Life Science Leader

Connect. Collaborate. Contribute.

SEPTEMBER 2014

Life Science Leader

Connect. Collaborate. Contribute.

SEPTEMBER 2014

Simplifying Oncology Success at Daiichi Sankyo

Glenn Gormley, senior executive officer and global head of R&D **p. 24**

MPI RESEARCH

ABOVE AND BEYOND

- COMPREHENSIVE CARDIOVASCULAR TELEMETRY CAPABILITIES
- SPECIALIZED *IN VIVO* CNS MODELS
- INTEGRATED STUDY DESIGNS
- CLIENT-CENTRIC FOCUS
- EXPERT AND FLEXIBLE STUDY EXECUTION

Developing a predictive understanding for a medication's safety profile from early phase preclinical research efforts is more important than ever. This is why the safety pharmacology experts of MPI Research continuously seek innovative ways to incorporate emerging technologies to drive enhanced insights. As your drug development partner, we understand the essentials promoting successful safety evaluation programs, and go beyond to deliver for you.

Meet the safety pharmacology experts at the 14th Annual Safety Pharmacology Society Meeting, in booth #216. Mention this ad and receive a unique gift.

For more information on our outstanding safety pharmacology program, visit **mpiresearch.com/LSL**

THE CRO LEADERSHIP AWARDS 2014 Regulatory Award
THE CRO LEADERSHIP AWARDS 2014 Reliability Award
THE CRO LEADERSHIP AWARDS 2014 Innovation Award
THE CRO LEADERSHIP AWARDS 2014 Quality Award
THE CRO LEADERSHIP AWARDS 2014 Productivity Award

Visit us at

ISPE Annual Meeting
Las Vegas - **Oct. 12-15**
Booth **49**

PharmaExpo
Chicago - **Nov. 2-5**
Booth **721**

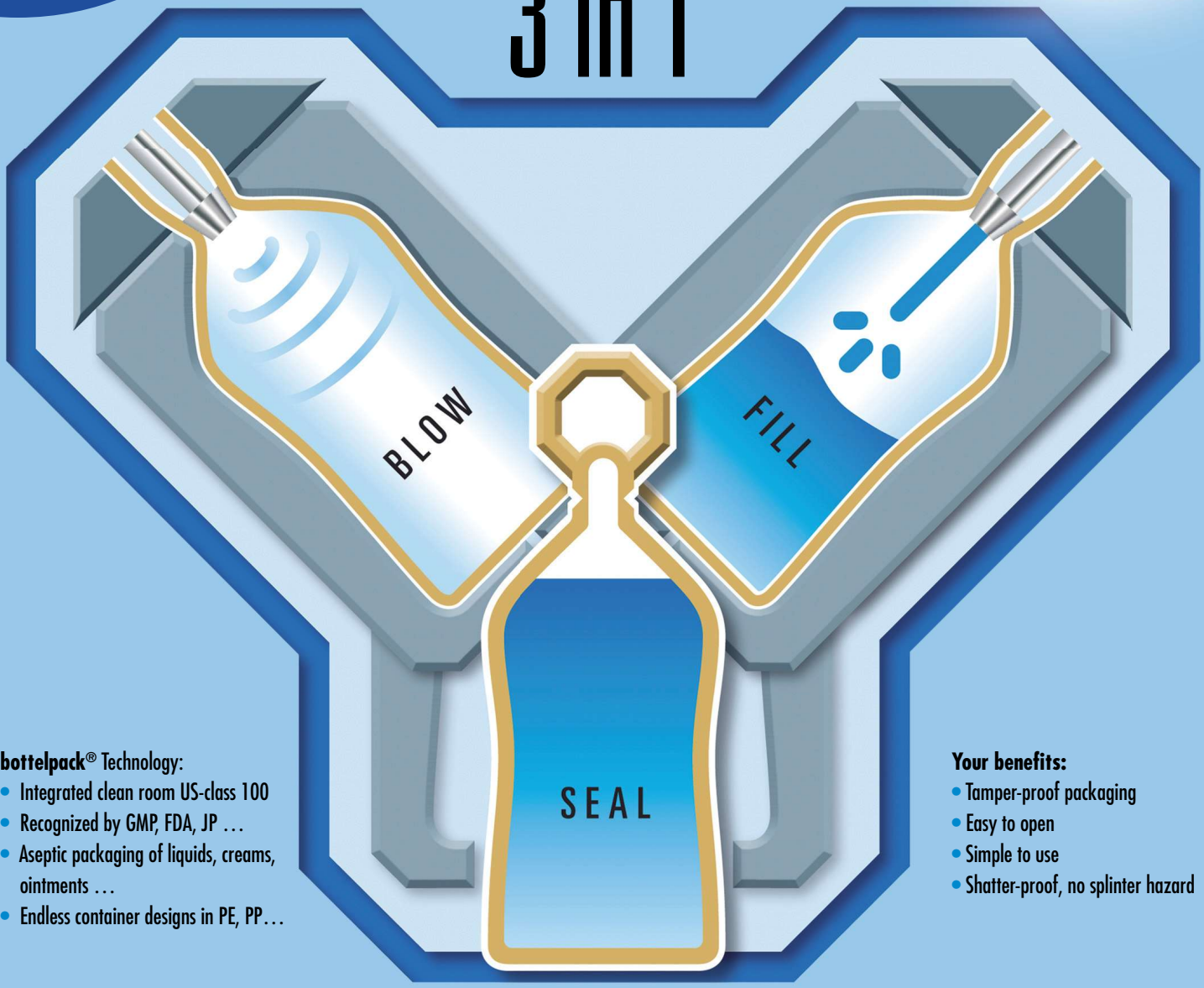
bottelpack®

BLOW-FILL-SEAL TECHNOLOGY

50 YEARS OF PASSION IN BLOW-FILL-SEAL
bottelpack rommelag

Advanced aseptic packaging in one operation cycle
Reliable – Simple – Cost-Effective

3 in 1



bottelpack® Technology:
- Integrated clean room US-class 100
- Recognized by GMP, FDA, JP …
- Aseptic packaging of liquids, creams, ointments …
- Endless container designs in PE, PP…

Your benefits:
- Tamper-proof packaging
- Easy to open
- Simple to use
- Shatter-proof, no splinter hazard

rommelag®

www.rommelag.com

rommelag ag
P.O. Box · CH-5033 Buchs, Switzerland
Phone: +41 62 834 55 55 · Fax: +41 62 8345500
E-mail: mail@rommelag.ch

rommelag Kunststoff-Maschinen Vertriebsgesellschaft mbH
P.O. Box 1611 · D-71306 Waiblingen, Germany
Phone: +49 7151 95811-0 · Fax: +49 7151 15526
E-mail: mail@rommelag.de

rommelag USA, Inc.
27905 Meadow Drive, Suite 9
Evergreen CO 80439, USA
Phone: +1.303. 674.8333 · Fax: +1.303.670.2666
E-Mail: mail@rommelag.com

rommelag Trading (Shanghai) Co., Ltd.
Room 1501 Xinyin Building
No. 888 Yishan Road · 200233 Shanghai, P.R.China
Phone: +86 21 6432 0166 · Fax: +86 21 6432 0266
E-mail: romcn@rommelag.com

CONTENTS

Welcome to

Life Science Leader

SEPTEMBER 2014 VOL. 6 NO. 9

@RFWrightLSL linkedin.com/in/robertfwright pinterest.com/rfwrightlsl facebook.com/LifeScienceLeader WWW.LIFESCIENCELEADER.COM

LIFE SCIENCE LEADER (ISSN: 21610800) Vol. 6, No.9 is published monthly by Jameson Publishing, Inc. at Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672. Phone (814) 897-9000, Fax (814) 899-5580. Periodical postage paid at Erie, PA 16510 and additional mailing offices.
SUBSCRIPTION RATES for qualified readers in the U.S. $0. For nonqualified readers in the U.S. and all other countries $97 for one year. If your mailing address is outside the U.S. or Canada, you can receive the magazine digitally if you provide a valid email address.
POSTMASTER: Send address corrections (Form 3579) to Life Science Leader, Knowledge Park, 5340 Fryling Road, Suite 300, Erie, PA 16510-4672. **PUBLICATIONS AGREEMENT** No. 40722524 c/o AIM, 7289 Torbram Road, Mississauga, ON L4T 1G8

CORRECTION
The article "An Update on the Buzz Around Oncology" in our July CMO supplement mistakenly stated "at present, there are still no FDA-approved drugs on the market that work using immunotherapy." Both Provenge and Yervoy are FDA-approved immunotherapy drugs.

MARKEN

GLOBAL LIFE SCIENCE SUPPLY CHAIN SOLUTIONS

SWITCH TO MARKEN FOR THE GREATEST CONFIDENCE IN TIME-CRITICAL SHIPMENTS

MARKEN MAKES IT HAPPEN

99.7% ON TIME, WITHIN SPEC | PRODUCT INTEGRITY | TEMPERATURE-CONTROLLED ENVIRONMENT

You're conducting a trial in Kiev that relies on biologic materials from the UK. Normally your supply chain logistics provider seamlessly executes a pre-planned process to keep the drugs on time and in perfect condition. But unprecedented political uncertainty, local unrest and potential military intervention engulf the region. When you work with Marken, we spend 10 days planning a strategic 8-day route in a temperature-controlled vehicle, protected 24/7 by armed guards and monitored by remote GPS. So the drugs arrive on time with temperature recorders showing perfect control.

TALK TO US ABOUT YOUR LOGISTICS CHALLENGES
EMAIL: EXPERT@MARKEN.COM WWW.MARKEN.COM

Want To Know The Secret To Discovering New Cures?

ROB WRIGHT Chief Editor

When I sat down to speak with the subject of this month's cover feature (page 24), Daiichi Sankyo's Glenn Gormley, M.D., Ph.D., I revealed that my father, Dr. David L. Wright, M.D., Ph.D., was also a trained pediatrician (retired). Gormley told me his early work at the chemistry bench, developing drugs for children with leukemia, served as his motivation for going to medical school. "I wanted to follow the compounds into the clinic," he said. Given that Gormley went on to become board certified in pediatrics and endocrinology, completed a post doc fellowship in oncology, and is presently working as the senior executive officer and global head of R&D at a company with one of the hottest oncology pipelines, some might argue he is living a *purpose-driven* life.

And that got me thinking about the purpose of drug development. Of course, the number one purpose of every business is to create revenues, and enterprises are created because of a perceived need not being met. But in drug development, that purpose has a direct undeniable link to the patient — your customer. And as we all know, keeping that customer is imperative to the success of any business.

Consider how one of the latest buzzwords in our industry is patient-centric. As is our industry's custom, we have been tossing it around as if we just discovered Ponce de Leon's Fountain of Youth and have taken to applying it to everything from how to deliver healthcare (i.e., patient-centric care) to how clinical trials should be designed (i.e., patient-centered clinical trials). But it was more than 60 years ago when George Merck, then chairman of Merck & Co., stated, "We try to remember that medicine is for the patient … It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear." As an industry, it is obvious we haven't done a good job at executing this vintage notion. Just look at the numerous stakeholders created to fill a perceived unmet need, such as biotech drug companies, patient advocacy organizations, and numerous consortiums. These, along with pharmaceutical companies, physicians, insurance payors, medical research centers, CROs, and government regulators, desire to play a role in drug discovery and development. While many of these can be defined as businesses, thereby being similar of purpose, this is not universal. Further, not all of these have the patient as their primary source of revenue. Thus, keeping the patient/customer is not their primary mission. If you want to discover new cures, you must have a sense of purpose that transcends revenue creation in order to motivate employees and place the patient at the center. To learn the fundamental organizing principles necessary to create such a purpose, check out *Combining Purpose With Profits* by Birkinshaw, Foss, and Lindenberg in the Spring 2014, *MITSloan Management Review*. Done well, the profits will follow.

Life Science Leader

SEPTEMBER 2014 VOL. 6 NO. 9

LIFE SCIENCE LEADER
5340 Fryling Rd., Suite 300
Erie, PA 16510-4672

Telephone: 814 897 7700
Fax: 814 899 4648

WWW.LIFESCIENCELEADER.COM

VP OF PUBLISHING
Jon Howland / Ext. 203
jon.howland@lifescienceleader.com

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

EXECUTIVE EDITORS
Wayne Koberstein
wayne.koberstein@lifescienceleader.com

Louis Garguilo
louis.garguilo@lifescienceconnect.com

Ed Miseta
ed.miseta@lifescienceconnect.com

Trisha Gladd
trisha.gladd@lifescienceconnect.com

SENIOR DIRECTOR OF PUBLISHING
Perry Rearick
perry.rearick@lifescienceleader.com

MARKET DIRECTOR
Robert Wilson
Robert.Wilson@lifescienceleader.com

PRODUCT DIRECTOR
Jenell Skemp
jenell.skemp@lifescienceconnect.com

PROJECT MANAGER
Megan Rainbow
megan.rainbow@lifescienceconnect.com

DIRECTOR, LIFE SCIENCE TRAINING INSTITUTE
Bill Beyer
bill.beyer@lifescienceconnect.com

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

PUBLISHER, CLINICAL & CONTRACT RESEARCH
Sean Hoffman
724 940 7557 / Ext. 165
sean.hoffman@lifescienceleader.com

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

PUBLISHER/OUTSOURCING
Cory Coleman / Ext. 108
cory.coleman@lifescienceleader.com

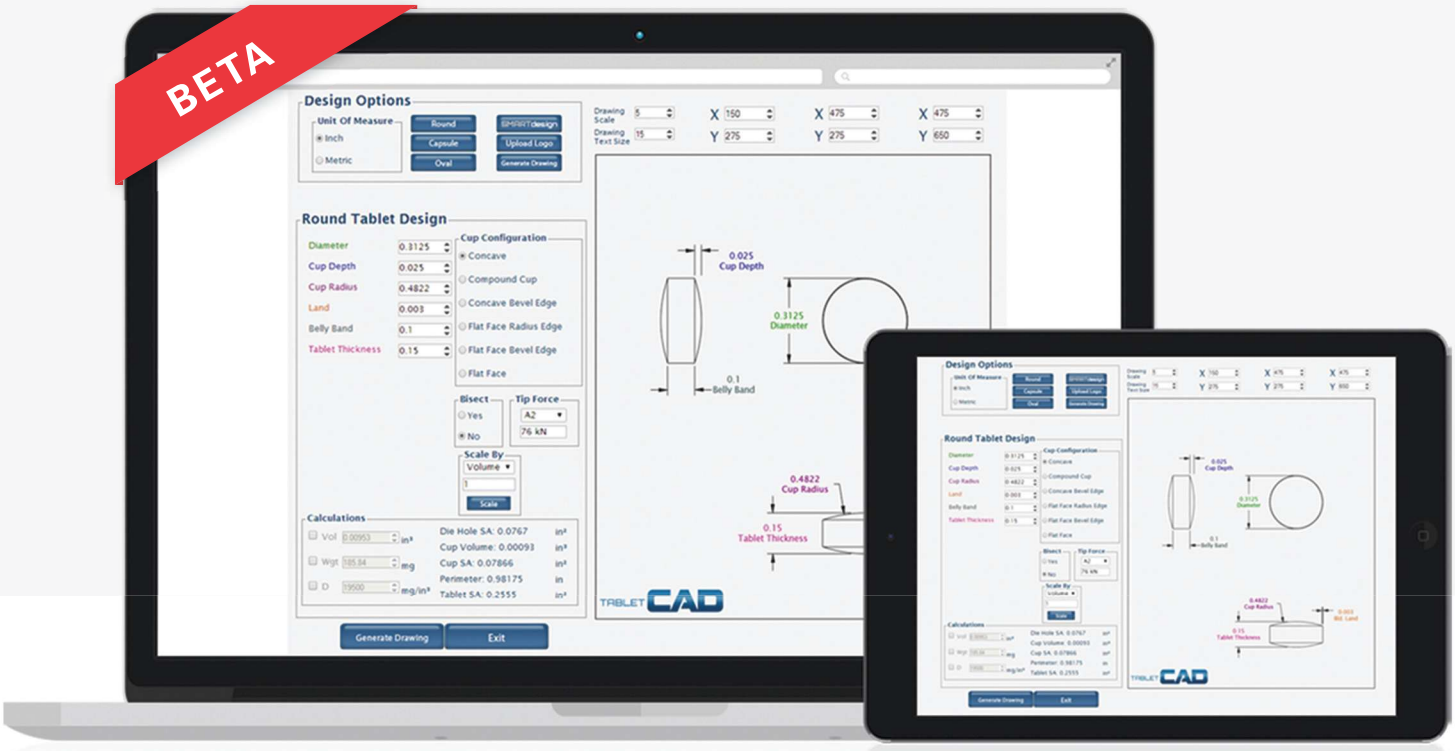
GROUP PUBLISHER/OUTSOURCING
Ray Sherman / Ext. 335
ray.sherman@lifescienceleader.com

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

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

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

DIRECTOR OF AUDIENCE DEVELOPMENT
Mindy Fadden / Ext. 208
mindy.fadden@jamesonpublishing.com



TABLETS ON YOUR TABLET.

Design tablets **online** with TabletCAD, Natoli Engineering's **web-based tablet design software.**

- Smart Design (guides you through creation of your tablet)
- Real time surface area, volume, and perimeter calculations
- Simple user interface with tooltip information and links between dimensions and their controls
- Real time geometry validation
- Add common bisects such as standard, cut flush, cut through, etc.
- Quickly determine tablet thickness and total surface area or film coat solutions required for packaging
- Online help documentation and walkthroughs
- Supports all major browsers

Participate in our beta testing!
Scan here to access or visit
natoli.com/tabletCAD

TABLET CAD

NATOLI
YOU DEMAND. WE DELIVER.

Q What is the best leadership advice you ever received?

A WHEN I TOOK MY FIRST MAJOR LEADERSHIP POSITION as chair of the Department of Microbiology and Immunology at the University of Michigan in 1986, I attended an event featuring the president of the University. During his speech, he indicated that his style of leadership was always to hire the very best individual available for the position, carefully lay out the expectations of the job, provide as much support as was possible, and then get out of that person's way. I've since tried to follow that advice, understanding that the academic industry and the pharma industry have differing goals and targets of performance. In both situations, though, accountability is required, and performance is both measured and appropriately rewarded.

BARRY EISENSTEIN
Barry Eisenstein, MD, is senior VP of scientific affairs at Cubist Pharmaceuticals and editor of *Antimicrobial Agents and Chemotherapy.*

A SHORTLY AFTER TAKING ON A SENIOR ROLE IN A FORMER ORGANIZATION, my manager (Dave Williams, former CEO of sanofi pasteur) told me, "If you are doing work, you aren't doing your job." As a new leader, I was working many hours to ensure good outcomes, and I wasn't relying enough on the team who had to deliver the outcomes. Leaders need to create and articulate a clear vision, understand the obstacles to achieve the vision, inspire the team to develop a strategy and plan to execute the vision, and coach them through the process. If you are doing the work yourself, you can only achieve the outcome of one person. Through leadership, you get the potential output of thousands of people and a more capable organization over time. Each day I need to ask myself, "Why am I here?" and reflect on this wonderful advice to keep myself grounded on how I bring value to the organization.

JIM ROBINSON
Jim Robinson is the VP for vaccine and biologics technical operations for Merck & Co. In this role, he supports the manufacturing strategy, process development, technical transfer, approval, and production of Merck's vaccines and biologicals at eight internal sites in the U.S. and Europe and several partner sites globally.

Q What best business practices have you seen utilized in clinical trials outside of the U.S. that you think should be incorporated into U.S. clinical trials? Why aren't these being used, and what roadblocks need to be removed for this to happen?

A TODAY, THERE REALLY ARE NO SIGNIFICANT BUSINESS PRACTICES used in clinical trials outside of the U.S. that are not already incorporated into U.S. clinical trials. Regulations may be different, and that can dictate different practices at times. However, the U.S. remains a leader in piloting innovation in clinical trials. Globally, clinical development is too slow and too expensive. This necessitates new approaches by both biopharma companies and regulators around the globe. Additional requirements and longer protocol review cycles are the roadblocks that need to be removed if we are to get innovative medicines to waiting patients.

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

ROPACK®

Your Trusted Packaging Partner

Solid Oral Dose Contract Packaging Services for North America

Certified cGMP Current Good Manufacturing Practices · FDA · Health Canada

Ropack brings exceptional solid oral dose packaging solutions to leading pharmaceutical organizations through its deep-rooted commitment to:

Quality

17% of Ropack's workforce dedicated to quality assurance

Facilities for low RH and controlled temperature production

Reliability

Verification by on-line vision systems

Customer-centric KPIs: on-time delivery, order accuracy and product quality

Regulatory

FDA, Health Canada and controlled substances licenses

Assistance with import/export process

Efficiency

Integrated business portal for real-time updates

Integrated OEE system throughout 33 packaging lines

ropack.com

Paul Dupont, *VP, Marketing & Business Development*
paul.dupont@ropack.com

ropack.com/download-5

Download "Blister's Competitive Advantage" for a chance to win an iPad Air.

Market Delivers Low Rx Costs, But The Left Schemes On Price Controls

JOHN McMANUS The McManus Group

As this column is published, Congress will be returning from a five-week recess ... I mean, "district work period" ... with only 10 days in September for actual legislating before it calls it quits to campaign for the midterm elections. Republicans stand a better than 50 percent chance of taking the Senate and will certainly maintain control of the House.

The 113th Congress cannot be considered a successful one in terms of advancing healthcare policy. While the committees of jurisdiction achieved a bipartisan breakthrough in developing a consensus on how to replace the dysfunctional Medicare physician payment formula, partisan disagreement on whether and how to finance that change prevented enactment. Moreover, paralysis on tax reform and high U.S. corporate tax rates sparked an incredible M&A run for life sciences companies in pursuit of inversions to lower their tax liability by moving their headquarters offshore.

Meanwhile, the Obama Administration refuses to contemplate ANY legislative changes to the Affordable Care Act (ACA) — repeal of the pernicious medical device tax, delay of the individual mandate that no one felt reasonable, repeal of benefit mandates that compel the cancellation of individual insurance policies — but for its own political convenience blithely halts, defers, or changes implementation of ACA policies that it chooses, despite clear language in the statute.

Congress may address several of these smoldering health policy problems in the lame duck period — after the November elections and before the new Congress is sworn in. But more likely, substantive policy decisions will be addressed next year with a new chairman of the House Ways & Means Committee (likely Budget Chairman and Vice-President nominee Paul Ryan) and possibly a Republican Senate. Democrats will remain influential even if Republicans capture the Senate and newly installed Finance Committee Chairman Ron Wyden (D-OR) will retain substantial input in health policy even if he is relegated to the post of Ranking Member. Democrats will certainly have more than 40 seats, enabling them to block legislation if they stay together.

