Life Science Leader
Connect. Collaborate. Contribute.
MARCH 2017

GABRIEL BAERTSCHI
Board Chairman & CEO,
Grünenthal

Grünenthal's Plan To Grow Globally & Expand Its Pipeline

Life Science Leader

Connect. Collaborate. Contribute.

MARCH 2017

GABRIEL BAERTSCHI
Board Chairman & CEO,
Grünenthal

Grünenthal's Plan To Grow Globally & Expand Its Pipeline

Why the private, European-based company is widening its base with new approaches and technologies for treating pain and, now, related conditions. **p. 14**


Pfizer CentreOne
Contract Manufacturing
When it's
YOUR
compound,
every step
matters.
www.pfizercentreone.com
API
STERILE INJECTABLES
HIGHLY POTENT SOLIDS
PC1-16-0005/R2-8.125x10.875in © 2016 Pfizer Inc. All rights reserved. Pfizer CentreOne is a Trademark of Pfizer Inc.

Expedite molecule to market

Launching a molecule from scratch. Enhancing capacity for a biologic. Introducing biosimilars to emerging markets. No matter your objective, speed is critical. Our services are designed to help you get to market as quickly as possible, with reduced costs, robust outcomes and full transparency.

GE's Fast Trak services solve your biomanufacturing challenges, empowering you to accelerate your bioprocess journey.

gelifesciences.com/fasttrak

GE Healthcare Bio-Sciences AB, Björkgatan 30, 751 84 Uppsala, Sweden.
29206530 AA 04/2016

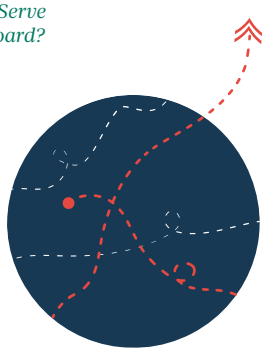
CONTENTS

Welcome to

Life Science Leader

MARCH 2017 VOL. 9 NO. 3

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



LIFE SCIENCE LEADER (ISSN: 21610800) Vol. 9, No. 3 is published monthly by Jameson Publishing, Inc. 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.

THINK UPGRADE

Optimize your capability

Taking your processing capabilities to the next level is a strategy for success; one that often demands upgrading equipment to meet new production goals and future requirements. For immediate access to the best technologies at the right price while maximizing returns from surplus idle equipment, Federal Equipment Company is ready to help you optimize operations while recovering equipment value through accurate appraisals, strategic liquidations and full logistical support.

Find us at Interphex Booth #3110

Federal Equipment Company

When you think equipment,
think Federal Equipment

1.877.536.1538 > www.fedequip.com

Gender Diversity – Can Biopharma Do Better?

ROB WRIGHT Chief Editor

This February I attended the 19th annual BIO CEO & Investor Conference in New York. Similar to its January counterpart (i.e., the annual J. P. Morgan Healthcare Conference in San Francisco), BIO CEO provides an opportunity for companies to conduct company presentations and Q&As (about 173 in total for 2017). However, where BIO CEO differs from JPM is that it also provides attendees with a number of educational forums. And while this year's selection included hot topics such as value-based therapy payment models, biosimilars, IPOs, and a post-inauguration market outlook, the session that captured my attention was "Embedding Diversity into Board and Executive Team Recruitment." Moderated by Julie Gerberding, M.D., EVP, and chief patient officer at Merck (and also the subject of our January 2016 cover feature), the session promised to explore how, despite biopharma's enormous growth, inclusion of underrepresented groups (i.e., minorities and women) in influential board positions has failed to keep pace. As a result, company boards are often neither a very good reflection of the employee bases they lead nor the patient populations they serve.

The challenge of achieving diversity among company boards is nothing new. For although 99 percent of S&P 500 companies have at least one woman serving on a board, the reality is that less than a quarter (21 percent) of these publically traded company board positions are presently filled by women. Perhaps this is one of the reasons why in January, the Massachusetts Biotechnology Council (MassBio) published an open letter to the "BioPharma Community" listing best practices for increasing gender diversity within our industry. Thus far the letter has been signed by more than 200 industry thought leaders, and I am proud to say, a number of *Life Science Leader* magazine editorial advisory board members. Should you concur with MassBio's open letter, I encourage you to show your support by signing. And while such an initiative is an excellent start, the goal of achieving diversity in the boardroom remains unfulfilled. Though the BIO CEO session provided attendees with some practical approaches and examples for improving the diversity of leadership recruitment efforts, the journey to the boardroom most often begins with the candidate. This is one of the reasons why I jumped at the opportunity to moderate a session entitled "Seeking A Board Seat" for BioBreak in Philadelphia this past December.

Following the publication of my BioBreak experience in my January 2017 "Editor's Note" (i.e., *What You Need To Know About Being Ready To Join A Board*), I received a number of emails from readers seeking advice. Thus, it seemed appropriate to share some expert wisdom from those currently serving on boards, which is why we created a three-part *Journey To The Corporate Board Room* Series. In this issue you will find Part 1 — *Are You Ready To Serve On A Corporate Board?* — providing insight on how to go about finding corporate board opportunities. In April we will dig into company considerations when building a board. We will conclude the series in May with insights on what corporate board service entails. We hope you enjoy the first *Journey To The Boardroom* installment, and, as always, we welcome your feedback. L

Life Science Leader
MARCH 2017 VOL. 9 NO. 3

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

SVP OF PUBLISHING/PRODUCT DEVELOPMENT
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

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

Cory Coleman / Ext. 108
cory.coleman@lifescienceconnect.com

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

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

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

PUBLISHER/BIOPHARM & LAB
Shannon Primavere / Ext. 279
shannon.primavere@lifescienceconnect.com

GROUP PUBLISHER/OUTSOURCING
Ray Sherman / Ext. 335
ray.sherman@lifescienceconnect.com

BUSINESS DEVELOPMENT MANAGER
Mike Barbalaci / Ext. 218
mike.barbalaci@lifescienceconnect.com

SR. ACCOUNT EXECUTIVE
Scott Moren / Ext. 118
scott.moren@lifescienceconnect.com

DIRECTOR OF DATA ANALYTICS
Kevin Morey
kevin.morey@lifescienceconnect.com

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

EVOLVE

There was a time, when a phone was just a phone. Then almost overnight it became a camera, computer, flashlight, compass and entertainment center. Now, you rely on it for almost anything you need. Imagine if this were our industry. Imagine if all your outsourced services were under one roof. We did.

DOHMEN®
LIFE SCIENCE SERVICES

BUSINESS PROCESS OUTSOURCING FOR TODAY.

www.dlss.com/**evolve**

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

Q Do you use dual sourcing to improve security of purchased materials supply?

A THE SIMPLE ANSWER IS "it depends." Our approach considers three main factors: (1) patient impact (i.e., is this a life-saving product, and is there an alternative available?), (2) business impact (i.e., risk to reputation and product revenue), and (3) raw material time-to-replacement. By applying these factors to all our products, we can identify our most critical products and their associated raw materials and develop an appropriate strategy for continuity of supply.

For sole-sourced critical materials (only one source exists), our continuity strategy is likely limited to holding additional inventory and/or qualifying another site for the current supplier. For single-sourced critical materials (only one source qualified), protection strategy options include dual-sourcing, alternate site with existing supplier, or inventory. Sub-tier visibility is important in determining single-source risk at the sub-tier level.

ANU HANS
is VP & chief procurement officer, enterprise supply chain for Johnson & Johnson, and is responsible for developing and executing supplier and spend-management strategies.

Q What are the opportunities for technology to further enhance clinical trial operations?

A ADDRESSING CLINICAL TRIAL ISSUES individually and through disparate systems is not sustainable. Technology that brings data together and analyzes the information in a comprehensive and centralized manner will not only allow for a much smarter focus but will also lead to a better understanding of root causes of performance and quality issues as well as provide key indicators to enhance oversight. Centralized monitoring and risk-based approaches to trial oversight, as suggested in the revision to ICH E6 (R2) and in the FDA guidance on risk-based monitoring, are supported by such technology. Strengthening the clinical operations arena today through technology is more cost-feasible than in previous years. And while technology can empower clinical operations teams to focus attention on areas of greatest need, no technology is effective without the expert judgment of a well-trained and educated clinical operations staff.

MITCHELL KATZ, PH.D.
has 30 years' experience in the pharmaceutical and biotechnology industries, including preclinical research, pharmaceutical operations, and regulatory affairs. He is the Head of Clinical Research and Drug Safety Operations at Purdue Pharma L.P.

Q What will be transformative to facilitating innovation in biopharma?

A TRANSFORMATION IN THE INDUSTRY is happening and at a faster rate than we could have anticipated. New biosensing technologies enable us to address one of the critical bottlenecks in drug R&D – the cost of collecting data, which until recently, was very high and limited. But a whole new set of emerging technologies is reducing these costs to nearly nothing. By outfitting patients with activity trackers and other tiny sensors we can collect millions of data points very quickly (e.g., as much as one gigabyte of data per patient, per hour). Historically we've never been able to see, in real time, what is happening inside the patient after taking a drug. While many think it is data that drives innovation, the reality is that it is our ability to collect it accurately, and eventually through the "smartification" of ordinary everyday objects (e.g., car seats) that will prove truly transformative.

BERNARD MUNOS
is a Senior Fellow at FasterCures, a center of the Milken Institute, and the founder of the InnoThink Center for Research in Biomedical Innovation. Previously, he served as advisor in corporate strategy at Eli Lilly focused on disruptive innovation and the radical redesign of the R&D model.

An
INTIMATE PORTRAIT
by Acurian

When we combine our proprietary statistical and lifestyle data with a profound understanding of patients' core needs and desires, you get...

patient enrollment certainty

Acurian's PatientPulse platform is the only patient-centric approach to trial enrollment that leverages data on over 17 million pre-screened patients, quantitative protocol insights from our proprietary database of over 100 million households, and unparalleled face-to-face feedback from our patient advisory board and patient advocates.

Let us show you how PatientPulse can deliver enrollment certainty for your trials. Email us at patientpulse@acurian.com

Acurian
The Global Enrollment & Retention Specialist

patientpulse™
In Touch with the Patients You're Looking For

Edge Therapeutics

In Phase 3 with an innovatively delivered drug to treat a deadly complication of ruptured brain aneurysm

WAYNE KOBERSTEIN Executive Editor
@WayneKoberstein

SNAPSHOT

Edge Therapeutics is a public company in Phase 3 development with a sustained-release form of nimodipine, coded EG-1962, to prevent delayed cerebral ischemia (DCI), a common fatal or debilitating complication of aneurysmal subarachnoid hemorrhage (aSAH), or ruptured brain aneurysm.

WHAT'S AT STAKE

In about three quarters of all cases, a patient with a ruptured brain aneurysm may regain consciousness, appear fairly normal for days or weeks, then abruptly die or suffer severe brain damage. The mechanism is simple but deceptive: When the balloon-like protrusion of an arterial aneurysm bursts, blood pools around the major arteries in the brain for up to about 21 days, where it slowly makes the arteries turn thin and fibrous until they close and no longer supply fresh blood to the brain. Short of dying, patients may be severely impaired or even fall into a vegetative state. The only real opportunity to intervene and save a patient comes between the initial hemorrhage and the subsequent loss of blood supply, called DCI. That is the chosen target of Edge Therapeutics' lead drug EG-1962.

Edge started up in 2009 after president and CEO Brian Leuthner got together with Dr. R. Loch Macdonald, arguably the leading researcher in cerebral vasospasm and DCI, to address the problem in a business enterprise. Macdonald knew the most promising approach with DCI would be to dilate the affected arteries while they were inundated with blood from the burst aneurysm so they could keep supplying oxygenated blood to the brain. But the only drug approved for that purpose was and is an oral vasodilator that causes off-target side effects. The Edge strategy was to deliver a vasodilator directly to the site of injury.

"Our story is a pharmacokinetics story," says Leuthner. "We incorporated nimodipine into micro-particles of a polymer that's used in sutures, so it slowly dissolves in tissue to release the nimodipine. To relieve increased pressure from swelling after the injury, the physician puts a catheter into the brain to drain cerebral spinal fluid. We deliver the medicine through the catheter. With one injection, as the micro-particles dissolve and release the medicine, we're bathing the vulnerable brain in the medicine for about 21 days."

Beyond scientific or technical hurdles, the biggest challenges for Edge were financial. After personal loans and contributions and some state and federal grants, the company still lacked adequate capital to move its development program beyond Phase 1. Moreover, in 2009, with the financial markets in shambles, no one seemed interested in putting substantial venture capital into such a risky space. The company turned to individual, "high-net worth" investors, and it found a friend in biotech veteran Sol Barer, a founder of Celgene and numerous other ventures. After an opportunistic meeting with Leuthner and Macdonald, Barer joined the board and helped raise enough money to finance a rewarding Phase 2 trial of EG-1962 in ruptured brain aneurysm patients, launched in 2014.

"We saw remarkable results," says Leuthner. "Of the patients who got our medicine, 60 percent were able to go back to work or take care of themselves within 90 days — compared to less than 1 percent historically. Almost 30 percent said they had returned entirely to normal." With the impressive data, Edge went on to its first of several VC rounds and other funding maneuvers as needed to keep the program growing. Today, really in relatively quick order after only eight years, it has a Phase 3 study with its lead drug underway. If approved, EG-1962 could bring a great leap forward in treating a shockingly stealthy and devastating condition, typically in younger people, especially women. But first, it must take a big step of its own in the final stage of development.

BRIAN LEUTHNER
President and CEO

Vital Statistics

31
Employees

Headquarters
Berkeley Heights, NJ

Finances

Total Raised
$208.3M

VC Rounds
2011 - $864,500 (Series A)
2012 - $3.6M (Series B)
2013 - $18M (Series C)
2014 - $16.5M (Series C-1)
2014 - $10M venture debt financing (Hercules)
2015 - $56M (Series C-2, led by Venrock)
2016 - $20M dual-tranche term loan (Hercules)

IPO
$83.3M (net)
October 2015

Latest Updates

July 2016:
Initiated pivotal Phase 3 NEWTON 2 study of EG-1962 in aSAH.

September 2016:
Reported pharmacokinetic data from EG-1962 Phase 1/2 NEWTON study supporting potential clinical and health economic impact in aSAH.

2017 HBA Woman of the Year event

Join over 2,000 attendees

11 May 2017 | NYC Hilton Midtown

Woman of the Year
Bahija Jallal, PhD
executive vice president, AstraZeneca and head of MedImmune

Honorable Mentor
Joaquin Duato
worldwide chairman, pharmaceuticals, Johnson & Johnson

STAR
Ceci Zak
principal and COO at Batten & Co (a strategic consulting firm within the Omnicom Group)

HBA Healthcare Businesswomen's Association
Connect Share Grow

Register by 4 April for the best rates
HBAnet.org | #HBAimpact

Pharmaceuticals Escape The Knife As GOP Mulls Medicaid Reform

JOHN MCMANUS The McManus Group

After bracing for the worst, pharmaceutical executives emerged from a White House meeting with newly installed President Donald J. Trump relatively unscathed. But they soon concluded that his ever-roving spotlight would be back on them in a matter of time and it was on them to develop proposals that would reduce the cost of drugs when patients show up at a pharmacy.

Eli Lilly CEO David Ricks later commented that the discussion focused on consumer out-of-pocket costs, and drug companies need to do a better job "getting discounts through to consumers."

Ricks' point was affirmed when the Centers for Medicare and Medicaid Services (CMS) issued a report revealing PBMs (Pharmacy Business Managers) in Medicare were reaping billions of fees in so-called direct and indirect remuneration (DIR) arrangements from pharmacies and drug manufacturers that did not assist patients at the time they filled their prescriptions.

The CMS report described how these fees were collected, often months after care was already delivered, and that they had skyrocketed in recent years — rising from $8.7 billion in 2010 to $23.6 billion in 2016, constituting about 17.2 percent of total spend in that year. CMS observed that because beneficiaries were not accessing the price concessions at the point of sale, they were moving through the benefit far quicker and hitting the catastrophic point where 95 percent of costs are covered.

