfect occasion to look to improve performance by examining data and fine-tuning the commercial plan. To do this effectively, though, companies need to deploy rigorous techniques such as machine learning, sales analytics, and primary marketing research. Those that examine their commercial operations each year using a data-driven strategy will differentiate themselves from competitors and enjoy many more birthdays to come.

— Jon Hesby is a partner; Melissa McDevitt is an associate partner; and Esin Izat is a manager; all with Beghou Consulting
Once Upon a Brand
The key ingredients for startups in building their brand story

Whether you are Nike, Starbucks, or a life science startup, you have a story to tell. A story about the moment when the spark of inspiration and discovery shaped a disruptive therapy that could help change lives. But the truth is, many startups are still in a research phase, or pre-commercialization. They are filled with scientists or engineers eager to get the facts and the data out there to investors or key physician influencers. So, building a brand story may seem premature, and frankly, a bit fluffy. And yet, the brand story is the key to success. If you build it, with these four critical brand characteristics in mind, they will come: simplicity, personality, consistency, and authenticity.

Simplicity
It is quite common for companies to use thousands of words to describe where they came from, and what they do. But the concept behind it is really quite simple:
1. There was a problem
2. We solved it
3. Success comes because of it

In short, your brand story should be simply and clearly told—“a short narrative that one could tell during an elevator ride.” But the challenge for many startups comes in determining what should be left out of the narrative. The key is to include only the compelling and differentiating points that keep the story moving. Simplicity breeds clarity, clarity breeds vision, and vision inspires multiple stakeholder audiences to want to be a “part” of the story.

Personality
We have all witnessed life science companies’ presentations to investors, usually fact-filled and data-driven. But sometimes, the presenter manages to connect the facts and the scientific points of difference by weaving in a distinct and ownable lexicon in a captivating way. This creates a personality, a personal voice for your brand. More companies are realizing the urgency of effectively communicating a story. It’s interesting to note that veteran actor Alan Alda is helping science professionals “communicate complex topics in clear, vivid, and engaging ways.” Remember, you yourself don’t have to be a “big” personality to build a brand story that has a personality.

Consistency
You might be surprised to learn that even with all the pre-market prep that goes into attracting investors, addressing KOLs, and appealing to practitioners and patients, the product brand storyline is often inconsistent, and the language used to express key ideas is not nailed down.

This happens because, in a life science startup, there are often different people presenting at different times, from the CEO to the CFO to the lead scientist. And without the boundaries of a brand story, there is a danger that each time someone describes the brand, they describe it differently than someone else in the same company. They might use different words, different key points, and not recount the story in the same way. Inconsistency leads to confusion about the brand and its purpose. To build a consistent story, the team must “define” and “align.”

While adept at explaining the science, life science companies don’t ordinarily micro-tune their messages using defined branding—a skill better suited to advertising agencies. Instead, their tendency is to rely on industry clichés and imprecise buzz phrases, such as “allowing for multiple shots on goal,” for example. So, in a sea of catch phrases, it’s critical to define the key messages to incorporate into your story, and the unique lexicon around your brand. To make this happen, the entire company must then align around that lexicon, and stay true to it. This is where advertising agencies can be an objective—and strategic support. Through exploratory workshops and brand foundation work, they bring key stakeholders together to ensure that there is a defining of the core messaging and true alignment around it.

Authenticity
By nature, life science companies are grounded in storytelling. It’s inherent in the scientific process to develop a hypothesis and prove it. So already, life science startups come from an authentic desire to tell a story that makes a difference. That authenticity should be in the DNA of every brand story. Authenticity builds trust. Many stories end up feeling like sales pitches, filled with marketing jargon and benefit bullet points. But it’s the simple, personal, and consistent story that screams authenticity. For a brand story to truly engage and inspire, it needs to have an authentic voice—not from one individual, but from the entire organization.

Communicating Your Narrative: A Pharm Exec podcast with Robert Finkel, CEO of FreshBlood Group
bit.ly/322fJ6a

ROBERT FINKEL is CEO and PATRICIA MALONE is Chief Creative Officer, both with FreshBlood Group
Quality goes up. Headaches go down. That changes everything.

Quality isn't just a box you check. It's not limited to a process or even a department. It's the ultimate differentiator. The MasterControl Platform helps you digitize, automate and connect critical processes, documents and data so you can improve quality across your entire product life cycle.

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