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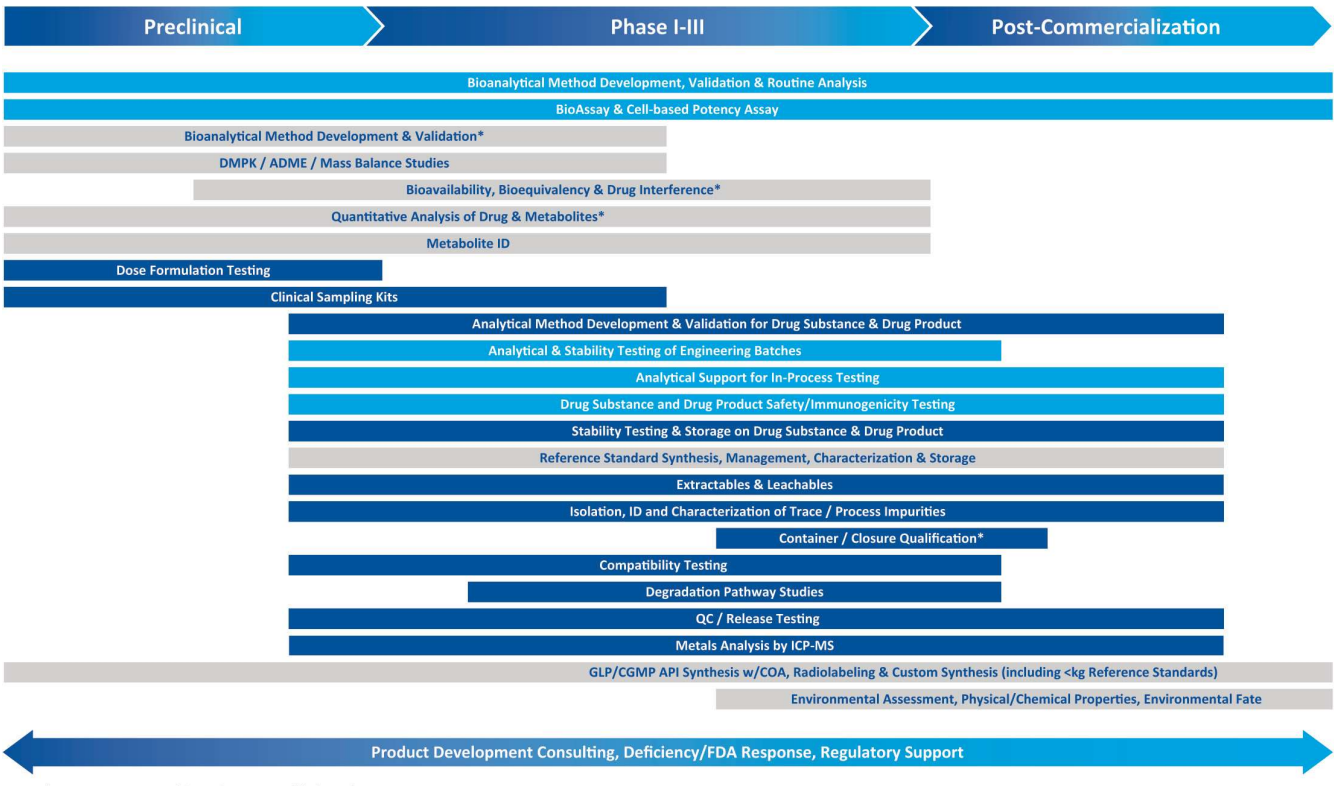

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How Astellas Makes Science A Sustainable Business

Jim Robinson, president of Astellas Pharma US, reveals how to avoid letting the allure of science sink your product's profitability. **p. 20**

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What Are The Top BioPharma Trends To Watch In 2015?

ROB WRIGHT Chief Editor

Prior to the end of 2014, we sent an email to every member of *Life Science Leader*'s (LSL's) editorial advisory board (EAB) listed on p. 8. In addition to thanking them for their service and making sure they were getting value from participating, we sought their insights. Specifically, we asked each to please provide a bulleted list of the top three trends, topics, issues, or people LSL should be covering in 2015. While the responses were as diverse as EAB member backgrounds, some common themes did emerge, starting with globalization.

One EAB member wrote, "All the attention on Ebola has served as a long-overdue wake-up call for other global health crises." While an Ebola epidemic in the U.S. remains highly unlikely, the cost of containment is not free. It took Nina Pham, the Dallas nurse who contracted Ebola while caring for the first U.S. person to have the virus, 13 days in the hospital and an estimated $110,000 to get her a clean bill of health. Experimental medications or care in specialized biocontainment facilities could easily push Ebola treatments in excess of half a $1 million per victim. In a global economy, applying first-world isolationist thinking to global health problems will eventually result in what were once perceived as third-world nuisances (i.e., Ebola) eventually becoming major second- and first-world problems — with dire ethical and economic consequences.

In addition to the economic impact of global health (or lack thereof), other trends highlighted as being global in scope include clinical trials, partnering and funding innovation, aging manufacturing facilities and their impact on drug shortages, supply chain risk mapping, the continued shift toward biologic drug development, and the impact biosimilars will have on biologic innovation. While not all are addressed in this issue, you can find insights on conducting clinical trials in Eastern Europe (p. 42); what Ireland is doing to facilitate partnering, innovation, and training (p. 44); as well as an in-depth analysis of the global biosimilars market (p. 40).

Other topics of interest to the EAB include personalized medicine, Big Data, the biotech IPO boom, expanded access and compassionate use, the coming of age of exon skipping, the melding of branded and generic businesses, and patient empowerment — which seems to be a new spin on "patient-centric." Eli Lilly's chief medical officer, Tim Garnett, provides some personalized medicine insights (p. 8), and financial expert, Dennis Purcell, gives his take on how the recent biotech IPO activity has led to a new era of interdependence (p. 32).

However, by far, drug pricing and reimbursement were the two biggest trends EAB members stressed for us to pay attention to in 2015. While John LaMattina shares his thoughts on the former (p. 8), with regard to the latter, look to this month's cover feature. Jim Robinson, president of Astellas Pharma US, shares how his company is leveraging commercial insights (e.g., conducting insurance reimbursement assessment during early drug development) to help make its science more sustainable (p.20).

We are grateful for having such a highly engaged EAB. And while we appreciate their ongoing input, some of the best industry intelligence often comes from you, our readers. Rather than waiting to get an email from us seeking your suggestions, why not take a more proactive approach? The best way for LSL to provide you with the content you want is for you to tell us what content you need. L

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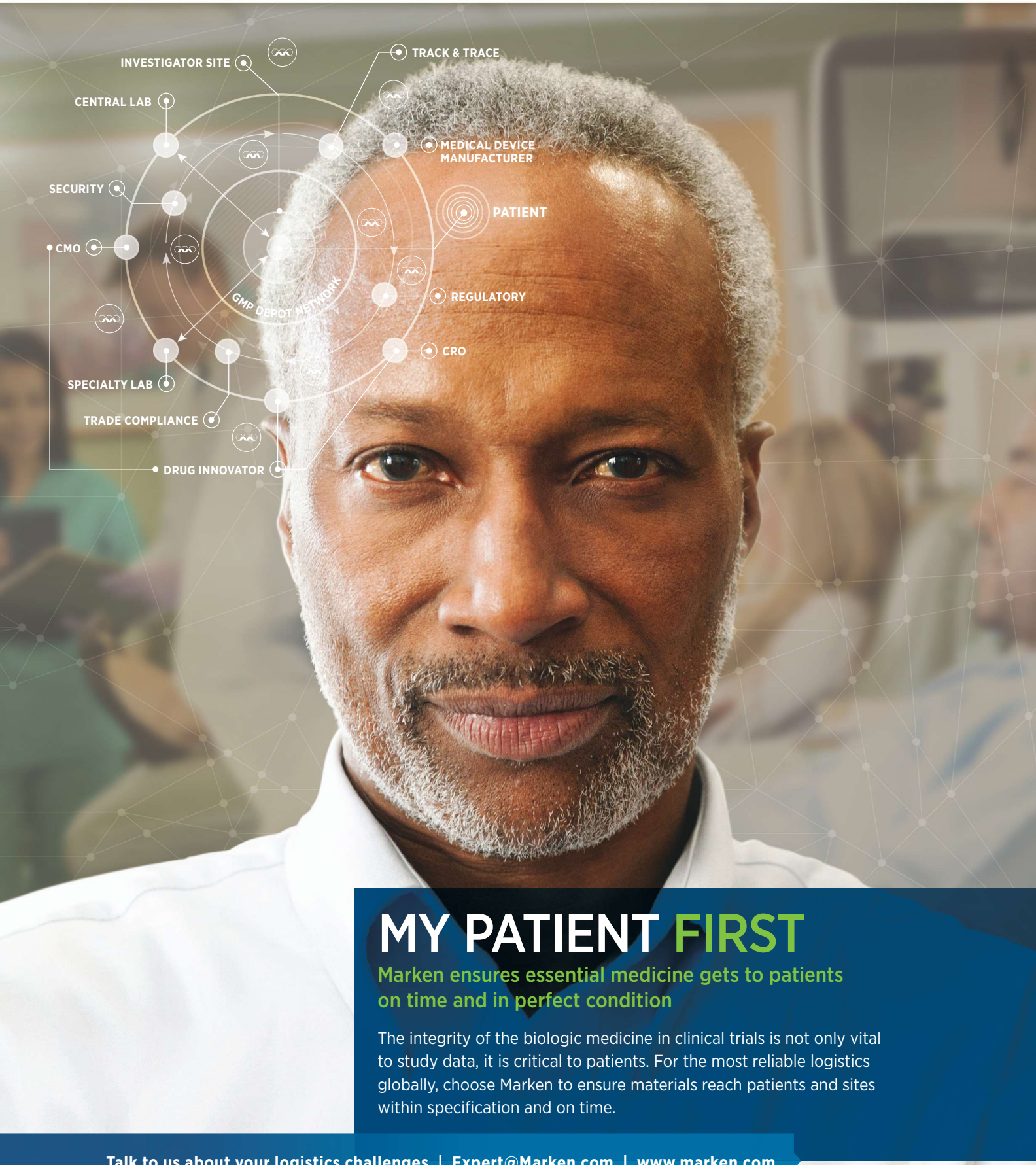

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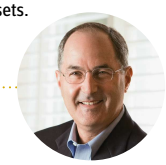
Q What innovations are needed to create better diagnostics for personalized medicine, and how can payors support them?

A NEXT GENERATION SEQUENCING (i.e., high throughput sequencing of genes via a panel) may enable more genetic information to be efficiently generated to best determine a course of treatment. Although this technology offers significant benefits, improvements in it are still needed for faster turnaround time, decreased cost of testing, and standardization of analytical methodologies. Liquid biopsy is another emerging technology creating the means for less-invasive sampling for patients. Rather than extracting tumor tissue via biopsy to test the tumor for molecular targets, sampling of blood may enable testing of tumor cells. Payors can ensure reimbursement for companion diagnostics, including those derived from novel technologies, to enable access to corresponding drug treatments. New business models should be created which view the companion diagnostic and drug as a single entity. They create value for the healthcare system when used together.

TIM GARNETT
Dr. Tim Garnett is the chief medical officer and senior VP of Medicines Development Unit (MDU) for Lilly and is responsible for medical, regulatory, global product safety, and global health outcomes.

Q From your perspective, what is the top trend/topic/ issue in our industry? Why?

A THE EBOLA SCARE SERVED AS AN OVERDUE WAKE-UP CALL about the potential spread of infectious diseases, including drug-resistant bacteria. Each year, more than five million people in the U.S. and Europe become infected with serious, resistant bacterial infections, and at least 48,000 die as a direct result of these infections. More than two million children, mostly in the undeveloped world, die each year of bacterial pneumonia alone. Without increased action, a nightmare scenario will continue to emerge. While the worldwide chorus advocating reforms has gotten louder, more needs to be done. We should enforce better surveillance and infection control in hospitals, use antibiotics only when necessary, and reform reimbursement policies to accelerate innovation. Additionally, we should develop new, targeted antibiotics through clear regulatory pathways and rapid diagnostics, which will promote antibiotic stewardship and appropriate use of these assets. Above all, we should remove barriers that prevent millions of people annually from getting the right medicine at the right time.



BARRY EISENSTEIN
Barry Eisenstein, MD, FACP, FIDSA, FAAM, is senior VP of scientific affairs at Cubist Pharmaceuticals

Q What is the top trend, topic, or issue in our industry, and why?

A DRUG PRICING. More drugs for cancer and rare diseases will be approved by the FDA. These will come with high price tags. While most of these drugs are priced responsibly, insurance companies will still howl when they come to market, as they did with Gilead's Sovaldi. Because many new drugs are priced extremely high, people are challenging the basis of these costs. Certainly, these prices aren't justified by the amount of R&D spent. Nor are they justified on the amount of money sunk into previous R&D failures. Drugs should be priced based on value. For example, if a patient with a rare disease costs the healthcare system $600,000 per year (i.e., hospitalizations, doctor care, home care), the introduction of a new drug that enables a patient to have a normal life, even if priced at $300,000 per year, still represents a win for all.

JOHN LAMATTINA
John LaMattina, Ph.D., is the former senior VP at Pfizer, Inc. and president of Pfizer Global Research and Development. In this role, he oversaw the drug discovery and development efforts of more than 12,000 colleagues in the United States, Europe, and Asia.

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SGR Offset: Replacing Individual Mandate With Late Enrollment Penalty

JOHN McMANUS The McManus Group

What if Congress could repeal Medicare's dysfunctional sustainable growth rate (SGR) payment formula for physicians — a budgetary gimmick that Congress has overridden 17 times in a dozen years — once and for all, as well as repeal the reviled individual mandate without fundamentally disrupting the marketplace in the Obamacare exchanges?

That package would represent a health policy coup and could come together as early as this spring before the current SGR patch expires on March 31st, after which physicians will confront a 21 percent pay cut. Last year, the House and Senate committees of jurisdiction developed a comprehensive, bipartisan replacement to the SGR, but the agreement failed to advance because consensus could not be achieved on whether or how to fund the $120 billion price tag of repealing the pending cuts.

Every sector of healthcare, including the life science industry, would cheer a permanent solution because the annual ritual of identifying offsets to fund temporary patches requires real cuts to address the gimmick. But it will require collaboration between the Obama administration and Republicans.

IMPLEMENTATION OF THE INDIVIDUAL MANDATE HAS COMMENCED

Americans have begun filing their tax returns, and millions are discovering the grim reality that their refunds will be dramatically reduced because they failed to obtain health insurance — in violation of the individual insurance mandate in Obamacare. This means they are subject to a tax penalty equal to the greater of $95 or one percent of their income (up to the cost of the average "bronze plan" premium of $2,448).

This is the first year the individual mandate will be enforced, and its bite will increase over time as it is fully phased-in. The minimum penalty for failure to have health insurance will skyrocket from $95 in 2014 to $695 in 2016; the Congressional Budget Office (CBO) predicts 4 million will be hit. Exemptions are provided for certain categories of people, including those with incomes below the filing threshold and those who obtain a hardship waiver (now with 14 different ways to qualify). The political ramifications of the penalty are just beginning to be felt.

