Life Science Leader

Connect. Collaborate. Contribute.

JANUARY 2018

Can Joseph Papa Save Valeant?

p. 16

JOSEPH PAPA
CEO, Valeant

FILLED WITH PRIDE

The Dedication and Persistence that Debbie Applies to Each and Every Client Project Makes all the Difference.

Fill finish manufacturers of biologics must have a strong understanding and appreciation of the innate properties of these large, complex molecules and the external factors that can adversely affect quality and stability. Althea's excellent first-time success rate and impeccable regulatory track record highlights the quality of our people and the work they do.

Learn more. Visit AltheaCMO.com

ALTHEA | THE POWER TO MAKE

A MEMBER OF THE AJINOMOTO GROUP

11040 Roselle Street, San Diego, CA 92121 | 1.888.425.8432 | 858.882.0123

PROCESS DEVELOPMENT • DRUG SUBSTANCE MANUFACTURING • DRUG PRODUCT MANUFACTURING • ANALYTICS • HPAPI & ADC

Enhance productivity with continuous bioprocessing

Continuous bioprocessing can positively impact product quality, improve process consistency, and debottleneck your biomanufacturing operations. Engage with GE Healthcare and our continuous bioprocessing experts today to conduct a needs-based analysis of your process to optimize and intensify your bioprocessing strategy.

gelifesciences.com/bioprocess

GE Healthcare Bio-Sciences AB, Björkgatan 30, 751 84 Uppsala, Sweden.
1038031017AD

CONTENTS

Welcome to

Life Science Leader

JANUARY 2018 VOL. 10 NO. 1

@LifeSciLeader1 linkedin.com/company/life-science-leader facebook.com/LifeScienceLeader WWW.LIFESCIENCELEADER.COM

16 Cover Story: VALEANT

When Joseph Papa took over Valeant Pharmaceuticals in May 2016, the company was in turmoil. We catch up with Papa and see how he's coming with what he calls "the turnaround opportunity of a lifetime."

Features:

Insights:

Correction: In the December issue we accidentally transposed Philippe Luscan's name in the article titled "Are You Ready For The Future Of Biopharma Manufacturing?"

LIFE SCIENCE LEADER (ISSN: 21610800) Vol. 10, No. 1 is published monthly by VertMarkets at Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672. Phone (814) 897-9000, Fax (814) 899-5587. Periodical postage paid at Erie, PA 16510 and additional mailing offices. **SUBSCRIPTION RATES** For U.S. based subscribers, $295 for one year. If your mailing address is outside the U.S. the subscription price is $445 for one year. **POSTMASTER**: Send address corrections (Form 3579) to Life Science Leader, Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672. **Publications Agreement**: No. 40722524 c/o AIM, 7289 Torbram Road, Mississauga, ON L4T 1G8.

CEO Tenure: When Is It Time To Move On?

ROB WRIGHT Chief Editor

How long should a CEO stay in the job? In a 2014 *Harvard Business Review* article, executive coach and INSEAD professor Manfred F. R. Kets de Vries said the most common response he gets to that question from CEOs is seven years, plus or minus two. Seems reasonable, as the nature and challenges of the position evolve over time, going through three distinct phases:

- **ENTRY** - honeymoon period when new CEOs are most open to learn, experiment, and innovate, but unlikely to perform to full potential, which is to be expected
- **CONSOLIDATION** - period when the CEO has alliances with key stakeholders, top executives are committed to the chosen course, has a good relationship with the board, good results, and is secure in the role
- **DECLINE** - few or no new products planned for the near future, no initiatives to find new markets, no new leadership blood, and everyone sings to CEO's same old tune as the job has become routine.

According to Kets de Vries, the best scenario for a CEO whose performance is declining is to get going while the going is still good. In other words, leave while they are at the peak of their performance, just before the decline.

Over the last several years we have witnessed some rather high-profile departures of CEOs within biopharma. For example, Bob Hugin spent five years as CEO of Celgene before being replaced by Mark Alles in 2016. John Lechleiter spent eight years in the top spot at Lilly prior to stepping aside for Dave Ricks in 2017. And just this past year, Joe Jimenez, having spent eight years as Novartis' CEO, announced Vasant (Vas) Narasimhan would be taking over this year. (Jimenez will remain available for advice and support until officially retiring on Aug. 31, 2018.)

It seems these executives are following some of the advice espoused by Kets de Vries.

In this issue, we feature another biopharma CEO, Joseph Papa, who in 2016 took the reins of Valeant Pharmaceuticals for what he has branded the "turnaround opportunity of a lifetime." But his rapid departure from Perrigo, where Papa had spent 10 years as CEO, was met with a good deal of criticism. For example, some have suggested that Papa didn't leave the company in as good of shape as he could have. Perhaps, but consider the data from Kets de Vries. Would Perrigo have been better served had Papa stayed on just a little longer, or had he already stayed past his peak and the sooner he moved on, the sooner Perrigo could begin moving on, too?

It's my understanding that Papa wasn't in search of a new job when he initially contacted Valeant; he was on a quest to fix part of Perrigo's pipeline problems by attempting to in-license dermatology and eye-care products. It was only after those product-focused conversations that he was approached about running the company. And while there are those who'd have preferred Papa stay and get the Perrigo ship righted prior to departing, the unfortunate reality is — despite best intentions — not every CEO gets to go out following an MVP-type year, and some CEOs stay long past their peak. L

Life Science Leader
JANUARY 2018 VOL. 10 NO. 1

LIFE SCIENCE LEADER
5340 Fryling Rd., Suite 300
Erie, PA 16510-4672
Telephone: 814 897 7700
Fax: 814 899 5587

WWW.LIFESCIENCELEADER.COM

CEO
Jon Howland / Ext. 203
jon.howland@lifescienceconnect.com

EDITORIAL DIRECTOR
Dan Schell / Ext. 284
dan.schell@lifescienceleader.com

CHIEF EDITOR
Rob Wright / Ext. 140
rob.wright@lifescienceconnect.com

EXECUTIVE EDITOR
Wayne Koberstein
wayne.koberstein@lifescienceleader.com

EDITORS
Louis Garguilo
louis.garguilo@lifescienceconnect.com

Bob Marshall
bob.marshall@lifescienceconnect.com

Ed Miseta
ed.miseta@lifescienceconnect.com

Anna Rose Welch
anna.welch@lifescienceconnect.com

VP OF AUDIENCE DEVELOPMENT
Michael Bennett
michael.bennett@lifescienceconnect.com

STRATEGIC PARTNERSHIPS/BUSINESS DEV.
Tim Bretz / 724-940-7555 / Ext. 123
tim.bretz@lifescienceconnect.com

Cory Coleman / 724-940-7555 / Ext. 125
cory.coleman@lifescienceconnect.com

Scott Moren / Ext. 118
scott.moren@lifescienceconnect.com

Denise Mosley / 724-940-7555 / Ext. 126
denise.mosley@lifescienceconnect.com

Shannon Primavere / Ext. 279
shannon.primavere@lifescienceconnect.com

Perry Rearick / Ext. 263
perry.rearick@lifescienceconnect.com

Ray Sherman / Ext. 335
ray.sherman@lifescienceconnect.com

Tracy Tasker / Ext. 297
tracy.tasker@lifescienceconnect.com

Derek Van Slyke / Ext. 217
derek.vanslyke@lifescienceconnect.com

Casey Weed / Ext. 219
casey.weed@lifescienceconnect.com

DATA ANALYTICS
Rick Miller
rick.miller@lifescienceconnect.com

Kevin Morey
kevin.morey@lifescienceconnect.com

PRODUCTION DIRECTOR
Lynn Netkowicz / Ext. 205
lynn.netkowicz@jamesonpublishing.com

CLINICAL LEADER FORUM

BRINGING TOGETHER A COMMUNITY COMMITTED TO BETTER TRIAL OUTSOURCING

Clinical Leader Forum focuses on clinical trial challenges impacting sponsor companies and their relationships with CROs and sites. Tailored for executives from sponsor companies that outsource, the sessions feature clinical professionals sharing their secrets on how to conduct more efficient and successful clinical trials.

Clinical Leader Forum is brought to you by *Life Science Leader* and ClinicalLeader.com

ClinicalLeaderForum.com

Have a response to our experts' answers? Send us an email to rob.wright@lifescienceconnect.com.

EAB

EDITORIAL ADVISORY BOARD

Q Why does it seem academia is moving away from participating in clinical trials, and what could be done to bring them back into the fold?

A **OVER 30 YEARS AGO** when I began my career, clinical trials were predominately the purview of universities. Now, out of 50 sites in a representative program at my company, only three are academic and only one entered a subject on a study. We tried hard to engage – advisory board involvement, conference meetings, site visits – but simply couldn't get the university sites open. Reasons included potential IP infringement related to knowledge sharing, contract language stalemate, exorbitant budget requests, Sunshine Act reporting, or simple inertia due to so many other competing priorities. The loss of the medical/scientific expertise and involvement by those most heavily invested in bringing better treatments to patients is detrimental to the industry. Perhaps it's time for an NIH initiative to remove the barriers to entice the academics back into sponsored research.

MARY ROSE KELLER
is VP of clinical operations at Heron Therapeutics. She has 30+ years of industry experience.

Q How can biopharmaceutical companies be more successful when working with payors in the future?

A **PHARMACEUTICAL COMPANY MANAGED-MARKETS ACCOUNT MANAGERS** can no longer rely on "selling" a health insurer or payor on a basket of products across a broad company portfolio. In today's environment, the relationships held by managed-markets account managers are still critically important, particularly for the largest payor, but they must be more focused on their messages. To be successful, account managers and the pharmaceutical companies they represent should focus on three things:

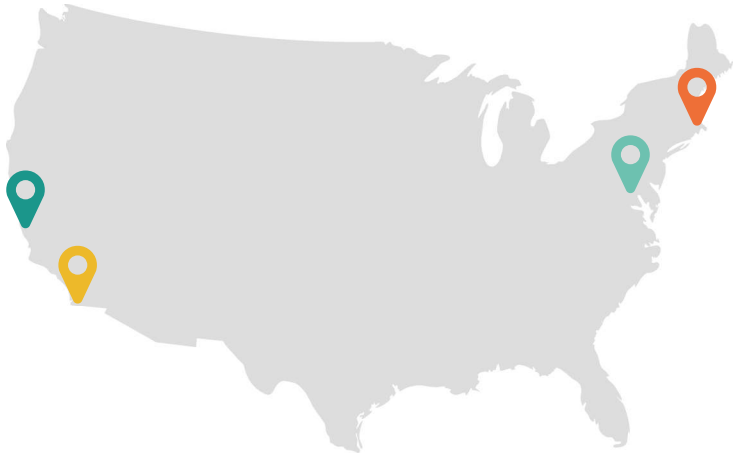
1. Start early: Account managers can't rely on bundling products together or expect to start discussions a few months before launch. They should be regularly updating payors on their portfolios and potential launches on a regular basis, even years before potential launch.
2. Be the architect of the story: Account managers should not let payors simply draw their own conclusions related to a particular product, therapeutic class, or competition. Account managers should do more than share the clinical attributes of their own products. Rather they should architect the entire story around their product, including class dynamics, generics, and competition.
3. Engage at the top of the house: While it is important for account managers to maintain good relationships with payors, the payor market has gotten so consolidated that it is equally as important to engage at the most senior levels of both organizations around product launches and critical products. Pharmaceutical company CEOs must be willing and able to engage with the largest payors throughout the life cycle of their product portfolios and particularly at launch of new products.

JEFF BERKOWITZ
is a 25-year industry veteran and has served in senior executive roles across the healthcare continuum with the likes of Schering-Plough, Merck, the Walgreens Boots Alliance, and UnitedHealth Group.

OutsourcedPharma
CONFERENCE AND EXHIBITION

THE OUTSOURCING INDUSTRY HAS NEVER TALKED LIKE THIS BEFORE.

Outsourced Pharma Conference & Exhibition is a vibrant forum that builds a community for networking and discussion. The focus is on topics most relevant to sponsor-provider partnerships and supply chain management in an open format that stimulates interaction.



JOIN US FOR A MEETING NEAR YOU IN 2018

BOSTON, MA	May 14-15
PHILADELPHIA, PA	July 18-19
SAN DIEGO, CA	August 21-22
SAN FRANCISCO, CA	October 29-30

For the agenda, speaker, and exhibition details visit **OutsourcedPharmaEvents.com**

CMS Opens Path To Reform Of Part D

JOHN MCMANUS The McManus Group

Pressure had been building for more than a year for something to be done about drug prices, and specifically inflated list prices to the patient at the pharmacy counter that do not reflect the substantial rebates manufacturers are providing.

Where was all the money going? How could the list price and patient copays for drugs keep rising when the net prices — accounting for manufacturer rebates — stayed level?

In November, the Trump administration asked the same question when CMS issued a proposed rule that could pave the way for a fundamental restructuring of how negotiated price concessions are passed on to the patient in Medicare Part D. It is the first substantial rulemaking of the Part D program since it was first implemented over 10 years ago. (CMS has been running the program primarily through annual, subregulatory "call letters.")

The rule makes the case that manufacturer and pharmacy fees must be passed on to patients at the point of sale in order to reduce out-of-pocket costs and correct emerging distortions in the program.

On the last day of the Obama administration, CMS issued a report noting that direct and indirect remuneration (DIR) — resources collected by plan sponsors from pharmaceutical manufacturers and pharmacies often months after the patient had received their prescription — had nearly tripled from 2010 to 2015, growing twice as fast as gross Part D costs.

That report, and growing ire from patients around the country at rapidly increasing prices at the pharmacy counter, prompted CMS to undertake a fundamental re-examination of this area.

At issue is how CMS interprets the term "negotiated price" in the statute. In the proposed rule, CMS noted, "To date, sponsors have elected to include rebates and other price concessions in the negotiated price at the point of sale *only very rarely*."

More troubling, CMS found that the current system has distorted pricing behavior. CMS stated, "Plans sometimes opt for higher negotiated prices in exchange for higher DIR and, in some cases, even prefer a higher net-cost drug over a cheaper alternative. This may put upward pressure on Part D program costs and shift costs from the Part D sponsor to beneficiaries who utilize drugs in the form of higher cost-sharing and to the government through higher reinsurance and low-income cost-sharing subsidies."

CMS went on to castigate current pharmacy benefit manager practices: "Sponsors have negotiated more high-price, high-rebate arrangements, especially in recent years, which has caused the proportion of costs for which the plan sponsor is at risk to shrink when those higher rebates are not passed on at the point of sale. Under current rules, therefore, Part D sponsors may have weak incentives, and, in some cases even, no incentive, to lower prices at the point of sale or to choose lower net cost alternatives to high-cost highly rebated drugs when available."

Because the structure of the Part D benefit requires the plan to cover only 15 percent of the costs once a beneficiary hits the catastrophic threshold while Medicare covers 80 percent, any rebates and other DIR the plan collects above its projected bid primarily contributes to profit, not lower premiums. CMS notes, "Our analysis of Part D plan payment and cost data indicates DIR amounts Part D sponsors and their PBMs actually received have consistently exceeded bid-projected amounts."

In the proposed rule, CMS solicits comments from stakeholders on how to reform DIR and its impact on

beneficiaries, competition, and efficiency in Part D. Specifically, CMS is contemplating requiring a minimum percentage (but not all) of cost-weighted average of rebates to be provided at the point of sale. It may limit application of this policy to "categories or classes that most directly contribute to increasing Part D drug costs in the catastrophic phase of the coverage or drugs with high-price high-rebate arrangements."

A key issue is how requiring more price concessions to be provided at the point of sale will impact beneficiary premiums. The average Part D plan premium has grown by about 1 percent, annually, in the last five years and is projected to decline in 2018. Rapidly increasing DIR is a major reason for this stability.

But rapidly increasing DIR has turned the fundamental concept of insurance on its head. The sickest beneficiaries with the highest drug costs are cross-subsidizing all other beneficiaries, many of whom have no drug costs at all, who benefit with a lower premium.

"PBMs have morphed from claim adjudicators into little-known and largely unregulated corporate giants."

NATIONAL COMMUNITY PHARMACISTS ASSOCIATION

CONGRESSIONAL EXAMINATION

Congress is now more intensely examining the drug supply chain. On December 13, the House Energy & Commerce Committee convened a 10-member panel of stakeholders to seek their views on how the drug supply system may contribute to the rising costs of prescription drugs.

Mark Merritt of the Pharmaceutical Care Management Association, representing PBMs focused on CMS's Part D proposal, said, "Requiring point of sale rebates in Part D would lead to adverse selection and would increase premiums for all beneficiaries while reducing costs for a small minority." He also cited CMS's estimate that it would reduce a manufacturer's cost for providing the 50 percent required discount for drugs in the coverage gap by $29.4 billion if 100 percent of the point of sale cost were passed through.

But Merritt failed to mention the reason the manufacturer's discount would decline: fewer beneficiaries will hit the coverage gap because they will be paying lower copays on drugs, which reflect the price concessions provided by the manufacturers in the first place. Therefore, beneficiaries will progress more slowly through the benefit, and fewer will require the manufacturer discount in the coverage gap.

In the hearing, the National Community Pharmacists Association attacked the growing influence and consolidation of the PBM industry. "Since their inception PBMs have morphed from claim adjudicators into little-known and largely unregulated corporate giants that exploit their strategic position at the 'middle' of nearly all drug transactions in the U.S. to extract profits from the upstream and downstream participants in the drug supply chain while providing questionable value to the ultimate consumer."

Lori Reilly of PhRMA lamented that negotiations between biopharmaceutical companies and payers do not always make their way directly to the patient. "Unlike care received at an in-network hospital or physician's office, health plans base cost-sharing for prescriptions filled in the deductible or with coinsurance on undiscounted list prices, rather than on prices that reflect negotiated rebates and discounts. Enrollment in high-deductible health plans and use of coinsurance for prescription drugs has grown sharply in recent years, increasingly exposing patients to high out-of-pocket costs based on undiscounted prices."

She also took aim at hospital markups of prescription drugs, noting an October 2017 Moran Company study showing, "Hospitals charge prices that are on average nearly five times higher than their acquisition costs and are reimbursed up to three-and-a-half times their acquisition costs by commercial insurers."

Energy & Commerce chairman Greg Walden (R-OR) concluded the hearing by warning all 10 stakeholders in the drug delivery chain that members of Congress are eager to develop solutions on drug pricing, and each stakeholder had to come to the table with solutions.

