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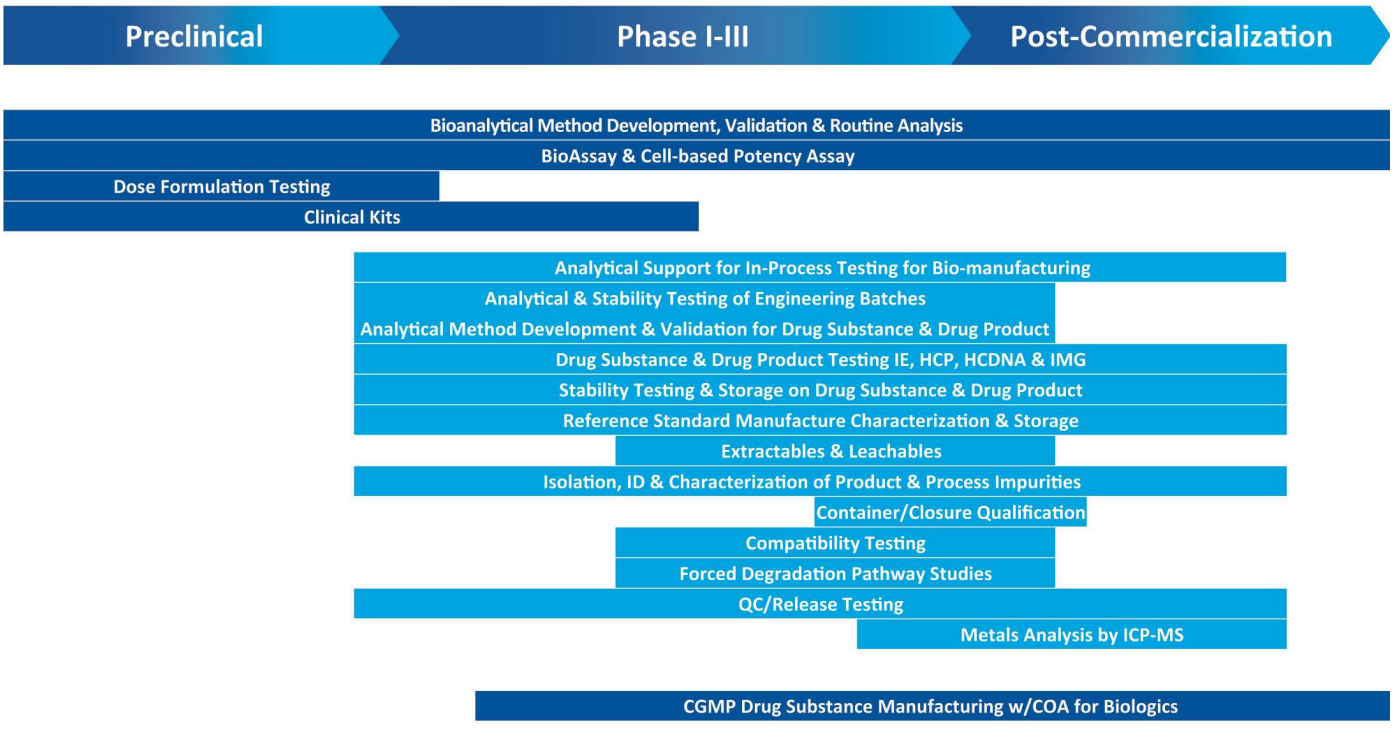

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ONO Challenges the Global Status Quo

Gyo Sagara leads Ono Pharmaceutical onto the global stage. **p. 18**

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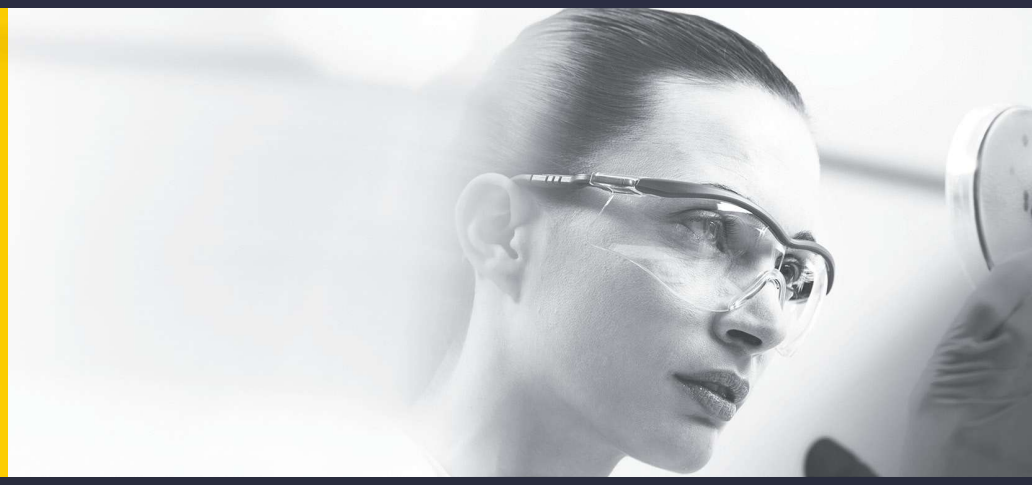

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Engage If You Want To
Capitalize On Opportunities

ROB WRIGHT Chief Editor

Commenting on his seemingly serendipitous scientific discoveries, Louis Pasteur said, "Chance favors the prepared mind." Though I agree with Pasteur's 100+ year-old sentiment, in today's hustle-and-bustle world, serendipity cannot reward a prepared mind if it is oblivious to its surroundings. However, situational awareness and a prepared mind are not enough for you to capitalize on opportunities presented by seemingly random interpersonal collisions. You need to be curious, willing to engage, and most importantly, not be in a hurry to rush your destiny. Consider the following example:

In 1981, musician and composer Peter Buffett, while living in San Francisco, needed a break from his keyboard. While washing his car, a neighbor with whom he had little more than a passing acquaintance happened by and struck up a conversation. When Buffett told him he was a struggling composer, he suggested Buffett get in touch with his son-in-law, an animator who was always in need of music. As it turned out, the son-in-law did have some work to offer Buffett — write a 10-second jingle for a newly conceived, unlaunched, cable TV channel. Not knowing whether his work would ever see the light of day, he took the work anyway. Today Buffett is an Emmy Award-winning composer. But his lucky break — that jingle was for MTV — began by first engaging with a neighbor while washing his car.

During the month of June, I had the opportunity to attend two of our industry's biggest events — DIA's 50th Annual Meeting and the 2014 BIO International Convention. Both occurred in back-to-back weeks in San Diego. Though I had many beneficial discussions from planned appointments, some of my most fruitful engagements occurred from seemingly random, interpersonal collisions. For example, at DIA, Julie Conry, senior director of advancement and outreach for Batten Disease Support and Research Association, struck up a conversation with me at our booth, taking the time to share the parents' perspective of involving their children in clinical trials. Though Daniel Kerner, at the age of six, became the first U.S. child recipient of transplanted stem cells from an aborted fetus, it was his parents, Marcus and Joanna, who agonized over the decision. I often hear companies speak of defining and improving patient engagement. Perhaps a topic for DIA next year could include parent engagement? During BIO, I had a chance meeting with first time attendee, Michael Flanagan, Ph.D. I soon learned that Flanagan, CEO and founder of a new startup company with the working name FlanaGen, was formerly the CTO for Arieso, a networking software company acquired by JDSU for $85 million. Inspired by the work of his son, who is pursuing a bioengineering degree at Penn State, Flanagan decided to ply his mobile technology expertise in the world of life sciences. As he shared his vision of improving the quality of life for patients, I pondered who to connect him with that could help.

Frequently at shows and in life, I observe people constantly interacting with their cell phones, thereby failing to truly engage with the world and individuals in their immediate surroundings. What a missed opportunity. Don't let this be you. Take the time to let people amaze you. This is what we try to do and why we were able to capitalize on the opportunity to strengthen the Life Science Connect editorial team. Be sure to check out the work of our newest executive editor, Louis Garguilo, author of this month's cover feature on page 18, which he developed from an interview conducted in Japanese (Osaka dialect, to be precise) and then translated into English. L

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Q What Is The Best Leadership Advice You Ever Received?

A IT CAME FROM DR. RICHARD COUTO, a professor of leadership studies. He taught me that adjusting to change is much like transitioning through the stages of grief. While the leader has had the benefit of understanding why the change needs to happen, those being led may need time to adjust and to come on board. Continuous communication and patience are critical. This knowledge has been invaluable to me both as a leader of change within biotechnology and as a teacher of leadership at Johns Hopkins. All too frequently, great change ideas are implemented but fail because not enough information and time are given. Put together a core, guiding coalition of believers in the change, articulate the vision early and often to everyone, and especially communicate small wins. Once people see that the change is working, more will come on board.

LYNN JOHNSON LANGER
Lynn Johnson Langer, Ph.D., MBA, is president emeritus of Women In Bio (WIB) and the director of enterprise and regulatory affairs programs in the Center for Biotechnology Education at Johns Hopkins University where she teaches graduate courses in biotechnology leadership and management.

A I RECEIVED SOME GREAT ADVICE WHILE IN MY FIRST JOB at a large pharmaceutical company. I had previously worked at a biotech where the environment was fast-moving regarding processes and decision making. While trying to move at the same speed at the pharma company, I encountered a lot of "That's not the way things are done here" and the perception that there was always a wall in front of me. One of my colleagues observed my frustration and suggested I, "Just run right through the wall as if it's not there." His point was that often we find ourselves in a box of our own making, thinking there is a rule or a reason preventing us from taking action. Another mentor and friend of mine put it this way: "We are far more empowered than we realize."

DR. JOHN REYNDERS
Dr. John Reynders is the CIO for Moderna Therapeutics. He has held senior R&D and technology leadership positions at AZ, J&J, Lilly, Celera Genomics, and the Los Alamos National Laboratory.

A MY FIRST MENTOR IN BUSINESS WAS ART BENVENUTO, the CEO to whom I reported at my first company, Advanced Tissue Sciences. I used to drive him crazy by adopting the perspective of whoever had presented the most recent reasonable argument about a given business issue; then someone would present a reasonable counterargument, and I'd appear to adopt that position. I wasn't necessarily agreeing with the position, I was just "trying on" each perspective to see how it fit. But to people around me, the behavior could come off as indecisiveness. Art insisted I not appear to "sway with each passing breeze" and helped me understand that there can be a fine line between considering options thoroughly and appearing to be wishy-washy. That advice helped me grow Acorda from just myself and a laptop to more than 420 people and over $300M in annual revenue.

RON COHEN
Ron Cohen, M.D. is president, CEO, and founder of Acorda Therapeutics, Inc., a public biotechnology company developing therapies for spinal cord injury, multiple sclerosis, and other nervous system disorders.

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Obama Administration: Driving Provider Consolidation And Increased Costs

JOHN McMANUS The McManus Group

The increasing consolidation of healthcare providers has undeniable, deleterious consequences for consumers; yet what is the Obama Administration doing about it?

Making things worse.

A *New England Journal of Medicine* study by Kocher and Sahni asserted that "U.S. hospitals have responded to implementation of healthcare reform by accelerating hiring of physicians. More than half of practicing U.S. physicians are now employed by hospitals or integrated systems, a trend that is fueled by the intended creation of accountable care organizations."

Hospitals that acquire physician practices argue that it helps them coordinate care and control costs. But why are hospitals often acquiring physician practices for a price that is far in excess of what they can possibly bill? It seems irrational.

They do so to capture the referrals for all types of services. Kocher and Sahni state that, "To break even, newly hired primary care physicians (PCP) must generate at least 30 percent more visits, and specialists 25 percent more than they do at the outset. Hospitals are willing to take a loss employing PCPs in order to influence the flow of referrals to specialists who use their facilities."

A May 2014 *Health Affairs* study also found that when hospitals buy physician practices, the result is higher hospital prices and increased spending. The study performed by Stanford University researchers examined 2.1 million hospital claims and validates insurance companies' and economists' contentions that the main motivation is negotiating higher prices and capturing referrals.

Researchers at the Center for Studying Health System Change examined nearly 600,000 private insurance claims and found that average hospital outpatient department prices for common imaging, colonoscopy, and laboratory services are *double* the price for identical services provided in physician offices or other community settings. For example, the average price of a colonoscopy in a hospital was $1,383 compared to $625 in a community setting (e.g., ambulatory surgery center). Similarly, physical therapy prices were 41 percent to 64 percent higher in hospitals than in community settings.

The Federal Trade Commission has only sporadically engaged in such mergers and acquisitions. For example, it blocked a proposed merger in Idaho that would have given Boise-based St. Luke's Health system 80 percent of the physicians in Nampa, Idaho.

The Medicare Payment Advisory Commission has recommended that Medicare pay hospital-employed physicians for routine evaluation and management visits at the same rate as physician offices. Such a policy would reduce hospital reimbursement for those services by more than 56 percent and save more than $10 billion over 10 years. Congress has not acted on that recommendation, nor has the administration endorsed it.

Indeed, increasing payment disparities between the physician offices and hospitals for identical services appears to be a deliberate public policy of this administration and has made it quite difficult for physician practices to remain economically viable. Payment cuts to cardiology for services often provided in the office more than tripled the number of cardiologists employed by hospitals between 2007 and 2012. Now the Center for Medicare and Medicaid Services proposes eliminating reimbursement for the "radiation treatment vault," which protects healthcare professionals, caregivers, and others from such radiation and is integrally tied to the linear accelerator itself. If this proposal is finalized, payments to physician-led,

"A May 2014 Health Affairs study also found that when hospitals buy physician practices, the result is higher hospital prices and increased spending."

community-based centers would be cut by more than 10 percent but leave hospitals untouched.

It should be no surprise that such policies have discouraged many physicians from continuing to operate free-standing practices. A recent study by Merritt Hawkins found a substantial shift toward the employed physician model with more than 90 percent of new physician job openings at hospitals and other facilities and just 10 percent in independent practice settings.

OBAMA PROPOSAL ON SELF-REFERRAL UNFOUNDED AND DRIVES CARE TO HOSPITALS

Despite these alarming trends and cost implications to the healthcare system, the Obama Administration offered a proposal that would make it illegal for integrated physician practices to provide "ancillary services," such as advanced imaging, radiation therapy, anatomical pathology, and physical therapy. The President's Budget proposed to eliminate the so-called "in-office ancillary services exception" (IOASE) provision that allows integrated physician practices to incorporate these services.

The administration argues that the IOASE provision has encouraged overutilization because physicians will consume more resources when they refer services to their own practices. A series of Government Accountability Office (GAO) reports supports that narrative ... at first glance.

But a deeper dive into the data offered by the GAO and analysis of all of Medicare claims since 2007 contradicts the assertion that physician-led care has resulted in overutilization.

- Advanced Imaging: Utilization of advanced imaging, which has drawn the most focus of self-referral opponents, has actually declined in the physician office recently. Medicare spending for CT and MRI services dropped from $4.1 billion in 2007 to $3.7 billion in 2012 and, at the time of the research, was headed toward $3.5 billion in 2013.

- More than three-quarters of these services are provided in the more expensive hospital setting.

- Radiation Therapy: In its report on radiation therapy, the GAO observed that although utilization of IMRT (intensity modulated radiation therapy) services for prostate cancer increased by self-referring groups, it was offset by decreases within hospitals and non-self-referring groups. "Overall utilization of prostate cancer-related IMRT services, therefore, remained relatively flat across these settings," the report said.

- Physical Therapy: the GAO found that "from 2004 to 2010, non-self-referred physical therapy (PT) services increased at a faster rate than self-referred PT services. During this period, the number of self-referred PT services per 1,000 Medicare fee-for-service beneficiaries was generally flat, while non-self-referred PT services grew by about 41 percent."

If physician practices are prohibited from offering these services through legislative fiat — as the Obama Administration proposes — this care will be forced into the more expensive and less convenient hospital setting.