Notwithstanding the expected political backlash, the Obama administration has insisted the individual mandate is critical in ensuring the healthcare marketplace functions properly, arguing that without it, healthy and young people who can help spread risk will defer enrolling. These gen-X hipsters are needed to balance out the high-risk individuals who benefit from the Affordable Care Act (ACA) provisions that prohibit insurers from charging sick more than healthy individuals, and also prohibit insurers from delaying or excluding coverage for pre-existing conditions. Without an incentive to purchase health insurance, adverse selection would ensue, whereby only high-risk individuals sign up for coverage and could result in an eventual death spiral of premium escalation.

But is an individual mandate enforced through the tax code the only way to solve the adverse selection policy problem? No.

ALTERNATIVE TO THE INDIVIDUAL MANDATE: LATE ENROLLMENT PENALTIES

Medicare operates effectively today with no individual mandate and instead relies on late-enrollment penalties to encourage individuals to sign up without delay.

- In Medicare Part B (covering outpatient services like physician visits), beneficiaries are automatically enrolled unless they opt out. The Part B penalty for failing to enroll is equal to 10 percent for every 10-month period the individual was eligible but did not enroll.

- Under Medicare Part D (the prescription drug benefit), individuals must affirmatively enroll in a prescription drug plan or Medicare Advantage plan. Failure to obtain prescription drug coverage through those sources or maintain coverage

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through another source (e.g., employer-sponsored care) results in a late-enrollment penalty that is collected by the Medicare insurer through its monthly premium.

Rather than collect a penalty through the tax code for those who have not yet enrolled in health insurance, a late-enrollment penalty could be collected by insurers upon enrollment through scaled monthly premiums. The IRS would be removed from the equation. But the policy would achieve the same goal: punish free-riders who wait to get coverage until they get sick.

The amount of that penalty could be defined in statute or deferred to the Secretary who would be tasked to develop an actuarial basis for assessing that penalty. It has worked in Medicare; why not apply it to Obamacare?

From a political perspective, it is critical that the Obama administration have a major hand in writing this provision, as it impacts its program.

REPEALING THE MANDATE RESULTS IN SAVINGS THAT CAN BE USED FOR SGR REFORM

Last year, CBO scored a five-year delay of the individual mandate as saving $169 billion over 10 years. Earlier CBO analysis stated that a *repeal* of the mandate would net $282 billion over 10 years, mostly due to lower projections of covered and subsidized individuals.

CBO predicted Medicaid and SCHIP (State Children's Health Insurance Program) savings of about $149 billion and $69 billion in lower federal subsidies in the health insurance exchanges. The savings derive from CBO's markedly lower enrollment projections in those programs without an insurance mandate, including 4 million fewer enrolled in employment-based coverage, 6 million fewer in individual-based coverage, and 6 million fewer in Medicaid and SCHIP. CBO also estimates that removing the mandate would result in $80 billion in increased tax revenue through reductions in employer coverage, as compensation would move from untaxed health benefits to taxed wages and profits.

Curiously, CBO clearly believes the individual mandate makes a material difference in enrollment for individuals who would *not be subject to the penalty* — the 6 million Medicaid/SCHIP beneficiaries who do not file taxes and are therefore exempt and another 4 million that are offered employment-based coverage. It is hard to understand why CBO expects enrollment to change so dramatically for these populations, as Medicaid subsidies and the employer mandate would remain intact. Would 6 million individuals dis-enroll from Medicaid and SCHIP or fail to sign up for those programs — which offer free healthcare — if the government repeals a provision that does not apply to them? Would 4 million individuals decline employer-provided care when most privately-insured individuals have been obtaining health insurance through their employer for years, with no individual mandate? That is unlikely; but it is precisely what CBO stated as recently as last summer.

Notwithstanding the flawed projections, all that is relevant from a scoring perspective is that CBO determined repeal of the individual mandate would create $229 billion in savings available from these two population groups. If a policy can be constructed to address the adverse selection policy concern, the savings are in essence "free money." What better use for this free money — gimmick money, if you will — than to permanently fix another gimmick?

Yet, there is some urgency on acting in this area, as the Supreme Court is considering the *King v. Burwell* case regarding the constitutionality of administering subsidies through the Federal exchange, notwithstanding the ACA's legislative text stating that subsidies are available only for exchanges "established by a state." Congress must act in this area and capture the savings before the Supreme Court issues its decision in June, or the free money is potentially lost forever.

Republicans would achieve a major victory in repealing the most reviled aspect of Obamacare — the government mandate to purchase a private product. In addition, they would dispense with SGR — a costly problem that requires them to own offsets for future patches and has the entire health community on edge.

Democrats are realizing that the individual mandate will continue to be a political albatross and has been largely gutted through hardship and other exemptions. Better to deal with it now in a comprehensive fashion that preserves a functioning marketplace envisioned in the ACA. Otherwise they might continue to lose even more seats and be tossed from the White House.

And both Congress and the administration would achieve a major policy breakthrough by finally repealing the SGR and initiating the physician payment reforms contained in that bipartisan legislation. This would be a productive way to achieve a healthcare policy win in the divided government of the 114th Congress. 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.

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WAYNE KOBERSTEIN Executive Editor
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SNAPSHOT

Tetra is developing a new class of phosphodiesterase 4 (PDE4)-inhibitor drugs to treat patients with a wide variety of "cognition-impairing" conditions. Its lead product, a PDE4D inhibitor (BPN14770), will enter Phase 1 human trials in Alzheimer's disease this year, and two other pipeline candidates are PDE4B inhibitors in preclinical development for treating neuroinflammation and traumatic brain injury.

WHAT'S AT STAKE

Bringing a new brain-affecting drug to practice requires overcoming a lot of scientific skepticism from past failures. Tetra's CEO Mark Gurney gathered a team of researchers to take a new look at PDE4, part of a chemical mechanism of memory in the human brain. Previous cognition-enhancing drugs designed to modulate the pathway by inhibiting PDE4 had the side effect of overwhelming nausea, which had discouraged and essentially ended further development. For Tetra's lead compound, BPN14770, the company focused on the single subtype associated with the side effect, PDE4D, and found a potential way around the problem.

"PDE4D exists in one of two states, an off-state in which it is partially inhibited, versus a phosphorylated, on-state in which it is fully active," Gurney explains. "Since the drug has little effect on PDE4D in the off-state, it has very good tolerability. Our team was the first to solve the crystal structures of the PDE4 regulatory domains, the first to exploit the negative allosteric mechanism, and the first to develop PDE4 subtype-selective inhibitors based on this new knowledge."

PDE4D affects the entire cAMP (cyclic adenosine monophosphate) signaling mechanism, giving Tetra's approach another advantage, according to Gurney. "BPN14770 potentiates cAMP signaling while maintaining the spatial and temporal patterning of information flow through brain circuits important for memory. As BPN14770 does not address a specific neurochemical deficit or disease pathway, it will have broad cognitive benefit across multiple neurologic and psychiatric illnesses."

Still, the company inevitably faces a steep uphill battle to overcome the lingering doubts of investors and prospective partners. It has adopted a "hybrid financing model" with substantial support from the NIH Blueprint Neurotherapeutics Network (BPN) to fund and conduct its R&D program.

"Through the BPN, Tetra received not just funding but also access to a network of industry professionals with deep knowledge of all aspects of drug discovery," says Gurney. "This meant we did not need to go it on our own, but instead, and from the outset, had a remarkable team working toward the goal of delivering a breakthrough drug for human clinical trials."

Gurney says he expects the company will have a commercial partner before it reaches Phase 3 trials but is prepared to go further alone if needed. "Given the important medical need and the potentially transformative value of BPN14770 to patients, their families, and their caregivers, Tetra should be able to raise financing all the way through late-stage clinical trials and market approval." Yet, he adds that, from an early stage, Tetra has received attention from licensing groups at larger companies, as well as access to regional and national venture capital funds.

Gurney points to another special hurdle common to CNS companies: to show, in early human clinical trials, that its drug reaches the brain and engages the target. "Cutting-edge CNS programs need to deliver both a drug and an imaging agent, typically a PET ligand, to demonstrate target engagement. This doubles the complexity of the discovery phase, as PET ligands have their own set of optimization criteria which are distinct from CNS drugs." Fortunately, he says, the company is "making rapid progress" in identifying a PET ligand it can use in early human trials of its lead product.

MARK GURNEY
Chairman and CEO

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The CDMO Model And Outsourcing Development

In 2014, the biopharmaceutical industry witnessed more and more contract suppliers take on the CDMO (contract development and manufacturing organization) acronym to identify their ability to assist at the development stage of drug manufacturing. These businesses can provide comprehensive services, from drug development through to manufacturing commercial supply, and are interested in differentiating their abilities from CMOs focused solely on large-scale manufacturing projects.

KATE HAMMEKE
Director of Marketing Intelligence
Nice Insight

> *"Larger companies tended to take advantage of outsourced development assistance with greater frequency than smaller companies."*

Theoretically, the CDMO is positioned for a strategic partnership, with expertise in areas the drug innovator seeks, whereas the CMO may be viewed as a tactical provider that has the available capacity to compete for the project. This perception has influenced many contract manufacturers to embrace the CDMO term as an additional advantage in the effort to develop long-term partnerships.

Utilizing a CRO or CMO for early-stage analytical, stability, preformulation, formulation development, and drug delivery method has become more common in the pharmaceutical industry and is anticipated to increase as the strategic partnerships between drug innovators and contract suppliers mature. This creates more opportunities to secure business from drug innovators across the drug's life cycle. In 2014, Nice Insight began tracking the development offering separately from commercial-scale production in order to keep abreast of buyer activities at the development stage and to identify whether CMOs offering development-stage services would have an advantage over the competition when it comes to strategic partnerships.

The results from the 2015 study (released Jan. 1) show that 10 percent of respondents stated their company will engage a CMO for small molecule API development, and 10 percent would outsource solid/semi-solid or liquid dosage form development. Thirteen percent stated they would engage a CMO for large molecule API development and 12 percent for injectable product development. In comparing the overall data for 2014 and 2015, there was little change in the percentage of respondents who anticipated engaging a CMO for assistance with API or dosage form development — only 1 and 2 percentage point increases. However, regarding the activities within the various buyer categories, the data showed more variances.

Interestingly, larger companies tended to take advantage of outsourced development assistance with greater frequency than smaller companies. While this results from a variety of factors, from larger outsourcing expenditures, to using CMOs and CROs for a higher number of services in general, and to having a larger pipeline for potential therapeutics, it conflicts with the notion that Big Pharma and Big Biotech have in-house development

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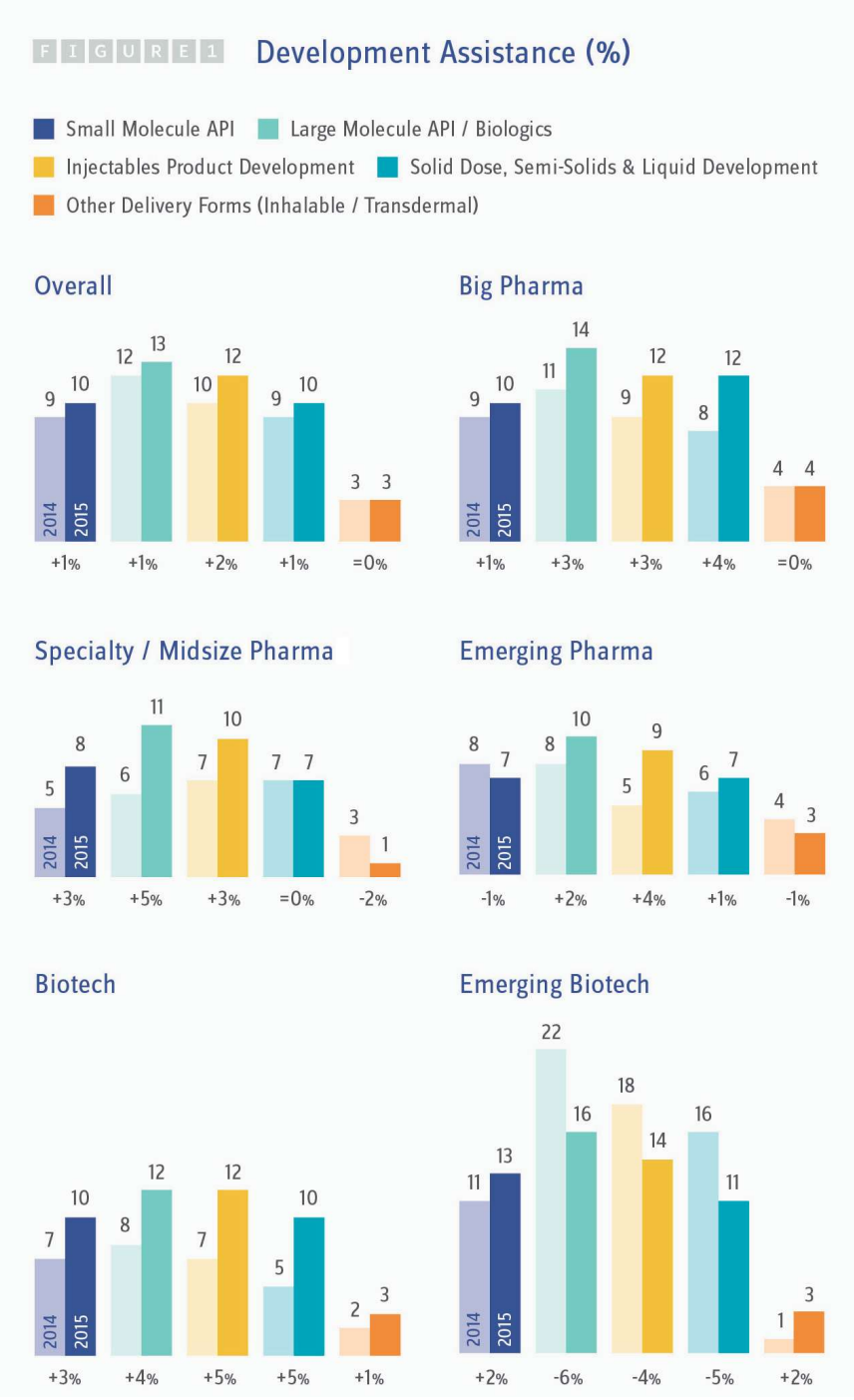
Federal Equipment Company

FIGURE 1 Development Assistance (%)



Survey Methodology: The Nice Insight Pharmaceutical and Biotechnology Survey is deployed to outsourcing-facing pharmaceutical and biotechnology executives on an annual basis. The 2014-2015 report includes responses from 2,303 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 ~125 CMOs and ~75 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.

expertise. This supports the finding that outsourcers, regardless of company type, are looking to CMOs for expertise — a shift in from historic usage where a CMO's primary purpose was to provide needed capacity.

OUTSOURCERS, REGARDLESS OF COMPANY TYPE, ARE LOOKING TO CMOs FOR EXPERTISE

Big Pharma and midsize companies showed an increase greater than 2 percentage points in three of five development categories, whereas emerging pharma showed increased outsourcing in only one category. Biotech companies showed an increase in four of five categories; however, emerging biotech did not have any increases greater than 2 percentage points. As a matter of fact, emerging biotechs indicated decreased outsourcing in three categories of development services when compared to 2014 behavior. It is important to mention that emerging biotech companies engaged a CMO for development assistance at the highest rates out of the five buyer categories in 2014 and 2015, despite these downshifts over last year predicted for 2015.

Biopharma companies' increased usage of CMOs for development activities corresponds with a significant rise in interest in strategic partnerships. These changes support the theory that offering development services will make the CDMO more appealing to a pharmaceutical sponsor and give an advantage over the traditional CMO.