Of course, retrospective rebates and pharmacy DIR fees are not peculiar to Medicare. In the commercial market, patients in high-deductible plans are charged list prices and do not realize the substantial rebates that manufacturers provide PBMs on their behalf. In Medicare, those rebates have helped keep the Part D premium stable, rising just $2 a month over the last six years. But policymakers are just starting to appreciate the complexity of the drug distribution system.

REPUBLICANS MULL MEDICAID REFORM

Meanwhile, Republicans are grappling with the reality that they will effectively own any replacement to Obamacare, so they must tread carefully. This realization has slowed action on "Repeal and Replace." Republican members are now appreciating that they are no longer shooting blanks but must deliver a real plan that stabilizes the disintegrating individual marketplace and provides a bridge to the millions of poor who were enrolled in the Medicaid expansion.

Central to the Republican replace bill will be how it addresses the Medicaid program, which now covers more than 70 million beneficiaries. Thirty-one states took the massive federal cash infusion from the Affordable Care Act to expand Medicaid, which resulted in coverage of 11 million poor, non-elderly adults. Many of those states have Republican governors and senators who are concerned that their people may lose coverage and the federal funds making it possible.

"Policymakers are just starting to appreciate the complexity of the drug distribution system."

Michigan, Indiana, and Ohio are emblematic of the complicated politics Republicans now confront. Michigan Governor Rick Snyder, a Republican, said, "We have over 600,000 Michiganders covered in Healthy Michigan, and we have lots of data showing good things going on in our state with this program."

Vice President Pence's home state of Indiana also undertook a creative approach to expanding Medicaid whose architect, Seema Verma, is Trump's nominee to

run CMS. In return for choice of their health coverage, the Indiana plan required enrollees to contribute some money to health savings accounts, then purchase their own insurance with help from the state. The idea was to make sure that the newly covered patients had some skin in the game when they made their healthcare decisions.

Ohio Governor John Kasich, a well-known and highly regarded Republican veteran who once chaired the House Budget Committee, commented, "We strongly recommend states be granted the flexibility to retain the adult Medicaid expansion." Senator Rob Portman (R-OH), a senior member of the Finance Committee, emerged from a closed door Republican Member meeting and said, "I want to keep those people in the system, covered in some way... whatever net savings there are from repeal [we need] to help people get coverage in transition."

But the 40-member House conservative "Freedom Caucus" issued a proclamation in mid-February that any Obamacare repeal bill must be at least as aggressive as the bill the House and Senate voted on in 2015, which provided no transition for newly covered Medicaid beneficiaries.

HOW TO NAVIGATE THESE COMPETING DEMANDS?

Republicans are now considering advancing a proposal known as Per Capita Caps, under which states would receive a lump sum per enrollee, and they would be provided with increased flexibility to provide coverage. The 1990s Medicaid reform proposal authored by then Rep. Kasich (R-OH) would have block granted Medicaid to the states, leaving the states on the hook if Medicaid rolls swelled because of a recession. The Per Capita Caps proposal represents a more refined approach that provides a fixed amount per beneficiary that can increase or decrease depending on the number of enrolled individuals.

However, it caps federal exposure on Medicaid spending based on a predetermined formula and leaves states at risk if costs exceed the cap because of increases in health costs or changes in technology that increase per-enrollee spending. The caps would be based on four different Medicaid populations:

- Children and mothers
- Disabled
- Elderly
- Non-elderly and non-disabled adults.

Potential savings to the federal government depend on how the caps are allowed to grow over time. The Congressional Budget Office (CBO) estimates that a cap that grows by the consumer price index (CPI) would save an astounding $583 billion over 10 years, a cap at CPI plus 1 percent would save $374 billion over 10 years, and congressional staff report that a cap established at a relatively generous medical CPI index would still save the program over $100 billion over 10 years. These substantial savings can be achieved because the Medicaid baseline has been growing at an unsustainable, compound rate of 7 percent over the past 20 years.

The proponents of a Per Capita Cap believe that states will have greater incentive to manage their programs if their own dollars are at stake, unlike the current system where more state spending results in more federal resources. States are eager to wield the increased authority the Per Capita Caps proposal would provide, including shifting resources to more needy populations, charging beneficiaries modest copays or premiums, and requiring work for certain able-bodies beneficiaries — without having to ask the federal government for a waiver.

While still in debate, the Republican plan would reportedly gradually reduce the federal matching funds from 90 percent to the underlying matching rate (generally between 50 percent and 80 percent, depending on the state) over a four- to five-year period.

CBO warns that nearly three-quarters of those who lose Medicaid coverage if states scale back the eligibility parameters could become uninsured. But Republicans like Governor Kasich argue that these individuals could be provided better coverage under a reformed and invigorated subsidized individual market. The Republican plan would replace means-tested subsidies with refundable and advanceable tax credits that would vary by age. They argue that insurance would be cheaper when they repeal costly insurance mandates and flex up the rating bands that have made insurance unaffordable to many young people.

But as the committees continue to draft the complicated legislation, Democrats feel increasingly emboldened to oppose any plan the Republicans develop. In an unprecedented move, Democrats boycotted even attending the confirmation hearing of the affable and studious Representative Tom Price, who was being considered for Secretary of Health and Human Services. And Republicans are becoming increasingly anxious to move the healthcare legislation so they can move on to items more in their wheelhouse, such as tax and immigration reform. L

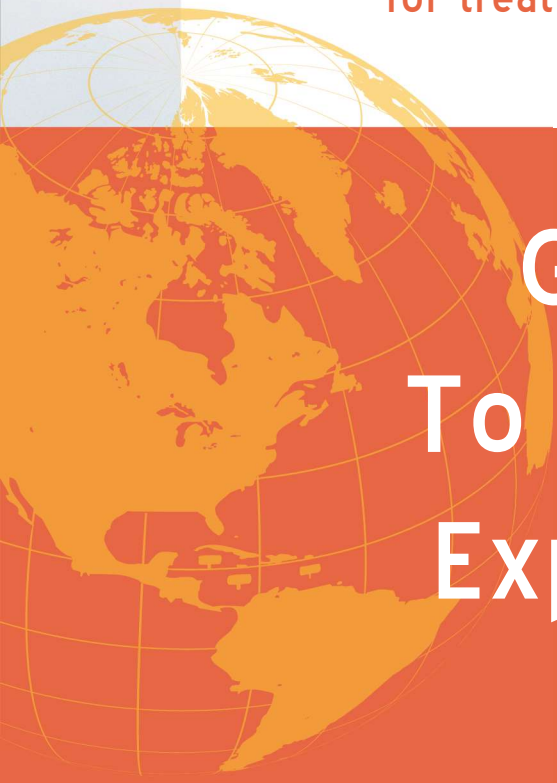
JOHN MCMANUS is president and founder of The McManus Group, a consulting firm specializing in strategic policy and political counsel and advocacy for healthcare clients with issues before Congress and the administration. Prior to founding his firm, McManus served Chairman Bill Thomas as the staff director 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.

GRÜNENTHAL'S PLAN TO GROW GLOBALLY & EXPAND ITS PIPELINE

By W. Koberstein

GABRIEL BAERTSCHI
Board Chairman & CEO,
Grünenthal

The private, European-based company widens its base with new approaches and technologies for treating pain and, now, related conditions.



Grünenthal's Plan To Grow Globally & Expand Its Pipeline

BY WAYNE KOBERSTEIN Executive Editor

If you can spot it through the dense cloud of opioid-epidemic news currently emanating from the United States, some companies are developing new modalities for the treatment of pain. Among them, Grünenthal is a recognized catalyst. Like other pain-focused companies, Grünenthal has mainly pursued innovation with "abuse-deterrent" technologies and products for the prescription-opioid market. But now, along with a slew of partners, the company is identifying, studying, and targeting specific types, or "segments," of pain, using new therapeutic mechanisms and technologies — even developing novel, non-opioid applications for its abuse-deterrent INTAC platform. It is also moving beyond pain into other, "adjacent," areas.

Headquartered in Aachen, Germany, the family-owned, heritage company is well-known outside the U.S. market but has been nearly invisible inside it. Some of Grünenthal's major products have reached U.S. patients by means of its partnerships with companies such as Depomed. But at this point, the company aims to establish a visible presence in the world's biggest market as it grows into a more global organization. At the same time, it is building a pipeline of new products that would expand its therapeutic focus and produce novel drug-device combinations for specialty areas such as cancer-care support.

A View Of The Entire Value Chain

Gabriel Baertschi has been board chairman and CEO of Grünenthal only since last October, when he came to the company after a long tenure at AstraZeneca. Even so, his personal story seems to harmonize with a key narrative of the company he now heads — in short, applying the art of turning scientific discoveries into viable new medicines.

Impassioned by science, but especially excited by its application in medicine, Baertschi felt drawn to the pharma industry even in his school years. He followed his university study of biology by joining Servier in his native Switzerland in 1997, beginning in sales. After coming to AZ in 1999, he led the launch of major brands and explored the interface between the R&D and commercial functions. Later on, as AZ's company president, first in Germany, then in Japan, Baertschi realized the positive results of integrating clinical and commercial development. He sub-

sequently applied the integration strategy when heading a key therapeutic area for the company — gastrointestinal.

"It was good to have had sales and marketing roles, because it gave me some insight on how you develop a drug from A to Z," he says. "Later in my career, having had both commercial and R&D responsibility gave me a view of the entire value chain from Phase 1 development to the commercialization of products. Now as the CEO of a company driven by innovation, I know we must put together the best science we have with the right commercialization efforts. And because it is not a huge company, we must accomplish the task in the smartest possible way."

A Segmented Approach To Pain

Baertschi believes Grünenthal leads other pain-focused companies in the depth and breadth of its R&D programs aimed at the many facets of pain, as manifested in dozens of conditions with unique causes and effects. "Pain is complex," he says. "We mapped out more than 100 types or sub-segments of pain, and many of them have no solution yet. The different approach we are taking at Grünenthal is to go after niche segments in pain. We are not interested in finding me-too solutions for broad-label indications."

One example of Grünenthal's segmented approach to pain is its development of potential treatments for the rare condition, complex regional pain syndrome (CRPS), an undeniably debilitating disease also known as reflex sympathetic dystrophy (RSD). CRPS is an orphan disease in the United States, with less than 200,000 sufferers. "CRPS is considered more painful than an amputation or giving birth," says Baertschi. "And there is no therapeutic solution yet available." The company has two non-opioid compounds in development for the condition: the bisphosphonates neridronate, or neridronic acid, in IV form; and zoledronate or zoledronic acid in oral-dosage form, which Grünenthal acquired with its purchase of Thar Pharmaceuticals in November 2016. "Our compounds really put us in the lead of bringing patient solutions to the CRPS space."

It is worth hovering above the CRPS space for a moment, just to appreciate how a chronic pain condition can be chronically acute. "Those patients cannot take their grandchildren in their arms because it's too painful. They cannot grab a glass of water. A patient explained to me that she cannot even stand the air-conditioner flow on her skin. Patients feel attacked the whole day, and that's why they also tend to develop depression and have higher suicide rates than the general population."

Other pain segments targeted by Grünenthal include gout, with the approved drug Zurampic (lesinurad), a URAT1 (urate transporter) inhibitor; long-acting local anesthesia and post-operative pain management, with neosaxitoxin, a natural toxin and sodium-channel blocker; and psoriasis and psoriatric arthritis, with

> But at this point, the company aims to establish a visible presence in the world's biggest market as it grows into a more global organization. At the same time, it is building a pipeline of new products that would expand its therapeutic focus and produce novel drug-device combinations for specialty areas such as cancer-care support.

candidate GRT6015, a PDE4B (phosphodiesterase 4B) inhibitor. A pipeline chart also refers to new therapeutic "options" in pain, gynecology, and CNS to be developed in regions such as Latin America.

"We tried to understand the physiology behind many conditions, and we realized some of the pain receptors are overexpressed in some of the organs," says Baertschi. "One of them is in the bladder, and we had a compound that fit very well against that receptor but was initially developed for a completely different condition, so it was repurposed for bladder pain." The candidate compound GRT6010 would be the first NOP (nociceptin opioid receptor) agonist on the market and the first therapeutic for bladder pain. It is a condition affecting a small group of patients, he says, "But these patients have to go to the loo 30 to 40 times a day, and they cannot even sleep. There is no treatment available for them. We just moved into Phase 2 with GRT6010 to explore the effect in bladder pain, but also in stump pain and other hypersensitivity disorders."

Although many of Grünenthal's development pipeline candidates employ non-opioid mechanisms, the most ancient of pain-relief modalities has not seen its last days, according to Baertschi. "Opioids have a somewhat bad reputation, but there are differences among opioids. Some opioids do not generate addiction as much as others; it depends on which opioid receptor you act on."

One avenue in the company's research line is the ORL1 (opioid-receptor-like 1) portfolio, a series of substances which activate a pain relieving pathway lacking typical opioid side-effects. "Given their unique expression in human tissues, these novel analgesics may serve to treat niche indications with high unmet need and currently being without standard of care," he says.

A North American partnership with Depomed also covers cebranopadol, an NOP receptor and opioid peptide receptor agonist, in development for low back pain. The two companies also have a commercial relationship in the U.S. market with Nucynta (tapentadol), sold elsewhere by Grünenthal as Palexia. Depomed sells the drug in immediate and

extended-release forms, formulating Nucynta ER with its own long-acting, oral-delivery technology, Acuform.

Broad Franchise & Beyond

Companies that play in the pain space tend to stay in the pain space, pretty much exclusively. But most of the historically pain-focused companies, such as Grünenthal and its close cousin Purdue, seem to have reached the point of expansion beyond old boundaries. Although Grünenthal's plans vary somewhat between geographic regions, new areas of research and development include perioperative care, cancer supportive care, and focused and specialty drugs, many combining drugs and devices. In Europe, the company also targets movement/bone disorders, neurology, and hospital-based products; in Latin America, women's health and the CNS areas. The common denominator, however, is still pain — the products in all of the focus areas will be for uses "adjacent" to pain.

As with similar companies under family ownership, the private company model gives Grünenthal the freedom to take a longer point of view than public companies can sustain. "You can really build value over time," says Baertschi. "But I would say there is no space for waste. When it's family money, you need to invest it extra carefully and prudently."

Will Grünenthal continue to expand its therapeutic and geographic horizons, becoming more like a publically owned, diversified company in the mold of Big Pharma? Or will the privately owned, more focused model, where pain is the hub of related products and services, endure as the most practical option for a company in this particularly difficult area?

There is no indication Grünenthal will morph into a Big Pharma in anyone's idea of a likely future. Even large companies concentrate on selected areas, according to their resident capabilities, Baertschi observes. "You focus on your area of expertise. It is not easy to acquire an area of expertise outside a field you have been building over the years. That being said, I'm not agnostic to building something beyond pain, and we have started that last year by building therapeutic fields that are adjacent to pain. You can look at pain from a CNS point of view or an inflammatory point of view, and the universe around pain is broader than just treating the pain symptoms. That is why we are building up the gout franchise and bought lesinurad [Zurampic] from AstraZeneca. We are looking at inflammation in general. Beyond gout, we have other products for which we are also seeking partners."