This radical proposal has sparked alarm and outrage among physicians. A coalition of more than 30 specialty physician groups and the American Medical Association, representing hundreds of thousands of physicians, wrote Congress to object to this proposal, stating that it would undermine the viability of the independent physician practice model and "result in the further centralizing of care around a few dominant hospital systems, which will undermine competition, and in turn, raise costs to the entire healthcare system over the long term."

Most Republicans have been unwilling to dictate how physicians should structure their practices or where care should be delivered. But the proposal has drawn interest from some Democrats who view it as appropriate to helping finance a long-term solution to pending Medicare physician cuts and other priorities.

While hospitals have not actively lobbied for the proposal, they certainly prefer it over further hospital cuts, such as site-of-service payment neutrality. That makes it a viable threat and just one more catalyst to further consolidation, which will only raise costs to consumers.

It is time to step back and take a longer view of healthcare policy. Where should most elective health care take place, in the hospital or community setting? And what policies should be pursued to reverse the current trend? 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.

ARSANIS BIOSCIENCES

A pioneer and crusader in the almost-abandoned field of antibiotics is out to show the world how to fight the nastiest bacteria with monoclonal antibodies.

WAYNE KOBERSTEIN Executive Editor

SNAPSHOT

Arsanis is one of a few small companies pioneering the use of monoclonal antibodies in antibiotic therapies. Now on the cusp of transition from preclinical to clinical development, the company's lead program is with a cocktail of antibodies directed against Staphylococcus aureus, the cause of severe hospital-acquired infections. Additional programs follow in gram-negative bacteria, Streptococcus pneumonia, and other infection areas.

WHAT'S AT STAKE

There is a good, if anthropic, reason why you have probably never heard of Arsanis: It qualifies under one of the natural selection criteria for "Companies to Watch" — obscurity. From its research origins in Vienna to its choice of the nearly deserted anti-infective area, the company has designed itself to fly under the radar of journalists prowling the halls of the recent BIO meeting to cover the hotter areas of biopharma innovation — cancer, diabetes, and senility. Its cofounder and scientific leader is similarly soft-spoken and understated in her description of the company's founding premise.

"I developed the idea of using monoclonal antibodies, which are very successful in the cancer and in the autoimmunity areas, in the new field of infectious diseases," says Eszter Nagy, MD, Ph.D., president and CSO. "It is a pioneering idea, but because of all my research and experience, I was convinced the antibodies are augmentative to antibacterial therapy." Dr. Nagy points to the obvious gap in the current priorities of biopharma R&D. "The infectious disease field is in a crisis. It is the only field of medicine where we are actually going backwards, and some fear we will soon reexperience the pre-antibiotic era, when we cannot really treat certain infectious diseases."

Companies have stepped away from developing new antibiotics partly because they are much less profitable than, say, cancer drugs, but also because they are used only for acute, not chronic conditions and face short product life cycles due to bacteria's ability to develop drug resistance quickly. The Arsanis strategy addresses the latter set of challenges — extending use to prevention and life cycle by avoiding resistance. Many of its products combine several mAbs (monoclonal antibodies) in a single treatment, targeting the most virulent and resistant strains of bacteria. Unlike vaccines, the mAbs are likely to work even in immuno-compromised patients, and they avoid another weakness of current antibiotics, which "do not support immune defense or prevent damaging inflammatory responses," according to the company.

Dr. Nagy worked for 12 years as an R&D leader at Intercell in Vienna and then moved on to join forces with Arsanis co-founder Tillman Gerngross, who is also the founding CEO of her company's main partner, Adimab. Vienna, the base for her continuing research, has spawned its own biotech community, belying the creative vein that runs beneath the city's conservative façade. With its corporate home in New Hampshire, however, Arsanis competes in the U.S. biotech sector, where its novel approach may have more opportunity but must also survive in the world's toughest life science industry environment.

Arsanis has a broad pipeline targeting various bacteria species and strains. "We think our technology is applicable to all or many infectious diseases, and every bacterium is different so we cannot apply the same approach to every one. First, there's a need to show that these antibodies work in various types of bacteria, and the first successes, not only clinical successes, but also when you publish your data for how they work in different disease models, can really help the field grow and encourage others to use this augumentative approach." With sufficient arrays of mAbs and mAb cocktails, physicians will have a choice of tools based on each patient's needs, in some cases guided by companion diagnostics. L

ESZTER NAGY.
President & CSO

Vital Statistics

34
Employees

Headquarters
Corporate:
Lebanon, NH, USA
R&D: Vienna, Austria

Finances

$30M
VC, 2 rounds (2010, 2013)
Investors:
OrbiMed, Polaris,
SV LifeSciences, NeoMed

$10M
R&D (Austrian Research Promotion Agency)
potential $20M next 3 years

Partnerships

Strategic partnership with Adimab LLC for antibody discovery against infectious targets

Latest Updates

Late 2013: Lead program, ASN-100, a monoclonal antibody cocktail to prevent and treat severe hospital-associated Staphylococcus aureus infections, enters preclinical development; due to enter the clinic within 18 months.

Follow-on gram-negative program, targeting multi-drug resistant Escherichia coli at candidate selection phase - lead selection planned for late 2014.

Q3 2013: $20M Series B round closed.

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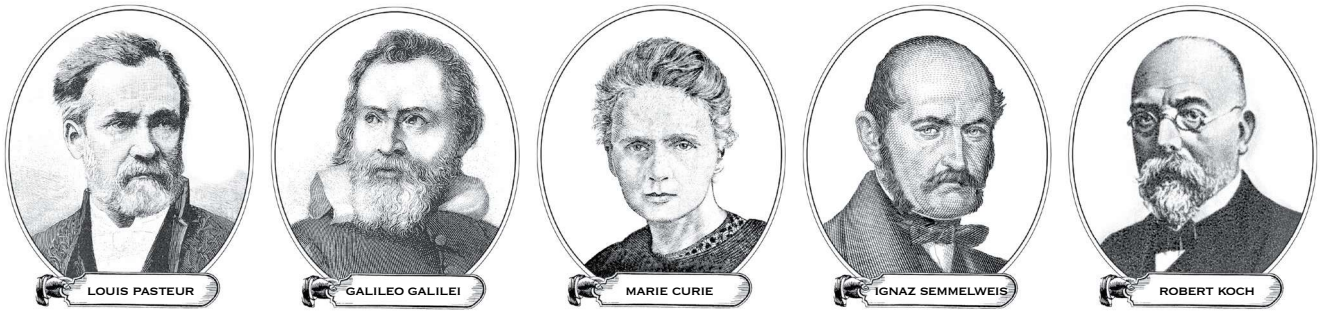

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Emerging Pharma and Emerging Biotech Value Different Traits in CROs

Much as when it comes to choosing a contract manufacturer, CRO selection practices and outsourcing needs vary. Whether it's business size, like comparing Big Pharma to emerging pharma, or business type, in comparing a biologics-focused company to a small molecule company, it is important to know which business traits contribute to a mutually successful partnership.

KATE HAMMEKE
Director of Marketing Intelligence
Nice Insight

> *"Emerging biotech respondents indicated a stronger interest in forming strategic partnerships with CROs than did emerging pharma respondents."*

And on the seller side, it is important to know which sales tactics reach the audience in need of your business' services. The results of Nice Insight's annual outsourcing survey show that there are many differences in how emerging companies perceive outsourcing to CROs, depending on whether it is an emerging pharma company or an emerging biotech.

Starting with how these businesses identify potential CRO partners, the methodologies differed. Emerging pharma companies place a significant amount of importance on referrals from colleagues (71 percent), followed by industry research (66 percent), and consultants (56 percent), whereas emerging biotechs showed less reliance on referrals (29 percent, placing third in priority) and more on industry research and consultants (tied for first priority with 52 percent). Emerging biotechs seek out CROs at trade shows and events (38 percent, and second most popular method for identifying a new CRO); however, it seems that their event focus may be more manufacturing centric, with more than half of emerging biotech respondents stating they attend trade shows to identify CMOs (53 percent).

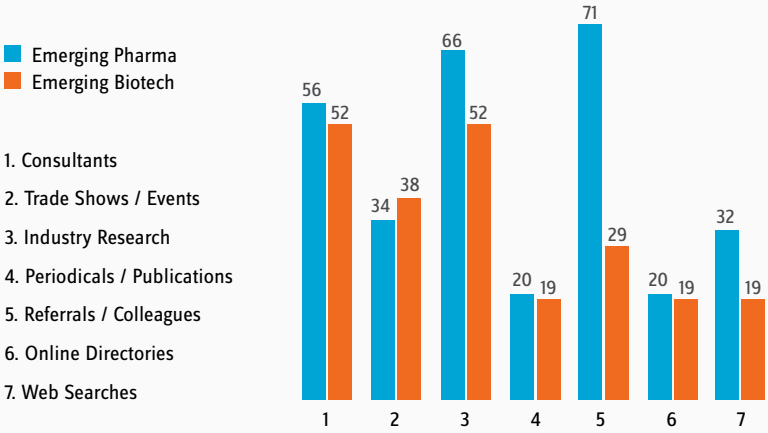
Behavioral differences continue when it comes to allocating projects to different categories of suppliers. Emerging pharma companies assign only 27 percent of their projects to tactical service providers, as compared to emerging biotechs that assign 34 percent of projects to tactical providers. Interestingly, emerging pharma companies are less likely to use tactical service providers for contract research work than they are for outsourced manufacturing projects (27 vs. 32 percent). It was also surprising to find that emerging pharma companies allocated slightly fewer projects to strategic partnerships with CROs than with CMOs (29 vs 31 percent) and assigned the bulk of projects to preferred providers (44 percent).

EMERGING BIOTECHS ARE MUCH MORE INTERESTED IN FORMING STRATEGIC PARTNERSHIPS WITH CMOs THAN CROs

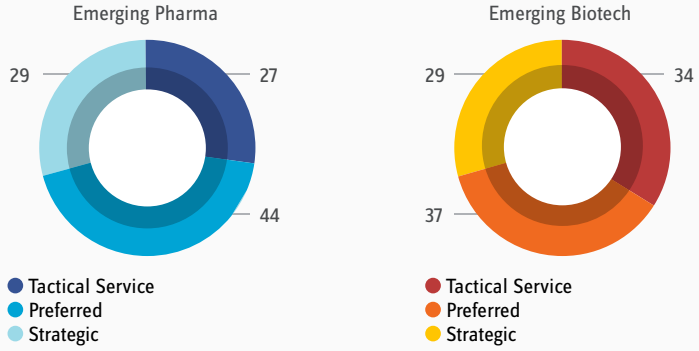
Meanwhile, allocating projects to the various supplier types was more consistent among emerging biotechs. This buyer group tends to use the three provider types similarly for outsourced work to both CROs and CMOs, with a slightly greater tendency to use preferred providers for CRO projects (37 vs 35 percent) and strategic partners for CMO projects (29 vs 31 percent, respectively). Emerging biotech respondents indicated a stronger interest in forming strategic partnerships with CROs than did emerging pharma respondents (52 vs 46 percent); however, these buyers were much more interested in forming strategic partnerships with CMOs than CROs (75 vs 52 percent). Conversely, emerging pharma companies were slightly more interested in forming a partnership with CROs than CMOs (43 vs 46 percent).

Emerging companies continue to show differences in outsourcing behavior with respect to the level of influence different traits have on CRO selection. For example, adaptability and a history of success tied for top influencers among emerging pharma outsourcers, while experience ranked first among emerging biotechs that outsource work to CROs. Some of the greater differences appeared in viewing how emerging pharma companies prioritized the range of services offered by a CRO (#3) versus how emerging biotechs ranked the offering (#6). Another area with strong differences in priority among

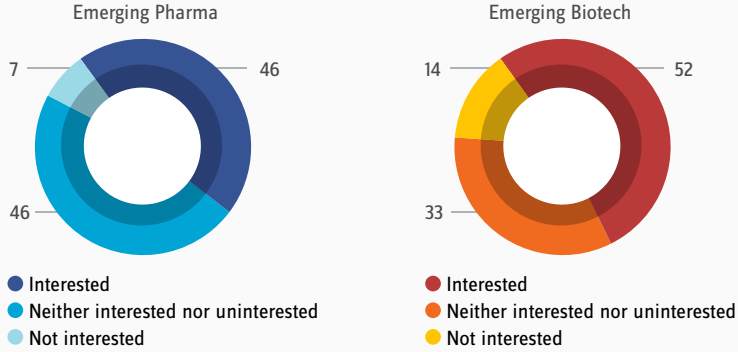
How Emerging/Niche/Startup Buyers Identify CROs (%)



Percentage of Projects that Will Be Contracted to Each Type of Outsourcing Relationship



Interest Level in a Strategic Partnership with a CRO (%)



Survey Methodology: The Nice Insight Pharmaceutical and Biotechnology Survey is deployed to outsourcing-facing pharmaceutical and biotechnology executives on an annual basis. The 2013-2014 report includes responses from 2,337 participants. The survey is comprised of 240+ questions and randomly presents ~35 questions to each respondent in order to collect baseline information with respect to customer awareness and customer perceptions of the top 100+ CMOs and top 50+ CROs servicing the drug development cycle. Five levels of awareness from "I've never heard of them" to "I've worked with them" factor into the overall customer awareness score. The customer perception score is based on six drivers in outsourcing: Quality, Innovation, Regulatory Track Record, Affordability, Productivity and Reliability. In addition to measuring customer awareness and perception information on specific companies, the survey collects data on general outsourcing practices and preferences as well as barriers to strategic partnerships among buyers of outsourced services.

these groups was using offshore contractors to save on costs — the lowest priority (#8) among emerging pharma businesses and fourth priority among emerging biotech companies.

Differences among emerging buyers continued when reviewing the less tangible attributes that influence CRO selection. Interestingly, while emerging biotech companies were less likely to use referrals as a source of identifying new partners than emerging pharma companies were, once a company has made it to the shortlist, references from colleagues became the highest-ranking trait for this group. Emerging pharma companies placed communication at the top of the list, followed by responsiveness and the rapport between teams — and references from colleagues came in seventh. Emerging biotechs also prized good communication and responsiveness, yet these attributes received a lower frequency of mention (by roughly 20 percentage points) and tied with other soft traits, such as willingness to go the extra mile and a company's reputation for doing quality work (second and third, respectively).

This information is especially useful to buyers of contract services when engaging a business for both research and manufacturing work. Be mindful of which traits are strongest for the services that your company will be engaging the provider for, and whether the contract service provider excels in the traits that matter to outsourcing peers who have formed successful relationships with CROs.

N. WALKER

If you want to learn more about the report or how to participate, please contact Nigel Walker, managing director, or Kate Hammeke, director of marketing intelligence, at Nice Insight by sending an email to nigel@thatsnice.com or kate.h@thatsnice.com.

Bio/Pharma Industry Improves Downstream Operations

Best Practices: Membrane Technology Options

ERIC LANGER
President and Managing Partner
BioPlan Associates, Inc.

Downstream purification includes multiple steps, such as intermediate and polishing chromatography and virus filtration. Many of those steps involve drug products at their most valuable — where a lot of work has already been done and a misstep can risk millions of dollars. So a lot of interest is paid to efficient operations. And as upstream productivity increases, running the downstream side of facilities without creating capacity problems has become a key concern. Challenging aspects of downstream operations include cost of chromatography materials, lack of single-use (disposable) options, cost of membranes, and cleaning and validation costs. Avoiding the high cost of Protein A affinity resins is a goal, but most biomanufacturers are reluctant to make any changes to existing processes, and there are, as yet, few alternatives proven at a larger scale.

As results from our *11th Annual Report and Survey of Biopharmaceutical Manufacturing* (see www.bioplanassociates.com/11th) attest, industry suppliers and end users are developing and evaluating new technologies for improving their downstream processes. As part of our annual survey, we evaluated factors that have led to improvements in operations as well as to the new technologies under consideration.