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.

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How To Make Your Science A Sustainable Business

BY ROB WRIGHT

JIM ROBINSON President of Astellas Pharma US

The term "sustainable business" is frequently associated with a company being "green" and minimizing its environmental impact. According to Jim Robinson, president of Astellas Pharma US, sustainability in biopharma should equally be associated with having a positive cash flow. "People fall in love with the science, which is always exciting," he attests. "Ultimately, however, scientists hope their idea will result in the launch of a commercialized medicine that will benefit patients." Robinson, a 20+ year veteran of the commercial side of biopharma, shares business insights to consider when taking your company's drug development dreams from concept to commercial reality and also reveals how to avoid letting the allure of science sink your potential product's or company's sustainability.

THINK SALES CAN'T HELP YOUR SCIENCE? THINK AGAIN.

Robinson and I have something in common — we both got our start in pharma as field sales representatives. "I find some people are hesitant to say they are in pharmaceutical sales," he shares. "When I encounter this, I tell them they should be proud, because sales is a noble profession."

Think you can't benefit from connecting more closely with the commercial side of the business? Think again. Some of the most successful pharmaceutical executives in the world got their start in sales. For example, Alex Gorsky, chairman and CEO of Johnson & Johnson, began his career at the world's largest pharmaceutical company in 1988 as a sales representative with Janssen. Another pharmaceutical executive fond of saying he "carried a bag" is Fred Hassan. A legendary pharmaceutical company turnaround expert, Hassan brought Pharmacia back from the brink to be acquired by Pfizer for $60 billion, as well as Schering-Plough, which was acquired by Merck for $41 billion.

Jim Robinson was an employee at Schering during Hassan's tenure as chairman and CEO. "I was very fortunate to observe Fred Hassan when he came into Schering-Plough to rebuild the company during a difficult time," he states. Hassan was a big proponent of leveraging salespeople to gain valuable insights to improve his strategic decision making, a concept captured in the *Harvard Business Review* (July 2006) article, "Leading Change From The Top Line." Robinson also is a believer of this strategy/model. Though his list of responsibilities at Astellas includes management of U.S. commercial operations across a diverse and growing portfolio of products, encompassing urology, immunology, oncology, infectious disease, and cardiovascular, Robinson interfaces a great deal with Astellas scientific and medical affairs (ASMA) and global medical development (GMD) in order to help the top 20 biopharmaceutical continue to build its U.S. business. "My organization represents what we call a strategic view of product planning," he states. "We [the commercial side of the business] are involved in the development phase, in terms of the stage gates of our development, from Phase 1 through Phase 3."

According to Robinson, sales and marketing play a pivotal role in developing the target product profile (TPP), which at Astellas is referred to as the product scheme sheet (PSS). The PSS provides a format for discussions between the company and the FDA throughout the drug development process — from preinvestigational new drug application (pre-IND) or IND phases of drug development through postmarketing programs that pursue new indications or other substantial label changes. If you have any experience in developing drugs, you are most likely familiar with the benefits of using TPP (e.g., serves as a living document to house the most current information on the intended product's characteristics and use, provides your R&D team vision and focus very early in the process as to what the actual product could look like). However, depending upon your level of commercial exposure, you may not be familiar with how to leverage the knowledge and experience of commercial leaders to improve your drug-development process, or even why you should.

> "Once you see a PoC, you definitely want to make sure there are clear and transparent partnering discussions taking place between commercial and development as to what makes sense in bringing a drug to market in the U.S. versus Asia or Europe."
>
> **JIM ROBINSON**
> President of Astellas Pharma US

SALESPEOPLE — YOUR LINK TO THE VOICE OF THE CUSTOMER AND COMMERCIAL SUCCESS

For those who wonder how and why commercial insights should play a pivotal role in your drug development process, Robinson explains it this way: "We provide the R&D department information on what the customer — the payor, patient, and provider — finds important. This kind of data helps us understand what these customer groups need to see from the clinical development program or, in the final submission, to make a worthwhile product for our organization to commercialize. There are processes at Astellas that enable us to have a very robust review at each step in the development cycle."

According to Robinson, at Astellas the commercial team becomes actively engaged in development when a product reaches Phase 2B. "Until this point, you're really looking at proof of concept," he states. "Once you see a PoC, you definitely want to make sure there are clear and transparent partnering discussions taking place between commercial and development as to what makes sense in bringing a drug to market in the U.S. versus Asia or Europe." However, Robinson suggests you not discount the value of involving your commercial team even earlier in order to develop the best product with the maximum opportunity for reimbursement and access for patients. With today's tradeoffs and limited resources, bringing commercial insights into a Phase 2A discussion could prevent working toward a PoC for a product that will never have any marketable value. "Why not kill it then," he asks, "versus spending money on Phase 2B, then getting into Phase 3 where you're spending a lot more money?"

Sitting across from Robinson during our interview, I must have unknowingly given him a look of skepticism as to the value of bringing the "voice of the customer" into a drug development discussion prior to Phase 2B, because he then leaned forward and stated, "I'll give you a real example." Astellas had a drug in early-stage development. "Clinically, it looked valuable," he relates. "Prior to the finalization of PoC, it looked *really* valuable." This is the point at which the commercial team conducts a thorough market evaluation. "Our marketing intelligence organization did exhaustive market research, beginning with the therapeutic area," he recounts. "They understand the market, the current products — if any exist — and make sure there is a well-defined and well-established unmet medical need. From there, we try to define the right product profile needed to be able to deliver on value,

outside of what the current treatment regiments are. Are we differentiated, or are we too similar to what the current standard of care is? If we are similar, what do we need to do to differentiate the product to be able to provide value?"

When assessing a potential market, another key component not to be overlooked is local, regional, and national insurance reimbursement and pricing. "When we looked at the current reimbursement environment, we found there were changes taking place," Robinson says. "In terms of reimbursement, there was basically almost what I would call a DRG."

In case you aren't familiar, a DRG (diagnosis related group) is a means of classifying inpatient hospital stays for payment purposes. By grouping patients of similar disease state and stage, hospital administrators can accurately determine the type and quantity of resources required to treat a particular group, thereby providing better cost of treatment predictability. The DRG system, conceived in 1982 by Yale University's Robert Fetter and John Thompson, is an effort to standardize hospital costs and reimbursement. Assigning patients to a specific DRG places the burden on facilities to work within a structured reimbursement system.

According to Robinson, assessing the reimbursement landscape for the early-stage drug revealed that payment would be capitated at a rate in line with other already-available treatments. These low rates of reimbursement would prevent the product from achieving profitability. Despite Astellas having a product that looked good clinically and with a clearly established unmet medical need, the decision was made to end the development program. "If there is no payment in Medicare Part B, and

Strong Mentors Don't Always Come From The Workplace

Jim Robinson, president of Astellas Pharma US, admits to having been the fortunate beneficiary of strong industry mentors, such as Masao Yoshida, current CEO of Astellas Pharma US; Roch Doliveux, recently retired CEO of UCB; and leaders such as Fred Hassan, former CEO of Schering-Plough. For example, Doliveux pushed Robinson out of his comfort zone of working in the field to take a home-office position. "It was one of the best things for my career," he relates. Observing Hassan played an important role in the development of Robinson's leadership philosophy. "I heard him define leadership as 'Know the way, show the way, go the way'," he recalls. "I have lived this leadership definition ever since I heard him say it." As for Yoshida, his current mentor, Robinson has been afforded the opportunity to enhance his team-building skills.

To be sure, any rising pharmaceutical executive would be blessed to have worked with and observed the above-mentioned leaders. But you might be surprised to learn the name of a mentor who prompted Robinson to do what he says is one of the smartest things he ever did. Prior to joining Astellas in 2005, he read the book, *The First 90 Days* by Michael Watkins. "My mom actually got it for me when I came from Schering to Astellas," he laughs. "It's the best advice — best book — I ever got for a particular career transition." Thanks to mentor mom, after reading the book, he approached going from Big Pharma to a much smaller organization (at the time) with humility and a willingness to learn. "I listened for the first 30 days," he relates. "I listened to the folks in the department; I listened to their frustrations, challenges, and issues. I listened to our internal customers in terms of the sales force, marketing, and finance." In the next 30 days, Robinson built a plan with some of the people he met in the first 30 days who "knew their stuff," as well as the folks experiencing the "pain points" and greatest level of frustration. "By the time the last 30 days rolled around, I had identified the low-hanging fruit and what was necessary to address in order to build momentum and belief and then foster long-term support for the department."

This small act of mentoring by his mom continues to leave a lasting impact on Robinson. "Every time I have had someone leave or join the company, I insist they read *The First 90 Days*," he shares. Like any good mentor, rather than relying on someone to go out and buy the book, Robinson, like his mom, provides a copy so they can get started on their first 90 days right away.

there's no payment from the standpoint of commercial insurers, then the commercial opportunity doesn't exist," Robinson affirms.

He cautions scientists not to interpret his insights as commercial folk seeking to become experts in clinical development. "We're not the ones who will know how to effectively power the study to achieve the optimal outcome," Robinson says. "Our value-add is bringing the voice of the customer into a partnering approach with development to help product differentiation that is best for the patient." That being said, Robinson suggests that partnering your drug development program with commercial expertise should not be approached as a short-term commitment where sales, marketing, or managed-markets people are brought in sporadically to share insights. If you think of the partnership between drug development and commercial running from at least Phase 2 through loss of exclusivity, this could be a 15-year commitment requiring continuity to maximize productivity. "We're not going to stop this relationship once the product' has been commercialized. Because, as you know, we have postmarketing approval commitments," he reminds.

With regard to the early-stage drug, had the sole focus on science been allowed to cloud the business decision behind killing its development, Robinson believes Astellas would have ended up selling the product for pennies on the dollar. To effectively determine a product's commercial opportunity, task the team first with determining the net present value (NPV) of the opportunity, being sure not to allow the allure of "cool" science to leak in and potentially sink your company's sustainability — something Robinson knows from personal experience (see sidebar, "Don't Let Your Science Go To Your Head" on p. 26).

DON'T LET CONFIRMATION BIAS OR LACK OF EXPERTISE WRECK YOUR COMMERCIAL OPPORTUNITY

Because so many biopharma start-ups are founded by scientists, the possibility exists for company founders to lack commercial experience. Virtual and small companies in early stages of start-up may have limited resources to gather the voice of the customer. Regardless of your background, the stage of your company, or the size of your company, the worst approach to product development is for leaders to think they know what is best for the customer based on their own biased opinion. Scientists might believe their training in applying the scientific method (i.e., developing a hypothesis and setting out to prove it wrong) prevents them from falling prey to personal bias. However, the reality is that scientists are also as susceptible to the phenomenon psychologists refer to as "confirmation bias" — the tendency to seek evidence to support, rather than challenge, one's beliefs. Even worse, according to author and philosopher Matt Ridley, confirmation bias seems to get worse with greater expertise.

When I asked Robinson how he would go about advising scientist leaders on how to avoid confirmation bias from getting in the way of commercial success, he responded, "I would ask them to tell me about the market for this drug and why it is needed. What unmet medical and patient needs will it fulfill? Do you believe you can successfully compete in the marketplace and win? Oftentimes, you'll have discussions with folks who will say, 'All we need is 3 or 5 percent of the market.'" According to Robinson, any time you hear leaders start with a caveat, you should question what they are trying to accomplish with the product. "When I hear the modifier, 'All we need is' at the beginning of an explanation, it sets off my antenna that either they've set their expectations too low, or they know the product does not have significant commercial potential."

When asked what advice he had for executives lacking commercial experience, Robinson advised them to become phone and road warriors. "Talk to physicians, payors, and patients, within the appropriate confines of what the FDA will allow, and ask them to define for you what the perfect product would be for the therapeutic category you may be seeking approval. If the drug you're developing doesn't come close to their definition, then you've got to rethink your approach." Robinson says, "If you want to know the answer as to whether or not a product will be reimbursed, best to pose the question to the person who's going to influence such a decision." Robinson says he has found

> "If there is no payment in Medicare Part B, and there's no payment from the standpoint of commercial insurers, then the commercial opportunity doesn't exist."
>
> **JIM ROBINSON**
> President of Astellas Pharma US

insurance customers to generally be very candid and more than willing to give advice.

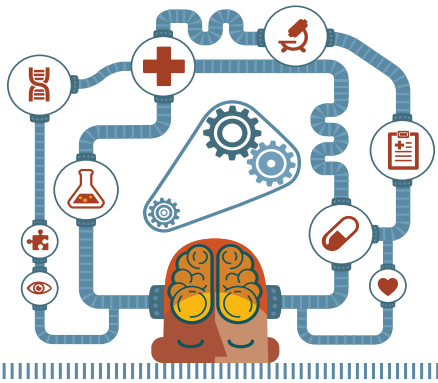
If you have access to a field or managed-care market sales force, he encourages you to get your scientists to go for a ride along with a field salesperson that doesn't involve a "milk run," and one that is possibly not in your home office's backyard. "A milk run is when sales reps set up a day of going to all their favorite doctors to make sure all is well," Robinson explains. While this might result in plenty of customer face time, it also is a biased sample. As for why to consider doing a ride-along away from your corporate office headquarters, despite the convenience and cost-savings benefits of doing it locally, the rationale is fairly obvious — cluster confirmation bias. While states like New Jersey and cities such as Boston can boast pharma and biotech clusters, if your company is in such a hub and seeking insights of local KOLs, odds are pretty good that so too are your competitors. And while KOL insight is always valuable, you would be wise to seek additional sources beyond those which are merely geographically convenient and perhaps more biased to tell you what they think you want to hear. Robinson's final piece of commonsense advice is to be open-minded to what the customer has to say. "Be willing to listen to what they have to say in helping you to understand the market, and be less concerned about how their insights impact the perspective you hold for the product you're developing," he suggests. Sustainable science and meeting patients' unmet medical needs require commercial success, which is predicated on having thoroughly studied the market first. L

Don't Let Your Science Go To Your Head

"Scientists getting too close to the science," is a theme I hear consistently in my experience in industry. The expression relates to scientists falling prey to their own biases and letting their love for a drug, device, or theory drive bad business decisions. But scientists aren't the only people susceptible to this phenomenon. We fondly remember how Steve Jobs proved doubters horribly wrong with Apple's successful launch of the iPad. Critics expected the iPad to flop, and yet, it went on to become the hottest selling consumer electronics device of all time. But let's not forget that Jobs, like many other entrepreneurs, had a lengthy list of failures (e.g., the Apple Lisa, Macintosh TV, Apple III, and the Powermac G4 cube), many the result of allowing his passion for a product to blind him to his personal bias.

Jim Robinson, president of Astellas Pharma US, can relate to Jobs as well as to scientists. "I'm better because of my failures," he admits. For example, when working at a company prior to Astellas, Robinson was adamant the company had a better product than its competition. "We believed this so strongly that we pushed the leader of our overall specialty organization for a head-to-head trial," Robinson recalls. "It'll be the proof point, once and for all, that we've got the better product, right?" Wrong. According to Robinson, the certainty of having a superior product translated into bravado, which resulted in pushing for an unnecessary study. Modeling showed there was little potential benefit to be gained. "But we pushed and pushed, and so eventually, it was done," he confides. What was the result? Turns out the expensive study revealed a tie. "The lesson learned is to know your boundaries," Robinson attests. "Know what you're good at, know what you're not good at, and share with the team the challenges you're facing." In this way, you can find multiple ways to address the challenges being faced and tease out the best approach. For example, Robinson says the company didn't have to do a head-to-head comparison. "We could have done a couple studies to show benefits in discrete patient populations."