Some partnerships are taking Grünenthal even further afield; the company is marketing Arcoxia (etori-

GRÜNENTHAL INNOVATION – LATE- AND EARLY-STAGE PIPELINE

Approved	Zalviso	Medical device containing Sufentanil tablets (strong opioid)	Treatment of moderate to severe post-OP pain in hospitals → EU
	Zurampic	Uricosuric Lesinurad	Gout 2nd line therapy
Late Stage	Palexia LE	MOR agonist + NA reuptake inhibitor	Life Cycle Management; acute and chronic pain
	Versatis LE	GRT7019 : NSAID + Na channel blocker (fixed dose combination)	Osteoarthritis pain Chronic LBP
	Lesinurad FDCs	Uricosuric in combination with Xanthine-Oxidase-Inhibitor (XOI)	Gout 2nd line therapy
	Cebranopadol	NOP receptor & opioid peptide receptor agonist	OA LBP NP [Partnering process for North America closed with Depomed in December 2015; process for Asia still ongoing]
	"CUTIS"	Medical device containing topical surgical adhesive	Topical wound closure of cuts and surgical incisions (for hospital market)
	Neridronate i.v. T-121 oral	Bisphosphonates	Orphan indication: complex regional pain syndrome (CRPS) → US
	New INTAC products	INTAC technology	Abuse deterrent formulation, several projects, also outside opioids → US
	Regional NTEs	(various)	Options: Pain, Gynecology, CNS → LatAm
	NCE GRT6010	NOP agonist	Hypersensitivity disorders
Early Stage	NCE Neosaxitoxin	Natural toxin - Na channel blocker	Innovative therapeutic option for long-acting local anesthesia and post-operative pain management
	NCE GRT6015	PDE 4B-inhibitor	Psoriasis and Psoriatric Arthritis (moderate to severe)
	Research pre-CS	Diverse, opioid receptors	Indications: various to be finally concluded in alignment with Pain Landscape

LBP = Low Back Pain, NP = Neuropathic Pain, OA = Osteoarthritis

coxib) in Europe for broad pain indications, but the company wants to explore the drug's potential at the far end of neurology: Severe Parkinson's. "Last year we made about 39 deals, and I hope we can continue at the same pace this year. It's very important that we focus on pain, but there are many conditions closely related to pain. It's the same doctor treating the pain syndrome and the cause of the pain, so it makes a lot of sense to offer a holistic solution."

In gout, emerging science shows the condition is a degenerative disease, not diet-related as popular myth maintains. This knowledge opens up a new world of possibilities for treating the age-old scourge. As Grünenthal entreats small companies with gout candidates to come forward as potential partners, it also prepares to educate the medical community accordingly. "We are actually trying to change the perception of gout," Baertschi says. "We would look at the companies with new compounds that could be interesting to use in one of our pain subsegments where we have a good understanding about the pathway, and perhaps the molecule they have could work. They may know the drug can work on some pathway, but they don't know how to develop it in pain, so we try to be the partner of choice in the pain field."

Geoexpansion Time

If you get the feeling Grünenthal has just stepped out from behind a curtain, you may be excused. Truth is, the company has been as quiet as its "private" status denotes. Only quite recently has it sought a higher profile, especially in the United States. It would also be logical to surmise Baertschi's arrival only three months before the new year was more than a coincidence with the emergence. The emergence is his agenda.

"I think there is much more we can do with Grünenthal in general," he says. "We're a €1.4 billion company. Our aim is to become a €2 billion company, and to do that we need to expand our global footprint, be more visible in the United States, in particular. We want to make sure we can access the best science in the United States as well, so one reason I'm trying to be more vocal about what Grünenthal has to offer is to power our research. Then we have compounds in the pipeline we would like to commercialize in the U.S. market, such as the CRPS drug. We currently don't have our own commercial infrastructure here in the United States, however, and we might need to find a partner for some of our products."

Although the company aims to become more global over time, Baertschi describes the present state of the company as international. About half of its business and infrastructure is in Europe, the other half, in Latin America, with both regions growing at a healthy 15 to 20 percent, but almost no standing in the United States, Japan, or Asia. In North America, where the Grünenthal subsidiary mainly operates the INTAC partnerships, the company's pharma presence is through commercial partnerships such as Depomed's sales of Nucynta — worth about $300 million now and growing rapidly. Grünenthal partners with Patheon in applying the INTAC platform to U.S. companies. Not only does Baertschi want to see the company grow in North America but also in Asia. "I cannot foresee a future for Grünenthal with no partnership or commercialization in Asia. There is a need for our products there."

Grünenthal's European perspective may prove to be an advantage these days as payers gain power worldwide, and the pharma value proposition faces new tests in the current populist ascendancy. Even in the United States, where private payers still present the greatest challenge, public power offers more a mixed blessing than unqualified support to the industry — a possible trade-off of drug-price negotiation for radical deregulation.

"Whether it's the private sector or the government challenging us, the principles are the same," he says. "You need to show that your product brings new value to society. Payers no longer want to pay for me-too medicines. In that sense, the value model has evolved more quickly in Europe, and also there is great science in Europe, as in the United States."

At the same time, Baertschi says the United States is also a very attractive place for Grünenthal. "We want to have more scientific presence and eventually commercial presence in the United States one way or another, either through a partnership or going it alone, depending on how our pipeline is moving."

Another intrinsic advantage for Grünenthal in the U.S. industry sector could be its moderate size. The simpler, more entrepreneurial organization could make the company especially attractive to industry talent laid off or alienated from large companies and looking for a new home. It might offer a kind of halfway house for industry veterans drawn to its startup-like agility, yet knowing it has the critical mass needed for all stages of R&D and commercial competition. Likewise, would-be entrepreneurs otherwise bound for the startup space may find the same qualities attractive. Baertschi would welcome both types to the company.

In-House Manufacturing

If there is any field where Grünenthal has a real lead, it may be in the continuum of formulation to production loosely called manufacturing. Though the company does some outsourcing where it lacks specific expertise, it maintains the capabilities needed to take compounds all the way from the bench to the clinic, from synthesis and formulation to full-scale production and supply. It even makes its own API. (See also "Grunenthal's Technology Model For The 21st Century," *Outsourced Pharma*, August 2016.)

"We really are a fully integrated company," Baertschi says. "It is nice to be in control of everything when

Global Pain, Patient Pain

A discussion with CEO Gabriel Baertschi about how various cultures and practitioners regard the treatment of chronic and acute pain with the medications Grünenthal and others make available.

HOW DOES THE PAIN SPACE OR MARKET DIFFER AROUND THE WORLD?

BAERTSCHI: Pain is a global burden. Starting with the United States, pain is costing the healthcare system $560 billion a year – half of it being direct cost; the other half, indirect cost of people being unable to work and so on. About 116 million people in the United States suffer from severe pain, indicating the dimension of the burden, and pain is universal. It is everywhere in the world. Now, the way pain is being treated is different from one country to another. In Japan, pain is traditionally something one should accept more than people do in the Western world, but that's changing. Grünenthal can contribute to educating physicians and healthcare providers in Japan about the need to treat pain there, because it has a societal impact. If you're not treating pain well, it costs money to society.

ONE OF THE DIFFICULTIES IS YOU CAN'T MEASURE SOMEBODY'S PAIN OBJECTIVELY OR PROVE THAT IT'S THERE.

Well, it's true that it's difficult, but you can measure it. There are validated scales used by regulatory authorities when you want to have a product approved.

IT'S JUST NOT USED IN DAILY PRACTICE.

Most general practitioners are not using it, but specialists do.

A PAIN PATIENT GOES IN AND TELLS A DOCTOR, "I HAVE PAIN," AND THE DOCTOR SAYS, "POINT TO YOUR PAIN LEVEL ON THIS 10-POINT SCALE." BUT THERE'S NO WAY TO PROVE THE NUMBER IS ACCURATE, SO IT BECOMES A SUBJECTIVE MATTER.

That is why we try to help physicians describe pain precisely, because then they can also look at the right therapy for that specific pain. We did a lot of work to actually map out these pain types and help understand what is the best drug that fits the condition. A typical neuropathic pain, for example, has a different component from acute pain. We have a big campaign in Europe called CHANGE PAIN, which is exactly about helping physicians understand the pain components and then make the right choices from a therapeutic point of view. We also did an initiative with the European Union on the societal impact of pain in Europe. Today, very little money goes into research of pain; in the United States, it's only about one percent of the entire research funds. And there is not always a willingness to pay for pain therapy. We have made some studies in Europe that found, for every pound you spend in the UK on Palexia rather than other pain therapies, you save two pounds on indirect spend.

you're small because you're not dependent on the API prices from another company. For some of our products, we beat the most cost-effective suppliers based in India. We can produce it cheaper because we know the best ways to do it. When we develop a drug, we use all of the steps in chemistry to engineer the molecule in the best possible way. That strengthens the resilience of our scientists and chemists, who might be tempted to give up more quickly on a product if they didn't have the know-how and persistence to do it right."

Baertschi says in-house manufacturing also gives the company a great deal of flexibility in packaging and quantity adjustment for various markets. "We are just more nimble having our own manufacturing sites. Will it always be necessary to have as many manufacturing sites as we have now? That's something I cannot answer today, but we will have to look at that."

More Partnering In Future

Four late-stage drugs in the pipeline — with high medical need indications in pain segments or adjacent areas — hold the potential to propel Grünenthal to its overall goal of expansion in annual sales during the next few years. Some of those may also push the company into building a greater infrastructure in the United States and elsewhere. Meanwhile, says Baertschi, the company will increase its presence in the scientific community and enlarge its network of external research partners — while continuing to strengthen its commercial capabilities in Latin America and Europe.

It seems natural: If we're going to have pain-focused pharma companies, they will evolve and spread to all corners of the world. If pain is global, so should be the medical relief of pain, even if all the accompanying issues apply: abuse, addiction, and let us not forget, denial of treatment to many who desperately need it. Some may call it self-interest, but Grünenthal is offering a well-founded alternative vision of pain as a complex set of conditions and mechanistic causes. Yet a steep education curve lies ahead, in Baertschi's view:

"Pain is penalized; it is regarded almost as a commodity disease, and I'd like to change this perception. There are still many pain areas that have no medical solution. We have patient days where we invite patients suffering from all kinds of pain, and when you listen to them, you realize there is still so much work left to do."

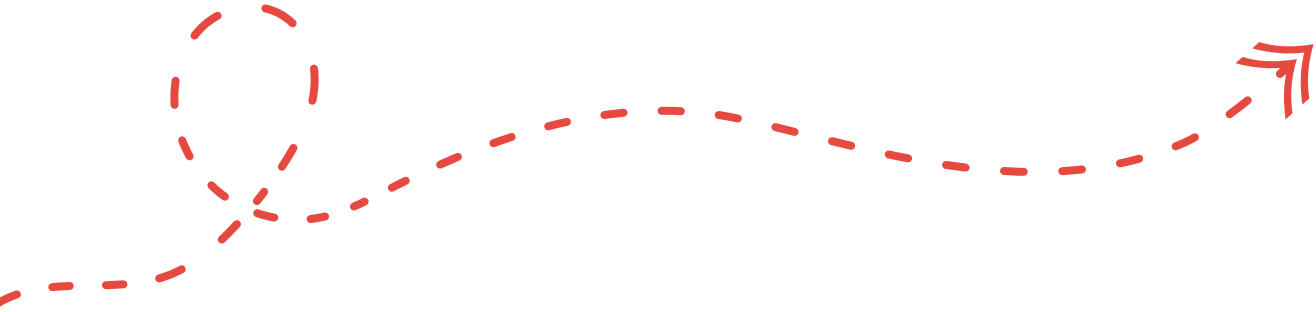
Pain patients — people in unbearable and perhaps intractable suffering — obviously hope someone is listening. As long as such pain exists, people will look to the medicine makers for solutions. And Grünenthal will be one to answer the call. L

ROB WRIGHT Chief Editor @RfwrightLSL

JOURNEY TO THE CORPORATE BOARDROOM

PART 1: ARE YOU READY TO SERVE ON A CORPORATE BOARD?

In December 2016, BioBreak and Militia Hill Ventures brought together about 100 biopharmaceutical industry executives in Philadelphia to discuss a rather important topic — corporate board service. You may recall my touching on this topic in the "Editor's Note" in the January 2017 issue of *Life Science Leader*, which caught the attention of a number of readers. One person (a recently retired manufacturing executive with over 30 years of industry experience) wrote, "For the last eight years I have held seats on non-profit boards, and I am now very interested in obtaining an advisory role/board seat." He went on to ask my advice on how to go about pursuing corporate board opportunities, and so we scheduled a phone call. During our conversation I found myself referencing the recommendations of those executives who had served on panels during the BioBreak event. As the wisdom seemed to resonate with this reader, *Life Science Leader* decided to put together a "Journey To The Boardroom" series of articles. In this first installment we explore how to go about finding corporate board opportunities. We conducted a Q&A with the following five executives: Madeline Bell, president and CEO of Children's Hospital of Philadelphia (CHOP) and Comcast board member; Nance Dicciani, Ph.D., former president and CEO of Honeywell Specialty Materials and former member of the U.S. President's Council of Advisors on Science and Technology (currently on the boards of Halliburton, LyondellBasell, Praxair, and AgroFresh); Don Hayden, company board chairman (e.g., Gloucester Pharmaceuticals, Insmed, RegenX), and company board member (e.g., Amicus Therapeutics, WindMIL Therapeutics, Otsuka Pharmaceuticals); Kirk Gorman, former CFO and EVP Jefferson Health Systems and board member of several companies (e.g., BioTelemetry); and Barbara Yanni, former head of licensing at Merck and board member of Trevena, Symic Biomedical, and Vaccinex.



LIFE SCIENCE LEADER (LSL): Explain your approach for determining on which boards to serve and why?

DON HAYDEN: In this industry, everyone knows that more things fail than succeed, so it's very important to interrogate the science, as it is the essence of what a company is built upon. The second thing I look at is the people (i.e., the management team, and if an existing board, who and what constitutes the board). In my experience, and in situations where I have had the opportunity to help construct a board, the best boards operate as communities or teams, not families. What you want is board members with competencies and experiences to enable the success of the company's management team. You want board members who can work closely together, because often they will be doing that at long and odd hours of the night, at times that aren't necessarily convenient and involving difficult circumstances. You might join a board believing there is an opportunity to build a company, but the real test of a board typically comes in those difficult moments when a program has failed, or the money's not there, or you have to raise money in a market where there is little or no support. When those difficult moments arise, you want to be on a board with a group of people that you not only feel comfortable with but also believe in. The third thing I look for when assessing a board opportunity is the challenge. A question I pose to myself is, "Will serving on this board challenge me, and can I add value to the work, the science, or the people who are already there?"

LSL: Some people might think serving on a nonprofit board could be good experience for serving on a corporate board. What are some of the differences between the two, and what advice do you have regarding serving on either?

MADELINE BELL: It's a very different experience serving on each of these kinds of boards. On a nonprofit board, you first need a passion for the mission, and you should be aware that you are going to be expected to give time and money. Oftentimes nonprofits don't have the ability to hire a deep management team, so you might find yourself "leaning in" to help in certain areas (e.g., audit committee, governance committee). And while certain components of nonprofit board experience can be helpful in understanding what governance is, it is very different from a corporate board where you typically have a strong management team, and you are there primarily to represent the shareholders. In a corporate board setting you are not "leaning in" at the same level to help management, and you are certainly not giving money. People shouldn't start working on a nonprofit board with the expectation it will lead to corporate board positions.

DON HAYDEN: Though nonprofits can be a great point of entry for gaining board context and experience, corporate boards evaluating such experience might give someone only partial credit when being considered for a corporate board. And, that credit is usually dependent on what you did for the nonprofit, as well as the nature of the organization. Experience at premier nonprofits is going to be viewed in a different light from experience at a local or regional organization. Another thing to think about when evaluating a nonprofit board is who else is serving on that board, as these people can be extraordinarily valuable from a networking perspective. When considering nonprofit board opportunities, you should have passion for what the organization does, perhaps gain some board experience, and benefit from networking with other board members.

LSL: What do you think boards were looking for when you began seeking/considering corporate board opportunities?

BARBARA YANNI: As my background is in business development (BD), I think the board saw that as being helpful. If you have a very small startup company, it may not have people with expertise in business development, licensing terms, or what to expect when trying to license its technology, which is often what a small company is interested in doing. Along with my BD background, boards were probably attracted to

IN THIS ARTICLE

DON HAYDEN, is the former global pharmaceuticals president for Bristol-Myers Squibb and current board member of several biopharmaceutical companies.

MADELINE BELL, RN, is the president and CEO of the Children's Hospital of Philadelphia (CHOP).

BARBARA YANNI, is the former VP and chief licensing officer for Merck, current board member for Trevena, Symic Biomedical, and Vaccinex.