Ryan and Wyden have collaborated in the past by developing a proposal for moving Medicare to a more market-oriented system known as "premium support," which would create more competition between private plans and the traditional fee-for-service Medicare program. This possible synergy could occur at a time when Medicare's private plans are more popular than ever before. The CMS Office of the Actuary's 2014 Report on National Expenditures noted that more than half of newly eligible Medicare beneficiaries enrolled in these private plans. The Ryan-Wyden plan would apply the competitive reforms to younger beneficiaries who are accustomed to and like private health plans.

A MORE ACTIVE AND INTRUSIVE FEDERAL GOVERNMENT

But while there are some rays of sunlight, it isn't all Yahtzee and mai tais. Senator Wyden envisions a much more active and intrusive federal government with respect to pharmaceutical pricing. In July, his missive with Senator Chuck Grassley (R-IA) to Gilead Sciences demanding a thorough and detailed explanation for its pricing rationale for Sovaldi, its breakthrough cure for Hepatitis C, sent a chill through the drug world. Their eight-page letter demanded documentation for

Q Polishing Reimagined

Remove Virus, HCP, DNA, Endotoxins... and Expense

Introducing NatriFlo™ HD-Q flow-through chromatography

The NatriFlo HD-Q anion exchanger, based on proven and universally-used quaternary amine chemistry, combines the capacity of the highest performance resins with the exceptional flow properties of membrane adsorbers. The compact NatriFlo Process 600 can polish up to 5 kg of monoclonal antibody in a single pass, typically in less than 2 hours. The NatriFlo family is fully scalable from 0.2 mL devices to production-scale.

True Q Resin Polishing Performance: Efficient and reproducible Q polish performance combining resin binding capacity with adsorber speed to achieve a new level of flexibility.

Polishing Workhorse: Purify 10 kg of mAb per liter membrane volume with sustained best-in-class clearance of virus, HCP, DNA and endotoxin.

Unrivaled Salt Tolerance: Purify without dilution in more buffer types at high conductivity, even in phosphate buffers.

Other important features:

- Single-use pre-packed column: equilibrate, run, and discard. No cleaning, handling equipment or storage space required
- Plug-and-play: No packing, no validation, no QC
- High flow rates: Process more in less time
- Easily scaled up as capacity needs grow

Learn More

For more information, technical details, and method development guidelines, please visit:

www.natrixseparations.com/hdq

Natrix®

Distributed globally by JSR Life Sciences

www.JSRLifeSciences.com

JSR Life Sciences
MATERIALS INNOVATION

"Let's hope a new Congress can address the vexing problems afflicting the healthcare system."

everything from financial analysis for every meeting related to acquisition of Pharmasset (the originating company for the drug), research and development costs of Sovaldi, and market and pricing plans used for launch of Sovaldi domestically and internationally. Wow!

One would imagine an intrusive inquiry of this nature would be prompted from exploding Medicare costs and spiraling Part D premium projections. But the Center for Medicare and Medicaid Services trumpeted Part D's effectiveness in constraining costs in a July 31 press release, crowing that monthly drug premiums would only increase by $1 in 2015. The premiums reflect prescription drug plans' projections for spending next year, obviously fully accounting for expected utilization of Sovaldi and all other covered drugs.

Perhaps Senator Wyden is responding to a highly orchestrated lobbying campaign by Express Scripts and the insurance industry to demonize pharmaceutical companies that have sought to invest in specialty drugs addressing unmet medical needs. Led by John Rother's National Coalition on Health Care's Campaign for Sustainable Rx Pricing, this media-focused activity is long on hyperbole and threats and short on responsible discussions and solutions.

The campaign's warning of a "tsunami of expensive medicines that could literally bankrupt the healthcare system," somehow failed to read Express Scripts' own projections for specialty meds to make up between 15 and 20 percent of total pharmacy costs for the future, just as they have for the past 10 years. This is the same Express Scripts that also recently let on to investors that its specialty pharmacy division would be its leading contributor to earnings in the future. Limiting access to history's most innovative and valuable medical products has never looked so good.

CBO REPORT OFFERS INSIGHTS ON DRUG COSTS

A newly released report by the Congressional Budget Office (CBO) also counters the alarmists by making clear that drug costs are down substantially because of less brand-name utilization. CBO's July report "Competition and the Cost of Medicare's Prescription Drug Program" notes that costs for 2013 were half of the original projections, largely because there has been substantially more generic utilization than initially projected. CBO attributes a combination of greater patent expirations and fewer launches of new drugs. The new Medicare trustees' report even has lowered its drug cost trend for the next 10 years.

Generic utilization in Part D shot up from 67 percent in 2007 to 78 percent in 2010 and has likely climbed higher since. In addition, Part D plans were brutally efficient in forcing generic switches when they were available — increasing the generic fill rate from a marketwide average of 72 percent in 2002 to 90 percent in Part D by 2007 to 2010.

As a result, beneficiary prescription premiums have remained virtually unchanged in the last four years. CMS proudly notes that in plan years 2011 through 2014, premiums have held steady at about $30 to $31 a month even while absorbing the costs of filling in the "donut hole" for beneficiaries with substantial drug costs.

So what is the motivating factor of all this outlandish talk? On the same week that CBO and CMS released data showing success of the Medicare Part D program, the left-leaning Medicare Rights Center issued a report calling for "Better Prices on Prescription Drugs," which included four proposals:

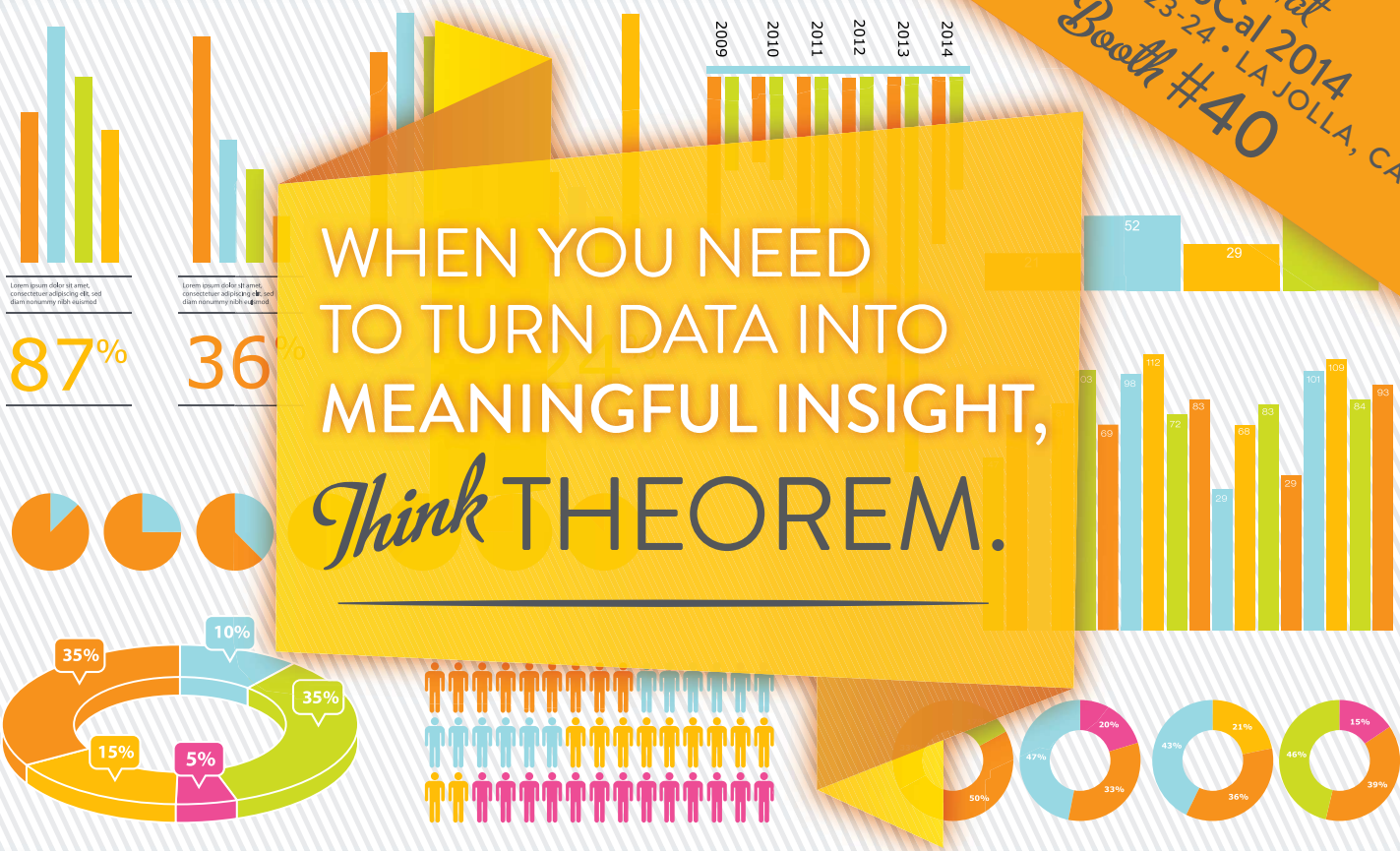
1. Impose Medicaid rebates — aka price controls — on Medicare drugs provided to low-income beneficiaries.
2. Allow Medicare to "negotiate prices" for a new public Part D option.
3. Increase manufacturer discounts in the "donut hole."
4. Establish price controls for Medicare Part B drugs administered in physician offices by using "least costly alternative" reference prices.

Oh, one more point the CBO report made about price control regimes like those advocated by the Medicare Right Center: "Firms would respond by curtailing drug innovation."

Let's hope a new Congress can address the vexing problems afflicting the healthcare system while allowing programs that are clearly working effectively to continue without ideological intervention that have no empirical basis. 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.

Visit us at OCT SoCal 2014
SEPTEMBER 23-24 • LA JOLLA, CA
Booth #40



WHEN YOU NEED TO TURN DATA INTO MEANINGFUL INSIGHT, *Think* THEOREM.

THEOREM'S ADVANCED VISUAL ANALYTICS TOOLS AND TECHNIQUES CAN SIMPLIFY YOUR COMPLEX TRIALS.

In the end, clinical trials are essentially about one thing: data. Throughout your study, we ensure data viability and make it available for review in real time. Theorem has developed visual analytics tools and techniques that allow us to present your complex clinical information visually to identify buried opportunities and risks so you can make heads-up decisions along the way. These techniques give you a quicker grasp and greater insight into the meaning the numbers actually represent. When you need a partner that can simplify your most complex clinical trial data from around the world, don't give it a second thought. **THINK THEOREM.**

- Real-time medical review and site performance visualization packages
- Fully integrated consulting services
- Integrated solutions or Functional Service Provider (FSP)

www.TheoremClinical.com

Simplifying the most COMPLEX TRIALS.

THEOREM CLINICAL RESEARCH™

Biopharmaceuticals \\ Medical Device \\ Diagnostics

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.

WAYNE KOBERSTEIN Executive Editor

SNAPSHOT

Based on its novel platform technology of flavivirus peptide inhibitors, Ennaid Therapeutics is developing "cures" for a number of infectious diseases, starting with dengue virus and west nile virus, ultimately in oral dosage forms. Mainly outside the U.S., the deadly mosquito-borne dengue virus infects 400 million people in 125 countries and poses a $1.8 billion economic threat worldwide. The WHO and the CDC have reported nearly half of the world's population is at risk for contracting dengue. Ennaid plans a four-year crash program for its dengue cure: a "comprehensive, IND [investigational new drug] -ready" preclinical program; a Phase 1/2a clinical development strategy; and use of orphan drug status in the U.S. and EU and compassionate-use trials in Australia or Thailand.

WHAT'S AT STAKE

Ennaid Therapeutics is one of the youngest companies to appear in Companies to Watch. Yet it barely seems to have stayed in the infant stage and may have passed the typically awkward toddlerhood altogether. Starting with its staff of three, the company appears on the surface to be much less than it is. In fact, the tiny group of "employees" hold together a team of senior executives and advisors that a much larger company would envy. Baby companies in preclinical development may be expected to have a chief scientist, but how many of them have two clinical manufacturing experts — covering everything from preformulation to packaging — on the scientific advisory board? And when Ennaid licensed its peptide-based antiviral technology, it also recruited the technology's inventor as its chief scientist, along with the co-inventor, a leader in HIV research, onto its SAB (scientific advisory board).

Just as impressive as the scientific expertise, Ennaid also brought an unusual amount of business acumen into its inner circle. Three solid financial and business experts lead the board of directors, and a separate board of advisors has a veteran start-up leader at its helm. Ennaid also has a head of regulatory affairs — another mature move.

"Once we acquired our product, it was evident that our company was built on a story that not only inspired others to do good professionally, but also inspired others to do humanitarian work, in that it was easy to build a team of dedicated, seasoned professionals from within the industry," says the dynamic CEO, Darnisha Grant Harrison.

Although identified mainly with the poorest nations on Earth, dengue virus infection is actually the world's fastest-growing pandemic, threatening many of the most advanced regions. Together, dengue and the target of Ennaid's second lead program, west nile virus, shadow over most of the world's continents. The current Ebola scare underlines why the biopharma industry should be more interested in diseases and epidemics originating outside its comfort zone, as well as access to healthcare in emerging countries, industry's role in public health, and public/private partnerships in drug development.

"Our drug will likely be an oral dosage form; therefore storage will be simplified at controlled room temperature. We will address this through strategic partnerships with organizations which have mature distribution programs to globally diverse regions," Harrsion says.

The recent headlines regarding Ebola are hammering some of those points home. The continuing news alone would be a factor in choosing Ennaid as a company to watch. Certainly, Ennaid will require all the help it can get and more from the Gates Foundation and other philanthropists — and it should get it — but this is not just another potential David and Goliath story. Harrison and her team are going at this as a business, along with the grand ambitions we look for in any healthy start-up. But benchmarked against many a lonely-inventor-turned-entrepreneur story, still so common in this industry, Ennaid looks positively light years ahead of the game. Perhaps its ambitions will turn out to be more realistic than merely grand.

DARNISHA GRANT HARRISON
CEO

Vital Statistics

3
Employees

Headquarters
Atlanta, GA
Office in New York City

Finances

$225K
round raised with self-funding & family/friends

Partnerships

Worldwide, exclusive rights to technology licensed from Tulane University, Rockefeller University, Florida Gulf Coast University, & Univ. of Washington

Latest Updates

June 2014: Invited to present at the BIO International Convention. (Not normally qualified as an update, but significant for such an early-stage company.)

If you have shipping needs that require temperature control, count on FedEx Custom Critical®. From ground services in the U.S. and Canada to global air solutions, we deliver.

Visit us at the Cold Chain Global Forum booth #402

For more information or to get a quote, call 1.800.255.2421 or go to **customcritical.fedex.com/temp**

FedEx. Solutions That Matter.®

"Shadow" Contract Manufacturing Industry Increasing

The combination of increased government healthcare coverage, ballooning government debt, and massive expiry of patent protection on originator drugs has spurred an interest in sourcing generic active pharmaceutical ingredients and finished drugs from lower-cost countries.

KATE HAMMEKE
Director of Marketing Intelligence
Nice Insight

> *"Strategic supply and marketing agreements can produce spectacular results for Indian manufacturers and American sellers alike."*

In this context, India has emerged as a powerhouse in supplying the Western pharmaceutical markets. India now ranks second to the U.S. only in terms of FDA-inspected facilities and number of active DMFs (drug master files), and it provides great value for a relatively secure supply of pharmaceuticals.

U.S.-based pharmaceutical companies now have numerous strategic supply and marketing agreements in place with the Indian pharma industry. Allergan and Pfizer with Nicholas Piramal, Wyeth with Bharat Biotech, and DSM with Lupin are examples of such strategic collaborations.

These strategic supply and marketing partnerships extract maximum value for their shareholders as they maximize capacity utilization in India and market share in the U.S. at minimum incremental expense. No up-front capital investment, lower manufacturing variable, and fixed costs in combination with higher sales volumes/prices are all powerful drivers in setting up these strategic agreements. This relationship, in fact, has obvious similarities with formal contract manufacturing arrangements. Nevertheless, due to the lack of transparency in these supply and marketing arrangements, the outcomes are not generally included in the contract manufacturing industry landscape.

Nice Insight market research shows now that this "shadow" contract manufacturing industry has been increasing spectacularly over the last five years and is expected to continue to provide great opportunities for both Indian and U.S. parties.

For example, Lupin has a strategic supply and marketing collaboration with DSM in the field of cephalosporines. Figure 1 shows that Lupin's number of shipments for four cephalosporin products will nearly triple by the end of 2014 when compared to 2009.

Wockhardt, another major name in the Indian pharma landscape, had a similar strategic agreement with U.S.-based Ivax* for anti-ulcer drugs.

Figure 2 shows a comparative view of Wockhardt's Q2 shipments to the U.S. for famotidine, lansoprazole, and ranitidine. The cumulative profile of the graph suggests that Wockhardt has quadrupled its shipments of anti-ulcer drugs to the U.S. between 2009 and 2013.

Dishman offers yet another example of synergies between American and Indian contract manufacturing companies. According to the company website, Dishman's focus is on high-value, cost-competitive contract services including process development, process optimization, and the manufacture of late-stage clinical and commercial supplies of prescription and over-the-counter drugs.

Dishman is a leader in the ammonium salts for food and drug use such as cetylpyridinium chloride (CPC). CPC is a bactericide used in OTC mouthwash, lozenges, and cough syrups. By way of example, CPC is used in the formulation of branded products such as Listerine (J&J), Crest (P&G), Colgate (Colgate Oral Pharmaceuticals), and ACT (Chattem). It is also used in a range of other no-name products sold by chains such as CVS, Walgreens, Target, and Walmart. Dishman's expertise in highly regulated manufacturing of

SCIENTISTS HELPING SCIENTISTS.

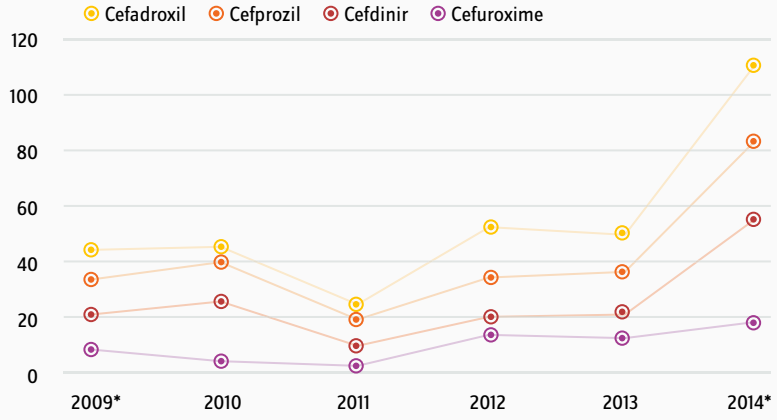
At Covance, we help move science forward. Your science. As your research partner, we act as an extension of your team, providing the deep scientific expertise and unique perspectives that have helped deliver over a third of all the therapies on the market today. From custom assays to unique insights on helping reduce timelines and regulatory hurdles, Covance scientists are your scientists too. Come discover more about our experienced researchers and scientific experts.

CALL TO LEARN MORE

The Americas +1.888.COVANCE | Europe/Africa +800.2682.2682
Asia Pacific +800.6568.3000 | **Or go to covance.com/scientist**

COVANCE
SOLUTIONS MADE REAL™

FIGURE 1 Lupin's Cephalosporins Shipments to the U.S.



Note: Cefalexin was left out since it was more volatile; nevertheless, the trend is growth.

FIGURE 2 Wockhardt's Anti-Ulcer Shipments to the U.S.

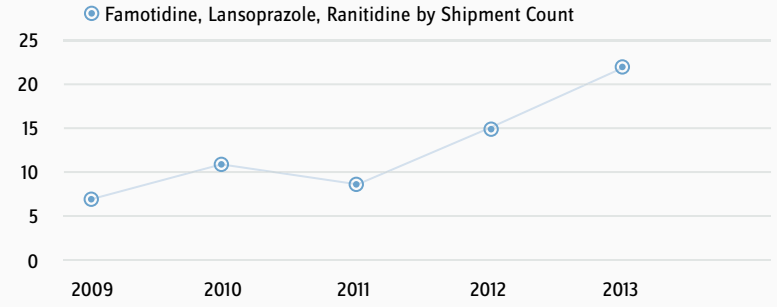
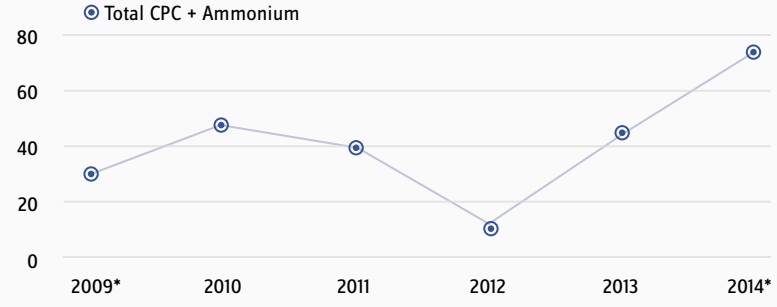


FIGURE 3 Dishman's Annual Quaternary Ammonium Salts Shipments to the U.S.



*Yearly sales for 2009 start in May and 2014 ends in June.

Source: PIERS, the Port Import/Export Reporting Service

quaternary ammonium salts in combination with the marketing power of P&G, for example, makes good business sense.

Figure 3 shows the number of annual quaternary ammonium salt shipments to the U.S. made by Dishman, including cetylpyridinium chloride. While the business displays considerable year-over-year volatility, the linear trend line clearly shows that Dishman's business has roughly doubled between 2009 and 2014. In fact, if Dishman shipments continue at the same pace in the second half of this year, 2014 will be a record year for the company's quaternary ammonium salt business.

In conclusion, our research clearly shows that strategic supply and marketing agreements can produce spectacular results for Indian manufacturers and American sellers alike. There is little market research publically available in the "shadow" contract manufacturing industry. Nice Insight research is now shedding some preliminary light on the spectacular growth rate of this market segment. L

** Ivax was acquired by Teva in 2013; therefore, data is available only to the end of Q2/2013.*

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.

American Airlines Cargo

With you all the way.

Our goal is to see things from your perspective and anticipate your every need – especially when it involves incredibly sensitive shipments. With a larger, expanding network, we're coming together to provide a global cold chain solution that ensures on-time, uninterrupted, temperature-controlled delivery, even in hard-to-reach locations.

ExpediteTC℃

Learn more about Expedite TC℃ℳ at aacargo.com/expediteTC

Outsourcing Economic Models Are Changing

Facilities are evaluating bottlenecks, risks, logistics, and inventory as part of cost modeling.

ERIC LANGER
President and Managing Partner
BioPlan Associates, Inc.

Amgen's recent slashing of manufacturing operations by 23 percent is the latest example of how operational pressures are affecting biomanufacturers' decision making. Now, even previously "core" operations such as media and buffer preparation are being scrutinized as biomanufacturers seek more efficiency with fewer people and lower costs.

Large-scale preparation of liquid-cell culture media and buffers for biopharmaceutical manufacturing has been discussed for decades, but only recently have the economics changed enough to warrant outsourcing of this process. This signifies a long-term strategy shift leading to the elimination of in-house bioprocessing of less "core" activities.