CMS is presently in receiving mode, and the various industries are now planning their lobbying campaigns to influence the final outcome of a rule that could substantially change Part D and also influence commercial practices. Since 2018 is expected to be a light year legislatively, all eyes will be on how the Trump administration decides to advance the ideas it has laid on the table. L

JOHN MCMANUS is president and founder of The McManus Group, a consulting firm specializing in strategic policy and political counsel and advocacy for healthcare clients with issues before Congress and the administration. Prior to founding his firm, McManus served Chairman Bill Thomas as the staff director of the Ways and Means Health Subcommittee, where he led the policy development, negotiations, and drafting of the Medicare Prescription Drug, Improvement and Modernization Act of 2003. Before working for Chairman Thomas, McManus worked for Eli Lilly & Company as a senior associate and for the Maryland House of Delegates as a research analyst. He earned his Master of Public Policy from Duke University and Bachelor of Arts from Washington and Lee University.

The Emergence Of New Gene Therapy Hubs

TIMOTHY MILLER, PH.D.

Within the broader field of biotechnology, the focus on gene therapy has expanded rapidly in recent years. The primary reason is that many promising development programs are reaching later stages and are headed for the finish line. Recently, the FDA's advisory panel unanimously backed a new gene therapy intended to treat a rare eye disease, potentially leading to the first FDA-approved gene therapy in the U.S. Our progress in this sector is expanding and may lead to gene therapies that can deliver curative treatments for many significant areas of unmet need in healthcare in the near future. As these development programs advance, a growing need is presented for gene therapy research and manufacturing centers.

More than 30 years ago, at the dawn of the biotechnology era, the first generation of companies set up shop in areas that offered several key attributes, including a science-educated workforce, proximity to leading research centers, access to capital, space to accommodate often custom-designed technologies, and tax breaks and other incentives. These factors gave birth to the established hubs in Cambridge and Silicon Valley and also have provided support for smaller hubs in locations including Ann Arbor, MI; Philadelphia; and Denver. With gene therapy, we are at the dawn of another era of potentially rapid growth in the sector. And companies planning for their futures will once again consider a range of factors in identifying the optimal locations for gene therapy research and production centers.

THE NEW BIOTECH HUBS

Since the founding of the first biotechnology companies, a few things have changed that will affect where gene therapy producers may choose to set up operations. Many of the established hubs are no longer as eager to attract new companies, and so tax breaks and other incentives may be less generous. There is also intense competition for employees and access to research centers in those areas. In some cases, housing costs and other quality-of-life factors present challenges in attracting employees. But one of the most important factors is that there are now many options for locations where access to science-educated employees, established research centers, capital, and state-of-the-art technology is possible. As a result, leaders in gene therapy have considerable flexibility in choosing a location for future facilities.

One well-positioned option is Chicago, which is now among the top locations in the U.S. to receive funding from the NIH as well as venture capital investment. Chicago's thriving Illinois Medical District (IMD) now includes 560 acres of medical and healthcare-related facilities, labs, and several major hospitals including Rush University Medical Center. Local institutions such as Northwestern University, The University of Chicago, and the University of Illinois at Chicago also offer potential support from academic leaders involved in research.

Also in the Midwest, Indianapolis is a prospective biotechnology hub with many advantages. It is the headquarters for Lilly and home to the growing Indiana Biosciences Research Institute, which currently includes 18,000 square feet of laboratory and office space and is situated between four major hospital systems. There are also many public and private universities that feed into the local biotechnology industry, including Indiana University and Purdue University. With these resources nearby, many companies will be able to find the talented workers and innovators they need to facilitate development of advanced gene therapies.

The Research Triangle Park in North Carolina is another quickly growing area for biotechnology compa-

nies. It is already one of the largest research parks in the world, with more than 250 businesses and a network of medical researchers from centers including the National Institute of Environmental Health Sciences and the North Carolina Biotechnology Center. These resources are well-positioned to meet the needs of many gene therapy companies.

> *"But the bottom line is that companies should not be afraid to be a big fish in a small and relatively unknown pond."*

On the West Coast, Los Angeles is building its reputation in the life sciences sector. While the area does not have as big a foothold in biotechnology yet, it is the home of notable research centers including UCLA, the California Institute of Technology, and the Los Angeles Biomedical Research Institute. There, employers can tap into a highly skilled pool of life sciences graduates and medical researchers.

Cleveland, the site for Abeona's new gene therapy manufacturing center, is now a leading area for investment in biotechnology. The area attracted more than $2.17 billion in funding in 2016 from sources including venture capital, angel investment, federal research grants, and state initiatives such as the Ohio Third Frontier. Companies received private investment worth $373 million in 2016 and estimates indicate at least $155 million has been invested so far in 2017. It is also the home of leading healthcare businesses and research centers including BioEnterprise, Cleveland Clinic, HealthTech Corridor, and Midtown Cleveland. The affiliation with Nationwide Children's Hospital, which is in nearby Columbus, also made Cleveland a highly attractive option for our company.

CONSIDERATIONS IN MANUFACTURING

One important factor that growing companies may not consider early on when choosing a location is the need for future expansion of their manufacturing operations. Companies focused on developing gene therapies especially need to plan for manufacturing needs at every stage of clinical development and be prepared to meet demand for products at commercial stage. They can face significant problems if they cannot expand their footprint as production needs escalate. Companies must consider future needs related to scale-out, use of off-the-shelf versus custom technology, and risks associated with variability as production needs escalate. Investing in facilities that can handle these complex manufacturing needs is critical.

It is also important to monitor the local workforce and educational resources to make sure they are continually positioned to support future staffing needs. Research centers and educational facilities must be able to produce trained workers with the advanced skills and experience gene therapy companies require. At Abeona Therapeutics, we are developing next-generation, adeno-associated virus (AAV) gene therapies. When choosing a location for our company, we had to confirm access to a pool of employees and suppliers who understand the complex manufacturing associated with our AAV vector platform. These needs will differ based on the specific type of gene therapy being produced, and it is unlikely that any company will find a team of experts in their unique manufacturing process available at every stage of their growth. In addition, many gene therapies are targeting treatments for rare diseases, which also can require specialized training. Companies must do their due diligence to assess whether a region can accommodate their future needs in both skilled employees and advanced technologies.

Many key regions are both underappreciated and undervalued, which can be an advantage to emerging gene therapy companies. They present compelling combinations of available space, affiliation with leading academic research centers, local incentives, good quality of life, and other advantages. Companies should consider all of these factors and many others — and assess each option based on multiple considerations. But the bottom line is that companies should not be afraid to be a big fish in a small and relatively unknown pond. There can be less competition, reduced operating costs, and a pool of eager untapped talent compared to the bigger hubs. Companies also can find locations that offer great flexibility for future expansion. For example, in Cleveland, we have found and developed a talented melting pot of academia, biotechnology, patient advocacy, and other expertise necessary for commercial success — a community that we are proud to call our own.

TIMOTHY MILLER, PH.D., is president and CEO of Abeona Therapeutics and has 16 years of scientific research, product development, regulatory, and clinical operations expertise.

Daré Bioscience

Bringing to commercialization women's reproductive health products – starting with a novel contraceptive

WAYNE KOBERSTEIN Executive Editor
@WayneKoberstein

SNAPSHOT

Daré Bioscience is a public company focusing on women's reproductive health and developing Ovaprene, a novel, vaginally inserted contraceptive ring about to enter clinical trials. Ovaprene is designed to prevent pregnancy by impeding sperm motility with slow-release of ascorbic acid and the iron compound ferrous gluconate from the ring's permeable mesh. Ovaprene is the first clinical candidate of Daré, which aims to be a global player in developing products that fill the unmet, often overlooked reproductive health needs of women.

WHAT'S AT STAKE

In a typical case, a small company discovers or licenses a promising reproductive health product, develops it up to or even through human proof-of-concept, but then fails to find a large company partner to take it all the way through late-stage clinical trials. "Big companies prefer to take on late-stage products," says Daré founder, president, and CEO Sabrina Martucci Johnson.

"The development gap was really the inspiration for Daré," she says. "We saw it time after time again — products that could make a difference never make it past proof-of-concept. That is true in all categories of women's reproductive health, not only contraception, but also vaginal health, fertility, menopause, and so on." The long-term model Daré chose to follow is to license-in products potentially in all of those areas, beginning with its novel, nonhormonal contraceptive, Ovaprene.

Johnson and her founding team had originally identified about 10 "interesting product opportunities" through her previous work in a nonprofit organization. "We were pragmatic enough to realize we couldn't do all 10 projects. We had to pick one. It was important for our first product to be really easy for investors to understand — to understand the market, why the product was important, and what its clinical development process and reimbursement landscape would be."

Ovaprene belongs in the classification of "short-acting" contraceptives, like condoms or vaginal rings. Most "advances" in birth control have come in the form of hormones, but Ovaprene is a nonhormonal contraceptive. Its vaginally inserted silicone ring surrounds a permeable mesh that slowly releases ascorbic acid, which keeps the local pH down below the sperm-friendly levels associated with ovulation, and iron, which slows sperm down. Significantly, the mesh also appears to impede the sperm. The dual modality led the FDA to designate the Center for Devices and Radiological Health (CDRH) as the lead review division. A pilot study with 21 women showed Ovaprene immobilizes sperm and prevents their progression into the cervical mucus. Other products that kept motile sperm from entering the cervical mucus in similar studies later demonstrated "typical use" contraceptive effectiveness of 88 percent in contraceptive studies evaluating pregnancy rates over time. That compares to 82 percent for condoms and 91 percent for hormonal contraceptives. Later in 2018, Ovaprene is due to enter a clinical trial for effectiveness in preventing the advancement of viable sperm.

Although Ovaprene technically meets the classification criteria, the term "short-acting" may mislead; the product functions and can remain in place for a month, or a full menstrual cycle. Convenience is, in fact, its main selling point. "It is readily reversible, meaning if someone wants to stop the method, they can do it themselves," Johnson says. "The easier and more convenient it is, the more likely users will be compliant and have the outcome they desire in reliable contraception. We can see that the most successful brands, both from a market-share perspective and dollars, have been the ones that focused on convenience and ease of use."

A reverse merger with Cerulean in mid-2017 coincided with the public offering of Daré on the Nasdaq, giving the company two years of cash — enough for the Ovaprene program as planned. But Johnson is still hard at work raising money to realize the bigger mission of bringing more new women's reproductive health products into the company's pipeline, and hopefully onto the market.

Sabrina Martucci Johnson
Founder, President, CEO

Vital Statistics

4.5
Employees

Headquarters
San Diego

Finances

Raised
$9+ M
via reverse merger
(July 2017)

Research Partnership Funding
Ovaprene licensor is a private company, ADVA-Tec.

Other Partners
CONRAD: nonprofit global reproductive health organization; to conduct Ovaprene postcoital test clinical trial

Latest Updates

July 2017:
Closed reverse merger with Cerulean Pharma; Nasdaq trading began under new stock symbol DARE.

What Drives CRO Preferred Provider Selection?

Using data from several market research reports, Industry Standard Research analyzed preferred provider arrangements across clinical development, eClinical, and contract manufacturing industries. Go to ISRreports.com/free-industry-resources to see the full infographic, which includes data for the contract manufacturing and eClinical markets.

Operational excellence

Top 5 driver for **47%** of CRO respondents

Therapeutic expertise

Top 5 driver for **37%** of CRO respondents

Prior positive experience with service provider

Top 5 driver for **36%** of CRO respondents

Global footprint

Top 5 driver for **34%** of CRO respondents

Expectations for data quality

Top 5 driver for **30%** of CRO respondents

Low cost

Top 5 driver for **28%** of CRO respondents

Project manager quality

Top 5 driver for **28%** of CRO respondents

Provider responsiveness

Top 5 driver for **22%** of CRO respondents

Metrics for meeting overall project timelines

Top 5 driver for **17%** of CRO respondents

ROB WRIGHT Chief Editor @RfwrightLSL

Can Joseph Papa Save Valeant?

JOSEPH PAPA
CEO, Valeant

There's no doubt about it — Joseph Papa took a huge risk and may have made a huge mistake. At the pinnacle of a firestorm of negative headlines and government investigations into Valeant Pharmaceuticals, Papa decided to take the helm of the embattled company, leaving behind a nearly 10-year successful career as chairman and CEO of OTC and generics drugmaker Perrigo.

It's a story that has been quietly unfolding since Papa succeeded Michael Pearson in May 2016. But a little quiet is something this company likely relishes these days. For now, free of the media's spotlight, Papa and his staff can continue with what he refers to as "the turnaround opportunity of a lifetime."

It would be an oversimplification to credit an increased salary (see sidebar) as the primary factor motivating Papa to join Valeant. After all, this is a pharma executive who had held the title of CEO or president at various pharma companies since 2001 and has been in the industry for 35 years. At Perrigo, he was credited with building the company up while also fending off an unwanted takeover attempt by Mylan, so he's no stranger to controversy. At this point in his career, taking a position like this at a company like Valeant is a big risk that could affect his legacy. He'll either be remembered as the hero ... or the fool — albeit, a well-compensated fool.

In talking with him, though, you don't get the impression that his legacy or public perception of his compensation package weigh heavy on his mind. Instead — and maybe understandably — he exudes an unwavering focus on reinvigorating the company internally while also crafting solutions to Valeant's mountain of debt. "From the beginning, my view was always that with some good leadership, we could turn this thing around, because this company has good products — and lots of good people," Papa says.

"Re-recruiting" Employees

Those employees were what Papa concentrated on first. More specifically, he aimed to change their perception of a company that had earned a reputation for, first and foremost, maximizing value and appeasing shareholders. The mission, and all of the internal messaging and branding that goes with it, had to change to emphasize "helping to improve people's lives through our healthcare products." Although a broad and somewhat obvious choice for a pharma company, it was still the type of positive message that employees could rally around. "One of the most important things a leader has to do, especially when you're trying to affect a company's culture, is define a model for what is going to be different," Papa explains. "So, we started with a mission, but then we wanted to make sure we branded that mission with the idea of Valeant being a turnaround opportunity of a lifetime. I like to say we were re-recruiting Valeant employees back into the company."

To help spread the new positive messaging, Papa began informally meeting with employees at all levels. Then he began having lunch with a group of about a dozen employees every two weeks, a practice he still does, but now on a monthly basis. "I use these meetings to get to know people, find out what they really like about the company, and learn some of the challenges we face other than what I see at the very top level." Papa says he didn't want to be sitting in his office believing everything was great while employees wondered why he hadn't addressed "X" — whatever X might be.

Tackling Debt — Harder Than Anticipated

Prior to joining Valeant, Papa did plenty of due diligence, reading every analyst report he could get his hands on just to understand what he needed to do if he took the job. But despite his best efforts to be prepared, he admits one thing turned out to be harder than he ever expected. "When I joined Valeant, I knew we had $32 billion in debt. But I didn't realize the implications of how such a debt load would impact nearly every strategic decision I was trying to make," he explains. For example, as Papa began looking at which core businesses to build upon for Valeant's future, he faced resource-allocation decisions. "If I have $100 million to spend, am I going to simply pay down my debt, or am I going to invest it in new products, and if new products, which ones?"

For Valeant to be able to invest where it wanted, it had to address its debt issue, and one of the quickest ways to do so was to divest some of its assets. "But before we started selling off assets, we needed to determine what was core to our future," he notes. "We decided to focus

on three areas: eye care [i.e., Bausch + Lomb], GI [i.e., Salix], and dermatology [i.e., Ortho Dermatologics]." Here's some of the rationale as to why. Valeant already had leadership positions in dermatology and eye care, and it's easier to build on a position of strength than try to shore up an area of weakness. In addition, Papa looked at pharmaceutical utilization. "The older you get, the more you utilize pharmaceuticals," he states. "For example, people over the age of 60 have seven times more use of eye care products." The aging population and changing demographics will lead to an increase in utilization of eye care products, he noted.

Once Valeant determined where it wanted to focus for the future, Papa then began to develop a divestment platform. He identified noncore assets with revenue of a set dollar amount that could potentially be sold for a double-digit multiple of EBITDA. In doing so, he then was faced with the question of how much should be sold. "We decided in August 2016 to make a pledge to reduce our total debt within 18 months by $5 billion. But I didn't want to identify only $5 billion in divestible assets; I thought it important to identify about $8 billion, realizing we weren't going to sell them all." Papa took this approach because he believed potential buyers would submit lowball offers, especially if they thought Valeant had to sell everything. "We told interested buyers we had a multitude of assets to sell, and our plans of paying down $5 billion in debt with proceeds from divestments and operating cash," he shares. "If we had an asset we thought had a value of 100, we'd entertain offers of 110 or 120 and not offers of 90 or less." Making the divestment basket bigger than what was actually necessary gave Papa the latitude for avoiding being put in a position of selling anything for less than he felt it was worth.

It all started in January 2017 when Valeant announced it was selling its CeraVe, AcneFree, and AMBI skincare brands to L'Oreal for $1.3 billion. "These were OTC consumer products with annual realized revenue of approximately $168 million," he explains. "We were able to get a good multiple for the sale, which gave us more flexibility when thinking about what additional assets to sell." Valeant sold its Vietnam subsidiary, Euvipharm, with the rationale that, though a good business, it wasn't going to have a major impact on whether or not the company was going to be successful in the future. Next, in

Valeant Pharmaceuticals — Analyst Insights

(NOTE: The following was written in early December 2017, so stock prices, company results, and analyst opinions could have changed since then.)

Following Valeant's 3Q 2017 reported results, analysts issued their thoughts on the company (NYSE: VRX). Wells Fargo believed the positive market reaction was unwarranted and maintained its "underperform" rating. Sales declined 10 percent year over year (YoY), and R&D spending was -20 percent YoY. "We cannot help but to think that a drug company that spends 4 percent of its revenue on R&D and still 20 percent lower than the year before is unlikely to have enough winners to offset the normal LOEs [loss of exclusivities]," noted Wells Fargo equity research on Nov. 9, 2017. However, Wells Fargo noted Valeant made some progress that should not be overlooked, such as getting Siliq (for psoriasis) and Vyzulta (for glaucoma) approved. "However, with Siliq not even registering a sales number in the 3Q results, we would wait on thinking that dermatology is fixed or that Valeant can robustly launch new products. Adding to our caution is litigation/investigation risk, as Valeant continues to have a wide array of pending suits and ongoing investigations." One of the major trials, where the defendants are Valeant and Pershing Square, begins Jan. 30, 2018.