KIRK GORMAN, is the former CFO and EVP of Jefferson Health Systems.

NANCE DICCIANI, PH.D., is the former president and CEO of Honeywell Specialty Materials, and current board member AgroFresh Solutions, Inc.

my finance and tax law experience. This combination meant I could be someone who could help with licensing from a big picture approach but do so with a small venture capital burn rate.

LSL: How did you come about your first corporate board opportunity?

KIRK GORMAN: When I worked for Universal Health Services, I was the investor relations finance guy. As such, I would make a dozen or so presentations a year at large investor conferences. Being able to explain the capital markets and M&A activity was highly valuable. But what truly benefitted me wasn't necessarily just having competencies, but being in a highly visible position where I was able to articulate and demonstrate my capabilities. Finally, and most importantly, don't underestimate the importance of working for a highly successful company. Personally, I think it's hard to get on a corporate board if you have a record of working for companies that struggle. For as people look around and think about who they want to staff their boards, they often start with people they see within industry who are doing well. My set of skills (i.e., strategic understanding of the delivery system on the service side of the business, coupled with finance, M&A, and capital markets experience) not only prepared me for board service but also positioned me well for being capable of serving as the audit committee chair (if needed). Though one of my board opportunities came through a recruiter, in all the other cases it was the result of industry contacts. So while I didn't initially cite networking as a skill boards are looking for, this is a skill you need to possess.

LSL: What were some of the key connections that facilitated your move toward future board service?

NANCE DICCIANI: There are three key connections that helped me with securing board positions. The first board I served on involved being recruited by the same recruiter who helped me get one of my earlier career-changing positions. That recruiter was looking for a board member possessing a combination of business and technology experience. As my background is in chemical engineering and business, it was a natural fit. Whenever a recruiter calls for advice or leads, I take the time to talk to them, and would advise others to do the same. Even if you aren't interested in a particular opportunity, by taking the time to consider whether you know someone who might be, you build rapport with people possessing marvelous electronic rolodexes, which is a place you want your name to be. For eventually the conversation moves from, "Are you interested in this job or do you know someone?" to your being able to express interest in finding board positions and the type you'd prefer.

The second contact that proved beneficial for me in securing board opportunities is trade groups. It is critical for people who are in decision-making positions about board membership to get to know you. Getting involved in trade groups and taking on leadership posi-

Your location. Your timeline. Your schedule.

We bring training to you.

Off-the-shelf courses can't fulfill every need of your team and are expensive for large groups. Almost every FDA 483 observation has a training component. Ongoing training is critical, but qualifying the right personnel to develop and deliver training is time-consuming.

Affordable and flexible customized training at your facility

The Life Science Training Institute (LSTI) client-site courses deliver more impact for less money.

- **Customized training that will weave your SOPs, case studies, etc. into the content to make it more relatable to attendees.**
- **Courses designed for adult learners by instructional designers, featuring plenty of interactivity and knowledge checks.**
- **Multiple delivery formats, including classroom, online (live and on-demand), plus blended sessions.**

LIFE SCIENCE
TRAINING INSTITUTE

To get started, visit **lifesciencetraininginstitute.com**

215-675-1800 x123 | info@lifesciencetraininginstitute.com

tions within them puts you in front of many c-suite people who can recommend you to boards, board members, and management teams.

Lastly, don't discount the power of personal connections and networking, as these too can lead to uncovering board opportunities.

LSL: What is your opinion on seeking a corporate board opportunity while also working full time?

DON HAYDEN: During my biopharmaceutical industry career, I was approached for a number of corporate board opportunities which I declined. While perhaps there are things I could have done differently, I remain convinced that I did not have the time necessary to serve on a board, do my job, and do both well. Since retiring from full-time employment, I have served on a number of boards at the same time. In my experience, it is a substantial requirement to join a board (more so for public than for private companies), and is a discontinuous experience. Sure, you have a set of planned meetings that you can build a schedule around. But the most important work for a board is often done around a business development opportunity where you need to have 15 board calls in a 10-week period, or when a program crashes and you have to have 10 board meetings in two weeks. It's important to understand that you need to be available when needed. If you are in a full-time role and you want to join a public or private for-profit board always think about why you are joining, as well. Is it a development opportunity for the role you are currently in, or is it something you desire to do in preparing for something in the future? Either way, you need to make sure you not only have your company's approval for taking on this board opportunity, but also that you have the full support of senior management. For there will be moments when you will need to ask for grace around some of the things you will be doing. The people I have seen benefit the most from serving on a board while working full-time did so because they had a plan for how board service would benefit them personally and professionally, and they had senior-management support.

LSL: What pre-work should a candidate do when considering if a board is the right fit?

BARBARA YANNI: For me, I'm only interested in biotechnology board positions, because that's my background. I approach being offered a board position the same way I deliberate over accepting a job, with the most important driver being whether the company has interesting and viable science. Now, I am not a scientist, but I have friends who are. So I consult with them when considering board opportunities. A second driver when weighing board opportunities is how I feel about my interaction with the people. I want to meet the other board members and the management team. While this tends to happen rather automatically as part of the consideration process, the length of time in these interactions can often be very short, so be highly attentive when having the opportunity to engage, and take advantage of additional opportunities, if provided, to engage as much as possible.

LSL: What advice do you have for people interested in serving on a corporate board?

MADELINE BELL: If you want to join a public board, expect long cycle times from the time you first hear about a board opportunity until the time you actually join (e.g., six months to a year). There will be background checks and many interviews for which you should prepare. And although "fit" is important and something you can't necessarily prepare, you should have an understanding of the company's values and history and the board members' backgrounds.

NANCE DICCIANI: Approach joining a board the way you would when seeking a job, because in many ways it is. Make sure your résumé is appropriate and distinctive, and be sure to highlight your key characteristics.

KIRK GORMAN: First and foremost is to be successful in whatever it is you are doing. Second, strive to be visible, especially among bankers and lawyers in your industry so people can find you. I've never looked for a board seat, but they have found me. Work for success in your personal life and career and what you're building.

DON HAYDEN: Develop examples of resiliency, because your ability to be resilient will be necessary on a regular basis when serving on a board. Your ability to work through some really tough times and being able to demonstrate that you enabled your group, department, or company to come out in a better place than where they were will be critical. Lastly, network early, often, and broadly, because you never know where or when the right board opportunity will turn up.

BARBARA YANNI: Serving on boards is all about networking and what it is you bring to the company as a board member. Figure out what you can bring to a board and be able to clearly articulate that when approached for potential board opportunities.

CLINICAL LEADER
FORUM

WHAT ARE YOUR BARRIERS TO A FAST & EFFICIENT CLINICAL TRIAL?

INTRODUCING CLINICAL LEADER FORUM.
A new conference all about sponsor-CRO partnerships and the issues that matter most to executives at small and mid-sized sponsor companies (or anyone who outsources).

PHILADELPHIA
MAY 10-11, 2017

REGISTER NOW
www.clinicalleaderforum.com

SPEAKERS INCLUDE

MICHELLE BERG
VP Patient Advocacy, *Abeona Therapeutics*

KAREN BROOKS
Sr. Dir. Clinical Operations, *Adare Pharmaceuticals*

ELIZABETH GARNER
CMO, SVP Clinical Development, *Agile Therapeutics*

MIKE COLLINS
Head Global R&D Vendor Mgmt., *Alexion Pharma*

RAMON MOHANLAL
Chief Medical Officer, *BeyondSpring Pharma*

BETH HARPER
President, *Clinical Performance Partners*

PAULO MOREIRA
VP Global Clin. Ops & Ext. Innovation, *EMD Serono*

BARI KOWAL
Head Clinical Trial Mgmt., *Regeneron*

GUY BOLTON
VP Clinical Operations, *Ferring Pharmaceuticals*

DAVID SLADE
US Asthma & Biologics Lead, *GSK*

ROGER MILLS
Sr. Dir Clinical Leader (Retired), *Janssen*

SEAN GHARPUREY
Exec. Dir. R&D Strategic Business Improvements, *Jazz Pharma*

MOLLY ROSANO
VP Clinical Development Operations, *Momenta Pharma*

DEIRDE BEVARD
VP Development Operations, *Nektar Therapeutics*

STEPHANIE PETRONE
Executive Dir. Medical Operations, *Novartis*

BARI KOWAL
Head Clinical Trial Mgmt., *Regeneron*

STEFAN SCHWABE
EVP, Head of R&D *Supernus Pharmaceuticals*

GREG FIORE
Chief Medical Officer, *Synedgen*

The Uphill Battle Of A Biotech That Switched Its Focus

DAN SCHELL Editorial Director

When Roger Crystal, M.D., says that he understands the importance of being "flexible" in the business of biotech, he's not spouting typical ambiguous CEO-speak. In his case, he's referring to his company's willingness to pivot, to "pause" a path that they had invested years of time and resources to and choose a new core objective. That's not an easy decision to make, and its ramifications stretched the definition of "flexible" for Crystal and his team at Opiant Pharmaceuticals.

AN INCREASED NEED AND A NEW MARKET

In 2009, the small biopharma company was working on developing a naloxone nasal spray for binge-eating disorder (BED), which is America's most common eating disorder. "The problem was — and is — a substantial one, and there is a serious need for improved treatment," Crystal says. The plan was to use naloxone as a pharmacological therapy to block the reward from bingeing.

But during the next few years an opioid epidemic in the U.S. continued to spiral, seemingly out of control. For instance, in 2014, an estimated 1.9 million people had an opioid-use disorder related to prescription pain relievers and an estimated 586,000 had an opioid-use disorder related to heroin use, according to the Substance Abuse and Mental Health Services Administration. Even more disturbing was the fact that the rate of overdose deaths involving opioids — including prescription opioid pain relievers and heroin — had nearly quadrupled between 1999 and 2014, according to the U.S. Department of Health and Human Services.

"Faced with the scale of this crisis, my colleagues [the company had three employees at this point] and I had a choice: We could continue on the project we had originally embarked on with BED, or we could reassess our priorities and attempt to fill the need for a new opioid antagonist treatment for opioid overdose," Crystal recalls.

At the time, injectable naloxone was already approved for the treatment of opioid overdose, but even in the hands of trained first responders, there was concern because of the risk of needlestick injuries, often the need for users to assemble the injection, and the potential for variation of absorption depending on the patient's body mass. Opiant's plan was to offer naloxone as a simple-to-use nasal spray that initially would be for first responders, but could be coprescribed with every opioid painkiller prescription. "We felt there was a huge market we could access if we could provide a safer and easier approach to delivering the naloxone," explains Crystal.

As a surgeon, Crystal had dealt with several overdose patients in the ER, so he understood the importance of delivering naloxone to a patient as quickly as possible rather than waiting for paramedics to arrive at a scene. "Every minute's delay in receiving naloxone can determine whether the patient survives," he explains. Also, through his management consulting and industry roles, he understood how to expand into new markets and the value proposition a naloxone nasal spray would offer once in the hands of patients, friends, families, and other first responders.

To further reinforce the decision to pursue this new drug, Opiant contacted and interacted with a lot of key opinion leaders and experts at the National Institute on Drug Abuse (NIDA) and harm-reduction organizations. Ultimately the company confirmed that the market potential was far greater than what currently existed for the injectable. Thus, in 2012, Opiant decided to make the switch.

SEEKING ASSISTANCE BEFORE GOING TO THE FDA

Although the company's small size enabled it to be flexible enough to shift focus, that same size hampered its ability to quickly execute on such an ambitious new goal. Opiant needed help, and it would get it from three sources: the FDA, NIDA, and another specialty pharma called Adapt Pharma.

"To an extent, we were venturing into the unknown because there was no precedent," Crystal recalls. "We wanted to develop the first FDA-approved naloxone nasal spray, so accessing investors who could appreciate the market potential was challenging. If this were another breast cancer drug, for example, then it would have been much easier for an investor to benchmark."

The first thing they did was hire a CMC (chemistry, manufacturing, and controls) consultant to oversee manufacturing and a regulatory consultant to oversee all interaction with the FDA. During this same time period, Crystal and his colleagues decided that having the support of a major stakeholder would be an important endorsement — particularly to investors — of their new program. So, they established a clinical trial agreement with NIDA in January 2013.

Representatives from NIDA also accompanied Opiant to the initial pre-IND (investigational new drug) meeting with the FDA. "We needed to get the FDA to support our drug development plan," Crystal says. "The FDA 'confirmed' that the development route was 505(b)(2), but also agreed with our development program that resulted in the rapid approval." This pathway allows a company to rely on the FDA's findings of safety and efficacy for a previously approved drug — naloxone in this case — so that the number of clinical studies required for approval is reduced along with time to market.

NIDA was able to sponsor a clinical study of three to four weeks duration to evaluate the pharmacokinetic properties of the new formulation of naloxone in human subjects. The study confirmed that the new novel formulation could be absorbed as quickly as injectable naloxone. "Having that information allowed us to explore all potential areas where a nasal spray could be used: schools, all first responders, addicts/needle exchange clinics, methadone clinics, etc. We even could explore opportunities for coprescribing it with any opioid painkiller prescription, because even patients who don't abuse opioids are at risk of an overdose and could benefit in having access to the nasal spray at home," explains Crystal.

The data from the clinical trial was made available in December 2014, and the product was launched in February 2016. "We had to wait for more stability data on the product before the NDA could be submitted," he explains. "Still, that time frame was significantly shorter than what's typical regarding the road from clinical studies to commercialization."

NEXT STEP: COMMERCIALIZATION

Again, Opiant's leaders knew the company's small size would require them to partner with a larger player to bring the nasal spray to market. That's where Adapt Pharmaceuticals comes into the picture.

> *"Being a small company enabled us to transition quickly to our new business objective."*
>
> **ROGER CRYSTAL, M.D.**
> CEO, Opiant Pharmaceuticals

"We were introduced to them by an advisor," Crystal says. "We needed a partner with a similarly nimble and entrepreneurial mindset to ourselves accompanied by deep commercial expertise in the U.S. in CNS specialty pharma. Adapt shared our passion for the product and has a great track record at Azur Pharma, their previous spec pharm business that was acquired by Jazz Pharma." He adds that the company did have significant interest — including a term sheet — from other larger pharma companies, but they weren't convinced that those companies understood the product potential, were committed to ongoing innovation around the product, or were willing to invest significantly in its commercialization.

Through the licensing deal with Adapt, Opiant could receive potential development and sales milestone payments of more than $55 million, plus up to double-digit royalties. Today, NARCAN (naloxone HCL) Nasal Spray is the first and only FDA-approved nasal form of naloxone for the emergency treatment of a known or suspected opioid overdose.

"Looking back, I am convinced making this transition was the right choice for our company," Crystal concludes. "Being a small company enabled us to transition quickly to our new business objective, but we also couldn't have done it without the cooperation of the FDA, NIDA, and Adapt. In the end, our flexibility paid off."

Lack Of Real Estate Prompts Life Sciences To Get Creative

ROGER HUMPHREY

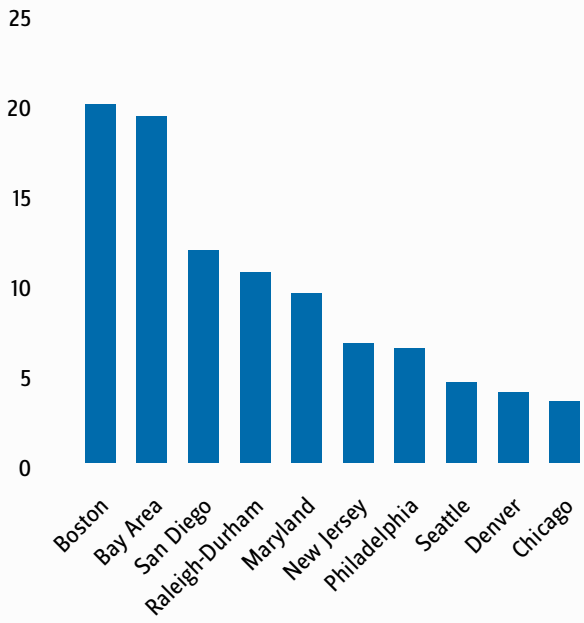
Curing diseases and other groundbreaking innovations are all in a day's work for life sciences companies. But that innovation mindset goes well beyond the lab; it helps industry executives find creative solutions to some of their biggest business issues. Attracting and retaining talent is one such challenge.