If put in a similar situation, Robinson says, given this experience, he would take a much more measured approach. His advice: "Spend the money to do the right studies and build a robust dossier so you can paint a good picture of patient populations that will benefit from your product, instead of going for the home run everyone thinks is always possible."



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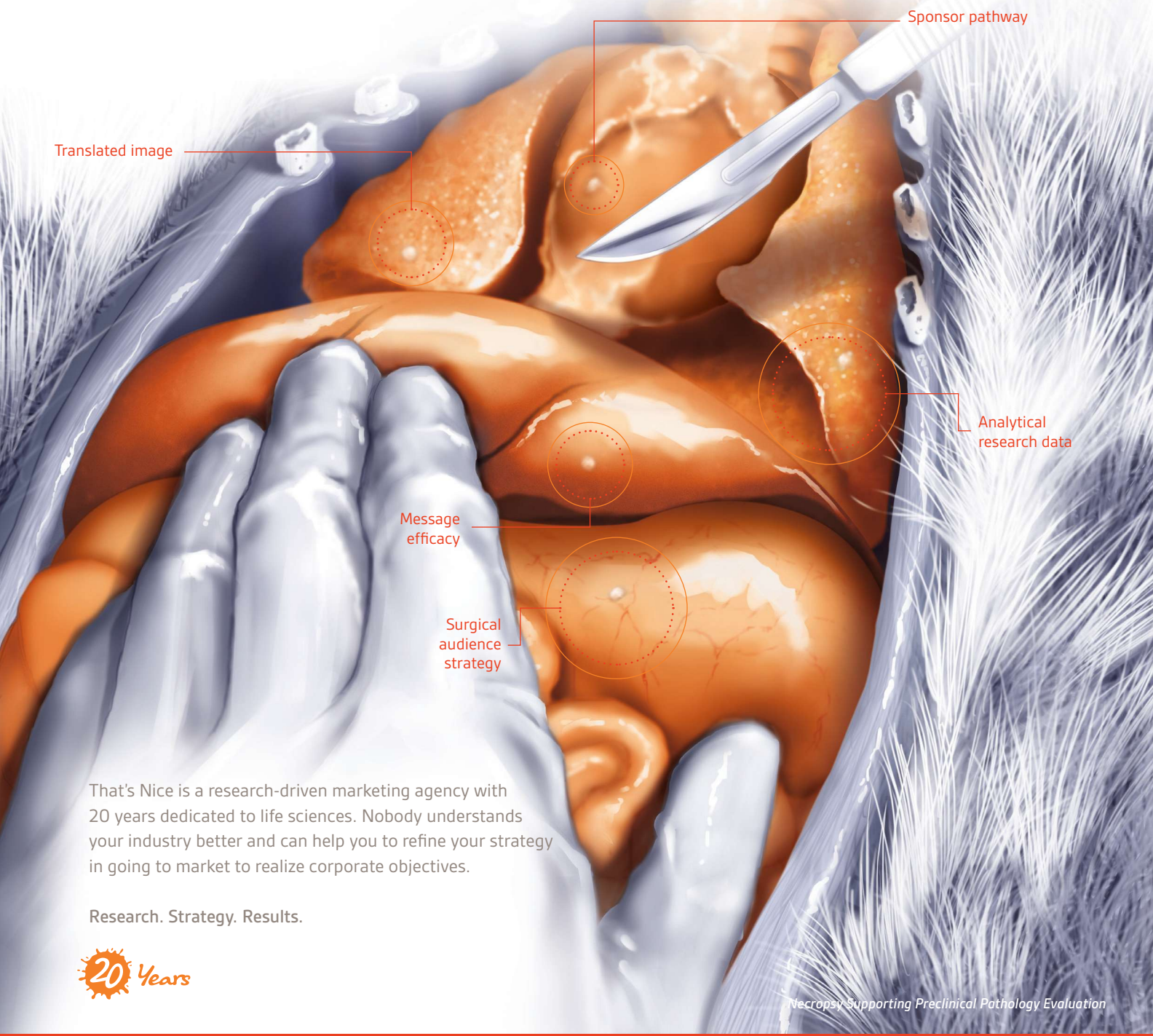

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COMPANIES to WATCH ROUNDUP 2014

WAYNE KOBERSTEIN, EXECUTIVE EDITOR

The "Companies to Watch" column appears in these pages every month, each time giving a brief but analytical look at a company with its own products in development, relatively little press coverage to date, and a recent milestone accomplished. Most important, the company must have an interesting and instructive story to tell, highlighting the key lessons it has learned in starting, scaling up, and steering the company toward its ultimate goal. This month, for the second year in a row, we share updates from the companies featured in the previous year. We rounded up the statements that follow from the leaders of our Companies to Watch 2014 lineup.

We asked each company executive to answer a single question: What have been the most important developments for your company since it was featured in *Life Science Leader's* "Companies to Watch," and what developments or milestones do you anticipate in 2015? Naturally, CtW companies covered later in the year tend to report less progress and more forward-looking objectives for the new year. Reflecting shifting priorities common in startups, a couple of companies chose not to respond at all, whether because they had no news or perhaps too much disruption, such as a turnover in management, to address in this context. Where public information was available, we supply updates about the nonresponding companies.

Almost all of our 2014 Companies to Watch did respond, however, and their comments reveal much about how they assess their own state of being in the new year. Their stories continue to unfold — blazing new trails, creating new models, and supplying new lessons for life science leaders.

JANUARY

Protagonist Therapeutics

The world has long awaited stable oral peptides as a potential replacement for many injectable drugs. Will this company be the hero?

Dinesh V. Patel, Ph.D., *President & CEO*

"Over the past year, Protagonist has made significant advances in progressing its 'oral peptide-based targeted therapy for inflammatory bowel diseases' from research to development. We have nominated our first development candidate, PTG-100, and expect to file an IND (investigational new drug) and initiate Phase 1 clinical studies in 2015. We also successfully secured the second tranche of our Series B financing, and are using these funds to progress PN-884 into clinical trials, expand our pipeline with other oral peptide assets, and build out a strong R&D and executive team."

FEBRUARY

NONE

The Companies-to-Watch Roundup for 2013 took the place of a monthly CtW column in this month. This year, in addition to the CtW Roundup 2014, the regular monthly column for February is back in place, featuring Tetra Discovery Partners.

MARCH

Otonomy

Not to build a platform, but to create new, FDA-approved therapeutics for unserved indications in the ear, this developer focuses on novel delivery.

David A. Weber, Ph.D., *President & CEO*

"We have made considerable progress in advancing our product pipeline, and significantly strengthened our balance sheet. In July, we announced the successful completion of Phase 3 trials for our lead product candidate, AuriPro, in the treatment of pediatric patients undergoing tympanostomy tube placement surgery and intend to file the NDA in the first half of 2015. We also recently announced the achievement of the patient enrollment target in the first of two pivotal studies for OTO-104 in patients with Meniere's disease, and expect to have results in 2Q 2015. We continue to advance our third product candidate, OTO-311 for tinnitus, toward an IND filing in 2015 and recently announced the licensing of nonclinical and clinical data for the molecule that will support our development and regulatory filing efforts. With regard to financing, we completed an oversubscribed Series D financing in April that totaled $49 million and included a number of well-respected public investors and then completed a successful IPO in August that raised net proceeds for the company of $104 million. The IPO was completed at the top end of the price range, and we increased the size of the offering in response to strong investor demand. We expect that the funds raised during 2014 will support the company through AuriPro's approval and commercial launch in the U.S. in 2016."

APRIL

Synthetic Biologics

Following a failed drug, a company retrenches and reinvents itself as a developer of new biologics with novel mechanisms focused on serious infections and other diseases.

Jeffrey Riley, *CEO*

"Synthetic Biologics made exceptional progress during 2014. By mid-2015 we plan to have two potential multibillion dollar pathogen-specific drug candidates in Phase 2 trials and expect topline cognition data from our Phase 2 multiple sclerosis drug (another potential multibillion dollar market). SYN-004 may be the first potential point-of-care therapy to protect the gut microbiome, thereby preventing C. difficile infection, an urgent public health threat for hospital patients receiving commonly used antibiotics. We initiated a Phase 1A clinical trial of SYN-004 in December 2014, with topline data expected by year end 2015, and a Phase 2 trial is planned for 2015. Another pathogen-specific candidate, SYN-010, is intended to reduce the impact of methane-producing organisms on constipation-predominant IBS (C-IBS). This groundbreaking approach targets the underlying cause of C-IBS, not just the symptoms, with potential application to obesity and diabetes. We plan to initiate a Phase 2 trial of SYN-010 in mid-2015."

MAY

Savant HWP

Industry experience and sound business principles guided the start-up and widened the portfolio options for this knowledge-rich company.

Stephen L. Hurst, J.D., *President and CEO*

"Savant HWP made outstanding progress in 2014, validating our business model, advancing and de-risking our addiction medicine and neglected disease programs, and acquiring yet another clinical-stage program, this one in headache pain. By completing the first-in-human phase of the 18-MC project without incident and in under two years from program initiation, the Savant team successfully demonstrated the strength of our leveraged approach to developing novel, high-impact products and the success of the 18-MC rational drug design program by eliminating in humans the dangerous side effects of the parent compound, ibogaine. The new clinical-stage program in headache pain positions Savant on the front lines of central nervous system drug development — medicines that address brain disease by altering the brain's regulation of neurotransmitters. The coming year will be marked by the advance of our programs into patients as well as healthy volunteers, the acquisition of additional clinical-stage opportunities, expansion of our operations in Europe, and our first significant equity financing."

JUNE

Protalix BioTherapeutics

Using plant cells instead of mammalian cells to produce protein drugs, plus a partnered product already on the market, possibly put this player in the lead.

[No response from company. The following updates are public information.]

Late last year, in September 2014, Protalix replaced then-president and CEO David Aviezer with the current president and CEO, Moshe Manor, who did not respond to our request for an update in the CtW Roundup. In August, Pfizer and Protalix BioTherapeutics had announced FDA approval of a pediatric indication for Elelyso (taliglucerase alfa), for treatment of Type 1 Gaucher Disease.

JULY

Second Genome

Beyond the human genome lies the much vaster field of the microbiome, where this company is finding new disease mechanisms, biomarkers, and therapeutics.

Peter B. Di Laura, *President and CEO*

"The biggest update is that the company has initiated a collaboration with Mayo Clinic to support research in up to eight disease areas. This includes metabolic disease and inflammatory bowel disease (disorders the company had previously discussed research in) and a new area — colorectal cancer. There will be up to five additional therapeutic areas disclosed at a later date. The company continues to move forward with its internal pipeline and existing partnerships."

AUGUST

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.

Eszter Nagy, M.D., Ph.D., *President and CEO*

"As part of its mission to target severe infectious diseases that are not effectively controlled by currently available treatments, Arsanis has recently identified and published a potential novel clinical biomarker for ventilator-associated pneumonia in a leading scientific journal. A further high-profile publication is expected in early 2015 describing the unique mAb which cross-neutralizes five different S. aureus toxins, including alpha-hemolysin, which is part of the ASN100 product, Arsanis' lead program targeting severe S. aureus infections. ASN100 is currently in development with a leading contract manufacturing company. During 2015, Arsanis will move closer to first clinical testing of ASN100 aimed at preventing S. aureus VAP and expects to nominate the lead candidate antibody for its E. coli program, targeting a globally spreading multidrug-resistant E. coli clone."

SEPTEMBER

Ennaid Therapeutics

Inspiration and business sense combine in this enterprise dedicated to developing the first cure for dengue-virus infection and other global disease threats.

No updates. Company did not respond.

OCTOBER

Nora Therapeutics

This company's novel and lonely development of a new fertility drug belies the industry's current lack of interest in the field.

Jeffrey Tong, *President and CEO*

"Nora Therapeutics' RESPONSE Research Study has been progressing as planned. RESPONSE is a randomized, double-blind, placebo-controlled, multicenter clinical study in Europe to evaluate the efficacy, safety, and tolerability of NT100 (our lead product) in women with a history of unexplained recurrent miscarriage. Top-line results from the RESPONSE Research Study are expected in the fourth quarter of 2015. We are optimistic that NT100's mechanism of action may reduce the risk of miscarriage by optimizing maternal-fetal immune tolerance. If successful, NT100 could fill a significant unmet need, as there are currently no approved therapies for women with recurrent miscarriage."

NOVEMBER

BEAT BioTherapeutics

With what it believes is a breakthrough gene-therapy approach, this early-stage company hopes to shake up the huge heart-failure space.

No updates. Company did not respond.

DECEMBER

OrgaNext Research

A European enterprise started by pharma veterans champions a product for age-related muscle-wasting — an overlooked but critical medical need.

Marjanne Prins, *Founder and CEO*

"Of course, we had little time for subsequent developments in 2014. But we are excited about the planning for next year. We also believe that we will see significant changes in our healthcare systems, as many people are determined to stay independent in old age. We see many technical innovations being implemented already, and it is very likely that pharmacotherapy will become more important to empower our elders to age independently. After many years of talking, I foresee that 2015 will be the year of real changes. And as 10,000 Americans turn 65 *every day,* these innovations will need to bring value-for-money to a group of very experienced consumers and critical healthcare payers. These are the challenges that we have put at the heart of our drug development program. With the promising results of the first clinical studies, we have come one step closer to making a difference in the lives of many. In 2015 we hope to make the next step!"

COMING IN 2015

- SECURE FINANCING FOR PIVOTAL PHASE 2B STUDY
- INITIATE ENROLLMENT IN EU AND USA
- EXPAND PIPELINE OF RECOVERY BOOSTER THERAPIES L

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Diverse interests converge to invest in a new wave of life sciences innovation.

DENNIS PURCELL Founder and Senior Advisor to Aisling Capital

The life sciences industry is entering a new "Era of Interdependence." The parties involved in bringing a product or service to market are realizing that cooperation, not competition, is the most productive, cost-efficient route to success. But that has not always been the case.

In the early 1980s, biotech, pharma, academia, and disease foundations were all wary of one another. They operated independently, and communication among them was rare. Wall Street also seemed at a loss as to how to value the life sciences companies. Some suggested that multiple scientists working at a company was an appropriate way to value it. Others suggested the R&D spend was the better indicator of value. Price earnings were irrelevant because most of the companies were not generating any earnings. Discounted cash flows were disregarded because the number of assumptions necessary to generate a model rendered them useless to an investor. How could investors not steeped in the science figure out how to invest in this growing industry?

It became common industry practice to rely on pharmaceutical companies as the experts. If a pharma company partnered with a biotech company, investors had at least some validation of the science underpinning the company. Pharma companies knew the leverage they had because it was hard to go public without the validation they provided. They drove good bargains for themselves, but they also provided some comfort for Wall Street investors. This relationship and coexistence enabled the biotech industry to generate many IPOs during the early days, and the industry became more mainstream. Genentech led the way for the industry with its IPO and spectacular first day of trading, opening at $35 per share and climbing to an $88 per share high. Wall Street had never seen anything like it.

GOING MY WAY?