CYCLING COLUMNS VS. INVESTIGATING NEW TECHNOLOGIES

Our study reveals that 57 percent of respondents cycled columns more frequently last year to improve their downstream purification operations; that's a big increase from recent years (~40 percent from 2011 through 2013). Ion exchange technologies are also being investigated to a significant degree:

- Slightly more than half of the industry used or evaluated alternative ion exchange technologies, such as higher capacity; and
- Slightly fewer than half used or evaluated ion exchange membrane technologies. (See figure 1)

Results from our study indicate that a significant proportion of industry respondents report changing buffer volumes, actively identifying/assessing bottleneck points, and investigated alternatives to protein A.

As in recent years, though, interest in Protein A alternatives is far greater than actual implementation. Although 3 in 10 purported to have *investigated* alternatives, fewer than 7 percent claim to have actually *made the switch* to using alternatives.

For nearly every implementation factor, CMOs report higher levels of adoption, with this likely a reflection of their dependence on efficiency, their managing multiple projects and high turnover, and their ability to pass the costs of new technology implementation onto developers. Indeed, the data is clear that CMOs lead developers in implementing new downstream technologies.

Protein A alternatives provide a good case in point: While biotherapeutic developers were almost twice as likely as CMOs to say they had investigated alternatives to protein A, CMOs were nearly four times as likely as developers to say they had actually implemented alternatives. The results suggest that the technology evaluation process is lengthier for developers than for CMOs, who are more willing to try out new technologies on the basis of the factors outlined above.

MEMBRANE TECHNOLOGY TAKES A LEAP

In addition to evaluating implementation of downstream technologies, our study looked at the new or alternative technologies respondents are considering currently by asking respondents, "Which new downstream purification (DSP) technologies are you actively considering to address bottlenecks and problems?" Note, this only asked about "actively considering," indicative of potential future adoption, with this not including those already having adopted these technologies and those considering, but not "actively" pursuing this interest.

On this front, while the use of high-capacity resins was again the most widely-considered technology, the largest indus-

try shift was toward membrane technology. This year, 49 percent of respondents indicated that they are actively considering membrane technology, roughly double the proportion observed in recent years (20-26.5 percent from 2010 through 2012). Consideration of membrane technology was high among both U.S. and Western European respondents and was a top-two consideration for both developers and CMOs.

CMOs showed greater levels of interest in most technologies identified in the study — prepacked columns (64 percent of CMOs versus 30 percent of developers) and use of filters instead of resin chromatography (45 percent of CMOs versus 23 percent of developers). Some of the largest discrepancies occurred in regard to single-use products.

There were some areas, though, in which developers showed keener interest:

- online analytical and control devices
- centrifugation
- development of mAB (monoclonal antibody) fragments
- 2-phase systems.

A small proportion of developers is also considering countercurrent chromatography and field fractionation, with these technologies not generating any interest from CMO respondents.

Interestingly, respondents in Western Europe outpaced those in the U.S. in consideration of the majority of technologies, with some notable exceptions being for disposable UF (ultra filtration) systems, in-line buffer dilution systems, and centrifugation.

SOLUTIONS ARE STILL FORTHCOMING

Our survey data continue to show that U.S. and European biomanufacturing facilities are considering — but slowly adopting — improvements and new downstream technologies. Overall, CMOs, not developers, are taking the lead in adopting new or streamlined DSP approaches, with CMOs much more motivated by cost savings and associated needs to develop and adopt standardized manufacturing platforms.

The survey captures continued concerns regarding the limitations of existing facilities to keep up with the relatively rapid increases in titer from upstream processes. There is no reason to think that this issue will go away. Upstream process development will continue to improve, and facilities that have a fixed DSP capability will therefore continue to push their DSP to feasible limits. L

FIGURE 1

Selected Options for Improving Downstream Operations, 2011-2014

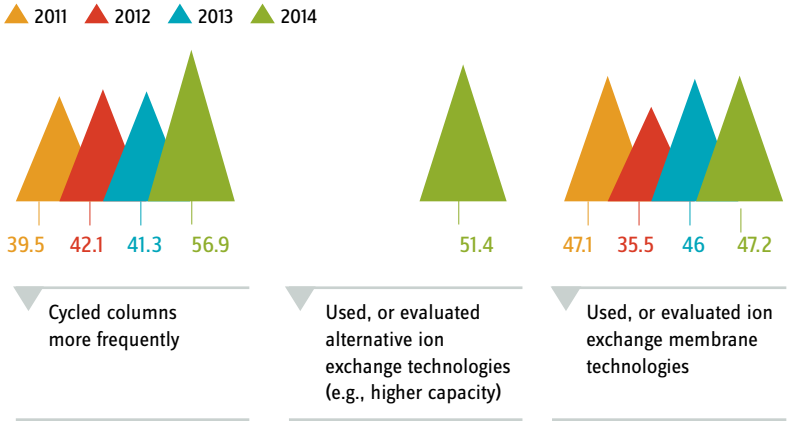
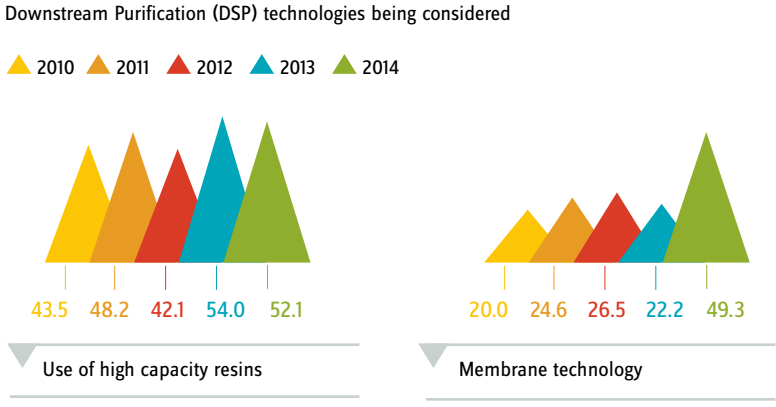


FIGURE 2

Top New Downstream Processing Solutions Comparison, 2010-2014



Source: *11th Annual Report and Survey of Biopharmaceutical Manufacturing,* April 2014, www.bioplanassociates.com/11th

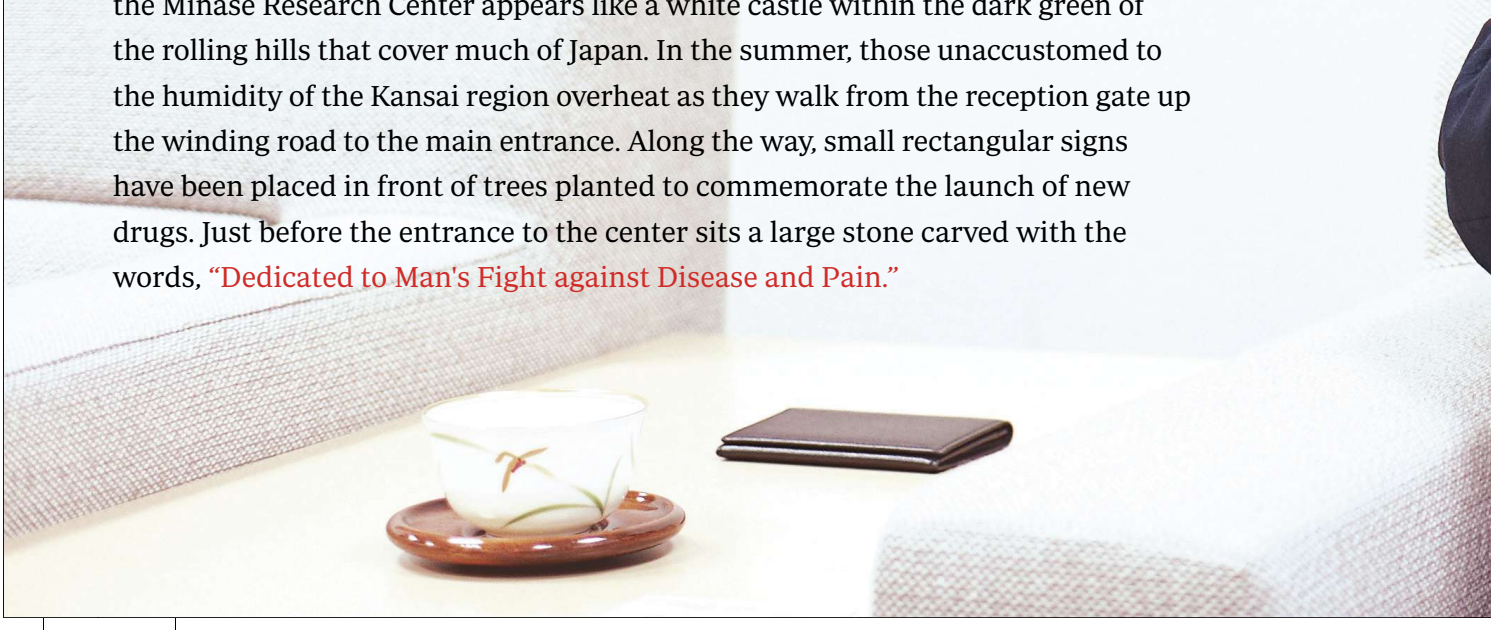
Survey Methodology: The 2014 Eleventh Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production yields a composite view and trend analysis from 238 responsible individuals at biopharmaceutical manufacturers and contract manufacturing organizations (CMOs) in 31 countries. The methodology also included over 173 direct suppliers of materials, services, and equipment to this industry. This year's study covers such issues as: new product needs, facility budget changes, current capacity, future capacity constraints, expansions, use of disposables, trends and budgets in disposables, trends in downstream purification, quality management and control, hiring issues, and employment. The quantitative trend analysis provides details and comparisons of production by biotherapeutic developers and CMOs. It also evaluates trends over time and assesses differences in the world's major markets in the U.S. and Europe.

ONO PHARMACEUTICAL STRIVES FOR GLOBAL SALES

Gyo Sagara, president, representative director and CEO, challenges his company to enter the cancer field and gain big-pharma relevance.

LOUIS GARGUILO Executive Editor, Outsourced Pharma

AS THE TRAIN PULLS INTO SHIMAMOTO STATION BETWEEN OSAKA AND KYOTO, the Minase Research Center appears like a white castle within the dark green of the rolling hills that cover much of Japan. In the summer, those unaccustomed to the humidity of the Kansai region overheat as they walk from the reception gate up the winding road to the main entrance. Along the way, small rectangular signs have been placed in front of trees planted to commemorate the launch of new drugs. Just before the entrance to the center sits a large stone carved with the words, "Dedicated to Man's Fight against Disease and Pain."



Most everything about Ono Pharmaceutical Co., Ltd., is quintessential Japan. That includes the determination of its trim, youthful, 56-year-old leader to make his the next Japanese company of global reckoning. And he believes he has the cancer immunotherapy drug to get him there.

I HAD THE OPPORTUNITY TO TALK TO GYO SAGARA, president, representative director and CEO, on a day spared the normal downpours of the early summer rainy season. Our discussion was in Japanese (Osaka dialect, to be precise) and translated into English for this article.

Sagara knows what he wants to talk about. "For the first time in our history," he says, "Ono will launch a cancer immunotherapy agent, Nivolumab. This is an antibody-based drug with a new mechanism of action that will have a major impact on patients, further research around the world, and Ono itself. We believe Nivolumab will have efficacy in several cancers, including malignant melanoma, non-small-cell lung cancer, and renal cell carcinoma. For the first time in the world there is a drug targeting the PD-1 [programmed death-1] pathway. We are determined to develop a new class of drugs based on Nivolumab. This will bring Ono international recognition and transform us into a true global pharmaceutical company."

Nivolumab was designated as an orphan drug indicated for malignant melanoma by Japan's Ministry of Health, Labour and Welfare on June 17, 2013. In December 2013, Ono officially filed an application to obtain "manufacturing and marketing approval for human IgG4 PD-1 immune checkpoint inhibitor Nivolumab." Sagara is optimistic approval is coming. "Maybe by the time this article comes out," he adds hopefully. (Editor's Note: Sagara and Ono got their wish: On July 4, 2014 Ono announced it had received manufacturing and marketing approval from Japan's Ministry of Health, Labour and Welfare [MHLW] "for the human anti-human PD-1 monoclonal antibody 'OPDIVO Intravenous Infusion 20 mg/100 mg' [OPDIVO] for the treatment of unresectable melanoma." OPDIVO is Nivolumab's product name for the global market.)

For Sagara, the story of Nivolumab reveals the type of company Ono is and what it wants to become on a much grander scale. The antibody work originated in the laboratories of Kyoto University, led by Professor Tasuku Honjo. In 2000, Ono selected Medarex, Inc., a biopharma company in the U.S. and a specialist in the field, as a partner to develop a drug. Ono out-licensed the U.S. market to Medarex, maintaining rest-of-world rights. In 2009, Bristol-Myers Squibb (BMS) obtained Medarex, and subsequently, in 2011, Ono granted the much bigger and more experienced BMS exclusive rights to develop and commercialize Nivolumab in rest-of-world outside of Japan, Korea, and Taiwan — Asian markets Ono has prowess in.

Ono is already being rewarded for its faith in BMS. In 2013, the FDA granted "Fast Track designation" for Nivolumab in non-small-cell lung cancer, melanoma, and renal cell cancer. Then in May of this year, the FDA further granted Nivolumab "breakthrough therapy designation" for the treatment of patients with Hodgkin's lymphoma after the failure of autologous stem cell transplant and Brentuximab. On June 24th, BMS announced that a randomized blinded comparative Phase 3 study evaluating Nivolumab versus Dacarbazine in patients with previously untreated BRAF wild-type advanced melanoma was stopped early because an analysis showed evidence of superior overall survival in patients receiving Nivolumab compared to the control group. Patients in the trial, named CheckMate-066, will be allowed to cross over to Nivolumab.

According to Michael Giordano, MD, head of oncology development for BMS, "The outcome of CheckMate-066 is an important milestone in the field of immuno-oncology, as it represents the first well-controlled,

randomized Phase 3 trial of an investigational PD-1 checkpoint inhibitor to demonstrate an overall survival benefit."

At Ono, Sagara ensures the value in leveraging this type of partnership is fully recognized. "I tell our employees that, like each step in the discovery, development, and commercialization of this new drug, they should always seek partnerships with the best scientists and companies in the world," he says. "This should work hand-in-hand with our own internal research and development. We'll benefit from combinations of internal and external expertise in all scientific and business areas," Sagara says.

EMERGING FROM THE VOID

Sagara is focused on the future, but he uses the lessons of the past as fuel to get there. He often reminds his employees that once before Ono gambled on a new scientific field of study to propel the company forward.

"Out of the poverty of post-war Japan came the seeds of great innovations and world-renown companies, such as Matsushita, Toyota, and SONY," says Sagara. "Ono was there as well. We put the survival of the company on the line, and in doing so we were in danger for a few years, focusing all our resources on the prostaglandins (PG) field. Outside of Ono and Upjohn, this was a field that no one else was pursuing. However, we fully embraced the challenge, and in 1968 we were the first in the world to synthesize prostaglandins. Although nowadays our situation is much more secure and stable, I want our employees to again embrace that same confidence and spirit."

It is not unusual, then, for Sagara to have Konosuke Matsushita, founder of Matsushita Electric Industrial Company, as one of his role models. In 1917, Matsushita started what remains today one of the largest commercial electronics companies in the world, now known globally as Panasonic. Sagara says it is very common to have Matsushita as a role model, "However, his management philosophy speaks directly to me in my daily activities. He believed that there is no value in establishing businesses unless the undertaking contributes to society at large. His most important teaching is to treat all things with an open heart. Look clearly at the essence of what is in front of you without prejudice. Make the correct decisions and judgments based on this openness."