The search for highly specialized talent is why life sciences companies tend to cluster around top research universities and why finding facilities in the top clusters can be very difficult. It's no surprise that seven of the top 10 U.S. biological science programs are at graduate universities located in the top life sciences clusters of Boston, the Bay Area, and San Diego.

In these cities, office and laboratory space opportunities can be few and far between — so a little innovation is needed to find locations that connect talent with top companies. The space crunch is real; across the country, vacancy rates remain unfathomably low in top clusters while rents continue to climb. For example, in Boston's East Cambridge submarket, the average rent for office and lab space of $70 per square foot isn't scaring away life sciences companies — the area has a vacancy rate of just 0.8 percent. On the opposite coast, the Bay Area's North County is experiencing a 0.5 percent vacancy rate with rent at $58 per square foot. Up-and-coming life sciences markets, such as Denver, Seattle, and Chicago, are seeing an uptick in leasing activities and a growing shortage of life sciences facilities.

As detailed in *JLL's 2016 Life Sciences Outlook Report*, expensive and competitive real estate markets are forcing life sciences companies to explore nontraditional real estate options to ensure innovation and productivity in their workforce. The lack of available space, particularly in urban clusters, is driving real estate solutions from new development to creative renova-

LARGEST CLUSTERS BY RENTABLE LAB SPACE*



*In million-square-feet

SOURCE: JLL 2016 Life Sciences Outlook

HOW RENT AND VACANCY COMPARE IN TOP SUBMARKETS

	2016	VACANCY
East Cambridge (Boston)	$70.12 PSF	0.8%
North County (Bay Area)	$57.84 PSF	0.5%
I-287 West (Westchester)	$52.00 PSF	11.0%
Torrey Pines (San Diego)	$47.40 PSF	3.3%
Lake Union (Seattle)	$43.87 PSF	2.6%
CBD (Philadelphia)	$28.00 PSF	1.5%

SOURCE: JLL 2016 Life Sciences Outlook

tions of existing space. Meanwhile, fierce competition for top talent is increasing the influence of employee needs in real estate decisions, including site selection, infrastructure, and amenities.

MOVING TO THE SUBURBS

Thanks to high demand and low interest rates, development of laboratory space is at an all-time high. However, the rising cost of labor and materials has made it increasingly expensive to develop sizable facilities, particularly the build-to-suit projects most favored by companies in need of highly customized laboratory space. With no space to be found in crowded urban clusters, the neighboring suburbs are welcoming life sciences companies as well as offering a similar talent pool.

> *"Thanks to high demand & low interest rates, development of laboratory space is at an all-time high."*

In Greater Boston, for example, life sciences tenants have recognized the added value the suburbs provide. In contrast to Cambridge — Boston's life sciences epicenter — where what little space is available may well be in older buildings, the suburbs provide the opportunity for office-to-lab conversions as well as brand-new development projects at a lower cost than building in Cambridge. Indeed, Boston's first suburban speculative laboratory facility is under development in the suburb of Lexington.

Similarly, San Francisco is seeing development rise outside the city center. High occupancy rates in the primary Bay Area markets of Emeryville and Berkeley are pushing life sciences companies into the suburban Tri-Valley area. Biotech and pharmaceutical companies in that area generated more than $100 million in venture capital funding in 2016, indicating that the Tri-Valley is emerging as a powerful life sciences hub in addition to neighboring cities in the East Bay.

TRANSFORMING OFFICE BUILDINGS INTO HIGH-TECH LABORATORIES

Life sciences innovation can only happen when the right scientists, doctors, and business minds come together. That's why talent recruitment and retention appeal are key deciding factors in site selection. For example, having a life sciences facility that is relatively close to leading research centers will enhance employee engagement and retention.

One solution is to transform office space into labs. In the Bay Area's mid-peninsula market, for example, 200,000 square feet of office space is being converted to laboratories.

The creative renovation of outdated facilities is playing out in several markets throughout the country, including Cambridge, where Blackstone is converting

a 90,000-square-foot office facility into highly coveted lab space.

Biotech companies in Los Angeles County are converting low-rise office-flex buildings into affordable multiuse facilities with spacious floor plates (i.e., the amount of rentable area on one whole floor), loading capabilities, high ceilings, and high-volume ventilation.

In Denver, real estate executives at life sciences companies compare the search for appropriate lab space in the market to "finding a needle in a haystack." To overcome this challenge, they've started repurposing second-generation restaurants or clean-tech spaces. In Denver's Boulder/Northwest submarket, the majority of product is first-generation conversion lab space and flex/office-to-lab conversion space. Longmont and Gunbarrel represent low-cost alternatives with access to the Boulder workforce. Longmont has a supply of flex and light industrial buildings that have infrastructure in place and could be quickly converted to lab space.

ADDING AMENITIES TO ATTRACT TOP TALENT

Whether in a new development or adaptive reuse space, life sciences companies are adding amenities and investing in space that improves the well-being and productivity of employees — as well as offers downtime and socializing among peers. Gone are the claustrophobic laboratories of the past, as life sciences companies seek modern facility designs with more natural light, open spaces, and interactive types of workspaces.

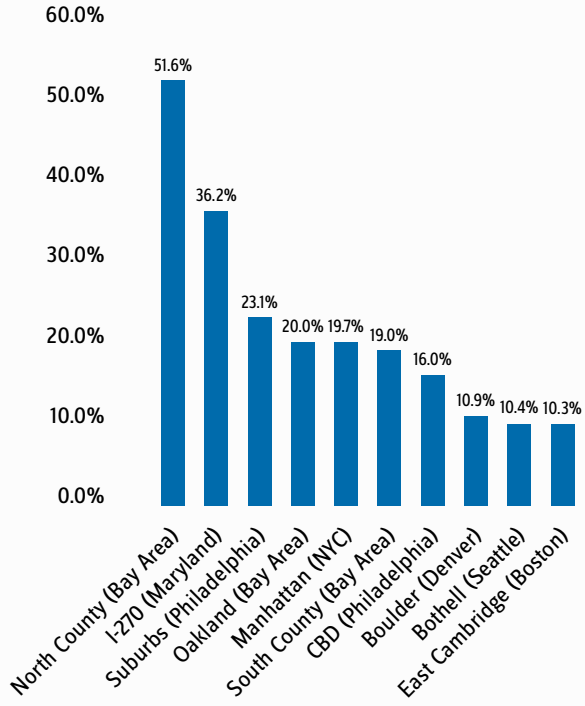
A noteworthy example is The Cove in San Francisco, currently the largest life sciences development underway in the United States. A seven-building, 1 million-square-foot campus, The Cove will feature a full-service amenities center with fitness and exercise rooms, a bowling alley, bocce ball courts, a café, an amphitheater, and hotel space.

Similarly, in the Torrey Pines submarket of San Diego, low vacancy and high rents in life sciences properties have led to a number of projects being upgraded. Alexandria Companies is in the midst of major renovations and upgrades at its Nautilus and Spectrum campuses within Torrey Pines and is converting a 90,000-square-foot building into The Alexandria at Torrey Pines. The latter will serve as a community center, providing Alexandria tenants with a gym and other amenities, including a restaurant open to the public. The facility also houses the local Biocom trade group.

On the opposite coast, the Alexandria Center at Kendall Square (ACKS) is under development in Boston. Located in East Cambridge, ACKS offers a rich urban environment that includes more than 10 hotels, 50 restaurants, 150 shops, and four Cambridge Athletic Club fitness centers — all within a mile radius. The development is attracting attention from the life sciences industry. Bluebird Bio will occupy the laboratory portion of the campus' 500,000 square feet of office and laboratory space at 50-60 Binney St., while Bristol-Myers Squibb will be the anchor of the 430,000-square-foot 100 Binney St. facilities.

In these developments and others across the country, companies understand that what is best for the individual aspirations of the talent pool is also beneficial for the company.

U.S. SUBMARKETS – YEAR-OVER-YEAR RENT GROWTH



*Submarkets with >1.5 million square feet of rentable supply

SOURCE: JLL 2016 Life Sciences Outlook

ROGER HUMPHREY is a former Merck executive and executive managing director and life sciences leader at JLL, a Fortune 500 professional services and investment management firm.

Building A Biotech Hub – **Austin Style**

CAMILLE MOJICA REY Contributing Writer

Austin, TX, prides itself on being called the Live Music Capital of the World. In recent years, it has also been aspiring to live up to the title of Silicon Hills. When it comes to high-tech, the name fits. Its high-tech industry is anchored by the likes of Dell, IBM, and AMD. In recent years, a growing number of high-tech startups and satellite offices of Silicon Valley favorites — such as Apple, Google, and Facebook — have also come to call Austin home.

Now, there is a serious push to make Texas the "Third Coast" of biotech and Austin, in particular, a new hub for the industry. "It took the Boston/Cambridge area 40 years of focused community building and economic redevelopment to become the biotech hub it is today, and that's what it's going to take for us," says Cindy WalkerPeach, Ph.D., director of health/biosciences at the Austin Technology Incubator (ATI). "Austin and Central Texas are probably 20 years into that process."

ATI is the startup incubator at the University of Texas at Austin. It helps companies that were started on-campus and in the larger community get funding. It accepts about 8 percent of its 250 applicants annually. WalkerPeach leads the bioscience effort — pharmaceutical, medical device, diagnostics — for the incubator's portfolio. In 2016, six out of the 19 companies that graduated from the incubator operate in the biotech sector – the highest proportion of biotech in the incubator's history. According to the Austin Chamber of Commerce, there are about 230 life sciences companies in Austin, including large healthcare providers. Most, however, have a dozen or fewer employees. The chamber says that about 16 percent, or roughly 37 companies, are focused on developing a pharmaceutical.

WHAT AUSTIN HAS TO OFFER

Austin is like a chemical solution just waiting for a catalyst to transform it from startup central to a hub for the biotech industry. John Burns, president of BioAustin, the life sciences industry organization for Central Texas, says, "All the ingredients are there."

- Workforce — Austin has a large entry-level workforce coming out of the University of Texas at Austin, nearby Southwest Texas State in San Marcos, and Austin Community College, which offers a biotechnology degree.
- Public Funding — State programs, such as the Cancer Prevention Research Institute of Texas (CPRIT), earmark money for research being conducted in the state.
- Quality of Life — Austin is consistently ranked among the best and most affordable places to live in the country. "Housing is cheaper than in California or Boston, and there's no snow to shovel like there is in Boston," Burns says.
- Low Taxes — There is no state income tax, and there are other tax incentives for businesses.
- Entrepreneurial Spirit — Austin is approaching critical mass when it comes to life sciences companies, "There are about 160 biotech companies within 30 miles of downtown Austin," Burns says. Most are small, having between one and 10 employees. (Burns includes device makers.)
- A Tier-One Medical School — The new Dell Medical School at UT Austin is the most recent addition to the life sciences mix in town. Burns says it's a great addition to the Austin biotech scene. "The medical school will bring many researchers and innovators who could drive up the number of local startups."

WHAT'S STILL NEEDED

With all of that going for it, there are still some key ingredients needed for Austin to fulfill its potential as a biotech or bipharma hub. At the top of that list is a large, successful company — either a homegrown success story or a company that relocates to the area. "There's an awful lot of opportunity here," Burns says. "We're just waiting for someone to make it big — and stay."

Ambion is Austin's most famous biotech success story. The maker of RNA (ribonucleic acid)-based consumables was acquired by Applied Biosystems (ABI) in 2005. ABI then merged with Invitrogen to form Life Technologies. That company is now part of Thermo Fisher Scientific. About 200 Ambion employees remain in Austin, while much of the manufacturing has been moved to Lithuania.

All of what makes Austin great for biotech makes it great for the pharmaceutical industry, says Greg Stein, M.D., founder and CEO of Curtana Pharmaceuticals, a graduate of ATI. Stein is intimately familiar with hubs, having started a company in San Diego, as well as having studied how high-tech centers develop. The former physician coauthored a 2007 peer-reviewed paper on the topic. He says that if a biopharma company does find success in Austin, it is likely to go the way of Ambion or be relocated to one of the coasts.

Stein started Curtana with Santosh Kesari, M.D., Ph.D., a University of California, San Diego professor of neurology who identified a potential drug target for the treatment of a type of brain cancer called glioblastoma. The target is a transcription factor that turns on the genes responsible for the initiation and growth of cancer stem cells in the brain. These genes are critical to a developing brain, but lead to tumor growth in adults. The treatment has shown promise, and clinical trials are expected to begin in late 2017.

After receiving a $7.6 million CPRIT grant in 2014, Stein moved the company to Texas. "We wanted to pick a place where we knew our employees would enjoy living." He agrees with the list of pros given by Burns and others hoping to encourage biopharma growth in Austin. Stein

VOICES IN SUPPORT OF AUSTIN

"We want to help companies grow and eventually build their own space in Austin."

TYLER DRAKE, PH.D.
Director of The Austin Community College (ACC) Bioscience Incubator

"We wanted to pick a place where we knew our employees would enjoy living."

GREG STEIN, M.D.
Founder & CEO
Curtana Pharmaceuticals

"There's an awful lot of opportunity here. We're just waiting for someone to make it big — and stay."

JOHN BURNS
President of BioAustin

"The state also realized that we didn't have huge barriers to working with startups."

LINNEA FLETCHER, PH.D.
Chair of Austin Community College Biotechnology Program

> *"Austin's biotech ecosystem could benefit from the added plasticity and venture development that a top-tier pharma company would add to the mix."*
>
> **CINDY WALKERPEACH, PH.D.**
> Director of Health/Biosciences, Austin Technology Incubator (ATI)

also agrees that the new Dell Medical School and its progressive dean, Clay Johnston, could be just the catalyst Austin needs to put itself on the biopharma map. "Clay is going to attract a lot of 'rock stars.'"

Stein says Austin is a great birthing ground for companies like his. But it lacks other key components, in addition to a large anchor company or two, that are keeping it from becoming a true biotech/biopharma hub. These include affordable wet-lab space, more highly skilled workers, and a larger community of top-level executives.

Austin will have all of this and more, Burns says. "Just give it time." The highly skilled workforce and biopharma community in Austin are growing, especially as more local companies lure workers looking for affordable housing, better commute times, and good schools from established biotech hubs on the coasts.

Now that Dell Medical School is coming on-line, WalkerPeach agrees with Stein and Burns that the next item on the biotech hub "wish list" would be the presence of a large pharmaceutical company to anchor ecosystem development and expansion. WalkerPeach points out that Austin already has a number of established public and private medical device and diagnostics companies. It also has quite a few small, private biopharma companies. "We have had some nice M&A and IPO activity in the last several years." Still, she says, "Austin's biotech ecosystem could benefit from the added plasticity and venture development that a top-tier pharma company would add to the mix."

THE BIRTH OF AN UNUSUAL WET LAB

Affordable wet-lab space, it turns out, is the biggest factor limiting the growth of Austin-based biotech/biopharma. A grass-roots effort has led to the state's first wet lab built in the most unexpected of places: a former shopping mall. The Austin Community College (ACC) Bioscience Incubator officially opened its doors in January 2017. The lab, which is accepting applications from startups, is funded by a $4.9 million grant to address the critical shortage of research space in the region.

"Austin has historically lacked this type of space," says Tyler Drake, Ph.D., the incubator's director. The flexible space will be a great launch point for companies, as well as providing hands-on training and internship opportunities for the school's biotechnology majors. The incubator will also provide companies with business support. "We want to help companies grow and eventually build their own space in Austin," Drake says.

Getting companies started — as well as staying — in Austin has been Linnea Fletcher's goal for 20 years. "When I came to Austin, I found people were moving out because they couldn't find jobs in the life sciences." Fletcher, who has a Ph.D. in microbiology, chairs ACC's biotechnology program, and heads up the AC2 Institute, funded by a Wagner Peyser Grant that allows the program to connect with industry, other education institutions, and government.