Morningstar analyst Michael Waterhouse wrote on Nov. 7, 2017, "Management's previous efforts to extend major debt maturities into 2020 combined with debt reduction and working-capital improvements have helped stabilize the business, but we still think the firm's high financial leverage remains a problem." Waterhouse also wrote, "Valeant's attempt to correct its missteps creates a highly uncertain outlook, and investors should remain very cautious, given the company's transition to a new CEO, financial distress from a high-debt balance, and investigations into business practices. Valeant's undisciplined use of debt and aggressive use of price increases and specialty pharmacies have tarnished the company's image." Waterhouse notes, "Some portions of Valeant — including its contact lenses, over-the-counter portfolio, and ophthalmology and gastrointestinal drugs — remain attractive. The legacy Bausch & Lomb assets, for example, should continue to grow and could theoretically fetch a decent sales price. Additionally, Valeant's new distribution partnership with Walgreens could salvage some product sales, particularly in dermatology."

As of this writing (12/12/17), average recommendation had the stock as a HOLD, with an average target price of $15.79 (Source – MarketWatch).

October 2017, iNova Pharmaceuticals was sold for $930 million in cash. As of this writing, Valeant has generated approximately $3.8 billion in proceeds from such divestments, and when combined with cash flow from various business operations, has succeeded in meeting its pledge. "As of Nov. 7, 2017, we reduced total debt by approximately $6 billion," Papa says. "We promised we'd do it, and we did it faster than we promised."

Though the company still has $26 billion in debt, the goal isn't to eliminate it all. Papa estimates that $15 to $20 billion is an appropriate amount of debt for a company of Valeant's size. "So we still need to pay down another $6 to $11 billion." In taking this approach, Valeant has freed itself from any debt repayments for any mandatory amortization between now and 2020, and can instead focus on improving operational results. "We now have the freedom to invest in the business, such as putting more resources behind the primary care sales team and Xifaxan (for irritable bowel syndrome with diarrhea). This year we also plan to invest more into R&D, which will help better prepare us for the future."

Measuring Progress

Beyond debt reduction and stock price, there are a variety of metrics Papa uses to measure the progress of the Valeant turnaround. "I like to look at simple data, such as employee turnover," he shares. "For instance, our turnover rate has dramatically improved versus a year ago, and we are now more in line with what I'd call a normal pharmaceutical company." Beyond turnover, Valeant also conducts an employee survey to get a feel for how things are going. "In 2017 we had a 79 percent response rate, which was the highest since the company first began surveying employees back in 2010, and a two-percentage point increase over 2016," he affirms. "That is a very strong result that indicates a high level of engagement among employees who are trying to help us get better." Here are some other results from a late 2017 survey:

- 82 percent of employees consider Valeant to be on the right track for growth
- 92 percent of employees would recommend Valeant as a great place to work (up 12 percentage points from 2016)
- 92 percent intend to still be working at Valeant a year from now.

"Think of what these employees have been through during the past few years," Papa says. "The company has replaced half of the 12-member executive leadership team and 10 of 11 board members. Our stock has declined significantly, and the company and some of its former leaders have been under tremendous public scrutiny. And yet, 92 percent of employee respondents still feel Valeant is a great place to work!" He knows there are still a number of people who continue to criticize the company for some of its past mistakes. But he says those criticisms are serving as a point of unification. "Our employees are responding with a 'we'll-show-you' attitude," he asserts.

There's no doubt that these kinds of incremental improvements are a good sign and serve as the core for a new business foundation at Valeant. But it's still too early to tell how the company will rebound — and to see how Papa's risk pans out.

A Pay-Package Storm

When Joseph Papa was chairman and CEO of Perrigo, he was looking for some new products the company could license in the areas of dermatology and eye care. He knew about the turmoil at Valeant and figured it might be selling some products to reduce its debt, so he called the company. He was told they'd put him on the list if any products became available. But the chairman of the board also broached the subject of Papa coming on board to run the company.

Eventually Papa agreed to join Valeant in April 2016. But almost immediately, his hiring — more particularly, his salary — added to the controversy surrounding the company and the scrutiny of top CEOs in general. His starting package of $63 million (over four years) was more than twice what he made at Perrigo, but consider the following. In order for Papa to keep just half of his new paycheck, he has to more than double Valeant's stock price from where it is currently (i.e., $20.50 a share as of 12/11/17). To keep all of his pay, Valeant's stock has to trade at or above $60 a share (a 193 percent increase) in roughly three years. In fact, Papa's compensation is so heavily incentivized that the actual value of his annual pay for 2016, $11.7 million, is less than a 2 percent increase over what he made at Perrigo in 2015. While Papa's pay package has the potential to net him nearly $800 million over four years, it would require moving the company's share price to all-time new highs (i.e., > $270 a share) — a feat that would not only make him a very rich man, but a corporate turnaround expert of legendary status.

Papa says all of the noise around Valeant not only caused problems for the company but also had a negative effect on the entire pharma industry. And if he could play a small role in improving Valeant, the impact would be felt well beyond the company's 21,000 employees. "I was eager to take on that challenge."

Not A Bad Year, After All

Peter Meath of J.P. Morgan

Perhaps the greatest heights of the biopharma sector will never be seen again — but don't overlook the good times now. That is the central message in the following interview with Peter Meath, who heads the Life Science Group at J.P. Morgan's Commercial Banking business. Meath also comments on the current industry environment and offers seasoned advice to novice entrepreneurs for turning a company's novel science into a viable business.

WAYNE KOBERSTEIN Executive Editor @WayneKoberstein

WHAT STANDS OUT ABOUT THE PERFORMANCE OF THE BIOPHARMA SECTOR IN 2017 AND THE TRENDS YOU SEE AS WE ENTER 2018?

PETER MEATH: The sector performed actually fairly nicely this past year. If you look at the public sector in general or just look at the IPO market, 2017 was a well-above-average year. There was more traction in public offerings in the second half than in the first half of the year, or even the year before, compared to historical averages, means, or medians. The "boom time" of 2014 and 2015 was an aberration, a statistical turning point. In those years, we saw massive volume and proceeds in the industry unparalleled in past decades. But on average and from a performance perspective, the sector has remained quite healthy.

IPOs by companies with Phase 3 assets and/or some good visibility with their late-stage topline data have typically done particularly well. Among the ones in earlier stages of clinical development, some have struggled, some have not. If there's any surprise, it's that the M&A environment hasn't been as active as many predicted it would be. The dollar volume is down from historical averages, particularly if you take out the largest deals during the past year. Partly, it is because of government regulatory issues, but the fact is that pharma is still sitting on significant cash, and that has to change at some point.

MIGHT THE LIMITED M&As REPRESENT SOME MATURING OF THE INVESTMENT COMMUNITY? IS IT LESS DRIVEN BY HYPE OR EARLIER-STAGE SPECULATION THAN IN PAST YEARS?

Yes, it speaks to a normalization that was inevitable in the last 18 months, after we came off the highs of 2015. Normalization happens not only in pricing and expectations, but also in the profile of the more successful recent offerings. That's not to say the companies with earlier-stage assets aren't sitting on an unbelievable opportunity, and some of them have performed extremely well, but, in general, it's just a natural normalization.

DO YOU SEE ANY KIND OF MATURING IN THE BUZZ-DRIVEN WORLD THAT HOVERS AROUND EARLY-STAGE RESEARCH?

"Buzz" is not unique to life sciences; it happens quite often in the tech world, as well. A lot of interest and future expectation is driven by the immense amount of technological change, and during the past five to 10 years in the life sciences industry the pace of change has accelerated massively. Whether it be CRISPR, some novel therapy, or whatever, a lot of people see the massive upside. But to your point, people should temper their optimism in the context of real-world issues that face the industry, such as uncertainties in the payer and regulatory environments. You have to take both sides into account and balance them accordingly.

Running At The Start

Meath and his group guide many startups and small to midsize biopharmas through the key steps of funding and building their companies. He discusses some of the nuts and bolts of running companies typically born of early research.

WHAT ARE THE KEY INTERNAL AND EXTERNAL FORCES A STARTUP OR A YOUNG COMPANY FACES THESE DAYS?

In early-stage companies, funding or access to capital is always item number one. It's no surprise that, in this industry, it takes an immense amount of capital to develop assets, regardless of the company size.

Maybe I'm biased because I've lived in the Southeast my whole life, but there has been a deterioration of extremely valuable earlier-stage regional institutional investors — the $250 million funds that were a great source of that startup capital for many young companies. A common theme we hear from companies is, "We've got a great thing going, but we're not in Boston or California. Where do we find access to that capital?" The vacuum tends to get filled somehow, and that points to the rise of extremely valuable angel groups or super angel groups, which have stepped in and become much more prevalent in the funding of early-stage opportunities. The trajectory of angel-funded deals has gone up precipitously recently. That's particularly true in the medical device arena where the lack of VC funding has been a little bit more pronounced. The other vacuum filler has been an increased participation from corporate VCs. Pretty much every large pharma now has some sort of VC-oriented activity associated with it, and a while back that wasn't necessarily the case.

WHY IS BIG PHARMA FOCUSING ON VENTURE CAPITAL NOW?

One reason is the increased globalization of the world in general and how it has affected the life sciences community. The young companies I worked with 15 to 20 years ago didn't talk much about international expansion and development or anything dealing with international concerns. Now you should be thinking about being an international company from day one. Whether it be licensing or partnerships, you need to be thinking about it at an extremely early stage. It is an opportunity, frankly, because it certainly opens the door to a lot more partners for companies, but it's also a challenge.

ENTREPRENEURS OFTEN COME OUT OF ACADEMIA WITHOUT KNOWING MUCH ABOUT BUSINESS AND STARTING OR RUNNING A COMPANY, BUT THEY HAVE THAT DRIVE. WHAT ARE THE FIRST THINGS THEY SHOULD LEARN?

First, you're going to get doors slammed in your face. Some people take that the wrong way when they should look at it as an opportunity. When that happens, ask questions. What are the holes in our value proposition? Absorb that information, which can ultimately be much more valuable than information from people who say, "I love everything you're doing." Investors may pass on your company, but that doesn't negate your value as a company. Many times, investors pass because of factors that are totally outside of your control. Perhaps it doesn't fit their investment parameters, or the timing for their fund isn't right, or they're conflicted with another investment, and so on.

Maybe it's just not the right fit, which leads to another point: Surround yourself with partners who share your vision — and not just your investors, but also your bank, your CPA firm, your lawyer, and others you depend on. Do they know your industry? Do they know your company? Do they share your values? The more you surround yourself with such people, the more doors they can help you open. All money is green, so look for value

outside of the color of the money that can be added to your effort. And the last point, which we have touched on — make sure you can communicate how you will turn your science into a business. How are you going to make money, and what is the ultimate return on that money?

HOW MUCH TIME AND EFFORT SHOULD COMPANIES SPEND ON THE LANGUAGE THEY USE TO COMMUNICATE TO THE OUTSIDE WORLD ABOUT THE VALUE OF THEIR PRODUCT AND APPROACH?

Companies generally need to spend more time creating clear language to communicate their value proposition. This shortcoming seems to be semi-unique to this industry. The difference I've seen in the life sciences space is the unique challenge of transitioning from a science-based company to an operating or commercial company. When that happens, it's always very interesting to watch because, at the earliest stages, companies tend to be extremely science-based. It is their bread and butter. They live and breathe it every day, so their communication tends to be heavily weighted toward the scientific aspect of what they're doing, whether it is the drug type, formulation, platform, and so on. Those companies often overlook the need to pay similar attention to the economic and market aspects of the products they are developing. What does the new product mean to consumers, and what does it mean to investors?

Looking Outside

While acknowledging the major uncertainties in the current political climate, Meath makes some reasonable predictions on the near-term future of drug pricing, healthcare reform, tax cuts, and regulatory streamlining.

THE DRUG PRICING CONFLICT OFTEN SEEMS INSUPERABLE, BUT HOW DO YOU THINK THE DEBATE MIGHT DEVELOP?

We should probably lump pricing into the overall regulatory and government policy changes, because they're all part of the same conversation. All we can do at J.P. Morgan is advise our clients on the uncertainties and how to move forward knowing those uncertainties. On the healthcare reform side, with the ACA, it's pretty obvious now that repeal-and-replace is stalled, at least in the near term. Where the government seems to be moving is on the tax side. That does not impact the life sciences community directly, except for maybe in a couple of ways. It seems we had some bipartisan support for rolling back the medical claims tax, an impediment to the med device industry. I'm assuming there will not be a large corporate tax overhaul as had been previously envisioned. But companies may be waiting to do M&As in case the big tax cut does happen.

HOW COULD REGULATORY CHANGES AFFECT THE INDUSTRY ENVIRONMENT?

Regarding the FDA, there are two competing messages coming out. One is, we want faster approvals. We want more efficient, more cost-effective means of doing this to encourage more competition. That might be a slight over-expectation. If you look at how clinical trials have always been done, it's been about safety and efficacy, and I don't foresee that changing in a massive way. There always will be checks and balances. If accelerated approval avenues exist, what does that really mean? For the generic drug industry, where the margins are already quite low and competition high, accelerated approvals could only exacerbate the challenges — as it would on biosimilars and specialty pharma as well. How that all works out could have an impact on cost and pricing.

A big part of this push for regulatory reform, along with the healthcare reform implications, goes back to systemic costs. You have to look at lowering the systemic costs. I find fascinating the blurred lines between high technology and the life sciences; it's becoming difficult to figure out where one ends and the other begins. How might the life sciences industry use tech-world talent and resources to improve processes in the life sciences world? A recent deal involves using AI to do early-stage drug discovery. There are other technologies with the potential to lower overall cost without lowering the safety of a process, which could be another avenue we see explored.

THE INDUSTRY'S CURRENT FOCUS ON SPECIALTY CARE PRODUCTS RANGES FROM REFORMULATING OLD DRUGS AND RAISING THE PRICE 1,000 PERCENT, TO SOPHISTICATED COMBINATIONS OF TECHNOLOGIES INTRODUCED WITH PREMIUM PRICES. WHERE IS THIS LEADING?

Only since about 2013 have we seen the rise of specialty pharma companies into their current prevalence. Specialty drugs have obvious cost and care benefits. There's a good financial reason why the prices are where they are; they have huge value for their unique patient populations. But the sector is still young, and over time I believe specialty pharma companies will learn to reach a better balance of benefits and cost.

LOOKING AT A HIGHER LEVEL, IS THE U.S. STILL COMPETITIVE IN EDUCATION?

Science education is a huge issue for the economy, and it is still not getting enough attention, but it's getting the right sort of attention now. You cannot build successful companies in the innovation economy without

good talent, drive, and passion in those academic endeavors. In the United States, with my experience over multiple years working with entrepreneurs, I can say our drive and entrepreneurial initiative in this country is by far our greatest asset. I continue to see young people with a huge amount of entrepreneurial drive, ability, and insight go way out on the risk curve to start their companies. It's in the DNA of a lot of people across the world, but it's very pronounced here, and it's a huge advantage.

Here is a secondary point: I recently met with a medical device "incubator" that helps match students who are interested in the engineering and scientific fields with promising young companies that need talent and engineering help, pro bono, in exchange for educational advancement. But there are many more students wanting these positions than there are companies that have the ability to fill them. Maybe part of the issue is that we need to do a better job helping the right people find opportunities in the space. At JPMorgan Chase, we have a $250-million initiative, New Skills at Work, and another, New Skills for Youth, focused on driving skill-based, demand-driven talent enhancement for adults and youth alike.

ARE YOU GENERALLY OPTIMISTIC ABOUT THE INDUSTRY?

At J.P. Morgan, we obviously think very highly of this industry, or we wouldn't be devoting the efforts of my group and many groups across the organization in investment banking. We all are highly focused on this sector because we see its potential in the future. The biopharma industry is not going away — it is here to stay. It's extremely important to us as Americans and as people in general. There are challenges to it, and those challenges are very complex, but again, my advice is surround yourself with people who understand those challenges and can help you navigate through them. We live in a really exciting time, and the one main takeaway I would add is this: Entrepreneurs will always find a way. That has been proven time and time again. They find a way, whether it's getting around capital issues or getting around scientific hurdles. They find a way to make things better and make things happen. That's extremely positive in my opinion, regardless of any headwind that might hit the industry. That is what we hang our hat on every day.

CHRISTI SHAW
Senior VP, Eli Lilly
President, Lilly Bio-Medicines

"Leaders with empathy," Daniel Goleman, the godfather of emotional intelligence, wrote, "do more than sympathize with people around them; they use their knowledge to improve their companies in subtle, but important, ways." That's what Christi Shaw intends to do as senior VP of Eli Lilly and president of Lilly Bio-Medicines, having signed up in April of 2017 to replace newly minted CEO David Ricks as head of its Bio-Medicines business.

In April 2016, Shaw stepped down as U.S. country head and president of Novartis to care for her older sister Sherry who was suffering from multiple myeloma. Sherry's condition had deteriorated since her 2013 diagnosis, and she was accepted into a promising clinical study in early April with the proviso that she have a full-time caretaker during the three-month trial. Shaw took up the mantle of caretaker, moving to Philadelphia with her sister where they stayed in Cancer Hope Lodge for the duration of the trial. "My own mother died at 51 of breast cancer, and this was back in 1996 in rural Iowa in the Midwest, and we didn't take her anywhere. I now know, had she gotten into a trial, the drugs they were studying were approved the same year she died, so she could have lived another 18 months to five years longer. That was a mistake that I've reflected on, and I wanted to be there for my sister."

AN EQUAL RIGHT TO CARE

In a *New York Times* opinion piece titled "A Toxic Work World," author and CEO of think and action tank New America, Anne-Marie Slaughter, argued that intense and toxic competition in the workplace was driving talented women — and men — out of the office, often in favor of raising their families or caring for aging parents. She spoke of the dangers of looking at it as a "women's problem" instead of addressing the deficit in an antiquated and broken work system. For Shaw, who has long championed diversity and equality in the workplace, the problem of the sandwich generation (women in their 30s to 40s who were "sandwiched" between young children and aging parents as their primary caregiver) is one that resonates.