2017: ONO'S PAST AND PRESENT MEET ITS FUTURE

Each day, the year 2017 drives Gyo Sagara. It represents the 300th anniversary of the founding of Ono and also its 70th anniversary as a corporation. Sagara wants to have realized the

Japan Pharma and the Nikkei

Ono Pharmaceutical and 16 other pharma companies in Japan belong to the Nikkei stock index. Next to the Dow Jones Industrial Average (DJIA) and the S&P 500, Japan's Nikkei 225 and its less exclusive partner the Nikkei 500 — both referred to as the Nikkei — are two of the most cited indexes in the world. The Nikkei is important because it tracks stocks in the third-largest economy and the second-largest pharmaceuticals market in the world, and also because of its advantageous time zone, which provides global investors a first look at how Asian investors are reacting to global news.

It seems a bit odd, then, that in our industry the pharmaceutical sector of the Nikkei receives such little attention and analysis. Nonetheless, it is a key barometer of the state of Japan's pharma industry. Pharmaceutical companies in the elite 225 are (Nikkei listing precedes the name):

4151	Kyowa Hakko Kirin Co., Ltd.
4502	Takeda Pharmaceutical Co., Ltd.
4503	Astellas Pharma Inc.
4507	Shionogi & Co., Ltd.
4508	Mitsubishi Tanabe Pharma Corp.
4519	Chugai Pharmaceutical Co., Ltd.
4523	Eisai Co., Ltd.
4568	Daiichi Sankyo Co., Ltd.
4581	Taisho Pharmaceutical Holdings Co., Ltd.

Ono and the following companies are added to form the broader Nikkei 500:

4506	Dainippon Sumitomo Pharma Co., Ltd.
4521	Kaken Pharmaceutical Co., Ltd.
4528	Ono Pharmaceutical Co., Ltd.
4530	Hisamitsu Pharmaceutical Co., Inc.
4536	Santen Pharmaceutical Co., Ltd.
4540	Tsumura & Co.
4569	Kyorin Holdings, Inc.
4578	Otsuka Holdings Co., Ltd.

All in all, these are quite impressive lists. Japanese companies may talk less to investors than their counterparts globally, but companies with steady earnings (and strong sales and pipelines) might be worth a look. For example, Ono's stock is up 27% for the last 12 months and has a total return over the period of ~36% when its dividend is included.

> "We are devoting resources to more aggressively take our compounds into Asia."

GYO SAGARA
President, Representative Director and CEO

pharmaceutical company of his dreams by then. He focuses on this historic juncture ... but only to a point.

"We are approaching 300 years of history, and like all CEOs I always think about our employees and their families, patients, and shareholders, but I'm careful not to do all this to the point of becoming too nervous!" he jokes, using an idiom often heard in Osaka. "I do feel responsible because we are approaching this particular milestone," Sagara continues. "Our real mission is to complete 300 years of history by establishing a bright future, filled with global aspirations and large ambitions. This is the focus."

A NEED FOR MORE SPEED

Sagara has provided us an overview of Ono's past and future aspirations, so let's discuss the here-and-now. Ono's top-line sales number has hovered near $1.5 billion (U.S.) for the past five years, increasing 6.8 percent from 2009 to $1.4 billion during the 2013 fiscal year (ending March 31, 2014). Net income has also remained relatively steady over the five-year period, coming in at $199.5 million in fiscal year 2013. The employee base has also stayed constant at just over 2,800 in 2013. Ono has a variety of commercial products on the market; the pipeline appears to be strong with a list of over 40 drugs in phase study in its 2013 annual report. It has focused discovery efforts on what could be global, high-value areas such as bioactive lipids, enzyme inhibitors, and membrane transporter regulators. And of course the newer focus on oncology, the first result of which is Nivolumab.

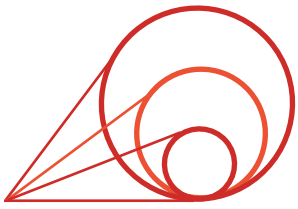
One thing is clear: With the bulk of Ono's sales — 98 percent — still derived from the domestic market, Sagara has his work cut out for him to gain a global share of drug sales.

Ono has forged international relationships to help grow overseas sales of its commercial products. For example, along with a strong relationship with BMS, Ono has codevelopment or licensing agreements with AstraZeneca, Merck Serono, Novartis, and Japan's Astellas. The company is open to working with CROs and CMOs around the world. It has announced discovery alliances with a variety of international partners such as BioFocus (U.K.), Domain Therapeutics S.A. (France), Receptos Inc. (U.S.), and Evotec (Germany). When asked how Ono selects its partners, Sagara replies, "We select these companies and relationships based on the specific science or technology necessary for a project, no matter where that may be, so the basic criteria differ in each case."

Sagara leans forward for emphasis. "At this point we are still a small company, and people from the outside may look at us as a bioventure," he says, choosing the term the Japanese use for small or specialty pharma, "but now we have a big agenda."

He continues, "We are devoting resources to more aggressively take our compounds into Asia, which has been an initial focus for us, and then the European and U.S. markets.

"Recently, we established a Translational Medicine Center (TMC) and new CMC Research Center (CRC). We have established a new office in Korea, OPKR, and in



Big Pharma: The Logic of Numbers And Scale

Not only does Gyo Sagara want to lead Ono Pharmaceutical into the club of "global pharma" (and if you are reading this for the first time, you have not been paying attention), but he also has thoughts regarding some of the current membership.

"Every company has to make its own business decisions," he starts carefully enough, "but I am concerned with the mega-pharma mega-merger syndrome." While Sagara says that nothing is for certain, "If this does continue, it will look like Big Pharma vs. fewer and fewer smaller companies, in a competition. They say 70 percent of drugs are not discovered by Big Pharma but by biotechs, bioventures, and universities. Therefore, this may not be the best way to move forward."

Sagara continues: "The logic of numbers and the logic of scale are gaining more and more influence over decision-making. Marketing and sales for certain employ the logic of numbers and scale, but now also clinical development and trials are based on this type of calculation. However, drug discovery — medicinal chemistry and other aspects — can't necessarily deliver reliable results based on this thinking.

"New drug discovery and development are at a reduced point," continues Sagara. "People in developed countries have longer life spans; populations in developing countries are increasing. Are more mergers really good for patients waiting for drugs, and for the industry itself? I am concerned we would somehow risk taking a step backward."

fact I will let you know we are reorganizing our presence in the U.S. at this moment, something not yet fully announced.

"Speed is holding us back," he suddenly interjects. "To compete globally, we need to speed up our activities, including planning and implementing of clinical trials, our approach to marketing and sales, and even in our labs and production facilities."

Since Japanese companies are not known for a management style that promotes quick decision-making, I asked if his plan to speed up included board decisions and executive management. "Yes, we need to organize our company hierarchy and speed up all activities," answers Sagara. "We need to make quicker decisions regarding scientific collaborations, for one thing. When we identify specialists around the world, we should reach out to them immediately. For example, we have hired a number of scientists from abroad as special consultants, including such well-known scientists as Dr. George Hartman, former executive director at Merck & Co."

Sagara continues, "We also need to adapt new technologies from around the world more quickly. We have a special team, Discovery Research Alliance (DRA), with members located here in Japan, the U.S. and the U.K., who are tasked with searching globally for specialists and leading technologies. We are taking on all these activities and moving in the right direction." Sagara says, "But if you ask me if there is one concern I have: It is that we still need more progress on what I call 'accelerating to the speed of global competition.'"

It might be expected that Sagara is all about moving fast; his ascension to his current role was born of speed. He started at Ono in 1983 and worked his way through the organization by holding leadership positions in operations and business and sales but then was suddenly named to replace Daikichi Fukushima, after Fukushima served as president and CEO for only two months. At the time (2008), Ono said the move would allow Fukushima to take on the newly created role of head of global research strategy to focus on Ono's R&D pipeline. The Nivolumab project actually originated in a research group headed by Fukushima, and according to Sagara, this re-organization is emblematic of a more agile company, both in the decision-making process and the resulting new organization.

The Human Reaction

Ono Pharmaceutical Co., Ltd., has been an active participant in global outsourcing across the drug discovery, development, and manufacturing continuum. I had the opportunity to work with the company for a number of years when I led business development in Japan for a U.S.-based CRO/CMO with international locations. In its pursuit of the best scientific expertise and strategic options applied to the stage and type of program it was outsourcing, Ono was very open to utilizing new facilities and locations. In fact, on some projects during our relationship, we had scientific teams working simultaneously at facilities in New York and Washington in the U.S., and Hungary and Singapore abroad.

Outside of the scientific and strategic considerations for a new location, Ono insisted on one other inviolable prerequisite: All facilities must participate "face-to-face" in combined video conferences. Unfortunately, as we added locations, my company started to realize that our conferencing equipment was inadequate. Since Ono was running projects from multiple sites in Japan, its equipment also became lacking in capacity.

The solution? Ono purchased a new video-conferencing system compatible with and able to bring together simultaneously all the sites at both parties working on the common project. In effect, the sponsor assisted the provider in meeting the sponsor's needs. This is surely an early example of the more mutual and deeper sponsor-provider relationships we hear so much talk about nowadays.

At that time, our main conduit for the Ono relationship, Takuya Seko (who is currently heading the newly formed CMC group), explained the strong stance on video conferencing: "Ono's executive management believes it is as important to see the human reaction as it is the chemical or biological reaction." Now, years later, having met Ono's new CEO, Gyo Sagara, it is clear that tenet starts at the top and still stands.

THE FIRE OF A CHALLENGER

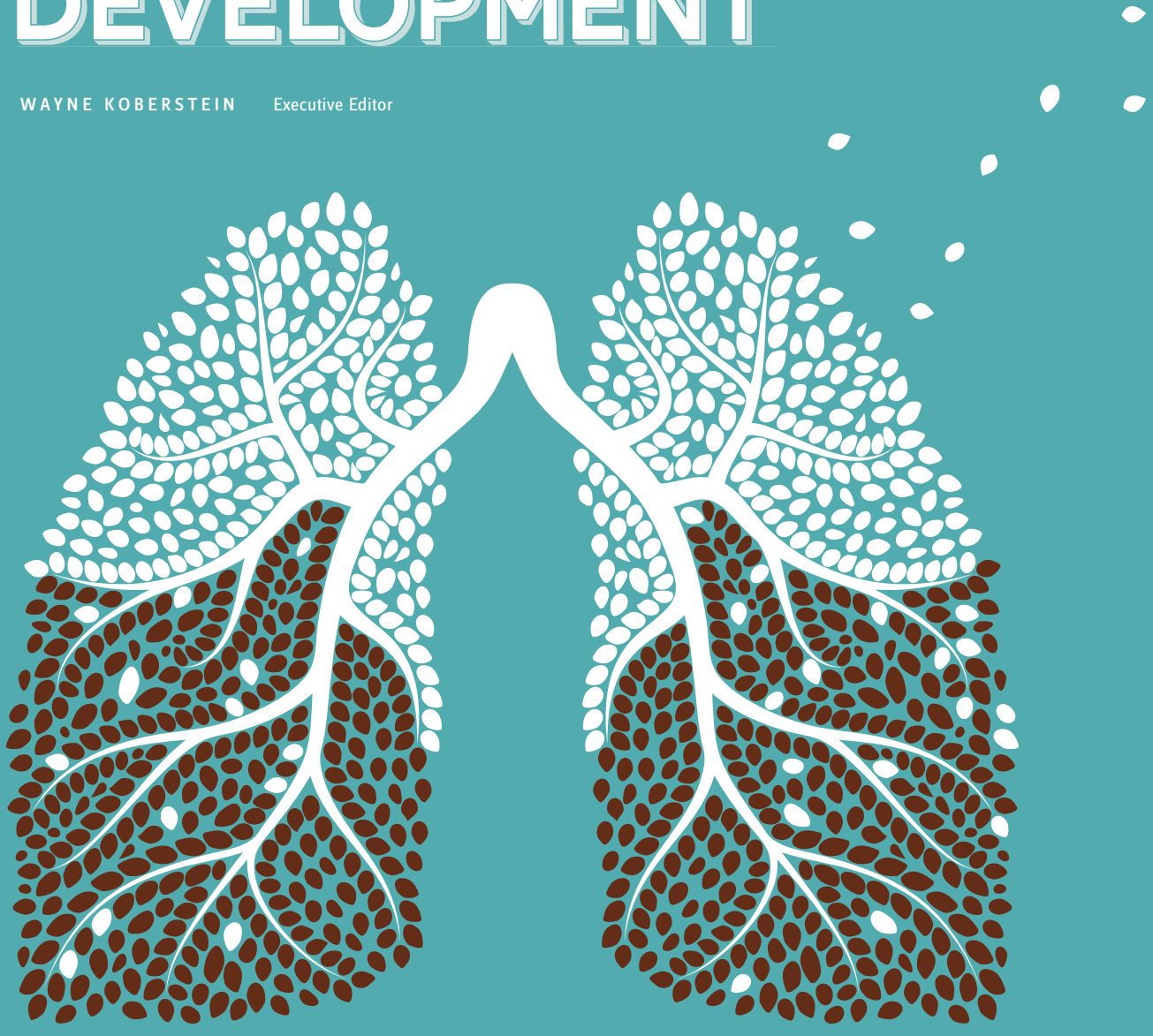
Throughout our conversation, Sagara used the word risk only as it related to his concern for "mega-pharma's mega-merger" syndrome and to the potential for a decrease in new drug output as a result (see inset). When discussing the future of his company, his philosophy, and Ono's employees, he intoned "challenge" and "challengers" repeatedly.

"What I want most to continue at my company is the understanding that employees must be challengers," he says. "They must challenge themselves and our company. Some 50 years ago we challenged the field of prostaglandins and produced first-in-class medicines. We bet the survival of our company on this, but we put everything we had into it and succeeded." He adds that Ono has adopted a company-wide slogan whose Japanese characters perhaps best translate to, "We are passionate challengers."

As the interview with Gyo Sagara comes to an end, I can't help thinking that although he loves golf (Sagara jokes he has gotten progressively worse over 30 years, so looks forward to training for another 20), his demeanor is more of the calm but resolute warrior-leaders of Japanese tradition. His personal challenge and the path to succeed are clearly set before him. He accepts them fully. He leaves one believing there is indeed little "risk" Ono Pharmaceutical will not succeed in becoming the global player of its leader's aspirations. And if Ono's entrée into the cancer field goes as planned, it will have happened in time for 2017. L

BENEFIT OVER BACKGROUND — BI'S BENT ON DRUG DEVELOPMENT

WAYNE KOBERSTEIN Executive Editor



RESPIRATORY LEADER BOEHRINGER INGELHEIM

UPS THE ANTE IN "REAL-WORLD" TRIAL DESIGN — AND PUSHES THE ENVELOPE IN TREATING LUNG DISORDERS.

Tunde Otulana, M.D., heads Boehringer Ingelheim's clinical development and medical affairs group. He is a former FDA reviewer who studied, learned, and finally got the chance to apply his knowledge of clinical trials when he stepped over into industry in 1997. As a pulmonologist who previously worked for about seven years in the FDA's pulmonary division, Otulana subsequently led related R&D efforts at several companies before coming to BI in 2011. He now plays a key role in the U.S. in preserving the company's position as a pioneer and leader in respiratory therapy, mainly in chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

BI belongs to a small handful of pharmas, such as its fellow German company Schering AG, that popularized the first metered-dose inhalers for respiratory patients — devices that became so familiar they appeared as props in a host of movies and TV shows. Until the mid-1970s, the company's largest products on the market were respiratory, but by then its R&D and product lines had branched into the cardiovascular and gastrointestinal areas. Eventually it got into antivirals, and more recently, launched its first cancer drug. In R&D, the company now lists four key research areas in addition to respiratory: cardio-metabolic, central nervous system, immunology/inflammation, and oncology.

Still a private, family-owned company, BI started nearly 130 years ago producing chemical acids and subsequently alkalines, then in the 1920s began to introduce some early medicinal products with the active substances isolated or synthesized from natural sources. One of BI's first respiratory medicines was an "antitussive," or cough suppressant launched in the 1930s, ensuring its claim on an area that proved rewarding over time as the company developed better active ingredients and delivery forms, culminating in inhalers. Now the company is striving to raise the bar again with new products that improve the condition of patients with respiratory diseases beyond what they have attained with their established treatments.