We surveyed 50 biopharma decision makers about their interest in core outsourcing, specifically media and buffer prep. We found that 47 percent would consider outsourcing large-scale media and buffer prep.

"We found that 47 percent [of respondents] would consider outsourcing large-scale media and buffer prep."

LARGE-SCALE OUTSOURCING OF MEDIA AND BUFFERS

Outsourcing of culture media and buffer preparation primarily involves hydration of media or buffer powder ingredients under GMP conditions. Today's economic currents are changing the make-vs.-buy equation and are beginning to favor buying prepared liquid culture media and buffers vs. end users preparing their liquids to cGMP standards from powders in-house. Of course, economics is just one of many factors. Others include regulatory, documentation, integration of inventory management, space availability, utilization of classified space, staffing, training, preferences for flexible and lean operations, and demand for bioprocessing sterility.

About 90 percent of current sales of culture media and buffers in bioprocessing are for dehydrated powders that require end users to hydrate and mix with highly purified water. Media and buffer powders have historically been used in large-scale bioprocessing. Powders have long been a core bioprocessing chore and have rarely been critically examined until recently.

There is room for greater scrutiny of traditional in-house media/buffer preparation from powders, and signs point to facilities beginning to assess their media-and-buffer preparation costs and options. With that in mind, BioPlan, in collaboration with end users, has developed a cost-analysis model to assess the value of in-house vs. external media and buffer prep.

ALTERNATIVES TO POWDER MEDIA AND BUFFERS

Outsourcing to local "hydration centers" that prepare finished liquids from manufacturer-provided powders offers just-in-time, local delivery of GMP materials. These facilities would form a regional consortium of customers that reserve capacity in an off-site facility. Primary users would include companies manufacturing at commercial scales, including single-use and hybrid facilities, biosimilars manufacturers, and even manufacturers in emerging countries that require GMP process fluids.

The purchase of liquid media and buffers can potentially free up capital, capacity, inventory, and staff overhead:

- Facilities Implications: Today's bioprocessing facilities include up to 20 percent of space and operational costs going to culture media and buffer prep from powders. In-house powder hydration requires utilities, dedicated staff, inventory, QA, GMP storage space, prep rooms, holding tanks, WFI (water for injection) operations, mixing equipment, and bulk liquids cooling or heating.
- Variability in Media and Buffer Prep: Differences between bulk liquid media and buffers prepared by suppliers vs. end users are not generally tested. Anecdotal data suggests that freshly

16:25
GMT

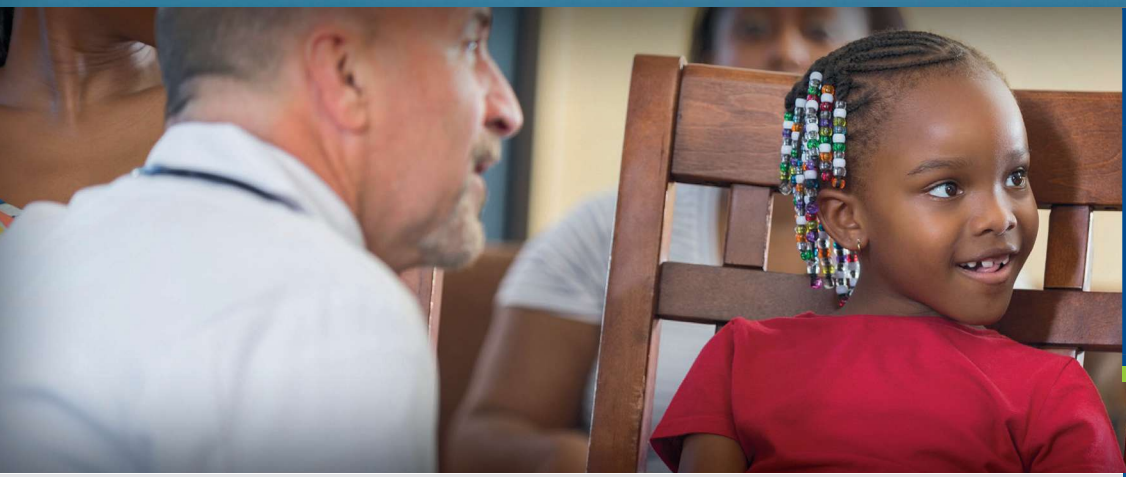
O'Hare International
Airport, Chicago USA
Ambient Temp. -15°C

Product Temp.
5°C

21:00
GMT

Caribbean Sea,
Altitude 36,000ft
Ambient Temp. -60°C

Product Temp.
5°C



14:20
GMT (+ 1 day)

Family Health Program
(PSF), São Paulo, Brazil
Ambient Temp. 21°C

Product Temp.
5°C

One World. One Cold Chain. One Expert.

CSafe
One world. One cold chain. One expert.

From our beginning 25 years ago, CSafe has grown to be a global force in temperature-sensitive bio-pharmaceutical transportation. We passionately believe that each and every shipment should arrive uncompromised and at The Right Temperature®. Our products help to successfully deliver temperature-sensitive bio-pharmaceuticals around the globe providing the Peace of Mind® you require. We are proud to be a leader and of our record for safety, innovation, design and reliability. We are committed to working to provide you the best passive, active and hand-held temperature-sensitive transportation solutions.

Call us and let's see how we can help you.

Discover how we are assisting clients achieve results at:
www.csafeglobal.com/whitepapers

To find out more, visit:
www.CSafeGlobal.com
or call: +1 937 245 6350

CSafe AcuTemp

delivered, expert facility-prepared liquid media may provide more productive and consistent bioprocessing. End users often use nonspecialized, less-than-optimal equipment in preparing powders.

- Costs Implications: Outsourcing of bioprocessing liquids can provide cost savings and flexibility for some facilities. Although existing facilities have invested in equipment, protocols, and staff, some are not designed to handle large volumes of bulk liquids, and few culture media and buffer suppliers promote bulk liquids over powders. Outsourcing liquid preparation can reduce a company's risk and provide more efficient testing and comprehensive cGMP documentation, warehousing, inventory, and management.
- Safety Implications: Culture media and buffers are one of the last key parts of bioprocessing that are not expected to be, or treated as, sterile. Powder ingredients are ground into powders, packaged, and handled in nonsterile environments. Culture media-associated virus contamination is capable of damaging companies. Consider Genzyme, which experienced facilitywide culture media feed-linked animal virus contamination.
- Improvements in Technology Creating New Expectations for Safety: Many large biopharmaceutical companies are implementing technologies like high-temperature, short-time (HTST) UV light and other culture media sterilization methods. Once large facilities implement HTST or other sterilization, the rest of the industry will be expected to follow.

REGIONAL BULK MEDIA AND BUFFER PREP

In our recent study of demand for local outsourced services, we evaluated media or buffer prep facilities. We asked which attributes would need to be offered, and cost-effectiveness topped the list at 38.7 percent. Nearly as many (35.5 percent) indicated quick turnaround, on-time/just-in-time delivery.

We then asked which critical attributes a media and buffer prep hydration facility must possess to be considered an outsourced supplier. Effective outsourcing will require a highly competent, service- and logistics-driven organization capable of addressing documentation, regulatory, and analytical challenges in a GMP environment.

ECONOMICS POINT TO OUTSOURCED SERVICE

To support the economic analysis and potential for outsourced media and buffer prep, BioPlan established an advisory board of experts in cGMP documentation and quality management, modular facility design, inventory/logistics, services management, client services and logistics, media and buffer reagent manufacturing, and single-use operations. The board defined cost-effective approaches to ensure high-quality, documented, just-in-time delivery of liquid media and buffers. This group has initiated a core facilities network analysis to service key biopharmaceutical manufacturing centers. The design includes a core-facility approach:

- facilities located within 20 miles of biofacility concentrations
- modular, flexible design to produce culture media and buffer powders
- either stainless or single-use equipment, sized to the largest required scales
- parallel/shared utilities, WFI, warehousing, storage, IT systems
- clients reserve capacity and order just-in-time (as needed) local preparation and delivery of bulk culture media and buffers
- operated by experienced dedicated managers, includes expertise from each media supplier, oversight from regional end users
- warehouse core facility, expandable to meet changing needs
- materials and methods fully documented and auditable
- end-user access to inventory systems for real-time data on liquids manufacturing
- logistics include just-in-time delivery and integrated LIMS (lab information management system) and IT systems
- full supply chain information and quality control testing
- regional facilities identical in design and documentation for consistency and efficiency
- cloned facilities enable the "same" fluids preparation at any facility to provide redundant backup manufacturing options
- core facility network to enroll established local CMOs, outside the U.S. to support global production.

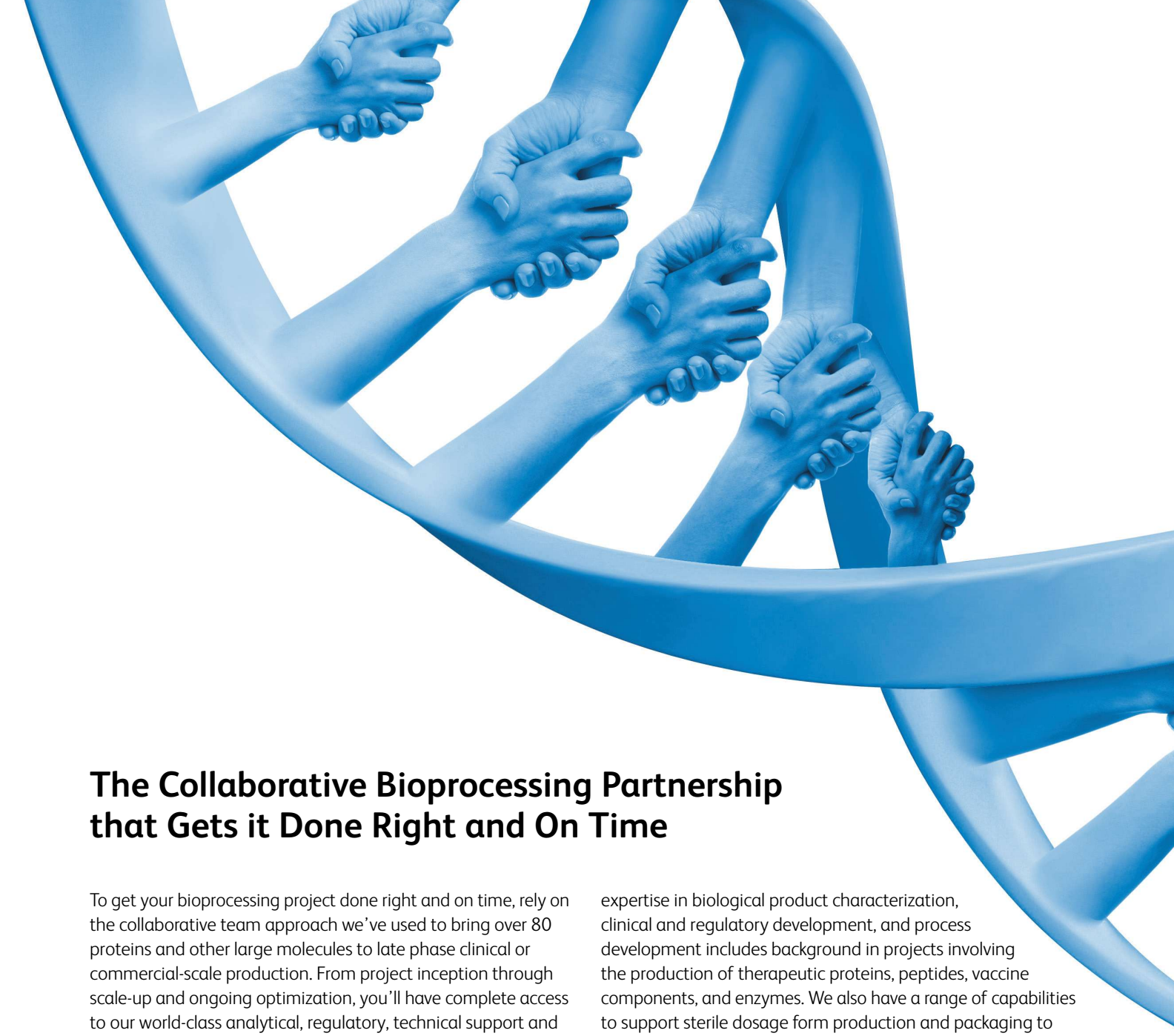
Regional hydration centers are just one example of economics-based outsourcing. When a service supplier can provide better products more quickly and with better control, then even core operations become viable outsourcing candidates. L

FIGURE 1 Selected "Very Important" Attributes in a Media/Buffer Prep Facility

Documentation & cGMP compliance standards / regulatory filing experience	74.2%
Analytical lab to support release and characterization testing	38.7%
Investigation support for full-scale manufacturing challenges	38.7%
Local, freshly prepared liquid culture media/buffers	32.3%

Source: June 2014 research by BioPlan Associates Inc.

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



The Collaborative Bioprocessing Partnership that Gets it Done Right and On Time

To get your bioprocessing project done right and on time, rely on the collaborative team approach we've used to bring over 80 proteins and other large molecules to late phase clinical or commercial-scale production. From project inception through scale-up and ongoing optimization, you'll have complete access to our world-class analytical, regulatory, technical support and production expertise – and the confidence that your project is managed with seamless efficiency by a dedicated team of experts, fully committed to your success. This allows us to offer more flexible solutions to your manufacturing challenges, and in accelerated timeframes.

No one brings more large-scale protein production experience to your project. We are fully conversant in microbial, mammalian cell, and other bioprocessing platforms. Our world-class expertise in biological product characterization, clinical and regulatory development, and process development includes background in projects involving the production of therapeutic proteins, peptides, vaccine components, and enzymes. We also have a range of capabilities to support sterile dosage form production and packaging to meet selected customer needs.

Get an initial project assessment within a week
Take advantage of the Pfizer CentreSource rapid assessment process to gauge your project's feasibility. We'll provide an initial assessment within five business days.

The Americas: +1.269.833.5844 Europe/Middle East/Africa: +32.2.714.6502 Asia Pacific: +65.6419.0248
centresource.info@pfizer.com www.pfizercentresource.com

Pfizer PfizerCentreSource

HOW DAIICHI SANKYO IS VENTURING INTO THE UNFAMILIAR TERRAIN OF ONCOLOGY R&D

ROB WRIGHT Chief Editor

Prior to 2011, Daiichi Sankyo, the second-largest pharmaceutical company in Japan, had very little oncology drug development experience, unless you include the 1977 launch of the anticancer drug, Krestin. Instead, the company, which is more than 100 years old, is probably best known for its expertise in cardiovascular (CV) disease, thanks in large part to the blockbuster success of Benicar (olmesartan medoxomil) — an angiotensin II receptor antagonist that generates approximately $2.5 billion in annual sales globally. Yet as of May 2014, the Daiichi Sankyo oncology pipeline consisted of 15 active clinical projects (nine in Phase 1, three in Phase 2, three in Phase 3), and one under application in Japan. As a point of comparison, in July 2014, Pfizer had 14 oncology compounds in development. If you are like me, you are probably wondering how a century-old global drug company known for valuing harmony and consensus (two of innovation's biggest roadblocks), and with essentially zero experience in creating cancer therapies, becomes one of the most innovative oncology companies in the world — in just under three years.

GLENN GORMLEY, M.D., PH.D., Senior Executive Officer and Global Head of R&D at Daiichi Sankyo Co., Ltd.

"One of the ways is that you find people who have been successful, and you let them continue to be successful, and you learn from it," says Senior Executive Officer and Global Head of R&D at Daiichi Sankyo Co., Ltd. Glenn Gormley, M.D., Ph.D. Indeed, this strategy seems overly simplistic. But Gormley, who also holds the position of chairman of the board, executive chairman and president of Daiichi Sankyo, Inc, the company's U.S. subsidiary, knows most strategies don't fail because they are too simple. Strategies fail because they are made overly complex in their tactical execution. Leonardo da Vinci said, "Simplicity is the ultimate sophistication." Gormley explains how Daiichi Sankyo is venturing into the unfamiliar territory of oncology R&D and building its cancer compound pipeline through partnerships and acquisitions, all while (and this may surprise you) shunning the notion of harmonizing the drug discovery process to the Daiichi Sankyo way of doing things.

> "For now, I'm very happy to work with smaller companies with expertise in developing biomarkers and companion diagnostics."

GLENN GORMLEY, M.D., Ph.D.,
Senior Executive Officer and Global Head of R&D at Daiichi Sankyo Co., Ltd.

GET ALIGNED INTERNALLY WHEN ENTERING UNFAMILIAR TERRAIN

When Gormley joined Daiichi Sankyo, the company already had begun delving into oncology R&D. For example, in November 2008, the company formed a strategic partnership with ArQule (NASDAQ: ARQL), a company engaged in R&D of next-generation small molecule cancer therapeutics. Two years earlier, the company acquired U3 Pharma AG, a German biotech focused on researching antibodies for the treatment of cancer. But someone like Gormley, called to cultivating therapies for cancer (see sidebar), knew Daiichi Sankyo's successful entry into oncology R&D required more than a couple of strategic moves. It necessitated getting directionally aligned on some key principles internally. "We had to be comfortable with *risk taking* in a field where there's a high level of uncertainty," he says. "Having a willingness to take risks is an important element of being successful in oncology." Additionally, because the company was in competition with some very experienced players, the organization had to also be able to make *quick* decisions. "In oncology you often don't know as much about the biochemistry or the biology as you might in cardiovascular disease," he explains. "You need to be able to move on innovation when it's discovered." Gormley believes that to make quick decisions internally requires a *simple* assessment system, such as Daiichi Sankyo's GEMRAD (global executive meeting of research and development). The GEMRAD committee serves as the supreme decision-making board for R&D. "All project teams report directly to this committee for either approval or challenge," he states. This makes the decision process very streamlined.

Another key area of alignment for Daiichi Sankyo was how best to couple the company's interest in building oncology into a major area of therapeutic expertise with a planned commitment to expand its biologics capabilities. "We had a lot of success historically in small molecules," Gormley explains. "But moving into biologics meant antibodies, many different kinds of biologics, companion diagnostics, biomarker discovery, and biosimilars." Unlike small molecule drugs, which are chemically based entities designed to treat the masses (e.g., Benicar), large molecule biologics often are more personalized to individual patients. Thus, when it comes to discovering and developing a biologic, it can be equally important to focus on developing a companion diagnostic (assuming one does not already exist) to determine if the patient is an appropriate candidate for treatment. Companion diagnostics play an important role in nonbiologics as well. For example, FDA approval (Aug. 17, 2011) of the oncology drug ZELBORAF (vemurafenib), indicated for the treatment of patients with $BRAF^{V600E}$* mutation-positive inoperable or metastatic melanoma, required the simultaneous approval of the cobas 4800 BRAF mutation test to serve as a companion diagnostic to determine a patient's eligibility for ZELBORAF treatment. ZELBORAF was discovered by Plexxikon (to be discussed later), a company acquired by Daiichi Sankyo. The cobas 4800 BRAF mutation test was developed by Roche Molecular Systems. The simultaneous approval of the drug and the diagnostic required a very coordinated effort. According to Gormley, if Daiichi Sankyo wanted to be successful in developing oncology as a key therapeutic area of expertise, it required a simplified structure to similarly coordinate its biologic R&D development efforts. In March 2013, the company announced a major organizational restructuring, including R&D. Within the R&D division, Daiichi Sankyo created the Biologics Oversight Function, which is charged with integrating *all* of the company's globally dispersed (i.e., Germany, India, Japan, and the United States) biopharmaceutical functions. Under the Biologics Oversight Function,

* **BRAF**, officially named "B-Raf proto-oncogene, serine/threonine kinase," is the gene that provides instructions for making a protein that helps transmit chemical signals from outside the cell into the nucleus. BRAF belongs to a class of genes known as oncogenes. When oncogenes become mutated, they have the potential to cause normal cells to become cancerous.

PHARMA EXPO™

Processing & Packaging Conference and Tradeshow

JOINT VENTURE

PMMI ISPE

November 2–5, 2014 • Chicago, Illinois USA

Smart Solutions for Lifecycle Innovation

At Pharma EXPO, meet solutions providers who understand the importance of controlling the integrity of your product throughout its lifecycle. Discuss your challenges with experts who know how the industry's systems work. Take away smart approaches to production so you can meet your goals for yield, performance, safety and security—from start to finish.

Register today at pharmaexpo.com

Co-located with:

PACK EXPO® ADVANCING PROCESSING AND PACKAGING

Daiichi Sankyo created two new laboratories — the Biologics Pharmacology Research Laboratories (drug discovery) and the New Modality Research Laboratories (technologies formulation). Gormley believes by aligning the two labs under one oversight unit, the company will benefit from having a highly coordinated biologic R&D effort — even if a biomarker or diagnostic requires an outsourced or partnership model. "It takes a lot of resources to develop both the drug and the diagnostic internally," he says. "For now, I'm very happy to work with smaller companies with expertise in developing biomarkers and companion diagnostics."

As you can see, the process of gaining alignment is not something done all at once, but is more of an evolution. To drive alignment within Daiichi Sankyo, Gormley utilized the company's core principles of integrity, innovation, and accountability. "We use these three principles to focus our efforts on putting the patient first, finding ways to make a difference, to test our decision making internally, and then do the same thing with our external partners," he states. Though Gormley believes you can easily establish these three guiding, core principles across any culture, when working with external partners there are other keys necessary if you want to realize the full potential of strategic partnerships.

EMPOWER PARTNERS TO FULLY REALIZE THEIR POTENTIAL

The saying, "Two heads are better than one," may explain why many companies enter into partnerships. However, the unfortunate reality is that most business partnerships don't live up to their full potential. Often compared to a marriage (50 percent of which end in divorce), estimates place business partnership failures at a whopping 80 percent. I asked Gormley how he goes about selecting organizations with which to partner. "I don't think of it as a selection process," he clarifies. "It is a mutual interest that creates successful relationships." According to Gormley, when Daiichi Sankyo approaches a partnership the conversation begins with asking, "What

The Creation Of Venture Science Laboratories

"I BELIEVE THERE IS A PERCEPTION IN THE PHARMACEUTICAL INDUSTRY that it takes a biotech mindset to drive innovation, and such a mindset can't be found in Big Pharma. I wanted to challenge that perception." That's how Glenn Gormley, M.D., Ph.D., explained why he spearheaded Daiichi Sankyo's formation of the Venture Science Laboratories (VSL). The concept was to establish an organization resembling a small biotech, within the walls of a Big Pharma, in order to create a more innovative culture at the company's research organization. In forming VSL, Gormley, senior executive officer and global head of R&D at Daiichi Sankyo, says he intentionally resisted the idea that to be successful VSL needed to be isolated from the broader R&D culture. "I want the biotech culture of VSL to coexist with our broader R&D culture so they can learn from each other," he shares. "If you create the right culture within VSL, people will naturally think and do things differently, while working in the same labs as their non-VSL colleagues." As a result, the VSL culture is evident everywhere Daiichi Sankyo has an R&D facility.