CHRISTI SHAW: EMPATHY KEY TO TRANSFORMING THE PATIENT EXPERIENCE

DEIRDRE COLEMAN Contributing Writer @DigitalDeirdre

"Being off for a year, I wasn't sure whether I'd come back to pharma. I thought maybe I'll retire and work part-time on boards. At a personal level, what drives me is being able to make decisions that affect millions of lives in a positive way. I felt obligated to come back and show, not just women, but employees in general, that if you have a family crisis, it's OK to take time off work. The best person to take care of your family is family. I wanted to be able to show that you don't just drop off the face of the earth; you can come back. It might not be the same job or the same company, but you can decide for yourself what it is you want," says Shaw.

Diversity and inclusion are very close to Shaw's heart, with Novartis coming first three years in a row in DiversityInc's annual survey of top-ranking companies during her tenure. "It's my goal to do the same here at Lilly and be a leader that promotes diversity and inclusion. We need to demonstrate that we truly represent the patients we serve and that the decision makers in the room are diverse and varied in their experiences and backgrounds."

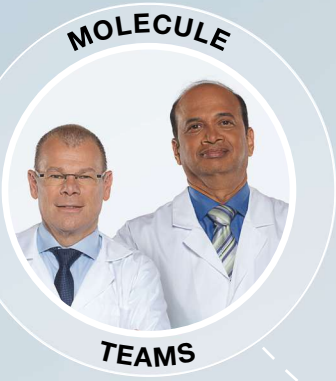
RETURN TO LILLY AFTER THE DROUGHT

Both personal and professional considerations impacted Shaw's decision to return to Indianapolis-based Lilly (she previously worked for Lilly from 1989 to 2002 in sales and marketing roles). "My sisters are now within a 3- or 4-hour drive, being located in St. Louis and Chicago, so that was an important aspect, especially with Sherry's illness. From a professional standpoint, a key consideration was Lilly being an integrated business, so I have responsibility from clinical development through commercialization; not many roles offer that unless you're the CEO." Another plus for Shaw was that she had not participated in a publicly traded board before. "That was a big development piece for me, to be on the inside when big decisions are being made and having responsibility for a global P&L."

Another draw was Lilly being in the midst of the most prolific period of new launches in the company's over-140-year history. Lilly is counting on its own crop of experimental drugs to pass clinical trials and be approved

The People and Science Behind

Patheon OneSource™ for Small & Emerging Pharma



2400+ scientists ready for your challenge

The Drug Substance Molecule Team collaborates with the Drug Product Team to ensure that your molecule becomes a formulation-ready API. The integrated Molecule Team is a key driver of the Patheon OneSource™ time savings.

Andreas Stolle, Ph.D., joined us in 2015
Vice President, API Process Development Services

560+ development programs in 2016

Whether you are working with a large molecule or a small molecule, your Drug Substance Project Manager proactively works to ensure your molecule has its best shot at success by maintaining timelines and minimizing potential rework during development.

Angela Colarusso, joined us in 2007
Sr. Director, Biologics Program and Proposals Management

Smart sourcing
Procurement experts assist with sourcing generic API and raw materials to ensure availability and reliable supply.

Simplified administration
If it works better for your business, we can establish one Master Service Agreement, one Drug Substance/Drug Product Contract and one Quality Agreement. This also means one taxation and regulatory structure, one currency and one invoicing process.

Faster Drug Development

We develop 75% of all dosage forms

For large and small molecules, close collaboration with the Drug Substance Molecule Team allows the application of right-fit science for formulation, process development, tech transfer and scale-up to ensure a smoother transition to market.

Anil Kane, Ph.D., MBA, joined us in 2000
Executive Director, Global Head of Technical & Scientific Affairs

CLINICAL TRIAL MANUFACTURING

112 NDA approvals in 10 years

More than 2x any other CDMO

For both large and small molecules, the Patheon OneSource™ methodology minimizes failures due to foreseeable events and maximizes your molecule's chances of out-licensing or making it to market.

DRUG PRODUCT PROJECT MANAGER

Stability and scalability

By collaborating with the Drug Substance Project Manager, the Drug Product Project Manager ensures your trial-level drug product is also suitable for scale-up.

Nicky Arvanitis, MBA, joined us in 1997
Director, PDS Project Management

CLINICAL PACKAGING AND DISTRIBUTION

Securely packaged for on-time distribution

Combining best-in-class robust primary and secondary clinical packaging and secure on-time distribution to meet quality standards and patient compliance.

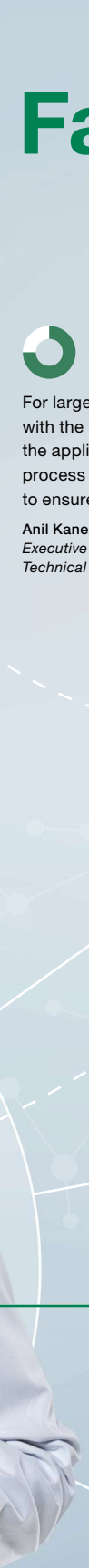
BACK-UP PROGRAM MANAGER

We always have a back-up plan

To ensure your molecule never goes off track, every team includes a Back-up Program Manager ready to step in any time life gets in the way.

Save an average of 14 Weeks & $44.7M[1]

Something needs to be done about the high cost of drug development. By combining drug substance, drug product, clinical manufacturing and clinical packaging into a single process, Patheon OneSource™ accelerates your molecule like nobody else can.



Speed through communication

The Program Manager is the architect of your drug development program. This single point of contact both within Patheon, and with you, simplifies every interaction and manages your molecule's critical path to deliver unmatched time and cost savings.

Aaron Williams, PMP, joined us in 2011
Program Manager, Patheon OneSource™

Patheon part of Thermo Fisher Scientific | OneSource™

www.patheon.com/onesource

1. Assessing the Financial Benefits of Faster Development Times: The Case of Single-Source vs. Multi-Vendor Outsourced Manufacturing, Tufts Center for the Study of Drug Development, 2017

in time to resurrect profit growth after the painful period of patent lapses, which Lilly has nicknamed "the X and YZ years."

"When I left Lilly in 2002, we had just gone through the heyday of Prozac and Zyprexa, and all of the neuroscience launches were going really well. Lilly has come through a time of not much innovation and survived, and we're coming into a period of abundant innovation. We're launching five new medicines in the next five years in my business alone (not including diabetes and oncology) and 10 line extensions in the next 10 years," says Shaw.

The company hopes that its emerging focus on non-opioid pain therapies will become fertile ground for new drugs. Overdose deaths involving prescription opioids have quadrupled since 1999, and so have sales of these prescription drugs.

Similarly, there is a great need for new migraine medicines, as more than 36 million Americans experience migraines, which costs the U.S. about $36 billion in healthcare and lost productivity, according to the Migraine Research Foundation. The size of the migraine market is expected to balloon to more than $10 billion in 2025 from $3 billion in 2015 in the United States and other developed countries, healthcare research firm Decision Resources Group predicted last year.

Lilly's bid to bring a new class of migraine therapy to market has just been lifted by a second positive trial that sets up first-marketing applications next year. If approved, lasmiditan would be the first acute treatment for migraines in more than 20 years. In addition, lasmiditan would be a good pairing for Lilly's other big migraine hope, galcanezumab, a CGRP (calcitonin gene-related peptide) inhibitor that works as a maintenance therapy to try to prevent migraine attacks from occurring in the first place. Lilly is competing with rivals Teva and Alder Biopharma to bring the first CGRP inhibitor to market.

Lilly, in partnership with Pfizer, aims to seek approval by 2019 for a new type of pain drug that could be an alternative to opioids for osteoarthritis, chronic back pain, and cancer pain. Tanezumab, given by injection

CHRISTI SHAW IN HER OWN WORDS

WHO INSPIRES YOU?

"It goes without saying that being side by side with my sister for the last three-and-a-half years, she has been such an inspiration. I've seen her almost die a couple of times and witnessed her go through 16 different therapies. She lost her hair multiple times; I've seen what she has had to do to try to survive. Because of that, she has walked our sister down the aisle, and she has been able to see her first granddaughter. Her will to live and the sacrifices and the physical toughness that she's had to possess have been inspirational. The other source of inspiration on a day-to-day basis is my husband. He's very strong, bold, and sure of himself. And as someone who always second-guesses myself, he inspires me to go with my gut and stick with it, instead of constantly questioning. It's a tendency I think women are often guilty of."

ON HAVING A PERSONAL STAKE IN IMPROVING THE LIVES OF PATIENTS

"When I took time off with my sister so she could participate in a clinical trial in Philadelphia, we noticed that all of the patients in the study were from the Philadelphia area except my sister. That's because many patients can't afford the ongoing costs over a couple of months for food, accommodation, and transportation. When we finished the clinical trial, and I discovered I wasn't a match for my sister's transplant (thank goodness, my younger sister was), I started to think what is it I can do to give back since I had time off. I had a vision to start a foundation that was for patients who needed to get in a clinical trial but who couldn't afford it. My younger sister and I dedicated the foundation to our mother and older sister, and it was launched in March. It's called www.moremomentsmorememories.org. We've already sponsored several patients for clinical trials. One patient we have is from St. Louis, who has four children, and her husband works and is her caregiver. They don't have a big enough income to travel the country and be in a clinical trial, and she wants to see her kids graduate."

ON LEADERSHIP LESSONS GAINED OVER THE YEARS

"People talked about me having a lot of courage to leave my role as president of Novartis. But I didn't see it as courage; I just saw it as something I needed to do. For me, my biggest consideration was thinking 'At the end of my life, what would I wish I could have done?' That gives me the courage to make the right decision. Maybe it's my parents dying young or because of my sister's illness that I think in those terms.

"The other piece for me is being yourself, being authentic. The more real you are, the more people want to follow you. Sometimes, we put unrealistic expectations on ourselves that we have to be the smartest person in the room because we're the leader. But actually it's more important to show your vulnerabilities and show others that you're human, as well. Instead of saying, 'I will make the decision,' it should be, 'We will make that decision.' I think that's what the younger generation is looking for as well – the team that will accomplish the big mission of changing people's lives."

every eight weeks, could be a far more effective and appropriate alternative for chronic pain than opioids, without their abuse potential.

"If you look at migraines alone, the research indicates that 43 percent of patients take opioids at some point. So having migraine assets not only for the treatment but also for the prevention of migraines that reduce the risk of using addictive opioids is pivotal to managing the current opioid crisis," explains Shaw.

UTILIZING EMPATHY TO DRIVE BUSINESS VALUE

Patient engagement is likely to become the most disruptive force in healthcare in the next decade, and this calls for a new type of leadership. The immersive patient experience that Shaw has come through as caregiver for her sister will undoubtedly affect her leadership and only serve to harden her resolve to better anticipate patient and caregiver needs and develop innovative solutions. "The key challenge to embedding a patient-centric culture in pharma is that it takes time. It also involves considerable empathy, bringing that emotional insight into the organization and drilling down into what will make patients' lives easier, whether it's through telemedicine, tracking their symptoms digitally, or facilitating access to care. Pharma used to be about the scientific rationale behind a medicine — now it is so much more than that. It's about relating to patients and understanding what they need on an emotional level."

Being side by side with her sister impacted Shaw at a very visceral level, and she considers empathy development as critical to transforming healthcare and improving the patient experience. "When I talk to my sister, we don't talk about the science of what's happening with the medicines she's taking. Diseases don't just affect patients; family members are also impacted both emotionally and in terms of their ability to work due to care duties. Bringing that emotional insight into the workplace is imperative even in manufacturing to help our employees understand how what they do every day is critical to the people using these medicines. It takes considerable time to do qualitative discussions because sometimes there is no right or wrong answer, and because it is an EQ (emotional intelligence) conversation rather than just an IQ conversation, relating to people and understanding what they need on an emotional level to make sure the medicines are effective."

Research shows that empathic leaders create emotional bonds and are therefore competent in understanding and addressing their team's and customer's needs. They appreciate and draw on people's talents, recognizing others' perspectives in problem solving and including them in decision making. This allows for a culture of trust, openness, and cooperation to flourish amongst teams and organizations.

> "PHARMA USED TO BE ABOUT THE SCIENTIFIC RATIONALE BEHIND A MEDICINE — NOW IT IS SO MUCH MORE THAN THAT."
>
> **CHRISTI SHAW**
> Senior VP, Eli Lilly
> President, Lilly Bio-Medicines

For Shaw, a big component of fostering a patient-centric culture is ensuring the workforce is reflective of their patients. "If most of the patients who get migraines are women in their 30s and 40s — do we have good representation of that cohort working on that product? I've learned with my sister that the lack of continuity of care and the amount of time patients or their caregivers have to spend getting what they need or what the doctor ordered really impacts the patient experience."

In September, Shaw's sister Sherry had completed a bone marrow transplant. "We won't know for sure if the operation has been a complete success until her 100-day bone marrow biopsy to check if the cancer is there or not. So far, the doctor is saying she's doing better than predicted. The transplant was supposed to be in January, but my sister's cancer was too aggressive for it to be successful. We thought that this could be it for her, as she had run out of all medicines to try. Then, in discussions with experts in the field who have always been there to help, we learned of a recent small study in Switzerland of 40 refractory multiple myeloma patients where researchers had combined an HIV drug with a cancer drug and two-thirds of the patients responded. Although we didn't know how long the regimen might work, her doctor agreed to try it as we just needed it to work long enough to get her to transplant. Although our expectations were not high, it worked! And it worked well. Her levels of active cancer significantly dropped within one month, and she was able to go to transplant and receive stem cells retrieved from our younger sister's bone marrow."

The journey they have been on together has left a lasting impression on Shaw. "It's amazing to me. If you had asked me before the transplant took place how she's doing, the prognosis did not look good. My sister had several medicines that gave her only one or two months. But here we are three-and-a-half years later, and probably the bulk of that experience has been positive. She's truly inspirational."

INDUSTRY EXPLORERS
BLAZE ON

The stories of longtime leaders, still active in the industry, sharing their historical perspectives on life sciences industry innovation.

WAYNE KOBERSTEIN Executive Editor @WayneKoberstein

Strive & Accomplish
Pat Andrews

Trying and failing has its place in science and many other human endeavors, because the failures hold valuable information. But in at least one occupation, executive management, it is necessary to match striving with accomplishment. Fortunately, and by hard work, Pat Andrews has carried on her family's tradition as strivers and achievers.

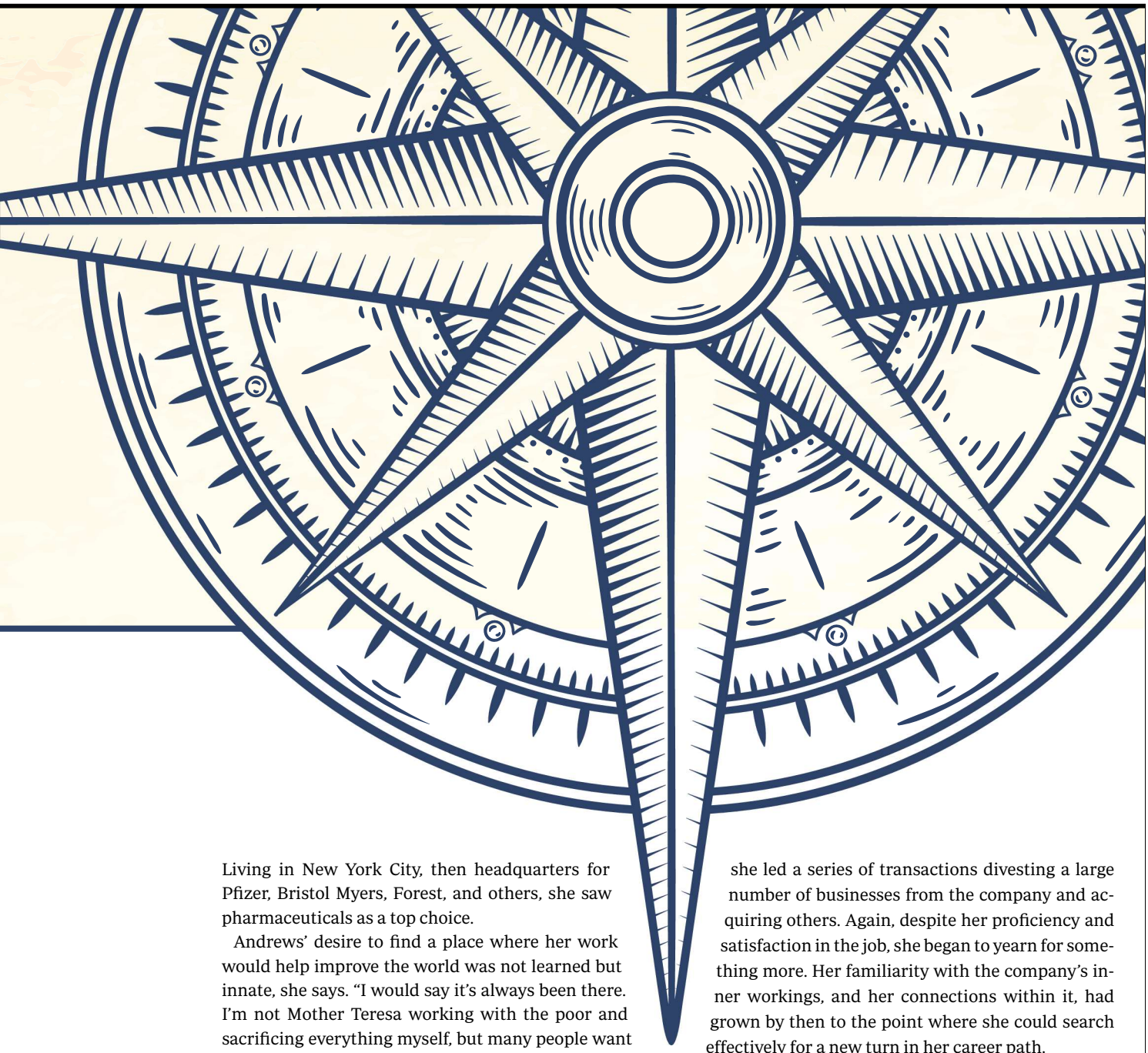
Andrews is now the CEO of Boston Biomedical, a relatively small biopharma company. Her 26-year career in the biopharma industry includes a long period of rising to the top echelons of Pfizer, through a succession of marketing, business development, and management positions, and eventually leading Pfizer's oncology unit. She then leapt into the small-company, entrepreneurial side of biopharma as the chief commercial officer at Incyte, and in April 2017, to her current job.