Fletcher, who previously worked at the National Science Foundation reviewing grants for undergraduate education, spent two years securing the grant for the current wet-lab incubator. "The idea of a community college having a wet-lab incubator was a bit foreign to the governor's office." ACC is the first two-year college to apply for and be awarded funding from the Texas Emerging Technology Fund Research Award Matching program. Partners include ATI, the nearby city of Georgetown, and the Texas Life Sciences Collaboration Center.

Fletcher was able to convince the state that the incubator would be successful, in part, because she and students from her biotechnology program had already been working with industry at ACC's Round Rock campus. "The state also realized that we didn't have huge barriers to working with startups. We don't talk about intellectual property rights, for example. Our driving force is combining economic development with best practices in education."

Austin is just as good a place as any for an innovation hub to thrive, Fletcher says. "I've always supported the underdog and the idea that innovation can come from anywhere. That's why I push to make it happen right here in Central Texas."

CMO LEADERSHIP AWARDS 2017

RECOGNIZING TOP-PERFORMING CMOs

Which CMOs will be recognized by customers as industry leaders?

CELEBRATE WITH US!

Award winners will be announced in a special March issue of *Life Science Leader* and recognized at our annual reception.

CMO Leadership Awards Ceremony and Reception

W Hotel | Lexington Avenue, New York City
March 22, 2017 | 7:00pm

Register today at cmoleadershipawards.com

Presented and Sponsored by

Life Science Leader · ISR reports · Federal Equipment Company · MEGGLE Excipients & Technology · WOMBAT CAPITAL MARKETS · CORNING

Pfizer's Response To Counterfeit Drugs

CAMILLE MOJICA REY Contributing Writer

This is the second article in a five-part Life Science Leader *series examining the current state of the counterfeit medicines problem. A previous story looked at efforts to quantify the crime. Upcoming stories will look at what is being done by one international coalition to fight the crime, describe efforts to educate patients, and profile a company working to put unique identifiers on individual pills*

In May 2016, the FDA warned consumers that fake versions of Viagra and Lipitor were being sold in Mexican border towns. In September, Polish police shutdown what was reportedly the largest laboratory in the world making phony versions of erectile dysfunction (ED) drugs. Authorities seized 100,000 pills for ED, including counterfeit Viagra.

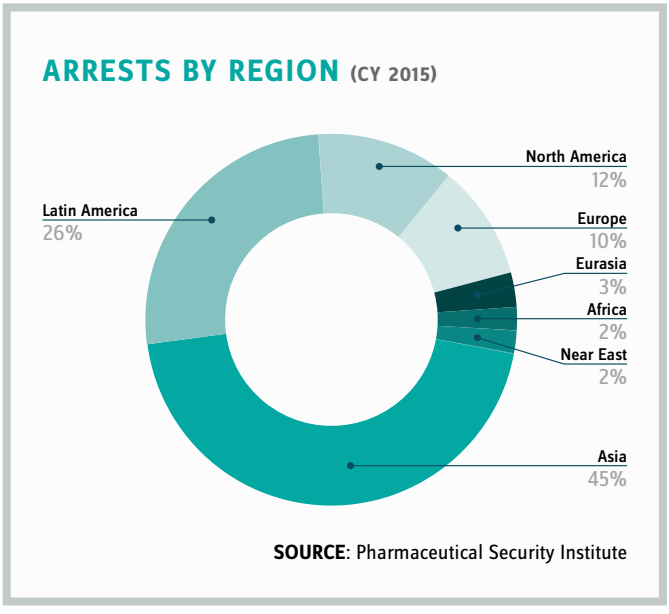
These fake drugs are easy money for criminals worldwide, says the Center for Medicine in the Public Interest, a New York-based research group partially funded by the pharmaceutical industry. The group estimates that counterfeit drugs will generate $95 billion this year, an increase of 26 percent since 2010.

"It's a huge and complex problem that continues to evolve and grow," says John Clark, chief security officer for Pfizer, which makes Viagra and Lipitor, as well as many other popular medicines. Especially in the age of the internet, the growth in the counterfeit drug market is driven by the low-risk/high-reward nature of the crime, Clark says. "We have heard reports of links between those selling counterfeit medicines and terrorist groups," he says.

In response to this mushrooming problem, Pfizer has created a global security team. Its members have a variety of backgrounds, from law enforcement to forensic chemistry. Working together, they initiate and develop cases with the goal of disrupting and dismantling major manufacturers and distributors of counterfeit Pfizer medicines. "Our efforts to combat the counterfeiting of medicines and our investment in addressing this problem are to ensure that patients who seek a Pfizer medicine obtain an authentic Pfizer medicine that is safe and effective," Clark says.

THE POPULARITY OF PFIZER'S MEDICINES AMONG CRIMINALS

This is a real concern, given that the company estimates that, to date, there have been 90 counterfeit Pfizer medications seized in 111 countries. In 2011,



Viagra accounted for 85 percent of seizures of Pfizer's medicines and products worldwide. That number dropped in 2015 to 49 percent of Pfizer seizures as the company's other drugs have grown in popularity. Lipitor, for example, is one of its drugs that is currently being widely counterfeited. Three years ago, Chinese authorities seized 3 million doses of the drug used to lower low-density lipoproteins, or LDL, the "bad" cholesterol. "Criminals are counting on Pfizer's reputation to sell their counterfeit products. Their intent is to fool patients into thinking they are getting an authentic Pfizer medicine," Clark says.

Most counterfeit drugs are made in China for export. In the last five years, however, there has been a shift to selling those drugs within the country. The 3 million doses of Lipitor seized in China three years ago were intended for sale to its growing middle class.

Clark called the recent discovery of the manufacture of counterfeits in the U.S. a worrisome development. The DEA recently shut down three separate operations making counterfeit Xanax in the San Francisco Bay Area, Texas, and Florida. Authorities found some of the fake Xanax contaminated with fentanyl, which caused a number of deaths in Florida.

SECURING THE GLOBAL SUPPLY CHAIN

Protecting patients from counterfeits means securing global supply chains. To that end, the industry and government agencies are turning to unique identifiers or bar codes. In the U.S., Congress passed the 2013 Drug Supply Chain and Security Act. The law requires drug companies to work in cooperation with the FDA to "build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States."

According to Clark, Pfizer is testing the use of unique identifiers on packaging. "We can check the pedigree of a medicine to see its last stop along the supply chain," he says.

The law sets 2023 as the goal for the full implementation of this system in the U.S. But even today, a patient in this country who goes to a brick-and-mortar pharmacy has a very slim chance of getting a counterfeit medicine. "The supply chain here is incredibly secure," Clark says. He recalls the last breach of a counterfeit Pfizer medicine in the U.S. supply chain occurring more than a decade ago. "When a rare breach occurs, our regulatory agencies ensure that these medicines are quickly pulled off shelves."

The bigger problem for Pfizer and other large companies is that they operate in a global marketplace. Implementation of a global track-and-trace system is happening, though slowly. The legislation required on an international scale to implement a global track-and-trace system is an enormous undertaking, so it is only slowly coming together. There needs to be consensus on the system that will be used to track medicines and whether the tracking markers will be placed on pallets, packages, and/or individual doses. This isn't just a pharmaceutical company issue but includes distributors, warehouses, pharmacists, and clinics. Each of the players has to invest in the same equipment so bar codes can be read, receipt of medicines can be verified, and forwarding can be documented.

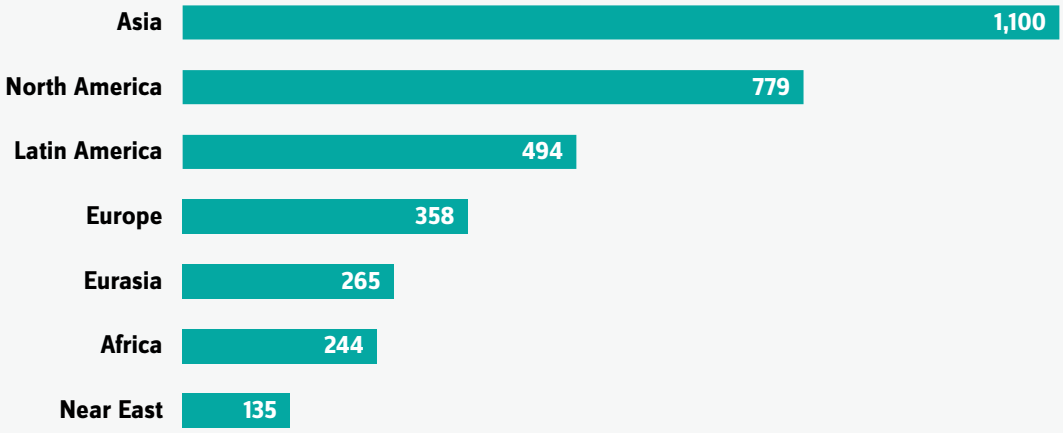
"Unique identifiers won't be the silver bullet to stop counterfeiting, but when you get the rare instance of counterfeit medicines breaching the supply chain, this kind of track-and-trace will be phenomenally helpful."

JOHN CLARK
Chief Security Officer, Pfizer

Getting global agreement on how to use unique identifiers has been difficult, Clark says. Where even to place the identifier — on the package or on the pallet — is being debated. "There are a lot of hurdles, but we are maybe two years away from having it formally implemented industrywide," he says. "Unique identifiers won't be the silver bullet to stop counterfeiting, but when you get the rare instance of counterfeit medicines breaching the supply chain, this kind of track-and-trace will be phenomenally helpful."

In addition to unique identifiers, Pfizer has been working on a variety of ways to track and trace their products. Clark's team works closely with Pfizer's manufacturing division to implement overt and covert capabilities on the packaging. "We have already instituted track-and-trace methods that allow us to know whether medicines from one market are being sold illegally in another market," he says.

COUNTERFEIT DRUG INCIDENTS – REGIONS OF THE WORLD



SOURCE: Pharmaceutical Security Institute

THE INTERNET PROBLEM

But it's the ability of patients to buy supposedly authentic drugs online from rogue pharmacies that is the biggest risk to patient safety. "That's when they really roll the dice," Clark says.

In 2013, the National Association of Boards of Pharmacy (NABP) did an assessment of 10,000 online pharmacies. Its survey revealed that about 97 percent did not meet pharmacy standards. "We are tackling that problem as best we can and targeting illegitimate online pharmacies," Clark says.

In fact, Pfizer is an industry leader in this area. The company partnered with Microsoft in 2012 to develop a computer algorithm that links what appear to be separate and distinct online pharmacies and identify the affiliate network behind them. "What we find is that there is really one organization running thousands of sites," Clark says.

As of June, Pfizer's security team has disrupted 21 affiliate networks consisting of 6,597 rogue online pharmacies. "We take a lot of pride in that fact," Clark says. Like the IACC (International AntiCounterfeiting Coalition), Pfizer works with payment service providers like VISA to ensure these criminals cannot do business anymore. "We limit their banking options," Clark says.

Pfizer's programs have been so successful that, at a recent meeting of security officers, five companies expressed interest in partnering with them and expanding their efforts to take down illicit online pharmacies. "It behooves us all to work together," Clark says. "We all need to be doing a better job of making it harder for this problem to grow."

SLOW PROGRESS WORLDWIDE

The pharmaceutical industry as a whole is slowly making progress in the fight against pharmaceutical crime. It's a difficult problem to combat when no one even knows the true extent of it. In any one country, people see only part of the problem. "There's no one country or agency to pull it all together," Clark says.

He points out that there is much more cooperation among law enforcement agencies around the world. Law enforcement officials in China, where most counterfeits are made, have been among the most collaborative. That's because the Chinese authorities see the negative impact the fake drugs are having on their population. "They will always work on a case when given the evidence," he says.

The work Pfizer and other companies do to train law enforcement around the world is helping both to raise awareness and detect crimes. Pfizer's security team has trained law-enforcement agencies in 151 countries. What the team encounters around the world, however, are inconsistencies in legislation. "If there is legislation, it is often weak and difficult to enforce, so it is becoming an attractive crime," Clark comments.

What is really needed is a universal outlawing of counterfeit medicines. Narcotics, Clark points out, are internationally recognized as banned substances. "If we can get counterfeit medicines universally recognized as illegal," Clark says, "then we can build up a global collaborative system." L

OutsourcedPharma
CONFERENCE AND EXHIBITION

THE OUTSOURCING INDUSTRY HAS NEVER TALKED LIKE THIS BEFORE.

BOSTON
APRIL 26-27, 2017
OutsourcedPharmaEvents.com

SPEAKERS INCLUDE

AGIOS PHARMACEUTICALS
Bob Sheroff | *SVP Technical Operations*

AMAG PHARMACEUTICALS
James Lucie | *Associate Director*

BERKSHIRE STERILE MFG
Shawn Kinney | *CEO*

BIOGEN
Tobias Blackburn | *Supervisor, Technical Dev*

BIOGEN
Evan Guggenheim | *Sr. Manager, Technical Dev*

BIOGEN
Clive Patience | *VP, Asset Dev & Program Mgmt*

BIOGEN
Thomas Holmes | *Senior Director Global External Mfg*

BRISTOL-MYERS SQUIBB
Keirnan LaMarche | *Senior Research Investigator 1*

CMC TURNKEY SOLUTIONS
Barbara Berglund | *COO*

ELI LILLY AND COMPANY
Mark Butchko | *Sr. Director QA - Development*

EMERGENT BIOSOLUTIONS
BJ Hull | *VP/GM*

FORTRESS BIOTECHNOLOGY
George Avgerinos | *SVP, Biologics Operations*

FREEDOM BIOSCIENCE PARTNERS
Brian Scanlan | *Managing Partner*

GENENTECH
Todd Mabe | *Head of Biologics, Drug Substance*

JOHNSON & JOHNSON
Milan Shah | *Head, Publishing, Global Capabilities IDAR*

LATHAM BIOPHARM GROUP
Susan Dexter | *Managing Director, Commercial Business*

MEDIMMUNE
Steve Cook | *Head, Global Biologic Supply Chain Operations*

MERCK
Anand Ekambaram | *Executive Director*

MERCK
Pamela Rizos | *Project Manager*

METRICS CONTRACT SERVICES
Charles Waldroup | *Director of Project Managemnt*

OUTSOURCED PHARMA
Louis Garguilo | *Conference Chair*

PATHEON
Franco Negron | *President, Drug Product Services*

RONDAXE PHARMA
Brian James | *SVP Operations*

SANOFI GENZYME
Piet Houwen | *Head of Contract Mfg Operations*

SNAPDRAGON CHEMISTRY
Matthew Bio | *President & CEO*

SUNOVION PHARMACEUTICALS
Vince Kosewski | *VP Supply Chain Operations*

TUNNELL CONSULTING
Julia O'Neil | *Principal*

VERTEX PHARMACEUTICALS
Michelle Bailey | *Associate Director*

XENETIC BIOSCIENCES
Henry Hoppe | *VP of Drug Development*

Pharma Field Trips: Is Hosting The FDA A Good Idea?

GAIL DUTTON Contributing Writer @GailLDutton

Inviting FDA scientists into your manufacturing facility or laboratory for one or two days may feel unsettling, but it can be rewarding when the visits are designed to bring FDA scientists up to speed on real-world issues and new technologies.

Drug developers can learn the extent of that potential benefit in 2017 when CDER launches the Staff Experiential Learning Site Visit Program. The educational program focuses on 17 areas of scientific interest, ranging from drug/device combo products to continuous manufacturing, nanotech, and APIs. It is expected to start during the first half of 2017, once CDER receives and approves appropriate applications from pharmas to host FDA scientists for one- to two-day learning visits.

WHAT CAN THE FDA GAIN?

The scientists and engineers at CDER's product quality office generally have industry experience and access to cutting edge equipment and techniques. "They're pretty savvy, so we have to wonder what they would gain from a site visit," says Darryl Sampey, president and CEO of BioFactura, a developer of biodefense countermeasures and high-value biosimilars.