The process of building VSL began with Gormley hand-selecting the two people he believed would be critical to its success — its leader and its head of business development. In choosing these leaders, he looked for openness, entrepreneurial spirit, and the ability and willingness to think differently. To fill the VSL leadership position, Gormley selected Takashi Fukuoka, DVM, Ph.D., a 27-year research veteran with a wealth of R&D change-initiative experience. Fukuoka also had held a number of positions with global responsibilities, such as working with the company's Reinvent Drug Discovery Program (RDP), GEMRAD, and the Change Excellence Team. "The number two person is the head of business development and licensing [BD&L], Go Saito, Ph.D.," Gormley explains. "I wanted VSL to have its own BD&L function and for it to be in a single person." Saito, who worked directly on initiatives with the likes of Coherus (a biosimilar company), Eli Lilly, Kai Pharmaceuticals, and NGM (a biotechnology company), brought significant external collaboration experience to the position. Because Gormley wanted the leaders to own the success of VSL, he let Fukuoka select his own group. Established in April 2013, VSL consists of 28 people.

Once the VSL team was assembled, they were given very few directions. "I gave them a blank slate and said, 'Your goal is to develop innovative, first-in-class medicines.' But there was one condition: Everything had to be done in partnership with an academic organization, although it could be government research if it made sense," he stipulated. When Gormley gave the team its small start-up budget, he reminded them they would need to demonstrate their value to the organization. "There would be no entitlements," he stated. "Bring us new, innovative ways to work on projects. If you can demonstrate value, you will get the funding you need." According to Gormley, demonstrating value eventually involves VSL giving a presentation to Daiichi Sankyo senior leadership. "They [VSL] need to convince us that what they are doing is worth funding," he shares. A recent example of an approved VSL project proposal, announced this past April, is a drug discovery collaboration with the UC San Francisco (UCSF) Institute for Neurodegenerative Diseases. UCSF focuses on developing novel therapeutics and molecular diagnostics for multiple neurodegenerative diseases, such as Alzheimer's, Parkinson's, Creutzfeldt-Jakob disease, and frontal-temporal dementia.

When creating this kind of company-within-a-company, Gormley says to expect people to be skeptical and challenge you. "We knew that one of our challenges would be to isolate this group so it could maintain its unique culture," he states. "But we also knew that people would be questioning whether we even needed such an approach." Here are Gormley's tips on how to create your own version of VSL:

- Choose the right leaders, and then let them own the success.
- Take a small group, and embed them in the organization.
- Give them a small budget.
- Ask them to demonstrate the value of what they want to do rather than guarantee funding.
- Require them to partner on every project.
- Stay out of their way, and see what they can do.

ONCE UPON A RIGHT-ON-TIME...

EVERYONE LOVES A GOOD STORY.

World Courier's customers have amazing tales of how we've moved their time- and temperature-sensitive products around the globe — sometimes at a moment's notice.

For example, one client advised us late one evening that it needed to transport a large volume of temperature-sensitive, clinical trial product from Finland to Israel for reformulation. During logistics planning, it became clear that any mistake in handling or moving the product would disrupt the clinical trial.

The problem-solving mindset and global presence of World Courier staff resulted in delivery within 48 hours, with no temperature excursions.

Stories like these show why more pharmaceutical companies rely on us than any other specialty logistics provider in the world.

Follow Us

For more market insights, visit, visit www.worldcourier.com.

Follow us on Twitter: @Worldcourier

WORLD COURIER
An AmerisourceBergen Company

do you need from us? What would we bring to you that would make a successful partnership?" To be successful and equal partners, Gormley ascribes to using a straightforward approach, striving for a win-win relationship. Gormley acquired this partnership philosophy while in his role as the CEO of a small biotech company, Gemin X. "I learned a lot about being on the other side of a partnership," he says. "I know the benefits achieved in creating a relationship where the potential partner is going to gain as much as we are at Daiichi Sankyo. I'm more attracted to win-win scenarios and less so to relationships that look to be very one-sided."

To determine how best to find and create these win-win scenarios, Gormley brought the senior R&D leadership team together. "We talked about what characteristics would lead to success in oncology. One of those, as mentioned previously, was our becoming more comfortable with uncertainty," he shares. The group concluded that just as being able to make *quick* decisions internally proved beneficial, this same principle would be advantageous for Daiichi Sankyo's external partners. "Our approach is to provide our partners with a high level of independence so they too can make quick decisions," Gormley states. "Let's identify successful organizations and let them continue to be successful. As long as they can demonstrate that level of continued innovation, why would we want to change it?"

Daiichi Sankyo has a number of business collaborations (e.g., Amgen and ArQule), as well as academic partnerships, such as the recently announced three-year alliance with Sanford-Burnham Medical Research Institute. To find these collaborative opportunities, the company utilizes initiatives such as the Venture Science Laboratories (see sidebar — *The Creation Of Venture Science Laboratories*) and the External Scientific Affairs (ESA) team — a group of scientists, Ph.D.s, and M.D.s charged with contacting academic and biotech organizations. "The ESA team works independently of me, making their own decisions on who to contact, as they know our interests and where we want to focus," he states. "I tend to get involved personally at a later stage once the group has determined both mutual interest and mutual benefit."

If you asked Gormley what he looks for when he gets involved in the partnership process, he would tell you *flexibility.* In addition, he would also tell you he seeks organizations where he can empower as many people as possible to think independently, even in the case of Daiichi Sankyo company acquisitions.

FOSTERING A DIFFERENT KIND OF PARTNERSHIP

In April 2011, Daiichi Sankyo acquired Plexxikon, a small Berkeley, CA-based biotech that had experience in oncology drug discovery and early development with its novel compound, ZELBORAF, that gained FDA approval just five years after the initiation of the first clinical trial. Gormley admits it was ZELBORAF which served as the initial attraction to Plexxikon. But as Daiichi Sankyo learned more about the organization, Plexxikon's targeted approach to oncology drug development became the real appeal. "We felt they [Plexxikon] would fit in well with our approach of developing companion diagnostics in biologics," Gormley recalls.

When it came time to execute the Plexxikon acquisition, Gormley decided to apply some of the lessons he learned at Gemin X, namely, he provided Plexxikon with a high degree of independence. He based this decision on the simple fact that the company had managed to maintain a high level of innovation discovery and success (i.e., ZELBORAF) with a staff of only 43! "If you want a different outcome, you need to foster a different kind of relationship," he states. "Plexxikon didn't approach discovery the way we might in our labs. That's great. We don't try to harmonize those approaches, but seek to take advantage of our differences." Further, the Plexxikon executive team was given a high degree of autonomy to run the company as they saw fit. Gormley feels some other best business practices from the Plexxikon acquisition include keeping the entire leadership team intact, making no attempt to change the size of the company, and not moving the Daiichi Sankyo organization into Plexxikon. Unless folks at Plexxikon want help or support, Gormley says they are allowed to establish their own annual objectives and timelines. "We give Plexxikon a defined budget for the year and let them choose how to allocate it to discovery and development, as well as what discovery areas they want to pursue. They have a tremendous amount of flexibility to decide the direction of the company."

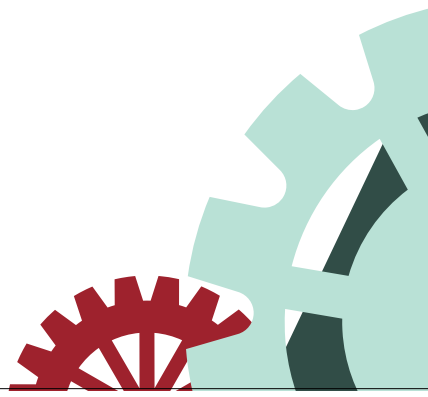
He admits that providing this high degree of autonomy is a continual learning process, but he believes the benefits far outweigh the challenges. "Where's the next area of breakthrough science or innovation going to come from?" he asks. "We don't all have the same answers to that question. It depends on one's background, experience, and contacts. If we want a better product, providing a better patient outcome, we need to encourage people to challenge each other in a very respectful way, so we can capture the benefits of diversity of thought." L

COMBINATION CANCER IMMUNOTHERAPY — A VIRTUAL ROUNDTABLE

A SERIES ON THE CHALLENGES AND OPPORTUNITIES OF USING NEW AGENTS TO RALLY THE IMMUNE SYSTEM AGAINST CANCER

WAYNE KOBERSTEIN, Executive Editor
LLEW KELTNER, M.D., Ph.D., Roundtable Moderator

Targets, targeting, targeted — these words get plenty of use in the biopharma industry as the field of drug discovery and development becomes more and more mechanistic. Drug targets usually consist of receptors on the surface of microbes or tissue cells, including cancerous cells, where certain compounds may bind and interfere with their growth or disease-causing activity. All such attempts to block tumor growth, however, have met with two main obstacles: tumor heterogeneity and what appears to be evolutionary ingenuity in adapting and developing resistance to drug treatment. From the earliest chemotherapy agent to present-day molecular-pathway targeting drugs, none has defeated cancer's defenses by direct, frontline assault. All along we've needed an ally, and we've known what the ally should be — the human immune system.



PART ONE: Key Opinion Leaders Benchmark the Science

WE TREAT YOUR JOURNEY LIKE SOMEONE'S LIFE DEPENDS ON IT.

BECAUSE IT DOES.

At PAREXEL we understand it can be a difficult journey bringing your new drug to market, which is why we are driven to solve the complex. We believe it is in our DNA to take on the toughest challenges, hurdles and obstacles that may stand in the way of your product reaching the hands of those who need it the most. From helping to write effective regulatory strategies for the emerging science of biosimilars to creating the most intuitive suite of clinical trial technology available, we are constantly focused on what's next. We understand that when we solve for the problems of tomorrow, we can create a smoother path for your journey today.

To learn more about how we can help your journey, visit **Solutions.PAREXEL.com**

PAREXEL®

YOUR JOURNEY. OUR MISSION.™

INCEPTION TO LONG TERM

CHOOSE YOUR GUIDE WISELY.

AFTER ALL, THE JOURNEY TO MARKET IS OFTEN QUITE LONG.

As your new drug embarks on the long journey to market, having a dedicated partner can make all the difference. At PAREXEL we not only understand this, we pioneered strategic partnerships between biopharmaceutical companies and their service providers. From reductions in outsourcing costs to enabling access to new patients and markets, a strategic partnership with PAREXEL can help streamline processes and accelerate development cycles. The result is greater efficiencies across all phases of your product's development. Here's to a better journey.

To learn more about how we can help your journey, visit **LongTerm.PAREXEL.com**

PAREXEL®

YOUR JOURNEY. OUR MISSION.™

Drugs that target the immune system, not the tumor, may have entered the long war on cancer at last. Although some still dispute the validity of cancer immunotherapy, others are charging ahead. Results of large Phase 2 trials showing durable responses from a new class of drugs called checkpoint inhibitors, along with progress on the vaccine/immunostimulator front, have fired up supporters and attracted new interest from former doubters. (See sidebar, "Brakes Off, Gas Pedal Down.")

Our virtual roundtable, a compilation of responses to questions from key experts and players in the field, considers the ramifications of a growing consensus that using cancer immunotherapies in combination, rather than as single agents, will be essential to have maximal effect for patients. In a matter of years, many cancer immunotherapies will be available, many combinations will be possible, and the choice of combinations will be quite challenging from a clinical, regulatory, and reimbursement perspective. Biomarkers and companion diagnostics may also play a big role in guiding the way, as will a deepening understanding of immunotherapy mechanisms and cancer response. But who should decide how combinations are tailored and delivered to individual patients, and on what grounds should they base those decisions?

In addition to this opinion-leader roundtable, the next phase of the series, beginning with Part Three, will offer and compare the views of company executives now working to develop and commercialize cancer immunotherapies. How well does the leading science match up with the development and commercial models of such companies? How well are companies adapting to the combination paradigm, and how may they continue to do so as the field advances?

We gathered the KOL (key opinion leader) responses in two ways — one, by an exchange of written questions and answers; the other, by in-person interviews — so some participants will inevitably sound more formal or informal than others. Another caveat: KOLs often disagree not just on theory but on facts. And where there is factual disagreement, there is error. Someone has to be wrong. In fact, if we show nothing else about this field, we will certainly reveal how many issues still need to be settled.

PANELISTS

Our panel members are all leaders in cancer immunotherapy research, and most are overseeing major clinical trials in the field. Two members are especially noted below because they represent opposite, yet overlapping, opinions on the readiness of the new therapies for wide adoption by oncologists.


A


B


C


D


E


F


G


H


I


J

A Moderator, Llew Keltner, M.D., Ph.D.
President and CEO, Epistat

B Pam Sharma, M.D., Ph.D.
Scientific Director, Immunotherapy Platform and Professor, Departments of Genitourinary Medical Oncology and Immunology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

C James Allison, Ph.D.
Executive Director, Immunotherapy Platform and Chair, Immunology, The University of Texas MD Anderson Cancer Center
Dr. Allison pioneered the concept of "CTLA-4 blockade" and the first checkpoint inhibitor on the market, ipilimumab (Yervoy).

D Lawrence Fong, M.D.
Professor, Department of Medicine (Hematology/Oncology), UCSF

E Mario Sznol, M.D.
Professor of Medicine (Medical Oncology); Clinical Research Program Leader, Melanoma Program, Yale Cancer Center

F Alan Venook, M.D.
Professor, Department of Medicine (Hematology/Oncology), UCSF
Chair of the Scientific Program for ASCO 2015 and serving on national practice-standard-setting boards, Dr. Venook is both a leading skeptic and an investigator doing exploratory trials in immunotherapy for GI cancer.

G Tim F. Greten, M.D.
Head, Gastrointestinal Malignancy Section Investigator, Thoracic and Gastrointestinal Oncology Branch, Center for Cancer Research, National Cancer Institute

H Walter Urba, M.D., Ph.D.
Director, Providence Cancer Center

I Neil Berinstein, M.D.
Director, Translational Research, Ontario Institute for Cancer Research (OICR)

J Jedd Wolchok
Chief, Melanoma and Immunotherapeutics Service, Memorial Sloan-Kettering

Diabetics do it better

envirotainer.com

What if we only hired diabetics to work in the active cold chain? Would they take more care handling health-care products? We think they would. They know what happens if they don't get insulin.

Of course we don't just employ diabetics. But we do share their understanding of the value of what we ship in our containers.

We educate the members of the active cold-chain on the difference they make to the lives of diabetics and others who rely on healthcare products. Because people do a better job when they understand the importance of why they are doing it.

Anna Klettner is one of those people. She is a diabetic and she works for us.

Envirotainer®

The Active Cold Chain

QUESTION: Cancer has shown an amazing ability to frustrate molecular-targeted therapies through mutation and adaptation. Why will cancer immunotherapy not be subject to the same ability of cancer to defeat interventions — in this case, to find a way around the therapy-induced immune responses in unpredicted ways?

KELTNER (Moderator): Most of our panelists see immunotherapy as a durable new paradigm for cancer treatment, though probably not one without surprises and setbacks during a period of experience and learning, not just about therapeutic results, but also about the mechanisms. The first two panelists to speak represent opposite poles of opinion, though both are dedicated researchers in the field.

ALLISON: A paradigm shift has begun, where you no longer focus so much on targeting specific mutations in the tumor, but you focus more on unleashing the immune system to attack the cancer. That's the new biology that has to be taken into account. You can't just look at the oncogenes and the "driver" mutations in tumor cells. In fact, those may be less relevant, and it may be more important to engage the immune system to recognize the hundreds of mutations that are inherent in all cancer cells, including driver and passenger mutations. What we need companies to do — as we are trying to do with the immunotherapy platform at MD Anderson — is to look beyond results with targeted therapies and chemotherapies. Just hitting the clinical endpoints with those agents is sufficient to move ahead, but we need to understand the salient molecular basis for the responses that are durable, as we have seen with immunotherapy, so we can begin to figure out the rational combinations and discover new targets. Unless the basic science keeps moving forward, the whole field will just stall out. In combining therapies, everyone wants a clear recipe — one from column A, one from column B — but to get there we need a better understanding.

VENOOK: The main issue is that cancer immunotherapy has just recently been shown to work. It is true that there appears to be efficacy in melanoma and prostate cancer, but at great expense and really in narrow areas. I am all for developing immunotherapy, but it is just fascinating to me that people think it is an amazing sea change and works in all the ways it is being applied. It's hype beyond hype. Acknowledging there is now some proof of concept, I am much

more optimistic than I might have been before. I hope it does work, but the problem will be knowing that the immune cells you affect have the capacity to do what you want them to do, that they are not already affected by the presence of cancer, chemotherapy, growth factors, or something else. None of the studies in my area of GI oncology have been positive, so far at least, so I remain skeptical.

SZNOL: What's already been published on checkpoint inhibitors is very significant and very good. I have a hard time believing the kinds of responses we're seeing in the clinic will just go away. It is reasonable for Dr. Venook to be a skeptic because he is a GI oncologist and we have not made many inroads against GI malignancies yet. But we have generated enough data and treated enough patients to know what kind of activity to expect. No, we haven't cured cancer. We have made new inroads, but not solved the problem yet. All the excitement here is related to two targets: CTLA-4, and PD-1/PD-L1. There are many other targets, so it is amazing how much success we have had with just those two. When we have other agents and start doing combinations, if even 20 percent of them work, it will still be amazing. Some patients are already deriving enormous benefit they would not have had with any other kind of therapy.

With anti-PD-1, for example, we are seeing activity across a half-dozen different malignancies, and in patients who are not responsive to other treatments. It is appropriate to be excited, not just about what anti-PD-1 or anti-CTLA-4 can do alone, but also the potential for manipulating the immune system in many different ways. We may incrementally improve outcome in many cancers. Some of the

> "The main issue is that cancer immunotherapy has just recently been shown to work."
>
> **ALAN VENOOK, M.D.**
> Professor, Department of Medicine (Hematology/Oncology), UCSF

responses we see now are amazing —not only does the disease go away, but we don't have to treat the patients anymore.

GRETEN: I'm not saying that Provenge or ipilimumab are the best therapeutics, but they have definitely changed many people's view of immunotherapy, and there are increasing results indicating that, indeed, patients may benefit. Obviously, we still mainly see the results in patients with melanoma, non-small-cell lung cancer, and prostate cancer. Alan Venook, like myself, is interested in GI cancers, where we have no clear results yet. It seems some mechanisms that work in non-small-cell lung cancer may not work in GI cancers. But I would also challenge anybody who does not believe in immunotherapy and wants us to focus more on toxic chemotherapy or targeted therapies — shouldn't we explore the new approaches? In GI cancer, there have been no significant advances in the past 10 years.

Obviously tumors can adapt; there's no question it is a potential danger. Years ago, people used peptide vaccines, aiming but mainly failing to induce a response against a very specific epitope. Yet a few patients actually responded to those treatments, and a retrospective analysis indicated the reason was not because they developed responses against the peptides used for the vaccination, but to other epitopes derived from the tumor antigens expressed in the tumors, indicating the treatment induced a wider immune response. If you have an immune response against marginal antigens on different epitopes, the tumor is less likely to develop escape mechanisms.

KELTNER: Some evidence now suggests the failure of early cancer vaccines was really due to the inability of administered antigens to elicit adequate CD8+ T cell antitumor responses, or to defective delivery of the antigens. For example, the data from simple raw peptide delivery of survivin compared to the recent (ASCO 2013 & 2014; AACR 2014) data on highly adjuvanted, depot delivery of the same survivin peptides is quite dramatic. (See sidebar, "Cancer Vaccines — A New Wave.")

URBA: Cancer immunotherapy is subject to some of the same frustrations faced by the use of molecular-targeted therapies. A close examination of tumors shows many mechanisms of escape from immune-mediated killing, for example, loss of tumor antigens or MHC-restricting elements. The major advantage of immunotherapy is this: like the tumor, it is adaptive. Over time the immune system can learn to recognize different antigens. The phenomenon of epitope spreading is an example of how the adaptive immune response could overcome the tumor's loss of an antigen to which it had been immunized. Another potential benefit of immune therapy is one can target a protein that is essential for the growth of the tumor, and if the tumor escapes by altering that key oncogenic protein, it is possible the tumor will be unable to maintain its malignant phenotype.

BRAKES OFF, GAS PEDAL DOWN

Cancer immunotherapies of various sorts have been around for a long time, but have never met the threshold of potency necessary to defeat the disease in most patients. In the past several years, however, four new approaches have excited — and some would say mesmerized — researchers: cell-based therapy, checkpoint blockade or inhibition, immunostimulation, and cancer vaccines, with the likely combination of more than one drug in one or more of these classes.

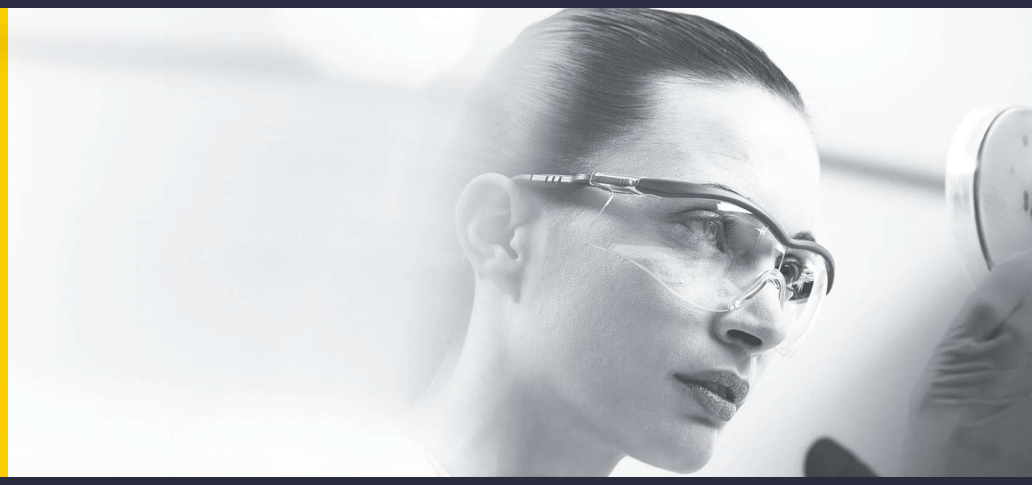
CELL-BASED IMMUNOTHERAPY. Exemplified by Dendreon's Provenge (Sipuleucel-T), this personalized form of immunotherapy involves removing immune and/or tumor cells from an individual patient's blood or tissue, transforming them through a biochemical process into specialized immune cells capable of an immune response to the patient's cancer, and injecting the transformed cells back into the patients. The approach is expensive and logistically challenging, but "industrialization" facilitated through central production sites may extend its practical application.