Born in England, with an English father, Andrews and her parents moved to the United States when she was an infant. "My parents were educated, accomplished, calm, rational people, and I had a really lovely childhood," she says. Her father was an engineer and her mother, an educator. As a young adult, grown up in private schools, she went to Brown for her undergraduate degree and to the University of Michigan for graduate school. She took a year off between the two, did some international traveling, and took a clerical job with a financial planning firm, where she got her first glimpse of business — in this case, not from the firm's own expertise, but from a specific lack of it.

"A question came from one of their clients getting a divorce: How could the party ensure the decree would stipulate their spouse would get a specific lump sum now based on a pension beginning many years in the future? But our firm didn't really know. I called my father, who was a Renaissance man in many ways, and asked him this question, and he explained to me the concept of a present value of a future income stream. And I thought, I should know things like that."

The experience led Andrews to apply to business school. "What is insurance? What is investing? What is the need for estate planning? How do taxes work? How do all these things work together? I thought I could learn to understand it all by getting a business degree."

With her MBA in hand, she worked in a bank for five years doing "highly leveraged transactions." But even though she liked the environment, she found she wanted more — to somehow contribute to the greater good.



Living in New York City, then headquarters for Pfizer, Bristol Myers, Forest, and others, she saw pharmaceuticals as a top choice.

Andrews' desire to find a place where her work would help improve the world was not learned but innate, she says. "I would say it's always been there. I'm not Mother Teresa working with the poor and sacrificing everything myself, but many people want to feel the work they do matters, and I found that in the pharmaceutical/biotech industry. I could have found it probably in others too, but biopharma is the one that combined all the right features for me, and I did well in it because I found it endlessly interesting."

SKYSCRAPER ASCENDANCE

In 1991, Andrews went to work at Pfizer in its 33-floor New York headquarters, which held the teams who run most of the company's integrated functions, from R&D to marketing, business development, and corporate management. She entered in corporate strategic planning, preferred for her financial background and experience with leveraged buyouts. For the next six years, she led a series of transactions divesting a large number of businesses from the company and acquiring others. Again, despite her proficiency and satisfaction in the job, she began to yearn for something more. Her familiarity with the company's inner workings, and her connections within it, had grown by then to the point where she could search effectively for a new turn in her career path.

"My boss was an officer of the company and reported to Hank McKinnell, who was CFO at the time," she says. McKinnell later became Pfizer's CEO and chairman. "I was in meetings all the time with these very senior people, and once I realized I wanted to get more involved in the business of pharmaceuticals, I asked Dr. McKinnell, where do I go, what do I do? And he said, 'Go to our U.S. pharmaceutical business — that's the place you will learn everything.' I didn't know if I could start over again in an area like marketing. But he said, 'You never have to be a great marketer; you just have to learn what great looks like.' I thought that was just so wise because my life was not to be a marketer, it was to do something broader. But to do something broader, first I needed to know what really good marketing looks like."

Pfizer in the early 1990s, though much smaller than today, still had billions in sales and employed tens of thousands. With surprising speed, mainly through blockbuster drugs and a series of increasingly large acquisitions, Pfizer became the leading company in the industry.

To Andrews, the company was an ever-expanding cornucopia of new challenges, skillsets, and experiences. "I loved Pfizer; the company was really good to me, and I learned a huge amount. When Pfizer decided to do something, it could really do it. It had such power, such might." The near-decade she spent in the marketing sphere began at ground level — the field.

"I started out in marketing in a local marketing function, which was unique to Pfizer at the time. Some marketing people were part of field teams, but they had the same resources, processes, and training as people based in headquarters. They were real marketers, not just salespeople assigned to local marketing. I did that for eight years in roles of increasing responsibility. I spent a lot of time in the field with sales, payers, physicians, nurses, and affiliated groups such as advocacy groups and lobbyists. That was a great training ground for seeing the world from the perspective of others, rather than the view of a pharma company looking out."

Among those who helped her the most at Pfizer, Andrews singles out the company's former vice-chair, Karen Katen. "Even though Karen clearly focused on the business, there was a personal touch in everything she did. People were enormously loyal to her because she created an environment that made people feel good."

BROADER BASICS

At the apex of her marketing role, Andrews had responsibility for new-product planning, late-stage clinical trials, and customer/payer relations in the specialty products business, which would grow to $2.5 billion in sales with her guidance. It was evident by then she had learned the marketing side well, but she was aiming to fill what she considered gaps in her understanding of the pharma business — discovery and early-stage development. Such knowledge would inform her increasing work in new-product planning — "in particular, how healthcare works outside of the narrow aspect of the drug."

Andrews was coming of age in pharmaceutical marketing along a parallel path with the emergence of new market forces such as managed healthcare, third-party payers in general, Medicaid and supplemental rebates, and premium drug pricing. New therapeutic modalities had also entered the scene, as with chronic therapy in oncology.

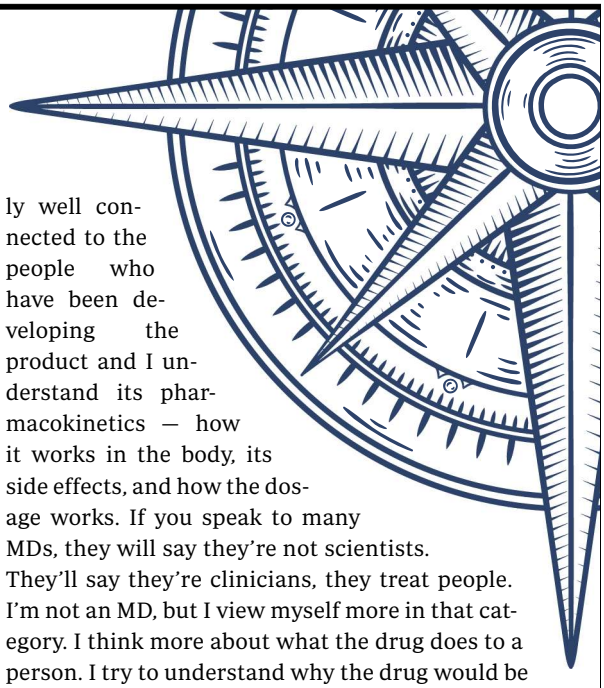
By the time Andrews moved on from marketing to head Pfizer's U.S. oncology business in 2007, she had seen all of those changes and more, and she had helped the company deal with them constructively. Oncology, as a market and therapeutic area, had transformed more than many others — from an almost pariah sector in the 1980s, to gold-rush territory drawing in nearly every large biopharma and many small ones. Pfizer had launched Sutent (sunitinib malate), an early molecular-pathway targeting drug, for kidney cancer in 2006. Ten years later, there would be hundreds of new cancer drugs on the market and many more in thousands of clinical trials. Pfizer's own oncology sales would grow far beyond the almost $1 billion of Andrews' unit.

It was not a sudden transition for her to take leadership of Pfizer's U.S. oncology. She had already overseen oncology marketing along with about a half-dozen other areas including ophthalmology, endocrinology, and infectious disease. At the time, Pfizer organized itself primarily by function. Her new assignment to head U.S.

TAPPING THE POWER — WOMEN ON BOARD

Pat Andrews, CEO of Boston Biomedical, has joined an elite and highly select club of women who head biopharma companies. Asked to address a top issue for industry women executives, she focuses on shifting the composition of company boards:

"Typically, the board-search people will say they're looking for someone who has prior experience on a board, and that perpetuates the status quo. What they're missing is new blood, new ways of thinking. Diverse ways of thinking are probably more important to the success of a company that is trying to do something new and innovative. People who have served on numerous boards over many years bring a lot to the table, but new, fresh perspective is also needed. The practice of turning down people for a board position because they don't have prior board experience keeps companies cycling within a small candidate pool and not tapping the larger pool of people rising up during the past two or three decades."



oncology coincided with a restructuring into business units defined by therapeutic area. The company's oncology portfolio had grown rapidly through M&As. Pfizer acquired Sutent with its purchase of Warner-Lambert. It also brought in Camptosar (irinotecan), Ellence (epirubicin), and others in acquiring Pharmacia & Upjohn. Andrews' business-development experience would prove useful in bringing and integrating new products and teams into her startup oncology unit.

Why oncology over other therapeutic areas? Andrews gladly accepted the cancer focus as the epitome of medical need. "There's something about the cancer area which is almost addicting because originally when people were diagnosed, it was a death sentence, and now we are bringing drugs to market that can really extend life," she says, speaking from personal experience on both counts. Her grandmother died of colorectal cancer in 1988, when treatment options were virtually nil, and now she would head a group marketing a colorectal cancer drug.

"In 1988, if you were diagnosed with a metastatic disease, you could expect to live maybe six months, but my grandmother went from diagnosed to dead in about six weeks. Now, with the newer, targeted drugs, the life expectancy is still way too short, but some make huge differences, and that's just incredibly appealing. When that was all beginning, it looked like science was on the verge of letting us know a lot more. And we have learned a lot more, though it has taken longer than we hoped."

Sutent had already made a mark in the targeted-drug race when Pfizer formed the oncology business unit. It had entered the market close on the heels of another early VEGF (vascular endothelial growth factor) inhibitor, Nexavar (sorafenib), which won the race to launch, but according to Andrews, Sutent surpassed Nexavar in use against renal cell carcinoma by about six months after its market entry. Her team followed Sutent patients and learned as much about the treatment process as the treatment itself.

"We met with the patients as a team to understand what they go through with the disease — not primarily emotionally because I think many of us can understand that — but their real journey: What physicians do they see? How do they handle the expenses? Do they need a patient navigator to get through the system? All of that and more. When you speak to cancer patients, they talk about their life before and their life after diagnosis."

SCIENCE TO BIZ — CAUSE & EFFECT

As a lay person in a business intertwined with science, Andrews has learned how to learn what she needs to know. "It's always been about making sure I'm really well connected to the people who have been developing the product and I understand its pharmacokinetics — how it works in the body, its side effects, and how the dosage works. If you speak to many MDs, they will say they're not scientists. They'll say they're clinicians, they treat people. I'm not an MD, but I view myself more in that category. I think more about what the drug does to a person. I try to understand why the drug would be different or unique."

Pfizer's sheer size worked to her advantage in understanding a drug's uniqueness, says Andrews. "Pfizer was a tremendous training ground. Maybe large companies aren't for everyone, but it's hard to get better, deeper learning than you can get there because you work with real experts in all of the relevant areas. When you go to a small company, people are more like all-around athletes rather than experts in a particular area. I felt lucky to have access to the variety of expertise at Pfizer and considered it a great foundation for moving to a smaller company."

The smaller-company opportunity came along swiftly and suddenly in 2008. Though she had not thought of leaving Pfizer, a search firm reached out to learn her interest in the position of chief commercial officer (CCO) at Incyte and, she says, "the job description sounded exactly like me." Her resume matched the number of years and areas of expertise required, and the company location would also bring her close to her family, including her ailing mother. "Incyte also struck me as a really interesting company," she says. "I liked what it had in the pipeline, it was a very science-based company, and I would be its first commercial person." She interviewed for the job, received an offer, and accepted it.

She says Incyte already had processes in place to ensure it did all the right preclinical work to understand the way a drug would work, what type of Phase 1 and Phase 2 trials it might do, how it would need to interact with the FDA, and so on. Pfizer's size had actually precluded such early coordination. "I almost never spoke to a preclinical person for the 17 years I was at Pfizer. But at Incyte, there was a lot of that communication and I got to see what it takes to fine-tune a drug so it has the best possible formulation to work well in the patients."

The example she mentions is Incyte's drug Jakafi (ruxolitinib), a JAK (Janus kinase) inhibitor launched in 2011 for treating myelofibrosis: "No one else has been

able to come close with a similar product. It's really rare that a drug can go six years with essentially no competition. Many small companies get pushed by financial pressures and timelines to move forward with less than optimal candidates, and Incyte didn't do that. It only went forward with the highest-quality compounds."

BUILDING FOR THE MARKET

Even with Incyte's early learning advantage, Andrews faced the considerable task of building a commercial organization with all of the required components. "Many people think a commercial organization is primarily sales with a little dose of marketing, but that's not accurate in a small company," she says.

"In a large company, there are many people who do all of the background operations needed to get a product to market. But in a small company, the commercial organization does it all — choosing what the drug product will actually look like, how it is packaged, whether it should come in single or multiple strengths, and how the final configuration may affect pricing. You have to make all of those decisions years before launching the product because it's highly recommended to use the same clinical trial material used in the Phase 3 for your commercial product."

Small-company commercial teams must also set up a supply chain before launch, addressing everything in the chain from warehousing to the possible need for specialty pharmacies or specialty distributors, according to Andrews. "The list is very long. You need to have a hub, with an information system that captures all of the processes and related data. You need to have certain licenses and policies in place. You need a separate incentive compensation program for your field force, designate your territories, and identify the prescribing physicians, which is all difficult to do when you're a first-in-class, first-in-disease product. What can you possibly use as a benchmark? That alone takes enormous time."

In a larger company, developing or launching a third or fourth product in its class or indication, Andrews observes how relatively easy it is to obtain much of the information needed for benchmarking. But for a small company carving out new therapeutic territory, by definition, no obvious benchmark exists. The only recourse is to look for analogous products already established in other areas.

"Am I talking about a $100 million or a $1 billion product? What you convey to the street is really important, but it has to be based on what you actually believe you can do, not overrepresenting or underrepresenting the opportunity. Many small companies are not successful at benchmarking and all of the other prelaunch preparations, but at Incyte, we were ready on time for the launch of Jakafi, which was approved slightly earlier than its prescription drug user fee act (PDUFA) date. We launched within five days of the approval, even though it was the week of Thanksgiving. It was really remarkable."

She elaborates on the difference between the ways large and small companies drive such prelaunch activities. "At Pfizer, when you launched a new product, you were just taking the product and putting it into a standard distribution system. Your field force was just adding another product. You didn't need to identify the territories, design a new incentive plan, and figure out how to recruit reps to a company that has no product yet."

Andrews confirms it is necessary to have a commercial team that will conduct all of the activities just described at an early stage, even when the company is just raising funds and doing business development, and even if it intends to partner out or sell the product to another company: "Having a chief commercial officer and a commercial team in place shows the company's confidence in the compound and its progress," she says.

"As more data on the compound gets into the public domain and it causes rising interest among potential

"Having a chief commercial officer and a commercial team in place shows the company's confidence in the compound and its progress."

PAT ANDREWS
CEO, Boston Biomedical

buyers, they will think the company just wants to be bought, unless it clearly shows it plans to launch the product and knows it can make a lot of money launching the drug itself. A lot of small companies miss that opportunity; they wait until they have Phase 3 data. That is too late to plan and take good strategic, cost-efficient steps, regardless of how good the commercial people you bring in may be."

It is important to distinguish the early commercial-team activities Andrews describes as aimed at enhancing drug development and investor confidence rather than selecting or deselecting candidates for development. The objective is not to "kill" development programs based on market evaluations, but to ensure the programs yield products ideally suited for the market conditions each one may face.

NEXT STEPS UP

Jakafi won FDA approval in 2011. In 2013, Andrews received another query from an executive recruiter. This time, the job offered, at Boston Biomedical, carried the same CCO title she had at Incyte but would give her broader responsibilities.

"It was really a chief operating officer job initially, with responsibility not just for starting up the commercial side, but also participating in more corporate functions: HR, legal, and for a time, medical affairs. They wanted someone who had worked successfully in a large company as well as a small company, and who was well-focused on oncology."

At the time, Boston Biomedical expected a near-term launch of its lead products, anti-tumor drugs napabucasin and amcasertib, so it needed someone who, like Andrews, was confident of taking the company from the R&D stage to the commercial. Although Incyte's drugs had addressed other diseases by other mechanisms, they had one thing in common with her new company's product: They would be the first in a new class. For Boston Biomedical, the new class would be cancer stem cell (CSC) pathway inhibitors.

She soon joined Boston Biomedical and for the next several years, developed the commercial plan and worked inside the management and drug-development teams. Just before she came to the company, Sumitomo Dainippon Pharma (then called Dainippon Sumitomo Pharma), acquired it, but the ownership has been benign, she says. "Sumitomo Dainippon Pharma allowed Boston Biomedical to prosper and develop very much on its own with support of the new owner's funding. Our parent company really believed in allowing the entrepreneurial biotech spirit to remain, so it was very hands-off. And we didn't need to worry about fund-raising or investor relations so much because we were largely shielded by the parent company."

Unlike Takeda's purchase of Millennium, which triggered a transformation of both companies, Sumitomo's acquisition of relatively tiny Boston Biomedical has made few waves in either organization. "We're a significant part of Sumitomo's future, and it is definitely investing in us, but not, at the moment, getting a return. That return will hopefully come in a few years when our products come out of Phase 3."

For a company of only 140 people or so, Boston Biomedical has an impressively large pipeline of programs in multiple indications for its two lead drugs and others such as a cancer peptide vaccine. According to Andrews, the programs have grown naturally out of the company's scientific activities and are all well-funded. The company is in an exploratory mode with the earlier-stage programs and may decide later whether to continue with some, but it considers all of them to have strong potential, she says.

One of the lead compounds, napabucasin, is in a Phase 3 trial for treating second-line colorectal cancer and in a separate Phase 3 trial for first-line pancreatic cancer. Both lead drugs target a cancer stem-cell pathway for self-renewal, a unique and unproven approach. "CSC-targeting has risk associated with it, but it also has huge potential because it may address an area of the cancer recurrence and metastasis other compounds don't address," says Andrews.

"The theory is a small subset of cells are particularly malignant and, after chemotherapy, remain dormant because they are inherently resistant to chemo. They stay dormant indefinitely until something in their microenvironment triggers them, and then like the roots of a plant, they sprout forward, and that's how metastatic disease occurs. They move throughout the body, so the tumor doesn't return to the spot that it originated."

Last April, recognizing the full depth and breadth of Andrews' talents, Boston Biomedical promoted her into the CEO position. One of the people she believes has supported and mentored her the most at the company is Dr. William Rutter, who was the founder of Chiron, as well as professor at UCSF, where a building bears his name, and is a member of the National Academy of Scientists. Rutter was on the Boston Biomedical board when she joined. "Bill is a true scientist with many amazing discoveries to his credit, and I find his advice enormously helpful to me."