The answer is "insight into new technologies and commercial-scale operations." At BioFactura, the key learning opportunity probably would involve its continuous manufacturing operations for bioprocessing. That is a relatively new approach to biomanufacturing and is garnering a lot of industry interest. As companies begin to adopt this linked method of biomanufacturing, it's only natural that the FDA also wants to learn the practical realities and what it takes to implement continuous manufacturing successfully.

EDUCATIONAL VISITS OR COVERT INSPECTIONS?

"People get stressed having regulators on site because they associate visits with audits," says Yaky Yanay, president and COO of Pluristem Therapeutics, an Israeli developer of stem cell therapies. "FDA site visits help make regulators more familiar with an industry that is changing rapidly. Therefore, there are a lot of advantages in having the FDA involved in learning and understanding the challenges in the technologies. Learning programs and site visits will only be beneficial." That's because regulators who thoroughly understand the processes, technologies, and issues involved in a product's development and scale-up are better qualified to review subsequent FDA submissions.

There's another benefit, too. By sharing knowledge with regulators, scientists on both sides of the regulatory milieu have had an opportunity to discuss any issues of concern. Therefore, companies can use new technologies more confidently.

"The focus of the visits is for staff in the Office of Pharmaceutical Quality to further develop their understanding of current industry practices, processes, and procedures," emphasizes Tralisa Colby of the CDER Trade Press. During the one-to-two-day visits, program hosts are expected to provide "experiential, first-hand learning opportunities" for visiting FDA staff rather than merely lectures or discussions. The goal is to improve FDA reviewers' understanding of the industry and its operations, including issues that affect drug development and a product's commercial life cycle. A facilities tour is integral to this experience.

To ensure confidentiality, CDER staff will be trained to handle information properly. Colby stresses the visits do not replace regulatory inspections.

This program is similar to others in the FDA. The Center for Devices and Radiological Health (CDRH), for example, began an experiential learning program in 2012 to close the knowledge gap between emerging and innovative technology and the premarket review of medical devices. "Since 2012, 1,557 premarket reviewers have gone on 130 site visits," Colby says. CDER also has a site visit program for regulatory project managers that was renewed in 2016.

Such on-site learning programs are very helpful to FDA scientists, stresses David Rosen, J.D, former regulatory counsel and special assistant to the director of CDER. Rosen currently is FDA practice group leader and co-chair of life sciences industry team at Foley & Lardner LLP. He says, "Looking at things that are difficult to formulate or manufacture helps FDA reviewers understand critical parameters. This helps them ask the right questions during the application review process."

CDRH reviewers say the visits expedite the application review probes by improving their understanding of how medical devices are developed, clinically tested, manufactured, and used. Biopharma executives expect CDER's new site visit program to extend similar benefits to drug development reviews.

ARE NEUTRAL SITES BETTER?

Any time a regulator visits a site, there is some degree of concern that something will be spotted that triggers an official site inspection. Rosen says, "If FDA reviewers do spot something during a site visit, one would hope they would inform the company and have a scientific discussion without triggering an inspection." He characterizes the risk that a learning site visit would trigger an official FDA inspection as extremely minimal. Nonetheless, there may be some concerns.

"As an investor, I think FDA site visits would raise a red flag," says Jeff Hausfeld, director of the board and chief medical officer of BioFactura. That said, "I support transparent communication between companies and regulators as long as we're all on the same page."

These site visits aren't the only way to provide learning opportunities for regulators. Interactions may be more productive when public entities serve as the interface, Sampey points out. He recommends meetings with reviewers, academics, and enterprises at neutral locations. For example, in 2016, the University of Maryland and the National Institute of Standards and Technology hosted the FDA, BioFactura, and other companies to discuss capabilities and commercial concerns. "It was very comfortable for the government and private sector to open this dialog on neutral ground. It was a very productive interaction," Sampey says.

Even in a neutral environment, industry can provide valuable insights into scale-up and commercialization that put real-world challenges into perspective. Neutral locations can't provide the full picture, however. "Meetings in neutral locations can be useful, but they can't replace visits to real companies to understand large-scale, commercialization concerns and practices," Yanay counters.

IF YOU PARTICIPATE…

If you decide to participate in CDER's new site visitation program, have a specific focus in mind that meets the FDA's learning objectives. As you craft a proposal as a learning-site host, involve your company's leadership and development executives to ensure your program is beneficial for everyone involved.

Yanay advises beginning the learning experience in a conference room to set expectations for the visit. This is a good place in which to provide an overview of the company as well as the technology or process that regulators are on-site to explore. Be sure to discuss how this process affects upstream and downstream processes and, if applicable, other areas of operations. For example, a discussion of APIs may involve supply chain risks and geopolitics if ingredients are sourced from a single site or even a single country, as well as the standard safety and purity concerns.

A PowerPoint presentation may help explain the equipment, critical process parameters and controls, and some of the actual issues your company has had to address during implementation or scale-up. Once regulators have a general understanding of the situation, they can tour the labs or manufacturing facility to see real-life operations.

Before touring the facility and talking with scientists and operators, Rosen cautions, alert your staff that guests will be coming through the facility. "Ensure that staff understand what's going on and what's expected of them, and be sure that the facility is clean and organized."

Rosen also warns against allowing visitors access to files. If an FDA scientist asks a staff member for information, it may be temping for that person to open a seemingly innocuous file and show it to the visitor. Instead, caution staff members to relay such requests to a designated individual who can provide the information without inadvertently sharing confidential data.

Details of this new program are listed in the Federal Register. When CDER requested hosts for its Regulatory Project Management Site Tours and Regulatory Interaction Program, only one company volunteered to host the program. The agency subsequently sent a request for additional participants. Therefore, although the deadline has passed to apply to host the Staff Experiential Learning Site Visit Program, companies may still have opportunities to participate.

Why Xellia Revived A Shuttered Pharma Facility

CAMILLE MOJICA REY Contributing Writer

As he walked through the former home of Ben Venue Laboratories, Niels Lynge Agerbæk didn't see the previous failures the facility had endured. No GMP violations. No recalls. No FDA-required supervision of drugs in critically short supply. Agerbæk saw only the "good bones" of buildings with lots of potential. He also saw a way for his company, Xellia Pharmaceuticals, to get its products to market faster than if they were to build a much-needed facility from the ground up. "We needed additional capacity to get our products to market."

Resuscitating a previously used facility is not an easy — nor an inexpensive — task. "There are a lot of unknowns when you start up a facility like this. You shouldn't do it if you are coming from a cost-saving perspective," says Agerbæk, Xellia Cleveland's general manager. The company purchased four of five buildings that once made up Ben Venue Laboratories in Bedford, a suburb of Cleveland. (The other building at the site houses Hikma's West-Ward Pharmaceuticals.)

Despite the risk of finding costly construction or equipment problems, Agerbæk and his colleagues have been pleasantly surprised by the conditions of the facility and how well it was maintained during its closure. While the site lay dormant, its owners kept a skeleton crew of maintenance workers on-staff until it was sold. "We are upgrading sterility to bring it to the highest necessary level, and there have been no major downsides."

Agerbæk and his team are one year into a two-year plan to bring the plant, which was closed in 2013 and now operates under a modified consent decree with the FDA, back into compliance and again begin manufacturing operations. Xellia got one step closer to that goal in November when the company received clearance from the FDA to begin packaging and distributing its drug products at the facility.

Xellia is a specialty pharmaceutical company that mainly produces injectable treatments for serious and often life-threatening infections caused by multidrug resistant strains of bacteria. The U.S. market represented 40 percent of the company's sales in 2015, and demand for Xellia's products is growing. "The two years

> *"There are a lot of unknowns when you start up a facility like this."*
>
> **NIELS LYNGE AGERBÆK**
> General Manager, Xellia Cleveland

CONSENT DECREES & THE FDA

By the time the FDA enters into a consent decree with a company, trouble has been brewing for some time. A consent decree is essentially a court order the agency turns to after numerous and repeated GMP violations or deficiencies. A consent decree is signed by the head of the company, the US Attorney, and the appropriate US District Court. It is filed with the court and submitted to the FDA. A consent decree spells out the steps the company will voluntarily take to rectify its violations and name a third party to verify that these measures have indeed been taken. In some cases, the decrees allow the company to continue to make and sell their products under FDA supervision. This was the case with Ben Venue Laboratories until it shut down in 2013. Xellia announced in April 2016 that it had entered into a modified consent decree with the FDA that detailed the parts of the facility that would have to be upgraded in order for the facility to resume operations. In November 2016, after a successful cGMP inspection, Xellia Cleveland received notice from the FDA that labeling and packaging of products from other sites could take place at the facility. Once the terms of the decree are met, Xellia Cleveland will also be free to commence manufacturing operations.

required to bring the old facility back online is about half the time it would take to build one from the ground up," Agerbæk says.

Once operational, Xellia Cleveland will be one of the largest sterile drug manufacturing facilities in the country. Agerbæk's current team of 107 employees is expected to grow to 170 by the time production begins in 2018. The Bedford site will be the second U.S. facility for the Denmark-based company, which already has its U.S. headquarters in Raleigh, NC.

A FACILITY'S NEW LIFE

Agerbæk, who has been in charge of production facilities in Denmark and China, is well-suited to lead the painstaking work now going on in Bedford. Once the renovations are complete, he says, the facility will be indistinguishable from a brand-new one. "We are treating everything as if we are building it from scratch." All equipment goes through commissioning and validating as if it had just arrived at the facility. Any equipment that doesn't meet the highest current standards is replaced. Even the buildings' plumbing and electrical systems have been regenerated. "We are not taking any shortcuts," he says.

Xellia is not taking any chances, either. It has been working very closely with the FDA, which first closed the facility owned by Boehringer Ingelheim (BI) in 2011. The plant was run by BI's CMO, Ben Venue Laboratories. Numerous quality and GMP violations led to the closure, but critical drug shortages resulted in a January 2013 consent decree and limited manufacturing under FDA supervision. BI invested $350 million to improve the facility but decided in late 2013 to shut it down because of the difficulty in bringing it back up to standards. It sold the entire facility to Hikma, a London-based pharmaceutical company, in 2014 for $300 million. Hikma has kept the R&D center and its staff for its own drug development operation.

Xellia's long-range goals include contract manufacturing and expansion of its own product line. That means every system must be flexible enough to accommodate planned expansions. Xellia has already seen interest in the opportunities provided by the future facility from existing customers, as well as new prospects.

A COMMUNITY'S HOPE

The physical structures at the Xellia Cleveland site are not the only things being rebuilt. The community of Bedford was devastated when the Ben Venue plant closed and 1,100 people lost their jobs. Xellia has not only breathed new life into buildings it acquired but also has brought back jobs to the community. It has also brought a new sense of purpose to the employees, especially those who worked at the site under its previous owners. "Everyone in the community is really excited to see this place come back to life," says Cheryl May, head of environmental health and safety and security at the site.

May began working for BI in 1998, and she helped decomission the plant in 2013. Later, she worked for Hikma. Today, May says her job is exciting and that neither the community nor the plant's current employees focus on the past. "To be able to be a part of bringing something back to life has been an amazing experience. Something that was terrible for this community, hopefully, will be something fantastic for it in the future." L

Academia Finds New Ways To Partner With Pharma

CHRISTOPHER LEO, PH.D., AND JONATHAN GERTLER, M.D.

For the past decade, academia and industry have become increasingly collaborative, finding ways to shed cautious attitudes and successfully advance programs together. Now, academia is taking a proactive, strategic approach that promises to further catalyze industry relationships and increase opportunities for commercialization and monetization of the most promising technologies.

The Great Recession of 2007 and the subsequent retreat of venture groups away from early-stage funding created a funding gap for early technologies and slowed innovation. To bridge this, top industry players, including Sanofi, Pfizer, and GSK, built dedicated units to establish and maintain relationships with leading academic clinical investigators and institutions.

Academia has responded in kind with enthusiasm and measured pursuit to engage industry. Many institutions, including Stanford, Harvard, Johns Hopkins, and the University of California, San Francisco, have found creative ways to fund high-priority technologies toward development and commercialization, monetize potential royalty streams, and collaborate with industry beyond the traditional structures.

For the first time, academia is creating dedicated business development teams to court pharma. These teams often are composed of seasoned industry professionals and investors who can creatively identify opportunities and enable this courtship.

- At the University of Massachusetts, Brendan O'Leary, Ph.D., executive vice chancellor for innovation and business development, has nearly tripled sponsored research dollars coming into the medical school via multiple mechanisms. In addition to courting pharma partnerships, O'Leary has implemented a range of new initiatives focused on funding of the university's technology. For example, he has assembled teams of entrepreneurs to review UMass technologies in exchange for an option to raise funding and negotiate a license around the program's IP. Another initiative involves identifying potential partnerships with CROs for access to their screening and preclinical platforms in exchange for UMass biologics or assay development expertise.
- David Greenwald, Ph.D., director, business development and corporate partnerships at Johns Hopkins Technology Ventures, sees several key benefits for universities being more aggressive in approaching pharma with these potential deals. Such agreements diversify the university's funding stream (particularly important given flat/declining NIH funding levels) and enable the pharma partner to guide the university's investigators throughout the development process, thereby increasing the value of the program and opportunities for commercialization down the road. Finally, many of these agreements include options to license the resultant IP for the pharma partner, thus incentivizing the investigator and institution to adhere to a research plan and timeline conducive to an early-stage pharma program.

Across academia, institutions are finding new ways to advance their technologies and catch the eye of industry: The University of California's (UC) QB3 program; Harvard University's Blavatnik Biomedical Accelerator; and The Engine, MIT's new venture to

support startup companies working on scientific and technological innovation, all provide resources, mentorship, lab space, and sometimes seed funding to support scientific and technology advancement.

These groups work closely with faculty to advance technologies and make them appealing and attractive to VC funding or industry partnership, with impressive results to date. For example, at the QB3 program, several large collaborations with industry have been established to advance UC science, provide funding, and link UC faculty to pharma expertise, including Pfizer, Roche, GE Healthcare, J&J, and Takeda.

This new approach is not without its challenges, however. As academia discovers creative ways to approach industry, it also must navigate through some difficulties:

- **Funding gaps** are still an issue for translational research to advance a program to a real inflection point, such as proof-of-concept in a second animal model.
- **Need for close management** is amplified. This new strategy requires a strong alliance-management function to serve as a liaison between the investigator and pharma partner and ensure ongoing dialog around research objectives, progress, and timelines. Johns Hopkins University hires a full-time employee as an alliance manager for each industry collaboration established.
- **Institutional culture adjustment** can be seemingly insurmountable. Adhering to a "pharma-like" research plan represents a real culture change for many investigators, particularly those with limited entrepreneurial experience. Therefore, a significant educational effort is required.
- **Industry stigma** can slow new thinking. Technology transfer is still too often viewed as a bazaar or open exchange of the university's assets, frequently driven by a principal investigator's preference. It's important to be transparent with goals and eventual outcomes to demonstrate mutual benefit.

As academia wends through these challenges, traditional options remain for advancing beyond the laboratory toward commercialization, including funding through angel investment, venture backing through licensing, and structured collaborations and licensing mechanisms that ultimately lead to acquisition of the technology/asset by the pharma partner. These options should be approached by academic investigators first with a thorough review of each asset.

Advancing a startup may be onerous to some and highly appealing to others. With industry-academic interactions, true commercial and transactional discipline should be applied. Technology development offices must triage priorities among faculty projects for intellectual property pursuit and strongly consider the various parameters that will ultimately predict commercialization success and optimal returns to the university.

Many offices of technology development claim success based on overall economic ranking. However, this can be an inaccurate measure of health. Close scrutiny may reveal that only one or two successes drive the lion's share of royalties and do not measure potential of future success. While many love the idea of a "home run" in academic-industry partnerships, a better indication of overall team health is a carefully strung together history of singles, doubles, and triples to advance a more sustainable program. Ultimately, these smaller, steady wins are a truer indicator of a university's ability to monetize assets.