As we entered the 1990s and the industry matured, the dynamics progressed as well. It seemed validation by Big Pharma no longer guaranteed a company's success. In fact, product failures seemed to occur equally for Big Pharma and biotech-derived products. Many investors and company boards decided going it alone was the best way for a biotech company to create value. The term FIPCO (fully integrated pharmaceutical company) was introduced into the biotech vocabulary. Many companies were asking, "If we went it alone, could we keep all of our product rights and evolve into the next Amgen or Genentech?" Those companies soon discovered, however, that product development was more complicated, costlier, and more time-consuming than expected. Those that successfully navigated those waters were rewarded. (Six of the top 20 pharma companies today are biotech-derived.) But many others struggled as the cost of developing a drug continued to increase, and companies had to routinely raise equity capital to advance their products. Large debt financings were not available due to the lack of company cash flows. Pipeline products were relegated to the second tier, as all of the focus and value were attributed to the lead product.

For pharma companies, it became apparent that R&D productivity was not satisfactory. Huge internal budgets did not guarantee success. They watched some of their best and brightest people go out on their own into entrepreneurial endeavors. Many Big Pharma executives and scientists saw the biotech industry as a more fulfilling career choice.

Biotech companies also realized that perhaps they did not have all the requisite tools to be successful. Manufacturing was not very straightforward. Resources to run multiple trials and determine the best path to registration were not always available. Sales, marketing, and distribution became more complicated once the traditional sales reps were no longer the key players. Reimbursement for successful products became more nuanced.

Wall Street and investors also recog-

nized the complexity of bringing a product to market. Other constituencies mattered. Wall Street developed its own due diligence techniques. Ph.D.s were hired in-house. Expert networks that matched experts with investors began to thrive.

Academic institutions recognized that developing their research to a later stage might help generate much-needed revenue for funding their core mission. By developing their findings further along the proof-of-concept path, they were able to access capital later and keep more of the upside for themselves.

At the same time, disease foundations decided typical fundraising events were not advancing their agendas fast enough. They could influence research more directly by using their network and expertise more effectively. They could have a more direct impact on their areas of interest by influencing the types of projects the industry developed. They would seek and find the researchers and companies working on the most promising projects.

Patient advocates realized they could learn and build upon the experiences witnessed with HIV/AIDS. By unifying their voices, cures could come sooner.

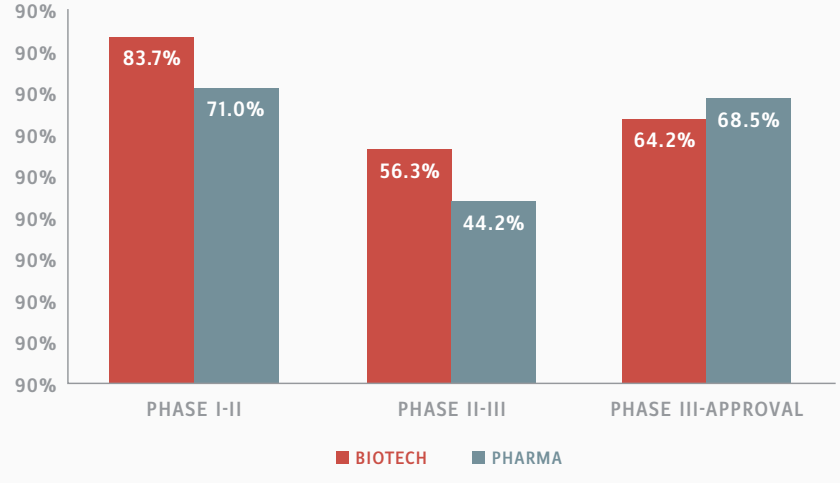
EMBRACING THE NEW ERA

We are witnessing many experiments as we enter the Era of Interdependence. We see virtual drug development efforts under way, whereby an entire drug development infrastructure need not be financed. We see transactions where the acquirer agrees to buy the asset and continue funding only as certain milestones are met.

New types of financing vehicles are also emerging. Corporations, disease foundations, and academic institutions are setting up their own venture capital funds. There is a rise in private/public partnerships, where each side brings its expertise to bear on a project. The democratization of financing as individuals is beginning to play a more important role. (During the ALS Ice Bucket Challenge, stocks of companies working on ALS increased by an average of 30 percent.) We see royalty funds buying royalties from academic institutions, thus freeing up much-needed capital for those institutions. And there are many other possibilities.

New models will continue to evolve in this Era of Interdependence. By thinking outside our own individual silos and focusing on how we can all work together in new ways, we may be able to find cures for diseases more efficiently and contribute to a healthier quality of life for everyone. L

TRANSITION PROBABILITIES FOR CLINICAL PHASES – BIOTECH VS. PHARMA



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Patient-Focused Drug Development: To Understand Patients, You Must Engage Them

CATHY YARBROUGH Contributing Writer

When National Health Council (NHC) official Marc Boutin, J.D., speaks to an audience of pharmaceutical company executives about patient-focused drug development, he underscores the topic's importance to the life sciences industry by stating, "Look at the person sitting on your right. Now, look at the person sitting on your left. One of them likely will be unemployed in five years."

The reason, Boutin said, is that the individual's company will have failed to effectively incorporate the patients' perspectives at multiple points along the drug development continuum, which he defined as encompassing R&D portfolio selection and prioritization; identification of research questions, outcomes, and comparators; clinical trial design and recruitment strategy; regulatory review; and commercialization and postmarket surveillance. "To understand patients, you must engage them," said Boutin, executive VP and CEO of NHC, whose member organizations include nonprofit patient advocacy groups as well as life sciences and insurance companies. "When people with chronic conditions are involved in a meaningful way through the drug development continuum, we greatly increase the probability of producing the kinds of drugs patients want, need, and use," he added.

David Verbraska, VP, worldwide public affairs and policy at Pfizer, agreed. "The patient perspective brings a universal truth to what we're doing. Patients help define the unmet medical needs, value of the science, and the patient-reported outcomes and surrogate or direct clinical trial endpoints that should be used in a clinical trial," he said. "By being patient-centric and adding transparency and interaction all along the R&D and market life cycle, patients help us achieve the best public health outcomes and avoid the worst-case scenario," added Verbraska. The scenario: a drug that is approved by the FDA but does not meet patients' needs. Through patient engagement throughout the R&D process, those needs would have been identified and addressed, he said.

Engaging patients in clinical trial design could help improve the study's efficiency by boosting patient recruitment, protocol compliance, and retention. It also could help insure that the study generates the type of information that will be most important to patients. For example, although Parkinson's disease impairs mobility, many patients have reported that they are more bothered by the impaired sleep patterns and depression that are associated with the neurological disorder. For these patients, a clinical trial of a new drug for Parkinson's disease should evaluate the agent's impact on these symptoms as well as mobility.

The Wall Street Journal recently reported on the role of patients in clinical trial design. The Sept. 29, 2014 article, "Design Power: Patients Play Researchers in Drug Trials," described a new clinical trial for a prostate cancer drug. Based on patients' suggestions, the researchers designed the trial to track such measures as the number of days when the patients felt well enough to go to work.

Until recently, the term "patient engagement" was usually used to describe programs to empower patients with the knowledge and tools to take responsibility for their health. Today, "patient engagement" is often used interchangeably with Patient-Focused Drug Development (PFDD), the name of the FDA's five-year study to systematically obtain patients' perspectives. "We want to learn about the clinical context of each disease from the patients' point of view and experiences," said Theresa Mullin, Ph.D., director of the Office of Strategic Programs in the FDA's Center for Drug Evaluation and Research (CDER).

At these public meetings, each of which targets a chronic, symptomatic disease, Dr. Mullin and other FDA officials also ask patients to assess their available treatment options and the therapeutic benefits that matter most to them. By the end of 2017, the FDA will have organized 20 patient meetings, each on a specific disease. Each meeting results in a "Voice of the Patient" report posted on the FDA's

website. The report captures the perspectives of patients who participated in the meeting either in-person or by webcast. Also summarized in the report are comments submitted during the 60-day period following each meeting.

The FDA's PFDD initiative has spurred several pharmaceutical companies to broaden the scope of their patient engagement activities. "In the past, the industry's approach to patient engagement was primarily anecdotal and *ad hoc*, with a project here and there," said Verbraska. "What is very different now is that Pfizer and other leading companies are more formal and systematic in soliciting the patient's voice, and we've gone from just listening to being more action-oriented in what we do, by taking what we've learned from patients and embedding that information into our decision-making processes."

SEEKING THE PATIENT'S VOICE

Pfizer is capturing the patient's perspective in a toolkit that will be broadly distributed to internal global project teams in the company's core therapeutics areas. The toolkit for each disease area targeted by Pfizer describes the patient's journey, including the impact of the disorder on such quality-of-life measures as relationships. The toolkit, which is now under evaluation in a pilot study, also suggests tangible ways that project teams can engage with patients to learn more about their needs. "We realize that systematically incorporating the patients' perspectives in decision making requires process and cultural changes, particularly in our R&D community," Verbraska said, "and the scientists are the most energized about making that happen. Our goal is to build an ecosystem in which the patient is at the center." To help build the ecosystem, Pfizer leaders have established a "community of practice," a group of colleagues whom Verbraska described as evangelists for patient engagement within the company.

For pharmaceutical companies such as Pfizer, there are several potential barriers to fully engaging patients in the drug development continuum, especially in portfolio selection and clinical trial design. The most imposing barrier is the industry's uncertainty about the impact of the FDA's restrictions on companies' communications about drugs that have not yet received marketing authorization from the agency. "Companies are understandably reluctant to discuss an unapproved drug for fear of facing enforcement action and fines by the FDA or the Federal Trade Commission," said Boutin. "How can we insure meaningful patient engagement at the front end of drug development while mitigating the risks of engagement for companies?"

That question will be on the agenda of an early 2015 invitation-only meeting of senior leaders of pharmaceutical companies, the FDA, patient advocacy organizations, insurers, and providers. NHC is organizing the meeting, which Boutin described as a dialogue of stakeholders that will begin to lay the foundation for a practical framework on how patients and their perspectives should be continuously integrated throughout the drug development continuum. Boutin said he hopes the stakeholders will develop a shared definition of patient engagement that embraces the concept of incorporating the patients' perspectives in the drug development continuum. Kenneth Kaitin, Ph.D., director of the Tufts University Center for the Study of Drug Development, has been quoted as saying, "There is agreement about how important patient-centered drug development is for pharma and biotech, but clearly no agreement on the definition of the term." Also on the agenda is a discussion of promising patient-engagement methods. In addition, participants will discuss barriers that hinder meaningful patient engagement and potential ways to eliminate them. The results of the dialogue will be subsequently communicated at an open-to-the-public event for a larger audience of stakeholders.

Pharmaceutical companies should not wait for the results of these meetings to broaden their patient-engagement activities. They should consider:

- Appointing senior executives to lead the company's patient-engagement efforts. Sanofi, Pfizer, Novo Nordisk, Boehringer Ingelheim, and UCB are among the companies that have created leadership positions with the responsibility for patient engagement.
- Changing the mindset of staff so they view patients as active partners rather than passive clinical trial subjects and end users of their products. Pfizer's patients' journey toolkit and community of practice leaders are examples of industry initiatives to transform staff members' views of the patient population in drug development.
- Making clinical trials more patient-friendly. Clinical trial participants are not routinely informed about the study's results after the completion of trial. In 2013, Pfizer conducted a pilot project to prepare lay summaries of clinical trial results for participants in select company-sponsored studies. Before sending the summaries to patients, Pfizer sought the FDA's comments. "The FDA was very supportive of the innovative, patient-friendly lay summary concept," said Verbraska.
- Taking advantage of the insights that are revealed at the FDA's PFDD meetings with patients and their representatives. Dr. Mullin said "Voice of the Patient" reports published after each meeting "serve an important function in communicating to both the FDA review staff and the regulated industry what improvements patients would most like to see in their daily lives."

  Dr. Mullin added that companies "could play an important role in collaborating with patient groups and researchers in follow-up work to develop clinical outcome assessment tools or patient-reported outcome measures for clinical trials that will better capture the patients' perspectives."

NHC has developed a tool that could help companies collect and organize data about patients' perspectives on their diseases, the quality of their lives, and treatment options. The "Patient Perspective and Disease Impact Stratification Tool" was originally designed to assist patient advocacy in preparation for the FDA's PFDD meetings. However, the tool will be useful to anyone who wants to understand the full scope of the patients' experiences with diseases, said Boutin.

In the past two years, Boutin said he has witnessed a dramatic shift in how individual companies and the FDA view patient engagement. "My sense is that we're in a very exciting place." L

Novartis Oncology Takes Cancer Trials To The Patient

ED MISETA Executive Editor @OutsourcedPharm

As executive director of clinical operations for Novartis US Oncology, one of Stephanie Petrone's responsibilities is discovering new ways to conduct trials, which will hopefully speed up the time it takes to get medicines to patients.

Petrone considers herself an innovator. She enjoys quoting a line attributed to someone from the patent office, which appeared in *Punch* magazine's "Almanack" back in 1899. "Everything that can be invented has been invented," it states, "so why do I need to file your patent?" That's the kind of thinking that can stop innovation dead in its tracks.

She also likes another quote, which defines innovation as taking two things that already exist and putting them together in a new way. She believes this is the approach Novartis took with its recent SIGNATURE Clinical Trial Program. "We took some things that clinical professionals will find very familiar," she says, "and put them together in a new and novel way."

The idea came about the same way many do in this space: an attempt to try and better meet the needs and expectations of a patient. Petrone's boss, Steven Stein, the head of development at Novartis US Oncology, became aware of an advanced breast cancer patient in Florida who was suffering from a particular genetic mutation. She was interested in participating in a clinical trial, but none were being conducted in Florida.

The patient's physician conducted a search and found the nearest site was in New York City. Luckily the patient had the resources available and was soon boarding a plane to the Big Apple. "Can you imagine that?" asks Petrone. "She is a breast cancer patient, probably not feeling well; yet, here she is boarding a plane to fly to NYC to take part in a trial."

Most of us don't like flying when we're feeling fine, much less when suffering from a debilitating disease. After hearing this story, Stein was left with one obvious question: Why was this happening? Why are we forcing sick patients to have to fly across the country, instead of letting them be treated in their own town and taking the protocol to them?

MEET THE NEEDS OF THE PATIENT

That simple but poignant question led to the creation of what would be called the SIGNATURE Clinical Trial Program. SIGNATURE is a series of clinical trials (eight at the current time) which are triggered by the patient. "There are two key aspects that made this project innovative," says Petrone. "They are the scientific and the operational models we are using."

Each of the SIGNATURE protocols is a Phase 2 proof of concept study looking for early signals of cancer. Novartis was hoping to learn if the drug was showing early activity, and, if so, should the company move on and perform additional research. The population for the study were all advanced stage patients who experienced a failure on at least one therapy.

"Cancer is scary and getting ever more complicated," says Petrone. "We are looking at therapies that target a specific pathway, which might be relevant to multiple cancers. The problem is, which ones? Do we need to run an individual trial for each tumor type? That process would take forever, and we knew we needed answers faster and in a more cost-effective way."

TARGET THE MUTATION, NOT THE CANCER

There are eight drugs involved in the SIGNATURE program, and more information on them can be found on clinicaltrials.gov. All are drugs in early development. For example, one of the drugs is a pan-P13K inhibitor (Buparlisib, also known as BKM120) that inhibits the P13K pathway. Unfortunately, a pathway being relevant still doesn't mean the drug is going to work.