Andrews is also a mentor to others and a strong promoter of women in the industry. (See "Tapping the Power — Women on Board.") Her career, spanning several decades, has evidently taught her not only what the industry *is*, but also what it *could be*. She has been, is, and will be an explorer who blazes new trails for herself and many others in this ever-evolving business. L

Creating A Contingency Plan: **Top 4 Pharma Concerns As Brexit Approaches**

JENNIFER RINGLER Contributing Writer

March 30, 2019 — Brexit D-Day — isn't as far in the distant future as some might hope. For U.S. pharma companies with headquarters or CROs in the U.K., much needs to be decided, planned, and executed before that time to ensure a smooth transition. A recent report from the Economist Intelligence Unit (EIU), titled "Healthcare in 2018," outlines the multiple challenges Brexit talks pose to the pharmaceutical industry.

ADOPTING EMA REGULATIONS

In order for currently existing drugs that have market authorization in the U.K. to be sold in the E.U. after Brexit, the EMA has said that pharma companies will need to set up additional offices elsewhere in the E.U. On Nov. 28, 2017, the EMA released its latest Q&A guidance about Brexit, which stated that marketing authorization holders (MAHs) established in the U.K. will need to be replaced with an MAH in one of the remaining EEA countries (E.U. countries plus Iceland, Liechtenstein, and Norway). This will require pharma to apply for a transferring of marketing authorization. It also means that the pharmacovigilance person (and pharmacovigilance master file) must reside and carry out business in an EEA member state.

"Of course, if the U.K. does reach a regulation deal before March 2019, then those E.U. offices may be unnecessary, but we can't tell at this stage," explains Ana Nicholls, healthcare analyst at the EIU and author of the report. The Medicines and Healthcare products Regulatory Agency (MHRA), U.K.'s pharma governing body, will take over responsibility for marketing authorization within the U.K., which means that in the future companies may have to duplicate applications unless a far-reaching mutual recognition deal is in place.

And that's just for completed and approved drugs; those still in clinical development have additional hurdles to face. In April 2014, the E.U. passed new clinical trial regulations, which were planned to take effect in October 2018. According to the EIU report, the implementation has now been delayed until 2019, and Nicholls says it's "not quite clear" whether the U.K. will decide to implement them or, essentially, create their own from scratch under the MHRA. Arguments for the U.K. forging its own way include the idea that doing so could cut through a lot of bureaucracy, allowing a much quicker drug approval process than the rest of the E.U. currently sees under the EMA. The argument against is that if the U.K. does adopt its own laws, drugs manufactured under those laws won't be recognized as approved outside the U.K., unless a deal is struck between the two countries. Meaning, the limited marketability of drugs developed under post-Brexit U.K. law will likely motivate pharma companies to concentrate on approval in E.U. markets, leaving the U.K. behind.

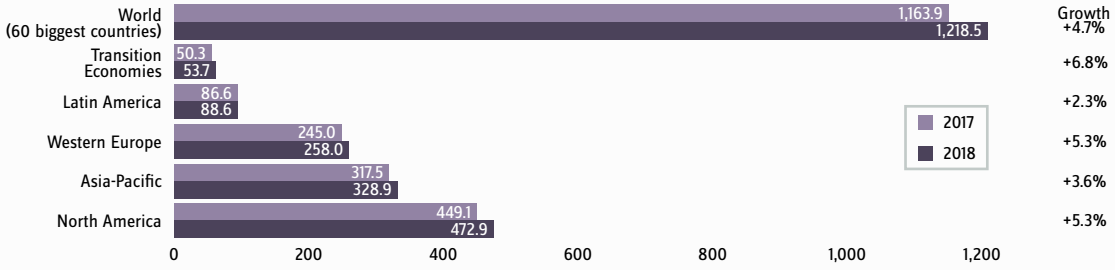
"If they can't ship things so easily, maybe it makes more sense to house the manufacturing in one place or the other, rather than swapping across borders."

ANA NICHOLLS
Healthcare Analyst, Economist Intelligence Unit

RECRUITING AND MAINTAINING A WORK FORCE

In terms of how, exactly, Brexit will affect the pharma-

PILL POPPERS: PHARMACEUTICAL SPENDING BY REGION IN 2018 (U.S. $BN)



SOURCE: The Economist Intelligence Unit

ceutical work force, "That's another issue that still isn't settled," Nicholls says. "At the moment, it looks likely that anyone who currently resides in the U.K. can stay; it's not that anybody will get kicked out." Pharma should be keeping an eye on ensuring top-quality talent is available down the line. Nicholls says it's likely that some type of "immigration system" will be implemented in the U.K., but the details of what that will look like are anyone's guess.

As mentioned in a previous *Life Science Leader* article by authors Cameron Cooley and Chris James, "Indications are that the U.K. government is pursuing a 'hard Brexit,' which would end the right for other E.U. nationals to work in the U.K. without visas." This could mean that recruiting top talent from the E.U. will become more difficult, as qualified candidates seek to work within the E.U. to avoid the complications of international work arrangements. Much like the red tape around post-Brexit EMA regulations, this complication could contribute to the newly independent U.K. becoming less desirable over time for pharma.

RETAINING MEDICAL FUNDING

Another major hit to pharma from Brexit could be the loss of scientific and medical funding coming in from the E.U. The U.K. has had significant funding from Horizon 2020, an E.U.-run research and innovation program offering €80 ($107) billion of funding over seven years (2014 to 2020) that is seen as "a means to drive economic growth and create jobs," according to the program's website. Nicholls notes that the U.K. has been one of the "biggest beneficiaries" of the program. The U.K. government has pledged to fund any research already underway until 2020, regardless of the E.U. negotiations. However, the U.K.'s involvement in future E.U. science programs is among the issues that still need to be discussed in ongoing Brexit talks.

But Nicholls sees the loss as an opportunity. "It could give us more motivation to work in scientific programs in the U.S., India, or China," she says. "One of the things about the U.K. science programs is they do get fairly widely cited; international citations are a widely used measure of the success of a scientific program. It may be that we still manage to get enough international programs from other sources to balance out the loss of that funding."

ENSURING THE SUPPLY CHAIN

There is a lot riding on the "what ifs" around post-Brexit supply chain; how negotiations play out here could potentially mean life or death for patients, as well as businesses.

"The main concern the pharma industry is having is, will there be a point after March 30 where all their goods are stuck in transit because they can't ship them across the border from the U.K. to the E.U. without the right paperwork?" Nicholls says. "It is conceivable that this might be the case for a few days."

Her advice for pharma on this front is to have contingency plans in place including a stockpile of currently approved drugs as well as raw materials for manufacturing, both inside and outside the U.K. "In the long term, pharma companies need to look at the whole supply chain and consider, if they can't ship things so easily, maybe it makes more sense to house the manufacturing in one place or the other, rather than swapping across borders." Such a contingency would require significant additional planning and cost on pharma's part.

THE WAY FORWARD

There are clearly still quite a few details that need to be hammered out before March 2019. "But I don't think they will be hammered out by then," concedes Nicholls. She's not the only one who has realized this; on November 28, the same day the EMA released its latest Brexit guidance, several associations representing the European and British life sciences industry collectively released a statement calling for a transition period and a post-Brexit cooperation agreement. "We urge Brexit negotiators on both sides to agree on a transition period that adequately reflects the time needed by companies, as well as all relevant authorities at E.U. and national level, to adapt to changes in view of the U.K. exiting the E.U.," the statement reads, in part. "Even in the context of the Brexit negotiations where all sectors are looking for clarity on the future, it's important to recognize that medicines are different. Our goal is ensuring that patients across Europe and the U.K. are able to continue to access safe and effective medicines through Brexit and beyond, and to ensure that there is no adverse impact on public health." L

A Celgene Exec's Unexpected **Trip To Washington, D.C.**

ROB WRIGHT Chief Editor @RFWrightLSL

Normally when we interview top biopharma executives for feature articles, we're looking for a unique story with personal insights about how they overcame some business challenge or implemented some business strategy. Recounting what an executive did while on sabbatical wouldn't normally fit into that model. That is, unless that executive is Richard Bagger, J.D., EVP of corporate affairs and market access for Celgene.

And it all started at 4 a.m. — in Tokyo.

CALLED TO SERVE

It was May 9, 2016. Bagger was in Japan on Celgene business and was up early reading news on his iPad. "I suddenly came across an article that I had an odd feeling about; I felt I may soon be a part of the story I was reading," he recalls.

The article was about presidential candidate Donald Trump announcing that New Jersey Governor Chris Christie would be chairing his White House transition team. "I was Governor Christie's first chief of staff," Bagger explains. "As I had worked closely with him on a number of assignments, I thought he might reach out about the Trump White House transition team."

He had been back in the U.S. only a few days when his prediction came true. Christie called asking if his old friend would consider taking a leave of absence from Celgene to serve as the pre-election transition planning team's executive director.

A TRUE LEARNING SABBATICAL

Intrigued, Bagger knew he had a difficult decision to make. On one hand, this was possibly a once-in-a-lifetime opportunity for him to perform a public service and support a candidate he favored. However, he would have to move to Washington, D.C. (he lives in New Jersey) for several months and work as an unpaid volunteer while also taking an unpaid sabbatical from Celgene.

After first discussing it with his family and getting their approval, he now had to broach the subject with his employer. "My plan was to complete the assignment and return to Celgene, but if I did not have their support, I would not have taken the opportunity," Bagger explains.

When he spoke with Mark Alles, Celgene's CEO, and Bob Hugin, the company's executive chairman, he recalls both men being not only very supportive, but enthusiastic about the opportunity. "They are each Marines and very patriotic people, and they saw this as a chance for me to serve and support someone who could be the next president," he recalls. "I think they also viewed it as an amazing learning and personal development experience that would benefit one of their employees, and thus, Celgene as well."

HOW TO BUILD A TEMPORARY "STARTUP"

In retrospect, defining his new "job" in Washington as a "learning experience" would be an understatement, according to Bagger. Instead, he likens it to creating a startup from scratch — something for which he had no experience.

At least he didn't have to worry about finding a location for the offices of the pre-election transition team. The Presidential Transition Act provides eligible candidates with federally funded office space as well as other resources such as IT, telecommunications, and office equipment/supplies. "It was still necessary for us to establish a 501(c) (4) organization to raise funds for any expenses and salaries to the extent anyone [certain transition staff] needed to be paid." (That IRS classification code provides exemption status to a nonprofit organized and operated to promote social welfare.)

In late May, when Bagger first showed up for work as executive director, it was just he and Christie. Deemed the preplanning phase, this part in the process involved "a lot of reading about the process itself as well as meetings with members of previous pre-election transition teams and members of the Partnership for Public Service [See sidebar "Understanding The Presidential Transition Process"] and its Center for Presidential Transition," Bagger says. "We were identifying deliverables and timelines and building a core team to begin operations after the national convention."

A MASSIVE STAFFING CHALLENGE

By Election Day, that team would need to number around 100 people, with a couple hundred volunteers working for extended teams. Unlike a startup that gradually builds its employee base over time, the clock was ticking for Bagger, and staffing quickly became a massive exercise.

"First we had to identify what positions to recruit for," he explains. "We approached this challenge similar to building a new company or a division within a company; we decided the first thing we needed was a leadership team." With Christie as the chair (i.e., CEO) and Bagger as executive director (i.e., COO), they proceeded to select a head of transition personnel (i.e., tasked with staffing the transition), a director of presidential appointments (i.e., who is the lead on developing slates of potential presidential appointees), a director of operations, general counsel, finance director (i.e., responsible for raising money to fund the nonprofit), and someone to begin vetting potential appointees through public sources.

The pre-election transition planning team had a number of deliverables, such as:

- Assemble prioritized slates of candidates for the most important presidential appointments.
- Develop memorandums for each department in the federal government so "landing teams" could hit the ground running. These 20- to 30-page documents might include:
  - basic background information

UNDERSTANDING THE PRESIDENTIAL TRANSITION PROCESS

We asked Max Stier to explain what the U.S. presidential transition process typically involves, so you could really get a grasp on the enormity of Richard Bagger's experience. Stier is president and CEO of Partnership for Public Service, a Washington, D.C.-based nonprofit, nonpartisan organization dedicated to making the federal government more effective for the American people.

"Historically, candidates have been loath to focus on transition planning," Stier says. This is because campaigns are designed to win an election. "Campaigns don't want to do anything that could get in the way of that focus, and pre-election transition planning made campaigns vulnerable to attack, i.e., measuring the drapes before the candidate had won the White House," he analogizes. However, this changed in 2010 with the passage of public law 111-128 (P.L. 111-128). An amendment to the Presidential Transition Act of 1963, it provided that certain transition services shall be available to eligible candidates before the general election. "This provided political cover for campaigns to do the right thing when it came to being ready to govern," Stier shares. "Waiting until after the election leaves 70-some odd days to prepare for taking over the world's most complex organization that operates on a $4 trillion annual budget, and employs about 4 million people."

Consider this, a new president has to select and place about 4,000 political appointees. "Imagine a biopharmaceutical company having to replace 4,000 of its top leaders in around 70 days," he says. "Of these 4,000 appointees, about 1,100 have to go through a grueling Senate confirmation process, and of those, about 500 are top jobs (e.g., secretary of state, deputy secretary of state) with line responsibilities and huge spheres of control."

It may seem unbelievable, but prior to the involvement of Stier's organization, there were no available position descriptions for these top political jobs during government transitions. "That's just one of the things we've built," he shares. While previous administrations were historically helpful to those coming in, transition planning best practices were typically shared via in-person meetings. "If you asked for transition documentation, you'd be lucky to be given a moldy, old box someone had kept in their attic," Stier states. "This is why we created the first-ever presidential transition learning system."

RICHARD BAGGER, J.D., EVP, CORPORATE AFFAIRS & MARKET ACCESS CELGENE (LEFT), CHRIS CHRISTIE, GOVERNOR, NEW JERSEY

- key departmental issues
- upcoming decisions needing to be dealt with right away.

- Develop and prioritize policy implementation plans for campaign priorities (e.g., healthcare, taxes) with timelines for what do in the first 100 days, 200 days, etc.
- Build a team of people tasked with framing how to utilize the 73-day period that starts with the day after the election, referred to as "day-next," and runs through the inauguration.
- Manage routine tasks such as president-elect logos, style guides, and websites. For example, 15 hours after the conclusion of the election, the Trump transition team had its website up and running, a positive outcome of the pre-election planning process.

Phase two — the planning phase — of the process begins immediately following the conclusion of each party's national convention and goes up until Election Day. The third phase begins on "day-next" and is the transition execution phase, which Bagger describes as the hardest, most complex, and most important.

"Prior to the election, this team goes about their planning quietly, heads down, and focused, so as to not be a distraction to the campaign," he explains. "Our goal was to build a strong foundation so the team was well prepared to execute if phase three needed to be implemented."

SHARING LESSONS LEARNED

Shortly after the election, the press made much ado about the transition effort headed by Christie being taken over by Vice President-elect Mike Pence. But Bagger says the pre-election transition team planned all along for a handoff after the election to the team for the execution phase. "I always expected to return to Celgene shortly after day-next. Had it made sense for me to stay further into the execution phase, I would have, though," he admits.

So, the Monday after the election, he found himself back at Celgene walking the halls and frequently answering one particular question: "What did you learn?"

Of course, he says he learned about presidential transitions, the structure of the federal government, and policy implementation issues. But from a business perspective, he says he learned a lot about building something from the ground up. "You have to think about how you're going to build the organization and who you're going to recruit next. What about defining and proposing objectives for others to ratify? How do you create an organizational culture [see sidebar] of shared purpose? How do you maintain team camaraderie and focus when there is a 50 percent probability that all of the work being done might never be used should your campaign lose?"

Aside from those kinds of takeaways, Bagger says the experience as a whole gave him a new and different perspective on how he viewed Celgene's business. "Just being away for a few months afforded me the rare opportunity to see our company from more of an outside-in lens. It's made me think more about Celgene's next phase and what we could not only do differently — but better." L

CREATING AN ORGANIZATIONAL CULTURE

Like an executive at a small startup, one of Richard Bagger's first tasks as executive director for the pre-election Trump transition team was to create a "company" culture.

"At the same time we were building the leadership team and the overall team, we were considering the type of culture we wanted to have once we were up and running," Bagger recalls. On the first day the leadership team was in its new offices, the 15 members spent a half day defining the culture and talking about ways to instill that culture.

"Tuesdays became my favorite day of the week," he says with a grin. "That was the day we'd have an onboarding meeting for new pre-election transition team members." At those meetings, Governor Christie would provide an update, as would other members of the leadership team if they had something needing to be addressed. Bagger would usually cover some key points for all team members to keep in mind. "I'd remind everyone that the campaign was the most important thing they should be focusing on, and that they were there to develop plans and not to substitute our judgment for the judgment of those who'd be executing these plans. Finally, I'd remind them as to the importance of doing our work in private, without making news and without talking to unauthorized people. We all needed to stay focused and get the job done." Bagger says he'd then conclude the meeting by saying, "OK, it's time for graduation," and he'd shake all of the new team members hands and give them a Make America Great Again hat. "It was a little 'Go team!' ritual. But those moments, in our open office landscape where everybody would crowd around, were particularly good for building team cohesion."

5 Leadership Questions **For Camilla Harder Hartvig**

DEIRDRE COLEMAN Contributing Writer

CAMILLA HARDER HARTVIG is SVP of Canada and EMEA for Alexion Pharmaceuticals. Previously she was president, Europe and emerging markets, at Glenmark Pharmaceuticals and also worked for companies such as Allergan, AstraZeneca, and Novartis in various managerial positions.

1. WHO HAS HELPED SHAPE YOUR LEADERSHIP STYLE?

Some of the leaders who have helped shape my style include David Brennan, former CEO of AstraZeneca; Philip Burchard, CEO of Merz Pharma; Lars Ramneborn, CEO of Xantis Pharma; and Paul Navarre, CEO, Ferring, U.S. All these leaders talk and care about people first before they get to performance and targets. I've adopted that approach, focused on developing people through a mix of challenge and support instead of just training or advice. My role is as an enabler, stretching and championing others and giving them the mix of support and challenge they need to excel. The best leaders enable the full potential in others. They are liberators, freeing up people to become the best version of themselves.