The path from academia to monetization combines several new disciplines for technology development, but during that journey it's important to remain close to the overall academic mission. Initiatives and investigators must stay dedicated to research and teaching.

The office of technology development should approach promising assets with the same level of scrutiny as would occur if the assets were embedded inside a biopharma company. This involves understanding the competitive intensity in the space, the groundbreaking nature (or lack thereof) of the asset in question, translational research requirements (e.g., animal models, preclinical tox studies), as well as the development and commercial hurdles that will render an asset appealing.

As academia learns to approach industry with key objectives in mind, assessment should broaden beyond the projected scientific innovation to matching the asset to the right structure for development (i.e., formation of a spin-out company, sponsored research collaboration, combinations of licensing deals, and continued sponsored research relationships). This leads to the greatest chance of success and requires scrutiny across the outlined parameters. With a wider swath of suitors from which to choose and unprecedented combined capital resources, academia has never been in a better position. L

CHRISTOPHER LEO, PH.D., is senior VP at Back Bay Life Science Advisors with over 12 years of strategic advisory experience.

JONATHAN GERTLER, M.D., served for many years as an academic vascular surgeon and investigator. He is managing partner, founder, and CEO of Back Bay Life Science Advisors.

New ADC Technologies: Deadlier For Tumors, Safer For Patients

ED MISETA Chief Editor, Clinical Leader @EdClinical

The concept of ADCs (antibody-drug conjugates) has been around for more than 20 years. The thinking behind them is that on the surface of cancerous cells there are overexpressed proteins (antigens). According to Anna Protopapas, president and CEO of Mersana Therapeutics, the "circuitry" around cancer cells goes haywire, causing the antigens to appear. ADCs attempt to use those antigens to attack the tumor cells.

"The hope is we can design an antibody that will only bind to those cancer-specific proteins," says Protopapas. "The antibody carries a cytotoxic drug that penetrates the cancerous cell. Once there, it will release the cytotoxic drug, causing the captured cell to die."

This seems, on the surface, to be a pretty simple idea. But getting to that final result has taken a good amount of time and research. Seattle Genetics and ImmunoGen pioneered the approach, and currently have products on the market. Kadcyla uses the ImmunoGen technology and is currently in its second generation while ADCETRIS uses the Seattle Genetics approach. ADCETRIS currently has sales of more than $250 million. It is also being used in trials for treatment of cutaneous T-cell lymphoma and in trials in combination with Bristol-Myers Squibb's Opdivo for the treatment of Hodgkin lymphoma. Kadcyla, Roche's late-stage breast cancer offering, has been shown to shrink tumors, slow disease progression, and extend life. Roche is currently spending $200 million to build a new manufacturing facility in Basel, Switzerland, to produce drugs like Kadcyla and some of the 25 ADCs in its pipeline.

Protopapas is no stranger to the technology. She worked on ADCs at Millennium and then Takeda (which sells ADCETRIS outside the U.S.) for almost two decades before joining Mersana. Although she saw some of the early challenges of those first-generation technologies, she was also able to witness some of the successes. She personally had the opportunity to meet patients who experienced incredible recoveries when using ADCETRIS. She believes the experience helped her to understand and appreciate the benefits of ADCs.

ADCs have improved and matured over the last 20 years, becoming more of an established cancer therapy. Protopapas notes that in that time, around 80 ADCs have made it into clinical trials. Currently there are approximately 60 ADCs in clinical studies.

BIGGER PAYLOADS BRING INCREASED TOXICITY

Since ADCs first hit the market, researchers have attempted to increase their efficacy by going to super-potent payloads including a highly potent cytotoxic agent called pyrrolobenzodiazepine (PBD). PBDs have been effective at delivering more potent payloads to tumor sites. Several ADCs using PBDs have made it into clinics recently, which Protopapas lauds as a major advancement in the field.

Of course, more potent payloads are also more toxic to surrounding tissues. To solve that problem, Mersana pioneered a new approach using a proprietary platform (Fleximer) that delivers a higher amount of payload to the cancer cells without harming healthy tissues.

"There is certainly a real concern surrounding these bigger payloads," adds Protopapas. "With higher levels of agents you have to worry about issues occurring when the payload is released after the tumor is killed. We are still very early in the review process, and unfortunately, we do not have a lot of clinical data. But the clinical data we do have demonstrates there is reason

to be concerned with these super-potent payloads." (*Editor's note: A December 27, 2016, press release from Seattle Genetics notes an FDA clinical hold had been placed on several early-stage trials of its ADC SGN-CD33A, designed to be stable in the blood stream and release a potent agent upon internalization into cells.*)

Protopapas believes Mersana has improved the approach to ADCs in two very important ways. In the traditional ADC approach pioneered by ImmunoGen and Seattle Genetics, the cytotoxic payload is attached directly to the antibody. She notes there is data published by both companies and academic groups showing the maximum molecules (cytotoxics) per antibody to be three to four. Mersana's technology can add four to five times that payload to a given antibody, delivering as many as 15 to 20 payloads.

"As you can imagine, the more payload you can deliver to the site of the tumor, the more efficacious you can be," she states. "We now have data showing we can cause complete tumor regression in preclinical models using our drug. That is to say, we have no detectable tumor at the end of the study. And, to the best of my knowledge, no other company is taking the same approach."

> *"From a clinical development standpoint, I don't think the path to development and approval of ADCs will really be that different from the path of approval of any oncology drug."*
>
> **ANNA PROTOPAPAS**
> President & CEO, Mersana Therapeutics

KILLS CANCER, SAVES HEALTHY TISSUES

The second way Mersana has improved the ADC approach may be the more important one. Although the company is delivering a greater payload, it uses what Protopapas describes as "very elegant medicinal chemistry" to minimize its impact on the patient.

"In any ADC, the payload released is toxic so as to kill the tumor," says Protopapas. "Unfortunately, that toxic payload also has the ability to permeate adjacent cells. In the ADC field we call this the 'bystander effect.' We do not want that payload to have the ability to travel to healthy tissues. The cytotoxic drug we use is extremely potent when released into the cancer cell, but it then becomes trapped in the cell and gets metabolized into a form that is a lot less toxic. It essentially destroys the cancer cell and then detoxifies itself, making it a lot more tolerable to patients."

The payload gets metabolized into a form that cannot penetrate the cell membrane. It enters the cancer cell and travels to adjacent cancer cells, effectively destroying them. But when the cancer cells are destroyed and released into circulation, the payload released cannot penetrate adjacent healthy tissues.

The traditional approach to ADCs had the payload attached to the antibody via a linker. The stability of the linker is important because you want the drug conjugate to be very stable while in circulation and to eventually release the payload once it enters the target cell. With Mersana's technology, there is a bond between the payload and the antibody, which is called a Fleximer. The Fleximer is a biodegradable polymer, and the payload is attached to the polymer.

ADCS READY TO ADVANCE TO PHASE 2/3

Protopapas notes there are three or four ADCs currently in Phase 3 trials, 16 that are in Phase 2, and approximately 40 that are in Phase 1. In pharma, outsourcing is the current method of conducting trials, and companies now work with sites across the country and around the world. It seems the movement of many of those 40 ADCs from Phase 1 to Phase 2 or 3 could be a significant event for the industry. She believes sponsors, sites, and CROs will be ready for that migration.

"From a clinical development standpoint, I don't think the path to development and approval of ADCs will really be that different from the path of approval of any oncology drug," states Protopapas. "The FDA would certainly look at the safety and efficacy of the drugs and make a judgment based on the risk/benefit in a similar way they would for any other oncology drug."

She notes the area where ADCs might be different from other oncology treatments is with the manufacturing vendors. Although the payload is similar to the small molecule payload, putting the antibody and payload together is what makes ADCs unique. There is a large number of global suppliers with expertise doing that, and Protopapas believes they will be ready to support the growing need.

When it comes to sites and CROs, she also does not believe more ADCs in trials will be a challenge. Patient recruitment channels already in place will enable them to get the volunteers they need. In fact, Protopapas believes new technologies and medications, including ADCs, will help to partially alleviate the patient recruitment challenge that has plagued pharma.

A Positive Outcome From Pharma Closures

DAN SCHELL Editorial Director

The large changes impacting biopharma in the Delaware Valley (i.e., Philadelphia metropolitan area) have presented a rather unique opportunity for capturing surplus biomedical research assets. As many of us know all too well, facility closures and downsizing initiatives usually result in the disposal of significant quantities of expensive chemicals, starting materials, equipment, consumables, and general and specialized industrial-grade glassware. That usually meant the safe disposal of the chemicals and the remainder of the materials being sent to landfill after appropriate washing and crushing.

But the Pennsylvania Drug Discovery Institute (PDDI) had another idea. Instead of disposing of these valuable resources, the PDDI offered to serve as a repository for these materials, archive and curate them, and then make them available for no charge to academic institutions and small biotech companies as a public service.

Presenting this proposition to a number of biopharma firms in the Delaware Valley resulted in PDDI receiving more than 22,000 reagents and starting materials, among many other consumables and related assets. "Our organization has its own liability insurance and assumes complete ownership of these donations on an as-is basis," explains PDDI President, Chairman of the Board, and Cofounder Allen Reitz, Ph.D. The reagent donations are incorporated into one consolidated collection, bar-coded, and clustered in functionality appropriate bins. Much of this work is conducted with the aid of medicinal chemists from the Fox Chase Chemical Diversity Center co-located with the PDDI at the Pennsylvania Biotechnology Center in Doylestown, PA. This curated repository has an estimated worth of >$2.5 million. But more important than its monetary value, it represents a valuable resource for the local biopharma and educational community.

AN INVALUABLE RESOURCE TO BIOTECH STARTUPS, SCHOOLS

Companies or organizations that want to access PDDI's repository of supplies must be either U.S.-owned small businesses or other nonprofit organizations working in the area of biomedical research. They cannot resell any of the chemicals or other assets received from PDDI.

The reagent collection has been made available to local high school chemistry instructors and professors at universities such as Villanova University and Immaculata University. Many of the small startup firms at the Pennsylvania Biotechnology Center where the PDDI is co-located also take advantage of the chemical repository. Doing so permits them to pursue chemical ideas they might not be able to address otherwise considering many of the starting materials in the collection are very expensive. "Were it not for the cooperation of many of the firms that have donated to our collection, these valuable reagents would be in a landfill or incinerated," says PDDI CEO and Secretary/Treasurer Dennis Gross, M.S., Ph.D.

As important as the chemical reagent collection is, it's the consumables that have turned out to be the most attractive part of the program, especially to the local educational community. These include test tubes, vials,

pipette tips, and an extensive repository of glassware for both chemistry and pharmacology. "All one has to do is look at a glassware catalog to note that a 100 mL volumetric flask costs $26, to see the need for this repository of surplus assets," comments Reitz. Many of these materials have been repurposed to a number of local high schools in Pennsylvania and New Jersey. In one instance, the PDDI provided glassware for a new biology instructor at a health sciences-themed high school in a nearby county. The school's mission is to provide focused programs in the health sciences for students interested in becoming nurses, dental assistants, and pharmacy technicians among others. Hands-on classroom and experiential opportunities help students to graduate with an employable skillset should they decide not to go to college. Gross adds, "It's very gratifying to see a high school biology or chemistry instructor accept a number of boxes of beakers, graduated cylinders, and Erlenmeyer flasks that will all be used to help support their teaching mission."

A similarly rewarding event took place recently when a PDDI alliance school, a small local university, was given enough glassware that enabled the faculty to create a second section of organic chemistry lab. All these activities did not just happen overnight, but represent the expansion of the vision of the founders of the PDDI, its senior management, members of its board of directors, and the cooperation of the many local firms that have embraced the PDDI vision of helping the local life sciences community.

The Pennsylvania Drug Discovery Institute (PDDI) was founded in Doylestown, PA, in June 2010 by Allen Reitz and Kathy Czupich and has obtained 501(c)(3) nonprofit designation from the IRS. PDDI's mission is to provide services to the local scientific community such as workforce reentry assistance for recently separated senior researchers via networking activities. It also provides courtesy faculty positions to enable displaced senior scientists to fill gaps in their professional resume as they pursue new career options. L

Companies or organizations that want to access PDDI's repository of supplies must be either U.S.-owned small businesses or other nonprofit organizations working in the area of biomedical research.

Leading Courageously Through Unclear Times

DAVID CARDER & PAT CORMIER

DAVID CARDER is a managing director at Kotter International, where he leads client engagements in the life sciences sector.

PAT CORMIER is a managing director at Kotter International, where she leads many of the firm's largest client engagements in the life sciences sector.

Over the past year, the pace of change in the life sciences industry has accelerated more than ever before, and 2017 shows no sign of slowing. From the shift to outcomes-based care and the rapid influx of new health technologies to growing pressure on cost controls and the ever-changing world of healthcare regulations, this year will bring even more change and uncertainty.

For life science leaders, uncertainty is not often a comfortable state, even as it increasingly becomes a familiar one. Next, we offer guidance from our experience working with leaders across the healthcare and pharmaceutical sectors to help you set an example, push projects forward, and find success — even when answers are unclear.

SPEAK LESS, QUESTION MORE

Leaders are often expected to confidently set direction and move the team forward. Yet amid the industry's uncertainty, leaders must be comfortable with not having all the answers. Leaders can't just lead through ambiguity, they must embrace it. A key way to build nimbleness and better identify the organization's needs and opportunities is to be become an inquisitive leader who queries and listens more, and dictates less.

REIMAGINE WHAT'S POSSIBLE

Incremental improvements are no longer enough to succeed. Success will depend upon seeking new ways to capitalize on internal resources — technology, people, or a combination of both — to create new paths forward.

DELIBERATELY AND CREATIVELY ASSEMBLE TEAMS TO GUIDE CHANGE

Building top-performing teams that push the envelope of innovation is less about getting subject matter experts together in one room and more about mixing up the roster. Build diverse teams of individuals spanning the organization and across silos who share the energy, mindset, and desire to overcome key challenges. Tapping into these multifaceted groups can reveal unique perspectives that look beyond "the way things are done" to push the boundaries of what's possible.

CHALLENGE TEAMS TO SET AGGRESSIVE GOALS

Diverse teams of problem solvers must collectively set and build their own path to achieve critical goals. But, as a leader, you can play an influential role in encouraging them to reach for the stretch goals they've set. When teams set audacious goals pegged to big opportunities for the business to thrive, they can help overcome inertia and complacency, and push the organization to achieve results they didn't think were possible.

EMPOWER TEAMS TO TEST NEW WAYS OF WORKING – AND MAKE IT OK TO FAIL

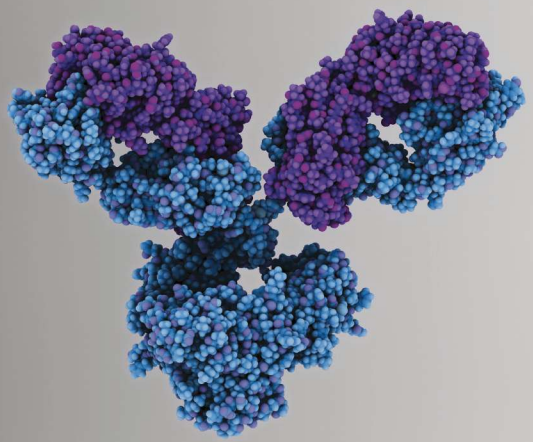
Fear of failure is often the biggest hurdle to overcome in tackling change. While there is no guarantee that reimagined ways of working will find success, leaders must give employees the freedom to test new ideas and processes, making clear that efforts to upend the status quo are valued in their own right for the lessons they provide to the organization—regardless of the outcome.

Finesse

Next stop: Never.

Continuous processing speeds up production and brings down costs.

Today, more and more biopharma companies are moving to continuous processes for their small- and large-scale operations. Find out why manufacturers are turning to Finesse for their continuous processing solutions. Finesse offers a universal control platform, plug-and-play flexibility, and the expert integration you need to get going fast. We'll also customize systems to fit your existing infrastructure, so you can keep expenses low. Learn more at www.finesse.com.



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.