CHECKPOINT BLOCKADE/INHIBITION. In "taking the brakes off" the immune system, checkpoint inhibitors block certain receptors or "checkpoints" expressed on T cells and other immune cells that allow tumors to avoid immune system detection and attack. Tumors essentially suppress the immune system by hijacking immune cell antigens, the "points" in "checkpoints," of which about two dozen have been identified. The first approved "off-the shelf" immunotherapy, Yervoy (ipilimumab), is a checkpoint "blockade" that inhibits the CTLA-4 receptor (cytotoxic T-lymphocyte associated antigen 4) on T cells, allowing the cells to proliferate and attack the cancer. Other agents in development target the PD-1 (programmed cell death protein 1) checkpoint, unleashing T cells and natural killer (NK) cells to proliferate and destroy the tumor, and PD-LI, a protein secreted by the tumor cells to the PD-1 receptor on T cells and to T reg cells that support the suppression of the immune system by the tumor. More inhibitory agents are in development for many of the other checkpoints now identified — each with its own unique role in rallying all of the immune system's armamentarium against cancer.

IMMUNOSTIMULATION. Besides taking the brakes off the immune system, many researchers and companies are "stepping on the accelerator" by combining checkpoint blockade with agents that directly stimulate proliferation of T cells and other immune cells. Although the most-often discussed are agents like anti-OX40, which cause proliferation of activated CD4+ and CD8+ antitumor T cells, immunostimulators may also include chemotherapy, monoclonal antibodies such as Rituximab, and autologous stem cell transplantation. (See sidebar "Cancer Vaccines — A New Wave.")

Synchronized
OUTSOURCED SOLUTIONS

from Norwich Pharma Services



CONTRACT
DEVELOPMENT
CONTRACT
CLINICAL RESEARCH
CONTRACT
MANUFACTURING
FROM A SINGLE PROVIDER

Using Synchronized Outsourced Solutions from Norwich you can consolidate all of the services you need throughout your product's entire lifespan: from development and clinical research to commercialization and manufacturing. Norwich aligns each step of the process and seamlessly transitions your project throughout its lifecycle. And by consolidating services with a single provider, you'll have greater security, efficiency and consistency, which will get your product to market quicker and more cost-effectively.

Synchronize your next project » **norwichpharma.com**

Norwich
PHARMA SERVICES

6826 State Highway 12, Norwich, NY 13815

KELTNER: "Epitope spreading" may be a potential benefit of the use of correctly formulated and delivered cancer vaccines in combination with checkpoint inhibitors — as long as the target antigens are fundamentally necessary for cancer-cell survival or malignancy.

QUESTION: Why should cancer immunotherapies be used in combinations rather than as single agents? Is it possible to envision a single, effective immunotherapeutic agent?

KELTNER: Many more than two constituents will possibly be needed to fully engage the immune system. In fact, some agents that have a negligible effect when administered alone may actually be quite active in the presence of others. But the current celebratory blush over surprisingly dramatic and durable responses in Phase 2 trials has some KOLs hedging their bets about single agents versus combinations.

WOLCHOK: It is not really a one-size-fits-all paradigm. There are some patients who have had long-term benefit, in fact, complete remissions from single agents, ipilimumab, or an anti-PD-1 drug, so some patients may not need a combination. It is very hard to make conclusions prospectively at this point.

SZNOL: Of course, the immune system is very complex. It would be hard to believe that just a single target would cover all scenarios, but that being said, a single-agent PD-1, PD-L1, or anti-CTLA-4 blockade or even interleukin-2 can produce amazing, durable responses in a subset of patients. It would be ideal if we could identify people for whom either single-agent or combination therapy is needed; we're not that good yet. For the majority of patients, combinations would probably be better.

ALLISON: Because a single drug will only work in some patients, two or more is inherently better — but only if you understand how they work. If they have overlapping fundamental mechanisms, they are probably not going to combine well. The best combination I've seen so far is ipilimumab, which is an anti-CTLA-4, which enables co-stimulation, and anti-PD-1 such as nivolumab, which enables T cell receptor signaling. It seemed to us they would be at least additive, and it looks like they worked even better than that.

Some patients who did not respond to CTLA-4 blockade did respond to PD-1 blockade, and vice versa; thus, it makes sense to put them together. But whatever the response rate, the survival rates may be higher. Response was dose-dependent, so there may be another inhibitory factor. When we were doing studies with anti-CTLA-4 biomarkers, we found a population of immune cells, the ones that actually show the anti-tumor activity, expressing a molecule called ICOS. ICOS is a positive test for CTLA-4 (Ng Tang et al, "Increased frequency of ICOS+ CD4 T cells as a pharmacodynamic biomarker of anti-CTLA-4 therapy," Cancer Immunology Research, 2013); it is genetically in the same family with CD28 and CTLA-4. But when you block CTLA-4, the cells that express ICOS appear. If you give a signal to the ICOS molecule, it boosts the anti-CTLA-4 response. You can find new targets just by studying the mechanisms.

URBA: Not only do I believe that it is possible to envision a single, effective immunotherapeutic agent, but in fact, they currently exist. Rituximab, trastuzumab, ipilimumab, and anti-PD-1 are all examples. So are vaccines against hepatitis B and HPV. But, except for the prophylactic vaccines, none of these strategies are optimally effective by themselves, and that is why combination therapy will be required. Tumors from each patient, and even

CANCER VACCINES — A NEW WAVE

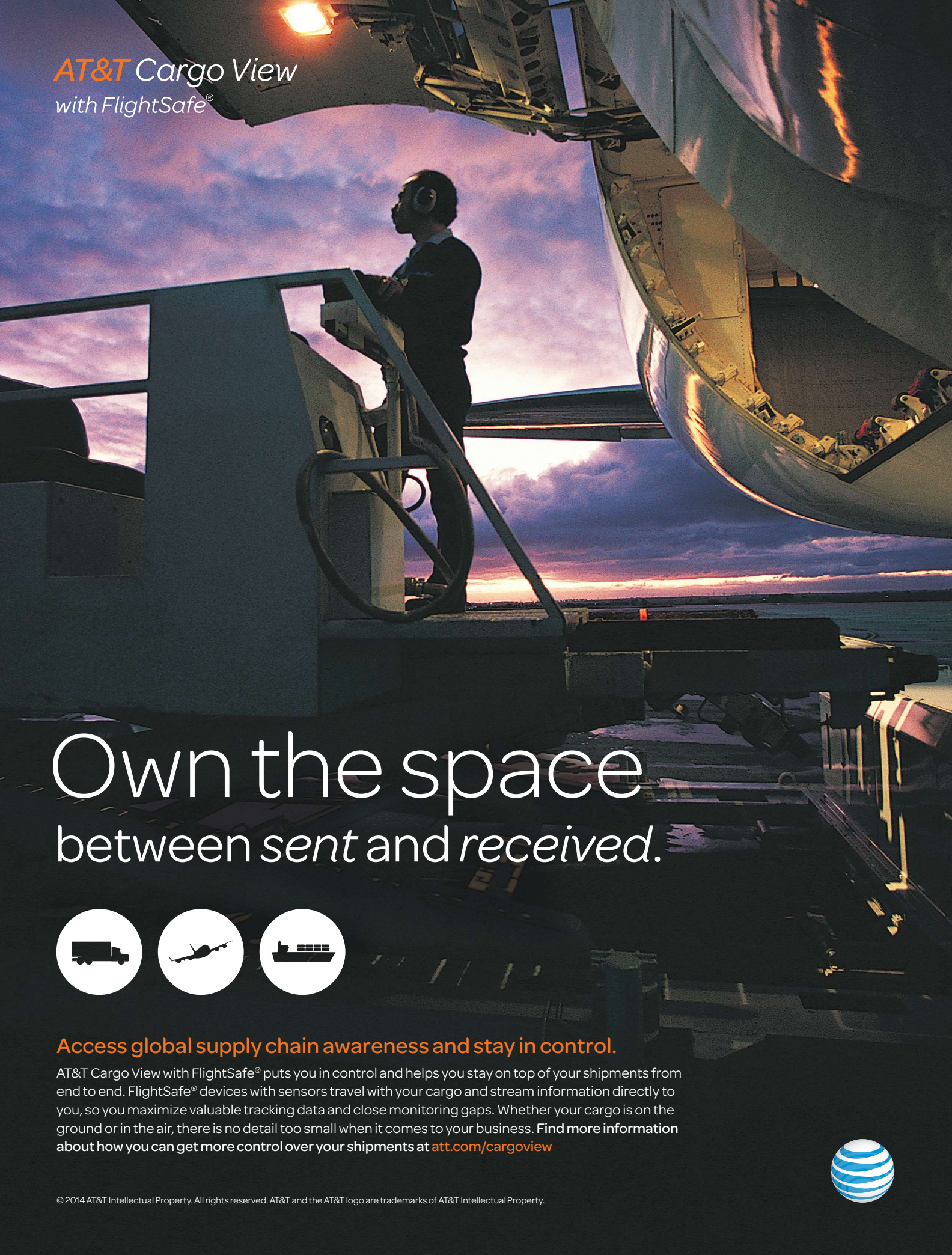
A creative approach to new cancer vaccines shows promise.

Where do cancer vaccines fit in the evolving paradigm for combination immunotherapy? The CAR-T (Chimeric Antigen Receptor Therapy) and autologous T cell technologies have shown that highly activated and targeted T cells can be home to tumors and provide a clinical benefit. The idea of activating T cells by using a vaccine technology is intuitive, particularly when combined with other immunotherapies that act on the tumor microenvironment and address its immune suppressive mechanisms, provided a meaningful T cell response is induced.

Not surprisingly, vaccines are generally believed to be ineffective; they only weakly activate T cells, and their use as monotherapies without addressing the immune-suppressive mechanisms has been an overwhelming weakness. But a new wave of rationally designed cancer vaccines has emerged, and the early data is intriguing.

The implementation of innovative technologies including viral vectors, DNA technologies, novel adjuvants, and formulations has demonstrated an ability to induce antigen-targeted T cell responses in cancer patients. Signals of clinical activity that conform with traditional endpoints in statistically modeled randomized studies, including response rate or disease progression evaluations, are emerging.

Going forward, the demonstration of a T cell-based mechanism of action in a meaningful number of cancer patients early in development will be an important gating event. Technological advancements in monitoring T cells will allow a sophisticated and rational evaluation of vaccines. A cancer vaccine may still be the underdog that enables highly effective combination immunotherapies.


AT&T Cargo View
with FlightSafe®
Own the space
between sent and received.
Access global supply chain awareness and stay in control.
AT&T Cargo View with FlightSafe® puts you in control and helps you stay on top of your shipments from end to end. FlightSafe® devices with sensors travel with your cargo and stream information directly to you, so you maximize valuable tracking data and close monitoring gaps. Whether your cargo is on the ground or in the air, there is no detail too small when it comes to your business. Find more information about how you can get more control over your shipments at att.com/cargoview
© 2014 AT&T Intellectual Property. All rights reserved. AT&T and the AT&T logo are trademarks of AT&T Intellectual Property.

> "I'm not saying that Provenge or ipilimumab are the best therapeutics, but they have definitely changed many peoples' view of immunotherapy."

TIM F. GRETEN M.D.
Head, Gastrointestinal Malignancy Section Investigator, Thoracic and Gastrointestinal Oncology Branch, Center for Cancer Research, National Cancer Institute

individual tumors within patients, have their own genetic composition. This leads to a unique repertoire of potential tumor rejection antigens and to individual evolutionary changes to adapt to the host's immune response. Add to this the heterogeneity of patients' immune responses, and you can immediately see the complexity of the tumor host response. There will be multiple problems to address from the presence of adequate numbers of antitumor T cells, the balance of checkpoint inhibitors, the presence of immunosuppressive cells and/or cytokines (perhaps produced by the tumors), and a host of other factors in the tumor microenvironment. This is likely not only to require combinations of immunotherapy, based on the biology of the patient's tumor, but also combinations with other therapies, including chemotherapy and radiotherapy.

GRETEN: Now is the time to evaluate possible combinations, because we are just about to get the first clinical data from the checkpoint agents tested alone, and a few combinations are being tested; this includes, for instance, checkpoint inhibitors with other enhancers of immune responses. But they are not being tested in combination with chemotherapy. My fear is, if you only combine checkpoint inhibitors with other immunotherapy agents, it may actually lead to premature negative data because there is insufficient immunological understanding behind it, including how the non-immune-based therapies affect immune responses. It is important to ensure the needed T cells are not depleted by the chemotherapy or any other agent combined with immunotherapy.

FONG: We have developed a method for cataloging the T cell repertoire, the T cells circulating within a patient. [Improved Survival with T Cell Clonotype Stability After Anti–CTLA-4 Treatment in Cancer Patients, Cha, et al., www.ScienceTranslationalMedicine.org, 28 May 2014, Vol 6 Issue 238, 238ra70.]. We use a next-generation sequencing approach to study the immune cells in the patient rather than looking for mutations in the cancer. That allows us to discriminate among the millions of T cells in a person's body — and see what happens to them when you give patients some of the checkpoint inhibitors. We found melanoma or prostate cancer patients who had improved survival after receiving anti-CTLA-4 antibody were maintaining a baseline of high-frequency T cells [i.e., the most common T cells, which may include "clonotypes" capable of recognizing tumors], whereas patients without survival gains had shuffled all their T cells around, replacing their initial high-frequency T cells with other T cells. Achieving prolonged survival seems to depend on whether there is a preexisting immune response. Some patients may lack this response, which is the context where it is important to use a combination therapy that helps them to generate these T cells.

KELTNER: Without major progress, immune-response detection may have little practical effect on the use of combinations versus treatment with a single agent. Patient segmentation is often murkier in practice than in theory. Most cancer patients' immune systems are compromised, so physicians will likely want to cover more than one base in any immunotherapeutic regimen — making combinations SOP. Yet immune-response testing will continue to grow in use and sophistication, if only to pursue the goal all of the panelists share: understanding immune and immunotherapeutic response in cancer at an ever-higher degree of resolution.

BERINSTEIN: Cancers have evolved very sophisticated biologic mechanisms to suppress effective immune eradication. Thus, successful cancer immunotherapy needs to incorporate a solid understanding of the different suppressive mechanisms in play for different cancers and different stages of cancer progression, as well as the potential antigen targets for immune rejection. It needs to utilize therapeutic platforms that can generate robust anti-tumor immune responses, which often require breaking immune tolerance to self-antigens. It also needs effective immune modulators that are safe and can inhibit the immune-suppressive environment of both the tumor and sometimes the patients themselves. These complex tasks are a tall order for a single agent. For this reason, it is likely that the most successful cancer immunotherapy will be a combination of two or more therapies that are very effective in doing their part, rather than a single, do-it-all treatment.

Plenty of competition exists among the growing variety of players to belong to the in-crowd of wide-use combinations. Our KOL panel wades more deeply into its discussion of therapeutic choices — by physicians, payers, and regulators — next month in Part Two of this series, Combination Cancer Immunotherapy — A Virtual Roundtable, Key Opinion Leaders Benchmark the Science. In the following month, Part Three will begin the next phase of the series, sharing the views and plans of company leaders in the combination cancer immunotherapy space. L

sartorius stedim biotech

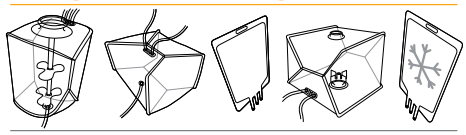
New Flexsafe Bag Family.

New PE Film. New Benchmark.

Cell Growth

Our new Flexsafe bags ensure an excellent and reproducible growth behavior with the most sensitive production cell lines. The optimization of the resin formulation, the complete control of our raw materials, the extrusion process and the bag assembly guarantee a consistent lot-to-lot cell growth performance.

ONE FILM FOR ALL



USP – DSP – F+F

Watch Videos:
www.sartorius-stedim.com/flexsafe

INDUSTRY PARTNERSHIPS WITH PATIENT FOUNDATIONS: THE BEST PRACTICES

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

WAYNE KOBERSTEIN Executive Editor

PART FOUR OF A FOUR-PART SERIES:

MANAGEMENT PARADIGMS

COMMITTEES, COMMITTEES.

It's in committee. Wound up in committee. Stuck in committee. Everyone has heard and repeated the pejoratives popularly attached to the committee model.

Forget those old saws. On a purely objective, scientific, and experiential basis, it turns out committees are the best way to manage organizations — certainly better than dictatorships, divine monarchies, and anarchies — but also simply the most effective way to get shared results out of a collaboration of disparate human beings. The committee is a basic paradigm of representation, resolution, and regard for the other's point of view.

In parts one, two, and three of this series we have drawn on the survey, "Successful Public-Private Partnerships," conducted by BayBio in collaboration with Merrill Datasite, BIO, and FasterCures. We have heard some of its key participants, or "voices," explore how life sciences companies and patient foundations can form partnerships around a common vision and goals, leverage their individual and shared resources, and create a formal agreement protecting both sides and the constituents they represent. When companies and foundations become allies, however, each side will likely have a very different style of operating than the other. That is why the fourth and final part of this series deals with the daily and long-term challenge of steering the partnership they have created in a coordinated and constructive way and thereby reaching the goals they have chosen together.

OLD MODEL TO NEW PARADIGM

For many life sciences companies, alliance management is a way of life. A standard model of partnering relations and operations exists, used mainly by large pharma companies but also by the wiser start-ups. Albeit with major exceptions, however, patient and disease foundations are not equally prepared for partnering, especially with for-profit entities, and young companies often mirror the lack. Thus, even though the "old" alliance-management model used widely by industry may be constructively applied to company/foundation partnerships, as the BayBio survey found, it takes on a new character and meaning in the process. For both sides, the model becomes a new paradigm for relationships between the quite different profit and nonprofit sectors.

Experience teaches best, especially in the creation of something new. As in the previous three parts of this series, this month, in Part Four, we hear from the voices of the BayBio survey — people who have founded, organized, run, and learned from such partnerships. Here they share their insights into the "best practices" emerging from their own and others' real-life experiences with alliances between and among life sciences companies and patient-disease foundations.

Establish a balanced, representative committee of people from both sides to manage the partnership's ongoing planning, operations, and progress toward set goals.

Part One of this series addressed how partners can establish a common vision and goals for their alliance, with an almost infinite variety of possibilities reflecting all the potential matches. But to progress from setting goals to reaching them, every partnership needs to organize itself in a practical, operational sense. Martha Brumfield heads the Critical Path Institute (C-Path) (http://www.lifescienceleader.com/doc/clinical-trial-upgrades-a-critical-path-to-innovative-consortia-0001), a nonprofit group that organizes, coordinates, and leads industry-government-NGO consortia in creating standard biomarkers and other tools to speed successful drug development. C-Path handles an extraordinarily diverse mix of partners in its consortia, maintaining a forum where they can all work together, not just in harmony, but to real effect.

MARTHA BRUMFIELD, President and CEO, the Critical Path Institute (C-Path): We don't form groups of people to sit around and brainstorm. Once we have a formal agreement on goals and milestones, we provide project management expertise that drives our collaborations forward. One thing we know about pharma companies — they don't want to make small talk for two years and see nothing happen, so we do our best to make sure we hit those milestones.

THOMAS P. SELLERS, Senior Director, Patient Advocacy and Corporate Philanthropy, Millennium: The Takeda Oncology Company: It is really important for both parties to be represent-

ed and have an equal voice, and sometimes that can be helped by some facilitation as well. Each party should select people for the steering committee who are well prepared to deal with the people on the other side. At the same time, the company people must understand that patients actually have something to contribute to the process.

The actual mix of people and functions needed for the steering committee varies according to the project. You might have a unique set of folks around the table for a patient-preference survey — a statistician, an epidemiologist, someone on the patient advocacy team, and maybe people from commercial or medical affairs. We have an approach we call Fit-for-Purpose — bringing together the right group of people who are fit for the purpose of the particular partnership or project. You have a core group, then you bring the people you need for that particular issue or decision.

Foundations now frequently match their company partners' expertise in adapting their own organizations to the collaboration.

TIM COETZEE, Chief Advocacy, Services, and Research Officer, National MS Society: What has changed is that our venture fund, Fast Forward, has recruited individuals with the expertise and competency in this area to understand how to run and manage a company's commercial research program. We've also bought IT tools to tackle the data to do professional due diligence as the venture capitalists do. We had to become more sophisticated about our finance function. We hold warrants in some of these companies, and as a nonprofit organization we never before had to worry about how to place a value on a biotechnology company. The changes have made us better because they've enhanced our capability to do more sophisticated research.

Ensure each side appoints a "point person" of equal rank with the point person on the other side, empowered as a project manager, facilitator, and committee liaison. BayBio's survey emphasized the importance of each side having a liaison and daily manager of the company/foundation partnership. On the company side, the point person would help executives "understand the issues from the patients' perspective" and be dedicated to knowing the foundation partner. Only people with special skills in management and communication need apply.

MICHAEL RICHMAN, President and CEO, Amplimmune: Most people in the point position do have special skills. We usually have an alliance manager in our relationships, and there is reciprocity on the other side; the foundation also has an expert who understands the science and the program. In reality, there are usually teams of people managing the alliance, because it requires a lot of expertise across the board.

SELLERS: Companies are hiring people who have been in roles in the advocacy organizations to work on patient advocacy and alliance development from within the company. And large companies have no corner on the market here. If anything, a small company may be more likely to attract someone from the nonprofit community because those people are accustomed to operating within small entrepreneurial environments.

Our partnership with the Multiple Myeloma Research Foundation and its Compass Initiative in building a thousand-patient database with tumor gene sequencing is driven by our translational research folks. But it also involves a relationship cultivated through our patient advocacy department. These partnerships generally work best when there is really a clear point of contact within the company working regularly with the patient advocacy groups across the board, shepherding the contacts among the various constituencies and stakeholders in both organizations.

Commit both sides to open, transparent, and frequent communications with each other – and with their constituents. Use the common meeting ground of the committee to integrate the cultural differences between the partners – and even turn them to advantage. Alliance management can be a powerful tool for cutting through and resolving wide differences in larger goals and priorities between the company and foundation partners.

GAIL MADERIS, President and CEO, BayBio: Make sure each side understands the other's goals. The more even in level of management the leaders are on both sides, the better. It is important to maintain open and honest communication channels, using appropriate program management tools and a meeting process. All of the mechanics are common, whether it is an industry/industry or industry/foundation collaboration. There are some key differences, however. Industry tends to shift its priorities based on dynamic factors such as competing projects in the pipeline, whereas disease foundations tend to hold constant. Even though there may be differences in the goals of the organizations at the highest level, the alliance management process can be very similar.

SELLERS: As a matter of course for each of our top partnerships, we have regularly scheduled monthly calls that cover the whole range of the relationship and its activities. We cover the programs and participation in them, especially around patient education. If a foundation wants to drive additional thinking around possible synergies between its R&D folks and ours, the issue can be raised on the call. The patient advocacy team will then transfer the request to the appropriate stakeholder in the company.

RICHMAN: Every group does partner meetings differently. Usually, there will be quarterly meetings or conference calls to update each other, and the schedule is built into the agreement corresponding to an annual report, semiannual report, and quarterly report. But sometimes they get so excited about the science and it's moving so fast, they will meet more frequently. Why wait for a quarterly meeting when you've got a great scientific update?