2. WHAT ARE SOME KEY MISTAKES LEADERS MAKE?

People will perform incredibly well from a platform of trust and strength. Leaders need to make sure employees have that. That's when you see amazing things happen. Leaders also should behave in a humble way; you have to often stand behind a team, not in front of them. I loved when Brent Saunders, CEO of Allergan, and the global leadership team took to the stage and they turned the chart on its head and said, "It's all of you who are up at the top and us down at the bottom; we serve you." That picture is just so powerful.

Leaders need to learn how to create a shared and well-understood vision among their organization's members in order to foster an atmosphere of purpose. Lack of communication is one of the worst things a leader can do in my opinion. If employees don't understand the vision or don't get an explanation of the vision — the why behind it — they can't understand their own purpose in it all.

3. EXPLAIN YOUR LEADERSHIP STYLE.

My entire leadership style is around collaboration; connecting people and making sure they have the right information and tools to make decisions for themselves and their teams. I'm always trying to drive more communication in any organization so people feel included, are aware of the shared vision, and hence have that clear purpose. For an organization to learn and grow, leaders need to act in a manner that encourages the sharing of information between all members of the organization.

4. WHAT IS THE MOST IMPACTFUL BOOK YOU'VE READ ON LEADERSHIP?

5 Voices: How to Communicate Effectively with Everyone You Lead. It's a profound book that deals with understanding your voice as a leader and listening to the voices of others. Once you realize what type of voice you have and understand the personalities of others around the table (namely, the Pioneer, the Connector, the Creative, the Guardian, and the Nurturer), you can remove 40 to 50 percent of the conflict immediately in a team setting due to miscommunication. This frees up time and removes unnecessary tension to simply get the job done better. I think it's a book that every leader could benefit from.

5. WHAT SHAPED YOUR POSITIVE LEADERSHIP STYLE?

I take huge inspiration from solo Atlantic rower and motivational speaker Debra Searle, who is a serial entrepreneur. Many years ago, she inspired me to get into this area of intentional and positive leadership. Searle's motto has become my motto: Choose your attitude. You have the opportunity every day to choose your attitude. Whether you're in a crisis or faced with a challenge or just in a discussion with someone, you can choose how you want to approach it. And I always say, don't worry about the things you can't control; that doesn't help you or anyone around you. 'Choose your attitude' every day as a leader. I have a big embroidery, created and given to me as a present by the most fantastic former employees, with that saying on it hanging in my office. Definitely words to live by.

Breaking The Mold — A New Perspective On Alzheimer's

JENNIFER RINGLER Contributing Writer @JenniferRingler

Casey Lynch, CEO and cofounder of San Francisco-based Cortexyme, has been fascinated by Alzheimer's disease throughout her career, even dating back to her graduate work at UCSF. And while other biotech and pharmaceutical companies have been needling away at the problem (without much success) for more than two decades, largely by looking to beta amyloid and tau proteins as the culprit, Lynch has long had the gut feeling that there was something else going on behind the scenes. As it turns out, she was right — looking at years of research, mounting evidence shows that a bacterial infection in the brain is at the root of Alzheimer's disease.

Simultaneously, UCSF psychiatrist Dr. Stephen Dominy was working with patients with HIV and dementia, and was therefore especially interested in infectious causes of neurological disease. Dominy's research led him to discover a pathogenic bacterium in the brain of patients; Lynch and Dominy met each other through investment group Life Science Angels, and the seed for Cortexyme was planted. Cortexyme can now identify the bacteria (which one, Lynch says, is still confidential) in the cerebrospinal fluid of people with Alzheimer's.

Cortexyme, which operates in lab space at JLABS, a nonprofit run by Johnson & Johnson, has now proven this correlation between the bacteria and the disease in the brains of mice as well as aged dogs. The company began Phase 1 human studies in December 2017.

LESSONS IN INVESTING

In the past four years since that first seed was planted, Cortexyme has raised more than $24 million in capital, with Pfizer and Takeda Ventures as backers — an achievement Lynch attributes to good timing, good data, and finding the right "champions."

As exciting as the discovery was, Lynch and Dominy knew they needed more to go on. For the first year, they operated on what she calls "friends and family money," doing their own experiments to corroborate what they had found in the data. This process was a lot like making a low-budget film — they sought out a scientist who was an expert in the bacteria they were studying and asked him to donate the leftovers from his own experiments — the brains of mice he had that were going to be thrown away. Lynch knew from previous experience that it was important to have something solid to present to investors. "We needed more than really interesting correlative human data, which is what we started with," she says. "There's a certain bar you need to reach before you go to venture or corporate folks."

Once the fledgling company had proven causation in mice, there still wasn't a lot to share with investors without a molecule to invest in. They surmounted this obstacle by seeking a grant from Breakout Labs (part of philanthropic organization the Thiel Foundation), which provides grants for early-stage scientific research. With that funding, Cortexyme had enough momentum to develop a proprietary drug program needed to convince corporate and VC investors to take notice.

Lynch's advice for startup biotechs seeking capital is to put themselves in investors' shoes. "Once you're in the pitching stage, it's important to show investors that you have a clear vision — from A to B to C to exit," she says. "This isn't a science project. Sometimes it isn't even about making revenue, although usually making revenue leads to an exit; you need to make it clear to investors that you understand their business as well as your own. Their business is giving a return to their company or their limited partners."

Even with strong data and a clear understanding of investors' goals, Lynch says, you're not likely to succeed without a personal connection. Finding a "champion" within the company you're courting is crucial; Lynch says to look for someone within the organization "who will really dig into your opportunity and get to know you."

GENDER DIVERSITY IN BIOTECH

In addition to looking at a new underlying cause for Alzheimer's and having an investment strategy that depends on human connection, Cortexyme stands out in yet another way; 50 percent of its staff, including the executive team, are female. Lynch doesn't think this is newsworthy, despite a September 2017 report from Liftstream and The Massachusetts Biotechnology Council that shows the C-suite of biotech is made up of 24 percent women versus 76 percent men. She insists the 50/50 split at Cortexyme was not intentional, but rather is "just what happens when you hire the best person for the job." She also believes the successful, collaborative dynamic at Cortexyme is not a result of having more women at the table. "My cofounder is incredibly empathetic; he's a great leader and a great motivator. And some women on our team are very assertive. I don't think any gender has a corner on certain qualities that are good for a company," she says.

"You need to make it clear to investors that you understand their business as well as your own. Their business is giving a return to their company or their limited partners."

CASEY LYNCH
CEO & Cofounder, Cortexyme

That's not to say that Lynch is blind to the impact that a lack of gender diversity in life sciences has on the industry as a whole. She acknowledges that biotech conferences and meetings where life science executives gather are often very one-sided. "I think the way it impacts the industry is that when there are fewer examples of successful women leaders, investors have fewer experiences to draw from," Lynch reflects. "And if they're thinking that they've never had an experience with a female founder or CEO who has been successful, this can create an unconscious cognitive bias as to who they invest in."

Despite the daunting odds, Lynch doesn't look for any credit or consider herself a hero or overachiever for her rare position among that 7 percent of female biotech CEOs. "I think all entrepreneurs have to push hard. It requires a lot of grit and passion and perseverance," she says. "Did I as a woman have to have more of that? I couldn't say. I don't know."

BREAKING THE CURSE

Hundreds of biotech and pharmaceutical companies have tried to find the needle in the Alzheimer's haystack over the years — the one therapy that would succeed in clinical trials, that could do more than just treat symptoms for a short period, that might actually find and treat the underlying cause. And while popular medications such as Pfizer's Aricept (donepezil) can give patients a small cognitive boost for a few months, research focusing on beta amyloid and tau proteins hasn't hit the mark in terms of curing disease — so far, every one has failed in the clinic. According to a 2014 study published in *Alzheimer's Research and Therapy*, "Alzheimer's disease drug-development pipeline: few candidates, frequent failures," of the 413 Alzheimer's trials that were registered to clinicaltrials.gov between 2002 and 2012, 99.6 percent failed. During the assessed time period, 72 percent of agents failed in Phase 1, 92 percent failed in Phase 2, and 98 percent failed in Phase 3. As of the publication of that study, only five drugs were approved for Alzheimer's treatment, and no new treatments have been approved since 2003.

With odds like these, what keeps Lynch and her team getting out of bed and coming to work every day? "It's easy because we're doing something so different," she explains. "I'm not sure how it happened, but in all of pharma, the targets in Alzheimer's disease were narrowed down very early on to one or two, maybe three. Compare that to oncology, where researchers pursue so many different targets — that just increases the chances of success." Lynch is not disheartened because she believes that "the lack of efficacy to date is likely because only small pieces of the puzzle are being addressed."

Lynch's optimistic mindset permeates the team at Cortexyme. She recalls a moment where she checked in with a new scientist about three months after bringing him on board, when he said to her, "I get up every day, and I'm excited to come to work because I know we could discover something new today." This turned out to be more than just a platitude; this same scientist later created the current diagnostic method Cortexyme uses to identify the bacteria in the cerebrospinal fluid — quite possibly the first step toward an unprecedented breakthrough for Alzheimer's patients.

One Small Startup's Quest For Funding Gets Creative

CAMILLE MOJICA REY Contributing Writer @CamilleReyATX

It's no wonder small biopharma companies are acquired by their larger counterparts only after clinical trials show a novel drug's potential for success. R&D costs are expensive, accounting for about half of the average cost to develop and gain marketing approval for a new drug. That leaves those small startups with the job of raising massive amounts of money just to stay afloat during the clinical trials process — and hoping for an acquisition exit.

As CEO of Ensysce Biosciences, a semi-virtual company with three employees, Lynn Kirkpatrick, Ph.D., knows all about the funding struggles of a small company. "Every small biotech understands that it costs so much and takes so much infrastructure to commercialize your own product that M&A is inevitably at the top of the list of options for getting a product to market," she says. "Seeking funding is a 24/7 job. As soon as we get money, I'm out looking for more."

MERGER IMPROVES ABILITY TO RAISE FUNDS

Ensysce, which relies on CROs and consultants to work on its products, was spun-off from Houston-based Carbon Nanotechnologies Inc. in 2009 to develop carbon nanotubes for the delivery of large molecule biologic therapeutics. In 2015, in order to increase its ability to raise funds and support the early-stage nanotube work, Ensysce chose to merge with clinical-stage Signature Therapeutics, developer of abuse- and overdose-resistant drug technology. Both companies were virtual at the time with only a handful of employees. "The merger allowed us to have two platforms for drug delivery in different stages of development, the clinical-stage opioid 'prodrugs' [Signature's abuse-resistant technology] and the R&D stage carbon nanotube delivery," Kirkpatrick says.

EXPLORING A VARIETY OF FUNDING SOURCES

With VC fund-raising on the rise, competition is fierce for those dollars. Statista estimates that between 2012 and 2016 there were more than 2,700 public and private biotech companies in the U.S. "If you are underfunded, it's hard to advance your technology because you are always out looking for your next dollar." That means many CEOs, like Kirkpatrick, need to look for funding from a variety of sources.

> *"Seeking funding is a 24/7 job. As soon as we get money, I'm out looking for more."*
>
> **LYNN KIRKPATRICK, PH.D.**
> CEO, Ensysce Biosciences

To date, Ensysce has been funded by a combination of state and federal grants, foundations, and funds from high net-worth individuals, friends, and family. Kirkpatrick has found that having a drug in clinical development has its fund-raising advantages. "Venture groups usually like to invest with a shorter runway to an exit, wanting drugs in the clinic versus R&D." She also has found that the ability to raise capital can be limited if you are trying to take on a major player in the industry. "There's always that 800-pound gorilla breathing down your neck," Kirkpatrick says. For Ensysce, that gorilla is Purdue Pharma, the maker of OxyContin, which holds 70 percent of the opioid market. Still, that kind of mar-

ket — one that is dominated by one player — means a new entrant like Ensysce that could challenge the status quo could be very disruptive. And that gets the attention of larger players.

"We're currently in a scenario where we have to prove to potential acquirers — and the FDA — that we have something that is far superior to the products already on the market," Kirkpatrick explains. "One of the biggest challenges will be educating physicians and others who prescribe OxyContin. They understand OxyContin, and that's why it has maintained its market share even though there are almost a dozen different formulations on the market."

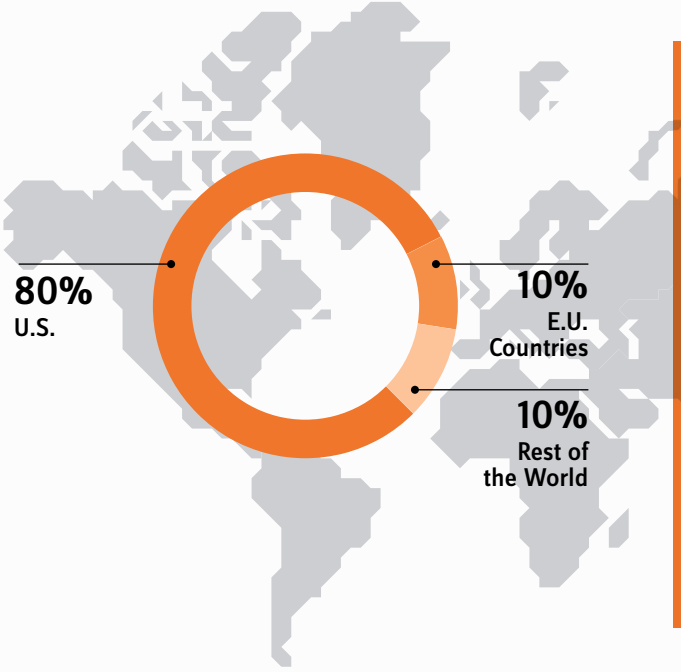
Kirkpatrick says she has already been approached by all of the major pharmaceutical companies that have pain products on the market. Some of these companies are in "wait-and-see mode," while others are having regular conversations with Kirkpatrick.

Recently, she has been exploring a number of funding options including a reverse merger into a public company that would give her access to capital without the lengthy, costly, and complex process of undertaking an IPO. Another option, available since 2015 when the Jumpstart Our Business Startups Act (the "JOBS Act") was amended, is a Regulation A+ offering. This offers small and midsize businesses the chance to raise up to $50 million through mini-IPOs from investors, both accredited and nonaccredited (i.e., the general public), by pitching and raising money online.

The costs associated with a mini-IPO are modest: an average of $50,000 in legal fees and an average of $15,000 for an accounting audit. These fees are much lower and there are fewer ongoing disclosure requirements than a traditional IPO. Companies interested in raising capital through a Regulation A+ mini-IPO must file an offering statement with the SEC and receive certification in order to begin selling securities. Companies also may file a draft offering statement for nonpublic SEC staff review and/or to "test the waters" by approaching investors between the time they file an offering statement and before certification. A company's leadership can decide not to proceed with the offering depending on the response they receive either from the draft review or the "testing-the-waters" phase.

No drug developer has yet to use Regulation A+, though Alzamend Neuro is working to move a mutant peptide-based vaccine forward using the crowdfunding source. As for Kirkpatrick, she says she is keeping her options open and continuing her constant quest to raise funds. "The life of a small startup is constantly evolving, especially when it comes to securing funding. Even I don't know until the last minute which of these fund-raising methods are going to happen — but they will happen." L

THE OPIOID EPIDEMIC



KEY FACTS

- Global opioids market $34B, anticipated to grow to $42B in 2021.
- North America is the largest market for opioid use:
  - U.S. accounts for 80% worldwide market share followed by Europe – approximately 10% market share.
- Southeast Asia has the world's highest opioid market growth with CAGR of 3.5% and is expected to increase at this growth rate until 2021.
- Abuse Deterrent Formulations (ADF) are the only source of market growth in North America and Europe.

Recurring Mistakes (And Remedies) For Life Sciences M&As

ODED BEN-JOSEPH AND THOMAS BUSBY

As members of a specialized life sciences investment banking group focused on private equity financing and M&A, we often note that life science management teams fall victim to recurring mistakes and entrapments. Below is a list of avoidable missteps in M&A transactions and their respective remedies.

1. GOING AT IT ALONE

What can get lost in these stories of M&As is the team of experts many executives depend on for areas such as M&A strategy, positioning, buyer identification, and negotiating and structuring the transaction to enable management to focus on running the company.

Lesson: M&A transactions are complex and require considerable expertise; seek expert assistance.

2. INWARD FOCUS

Maintaining an objective mindset during an M&A can be challenging. The result of failing to do so, however, is succumbing to heavily biased judgement, which is why boards and management must consider external market forces. A private company might never be concerned with public market movements until a public buyer is interested in acquiring them. Changes in a buyer's corporate leadership or strategy, buyer M&A activity, public market sentiment, and macroeconomic forces constantly alter deal dynamics.

Lesson: Expand your view to include external forces that need to align for your transaction to close; be prepared to refine and recalibrate your strategy.

3. FAILING TO CREATE A COMPETITIVE SALES PROCESS AND IDENTIFY ACQUISITION DRIVERS

Before commencing an M&A process, executives should conduct a broad market analysis to identify synergies and acquisition value drivers with potential buyers. Sellers should be armed with relevant financial parameters and strategic acquisition drivers, including revenue and profitability multiples, industry margins, and growth rates in order to estimate an expected transaction valuation. Most importantly, the seller should identify a number of buyers that could leverage the company's value proposition and quickly integrate for growth and profitability.

Lesson: Consider every financial/strategic player that stands to gain or lose from your company being acquired.

4. INADEQUATE UNDERSTANDING OF THE COMPETITIVE LANDSCAPE AND COMPARABLE TRANSACTIONS

Significant effort must be taken to grasp the particular dynamics of each small life sciences industry niche. Executives will commonly benchmark their technology against companies that play in different markets and expect the same valuation. Insofar as comparable transactions are concerned, market identification is crucial.

Lesson: Avoid futile discussions about valuation by disregarding transactions that are not relevant to your value proposition. If they are not a key competitor, do not benchmark yourself against them.

5. OBSESSIVELY FOCUSING ON FINANCIAL TERMS WHILE IGNORING THE PROBABILITY TO CLOSING

Executives are often overconfident about their chances of success with an M&A. However, when a multinational company offers a term sheet, they are seldom inclined to engage in extensive discussions about specific valuation metrics. As the buyer's BD team is likely

strapped for resources, they will lose patience negotiating superfluities. It is imperative that management focus their time on closing instead of engaging in never-ending discussions.