"We start with it being patient-triggered and target-specific," says Petrone, "so the patients are pre-identified using standard-of-care mutational testing that physicians are already performing in their offices. Once they have the result in hand, they pick up the phone, call Novartis, and register."

But Petrone notes there is another unique aspect of the protocols. They are all tissue-agnostic, meaning every one of those protocols can accept any patient with any cancer, as long as they have the relevant mutation. In the Buparlisib example mentioned earlier, any patient with a P13K-mutated cancer would be accepted.

"This is not a breast cancer study," notes Petrone. "It is not a prostate cancer study. It is open to all types of cancers with that mutation. When we have enough patients with a certain tumor type, we break those patients out as a cohort and analyze them while the trial is ongoing. This allows us to generate data quickly, in real time, with as few patients as possible. We want to know if there is a signal there, or if the trial is negative and we need to move on. The whole idea is not to get more patients into a trial, but to get those patients who have a higher probability of being positively impacted by the drug."

STANDARDS SPEED THE PROCESS

Once patients are pre-identified, they are enrolled in a 16-week treatment period after which the data is analyzed. Novartis is looking at approximately 70 to 100 patients per trial, who are then followed for a minimum of two years for proof-of-concept.

Novartis is using CLIA (Clinical Laboratory Improvement Amendments)-certified labs to do the local testing, which are overseen by CMS (Centers for Medicare and Medicaid Services). There are no preselected sites for the trial, which eliminates the need for any patient to have to travel to a site. Once the patient is identified and registered, Novartis performs the rest of the screening procedures. There is also no prescribed number of sites participating, and, more importantly, no sites being paid to deliver zero patients.

Once patients are registered, a rapid study start-up model, which is contingent on standards, is used to qualify the patient for the protocol. There is a fixed budget for each of the protocols, and Petrone states the company has never wavered from that budget. A central IRB is also being used.

"Every site in a trial is using that central IRB," adds Petrone. "We will not waver

> "As part of this effort, we worked closely with our field-based colleagues to ensure they had the information and training they needed to be ambassadors in the community. The team was dedicated to providing 'concierge-level' service to potential sites and partner CROs. With this approach, we prioritized potential issues enabling us to accelerate all aspects of the study start-up process."

STEPHANIE PETRONE
Executive Director of
Clinical Operations, Novartis

from that requirement either. If a prospective site says it can't use the central IRB, we thank them for their time, but tell them they can't participate. We expected to get some pushback from academics, but that has not happened. We have 12 academic institutions on board that have accepted our standard procedures. We also have a standard contract and a standard informed consent agreement with adjustments for state-law provisions."

Generally it takes fewer than five weeks from the time a patient is identified until the drug is shipped. Many community-based sites have been accomplishing that task in only three weeks. Academic sites have been averaging 12 weeks, but that is still an accomplishment considering the start-up period for a major academic site generally averages six months to a year.

One of the fastest P13K mutations occurs in colorectal cancer, and that cohort has already closed. Novartis is now in the process of analyzing the data to get an early read on whether or not there is a signal present.

OVERCOMING THE CHALLENGES

The SIGNATURE program had been in place for fewer than two years, and during that time Novartis opened eight protocols, prescreened 700 patients across 35 different cancers (without a single one having to set foot on a plane), and already has seven tumor cohorts across three protocols waiting to be analyzed using adaptive statistics.

The entire process was certainly not as easy as it sounds. Once the first protocol was written, everyone got into a bit of a cadence with the others, but it still required a lot of time and effort up front. There were weekly meetings that even got a bit heated at times. Many questioned the possibility of opening sites in just three weeks, while others doubted the chances of getting so many sites to all agree to accept a central IRB. Petrone gives a lot of credit for the success of the project to August Salvado, VP, early development, strategy and innovation and head of the program. On a weekly basis, he would look employees in the eye and say, "Yes, you will make this happen." The company stuck to its guns, and its principles, and ultimately did make it happen.

To work through these potential obstacles, Novartis Oncology established a central team augmented by operational experts within the company. The team met weekly with the sole purpose of reviewing potential operational challenges and brainstorming possible solutions. "This enabled us to rapidly respond to inquiries and clear roadblocks in real time," says Petrone. "As part of this effort, we worked closely with our field-based colleagues to ensure they had the information and training they needed to be ambassadors in the community. The team was dedicated to providing 'concierge-level' service to potential sites and partner CROs. With this approach, we prioritized potential issues enabling us to accelerate all aspects of the study start-up process."

Two steps were critical to the success of the project. First, the company established a SWAT team of study start-up experts that rapidly responded to site start-up requests. By using a central IRB, the protocols were approved up front, and only the site itself needed to be approved. By using standard contracts and budgets, the company was able to eliminate negotiation time with sites.

For those sites that initially did not accept the model of an independent central IRB, the SWAT team worked closely with an investigator "champion" at the site, the site IRB staff, and the independent partner IRB. Teleconferences were used to explain the SIGNATURE model and why a central IRB was necessary in order to meet the rapid study start-up timelines. A key success factor was having an investigator agree to be that site champion for the project, to speak to the local IRB personally and explain the scientific rationale for the project.

"Using the old oncology model, we would have to take every one of those tumor types, start a trial, do the study start-up, enroll patients, perform the study, and read and report the data," says Petrone. "And that is just for one trial. That process would then have to be repeated for the other trials as well. Being able to do them all simultaneously in one trial is fairly significant, and we are proud of the results we are seeing."

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A New In-Depth Analysis Of Global Biosimilar Markets

FRED OLDS Contributing Writer

By the end of this decade, nearly $100 billion of biologics will be exposed to competition due to patent expiration. This tantalizing prospect has led to the formation of an entirely new market – biosimilars, says Mari Serebrov, analyst with Thomson Reuters Bio World.

She is the author of "Biosimilars: A Global Perspective of a New Market, Opportunities, Threats and Critical Strategies 2014." Released by Thomson Reuters, it is a comprehensive, 268-page analysis of global biosimilar markets.

The report profiles 245 companies, 25 markets, and 18 biosimilar pathways to commercialization. It charts the opportunities of biologics coming off patent and provides strategies and marketing insights. Serebrov points out that with the opportunities, there is also the sobering 50 percent failure rate for biosimilars. Obstacles such as uncertain regulations, substitution, pricing, naming, funding, and brand loyalty demand a clear and thoughtful business plan for a biosimilar company to succeed.

CONSULT CLOSELY WITH REGULATORY

Serebrov says, "The most important thing to understand is that this is a new market. It's still in formation." She adds there are fewer than 20 countries that have a regulatory pathway to market for biosimilars. A biosimilar path was authorized in the U.S. in 2010 with passage of the Biologics Price Competition and Innovation Act of 2009 (BPCIA). The FDA issued draft guidance in May 2014, and it is currently formulating approval processes. Many emerging markets may never have a biosimilar path and will likely rely on approved biosimilars coming from other markets.

Manufacturers of biosimilars are finding a very uneven regulatory landscape. "It's an iffy proposition. A company doesn't know going in how many steps they are going to have to go through," says Serebrov. Even where regulations and laws exist, she says, it's something of a learn-as-you-go process, and regulations are being changed as governments gain new knowledge and experience.

"Regulators are taking a stepwise approach to the approval of biosimilars. They are designing methods to squeeze out as much data from clinical trial analytics as possible," says Serebrov. The goal for the developer of a biosimilar is to prove its compound is highly similar to the reference molecule. If that can be proven, regulators will accept that the compound is as safe and effective as the reference drug. The foci for regulators then become immunogenicity, pharmacokinetics, and pharmacodynamics. Yet without a well-established framework, biosimilar developers may find it hard to know exactly how to design clinical trials to demonstrate similarity. It will be critical for them to work with regulators to determine what data the government will require and which patients to test.

SIMILAR, BUT NOT GENERIC, SCIENCE

Deep discounts and laws providing automatic substitution led to the success of the generic drug market. No country has yet authorized automatic substitution of biosimilars. The BPCIA provides for "interchangeability" of a biosimilar if it can be demonstrated to have fingerprint-like similarity to the reference biologic, but the FDA has yet to establish how that can be done. For now, experts argue against automatic substitution of biosimilars for patient safety.

As the name denotes, these products are similar to, but not exact copies of, the innovator products. Biologics are large complex molecules. Similar proteins share a primary structure but possess intrinsic characteristics that open them up to potential biological or chemical actions such as glycosylation or sulfation, which can differentiate them from one another. Variations can also arise from using different cell lines, manufacturing processes, or something as simple as a different vial stopper. These variations could affect activity in humans.

WHAT'S IN A NAME?

Recognition of these differences has caused a dispute about nomenclature. "Perhaps the most divisive regulatory challenge facing industry and regulators today is the naming of biosimilars," says Serebrov. Innovators say the products should have distinctly different international nonproprietary names (INNs). That would facilitate identifying a product if adverse events arose. Manufacturers of biosimilars, some governments, and advocacy groups contend that naming these products differently will only add confusion to the marketplace and inhibit the adoption of the biosimilars. They argue this would deprive patients and countries of the benefits of the biologics.

While there's no universal solution to this issue, the WHO and some governments have suggested protocols that may resolve both sides of this argument.

SIMILAR, BUT NOT GENERIC, PRICING

When generics were introduced, the distrust of them was quickly overcome by education and deep discounts of as much as 70 to 80 percent. Innovators could not compete on price with the cheaper products, so these markets were left to generic manufacturers. Biologics, on the other hand, are very expensive to develop. Biosimilars have to conduct clinical trials, an expense not required of generics. The manufacturing equipment, processes, and quality control are more complex than that of small molecule drugs. So discounts with biosimilars average 20 to 30 percent compared to the reference products.

This price differential was not significant enough to lead to rapid adoption. In the EU, adoption of biosimilars had a much slower uptake than predicted. Serebrov says 14 biosimilars were approved and on market in the EU in 2011; yet, they only had 11 percent of the market versus the products they referenced. Innovators found it financially feasible to lower prices to match that of the biosimilar companies. Practitioners and patients were reluctant to switch brands, and there was very little incentive for payers to recommend the biosimilars.

MARKET TO PRACTITIONERS, PATIENTS, AND PAYERS

In part, the slow adoption of biosimilars in Europe was due to a reliance on marketing using the generic model based on price. "The question is, 'How do you compete when price isn't a differential?' That's something biosimilar makers have to figure out," says Serebrov.

Yet, she points out, companies like Sandoz, Hospira, and Teva are making a go of it. These companies realized they needed to differentiate their products to compete successfully, and price alone was not a sufficient differentiator. Hospira, for instance, developed a marketing plan focused on education of physicians and payers to build confidence in their products. They now market three biosimilars in the EU.

WAITING FOR THE U.S.

The U.S. market may be the most anticipated entry point for biosimilars. It is the most lucrative market; although patent laws are complex and pricing opaque, there are no price controls, law provides for interchangeability, and the population can afford the medications. Innovators are taking steps to protect and extend patents while other companies develop biosimilars to challenge them. In some cases, the innovators may be doing both. Uncertainty will yield to formation as the FDA creates a path to approval and ensuing patent infringement cases are resolved.

INDIVIDUALIZE STRATEGY – A START-UP'S PERSPECTIVE

"The most important question is, 'How do you make money with biosimilars?'" says Amit Munshi, CEO of Epirus Biopharmaceuticals. Many companies can make biosimilars. "You have to figure out how to do that profitably without putting thousands of reps on the ground in the U.S.," he says.

The feasibility of building a biosimilar company comes down to three things, according to Munshi: Is there a regulatory landscape you can navigate, can you get clear legal sailing and avoid legal challenges, and can you find a tractable commercial model to build a business?

He says it's classic marketing. Where's the money, and can one access it? Where's the best patient opportunity? Segment the market, and develop a tactical game plan for each of those markets.

Epirus is a small start-up. Strategically, Munshi felt it would be difficult to compete in the U.S. successfully. The U.S. has no regulatory precedent, it has a complicated patent environment, and a small company would have to compete with pharmaceutical giants. Finally, he says, "Ninety-five percent of patients who are eligible for biologic drugs already have them in the U.S. That means your entire business in the U.S. is switching patients, and that has to be done doctor by doctor. That's a very difficult and expensive challenge."

Epirus chose to enter international markets. Half of the global opportunity for biologics is outside the U.S., and international markets have the cleanest regulatory framework, according to Munshi. The markets are fragmented with small dollars but large populations. "$100 million in Brazil or Russia would not move the needle for Amgen or Samsung, but does drive a revenue line that matters to us," says Munshi. So Epirus creates partnerships and commercial agreements in China, India, Latin America, and elsewhere to produce biosimilars.

There are benefits for small companies entering into partnerships in these markets. They can be satisfied with the profits there and enjoy the benefits as those profits increase when the markets grow. In many cases, the products will be protected from competition by the government. It's likely there will be little competition from the reference drug because the reference drug was too expensive to penetrate the market. Partnering with domestic manufacturers can lead to government tenders and improve the chances of getting on essential drug lists.

BUILDING FRANCHISE MANUFACTURING

Emerging markets may lack the manufacturing technology to produce biologics. To meet this challenge, Epirus has developed single-use manufacturing processes that can be transferred and constructed globally. The manufacturing process is developed, tested, and validated in the U.K., and recreated in the host country. "We take a franchise mentality. We do all the training and help in hiring. We make sure the media, filters, bioreactors, and columns are all identical to those developed in the U.K.," says Munshi. The end result is a process capable of producing a more consistent product, in higher quantities, in a shorter period of time, and with less expense.

Why Eastern Europe May Be The Best Location For Your Next Clinical Trial

GAIL DUTTON Contributing Writer @GailDutton

Eastern Europe is becoming the new bright spot for clinical trials by offering significant opportunities and the fewest challenges of any of the emerging regions, according to a recent IQPC survey of pharmaceutical executives.

Benefits include an eagerness to participate in clinical trials to access cutting-edge medications and many treatment-naïve populations. Additionally, the complexities of conducting clinical trials and of importing and exporting materials and patient samples into or out of these countries are well-known, so challenges can be addressed proactively.

"Clinical sites in Eastern Europe are excellent contributors, delivering timely, high-quality data," says Stanislaw Mosiej, clinical development operations and EEMEA regional head at Roche. "Conducting trials in Eastern Europe also gives the best investigators there the opportunity to create links with the international medical community. This promotes knowledge exchange and the continuous improvement of healthcare standards in Eastern Europe."

Some of the benefits of working in Eastern Europe come from the expertise of its professionals. "In Russia, principal investigators must demonstrate five years of experience participating in clinical trials," says Francisco Vega, Ph.D., VP of study start-up and global clinical operations at inVentiv Health Clinical UK. Similar requirements exist throughout many Eastern European countries, producing investigators with several years of experience conducting high-quality clinical research that can be verified before sites are qualified.

Additionally, Eastern Europe offers willing participants. "There's significant interest throughout Eastern Europe for any product that could increase the standard of care," Vega notes. Biosimilars, for example, are particularly popular in Eastern Europe because the innovator drugs aren't widely available. Therefore, participating in clinical trials increases patients' treatment options. Consequently, Mosiej says, "Patients and investigators are very motivated to participate in clinical trials, so they adhere to the required standards."

Participating in clinical trials, regardless of where they are held, increases patients' treatment options. The difference is that patients in Western Europe and North America already have wider options than patients in Eastern Europe. The drugs undergoing trials in Eastern Europe may not be considered novel in Western markets and may even be commercially available. That's also true, albeit to a lesser extent, in Asia-Pacific nations in which the standard of care generally is improving.