MADERIS: To some extent, these disease foundations can be more like the small, scrappy biotechs than pharma. Even though one is nonprofit and the other for-profit, their cultures and their drives are often very aligned. Some companies tell us disease foundations are so tremendously committed to the disease that it is actually easier to raise issues around the things that aren't working and to deal

THE POWER OF
COMPLEMENTARY CAPABILITIES

GLOBAL REACH | SECURITY OF SUPPLY | EFFICIENCY

Let's talk

KNOWLEDGE | EXPERIENCE | EXPERTISE

Call +1-224-212-2267 or +44 (0) 1926 835 554
or e-mail one2one@hospira.com

ONE2ONE™

PARENTERAL CONTRACT MANUFACTURING
SERVICE OF HOSPIRA

Hospira

Hospira, Inc., 275 North Field Drive, Lake Forest, IL 60045
P14-0381-3-8.25x10.875-Aug., 14

PLEASE VISIT US AT

Contract Pharma 2014 | iCSE/CPhI | PDA Universe of PFS | AAPS

with problems in an open way, because the foundations are less likely to give up. People said, "We had some really tough problems, and we were completely open about the issues. We worked together knowing our partner was 100 percent committed to solving whatever the problem was." The sense of urgency in disease foundations aligns very well with the sense of urgency the small biotechs have — every day matters; every product in their pipeline matters.

Plug into the growing community of industry/foundation collaborations – and keep learning best practices. Umbrella groups, consortia, and all kinds of hybrid partnerships involving the life sciences industry, patient/disease foundations, and many other players mean one-on-one alliances are no longer the only option.

SELLERS: There's an emerging body of patient opinion leaders who have weighed in on what the companies are doing, as well as what the regulators are doing, causing a shift toward patient-focused drug development that has really driven the creation and nurturing of these partnerships. Companies now consult with KOLs in designing a clinical trial, but you will start seeing companies consult with POLs (patient opinion leaders) in the same way and using some of the same mechanisms. There has been a recent acceleration in attention to patient-focused drug development. We have reached a tipping point around engagement with patients to find therapies faster and get them available to patients as soon as possible.

BRUMFIELD: In addition to enhancing collaboration within our consortia, we make sure we collaborate with other groups so we do not duplicate efforts. For our Predictive Safety Testing Consortium, we have a legal agreement with the Innovative Medicines Initiative's Safer and Faster Evidence-based Translation (SAFE-T) program in Europe, because it is doing something similar. We are now fully embedded in each other's work plan, sharing data, attending each other's regulatory meetings, and trying to help each other be successful. This is not about competition; in our minds it is about moving things forward.

SHARON HESTERLEE, VP, Research, Parent Project Muscular Dystrophy (PPMD): There is a novel group in Europe called Treat-NMD, originally formed with a 10-million-Euro grant from the EU to focus on drug development for neuromuscular disease. Its focus is infrastructure, and it has put together the group TACT, Treat-NMD Advisory Committee on Therapeutics, which reviews funding proposals. Now, we insist that all of our project requests undergo TACT review. TACT is a pool of expert reviewers that includes pharmacologists, statisticians, ethicists, regulatory specialists — a whole gamut of people with drug development experience — along with 50 ad hoc reviewers to consult as needed.

SELLERS: The other sort of mechanism that we use for driving these kinds of partnerships is a group that we convene one or two times a year called The Cancer Advocacy Council. It's by invitation only, and it's 15 to 20 of those POLs at the C-suite level in patient advocacy groups. About one-third of the groups are legacy relationships; one third, pan-tumor organizations such as the American Cancer Society and patient support groups such as Cancer Care; and one third, patient advocacy groups with whom we want to build a relationship before we have an immediate reason to engage with them. We convene them to work on a mutually interesting topic. One of the early meetings of the Cancer Advocacy Council was focused on how to get patient input into development of patient-reported outcomes or patient-preference surveys, and out of that we formed a collaboration between our epidemiology and outcomes research people with a patient group, as well as "patient ambassadors," who are speakers on behalf of Millennium, to develop and field a patient-preference survey for myeloma patients. No need for focus groups. We have a patient advocacy organization with ready-made access to patients.

HESTERLEE: Even in the small Duchenne space, we have some highly competitive players, but we are able to serve as a neutral territory. Our Duchenne Drug Development Roundtable has involved about a dozen companies in the discussion. We have talked about common issues, such as the potential for using a natural history control instead of a placebo arm. We have multiple rival companies talking about their strategies. That is an emerging paradigm: As a nonprofit group, if we do it right, with strong firewalls to prevent bias toward the companies we fund, we can be that neutral platform.

This ends our four-part series, "Industry Partnerships with Patient Foundations — The Best Practices." Many thanks to the BayBio team for its help with this series. (See BayBio's white paper on the survey at http://baybio.org/?s=public-private+partnerships.)

BIO BOOSTS PATIENT FOUNDATIONS

The avalanching advance of industry/foundation partnerships has not escaped the industry's largest association, the Biotechnology Industry Organization (BIO). At the 2014 International Convention, BIO provided foundations with access to its partnering meeting system, sparking nearly 600 meetings in the BIO Alliance Pavilion between about 60 participating patient groups and academics and the biotech companies at the convention. BIO has also scheduled several other events this year to encourage and facilitate more industry/foundation partnerships. On October 14 and 15, BIO will hold the third annual Patient & Health Advocacy Summit in Washington, DC, convening leaders from patient advocacy organizations, medical and professional societies, and the biotechnology industry for two days of programming and networking opportunities. Generally, BIO is also reinforcing BayBio's message to companies that patient foundations, in addition to funding drug development, bring almost incalculable value to companies in their expertise, resources, and rapport with patients.

MULTISORB Technologies

The World Leader in Active Packaging Technology™

StripPax System

Versatility Doesn't Guarantee Efficiency

You could try using a versatile multifunctional tool to chop down a tree, but it wouldn't be very efficient. Versatility is only useful when you are using the correct tool for the job. When it comes to sorbent packet dispensing, Multisorb has the tools you need! Unlike another supplier who claims its versatile product can run on any machine, Multisorb's StripPax® System components (StripPax Sorbent Packets and StripPax Dispensers) are engineered to run together effortlessly, providing unmatched efficiency and precision that you cannot obtain with unrelated sorbents and dispensers. If you need efficient and precise sorbent packet dispensing, then you need Multisorb's StripPax System!

www.multisorb.com

Protecting Biotech And Pharma Innovations Under New USPTO Guidelines

NOEL DAY, Ph.D.

In two recent decisions (see below), the United States Supreme Court issued opinions that have a drastic impact on the biotechnology and biomedical industries. The impact of the cases, which involved claims to diagnostic methods and gene patents, were originally anticipated to be limited to these industries.

However, the resulting United States Patent and Trademark Office (USPTO) guidelines made final on March 4, 2014 are extremely broad and will have a detrimental effect on the pharmaceutical industry, as well as any business with intellectual property involving "natural products."

In order to obtain a patent, a claimed invention must meet the requirements of Title 35 of the United States Code. An initial question is whether the claimed invention meets the requirements of subject matter eligibility under 35 U.S.C. § 101. Only after a positive determination has been made does the analysis for the novelty and nonobviousness requirements begin. In a previous Supreme Court decision involving genetically modified organisms, the § 101 requirement was interpreted to include anything "touched by the hand of man" as patentable subject matter.

On March 20, 2012, in what would seem to be a change of position, the Supreme Court decision in *Mayo Collaborative Services v. Prometheus, Inc.*, held claims to a diagnostic method unpatentable under 35 U.S.C. § 101, because the claims merely observed a correlation that was the result of a law of nature. On June 13, 2013, a little more than a year later, the Supreme Court issued a unanimous opinion in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, in which it held that naturally occurring "isolated" DNA is not patent eligible subject matter under 35 U.S.C. §101, finding that isolated DNA falls within the law of nature exception.

In *Myriad*, the Court noted that the holding applies only to isolated DNA. Claims to methods, new applications of knowledge regarding genetic sequences, or DNA in which the order of the naturally occurring nucleotide sequences has been altered were not addressed by the court, and synthetically created complementary DNA (cDNA) was held to be patent eligible under § 101. Nonetheless, in response to these decisions, the USPTO drafted guidelines for its examiners, titled *Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products*, which extend the holding to all claims involving "natural products" or natural principles. The guidelines were not open to comment from the public before being finalized; however, the USPTO held a forum on May 9, 2014, during which it became undeniably clear that patent practitioners, industry organizations, and biotech and pharmaceutical companies all have serious concerns about the new examining procedures.

WHY THE GUIDELINES HAVE GARNERED CRITICISM

The basis of the concerns is that the guidelines are overly broad and complicated, such that they improperly restrict the ability of innovators to protect their inventions and often make it difficult to determine from the outset what will and will not be patentable-eligible material. While the law regarding patentable subject matter in the United States provides that "Whoever invents *or discovers* any new and useful process, machine, manufacture, or composition of matter ..." may obtain a patent, the new guidelines have written the discovery component out of the law by making natural products and natural laws ineligible. According to

Visit us at Chem Outsourcing Booth #87 and at CPhI Booth #3C100

MovinScience

Moving Science To Commercialization

Ash Stevens®

Small Molecule API Manufacturing

Call our team +1 734 282 3370 www.ashstevens.com

Benefit From 50 Years Of CMO Knowledge

Ash Stevens has over five decades of experience developing and manufacturing drug substance. From our earliest origins to our present day state-of-the-art cGMP manufacturing facility in Riverview, Michigan, Ash Stevens has remained committed to moving projects forward to commercialization through high quality science, regulatory excellence, safe operations, integrity, and customer satisfaction. We serve clients of all sizes, from virtual biotech to large pharma, and from grams to metric tons.

the guidelines, a natural product must be "markedly different" from how it appears in nature to rise to the level of patent-eligible subject matter. It was revealed during the USPTO forum mentioned above that the USPTO's definition of "markedly different" requires a difference in structure and that a difference in function will not suffice. The USPTO has clearly stated that a combination of multiple natural products is not patent-eligible simply because the combination does not exist in nature. To demonstrate this, the USPTO materials reference a pair of primers having two different sequences. A claim to the pair is not patent-eligible, because the primers are not markedly different (meaning structurally different) once they are combined. In another example provided by the USPTO, a claim to a beverage composition comprising: a) pomelo juice; and b) a preservative is discussed. The USPTO first notes that the term "preservative" could cover both naturally occurring and non-naturally occurring preservatives. The office analyzes the potential argument that a combination with a naturally occurring preservative would be patentable because it is a non-natural combination, as pomelo juice does not naturally contain the preservative. According to the USPTO materials, this argument is not persuasive because "A marked difference requires a product to be both (1) non-naturally occurring and (2) markedly different in structure." Presumably, the outcome would be the same for a pharmaceutical composition containing a natural active ingredient and a preservative.

Another particularly problematic result of the guidelines is that a product that occurs in nature will not be patent-eligible even if it is made synthetically. For example, vitamin B was first found in nature but is now made by a synthetic process; the synthetic product would not be patent-eligible if vitamin B were discovered today. In fact, the list of synthetically derived natural products that would not meet the new requirements for patentable subject matter includes many antibiotics, cancer therapeutics, and treatments for cardiac afflictions.

One issue with the guidelines is that the determination is overly complicated and cannot easily be predicted when business decisions are being made as to whether to pursue developing a technology and how to protect it as intellectual property. From another perspective, it may also be difficult to determine when a license is necessary if another party holds the rights to an invention that is being used in the course of a company's business. The reason is that the guidelines do not provide a definition of "markedly different"; rather, they provide several factors for narrowing claims to attain eligible subject matter. The problem this raises is that the decision rests on the opinion of the examiner, which could vary from one examiner to the next and could even be motivated by factors that are irrelevant to the case being examined. A demonstration of the unpredictability of the analysis can be seen in Example F of the guidelines, where it states that the claim element of contacting a blood sample with antibody XYZ and using flow cytometry does not satisfy factor E, which is the machine or transformation factor. Additional materials prepared by the USPTO explain that while flow cytometry inherently recites a machine, the claim is not particular or specific, because it does not specify whether the flow cytometer is a bench top machine, high speed, etc.

WHAT TO REMEMBER FOR PROTECTING INNOVATIONS UNDER THE GUIDELINES

It is important to note that the current guidelines are only for the U.S. However, many other jurisdictions look to the U.S. for guidance, so similar changes in some countries can be expected in the future. Some jurisdictions are historically very independent and will likely not revise their system based on changes made by the U.S., but others are likely to follow suit in the near future.

The potential ramifications in the U.S. include the possibility that companies will stop pursing patent protection on their discoveries related to natural products and may choose to maintain the discoveries as trade secrets whenever possible.

"One issue with the guidelines is that the determination is overly complicated."

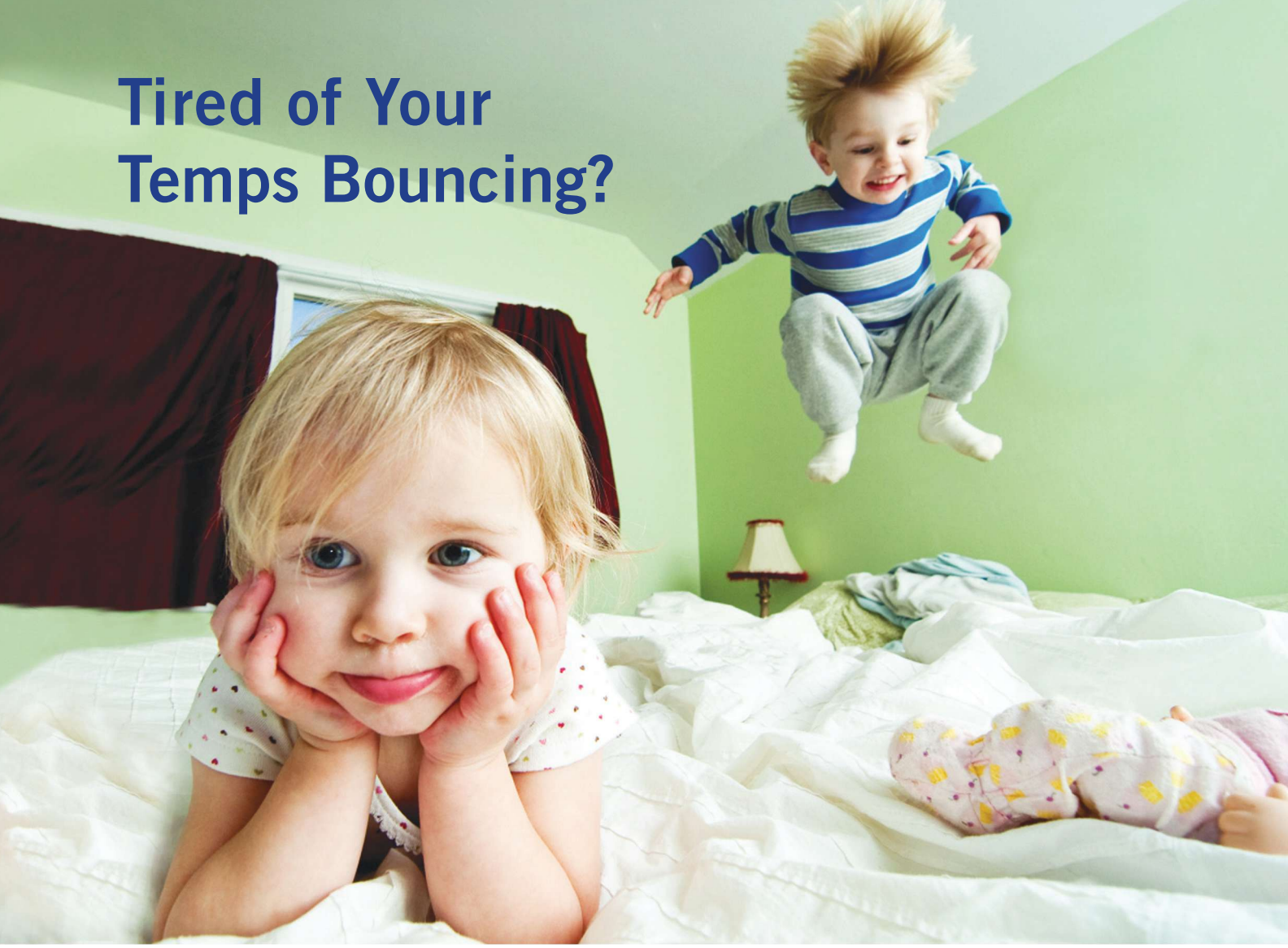
NOEL DAY, Ph.D.
Partner At Law Firm
Honigman Miller
Schwartz And Cohn, LLP

A more extreme, yet quite conceivable and very unfortunate, possibility if the guidelines remain in place and are strictly implemented is that there could be a reduction in innovation and some biotech and pharmaceutical companies may choose to relocate to jurisdictions that are not as restrictive.

There is hope for a more reasonable interpretation of the Supreme Court's decisions in the future. However, when and in what form the change will come is yet to be determined. In the meantime, it is important not to surrender any subject matter that may be patentable in other jurisdictions or as a result of more reasonable future guidelines in the U.S. It is highly recommended to layer claims such that the disclosure of the natural product is not sacrificed when drafting and prosecuting applications in light of the guidelines. Whenever possible, patent counsel should provide details that will allow the claims to be narrowed to achieve patent-eligible subject matter in the U.S. and to distinguish a product from its natural counterpart where practical. For example, when claiming a biomarker for patient selection, it may eventually be required to indicate a particular antibody or other specific method for detecting the biomarker in order to obtain patentability. L

Noel Day, Ph.D., is a partner at law firm Honigman Miller Schwartz and Cohn, LLP. Her practice focuses on pharmaceutical and biotechnology patent prosecution and transactional matters.

Tired of Your Temps Bouncing?



eurofins | Lancaster Laboratories

Partner and prosper with our award-winning PSS.

Eliminate the ups and downs of continually replacing and retraining temps by retaining our scientists at your site. Hired, trained and managed by us, our award-winning Professional Scientific Staffing[sm] (PSS):

- Eliminates headcount, co-employment and project management worries
- Avoids Temp turnover rate with managed insourcing
- Costs you less than your own full-time employees
- Delivers a 50-year history of regulatory compliant technical expertise in your lab
- Holds numerous client awards as the top insourcing service provider for the past 10 years

Choose the Professional Scientific Staffing solution that enables you to keep staff grounded.

www.EurofinsLancasterLabs.com

Life Sciences And Taxes: The Elephant In The Room

BARBARA RYAN

Last year marked an extraordinary time in the global life sciences market — record setting, in fact — and 2014 is already off to a roaring start. There were 60 mergers and acquisitions (with the average deal size 49 percent larger than the previous year's).

And, almost 60 percent of investors responding to FTI Consulting's fourth annual "Life Sciences Investment Survey" said they expect to see a significant to moderately significant increase in M&As in 2014.

What's driving this urge to merge and acquire? In a recent panel discussion hosted by FTI Consulting, the action in the M&A space last year (and going forward) was largely driven by companies and their investors in the specialty pharma/generic category looking for their portfolio companies to grow and diversify.

For example, one of the more significant deals last year was Perrigo's $8.6 billion acquisition of Ireland-based drug manufacturer Elan. Perrigo, a $22 billion company, is the largest manufacturer of OTC pharmaceuticals in the U.S., and Elan has a pipeline of experimental drugs for serious conditions, with its most notable success the multiple sclerosis drug Tysabri.

As Perrigo Executive VP and CFO Judy Brown told the FTI panel, the Elan acquisition was driven partly by the company's desire to expand outside the U.S., giving its "booming" generics business a global platform to bring "quality, affordable healthcare to more markets" and partly to build a balance sheet that would allow the company "to do more and larger transactions than we would have been able to do in the past."

As part of the transaction, Perrigo is reincorporating the combined company in Ireland, taking advantage of Ireland's corporate tax rate of 12.5 percent, as opposed to the U.S.'s 35 percent. "By having a footprint in Ireland, by now being an Irish company," Brown said, "we have more flexibility in our cash flow utilization, where we're going to deploy cash, and how we're going to be able to invest effectively globally."

But switching domiciles to take advantage of lower corporate tax rates is not without its risks. Indeed, as FTI Senior Managing Director Tom Crawford told the panel, the practice, often called inversion, is "like Voldemort [in the Harry Potter books]. It's not something we like to say out loud."

THE ELEPHANT IN THE ROOM

Apple has done it. Starbucks has done it. Google has done it. Many multinational corporations have taken advantage of lower tax rates in foreign jurisdictions through a variety of strategies, including inversions, transfer pricing (charging prices for goods and services between divisions in a company for the purpose of either lowering profits in high-tax jurisdictions or raising them in low ones), and intellectual property (IP) migration (in which IP developed in a high-tax jurisdiction is moved to a low-tax one, enabling a company to recognize its revenue in the low-tax jurisdiction even if its sales take place in the high-tax one). IP migration particularly is common in the pharmaceutical industry, which has made large investments and built large facilities offshore.

Apple, Starbucks, and Google, among others, have been taken to task publicly for these strategies which, although legal, are viewed by consumers — rocked by the 2008 financial meltdown and still adversely affected by the slow economic recovery — as less-than-ethical business practices. As Crawford said, "You pick up the paper and you read every day some outrage about how much money is pooled offshore, avoiding taxation somewhere, and people want to do something about that." (The headline for the *Boston Globe*'s June 17, 2014, story on the purchase of Dublin-based medical device manufacturer Covidien by Massachusetts-based Medtronic, another device manufacturer, read: "Address in Ireland may be Covidien's sweetest asset.")


WE GET
SHIP DONE.®
When you need to ship air cargo, there's one Team you can count on. One Team delivering Relentlessly Reliable® service to destinations across the map. When you need someone who'll get the job done, you need Southwest Airlines Cargo.®
SOUTHWEST
CARGO
RELENTLESSLY RELIABLE®

Governments, responding to their disgruntled citizens, increasingly are prone to viewing these corporate financial arrangements skeptically and often as mere tax avoidance schemes and consequently pondering regulatory remedies. Right now, the Organization of Economic Co-Operation and Development (OECD), the European Union, and the G20 are all working on rule changes that would require companies to maintain significant facilities, management, or personnel in the offshore location in order to be able to report the revenue there. The U.S. is also saying that if a company is not managed and controlled in the jurisdiction where it's reporting revenue, it will be disqualified from taking tax deferments.

As Crawford told the panel, if a company wants to be in a jurisdiction, "You have to demonstrate that it's not solely for the purpose of avoiding or paying low tax." There have to be "boots on the ground, or facilities, or some sort of management in control of operations for the overall business," said Crawford.

Given the competitive demands on pharmaceutical companies and the benefits that accrue to corporate cash flow and the bottom line by the mitigation of tax liabilities, how can companies stay within the letter and spirit of these new and forthcoming regulations without risk of being placed at a disadvantage? The answer, both Brown and Crawford agreed, is understanding, openness, and engagement.