Lesson: Time is the enemy of transactions; move with haste and focus on what is truly important.

6. BEING UNPREPARED FOR THE EXTENSIVE EFFORT AND TIME THE TRANSACTION WILL CONSUME

Executives should allocate appropriate resources and expect the M&A process to last six to eight months. If there are internal company issues — for instance, options plans or AR issues — the M&A process can magnify their complexity. Compounding the challenge to resolving these issues is a management team preoccupied with closing. It is the seller that usually constricts the flow of information. Activating a key group of employees in your company can greatly shorten time to closing and showcase operational strength.

Lesson: Prepare your operations team accordingly and "button up" all outstanding governance issues — they will only fester and worsen with time and confirm to a buyer they are dealing with an amateur.

7. ALLOWING BIASES TO IMPACT DECISION MAKING

With M&A transactions, executives often rely on "rules of thumb" (heuristics) that may seem reasonable but lead to severe errors. They plan an M&A strategy haphazardly and make predictions about acquisition price and various other terms. Their point of view is heavily dependent upon the information available to them as well as their personal judgements based on individual experience.

Lesson: Accept that human error is rampant. Adopt a statistical mindset, and substitute human judgment and intuition with formal thinking.

8. FAILING TO PRESENT A CLEAR AND COMPELLING VALUE PROPOSITION AND STRATEGIC FIT WITH ACQUIRER

Management teams often inaccurately assume that corporate BD teams rigorously analyze each potential deal that comes to them. This belief, however, can cause otherwise value-enhancing transactions to never leave the runway. A clear and differentiated value proposition must be communicated to buyers from the initial point of contact. Sellers should take the time to formulate and articulate a strategic fit tailor-made to each potential buyer. The strongest letters of intent (LOI) are products of thoughtful strategic discussions centered on how an asset is better used in the hands of buyer.

Lesson: Identify your company's true value to its market and how its value is differentiated (and defensible) from competitors. Then, review each potential buyer separately and identify unique value enhancing synergies.

9. ABSENCE OF CREDIBLE FINANCIAL PROJECTIONS

Buyers spend considerable time evaluating a seller's current and projected financials and often employ valuation methodologies, such as the discounted cash flow (DCF), to assess value. A seller's unrealistic/unreasonable projections will adversely affect management's credibility and will create buyer distrust — the killer of all deals. Unique to private transactions, there is no such thing as the "right price" or fair market value of an asset; what a buyer pays is based on its views of the financial future value of the seller. Thus, the inputs into a DCF model to determine value will be different from buyer to buyer, and these are different from the view of the seller, who sees its company on a stand-alone basis.

Lesson: Ensure your financial projections are realistic and in line with market benchmarks. Allow for a valuation range.

10. NOT NEGOTIATING KEY TERMS EARLY IN THE PROCESS

A detailed LOI is likely to result in more favorable terms for the seller and will reduce the time to executing a definitive agreement. Once an LOI is executed, leverage migrates from seller to buyer because of the exclusivity provision that prohibits the seller from negotiating with other bidders. Some of the terms to be included in an LOI are price, structure (up-front cash, milestones, royalties), the calculation for price adjustments (working capital, cash-free, debt-free), amount and duration of escrow holdbacks, treatment of employees, representations and warranties, and conditions to closing. A seller must be clear, early on in M&A negotiations, about what the expectations are and what "third rails" to avoid.

Lesson: Choose early on in the process what key terms must be met for a deal to be consummated; communicate to buyers those terms, and do not waste valuable time negotiating less important issues. L

ODED BEN-JOSEPH is managing director at Outcome Capital, LLC.

THOMAS BUSBY is senior analyst at Outcome Capital, LLC.

Classifying Independent Contractors: 3 Things Pharma CEOs Should Know

REBECCA CENNI

Pharmaceutical companies abide by strict regulations and ensure compliance during drug development and manufacturing, but when it comes to regulations surrounding employment, it's imperative to exercise the same level of care. Not unlike a clinical trial setback, misclassification of independent contractors (ICs) can have a substantial negative impact on the business. Here are three key IC considerations pharma execs should ensure are addressed by compliance efforts.

1. THE RELATIONSHIP IS KEY

So you've identified a potential IC with truly impressive experience? Don't jump the gun — a sterling pharmaceutical industry track record doesn't automatically mean they are qualified to serve as an IC. What counts is the relationship they will have with your company. It is important to assess the level of behavioral control you'll be exerting over their work routine. In general, the more control you exert, the less likely they are to qualify as an IC. A genuine IC should require little supervision, should not be financially dependent on a single client, and should have the autonomy to determine how and when work is performed. When planning the project, if you anticipate treating an IC like your full-time employees by offering substantial training or regular oversight, it may be better to hire them as a W-2 employee. This is especially true if there isn't a definitive, planned end to the project; an indefinite end date is more characteristic of an employee than a consultant.

2. DETERMINE WHAT'S AT THE CORE

Are you asking ICs to perform any type of drug development? If so, you may not be compliant with local laws. Twenty U.S. states — as part of their three-pronged "ABC" test for IC compliance — include a key component known as the Core to Business (C2B) law. Essentially, the law mandates that services performed by an IC cannot be core to your company's business or a core competency of your business. In the state of Massachusetts, for example, the C2B law states, in part, that "for an individual to be classified other than a [W-2] employee," a service must be "performed outside the usual course of the business of the employer." As a result of this restriction, pharma companies in Massachusetts cannot hire ICs to perform projects related to drug research and development. In contrast, engaging contractors to provide expertise on business support functions, such as finance or IT, falls outside the category of "core activities" and is not subject to such restrictions.

> *"Not unlike a clinical trial setback, misclassification of independent contractors (ICs) can have a substantial negative impact on the business."*

3. ASK AN EXPERT TO ENSURE COMPLIANCE

As the head of your company, you are ultimately responsible for ensuring you have access to the best talent to move strategic initiatives forward while ensuring sound business practices that are compliant. Sometimes, it can feel like a false choice. Your need for IC expertise may grow as you ramp up your work force for late-stage research, product approval, or pipeline expansion. Your HR or legal departments should ensure your IC compliance; they can leverage their employment-related expertise or use an external company to help evaluate potential ICs. Whether the task is handled internally or externally, having an established process to determine the proper designation is key to avoiding costly fines and penalties in the future.

Being mindful of these items is advisable for any company utilizing ICs. The potential of working with talented individuals is great; the risk of misclassification shouldn't be. L

REBECCA CENNI is founder and CEO of Atrium Staffing, a New York City-based talent solutions firm.

In M&A, The Devil's In The Details ... **Of Your Insurance Policy**

DAN BRETTLER

In today's competitive marketplace, many pharma companies are diversifying their offerings and investing in early-stage technologies. Diving into a new business segment, line of product, or service can be risky. While the financial investment may be considerably less than targeting a later-stage firm with proven products, prioritizing R&D potential means seeing products through development, clinical trials, and approvals.

Many companies overlook crucial details in their insurance policies — a potentially expensive mistake. Companies that don't emphasize risk management and insurance due diligence while adding exposures from new products or services to their policies will see the far-reaching impacts on their budgets. They may be surprised when year-over-year financials come due for review, and the acquisition budget has been reconciled. The suppositions factored for adjusted insurance costs may be way off base. This can be costly in terms of premium overruns and also direct cost of claims. Not to mention, it could be embarrassing.

Life sciences companies need to understand their insurance coverages for exposures associated with these types of transactions. Particularly for a larger company looking to acquire a development-stage firm, loss and/or litigation could stem from "off the radar" issues, seemingly nonmaterial by measure of small financial metrics in relative terms at the time. Two major areas where companies get into trouble are successor liability and due diligence on their expanded product /service portfolio.

SUCCESSOR LIABILITY

When scheduling an acquired entity on your insurance policy, you will likely consider and cover the risks you anticipate post close — for products in clinical trials, on the market, and in development.

Most insurance policies have limitations for loss that occurred in whole or in part prior to acquisition. For example, if a product liability claim related to a product sold or manufactured prior to the acquisition were to be made post close, your policy may contain an exclusion that would leave you without coverage, even though you may have thoughtfully scheduled on your insurance policy the acquired entity as an "Insured."

Companies may not realize this exclusion exists until a case is presented and their coverage is denied. Tending to this detail while updating your policy in anticipation of a transaction and after proper due diligence can make all the difference.

Your broker should not only examine acquisition provisions in your policy, but also how the acquired company is defined within the policy to ensure you have adequate coverage. Not every entity assumed to be considered a "subsidiary" is covered automatically in insurance policy language, and if it is, the duration of coverage may be temporary.

DUE DILIGENCE

A company diversifying its product portfolio will devote resources to understanding the supply chain and financial and operational considerations. But they may overlook how their insurance policy protects (or doesn't protect) new products or new services.

Most product liability policies have exclusions for using specific ingredients or even treating particular conditions. Depending on the nature of the products they're acquiring, life sciences companies may see their rates increase dramatically or learn their current insurer is not able to cover particular areas of the business. This is especially troubling post close.

We often see this when a company moves into pain products, narcotics, weight management products, and different patient populations such as pediatrics. Insurance companies will raise rates and/or retentions for these exposures or exclude them from coverage altogether. Companies should carefully audit the products and individual ingredients they'll be adding to their product portfolios — and not assume that coverage or similar cost will be guaranteed under their current insurance policy.

DAN BRETTLER is the life science practice leader for Conner Strong & Buckelew where he delivers risk management and insurance products and services to life sciences and technology clients.

Unleashing Breakthrough Innovation

MELISSA SCHILLING

MELISSA SCHILLING is a professor at New York University's Stern School of Business and is one of the world's leading experts on innovation and strategy.

What can breakthrough innovators like Elon Musk, Steve Jobs, Marie Curie, and Nikola Tesla teach us about managing innovation in organizations? A lot, it turns out. Serial breakthrough innovators — those people who dedicated their entire lives to introducing one game-changing innovation after another — have some interesting commonalities that serve up some important lessons for how we can unleash the breakthrough innovation potential in us all. Here are three of them.

1. GIVE PEOPLE AUTONOMY AND DEMONSTRATE A TOLERANCE FOR THE UNORTHODOX.

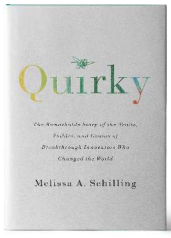
George Bernard Shaw once noted, "The reasonable man adapts himself to the world: The unreasonable one persists in trying to adapt the world to himself. Therefore all progress depends on the unreasonable man." Serial breakthrough innovators demonstrate this in spades. Albert Einstein, for example, revolutionized science by radically casting off many of the most well-accepted principles of Newtonian physics. He challenged the existing paradigms, and at first other physicists were deeply skeptical of his ideas. A more "reasonable" scientist would have incrementally extended the theories of those who had gone before him, but Einstein was not interested in being reasonable — he was interested in discovering truth, and it was not in his nature to be deferential. Elon Musk similarly pioneered reusable rockets — something the space industry said was impossible — in part because he was not part of the space industry, and in part because he wasn't the kind of person who let other people define what was possible for him. Well-defined hierarchies, norms encouraging consensus, and rewards for being a good team player will all foster smooth operations in an organization, but they are the enemies of breakthrough innovation. If your organization seeks breakthrough innovation, you need to give people the space and freedom to generate and pursue unconventional — and potentially disruptive — ideas.

2. FIND AND NURTURE IDEALISTIC GOALS.

Marie Curie, Nikola Tesla, Steve Jobs, and Elon Musk all endured intense criticism, hardship, and failure. Yet each tenaciously persisted in pursuing their goals. Why? They believed they were pursuing an ideal, something more important than their comfort, their leisure, or what others thought of them. Curie pursued science because she believed it was intrinsically noble and would help preserve Polish heritage. Tesla believed that through creating free energy and wireless communication he could obviate human toil and war. For Jobs, the computer was not just a profitable product; it was a revolutionary tool to expand the capacity of the human mind. Musk believes that through creating affordable space travel that enables us to colonize Mars, we will help avoid extinction of the human species. These lofty goals provided intrinsic motivation that fueled intense effort and became an organizing principle that helped these innovators make tough choices. When a firm has lofty goals that are well-ingrained throughout the organization, these goals can guide employee behavior even without direct oversight or incentives, and fuel greater effort and commitment.

3. BUILD A KNOWLEDGE WEB IN YOUR ORGANIZATION THAT ENABLES ANYONE TO FIND ANY EXPERTISE.

Jobs had brilliant ideas and vision, but he needed Steve Wozniak, Jonathan Ive, and others to enact his ideas. Musk came up with his plan for a reusable rocket, but then turned to rocket engineer Tom Mueller and other space experts to help him implement his plan. These innovators show us how important it is to create ways for people with ideas to gain access to others with the expertise needed to execute those ideas. L



WORKFLOWS

Built for Your Biosimilar Pipeline

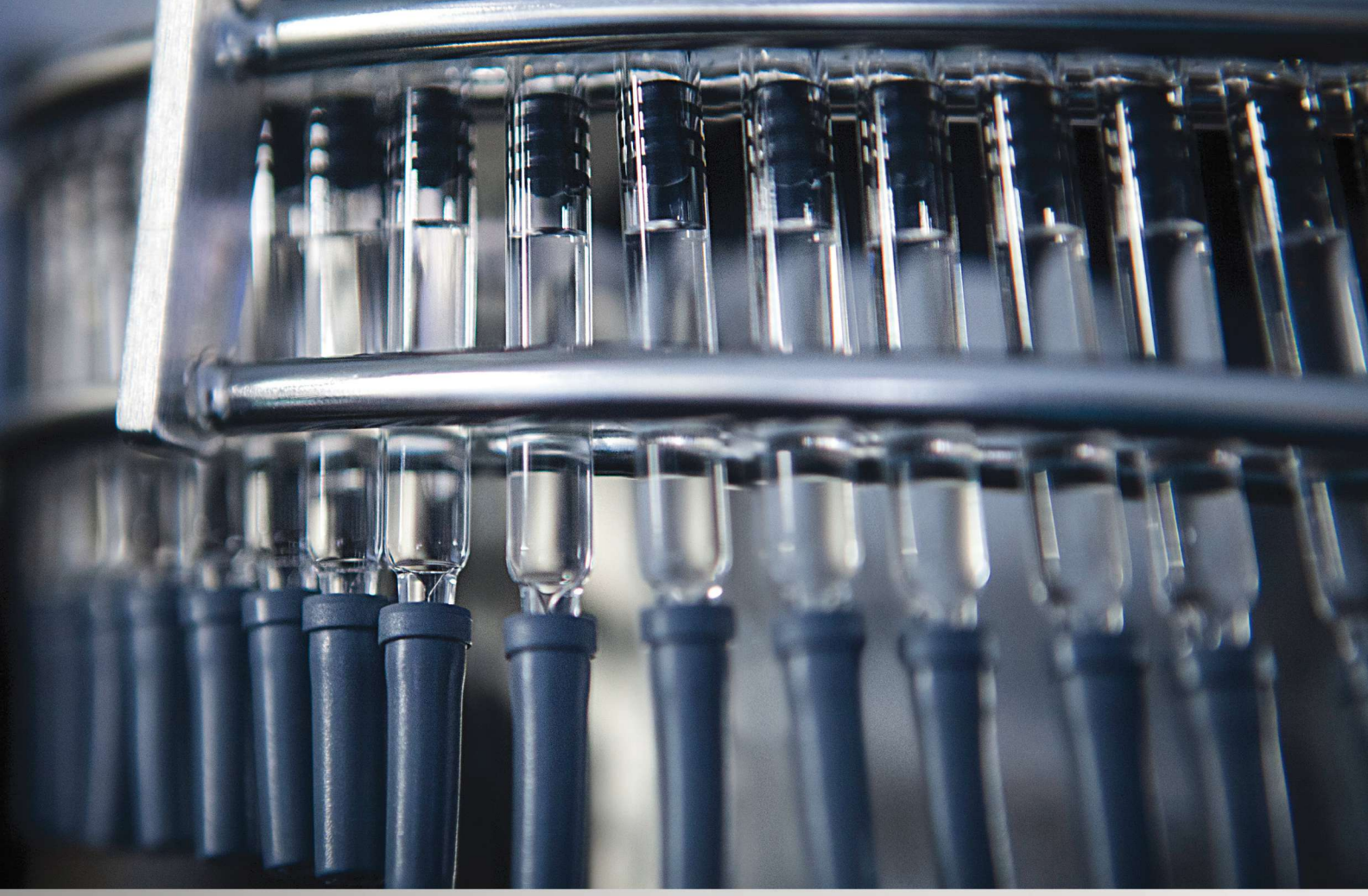
Get to market faster with customized solutions

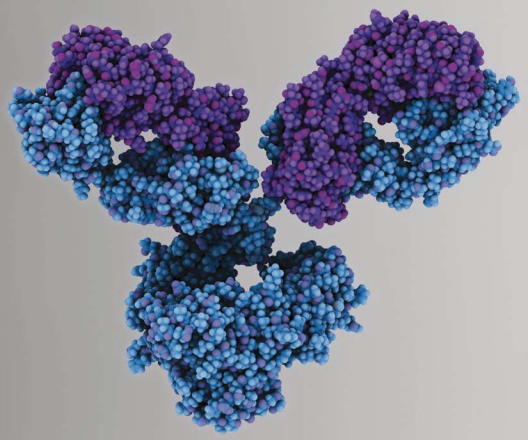
Every biosimilar takes a different path to market. This is why we support you during each step of your biosimilar development with innovative and customizable solutions that include resins for lab- and manufacturing-scale purification, an award-winning cell analyzer for comparability studies, and off-the-shelf anti-biotherapeutic antibodies for PK and ADA assay development.

Pharma Starts with **You**

Explore biosimilar workflows at bio-rad.com/info/biosimilar

BIO-RAD





IgG1 monoclonal antibody

Vital solutions. Delivered.

We've developed over 240 projects across our fully integrated global network of cGMP drug substance and drug product facilities in Europe, North America and Australia. We offer smooth scale-up from clinical phases and have extensive experience in technology transfer. And every day, our development and commercial fill-finish operations work in sync to ensure that new biologics scale and commercialize quickly. All to provide a secure supply chain for bringing your biologics to life.

Patheon®

A HEALTHIER WORLD. DELIVERED.