Such an ambitious strategy for clinical development requires a corresponding change in how the company qualifies patients, sets endpoints, and evaluates the data in trials of the pipeline candidates. Rather than testing its new COPD drugs against placebo in treatment-naïve patients, BI is studying their effects when added to the "background" of existing treatments the trial subjects are undergoing. Obviously, the "benefit over background" strategy represents a high-stakes play, informed by the company's confidence that clinical outcomes will clearly show additional benefits in sharp contrast to the background. BI has dubbed its innovative study design the "real-world clinical trial."

CONTRASTS IN EFFICACY

"It is not inaccurate to say that we have been very innovative in the way we do our studies," says Otulana. "We tend to do studies that will answer questions that will address specific issues with our drug or with the disease in general."

As examples, Otulana cites two Phase 3 trials — UPLIFT (Understanding Potential Long-term Impacts on Function with Tiotropium), a 6,000-patient study, and TIOSPIR (Tiotropium Safety and Performance in Respimat), a 17,000-patient study — conducted a few years ago in COPD patients. Both trials looked at the disease progression, based on measuring patients' lung function, not only to win regulatory approvals but also to increase the company's understanding of the disease and the ways tiotropium impedes its progress. Importantly, he says, the trials enrolled patients who continued on their other meds.

"In the past, many new-drug studies required patients to go off the background treatment. We would divide patients into two treatment arms and then randomize them to receive new drugs or a placebo. The benefit of the old method is it reveals the effect of your drug very clearly if it makes a difference, and you can amplify your drug's effect because patients are not taking any other medications that may

crowd out the added benefit. But that is not the real world, where physicians want something they can add to existing treatments for even potentially more benefit."

BI is now developing a new class of COPD agents, the long-acting beta-agonists (LABAs) — such as olodaterol, which it found could be added to its older product Spiriva (tiotropium) for greater symptom control. So now it is also developing a fixed-dose combination of olodaterol and tiotropium for COPD. Again, the new products are tested against background treatments.

"If a patient is receiving various drugs to treat COPD, we will let them continue those drugs in our trial as long as the drugs are not in conflict with the new drug we are introducing," says Otulana. "It cannot be of the same class as the new drug, for instance, because that will make the data incomplete. We have chosen the 'real-world' design because we believe our studies should be as close as possible to what physicians actually do. We believe our studies reflect the real-world environment and that the data that we provide to physicians will actually mimic what happens when the drug becomes available and they use it in their patients. It's a very innovative design, and we've been very pleased with the data we have collected, and I believe the data has also been appreciated by the physicians who looked at it."

Although the main, if not only, examples of the new trial design are with respiratory drugs, Otulana claims no credit on behalf of his unit for originating the design in the company as a whole. "The real-world trial ties in with the BI way of doing things," he says. "We are constantly seeking new ways we can tailor our research to meet the needs of treatment in actual practice. Physicians want data that shows how to use our new drugs in real patients, not theoretical patients. It is the way BI looks at its drug development overall."

SYMPTOMS AS CAUSES

BI has products on the shelf and in development for other respiratory conditions, but COPD remains its largest market area, with about 26 million patients in the United States alone, according to Otulana. Decades ago, when BI pioneered treatments for the disease, launching the anticholinergic Atrovent (ipratropium bromide) in 1975, it had few potential competitors. Later, it was the first company to develop a combination of short-acting bronchodilators, Combivent (ipratropium bromide and salbutamol) to boost airway-opening capacity over single-entity inhalers. The long-acting bronchodilator Spiriva, first launched in 2002, is now the world's most prescribed drug for COPD.

"Fifty years ago, many respiratory diseases were treated with oral medications, so the introduction of inhalers was a significant milestone," says Otulana. "The benefit of inhalation is it delivers the drugs directly to the site of action in the lung, minimizing drug exposure to the rest of the body and allowing a smaller dosage. Another milestone was the development of inhalers with longer-acting medications so that patients use the inhaler just once a day." He also notes a third milestone for BI: the transition from propellant-induced inhalers to its Respimat device, which uses a propellant-free technology. Respimat is the platform for Combivent and the company's future inhaled drugs.

Such apparent maturity as a market leader brings up the question: If current treatments for COPD are so effective that physicians will continue using them even when new treatments come on line, why should BI or any company develop new ones? What possible benefit could it add to the short- and long-term symptom relief already available, short of curing the disease? The answers turn out to be rather interesting. Sometimes, prevention of some symptoms can really be worth thousands of cures.

Because COPD is the result of permanent damage to the lungs, actual treatments for its root causes, which would reverse the damage, lie many years in the future at best. Thus, current COPD drugs on the market and in the pipeline all address the extremely serious symptoms of the disease. Those symptoms — mainly chronic cough with mucous, restricted breathing, and hypoxia — can actually cause further damage, making the overall condition even worse, as Otulana explains.

> "We don't want to go into the cancer space just to have a drug on the market."
>
> **TUNDE OTULANA, M.D.**
> Head of Boehringer Ingelheim's Clinical Development and Medical Affairs Group

"Part of the manifestation of COPD is 'exacerbations,' dramatic crises in breathing when patients have acute worsening of their disease. A COPD exacerbation is a major setback for patients when one develops, and it does in half of all patients. Exacerbations often lead to emergency room visits or hospitalization, and patients who experience them have an increased likelihood of mortality or worsening morbidity. By reducing exacerbations, we hope to improve the overall symptomatology for patients in the short and the long term, and that's why we're continuing to develop new drugs in the respiratory area."

In addition to its COPD pipeline, BI is developing a number of other drugs in other respiratory conditions such as asthma and sometimes much rarer respiratory conditions, such as idiopathic pulmonary fibrosis (IPF) — a "natural step for a leader in the respiratory field," as Otulana describes it. In asthma, another condition in which exacerbations occur, the company first looked for and found a candidate among its existing COPD drugs: Spiriva. It is currently conducting a Phase 3 trial and has released some positive data from the trial, indicating tiotropium "improved lung function and was well tolerated in patients with asthma who remain symptomatic while receiving maintenance ICS [inhaled corticosteroid] treatment."

BI has completed Phase 3 trials of a new compound, nintedanib, in IPF — a

rare, progressive, and rapidly fatal disease, considered an orphan condition in the United States with around 130,000 patients who have no FDA-approved treatments. According to Otulana, about 50 percent of IPF patients die within three to five years of diagnosis. The trial results show nintedanib "slows disease progression by reducing annual decline in lung function by approximately 50 percent," according to data published in May, and BI has since filed for market authorization of nintedamib with the European Medicines Agency (EMA).

FAMILY VALUES

In what might appear as an unusual turn in therapeutic targeting, BI's research has also led it into cancer. It launched its first oncology drug, Gilotrif (afatinib) in the United States last December with an indication for lung cancer patients with 13 specific mutations. Without giving away much about how the company singled out afatinib and identified the mutation-based patient set, Otulana implies the long-term commitment and planning needed for such efforts is a unique advantage of the company's private family ownership.

"The family has certain guiding principles for where they want us to focus our development, and since its beginning in 1885, the company's focus has always been long term. We are patient enough to look at the needs and do clinical trials until we get to a point where we feel we can make a difference. We don't want to go into the cancer space just to have a drug on the market. We have developed a strategy for what we're going to do, we've identified the areas with unmet needs, and we've come out with a drug that will specifically target these populations."

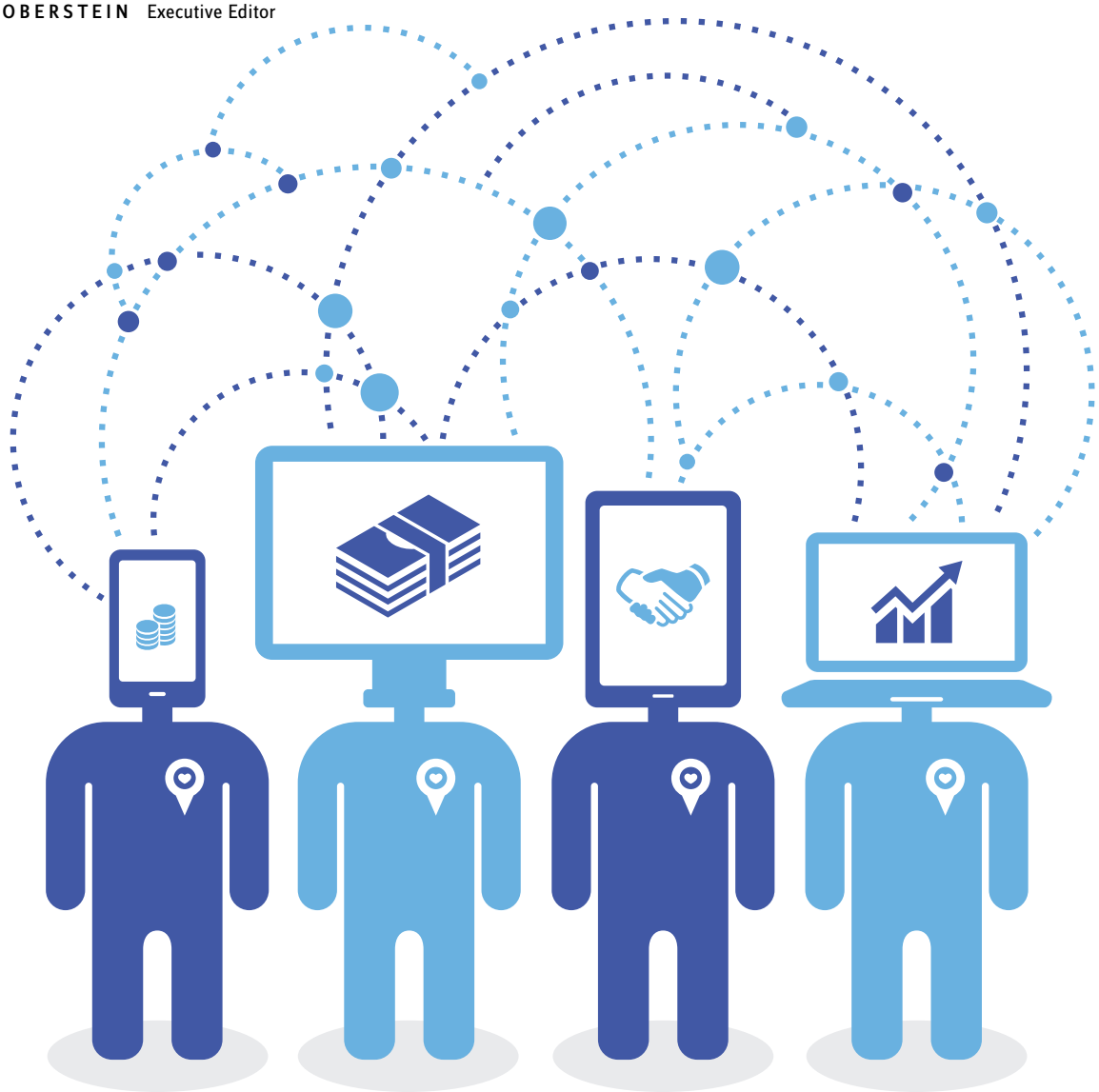
New rules, product-approval requirements, and data preferences by the regulatory authorities, as well as pricing and other restrictions by payers and providers — Otulana says BI has to pay attention to all those factors, just as other companies do. "But the actual development of our products is under our control. BI has a long heritage of focusing development on areas where we can bring the most benefit to patients and carrying out development with a long-term view."

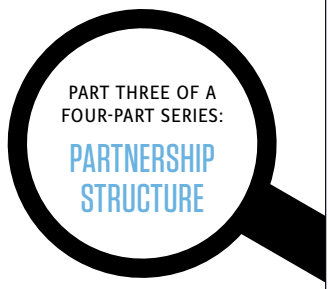
Respiratory diseases are notoriously tough conditions to treat, and despite all of the advances in inhaled medicines to open and protect air passages for breathing, patients routinely continue to suffer serious, intractable symptoms. Otulana and his company see plenty of room to add new drugs, and thus new relief, over the background of existing treatments. Such is BI's simple but real-world strategy for remaining "the leader in respiratory." L

INDUSTRY PARTNERSHIPS WITH PATIENT FOUNDATIONS: THE BEST PRACTICES

Voices of BayBio's "Successful Public-Private Partnerships" Survey

WAYNE KOBERSTEIN Executive Editor





TWO OR MORE WIDELY DIFFERENT ENTITIES

have worked their way to a united vision. They have set the ground rules for their relationship. They have defined goals and plotted a path for achieving them. They have assessed and balanced their resources, individual and shared. Now comes the hard part — creating a formal structure, drawn up in a contract that will ensure long-term success for operating, maintaining, and developing their collaboration.

Structure is the topic of this third installment in our four-part series on best practices for partnerships between life science companies and patient foundations.

Part One of this series (May 2014) introduced several models of industry-foundation partnerships and showed examples of how the partners must rally around a common vision and goals. Part Two (June 2014) dove into the practical challenges of assessing, managing, and leveraging the partners' resources for maximum alignment along their common path. This month, in Part Three, we again hear the voices of people with experience in such partnerships who were also key participants in "Successful Public-Private Partnerships," the survey that inspired this series, conducted by BayBio in collaboration with Merrill Datasite, BIO, and FasterCures.

FROM VISION TO SIGNATURE

It becomes increasingly obvious that no hard lines exist between the four general areas we have conveniently defined for this report, and in fact there is plenty of overlap among them all: A common vision and goals serve as the template for everything that follows or, in some cases, must happen in parallel. Resource alignment, last month's topic, not only takes its direction from the shared vision but also places conditions on the envisioning process, beginning at its earliest stages. A contractual agreement formalizes what should be a well-thought-out structure based on the shared vision and goals — and, in some cases, may foster new organizational paradigms for industry-foundation partnerships, the topic of Part Four. The particular form or structure of any given partnership may conform to a standard model or be unique to the circumstances and plans of the partners.

Nevertheless, the people who run many different kinds of partnerships seem to agree on a few principles that may apply to nearly all. Based on their words and shared experience, the following "best practices" offer some reliable guidance to companies and foundations that have reached the point of formalizing their partnership structure.

TIE MILESTONES TO FUTURE SUPPORT – FLEXIBLY

One foundation leader's own career suggests the wide range of structures such partnerships may adopt or build for themselves — from the simplest funding mechanisms to complex agreements involving performance incentives, reviews, and reserve clauses to protect development candidates from being sidelined for "non-scientific" reasons. At her former position heading the translational research program at the Muscular Dystrophy Association (MDA), Sharon Hesterlee founded the "MDA Venture Philanthropy" fund, initiating a shift from MDA's traditional support for academic research to funding companies in drug development. Now she heads the research funding of a much smaller foundation making fewer but still sizeable grants to companies. Like most others participating in this series, she emphasizes

the importance of setting drug-development milestones in the formal contract, each one tied to a round of funding.

SHARON HESTERLEE, VP, Research, Parent Project Muscular Dystrophy (PPMD): A grant to a company is usually milestone-driven, and we will have payments tied to completion of the milestones. Some of the milestones might be a go/no-go point, but in other cases, if the milestone doesn't work out and no longer seems appropriate, we have a small steering committee that will review it and perhaps set a more realistic one. That procedure is all supported by language in the contract. "Good fences make good neighbors." But we have also learned at the front — if you're too rigid about those milestones, you end up actually holding up the project because things take twists and turns that you can't always predict, and you don't want to throw the baby out with the bathwater.

Hesterlee's point about balancing goals with flexibility draws agreement from a legal expert whose firm specializes in life science industry-foundation partnerships.

DAVID LUBITZ, Partner, Schaner and Lubitz, pllc: To maximize the coordination and efficiency of the relationship, the two ingredients both sides should want in the contract are 1) setting very clear and concrete, but also realistic, goals for the collaboration, and 2) being reasonable. Sometimes companies go into negotiations with the attitude that, because they are dealing with non-profit organizations, they should "just give us the money" in the same way they might give money to academic researchers, without any return, financial or otherwise. But that is not what foundations are interested in. They are beholden to their patient and family constituents, and that community wants to see results.