SHRINKING THE ELEPHANT

Brown stressed the importance of keeping a company's management team briefed both on current and proposed regulatory shifts. Management, she said, is making long-term investment decisions that will, of necessity, be affected not only by U.S. but also by foreign policy makers. When a company's leadership is properly informed, it can make strategic investment decisions without running the risk of being surprised by events down the road. Furthermore, informed leadership can create a narrative that it can communicate to regulators that positions a company on the side of the angels.

Crawford worked with Perrigo to create and communicate that narrative. "The key for us in differentiating what Perrigo did from the standard tax avoidance, tax structure game that's going on with inversions was that we made the business case for what Perrigo was doing," he said. "We didn't start at the point that we decided we wanted to acquire Elan. We started two years before the acquisition talking about the need for U.S. tax reform. We started telling the story about Perrigo's contributions to the healthcare system. We talked about how what we do could be exported around the globe and the benefits of what we do in the U.S. That allowed us to go into the merits of the deal instead of talking about inversions."

Brown testified before the U.S. Ways and Means Committee, engaged with its members, and argued that the U.S. needed lower tax rates to become more competitive globally. She pointed out that in order to continue adding jobs in the U.S. and to grow the company, Perrigo needed to compete with firms taking advantage of lower tax rates abroad. However, while Brown acknowledged that tax was a component of Perrigo's acquisition of Elan, it was not the driver for the business decision. That, she told the committee, was growth.

Perrigo's narrative and engagement strategy, said Crawford, has become "something of the white hat example of a U.S. company that is struggling to remain competitive for share outside the U.S." Ultimately, instead of opposition or blowback when the acquisition was announced, according to Crawford, the Chairman of the Ways and Means Committee said, "I don't blame you for what you did. You've been up here for two years telling us we need to do something. You can't wait for us to go and do your business."

The lesson from the Perrigo-Elan acquisition, Crawford said, is that "Policy makers are not looking to crucify people who explain themselves and who have a rationale for what they're doing. I think they're looking at people who try to arbitrage the system in a way that doesn't appear to be about anything more than getting a tax benefit."

THE TAX FUTURE

It's becoming clear that governments are going to get tougher on companies that appear to be gaming the system to avoid taxes. Crawford recounted a meeting with the Finance Minister of Ireland who told him, "I'm going to keep our Irish rate – we're not going to give that up – but I'm going to call the bad guys in and tell them you've got to get right or you're getting out."

That attitude is something new, and companies that don't "get right," that don't implement controls and management in the jurisdictions in which they recognize revenue, risk alienating both governments and investors. At the FTI panel, Alan Hartman, a partner in Centerview Partners, an investment banking and advisory firm, said that investors "should just not be around those companies that have inverted or those that are otherwise in offshore jurisdictions. This issue is a big one for all Pharma."

If, Hartman posited, pharmaceutical companies suddenly, without planning for it, find themselves paying 30 percent tax instead of a rate in the low twenties, "The math of those companies looks very, very different." And the multiples at which they've been trading will look very, very different, too.

It behooves pharma leadership to begin planning for this future now. That means making sure their tax policies align with their corporate values and that they're engaging thoughtfully with the investors and regulators who hold their financial futures in their hands. L

Barbara Ryan is consulting managing director in healthcare capital markets and strategic communications at FTI Consulting. She has more than 30 years of Wall Street experience as a sell-side research analyst covering the biopharmaceutical industry.

UPM Pharmaceuticals®
Formulating Your Future™

Introducing a Commercial Facility for Today's Market

UPM Pharmaceutical's new 500,000 square foot commercial facility in Bristol, Tennessee serves customers with large-scale manufacturing capabilities for solid oral dosage tablets and capsules, as well as semi-solid creams and ointments.

KEY SITE FEATURES:

- 500,000 square foot manufacturing facility
- 70,000 square feet of general warehouse storage
- 7,400 square feet of controlled substances storage
- Excellent regulatory inspection history (DEA-licensed)
- Comprehensive tech transfer support
- Pilot plant with scale-up capacity
- Analytical and microbial testing laboratories with dedicated suites for potent compounds

LARGE-SCALE OPERATIONS:

- Blending
- Drying
- Compressing
- Semi-Solid Processing
- Milling/Sifting
- Granulating/Coating
- Encapsulating
- Packaging

ANNUAL PRODUCTION CAPACITY:

- 3.5 billion tablets
- 700 million capsules
- 43 million packaged bottles
- 138,000 kilograms of cream/ointment
- 5 million packaged tubes/jars

To learn more, visit **www.upm-inc.com** or call **+1 410 843 3738.**

Visit us at Contract Pharma Booth #61
& Chem Outsourcing Booth #81

THE CMO LEADERSHIP AWARDS 2013 | WINNER
REGULATORY PRODUCTIVITY INNOVATION

Reengineering The Pharma Supply Chain

GAIL DUTTON @GailLdutton Contributing Editor

The life science supply chain shouldn't be the same as it was 10 years ago. Reengineering is imperative to deal with pressures that include transforming the industry from a volume-based to value-based model; ensuring profits despite reduced margins and the patent cliff; and addressing the complexities triggered by increased regulations, new product types, and globalization of both R&D and markets.

"The big players estimate reengineering will reduce distribution costs by at least 25 to 50 percent," says Siddharth Dutta, Ph.D., life sciences industry manager, Frost & Sullivan.

Savings will be accomplished through a combination of cost reduction and new opportunities. For example, Reenita Das, partner and senior VP of healthcare and life sciences at Frost & Sullivan, points to expanding products' scope to lower costs and streamline logistics. As products are approved for more indications, she says some organizations can "expand beyond the acute care setting to create models" to compete with Walgreens and CVS, which are increasing the numbers of their in-store clinics and turning healthcare into a retail experience.

"Online ordering of drugs, customized delivery, and reduced delivery time will be the new paradigm in the supply chain," Dutta adds. Already, the 2014 Biopharma Cold Chain Sourcebook reports that it is becoming increasingly popular to see a direct distribution model that mails individual doses directly to patients or specialty clinics. Like other pharmaceutical shipments (from APIs through finished products), these shipments to individuals and clinics often are managed by third-party logistics providers.

LEVERAGE 3PL INSIGHTS

Leading third-party logistics providers (3PLs) understand the need to do more than move packages. Many have developed life science divisions capable of providing logistics and consulting support to help clients transition from volume to value. "The supply chain must be solutions-driven," says David Bang, CEO of DHL's LifeConEx unit. "Shippers need an integrated, whole-package solution." He advocates one solution that incorporates infrastructure, networks, and standards to provide visibility into each link in the chain rather than a host of options that must be cobbled together and managed.

The complexity of the products may require special handling. For example, shippers need to account for differences between "room temperature" and "ambient temperature" requirements, as well as the increasing number of products that need 2° to 8° C, -75° C, or deep frozen -150° C temperatures and the purpose-built packaging and temperature monitoring solutions that are tailored for those specific temperature ranges. Also, as packages travel globally (even for clinical trials), shippers must be aware of customs requirements and policies regarding work schedules, holidays, and storage facilities at customs clearance facilities to help ensure temperature-sensitive items aren't left sitting .

"Go back to the regulatory environment and the basic quality agreements. Shippers and carriers need to agree to maintain GDP-based quality (which, increasingly, is an extension of GMP practices) throughout the supply chain. Life science KPIs (key performance indicators), for instance, go beyond typical transportation KPIs and may require additional analysis." In life sciences, it's not enough to know that packaging is effective; it must be certified effective, along with any changes to that material which may occur if manufacturers change suppliers of foam, foil, or other protective packaging elements.

Changing suppliers or countries of origin for APIs or products also creates potential hazards. While APIs from India, China, or Turkey, for example, may be identical, customs clearance documentation may differ. When suppliers are changed rapidly, importation documents may not be

updated to allow timely clearance. Even if the change is just from one manufacturing site to another within the same company, additional site inspections and due diligence may be required to ensure that the facility and its suppliers meet GMP standards. APIs also may need to be reevaluated. For example, the skikimic acid extracted from the pods of star anise grown in four regions of China is notably more potent than skikimic acid extracted from anise grown anywhere else in the world. If a supplier changed its source of skikimic acid, the potency of the drug (in this case Tamiflu) would be diminished.

LEARN FROM OTHER INDUSTRIES

The life sciences industry can learn a lot from the automotive industry. As one example, Bang points to automotive forecasting systems, which enabled just-in-time delivery. CSL Behring takes a similar approach to manufacturing. "We postpone product differentiation as long as possible," notes Mary Sontrop, EVP, manufacturing and planning, CSL Behring LLC. CSL holds product at various processing stages, filling final product containers at the last possible moment. This increases shelf life and flexibility. The pharmaceutical manufacturer also applies one multilingual label for multiple markets, increasing inventory flexibility by letting one product be shipped to many destinations as needed. Before, small batches with different labels had to be produced and inventoried, taking extra management time. CSL uses predictive analytics to preposition goods where they will be most needed. The company also is installing equipment in its warehouse to simplify order fulfillment and is implementing a paperless inventory management system that is expected to minimize inventory fluctuations.

Additionally, Dr. Dutta advises life science companies to develop one inventory system rather than multiple inventories managed by different divisions of the company and an electronic catalog that lets customers order from the entire catalog, day or night.

ACCOMMODATING LOCAL REGULATIONS

"Emerging markets' GMP, GDP, serialization, and customs standards are similar to those of industrialized markets, but the infrastructure is not the same," Sontrop says. Operating in Brazil, for example, requires a warehouse there because of concerns about temperature control, cargo theft, and poor inland infrastructure. "This is a big inefficiency that requires additional CSL energy to manage and ensure that products shipped to that country receive adequate protection," Sontrop says.

"Manufacturers must prove that product storage technology is robust enough to ensure adequate protection," Sontrop says. Particularly in emerging nations, storage capabilities vary among customers. "Some have a refrigerator and thermometer they check daily. Others have a 24/7 monitoring

and alert system."

Serialization introduces another hurdle. "As introduced globally, serialization regulations won't be harmonized. Nor will the technology," Sontrop predicts. "Companies may have to adhere to different standards for different countries." That implies deploying technology and solutions that can adapt and respond to multiple standards. "That's challenging," she says. "We're working with serialization requirements in about 30 countries."

TRANSPORTATION

Shipping options for life science products are increasing. "Marine shipping is a new, lower cost option for the life sciences," Bang says. "The top five marine operators are the core carriers," and others that never transported pharmaceuticals now are allowing these high-value products as cargo. The catalyst has been the introduction of more reliable reefers and temperature monitors that offer high-performance temperature control or monitoring and visibility to both the carrier and the shipper.

CSL Behring ships some of its mature products by sea. "Plasma from the U.S. to Europe ships at -30°C, and products return at 4° to 8°C or room temperature," Sontrop says. "To further reduce shipping costs, we do the first processing steps in the U.S. to remove water from the plasma and then ship the intermediate concentrate to the EU. It's about one-fourth the cost of shipping whole plasma." Marine transportation between the U.S. and EU adds about three weeks to the transportation cycle.

When changing transportation modes or destinations, "You may need to change packaging," Sontrop adds. "In the U.S. we ship palletized products with cardboard on the outside in temperature-controlled trucks." To ship the same products to developing regions, the polystyrene packaging is thicker, and temperature indicators or monitors are used to document temperature excursions.

Whichever mode is used, "Look at the overall picture," Bang advises. "Know the carrier and container companies, the handoff process, and the technology used to maintain and monitor the environment. If monitoring provides real-time visibility into the status of shipments, learn whether intervention is possible if things go wrong. Know, for example, whether cold-chain items can be re-iced before they are ruined by too warm temperatures and whether damaged products can be diverted before reaching the customer. "Real-time visibility is valuable, but for it to be most worthwhile, monitoring technology must be integrated into the cold chain platform rather than merely slapped onto a package and checked upon arrival."

TEMPERATURE CONTROL

"Global life science regulatory guidelines are mandating temperature control — often before the infrastructure to ensure it is in place," says Mark Seegres, president and CEO of BD (formerly Becton, Dickinson and Company). For example, Brazil mandates temperature control, but temperature-controlled warehouses are not yet routinely available nationwide to support a wide range of temperature thresholds. Instead, as in many developing regions, facilities are available mainly at major ports.

DHL, like many major carriers, is working with local authorities to expand its temperature-controlled infrastructure globally. "In Mumbai, Bangalore, and Hyderabad, for example, we have 2° to 8°C facilities in a bonded warehouse with more than 1,000 square meters," Bang says. "That's not something we just built. We did this in consort with the airport authority to develop solutions that will remain viable for many years." DHL has taken such long-term, cooperative approaches in many locations globally.

Pharmaceutical companies are trying to eliminate temperature issues, particularly for new products, by designing ambient temperature formulations. CSL Behring developed an immunoglobulin product that can be stored at room temperature versus the usual 4° to 8°C, for instance. "However," Sontrop adds, "there's only limited opportunity to do this because if you make changes in the process, you may need to redo clinical trials or, for minor changes, demonstrate comparability."

ASIA-PACIFIC SHIFTS SLOWLY

"In the Asia-Pacific (APAC) region, distributors are developing integrated business models to enhance efficiency," Dr. Dutta says. "For example, the large Indonesian distributor PT Enseval Putera Megatrading has opened one-stop healthcare chains like Mitrasana Clinics, which combine a family doctor, pharmacy, laboratory, and convenience store."

PT Enseval Putera Megatrading uses a unified inventory system to shorten distribution channels, saving time and expense. According to Dutta, APAC distributors are investing heavily in IT to increase efficiency and allow access to customers for online purchasing. He calls IT investment, which minimized inventory fluctuations, a major catalyst for PT Enseval Putera Megatrading's growth and 12 percent market share in Indonesia.

Mid-to-large players in India and China also are planning cold chain investments, particularly near major metropolitan areas. In Indonesia, Dutta continues, "Only selected distributors have cold chain facilities. APL Zuellig is the only company handling cold chain with international certification, with the assistance of a German monitoring system. The other big distributors are planning similar arrangements."

REENGINEERING IS PLANNING

"There's no magic bullet solution to supply chain optimization," Bang says. Reengineering the supply chain requires detailed planning that takes into account the new options, new challenges, and broad contingencies faced by a global, highly regulated, cost-pressured industry. Don't attempt to redesign the supply chain alone. Instead, work with reliable logistics experts who know your business and with your suppliers and distributors to design a system that addresses today's pain points for well into the future. L

A New Model for the New Marketplace

Today, trial decisions must be made more quickly and efficiently than ever before. Success demands a new kind of CRO partner — one with strategic and flexible solutions that assure the fastest possible route to quality clinical results.

At inVentiv Health Clinical, we are that next-generation CRO. A top provider of Phase I-IV global drug development services, we take a patient-centric approach and apply smarter, fresher thinking to go well beyond traditional outsourced services.

And, as part of inVentiv Health, we leverage the expertise and resources of a much larger organization to apply real-world commercial and consulting insights for clients in over 70 countries.

Advancing clinical innovation — that's what we do best.

inVentiv Health clinical

inVentivHealthClinical.com

Driving A Data Analytics Strategy From The Inside

GEORGE BRUNNER

The following is part one of a two-part series depicting the personal journey of a fictional CEO as he develops a data analytics strategy to shorten his drug development timeline and predict and prevent problems before they occur.

Cabot Harrington is a CEO of a midsize pharmaceutical company called Helioarc, and like most CEOs, he has an insatiable appetite for information, especially information that will help him better position his company in the market. His is a three-drug company with one in clinical trial, the second a mini-blockbuster in 24/7 production, and the third a bulk-powder product going to a Big Pharma partner. In total, his partnerships number nine when you include contract packaging partners, CROs, and logistics companies.

To satisfy his appetite for information he seeks data at every moment, and he reads constantly. He recently read something about Big Data and realized that he might have a Big Data problem at Helioarc, because his team seemed to spend more time reading reports than using data to move the company forward.

He grasped that his organization and the life science industry in general were huge collectors of data, and primarily data that looked back in time — for example, last month's financial and clinical trial results. That got him thinking about how his teams currently interacted with data.

During his regular walks throughout his company's laboratories and manufacturing floors, he noticed laptops, desktops, tablets, spiral bound notebooks, black leather laboratory notebooks, and tons of instrumentation with digital data. He knew that his contract packaging and clinical research partners delivered data to his company in Excel spreadsheets, often sent in emails. They weren't on the same platform as Helioarc, and thus, all of that data had to be re-entered into his company's software. Finally, when his CQV (commissioning and quality validation) department was working with the FDA last month, it was astonishing to Harrington how much validation data was still kept on paper and how much time it appeared to take to access relevant information.

WHEN DOES DATA LOOK AT THE FUTURE?

In one of those middle-of-the-night ruminations we all have, Harrington realized how to dramatically improve Helioarc's position in the market — both on the clinical and commercial sides of the business.

He concluded that a majority of companies were still in the sense-and-respond stage, and he knew Helioarc still languished there as well. They were using data, post-generation, only to sense and respond, rarely discussing the future state with anything more than a rush to prepare for that quarter's board meeting. Sometimes, during his midnight, home-office, caffeine-induced moments, Harrington could see the possibilities of predictive, comparative data collection. Last night, he looked at clinical data from a 2009 study that seemed eerily similar to a study being conducted by one of Helioarc's current CRO partners. Now they were paying to do the same testing again. Did that make sense?

Harrington decided to set some goals that he was not sure were yet possible, or plausible, but they were a start:

1. shorten and improve the outcome of his clinical trial programs
2. develop better data sharing between his company and its contract packaging, contract manufacturing, and other outside vendors
3. use historical data from clinical trials to inform future trials, patient populations, and molecular studies
4. find a way to access data for regulatory agencies more quickly.

It was an ambitious set of goals. Harrington realized that his first step was to communicate his vision to his IT group, the executive team, and board members. He needed to "talk the talk", or at least understand some of this new language. If he were going to encourage his organization to develop a predictive analytics strategy for its clinical and regulatory/compliance areas, he also needed to make everyone part of the discussion.

PREDICTIVE ANALYTICS

If you can relate to any of Harrington's revelations or challenges regarding Big Data, your goal should be to build a predictive analytics strategy. In other words, lead your organization to use the data that exists, improving its quality where necessary, to make better decisions for the future.

To do so, first huddle with your executive team and prioritize the specific data types to address. Then, make it clear that the entire company will be eliminating data silos and streamlining data entry. At most midsize pharmaceutical companies, accomplishing these three steps will take at least a year. It's likely the whole implementation will take two years. Explain these time frames up front to your staff to ease some of the pain as the project drags on. You should also prepare your teams for significant infrastructure and procedural changes as they choose which data types to address first.

This series of articles will focus on prioritizing clinical data, although the process described here could apply to multiple areas inside your organization.

Help your team to imagine the possibilities. When clinical data becomes more accessible, portfolio management and pipeline evaluation could improve — a lot. If opportunities can be viewed across multiple studies, and different years of research can be evaluated together, it can open up possibilities never before considered. Use the term Analytics-as-a-Service (AaaS) when you speak to the team about this vision.

Data silos will come down between departments, as they should. Use the term "governance" when discussing who will become the new owners of various types of data. These new individuals or teams will undoubtedly be cross-discipline.

Ask IT about your EDW (enterprise data warehouse), which is a repository of information used for reporting and analytics. According to Forrester Research, an EDW includes key data management functions such as concurrency, security, storage, processing, SQL access, and integration. Although this conversation might get too technical, simply convey to your IT team that you do not want to commit to one vendor too early or consider only legacy enterprise solution providers (e.g. HP, IBM, Microsoft, SSAP, Pivotal, Teradata, Amazon Web Services, ParAccel). It is critical to evaluate the current state of your data situation with a neutral eye.

As mentioned earlier, data cleansing and aggregation of your own data is the single most difficult step. No matter where you start, it is arduous. Aggregating data in a new data repository and instituting guidelines for entering the data consistently, so the data is "clean," take time.

For over 25 years George Brunner, CTO at Acumen Analytics, has been lending his vision and leadership driving technological innovation in pharmaceutical, biotechnology, medical devices, and other life sciences sectors.

A Global Systems Approach To Clinical Research

FRED OLDS Contributing Editor

"It would be an enormous benefit to pharma and humanity if we had a more efficient and systematic way to bring safe and effective drugs to market," says Greg Koski Ph.D., M.D., CEO, president and cofounder of the Alliance for Clinical Research Excellence and Safety (ACRES). He asserts that the current approach has evolved into a multisiloed proprietary arrangement.

"Everyone knows it's an inefficient mess, and many believe it's unsustainable." He proposes a better approach — a system.

Koski and collaborators envision ACRES as the nexus of a global research system. They propose establishing a worldwide network of accredited clinical study sites and research professionals supported by a shared information technology platform. These would operate under common standards and use common procedures agreed to by international stakeholders in clinical research.

ACRES was conceived out of frustration with attempts to bring harmony to the current state of clinical research. There were, and are, many good organizations working to fix or improve specific areas of research, but, Koski says, "That's like having a 1954 Chevy that you work on to improve. You can replace parts and repair all you want, but in the end you still have a 1954 Chevy." What is needed, he says, is a revolution of thought and behavior. He says, "ACRES isn't a piecemeal fix; it replaces the current inefficient processes with a true system. Think of it as 'next generation.'"

He points to the International Air Transport Association (IATA) which led efforts in the development of universal standards for aviation. ACRES patterns itself on the success of the IATA. Like IATA, it is both a forum for the exchange and implementation of ideas as well as a vehicle for establishing standards. It is an alliance of stakeholders in clinical research including sponsors, investigators, vendors, and regulators. It was founded as a not-for-profit organization to remove any doubt about its motives, actions, and recommendations.

THE RATIONALE OF QUALITY, TIME, AND MONEY

The alliance is based on the concept that a universal system of standards, accreditation, and technology will reduce costs and speed time to market for therapeutics, while enhancing quality and safety. Koski contends the current processes are inefficient. "Of the $70 billion spent on clinical trials, about 30 percent is wasted," he says, "That's more than $20 billion left on the table." For example, even with the best selection techniques, fewer than one-third of trial sites will enroll more than one or two patients, and 10 percent will enroll none at all. Costing $25,000 or more, development of a site can be a large investment with nominal returns.

Having established/accredited sites means improvements in quality, time, and money related to the trials. Koski estimates that access to high performing sites can shave two to three years off time to market. A comprehensive global database will speed screening for appropriate sites based on, for instance, desired patient populations or site capabilities. Access to existing equipped sites that are staffed by trained professionals will cut start-up time. The ACRES global technology network will provide real-time monitoring so potential issues can be identified and resolved early. Application preparation will be easier because data will have been collected in real time and in a uniform manner. Regulators relying on ACRES accreditation may find reviewing applications easier, because all sites used standard operating procedures.

Koski believes it is imperative to establish consistent global standards. "Seventy percent of clinical trials are now conducted in North America and Europe. In the next decade, that is predicted to change, as trials shift to China, India and other parts of the world," he says. With conflicting regulations, standards, and local customs, there are difficulties in reconciling policies and procedures in one part of the world with those used in another.