The centralized healthcare systems common throughout Eastern Europe funnel patients into a few specialized centers, making it easier to identify patients who meet protocol criteria and to treat a large number of patients at one site. Eastern European populations remain more homogeneous than those in North America and Western Europe, Vega says, which can be beneficial for testing drugs in which pharmacokinetics vary according to genomic differences that are reflected as ethnicity.

CHALLENGES INCLUDE REGIONAL CONFLICTS, REGULATIONS

Eastern Europe can be divided into nations that adhere to European Medicines Agency (EMA) guidelines and those with their own internal standards. "There are no issues getting drugs into EMA signatory countries (which include Czech Republic, Poland, Romania, Lithuania, and others)," notes Robert Arbeit, M.D., VP of clinical development at Idera Pharmaceuticals. Russia, Ukraine, and Serbia, however, do not adhere to the EMA guidelines for clinical trials.

Despite the opportunities in Eastern Europe, the conflict between Russia and

the Ukraine is making some sponsors nervous. "Aside from the areas of fighting, however, the ability to get drugs into or out of those countries, distribute drugs inside the countries, and access patients hasn't been affected," Vega maintains. That said, inVentiv uses remote monitoring in the eastern Ukraine because military operations have prevented the site consultant from traveling to some trial locations.

Eastern European nations typically take longer than the EU to approve requests to conduct clinical trials. Vega says the regulatory burden in Eastern Europe is similar to that of China, but applications move through the system faster and with more assured outcomes. "In the EU, companies can expect a request to be approved within 60 calendar days. But in Russia the period is 60 working days, and authorities start and stop the clock to send questions, so the review time is extended and may total three to four months." Ukraine, with a hybrid version of the EU and Russian systems, also takes longer for reviews than EU nations.

Once approved, expect to provide additional support to study sites, too. "When running clinical trials in Eastern Europe, it is often necessary to provide support in terms of infrastructure — developing standard terminology. For example, "stillbirth" is defined differently in various countries. "Study-specific training and sometimes any accompanying treatments also must be provided," Mosiej says. Study sponsors also may need to translate trial protocols, informed consent documents, and other materials into local languages.

IN-COUNTRY DEPOTS ALLEVIATE PERMIT AND LICENSE BURDENS

The key question when shipping medicines to nations that do not adhere to EMA guidelines is whether they will issue a blanket import license for all shipments of that drug or whether each shipment will require a separate import license. Arbeit says if they require separate import licenses, "Delivery is no longer predictable because of this added layer of bureaucracy, which is out of the shipper's control."

Among EMA signatories, the challenge is to establish a drug depot and a qualified person, Arbeit says. "Qualified person" refers to a designated individual who is professionally responsible for reviewing the documentation and guaranteeing that, according to those documents, good manufacturing practices were met. "This is not a situation in which you can fax documents and expect them to be signed off," Arbeit says. "That person will want to see audits, batch records, and certificates of analysis, even if the drug is FDA-approved. The process can take at least one month."

Arbeit recommends establishing a depot within the EU from which companies can ship into EMA-signatory countries easily. Even in countries that have not agreed to the good distribution practices (GDPs) advanced by the EMA, establishing an in-country distribution depot is a good idea because it adds flexibility to clinical trial supply.

Without a depot, manufacturers would ship directly to trial sites. "Those sites aren't required to maintain GDP standards," Arbeit explains. "They can use refrigerators with monitors, with or without dual-power backup." Once at a trial site, however, product can be dispensed to patients but cannot be moved among sites.

Working through a GDP depot in-country, however, sidesteps the challenges of restocking multiple sites as well as the need for multiple import licenses. With this approach, the trial sponsor can export the drugs that will be needed for one year, for example, under one license and dispense them to trial sites as needed. "And, because the depot is a GDP facility, you can recover unused drugs once the trial ends," Arbeit says. "It makes the drug supply very predictable."

PARTNER TO CLEAR LOGISTICS HURDLES

The primary challenges in conducting clinical trials in Eastern Europe and many other regions are logistical — getting drugs into a country and patient samples out. Therefore, partner with experienced vendors and customs brokers. Ukraine, Russia, and Serbia, in particular, have specific transportation requirements. The differences include using a different rail gauge for railways, thus requiring cargo to be transferred to other rail cars when they reach the border.

Vega suggests verifying all of the documentation accompanying the products is approved by customs brokers and that the declared value is accurate according to their definitions prior to shipping. He recommends testing this with a dummy shipment.

At the border, Vega warns, products may sit in customs for three days with cold chain packages mixed with those lacking temperature requirements. Therefore, he recommends either active packaging or passive packaging with long hold times. Cold chain issues go beyond that, however.

"The airports we use in Moscow and Saint Petersburg each have large refrigerated rooms with expected temperatures between 2° and 8° C," Vega says. "However, these rooms aren't certified for life sciences. Temperature fluctuations occur. Airport management can't guarantee conditions within the rooms." Ukraine's Kiev International Airport also has temperature-controlled facilities. But even before the outbreak of hostilities, staff didn't follow strict procedures during customs clearance, according to Vega.

To resolve that challenge, Merck works closely with local vendors. Several well-known CROs work in the larger Eastern European countries. "We advise verifying their ability to operate in smaller countries in that region [e.g., Belarus] and manage shipments and translations in a timely and effective manner," Mosiej says.

Choose contractors with close ties to the countries in which they work. They have a vested interest in the trial's success and, therefore, are likely to take greater care of the shipment, even walking it through customs to ensure it is handled appropriately by customs officers. "Some vendors have their own temperature-controlled facilities and are licensed for customs procedures," Vega says. "In those cases, shipments are transferred directly from planes to these facilities, so customs checks are performed on their premises." By choosing depots with robust temperature controls, manufacturers can ensure their drugs are not released to sites until temperature maintenance throughout transit has been confirmed.

All these factors are important, but so are language skills and cultural fluency. When considering Eastern Europe, ensure your partners have not just the medical and logistics skills needed to run a trial smoothly, but that they speak the local language fluently and know how the clinical trials bureaucracy works in the country in question. Only then can all the pieces of running a successful clinical trial fit together.

Ireland: A Training Hub For Life Sciences Innovation

BARRY HEAVEY

Barry Heavey is the head of life sciences for IDA Ireland and a former research scientist.

In the last decade, the global life sciences industry has seen tremendous growth, which has necessitated a commensurate growth in its infrastructure, including training centers and R&D facilities. In Ireland, it seems like everywhere you turn these days there is another biopharmaceutical facility being built by companies such as Alexion, Regeneron, Amgen, BioMarin, and Pfizer. The country has amassed more than 30 FDA-approved sites employing more than 47,000 people in the areas of pharmaceutical, biotechnology, medical devices, and diagnostics. Just two years ago the global budget for R&D facilities was $103 billion. With this growth comes the opportunity for companies to prioritize real-world, hands-on training for graduates and those new to the industry. This, in turn, drives escalating levels of innovation. Let's take a look at how education and training helped Ireland grow to become one of the world's leading life sciences hubs.

TRANSITIONING FROM CLASSROOM TO REAL WORLD

Some of the best biopharmaceutical programs in Europe are found in universities and institutions across Ireland. At colleges such as University College Dublin and National University of Ireland at Galway, students have the privilege of learning from well-educated professors. But what happens to students after graduation? Are they being provided with an education that allows them to enter the biopharm workforce and begin hands-on work immediately?

Not everything that takes place in a work environment can be learned from a textbook. Previously, biopharm manufacturing centers often didn't have machinery reserved for training new graduates. This made it difficult to give new recruits the hands-on experience they needed. Additionally, any training provided could affect a facility's budget and interfere with the daily production schedule.

Today, some manufacturing centers are starting to designate sections for trainee machinery, which allows graduates to finally put down the books and learn in a real-world environment. This competency-based training gets new employees involved in process development immediately, but it is expensive for each facility to incorporate.

Ireland's National Institute for Bioprocessing Research and Training (NIBRT) is taking the research and training center to the next level for graduates. Think about a training and research center that works in the same way as a flight simulator. With the approach taken by NIBRT, training centers are able to quickly bring trainees up to speed in a real-world setting. The institute can be used by all of the local companies, which can significantly reduce both the cost and time of getting new recruits up and operating.

SETTING THE STAGE FOR SUCCESS

At NIBRT, training is focused on cross-functional teams, so trainees are equipped to succeed in the workforce. Education never stops in this industry, and it's necessary to keep up with innovation. When looking to build new facilities, companies in Ireland must not only build for the now, but also for the next 10 to 20 years. Biopharm companies expect the number of treatments to quadruple in the next 10 years, and it is this that is driving the factories of the future with shorter production runs, disposable systems, and a more flexible workforce.

COLLABORATION WITHIN THE INDUSTRY

While it's generally accepted that a healthy amount of competition among companies is a good thing, the same could also be said for collaboration. Biopharm companies with operations in Ireland keep their trade secrets close and their competitors closer. True innovation in Ireland comes from companies feeding off one another. Training centers allow for education and growth, but providing trainees with experience in more subsets of biopharmaceutical categories expands upon their existing knowledge base. This can be done by partnering up companies in the same building, which enables collaboration among companies to identify challenges and find solutions.

JOB CREATION

It is impossible to innovate without talent. By expanding the workforce to include more jobs and different roles and responsibilities, life sciences will continue to prosper in Ireland. Ireland has one of the youngest workforces in Europe. Since the end of 2012 alone, the Irish workforce has expanded by more than 60,000 full-time employees. With more positions opening up, the industry can bolster the workforce with processes, research, and trainers/trainees — many with third-level (i.e., higher education) qualifications. In Ireland, 50 percent of the direct employment within the pharmaceutical industry has a third-level qualification. A larger workforce with all levels of qualifications leads to better processes, which leads to more solutions. L

BIOCOM GLOBAL LIFE SCIENCE PARTNERING Conference

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Biocom's 5th Annual Global Life Science Partnering Conference is an exclusive global partnering and networking forum that brings together senior executives, bankers, venture capitalists, and business development professionals from leading pharmaceutical and biotech companies. The conference will include panel discussions on relevant topics with senior industry leaders, individual company presentations, one-on-one meetings, and numerous networking opportunities.

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Day 1 Agenda (Wednesday, February 25th)

5 Secrets of Business Development

- **Karen Bernstein**, Chairman & Editor-in-Chief, BioCentury (Moderator)
- **Richard Brudnick**, SVP of Corporate Development, Biogen Idec
- **Iain Dukes**, SVP, Licensing & External Science, Merck
- **Chris Haskell**, Head, US Science Hub, Global External Innovation & Alliances, Bayer Healthcare
- **Bob Smith**, SVP, Business Development, Worldwide Research & Development, Pfizer
- **Jack Tupman**, VP, Corporate Business Development, Eli Lilly

Eavesdropping on a Trendsetter

- **George Golumbeski**, SVP, Business Development, Celgene
- **Ed Saltzman**, President & Founder, Defined Health (Moderator)

Lunch Keynote

- **Peter Schultz**, Professor of Chemistry, Scripps Research Institute

VC Panel

- **Nancy Hong**, PhD., Senior Associate, BioMed Ventures (Moderator)
- **Carol Gallagher**, Partner, New Enterprise Associates, Inc. (NEA)
- **Heath Lukatch**, Partner, Novo Ventures
- **David Kabakoff**, PhD, Executive Partner, Sofinnova Ventures
- **Carole Neuchterlein**, Head, Roche Venture Fund
- **Sam Wu**, MD, Ph.D., Managing Director, MedImmune Ventures

IPO Panel

- **Bharatt Chowrira**, Chief Operating Officer, Auspex Pharmaceuticals
- **Cheston Larson**, Partner, Latham & Watkins LLP
- **David Shapiro**, MD, Exec VP, Development & Chief Medical Officer, Intercept Pharmaceuticals
- **David Weber**, PhD, President & CEO, Otonomy, Inc.

$50 rebate if you book a room at The Lodge at Torrey Pines by Tuesday, February 3, 2015. To get the rebate simply book a room at the hotel under the room block and forward your confirmation email to Ashleigh Berry at aberry@biocom.org

Day 2 Agenda (Thursday, February 26th)

Pharma BD Trends

- **Miranda Biven**, Partner, Wilson Sonsini Goodrich & Rosati (Moderator)
- **Adam Keeney**, Global Head, External Innovation, Sanofi
- **Damien McDevitt**, Ph.D., VP Business Development & Head of R&D West Coast, GlaxoSmithKline
- **Corinne Savill**, Head of Business Development and Licensing, Novartis
- **Naoki Okamura**, Corporate Vice President, Global Head of Business Development, Astellas Pharma
- **Neela Patel**, Ph.D, Director, Licensing - Search & Evaluation, AbbVie
- **Jeffrey W. Warmke**, Ph.D., Senior Vice President, External Scientific Affairs, Daiichi Sankyo Group

M&A Panel

- **Bradley Wolff**, Managing Director, Senior Investment Banker, Bank of America Merrill Lynch (Moderator)
- **Dan Burgess**, Former CEO, Rempex Pharmaceuticals
- **Mike Grey**, Former President & CEO, Lumena Pharmaceuticals Inc.; Venture Partner at Pappas Ventures
- **Rich Heyman**, CEO, Seragon Pharmaceuticals
- **Michael Martino**, President & CEO, Ambit Biosciences
- **Ted Schroeder**, CEO, Cadence Pharmaceuticals

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Motivating Improvements In Process Development:

The BITE Awards Program At GSK

CHIP REUBEN, M.S. Contributing Writer

When project teams have an opportunity to compete for funding for what matters to them, the scientists start to think of new ways to improve processes toward more efficient pharmaceutical product development.

According to S. Joseph ("Joe") Tarnowski, Ph.D., SVP chemistry, manufacturing, and controls Biopharm R&D at GSK, when project teams compete for funding what matters to them, the scientists start to think of new ways to improve pharmaceutical product development. Tarnowski created the Biopharm Innovation and Technical Excellence (BITE) Awards program within the organization. He joined GSK in 2010, and the BITE Awards officially kicked off in 2011.

"When you get into biopharmaceutical process development and clinical manufacturing, you are dependent on project teams that 'own' the project, funding the work we do in process development," says Tarnowski. What is not otherwise available is money to do innovation and improvement, because such goals are normally supposed to have been done in the discovery and research phases. The BITE program would allow Tarnowski's teams to get funding during the manufacturing stage, for example, to improve the process of producing pharmaceutical products for toxicology studies and clinical trials. Tarnowski had about 40 requests from his teams within GSK for these types of process improvement ideas, but had no budget for such work because the project teams hold all money. "It put me on the spot," says Tarnowski, who found it difficult to evaluate the large number of requests to determine which goals would be worthy of pursuing. With so many disparate projects, Tarnowski was unlikely to have all the knowledge required to make all of the approval decisions. So he decided to make it a contest and organized a selection committee to represent a broad range of talents and skills ranging from manufacturing to discovery.

BITE AWARDS: IMPLEMENTATION AND EXPERIENCE

Tarnowski is on a committee that evaluates applications for BITE Awards and looks for innovative projects that have a broad range of applicability. This committee of 11 members includes heads of various departments in the company, including CMC (chemistry, manufacturing and controls), biopharmaceutical development, R&D, business development, patents/legal, and finance. Projects have to be cross-functional; they can't just pertain to one particular silo of the company. They have to engage other parts of the organization. "We wanted to promote collaboration," says Tarnowski. Additionally, projects can't include the normal day-to-day responsibilities ordinarily considered to be part of the applicant's day job. A broad range of projects has been proposed, including both those aimed at incremental innovation (i.e., stepwise improvements) as well as "moonshot" or "blue sky" projects (i.e., monumental improvements). "We are looking for breakthroughs," says Tarnowski. "We often say, 'Let's change the way we do biopharmaceutical manufacturing, and let's do it differently.'"