STIPULATE THE RETURNS ON INVESTMENT

Contracts with foundations can go beyond milestone-driven funding clauses. Many disease and patient groups expect and receive modest payback for their early investments when one of their supported drugs passes all development milestones and achieves regulatory approval. Though not applicable to groups like The Myelin Repair Foundation and the Critical Path Institute, which deal in scientific tools and information rather than finances, partnership agreements with funding foundations will likely ensure them a certain return on investment from successful outcomes for patients.

LUBITZ: With diseases for which we don't even know the causes, the issue of a financial return from a therapeutic product really isn't on the table; foundations are focused on research for developing biomarkers or figuring out causes for the disease. But when the knowledge chain is sufficiently advanced with the potential for therapeutics, and companies with those potential technologies are looking for funding, the foundations do two things that justify their request for financial return: They are willing to invest in the technology during the period of development known as the Valley of Death, where the risk is extremely high and private money is scarce or unavailable. And, unlike profit-maximizing investors or private investors, when foundations obtain a return on their investment, they always put the money back into support for scientific progress. There is no charitable requirement on private investors who obtained a return — they can take the money and do anything they want with it. But when the disease foundations are plowing money back into scientific research, there is a virtuous cycle in giving them a contractual return for their investments.

HESTERLEE: One of the things our donors really appreciate — when we give money to a for-profit company, we typically arrange some kind of return on that investment, and the return, of course, is rolled back into our non-profit mission. It is actually a way to leverage dollars from donors. They understand it's high risk; we may not see any return at all, or it might be years before we do, but there's a chance the money they gave early on could turn into bigger dollars, and of course it's a potential source of income for us. We typically develop some kind of royalty-sharing agreement, though other organizations have different processes. We don't take an equity stake, any shares, stock, or ownership of IP. As a non-profit, we have to look at any equity stake as an asset, and that means every year you have to value that asset, and at some point, you will probably have to write it down.

Another foundation leader shows how greatly the contractual forms of ROI can vary among the disease or patient groups partnering with companies. But the common denominator is still a concern for maintaining reasonable flexibility in the agreements.

TIM COETZEE, Chief Advocacy, Services, and Research Officer, National MS Society:

When we put money into a company, we expect some level of a return if the program we fund is successful. It is not about our trying to extract a pound of flesh but really more about the company's responsibility to the community that helped get the program going. We never get an argument from companies on that. As part of our agreement, we have some sort of return vehicle built into the transaction.

Sometimes, it consists of warrants or options in the company at a negotiated rate with potential upside if it achieves a certain coverage. Oftentimes, it's more of a capped-cash royalty based on specific development milestones. When the company reaches a point where it is receiving money from another partner for specific assets of the program, we also receive some of the money, so everybody participates in success.

We don't aim to secure a royalty based on percent of sales of a future approved drug, in part because the development timelines are so long and fraught with uncertainty, and we just don't believe it is the right strategy for our organization. Royalties can quickly become stacking royalties that make the development program commercially unviable because of financial downstream challenges. We aim to make sure our royalty appropriately reflects the mission but also will not create an impediment to future developments.

Because some foundations may have made unreasonable demands in the early days of partnering with companies or because ambiguous ethical issues may arise wherever funds change hands, it is only fair to include two cautionary views of "foundation ROI" from the industry side.

ANDREW GENGOS, President and CEO, ImmunoCellular Therapeutics: If foundations start to act like venture capitalists, saying, "Here's $200,000, but we'd like some stock in your company," or, "If the drug reaches the market, we'd like a royalty from sales," now you've got a 501(c)(3), tax-exempt, not for profit disease organization, financially benefiting from an approved drug that serves its constituent patients. If the drug gets priced at $100,000 a year instead of $50,000 a year, the foundation may earn even more from it, but there's blowback risk from the potential misperception that higher pricing restricts patient access. By the way, ROI mechanisms aren't categorically bad ideas; financially, they can make sense especially in underserved disease areas. However, all parties need to be mindful of the potential conflicts of interest.

MICHAEL RICHMAN, President and CEO, Amplimmune: Conflict of interest will always come into play, not so much with the foundations because the foundations usually don't take a royalty, and they're not involved so much in the clinical trial as their developer partners are. But a real conflict of interest may arise when a key opinion leader receives funding from a foundation and also from a company involved in the foundation-supported trial. Such arrangements can only be dealt with on a case-by-case basis.

DEFINE INTELLECTUAL PROPERTY AND DATA-ACCESS RIGHTS

Foundations may also want to protect the drug in development from the opposite of success — being put on the shelf for non-scientific reasons such as new organizational priorities in a merger or acquisition. Likewise, companies usually should not fear their partners' limited efforts to ensure timely patient access or at least a fair shot at it.

HESTERLEE: Most organizations in this space ask for some kind of interruption license or march-in rights, meaning that if a company drops the work on a therapeutic in development, then we have the right to sub-license to another developer to finish the work. Companies tend to hate this requirement because it may appear we have a right to grab their assets, which could be a problem for them in future deals. But companies can have many internal projects, and they have boards and often shareholders they report to. If the company's priorities change, and it drops a project for a non-scientific reason, we want to make sure the particular project is not lost. Of course, if they drop it for scientific reasons, and everybody agrees it failed, we don't have a problem. It is usually a contingent issue. We have not exercised our march-in rights before, though we have discussed them. They are really worst-case-scenario safeguards. We are business partners, and that's the best way to look at our rights in the contract, because it is a business arrangement.

LUBITZ: Disease foundations are certainly no more difficult for companies to work with than private investors, and perhaps easier. Typically, in addition to interruption rights, they may ask for things like research licenses for technology but only on a non-commercial basis. The point of disease foundations, of course, is to further scientific research broadly, and they are certainly quite flexible in their research licenses or publication requirements so that they don't negatively impact the company's intellectual property protections. Once the companies see the foundations are not making outrageous requests or demands, they realize foundations can be quite helpful collaborators.

HESTERLEE: If we don't have the license, which would only occur in a rare exercise of march-in rights, it doesn't really matter if we own all of the data. We have all the data reporting we need built in already, related to milestones. We usually ask our partner companies for reports on communications with regulatory agencies, shareholders, and other types of prospective information, and they typically agree to share it.

BUILD A DYNAMIC STRUCTURING PROCESS

When people speak about incorporating flexibility and reasonableness into the partnership structure, they generally mean establishing some kind of steering body that represents all the players in the program. Without exception, the experienced voices in this series stress the importance of establishing an inclusive system that ensures dynamic restructuring of the partnership as new challenges and opportunities arise.

MARTHA BRUMFIELD, President and CEO, the Critical Path Institute (C-Path): Ideas for new projects come to us from many directions. Sometimes the FDA or EMA, oftentimes foundations such as The National Multiple Sclerosis Society or the Gates Foundation, or other times from industry. In complex consortia, we bring multiple players together to share data we can aggregate into databases that help us construct predictive models and biomarkers that address wide-interest medical issues, such as drug toxicity and effectiveness. When we take on a project, we reach out broadly to those who have expertise or interest in the area and invite them to join the consortium. We want everyone's voice in the discussion, including patients'.

KLAUS ROMERO, Director of Clinical Pharmacology, the Critical Path Institute: Every C-Path consortium is founded on a legal agreement that defines the breadth of participation and the expectations and the roles for each of the participants, including the regulators and the companies. Sometimes we bring in independent consultants or even CROs for specific portions of the hands-on work, and we also leave the door open to external collaborators, such as key opinion leaders, to participate under a confidentiality agreement.

Whether developing therapeutics, new science, or data tools is the goal, a "family" approach to managing and making structural changes in the partnership is the ideal path to take, as the following company executive and his peers in this report unanimously testify.

JEFFREY M. OSTROVE, Former CEO, Ceregene: In Ceregene's partnership with the Michael J. Fox Foundation [MJFF], representatives from the foundation attended all of our key company meetings, including Board of Directors, scientific advisory board, and our "expert panel" meetings, where we assembled world experts in Parkinson's disease. The MJFF people didn't just *attend* the meetings, they *participated* in them, because the whole community was pulling together.

To guide the spirit of the community formed in any company-foundation partnership, a few final words of wisdom from another experienced hand:

DIANE STEPHENSON, Executive Director of C-Path's Coalition Against Major Diseases: In some of the areas we work, even the experts in the field don't agree on the best approach; for example, on the details of developing outcome measures for Alzheimer's. So, it's extremely difficult to gain consensus. We work with so many diverse stakeholders that we've learned to say, "It's okay if you don't agree, but we're still going to continue working on this goal together." That's really rewarding because then people in the consortium realize that everybody brings something to the table, that we respect your opinion, that what you have to say is extremely important and we hear it, but let's all realize that that's not going to block our progress."

So ends Part Three of our four-part series, "Industry Partnerships with Patient Foundations — The Best Practices." Watch for Part Four, "New Partnership Paradigms," in next month's Life Science Leader. Many thanks to Travis Blaschek-Miller at BayBio and the BayBio team for their help with this article series. (See BayBio's white paper on the survey at baybio.org.)

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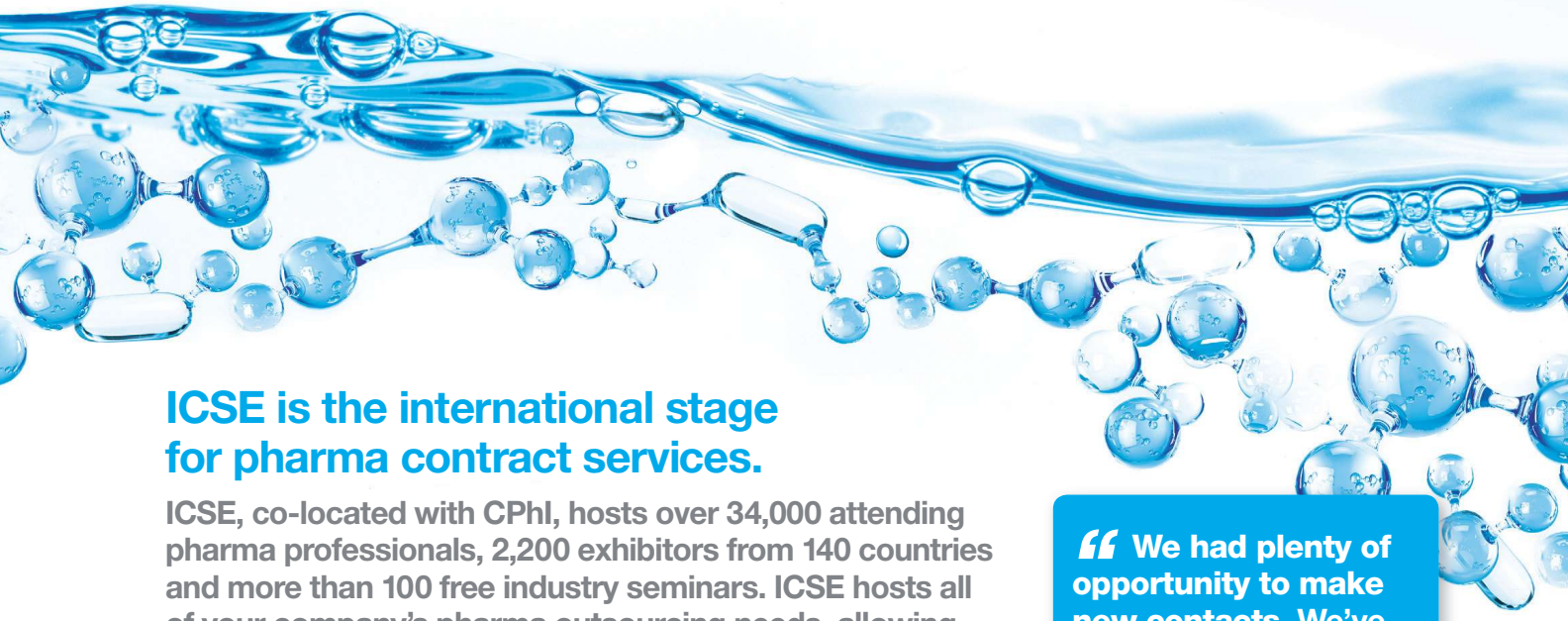

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Pharma And Life Sciences Confront The Evolving Role Of The Consumer And Intensifying Competition

MICHAEL SWANICK

The pharmaceuticals and life sciences (PLS) industry today faces unprecedented challenges, and around the globe, sector CEOs are pondering how their businesses need to adapt. Insights into their thinking about the hurdles and opportunities ahead can be found in the recently released 17th edition of PwC's Global CEO survey.

The firm surveyed 1,344 business leaders across 68 countries around the world, in the last quarter of 2013, and conducted further in-depth interviews with 34 CEOs. PLS was well-represented — nearly nine percent of the sample, 119, were PLS CEOs.

Those PLS CEOs told us they face three key challenges:

1. They have to chase a moving target, as consumers evolve in different ways in different markets.
2. They have to address the needs of more diverse — and demanding — customer segments.
3. They have to fight off increasingly intense competition.

Our overall survey sees a leap in CEOs' confidence in the global economy — but there is caution as to whether this will translate into better prospects for their own companies. The search for growth is getting more and more complicated as opportunities in both developed and emerging economies become more nuanced, leading CEOs to revise the portfolio of overseas markets they will focus on.

Addressing the growth search, Coviden Chairman and CEO José E. (Joe) Almeida told us, "Growth is being driven primarily by major investments in emerging markets and secondly, by investments in technologies. We find that with the combination of emerging markets and those technology initiatives, plus a great deal of product development and pipeline coming in the next five years — up to around 30 products a year — Coviden will be able to deliver above market growth."

THE TOP LINE

PLS CEOs believe technology is transforming the sector, and they're using strength in innovation to make the most of it. They're also focused on regulation and integrity. Facing the talent challenge is a key priority too, particularly with demographics and shifts in wealth also radically reshaping where manufacturers will need to focus their efforts in the sector.

➔ TECHNOLOGY, DEMOGRAPHICS, AND SHIFTS IN WEALTH ARE TRANSFORMING THE SECTOR.

PLS CEOs are even more convinced than their peers that technological advances will transform their businesses in the next five years. And they're more conscious than other CEOs of the huge role demographics will play — 72 percent see it as a transformative trend, compared to 60 percent across the sample. More are also expecting a big impact from global shifts in economic power.

That combination of factors was captured succinctly in our conversation with Joseph Jimenez, CEO, Novartis, who told us, "The biggest trend is the aging population. This is going to create both a massive risk and a massive opportunity for the world. On the risk side, who is going to pay for the healthcare as the big cohort moves through? If you look at the number of people who will be over 65 in a few decades, it is a staggering figure. But then you realize this is going to create a demand for disease-modifying new agents. The IT explosion and what we are working on right now is going to lend itself to managing the challenges that come with the aging population."

➔ PLS CEOs BELIEVE TECHNOLOGY WILL HELP MORE THAN HINDER.

Only around a third of sector CEOs are concerned that the speed of technological change may negatively impact growth, compared to nearly half of CEOs across the overall sample.

INNOVATION IS A TOP PRIORITY – AND PROTECTING INTELLECTUAL PROPERTY IS A WORRY.

Sector CEOs are already transforming their R&D function to cope with transformation — 38 percent say they've completed or have in progress a program to change their R&D and innovation strategies, more than across the sample as a whole. And the same number believe that their R&D departments are well-prepared for the challenge. Importantly, "innovation" means more to these CEOs than new product development.Innovation can also help improve processes or create new services or business models.

The CEOs we surveyed are not as confident about their ability to benefit from their discoveries, though. Sixty-four percent of PLS CEOs are somewhat or extremely concerned that an inability to protect intellectual property will hamper growth, far more than across the sample as a whole.

TOO RELAXED WHEN IT COMES TO CYBERSECURITY?

A surprising 57 percent of PLS CEOs are not concerned that cyber threats including lack of data security could threaten growth. That's despite a boom in Big Data and data analytics — 79 percent agree there's a need to change strategies in that regard, although just 23 percent have already started.

REGULATION IS NOT ALL BAD.

Nearly four-fifths of CEOs (79 percent) are concerned that overregulation could put the brakes on growth. That said, a full 72 percent believe that their production and/or service delivery quality standards improved over the past 12 months as a result of regulation.

SUPPLY CHAIN INTEGRITY AND SECURITY IS A BIG ISSUE.

The industry is taking safety seriously; more PLS CEOs strongly agree that it is important to them to ensure the integrity of their supply chain (76 percent vs. 58 percent overall). They also worry about the impact of bribery and corruption. Sixty-one percent believe it could slow down growth, compared to 52 percent of CEOs overall.

SECTOR CEOs ARE POSITIVE ABOUT FACING THE TALENT CHALLENGE.

While about half of PLS CEOs remain concerned about the availability of key skills, this year that is far less than their peers across the sample. Fewer are concerned about rising labor costs in high-growth markets, too. That may be because many have already taken steps to revamp their talent strategy to capitalize on major trends — 43 percent say they've already begun or completed a change program, compared to 32 percent overall.

THE DRILL DOWN

This changing landscape doesn't lack for threats — and the top three identified by our global group of CEOs are overregulation, debt and deficit responses by governments, and a slower economy.

OVERREGULATION

More than three-quarters of PLS CEOs believe overregulation could sidetrack growth prospects. That's far more than across the sample as a whole (percentage concerned about overregulation — 79 percent).

DEBT AND DEFICIT RESPONSES BY GOVERNMENTS

PLS CEOs, like their peers overall, are concerned about the ability of debt-laden governments to tackle soaring deficits. It's a worry that's been increasing over the past several years (percentage concerned about government responses to debt and deficits — 76 percent).

POOR GROWTH IN DEVELOPED ECONOMIES

PLS CEOs are slightly less worried about this poor or negative growth in developed economies than the sample as a whole. It's "business as usual" for them as growth rates in these markets have been low for some years now (percentage concerned about poor growth in developed economies — 65 percent).

CEOs ARE ALSO CHANGING THEIR APPROACHES TO BUSINESS MODELS

New strategic alliances or joint ventures are the main restructuring activities planned. The PLS industry's appetite for collaborative cocreation continues. The sector's CEOs are more likely than other industries to be looking at alliances, JVs, or outsourcing. When it comes to M&A, they're keeping things close to home, with less desire for cross-border deals than their peers in other industries.

HALF OF PLS CEOs ARE ACTIVELY CHANGING THEIR TRANSACTION STRATEGIES.

PLS CEOs are ahead of the curve when it comes to changing programs around their transaction strategies. Over one quarter (28 percent) have programs completed or under way, compared to 21 percent cross-industry, while a further 22 percent have firm plans to take action.

PLS CEOs ARE EMBRACING INNOVATION AND TECHNOLOGICAL CHANGE.

More PLS CEOs (44 percent vs. 35 percent overall) see product and service innovation as their main route to growth. The sector's CEOs are confident in their ability to keep up with a changing world. Just 32 percent of PLS CEOs are concerned about the speed of technological change — lower than across the overall sample (47 percent). And more believe that their R&D department is ready to cope. Thirty-eight percent say it's well-prepared, compared to 28 percent overall.

Our research shows that successful CEOs are doing three things to innovate their product and service lines — make them repeatable, dependable, and scalable. They're focusing on innovation in all its forms, putting disciplined innovation techniques in place, and collaborating much more actively. Going beyond new product development, innovation can also help improve processes or create new services or business models.

FINALLY, THESE SHIFTS CARRY IMPLICATIONS FOR THE PLS WORKFORCE

More PLS CEOs are taking on staff than letting them go. Nearly half of PLS CEOs say headcount will increase in the coming 12 months. But this is less than the overall sample predicts. A quarter expects to reduce their workforce, compared to one-fifth overall.

CEOs ARE CONCERNED ABOUT DEVELOPING A WORKFORCE THAT CAN COPE WITH A CHANGING WORLD.

Talent is one of the main engines of business growth. So one of the biggest issues CEOs face, as these huge demographic changes occur, is finding and securing the workforce of tomorrow — particularly the skilled labor they need to take their organizations forward.

Fifty-one percent of PLS CEOs continue to be concerned about the availability of key skills. As consumerization dramatically changes the delivery of healthcare, traditional business models need to change, and that includes people and skills. Thirty-seven PLS CEOs believe that creating a skilled workforce should be a government priority, but only 19 percent believe that the government has been effective. As a result, many are taking action themselves — 64 percent say creating a skilled workforce is a priority for their company.

In the future, a company's value may be judged on how well it establishes and maintains a robust talent network that spans traditional boundaries. Our research shows that the quest for talent must be in harmony with new collaborative R&D models in the life sciences industry. Companies must involve HR in strategic planning and organizational design to successfully identify skill gaps, align employee incentives with company goals, boost staff morale, and solidify external partner relationships.

Adopting the innovation practices of successful CEOs and taking concrete steps to align an enterprise's search for talent with the new collaborative models that are allowing PLS leaders to push the envelope for research are tactical approaches that address key concerns we heard from our CEO survey respondents. L

MICHAEL SWANICK
Partner, PwC, Global Pharmaceutical and Life Sciences Industry Leader.

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5 Real Estate & Facilities Management Strategies To Drive Top-Line Value

In a new paradigm of the life sciences industry, corporate real estate can be a source of top-line value.

ROGER HUMPHREY

The patent cliff was only the beginning of cost pressures in the life sciences industry. Today, new healthcare reform initiatives in the United States and elsewhere are transforming the business of life sciences around the world. New pressures are emerging from the shift to value-based product pricing, while regulatory and cost pressures continue to grow.

To thrive in this dramatic new landscape, life sciences companies must push for even greater research and manufacturing productivity — without compromising the integrity of their systems and facilities.

It's a paradigm shift that requires biopharmaceutical companies to take innovation beyond R&D and into their operations. One area ripe with potential is corporate real estate and facility management. After R&D, real estate costs are among the most significant expenses for life sciences companies, encompassing offices, highly technical laboratories, and sophisticated facilities necessary for producing drugs or biological medicines in compliance with complex quality and safety regulations.

As life sciences companies continue their quests for efficiency, corporate real estate and facilities management strategies have the potential to support shifting business priorities and to drive top-line value. These strategies are not just the purview of the global corporations, but can also be adopted by middle-market companies facing equally severe cost pressures.

STRATEGY #1: CHOOSE THE RIGHT SPACES IN THE RIGHT PLACES

Now more than ever, strategic site selection and optimal use of resources are crucial for the success of biopharma companies. Whether a company owns or leases its facilities, the costs of real estate operations can be considerable, especially if facilities are located in high-cost cities.

Given today's narrow profit windows, the challenge lies in balancing real estate costs in a particular city against the potential advantages of gaining vital access to multidisciplinary research talent, new market opportunities, potential business partners, and production facilities. Sometimes it is worth paying more for facilities with proximity to potentially game-changing resources, and that is exactly what some companies are doing.

As noted in JLL's annual *Global Life Sciences Cluster Report*, life sciences companies have been right-sizing their corporate real estate footprints in mature U.S. and European markets to improve their operating efficiency. Nonetheless, cities such as Boston and Zurich continue to be top clusters of life science activities despite extremely high real estate costs because these cities provide access to top research institutions, promising biotech start-ups, and capital. Concurrently, some life sciences companies are expanding operations in emerging markets where new markets and clinical trials resources abound.

STRATEGY #2: DON'T OVERLOOK FACILITIES IN MERGERS & ACQUISITIONS

Mergers, acquisitions, business unit spin-offs, and creative joint ventures complicate the facilities picture, which is why a company engaging in these activities should include a knowledgeable facilities strategist in the decision making. Although the hope of greater efficiency is a major motivation for M&A, some companies overlook or mismanage a major source of potential value — the corporate real estate portfolio.

Mergers and acquisitions are occurring more frequently among large biotechnology and specialty pharmaceutical companies than among the global concerns, according to Ernst & Young's January 2014 *The Shifting Balance of Firepower.* Overall, executives in the sector anticipate significantly more acquisitions in 2014 than in 2012 or 2013.

Engaging the corporate real estate team during the high-risk due diligence phase will help a company better understand the value and the risk that may be hidden under layers of leases and building valuations. Regulatory restrictions, of course,

mean that a company never has all the advance detail it wants. However, having an external real estate partner can provide quick access to real-time global real estate market intelligence to support facilities decisions and detailed scenario analyses.

The corporate real estate team should include a program management function to streamline integration activities. A well-rounded execution team will include commercial real estate brokers experienced with M&A, along with workplace strategists, CPAs, legal specialists, architects, and project managers. Change-management specialists are also essential for engaging employees during facilities transitions.

Companies need to ask the right questions during the M&A due diligence process to drive the most value from the corporate real estate portfolio — not to just cut costs. What locations will attract the best and the brightest scientists? Where do portfolios overlap? What is the value of surplus facilities? Are there hidden risks in the portfolio that will hinder integration? What will the fully integrated portfolio look like and when?

The real estate team must be equipped to address a potentially large and complex portfolio of diverse property types. A company's portfolio may include not only office and laboratory facilities, but also data centers, a product distribution network, traditional and biologic manufacturing facilities, global sales team offices in emerging markets, and other specialized properties.

This team should plan in advance where redundant facilities can be quickly consolidated when the deal is closed. Otherwise, the lag time between executing a business strategy and aligning the corporate real estate with the strategy can be lengthy and costly. The more quickly the corporate real estate team moves, the more quickly a company can realize the advantages of consolidation.

For example, when Merck acquired Schering-Plough in 2009, the corporate real estate team reduced the combined companies' occupancy costs by $300 million within three years — making a significant contribution to the $3.5 billion merger synergy goal. For Merck, the value hidden within the corporate real estate portfolio was the "X factor" that contributed to the transaction's success. However, Merck's corporate real estate goal was to build long-term productivity by creating highly efficient and effective business and laboratory locations and workplaces, rather than focusing solely on short-term savings.

STRATEGY #3: INVEST IN FACILITIES-COMPLIANCE EXPERTISE

Always a critical issue for life sciences companies, regulatory compliance is ever-pressing as companies seek new markets and R&D opportunities in emerging markets such as Southeast Asia, India, and Latin America. As the life sciences industry continues to evolve, organizations that maintain the highest quality standards throughout their facilities will find the greatest success.

Training and managing highly skilled facilities workers around the world, however, can distract from the core businesses of a biopharma company. One way to maximize efficiency and improve facilities regulatory compliance is to outsource facility management to a qualified organization that has already established a reliable presence in the area with personnel who have the breadth of technical capabilities required.

Many leading organizations are seeking best-in-class outsourced services to manage a wide range of technical facilities functions, extending outsourcing even into highly regulated areas. A specialized facilities management vendor can provide equipment maintenance, hazardous waste management, regulatory compliance, environmental and health safety, technology, critical environment, and other specialized functions in R&D and production facilities.

STRATEGY #4: PRIORITIZE A HIGH-PRODUCTIVITY WORK ENVIRONMENT

Workplace productivity depends on the people who work within it — but the workspace itself can go a long way in inspiring them to excel. From fostering collaboration in open discussion areas and providing distraction-free focus in private spaces, to simply increasing the amount of natural light to make a workplace more attractive, the facility itself can be a powerful tool in talent recruitment and retention, which can ultimately trigger greater innovation and drive productivity forward.

In some cases, uncovering underutilized space and better managing overall use can actually provide the cost-reducing benefit of shrinking a facility's footprint or square-foot-per-employee ratio. The trick is to rethink the corporate approach to space such that it sustains operational efficiency while actually functioning as a "nice place to go to work."

STRATEGY #5: TRANSITION REAL ESTATE TO SUPPORT BIOLOGICS

According to BCC Research, the biologics market is estimated to reach $252 billion by 2017. With so much of today's growth coming from biotech medicines, traditional pharmaceutical manufacturing facilities are quickly becoming industry dinosaurs.

In previous eras, production facilities were fairly adaptable and could be fairly easily transitioned from one type of drug production to another. In contrast, re-equipping facilities originally built for small molecule drug production to house biological and biosimilar medicine production is anything but minor. In some instances, a new facility may be the most cost-effective option.

Not only are production processes entirely different, but also the facility management requirements for biological products are necessarily complex, as any changes in environment can affect product quality and safety. To comply with these tougher regulations, expert management of such functions as air filtration, temperature quality, and equipment maintenance to maximize uptime is critical.

ADDING IT ALL UP

Taken together, these strategies can maximize value in the corporate real estate portfolio. The tough life sciences regulatory landscape may be pushing the industry in new directions, but with a proactive approach to facility real estate and management, today's industry paradigm could actually help life sciences companies drive innovation and value.

The Strength At The Interface: Academia Meets Industry

Collaborations between academia and industry are becoming more common as biopharma companies, both large and small, see the value gained from different approaches.

SUZANNE ELVIDGE Contributing Editor

The biopharma industry is changing, as outsourcing and collaborating becomes a more common route to drug development. Biopharma companies are starting to recognize the value of tapping into the wealth of experience and expertise that is academia.

There will be challenges, of course, as the two sides learn to work together, but the benefits in the long term work both ways, as working with industry can help support research for academia too. As always, the best collaborations will be those that benefit both sides.

WHAT'S THE DRIVER?

The aim for academia-industry collaborations is improving scientific knowledge about diseases, drugs, and their pathways, as well as finding ways to apply this knowledge practically that will benefit patients. A key driver for the biopharma industry is to broaden the application of marketed drugs. Companies developing drugs generally want to get their products to market as quickly as possible to begin to recoup their investments. One route to speeding up approval is to carry out monotherapy trials in large populations. Doing so provides the type of data that regulatory authorities require. However, particularly in areas such as cancer, effective treatment relies on combinations of drugs rather than single treatments.

The Combination Alliance, part of the Experimental Cancer Medicine Centre (ECMC) network launched in 2006, works with pharmaceutical company partners to run early-phase trials of combinations of cancer therapeutics. These allow investigators from academia to run clinical trials that look at how combinations of different therapeutics can work, often in smaller and more focused populations. These smaller trials benefit industry by providing the early tolerability and rationale from pharmacodynamic endpoints that the biopharma companies need to plan their pipelines and include combination options for broader patient benefit. "Academics benefit because they can access the drugs earlier, and patients benefit from early access too, particularly those in countries outside the large-scale regulatory studies," says Hazel Jones, head of combination therapies at Cancer Research UK.

The ECMC network is backed by Cancer Research UK and the U.K. health authorities, and it began as a partnership with AstraZeneca in 2010. As of March 2014, it includes 14 collaborations covering 11 compounds, and agreements with Eli Lilly and an as-yet-undisclosed UK biotechnology company.

"Advances in cancer treatment are driven by drug combinations, and the ECMC network allows academics and industry partners to discuss ideas and suggest combinations of drugs," says Jones. "The industry collaborations mean that the academics may have the opportunity to pick and choose across the different companies' portfolios to create the best possible combinations. This allows research to move away from combining known drugs and toward novel-novel combinations which could have further benefit for cancer patients."

By working together, academia and industry can achieve important breakthroughs, but the relationships have to be managed to ensure that the benefits are maintained long term. For academia-industry collaborations to work, companies have to be prepared to be more open at a much earlier stage. Confidentiality also needs to be built into the alliances, including nondisclosure agreements and working in the precompetitive space. GlaxoSmithKline's approach includes open innovation, sharing precompetitive information. "We see a value in sharing best practices," says Malcolm Skingle, director, academic liaison, GlaxoSmithKline. "We gain from tapping into an expanded science network and learning more about the science underpinning our molecules."