The application process requires a write-up of no more than two pages consisting of approximately 200 words describing the project and its purpose. Those who receive awards need to demonstrate ownership and responsibility. Furthermore, the idea had to meet the established criteria and come with a passionate chief investigator. The committee spots formulaic approaches such as submitting a lot of applications for a higher probability of success. "We see through that right away," says Tarnowski.

The BITE Awards committee designed the scoring system to evaluate the applications. Each member of the committee rates and ranks each of the applications on their relevance and percent weight of importance on the following criteria: manufacturability (40 percent), innovation (20 percent), technological feasibility (30 percent), and time and resource requirements (10 percent). Each of the committee members enters a score of 1, 3, 5, or 10 for each criterion, and a weighted average is calculated. In 2014, a sustainability measure was added.

The project received a bonus point (+1 added to the weighted score) if it addressed at least one issue that makes processes more environmentally friendly and reduces the carbon footprint. Subsequently, the committee ranks the proposals from highest to lowest total scores. Projects receive awards in that order until the cumulative budget for the projects exceeds the total budget allotted for that year.

Award recipients essentially run their own entrepreneurial businesses, including managing budgets and committing to timelines. Thus, they become teams in their own right. Furthermore, the company holds them accountable through quarterly meetings that serve as progress checks. Either the committee or the investigator can stop the project. "I have an easy way to monitor progress," says Tarnowski. "I go to my finance director and ask how the spending rate is going for a project. If they are not spending at the rate they had projected, I know they are behind. I give them a nudge to start making progress and remind them that we reserve the right to cancel the project."

Tarnowski says about half of the ideas concern "incremental" (i.e., relatively minor) process improvements, and the others show an ambition for making major breakthroughs that would revolutionize the way pharmaceuticals are manufactured. Some of the ideas are very risky. The committee does not award funding if it does believe the team can achieve the proposed technical advancement. However, the chief investigators have an opportunity to resubmit if they come up with a new idea or a "repackaged" previous plan. "Nobody gets too disappointed or feels slighted, because we do it with a spirit of taking ideas forward and doing what people want done," says Tarnowski. "It energizes people, and the feeling of ownership is a huge benefit. It gives them a lot of pride." Funding awards are typically around $100,000 for a project. "But they have to get creative about how they partner and get resources to help them do the work," specifies Tarnowski. Awards go to participants both in the U.S. and U.K., as the company wants to balance the funding throughout the company's geographic locations. This approach forces collaboration because they've got to bridge the international corporate channels.

GROWTH AND SUCCESS STORIES

Since its inception in 2010, the BITE Awards program has been well-received. The committee has reviewed 117 proposals, awarding funding to 35 of them. The program had 34 proposals and 11 awards in 2011, 24 proposals and 6 awards in 2012, 33 proposals and 12 awards in 2013, and 26 proposals and 6 awards in 2014.

As a working example of the value of one of the funded programs, Tarnowski shared a particularly fruitful rediscovery of a technology the company had that was "sitting on the shelf." Some of the compounds they have were engineered to bind to the blood protein albumin. This protein serves the important function of binding to many molecules such as vitamins and other nutrients in the circulation. Accordingly, albumin also has been found to play a role in transporting drugs throughout the body, hence the idea to engineer potential therapeutic molecules to bind to albumin.

One of the BITE Awards programs was a project in which Tarnowski asked his development team and separation scientists if they could come up with a molecule that has albumin's same kind of binding affinity. So they started reviewing some of the X-ray crystallography data (a method used to study molecular structure) and found that they had some spots on their molecules that looked as if they would have a high potential for binding to albumin. Subsequently, they reviewed their library of therapeutic compounds and found more molecules that had albumin-binding potential. "We turned those hits into molecules that we now want to immobilize on a chromatography resin. We want to set up a novel separation material such that drugs could now be purified in a novel way. We are having one of the big vendors in chromatography separation partner with us on this endeavor," says Tarnowski. "We're filing patents. We've found things that were completely unintended for this type of purpose, but by using good scientific methods, we've been able to find interesting molecules to do bioseparations."

The albumin-like molecule Tarnowski described works well with one of their commercial products, Tanzeum, which is a type-2 diabetes drug. They validated their research by immobilizing the binding molecule on a column and showed that they could use the column to purify Tanzeum. The current process is to buy separation columns from other vendors. By inventing a new bioseparation method, GSK now may have a way to protect its processing science long term. The company may be able to purify many biosimilars and biogenetic products using their novel method.

> "We often say, 'Let's change the way we do biopharmaceutical manufacturing, and let's do it differently.'"
>
> **JOE TARNOWSKI, PH.D.**
> GSK

Tarnowski gave another example related to the storage of proteins. "There is a dogma within the biopharmaceutical industry that protein-based therapeutics are very fragile and must be freeze-dried and stored at –70 C," he explains. This practice is problematic, because it makes for a complicated and laborious supply chain. So one of the BITE Award programs looked at whether you could spray dry proteins and make them into a powder that could then be dissolved in a unique way and stored in the refrigerator or at room temperature. This new method avoids the complications and expenses associated with freeze-drying and storing at very cold temperatures. This method has been successful, and is starting to be industrialized. "You've got to test the old ways and ideas that nobody wanted to challenge, and this BITE program is the place to challenge them," said Tarnowski.

Dr. Tarnowski also notes that a program of modest expense can yield a large improvement in process efficiency, which translates to cost savings. As such, he believes that management will continue to fund the BITE Awards. L

The New Regulations: Will They Hurt Your Business?

AMBRISH MATHUR

Ambrish Mathur is VP strategic development at ArisGlobal. He has worked in the life sciences industry for more than 20 years. He has led the development of systems at ArisGlobal for drug safety, electronic submissions, clinical trial management, registrations tracking, medical communications, and document management.

Accurate and timely safety/pharmacovigilance (PV) reporting is required to avoid embarrassing Warning Letters and potentially huge fines and penalties. Recently, the reporting format was revised, and the new structure, E2B(R3), has been finalized and is targeted for adoption in Europe in 2016. Also, the FDA has recently issued regulations requiring mandatory electronic reporting of ICSRs (individual case safety reports) for drugs, devices, and vaccines, effective in 2015. Marketing authorization holders (MAHs) need to start planning for these changes now or face the risk of not being in compliance when the new rules go into effect. The following are some key business issues you need to be aware of as you plan for these mandates.

THE CHALLENGES

Compliance to the new standard will require a significant investment in your drug safety/PV department. Your adverse event data capture, management, and submission process will need both business- and system-level changes. The need to collect and process additional data related to safety issues may require changes and training at various collection and processing points, including all your local safety offices and external partners. You also need to assess the impact of the changes on other departments that provide or process safety-related data, such as clinical-trial data management and regulatory affairs.

Another challenge concerns how your company's products are identified in the new format. Companies now have to maintain their product master data to comply with the Identification of Medicinal Products (IDMP) standard. The IDMP is used to identify all regulated products through the product life cycle (premarket to postmarket). European regulations mandate MAHs to adopt the IDMP terminology by 2016, with the FDA and the rest of the world indicating their adoption mandate will follow soon thereafter.

While submitting ICSRs is a primary safety/PV function, maintaining product data and implementing product dictionaries such as IDMP is typically managed by your regulatory affairs function. As the IDMP terminology will be needed for the new-format ICSR creation, the two departments will need to work collaboratively to plan an appropriate level of interface.

Industry experts estimate that a complete IDMP assessment and solution implementation for a large pharma could take 12 to 21 months, depending on their current processes and data-store configuration. Research has shown that barely 20 percent of pharmaceutical companies have fully implemented a strategy for managing their information to meet the new IDMP guidelines.

THE OPPORTUNITIES

While assessing how you will ensure compliance to both E2B(R3) and IDMP, each responsible department has an opportunity to improve efficiencies. You can implement these optimizations in conjunction with deploying/updating a technology solution, providing added business value from the projects, and maximizing use of already planned budget expenditures.

On the data center/IT front, this may be a good opportunity to assess any system upgrades, integrations, or replacements you may have been putting off (e.g., transition to SaaS and/or cloud-based computing).

The linkage between the submission and product identification standards offers that final justification to include a shared repository of product information in your budget. For your regulatory affairs function, this is your opportunity to affect those product master data management strategies that may have been on the back burner.

The challenges in reaching compliance with the new requirements should not be underestimated, and you need to start developing a clear action plan across business lines and regions now if you want the best ROI.

THE PLANNING

Begin by appointing a planning and oversight committee spanning safety/PV, regulatory affairs, and IT to ensure appropriate collaboration and harmonization across projects. If applicable, a phased approach that addresses the FDA medical device and vaccines electronic reporting requirements in 2015 can provide an interim step, leading to the 2016 readiness for IDMP and for drug ICSR reporting using the new format.

Perhaps this is the ideal time to explore and introduce global operational efficiencies while implementing these new compliant solutions. This is the time to rethink — and perhaps further optimize — your affected business processes and ensure this is a strategic business effort, not just regulation-mandated new resource investment and IT spending. L

6:30 AM

Enjoy the Miami sunrise on a jog with fellow fleet-footed attendees

9:40 AM

Wow the crowd during Biotech Spotlight presentation

1:10 PM

Make new friends over delicious catered lunch

4:00 PM

Private 1:1 partnering meeting with top prospects in private suite overlooking the ocean

5:50 PM

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The Best Metrics To Measure Performance

JOE TRAMMELL

Leaders must encourage constant improvement and consistently drive performance. The best way to do this is to ensure that all goals are tied to metrics that help predict business success. Selecting the correct measurement is critical.

The "ideal metric" possesses as many of the following characteristics as possible:

- EASILY MEASURABLE
- DIRECTLY CORRELATED WITH BUSINESS PERFORMANCE
- PREDICTIVE OF FUTURE BUSINESS PERFORMANCE
- COMPARABLE TO THE COMPETITION
- ISOLATED TO FACTORS CONTROLLED COMPLETELY BY THE GROUP THAT IT IS MEASURING.

No metric in the real world is perfect, but this list is a good place to start.

TURNOVER METRIC

Every manager in a company should be judged by the number of A-rated employees who leave the organization. I define A-rated performers as those ranked in the top 15 percent in the industry, considering their job and pay.

Any time an A-rated employee leaves, the organization should conduct a thorough postmortem to understand why and what can be done to prevent further losses. When top performers leave for other jobs, it is often an early sign that things are going wrong in a department.

SALES METRIC

Contrary to popular belief, total revenue is often NOT the most important metric for sales. First, it's not predictive of future revenue. Second, sales groups are often impacted by conditions outside of their control (quality of product, economic conditions, etc.). Because low revenue doesn't necessarily correlate to a bad team or poor effort, it's not a great sales metric.

I believe the best metric for sales is the accuracy of revenue forecasts. As any good salesperson knows, making a sale is a process. The better you understand the process, the better you will be at maximizing the revenue possible within the given market conditions.

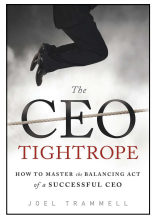
Therefore, the ability to predict revenue measures how good a sales team is at understanding the sales process. For example, at one of my former companies we expected the final sales numbers to be within 5 percent of the forecast at the beginning of the quarter. Building excellent forecasting into the company's sales culture gave us a strong competitive advantage.

EMPLOYEE SATISFACTION METRIC

Another metric I include for every department is employee satisfaction. I use the Gallup Q12, which is a 12-question survey of engagement created by the Gallup Organization. By giving this survey anonymously every six months, you can closely monitor employee engagement, which is crucial to success. This metric is easily measured, it's predictive, and it's somewhat reflective of factors unique to individual departments.

As a leader, you want to build a business culture that is constantly seeking to understand and improve performance by measuring it intelligently. If people understand that they will be held to a high standard, the productivity of the company will be maximized. Choosing the right goals and metrics, and then verifying performance regularly, will help build that culture and a winning team.

Joel Trammell is author of *The CEO Tightrope* and CEO of Khorus, which provides business management software for executives. His leadership as a CEO has resulted in successful nine-figure acquisitions by two Fortune 500 companies.



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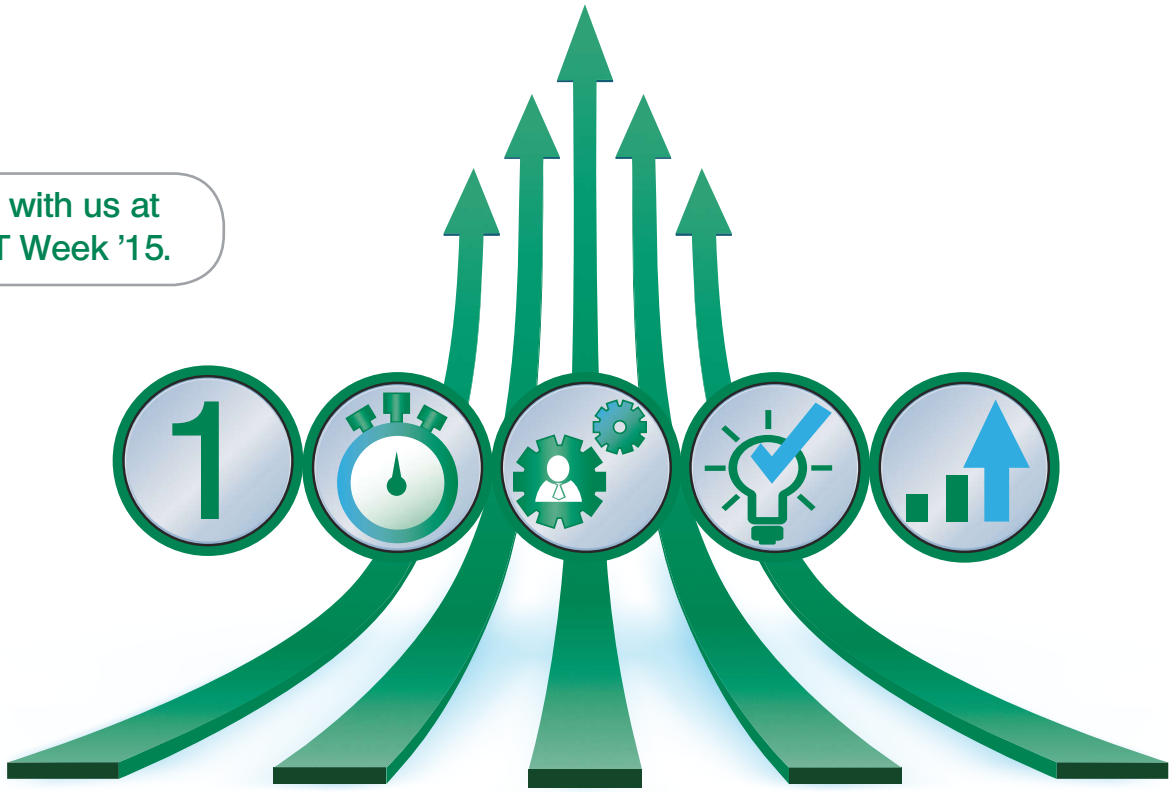

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