REAPING THE BENEFITS

The most effective and long-lasting academia-industry collaborations will be those that benefit both sides, but also where both sides bring resources in an equal relationship. The benefits for industry include access to interesting and cutting-edge research, knowledge on basic science, and the opportunity to make contact with key opinion leaders who provide a range of different viewpoints.

"Companies collaborate with academia to tap into their research and platforms — this could be described as 'try before you buy.' Collaboration also provides an opportunity to impart and exchange the knowledge that drives science or creates a larger pool of people who can think about a problem," says Skingle. "We gain a deep understanding of the biology from academia, and we provide scientific direction and access to resources."

Academic support and collaboration is of great benefit to small companies, which don't have the range and depth of resources in-house, as Simon Fredriksson, president and CEO at Olink, explains. "For us, collaborations with academia are a vital part of what we do. Through collaborations, we get the opportunity to 'test drive' technology in the real world, which would be very hard without access to academics."

Academia also benefits by gaining access to a range of proprietary platforms and compound libraries, along with early-stage and industrial-scale technologies. The academic partners can also benefit from industry's applied therapeutic knowledge and may be able to access new funding sources, whether directly from larger companies or as part of a collaborative application with smaller companies.

"We are a small company, and so while we can't invest large quantities of money, we can bring our time and skills to collaborations," says David Bejker, president and CEO at Affibody AB. "We invest in-kind rather than in cash — we can raise money together."

Collaborating with industry allows academics to have the opportunity to think more broadly and to put their knowledge to practical applications by transferring their innovations and translating them into uses in healthcare. "The academic research can push forward the scientific frontiers and test the theory behind the drug's activity in combinations, focusing on synergistic effects and blocking resistance mechanisms," says Jones.

MEETING THE CHALLENGES

There are differences in mindsets between academia and industry, and this can lead to challenges in the burgeoning relationships. These include building trust between the partners and understanding not only how much information to share but also when and how it will be used. However, being aware of these up front will help both partners work together to build a fruitful collaboration.

"Biopharma companies are primarily interested in successfully translating research from drug discovery into the clinic, and they focus on following the positive results. Academics tend to want to know more about the science, about how and why the drugs do (or don't) work," says Jones. "The Cancer Research UK Drug Development Office sees both perspectives and can act as a bridge between the two, setting up initiatives such as the ECMC Combination Alliance and the Clinical Development Partnership (for deprioritized projects)."

One of the key drivers within academia is the need to publish — to support funding streams and to maintain the profile of the academic institution. According to Bejker, this can be a sticking point in a relationship, as biopharma companies do need to exclude certain pieces of information to protect their IP. Skingle sees the flip-side of this, however. "Published papers produced as part of collaborations have a higher impact than those from either academia or industry alone," says Skingle. "The whole *is* greater than the sum of its parts."

Another challenge faced by academia is its reliance on biopharma companies' pipeline decisions, which can result in drug development ceasing for strategic rather than efficacy reasons. These can be solved, or at least mitigated, through open communication. Sometimes ideas from academia are too visionary and have to be distilled into a practical and pragmatic form by the company.

WHO'S DOING IT?

Collaborations between academia and industry have benefits for both small and large companies. GlaxoSmithKline includes discovery performance units (DPUs) made up of 10 to 70 people, and each is responsible for a specific area. "Our DPUs can source R&D internally or externally, and the proportion varies. For example, all of the research in the ophthalmology DPU is external, as part of a £6 million [around $10.1 million], six-year collaboration with Moorfields Eye Hospital, London," says Skingle. "GlaxoSmithKline has more collaborations with academia than any other U.K. company. This includes 310 undergraduates in our laboratories and IT offices and 240 Ph.D. CASE (Collaborative Awards in Science and Engineering) studentships." For GlaxoSmithKline, the collaboration works both ways. For example, scientists from the company go into universities as visiting professors, taking in information about science with a different perspective.

From a big company to a smaller one — Swedish company Olink was founded by academics from Uppsala University and relies on ongoing relationships. As Fredriksson explains, "Collaborations between academia and industry are essential for a company like Olink to generate products. Academics have lots of ideas that could be commercial, and they need to think about how these ideas can translate into products and services. That way they can become useful for the general public who often actually paid for the research through taxes."

Another smaller Swedish company, Affibody, has a long collaboration with Uppsala University, including the development of ABY-025, a small reengineered Affibody molecule targeting the HER2 receptor. A radiolabelled form of this molecule is in Phase 2 clinical trials as a breast cancer diagnostic. The relationships between academia and industry are likely to be a cornerstone of research in the future. As Skingle concludes, "Big science needs multiple parties involved, sharing both the risk and the reward."

Big Data In Life Sciences: Trends, Challenges, And The Payoff

RICH SOKOLOSKY

Information is playing a critical new role in the business of life sciences, from discovery to commercial operations. Big Data is a major agent of change in the trends, challenges, and payoffs for this emerging focus, and now is a good time for informatics and analytics professionals to step back and see where we are and where we can go.

A good starting place is to look at these four commercial life sciences information trends:

1 PATIENT-LEVEL INSIGHTS ARE DRIVING COMPETITIVE ADVANTAGE.
Organizations are looking to patient data for real-world drivers of brand use — to explain the drivers behind the trends and better inform commercial activities from brand planning to sales targeting.

2 WE ARE MOVING BEYOND THE DATA WAREHOUSE TO THE "DATA LAKE."
Companies are building data hubs to provide comprehensive access to the information necessary to create new insights that data warehouses cannot deliver.

3 THE DATA SCIENTIST IS BECOMING A KEY ROLE IN COMMERCIAL ORGANIZATIONS.
New insights drive decisions when market conditions are changing, and new products are being launched. Data scientists provide the necessary link between business knowledge and analytics expertise to provide these insights.

4 NEW TECHNOLOGIES ARE RAPIDLY CHANGING COST & CAPABILITY DYNAMICS.
NoSQL databases, Hadoop, and cloud-based platforms are significantly driving down the cost and time necessary to create value from information initiatives.

The common denominator to these trends? Big Data — and the analytics that life sciences businesses need to make profitable sense from the unparalleled amount of information now available to them. But this opportunity is presenting a new set of challenges, too.

THE CHALLENGES

Life sciences businesses want to know what Big Data really means and where new approaches can deliver value to commercial operations. And then there is the big question: How do I start?

Here are some common issues we see at this stage:

"The data warehouse team says my request to add patient-level data sources and analytics will cost $3M and take 18 months to complete. I am launching the product in 12 months, and don't have that kind of budget or time."

"My analysts spend 80 percent of their time finding and acquiring data, and those are all one-off efforts. How do I get them ready access to all of the data they need? Where do I start? How do I develop a strategy that all the change agents can get behind, including IT?"

"None of the data integration firms I have talked to understand commercial pharma, and I cannot take the time to educate them on the analytics I am looking to create."

Meanwhile, data scientists and analysts play increasingly important roles as commercial analytics drivers, providing the new analytics that drive business decisions in a dynamic environment. They need access to all of the data to support business decisions and create competitive advantages. In fact, 80 percent of data scientists and analysts want access to comprehensive sets (subject areas) of integrated data rather than direct source data.

That's a big demand. A single "uber" data warehouse cannot deliver the agility and information necessary for commercial reporting and analytics across all of its dimensions and uses. This is where cloud environments and open source (Big Data) technologies have dramatically changed the cost and capability parameters for these adventures in information.

THE PAYOFF

The payoff begins by recognizing the new analytics requirements and the opportunities they represent. Today's data scientists and analysts can start with hypotheses and iterate through them; faster iterations lead to more insights. They can search and explore all of the data across its life cycle stages to find the answers and perform work in a "sandbox" outside the data warehouses. Data sets are not perfect, but they are directionally correct, and they deliver results quickly. Analysts can work with current information for immediate business decisions.

The result? Big Data claims are not exaggerated. Working from such a Big Data analytics platform, life sciences providers have been able to deliver results at one-tenth the cost and duration of a traditional implementation.

Data scientists and analysts spend the majority of their time exploring the data and creating new analytics vs. acquiring and understanding it. Analytics run in minutes vs. hours, leading to more iterations and reducing "information depreciation." And this environment can accommodate new data sources of any size.

In the commercial operations of pharmaceutical companies, understanding real-world patient behavior is critical to brand messaging and sales activities. Here's an example:

A top-20 pharma company needs to know if its patients are taking medication as directed (adherence) and how long patients are continuously staying on their brand vs. the competition (persistence). The company delivers this information to its sales force so they can work with physicians if there is an issue in their territory and to adjust marketing content if necessary. The company also needs a way to measure results from both activities as soon as possible to see if further actions are necessary.

The company receives weekly claims data for their brand and the competition, but it takes two to three weeks to create the adherence and persistence information, and by then the insights are not useful. They turned to a hosted Big Data platform to see if they could do better. With cloud and open source technologies, they were able to run the analysis in 20 minutes. The data lag went from four weeks to one week (the lag inherent in the data itself), and it took one month to implement — after the data-warehouse team had anticipated that the effort would take eight to nine months. While the company relied on Big Data expertise from a consulting company for the initial proof-of-concept, the end result was compelling enough for them to start building a Big Data platform and start training internal resources to handle the processing.

WHERE DO WE GO FROM HERE?

Big Data can be described in many ways, but the real value lies in providing a set of technologies and capabilities that data scientists and analysts can use to better inform business decisions at all levels of the commercial organization. The traditional data warehouse still has a role, but organizations need to rethink the data eco-system to incorporate the new discovery analytics that are so important to staying competitive in today's market. By incrementally testing these new technologies and resulting insights, life sciences organizations can determine the best way to integrate Big Data with their existing data warehouse investments.

Rich Sokolosky is partner, life sciences practice leader for NewVantage Partners, a consulting firm that provides expertise and guidance to Fortune 1000 business and technology executives who are seeking to leverage data and analytics to gain business insights and derive business value.

The Next Hotspots For CMO/CRO Growth In China

DAVID FRIESEN

Mr. David Friesen, a British writer and editor, has been living in China since 2005. His current roles include managing editor of *China-Britain Business FOCUS*, copy editor for *LittleStar* magazine, and contributor to *Financial Times* and *CKGSB Knowledge*.

A number of forward-thinking development zones (i.e., regions) in China are now investing more into creating and fostering CROs and CMOs. This makes sense considering these types of organizations are usually associated with innovation, and China already has an environment fit for innovation with its large population and corresponding ability to test and enhance new ideas. In addition, through the "Healthy China 2020" program, the country is making biomanufacturing a major priority.

Overall, China's share of the CRO and CMO market globally is predicted to grow from its present 7 to 10 percent to near 20 percent in the next three to four years, according to a report by the Chemical Pharmaceutical Generic Association (CPA), an organization representing manufacturers of generic APIs in Italy. Much of that growth is likely to come from China's top industrial zones where innovation and R&D are key areas of emphasis.

The proximity of firms and advanced infrastructure at such zones allows companies to collaborate and develop research much more effectively than on their own. One example is the Tianjin Economic-Technological Development Area (TEDA), which has been ranked China's top development park by the Ministry of Commerce for every consecutive year since 1998. The Tianhe-BGI Bioinformatics and Computing Joint Laboratory, launched in the Binhai New Area in 2012, is another success story. This cross-disciplinary joint venture uses the Tianhe-1A, the world's second-fastest supercomputer, to research biological sciences, completing human genomics association studies in 3 hours as compared to the previous time of more than 300 days.

FOSTERING THE VALUE OF PARTNERING/COLLABORATION

To further CRO and CMO growth in China, it's imperative to foster synergy between firms in industrial clusters. That's why TEDA continues to evolve, creating specific areas for CRO, biologics, plant medicine, generics, and medical equipment. This clustering strategy also creates a more integrated approach to the local market, which is a trend that Accenture notes is becoming more popular. "An approach focused around clusters helps a company develop a more targeted, therefore more customer-centric, strategy," says Anne O'Riordan, global industry managing director for Accenture's Life Sciences practice.

Developing such links isn't always easy, however, which is where industrial zones such as TEDA come in by helping to forge closer ties between firms and provide the infrastructure for CROs and CMOs to thrive. For example, thanks to TEDA's brokerage, CRO and CMO firm AsymChem successfully got $47 million (US) in loans from the China Development Bank. This helps to trigger a radiating effect in the area, attracting more businesses and further increasing links.

According to Li Hongliang, deputy general manager of TEDA Science and Technology Development Group, "What is important for pharma companies to survive and thrive not only consists of top-level 'hardware facilities', but more importantly, a holistic approach in support programs." He further elaborates that the TEDA administrator provides "all-cycle" support to the pharma tenants, with services such as licensing, financing, talent support, marketing and business development, legal, and environmental policy compliance.

BIG GROWTH EXPECTED

TEDA's ecological-circle strategy has allowed for some of the most innovative links and drug research collaboration between foreign and domestic firms anywhere in China. For example, in May 2012, TEDA tenant company CanSino started to collaborate with Maryland-based Aeras on the development of CanSino's tuberculosis vaccine candidate Ad5Ag85A. With TEDA's support, these novel vaccines are now beginning to near clinical development, showing how far China's contract pharma industry has come in the last few years through the help of forward-thinking industrial parks.

In 2013 alone, more than 10 new drug discovery projects at TEDA were selected as nationally significant R&D projects, and another 10+ ventures obtained clinical trial approvals. By 2015, TEDA's biomedical industry output will reach an average annual growth of 25 percent. There are expected to be more than 20 firms with annual output value of $79 million (US) or above, 30 R&D institutions, and over 150 new- and high-tech biopharma companies. And with R&D expected to account for more than 10 percent of total revenue, further collaborations and innovations are surely on the way.

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The Importance Of Perspective-Taking In Leadership

DANIEL PINK

Try this simple experiment. First, with the hand you use for writing, snap your fingers five times quickly. Now, with the forefinger of that hand, on your forehead draw a capital E. Believe it or not, how you drew that letter might reveal how you act as a leader.

This "E Test" is a technique that social scientists have used since the early 1980s to measure what they call "perspective-taking." Researchers control for handedness, distract participants with finger-snapping, and then ask them to scrawl the vowel on their forehead.

There are two ways people can draw the E. They can draw it so someone else can read it—that is, with the open side of the E facing to their left. Or they can draw it so they can read it – with the open side of the E facing to their right. The test measures what we do out of habit and instinct. When we don't know what's being measured, what's our go-to move? Do we take the other person's perspective? Or do we stick with our own?

Whether you're selling a product, pitching an idea, or trying to get employees to do something different or do something in a different way, perspective-taking has become an essential element in moving others. Over the last decade, social scientists like Adam Galinsky of Columbia University have deepened our understanding of perspective-taking. Their work yields three ways leaders can become more effective.

1 **CHECK YOUR POWER.** Galinsky and others have found that when people feel powerful, their perspective-taking abilities degrade. The more powerful we feel, the more we anchor in our own perspective rather than adjusting to another's. And that can make others less likely to go along. But briefly reducing one's feelings of power ("Maybe this employee I'm asking to do something needs our company much less than our company needs her.") can increase the acuity of our perspective-taking, which in turn can make us more effective.

2 **PERSPECTIVE-TAKING ISN'T TOUCHY-FEELY.** Perspective-taking sounds a lot like empathy, but the two qualities are siblings, not identical twins. Empathy — the ability to understand another's emotional state — is an essential human quality. But research has shown that, in commercial settings such as negotiations, understanding the other side's thoughts and interests, not simply their emotions and feelings, can be more effective in forging a deal. So if you're in a high-stakes leadership situation, definitely be emotionally intelligent. But use your head as much as your heart.

3 **DON'T FORGET MIMICRY.** Mimicking others' posture, gesture, and expressions sounds like the sleazy tactics of a used car salesman. But ample research has shown that mimicry is a natural part of human behavior, an instinctive way we understand others. You can enhance your attunement skills, and thereby your leadership, simply by being conscious of how the other person is standing, moving, and talking and ever so slightly mirroring what they're doing. L

Daniel H. Pink is the author, most recently, of *To Sell is Human: The Surprising Truth About Moving Others.* (www.danpink.com)

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