Under the ACRES umbrella, sites will

Enhance Your Commercial Success

Kim, Cell Culture Manufacturing

Go to Market With Gallus

Gallus' exceptional record in commercial manufacturing reflects the experience and reliability you need to have confidence in advancing your protein therapeutic to market. With an exemplary regulatory record, Gallus is now delivering multiple molecules to Phase III and product launches for our clients. As your strategic CMO partner, Gallus offers a collaborative approach and flexibility in manufacturing and business models, working with you to achieve success.

Contact Gallus to learn how far we will go to work for you.
info@gallusbiopharma.com | **www.gallusbiopharma.com**

gallus
Uniquely Flexible CMO™

THE CMO LEADERSHIP AWARDS 2013 | WINNER
REGULATORY PRODUCTIVITY

be interoperable; they will be using the same systems. That means communications and oversight of multicenter studies will be consistent, regardless of location. Researchers won't have to deal with computer interface difficulties nor differences in procedures because of local variations in equipment or practices.

A GLOBAL TECHNOLOGY NETWORK

Connectivity is at the core of the system. "Develop the system, and the system will drive standardization," says Koski, "Standardization will improve efficiency, quality, and safety. If there is no system, then sponsors will have to adapt studies to each country."

Systems engineers are creating a global technology network using off-the-shelf equipment. Doing so is economical and creates a network that is capable of aggregating, analyzing, and sharing information globally in real time. Koski says an authorized researcher or regulator anywhere in the world will be able to access the system to find the required information. "It's much like our ability to find flight schedules on the other side of the globe because of IATA's database," he says.

DYNAMIC ACCREDITATION AND EXCELLENCE

"Industry has failed to recognize the value of promoting excellence at research sites," says Koski. Accreditation will reward site excellence. Sponsors looking to place studies will be able to screen sites, looking for those that perform efficiently and quickly. Site operators wishing to draw studies to their centers will manage their operations to meet the standards of the highest-performing centers. "Not everyone wins. High quality wins — inefficient, poor-quality sites will not be sustainable," says Koski.

Sites will be accredited by agencies empowered by stakeholders in the ACRES system. Once approved, a site will continue to be accredited dynamically. Work at study locations will be captured in real time. Systems will continually monitor the environment, equipment, and media for review and analysis. Input by staff will provide current progress on research. All of this will give assurances to the sponsor, public, and regulators that research was conducted properly and allow accreditors to assess the work conducted by the research site. Koski asks, "Does it make sense to go eight years developing a new molecular entity only to have it fail to win approval due to an error in process?"

Site accreditation is one of the core initiatives ACRES is tackling. At present 120 international experts from all sectors of clinical research are engaged in ACRES' initiatives, including development of procedures and standards for clinical trials. It is reviewing international regulations, science, and best practices to seek consensus on, and then establishment of standards for, adoption by ACRES. The first version of site accreditation standards should be available for testing by early 2015. Round one of actual accreditation should take place by the third quarter 2015.

HURDLES TO EXPANDING HEALTHCARE IN THE THIRD WORLD

"A big challenge for healthcare is that the majority of people in the world don't have access to medicine or medical care," says Koski. Much of the research in the third world is "one-and-done." It's helicopter research. A company comes in and completes a trial then departs without leaving any lasting benefit to the country or its people.

ACRES established the Global Challenge initiative to develop world-class permanent clinical trial sites in the developing world. It believes a location staffed with medical and research professionals will not only draw research but also serve as a hub for medical services to the people of the country. The first accredited pilot project for the challenge is planned for Bangladesh.

Changing the world in a big way has big challenges. Funding is an immediate one. ACRES is embarking on a $50 million director's campaign to build infrastructure and core systems components. These components are key to operations because they form the backbone of the global technology network.

Once online, ACRES can be financially self sufficient in three and a half years. It has identified potential funding streams from site-related connection fees, user fees, and royalty streams. In time, there should be as many as 180,000 sites in the network. Revenues of about $250 from each of 65,000 of those sites would be sufficient to support the global system.

"Of the $70 billion spent on clinical trials, about 30 percent is wasted."

GREG KOSKI Ph.D., M.D.
CEO, president and cofounder of ACRES

Inertia may be the greatest obstacle for ACRES. Changing the culture of secretive siloed research is not easy. Koski agrees it will be a challenge to convince sponsors to provide open, transparent data on their trials. Countries may resist adopting universal standards. Habits and suspicions are difficult to change. The fear of losing intellectual property or local customs is a difficult psychological and practical obstacle.

While accepting the challenges, he says there are currently 46 strategic allied organizations that believe in the value of ACRES and are actively involved in the effort. ACRES is relying on them as advocates. As major sponsors like Pfizer or AstraZeneca make clear they intend to use ACRES standards for their trials, countries interested in working with them will strive to raise their standards to attract the trials. If the allied companies do cut time to market and enjoy easier coordination of research, others will follow.

"It is safer to fly from an airport in one country to an airport in another country than it is to drive to your local airport," says Koski, "That's because of the system that IATA has helped build." He believes ACRES can be the correlative agent to bring higher quality, efficiency, safety, and standards to clinical research.

Minnesota Thermal Science and Cool Logistics have combined to provide the largest global reach and widest range of passive thermal packaging solutions available in the industry!

Exceptional services & support delivered globally

Innovative Leading Technology options

Unsurpassed Global Reach

All designed to deliver.....

REDUCED payload risk.

REDUCED distribution costs.

REDUCED environmental impact.

PELICAN BioThermal™

Credo® THERMAL PACKAGING SOLUTIONS

COOLPALL™ VERTOS

Sherpa Systems

CHRONOS™ ADVANCE

PELI BioThermal™

877.537.9800 3020 Niagara LN N Plymouth MN 55447 USA

The Supply Chain Of The Future: A Strategic View

PETER BIGELOW

Peter Bigelow is president of xCell Strategic Consulting, a consulting firm to the life sciences industry. In this position he provides management consulting services to a number of pharmaceutical clients.

Evolutionary theory teaches us it is neither the strongest nor the most intelligent of the species that survives. It is the one that is the most adaptable to change. Ingredient suppliers, manufacturers, quality standards and audits, and logistics are just a few areas where we can expect to see many changes. Adapting to these changes will be critical to everyone involved in the process and in ensuring that medicines are delivered to patients safely and effectively.

The pharma supply chain has certainly undergone significant change in the last 40 years. In the 1970s and 1980s very little outsourcing was performed in pharma. Companies had separate domestic and international divisions, each with its own manufacturing. In the 1990s, API manufacturing became globalized, global quality standards were rolled out, and generic and biotech manufacturers emerged.

In the first decade of the 21st century, dosage-form manufacturing went global, companies instituted operational improvement programs, external supply departments were established, and outsourced products were managed more consistently. There was also greater scrutiny, with regulatory actions increasing exponentially. Business interruptions are now pervasive, with plant shutdowns resulting in drug shortages and higher manufacturing costs.

TAKE A STRATEGIC APPROACH

To improve supply chain performance and avoid costly and disruptive delays, companies must take a strategic approach. This begins with setting goals that redefine performance. First and foremost, pharma must make 100% customer service levels their top priority. Pharma should strive for short cycle times, low inventory levels, and no products on the drug shortage list. Quality levels should be set that consistently beat expectations, including zero regulatory actions, processes with advanced warning systems in place, and value driven decisions being made at every level. Waste elimination must also be a top priority.

Part of a strategic approach involves the preparation of a strategic plan. Several factors should be considered when preparing this plan. Counterfeiting and diversion are things the industry has to attack smartly and aggressively. To do this effectively, everyone in the supply chain has to be held accountable. Counterfeiters must be identified and prosecuted wherever in the world they happen to be. We must also devise creative solutions to fight counterfeiting quickly and effectively. These solutions must be supported by everyone, including regulators.

Pharma companies must take needed steps to reinvent outsourcing. To assist in managing suppliers, firms should establish a set of GSPs (good supplier practices). Part of this is developing a set of metrics for suppliers and improving the way customers and suppliers communicate with each other. Cracking down on poor cGMP practices will require drug developers to support the audit services industry and the push for manufacturing uniformity. This should consist of an alignment of standards for product classes, consistent penalties for risky behavior, a drive for consistency across regions, and a consolidation of industry support organizations. We also need to see stronger integration of information technology in the supply chain, a seamless integration of data with suppliers, and investment in continuous manufacturing, electronic batch records, automated processes, and other IT advancements we have seen in other industries.

Finally, there needs to be a greater focus on getting operational excellence right. Manufacturers must attack variability, waste, and inefficient processes with a vengeance. Managers must engage and motivate employees from top to bottom, while focusing on mindsets and behaviors. A focus on training will be essential, and when new ideas are adopted, they cannot be hypothetical. Managers must make sure the improvements are actually happening on the factory floor.

ARE YOU MAKING PROGRESS?

Once changes are made, how can you know progress is being made? There are several metrics that can be used to gauge progress.

Critical drug shortages should be rare, and customer service metrics should indicate a 99% or greater shipment completion rate. The pharmaceutical industry should be managing suppliers better than any other industry in the world. When regulatory actions have been all but eliminated, medicines are available to all at an appropriate cost, and when we have altered the risk/reward situation for diverters and counterfeiters, we will know we are making progress.

If changes are done correctly, drug manufacturers will not only secure their supply chains and reputations, but also will have the highest levels of compliance and customer service. The result will be safer medicines, fewer adverse events, and lower costs for pharma. L

UNITED CARGO

SM

right temp
right time

friendly

TempControl™ provides secure around-the-clock delivery of sensitive cargo.

fly the friendly skies℠

Keeping Pace With Adaptive Design

MICHELLE MARLBOROUGH

Michelle Marlborough, VP of product strategy at Medidata Solutions, is responsible for product direction across the entire Medidata Clinical Cloud. She works with the company's development team to create new modules and capabilities within Medidata's cloud-based platform.

Adaptive trials are increasingly used to accelerate studies and reduce the risk of clinical drug development. The Tufts Center for the Study of Drug Development estimated in 2013 that approximately 20 percent of clinical trials already use simple adaptive designs. However, the adoption of complicated adaptive designs such as Bayesian methods may require new technology and working practices.

Adaptive trials require more frequent analysis of study data than traditional clinical trials, yet the frequency and complexity of these analyses vary, depending upon the adaptive trial method. Simple methods may require only a few interim analyses of blinded data with minimal demands on technologies, while complex methods may analyze diverse forms of unblinded data daily. Methods requiring such real-time access to data are only cost-effective when using advanced clinical trial technology.

THE REAL VALUE OF INTEGRATED EDC

Traditionally, electronic data capture (EDC) was a transposition of manual methods of recording data into a web-based media (simply putting the "e" in "eCRF"). However, to support adaptive trials, EDC systems must integrate a wider range of data sources (e.g., clinical assessments, lab data, patient reported outcomes) into a single homogenous data source with minimal manual intervention. Instead of manually combining data once at the end of a study, these technologies integrate the data as it is collected, allowing data to be extracted and analyzed at any point during a trial.

The simplest adaptive design uses an interim analysis to evaluate whether to change a trial's path at some point during the study. In most cases, sponsors will undertake this analysis only after all patient data has been collected and examined by a third-party monitor. But this adds significant time to decision making and restricts the ability to do more complex adaptive trials. Further, the process of verifying every entered data element is increasingly being challenged by the FDA as well as other drug development participants, and research has shown that little data is actually changed post-entry.

Instead, having a single integrated source of all trial data speeds monitoring and verification and eliminates the need for traditional data cleaning prior to analysis. Risk-based data selection enables a targeted verification approach that has proven at least as effective as traditional data monitoring.

REMOVING TRIAL BOTTLENECKS

Having an EDC solution that is part of an interoperable platform also helps when using Bayesian analysis methods, which can add another level of demand on data systems because they include historical data into analyses. After all, aggregating data in a common format for modeling is difficult. (Of course, alignment with CDISC [Clinical Data Interchange Standards Consortium] data format standards will help you receive data in a consistent format regardless of the system used to gather the data.)

Trials like the I-SPY2 trial for breast cancer and the Lung-MAP trial for advanced squamous cell lung cancer (both public-private partnerships led by the Foundation for the National Institutes of Health) show where clinical trials may be headed and how these trials need to be supported by new technology. Both are multi-drug, multi-arm trials that use biomarkers to establish treatment arms. Integrated electronic tools such as EDC and clinical trial management systems, as well as randomization and trial supply management, will ease the operational complexity of these trials as changes are made throughout the study.

The rollout of trials like I-Spy2 and Lung-MAP points to the exciting opportunities that will come when the industry begins to change the way clinical trials are designed based on the data available. But those opportunities are only possible if sponsors are able to tap into real-time flows of data and integrate disparate data sources.

Bugaboo Provincial Park, British Columbia

At a life science meeting in Canada, your delegates will exchange breakthrough ideas with some of the leading minds in medical research, medical equipment and pharmaceuticals. And afterwards they can experience some of the best leisure activities anywhere. Put the Business Events Canada (BEC) team to work for you and set the bar high for your next meeting, convention or incentive. As part of the Canadian Tourism Commission, we'll ensure your delegates have exciting landscapes to explore, both natural and urban. And of course, incredible venues to inspire them. **BusinessEventsCanada.ca**

BUSINESS EVENTS CANADA

KEEP EXPLORING

BioNetwork

The BioPharma Industry's Most Exclusive Partnering Summit...

Where Your Next Multimillion Dollar Deal Is Just A Handshake Away

---

October 27 – 29, 2014
The Ritz-Carlton, Laguna Niguel, CA
www.BioNetworkUS.com

Pharma & Big Biotech receive 25% off with the code: BN14LSL

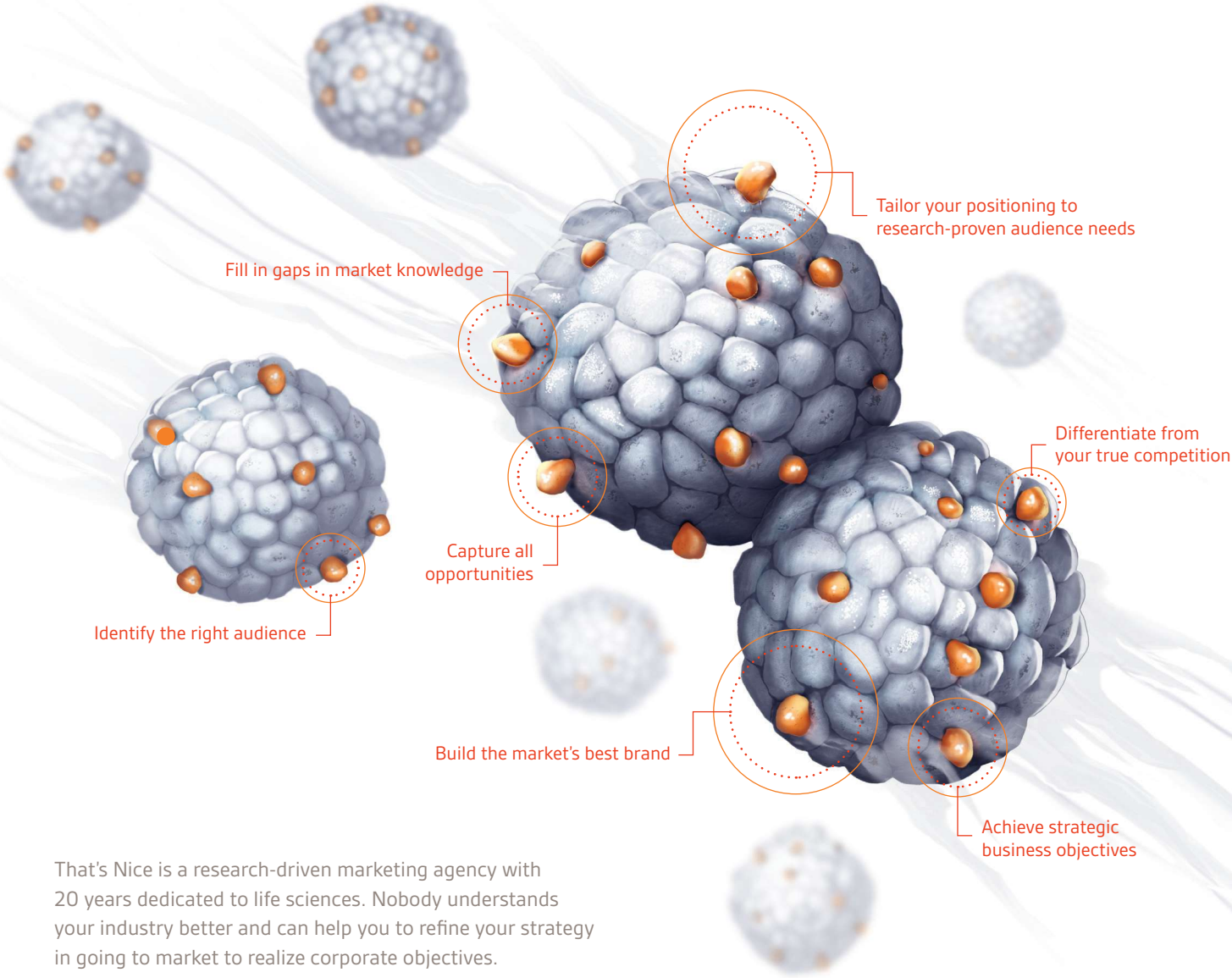
Lead Sponsors: CDRI CAPITAL · Evaluate™ · FOLEY HOAG LLP · GE Capital Healthcare Financial Services · INTRALINKS DEAL SPACE · MORRISON FOERSTER

Organized By: WORLDWIDE BUSINESS RESEARCH

Register Now: Call 888-482-6012 or 646-200-7530 · Email bionetwork@wbresearch.com · Web www.bionetworkus.com

thats nice
A Science Agency

Your science is targeted. Your message should be too.



That's Nice is a research-driven marketing agency with 20 years dedicated to life sciences. Nobody understands your industry better and can help you to refine your strategy in going to market to realize corporate objectives.

Research. Strategy. Results.

Proteins targeting prostate cancer cells

For more information, call +1 212 366 4455 or visit www.thatsnice.com

Meet your personal expert advisory board for managing external relationships.

Only at Outsourced Pharma West, a conference about partnerships for pharmaceutical development & manufacturing. Our panelists will lead you in discussion on business challenges to managing outsourcing relationships:

Andy Skibo,
RVP and EVP
ASTRAZENECA AND MEDIMMUNE

David Lowndes
SVP Supply Chain Management
SHIRE

Junning Lee
SVP Technical Operations
THERAVANCE BIOPHARMA

Christopher Haskell
Head US Science Hub
BAYER HEALTHCARE

Gerd Kochendoerfer
VP Technical Development & Quality
DEPOMED

... and MANY others!
View all panelists at outsourcedpharmawest.com

"I don't think we are very good at all in this industry with creating true and useful partnerships. At Outsourced Pharma West, we will be able to say, 'Listen, you've got to start thinking about this if you are really going to get the most out of strategic relationships.'"

PETER BIGELOW, PRESIDENT, XCELL STRATEGIC CONSULTING
OUTSOURCED PHARMA WEST PANELIST

PANEL DISCUSSION TOPIC HIGHLIGHTS:

- Establishing a balanced quality agreement
- Matching a vendor to your stage of development
- Supply chain planning/contingency planning best practices
- Phase to phase scale-up strategies
- FDA quality initiative update
- Qualifying CDMO capabilities

OutsourcedPharmaWEST
CONFERENCE AND EXHIBITION

HYATT REGENCY SAN FRANCISCO
NOVEMBER 10 & 11, 2014

814.897-7700 | INFO@OUTSOURCEDPHARMAWEST.COM
WWW.OUTSOURCEDPHARMAWEST.COM

co-produced by
BAYBIO Life Science Leader Outsourced Pharma

with support from
LIFE SCIENCE TRAINING INSTITUTE RONDAXE LIFE SCIENCES FOUNDATION

Seating at panel sessions is limited.
Rates increase on 9/10/14!

Register **today** and save with code EARLYt72uW

Special rate for BayBio members,
Portion of fee benefits BayBio Institute.
Call 814-897-7700 x174 for details

outsourcedpharmawest.com/attend/register

Empowered to Innovate

HBA 2014 Conference

Join us as we celebrate 35 years of empowering women as business and thought leaders in healthcare.

Meet **inspiring** leaders.
Gain **career** perspectives.
Make lasting **connections.**

Don't miss **your opportunity** to **attend** the HBA Conference, November 12-14, 2014, **in Chicago.**

Register at **www.hbanet.org**.

HBA HEALTHCARE BUSINESSWOMEN'S ASSOCIATION
REQUIRED EXPERIENCE FOR HEALTHY CAREERS

HBA | *Inspiring Leaders* Powering Innovation

25 Essential 21st Century Leadership Skills

JAMES STROCK

There are aspects of effective leadership that speak across time. For example, even after more than 150 years, Abraham Lincoln's Gettysburg Address still resonates. Vince Lombardi's coaching for excellence is every bit as timely now as 50 years ago. Nonetheless, one also recognizes differences. Would Lincoln have been able to succeed in today's media environment? Would Lombardi's "tough love" approach be accepted in our time? No one knows how historical figures might fare today, yet we can isolate leadership lessons that meet the needs in our time and place. The list that follows attempts to capture enduring leadership lessons within the unique, fast-moving circumstances of the early 21st century.

1. SERVICE FOCUS: In the Information Age, everyone is a potential relationship. A service mentality is not an ethical plus; it's required.

2. COURAGE AND SACRIFICE: Higher levels of service are the binding elements of effective leadership.

3. RELATIONSHIPS: Gaining advantage in isolated transactions cannot be the basis of a sustainable business model.

4. VALUE CREATION: Value is not based on how hard you've worked, or what you think you deserve, but solely on your customers' judgment.

5. VALUES CREATE VALUE: In a time of customer empowerment and commoditization, advancing the values of customers can be a potent differentiator.

6. VISION is the essential element of leadership.

7. MANAGEMENT is part of leadership: In an age of accountability, the boss is out, the coach is in.

8. BEST IN WORLD is the only sustainable model in our connected world.

9. LISTENING is the master skill in a relationship-based world.

10. QUESTIONS are better than answers; substitute the open ends of question marks for the closed ends of periods.

James Strock is an entrepreneur, professional speaker, and citizen servant. His books include *Serve to Lead: Your Transformational 21st Century Leadership System.* He can be reached at servetolead.org.

11. INFLUENCE: "The power to persuade" is now as necessary a skill for corporate CEOs as for politicians.

12. COMMUNICATION SKILLS cannot be delegated or outsourced; effective leaders must master an ever-evolving range of communications and expectations.

13. COLLABORATION: The smartest person in the room is always the room.

14. CREATE A STIMULATING ECOSYSTEM: Have a personal board of advisors. Search out mentors. Connect with people of accomplishment through social media.

15. INTERGENERATIONAL LEARNING: What are you learning from various generations?

16. INTERNATIONAL LEARNING: A world of customers, competitors, prospects, and resources is just a mouse click away.

17. RESILIENCE: You're less likely to have your falls hidden behind the walls of large institutions. Are you able to get off the mat, get back into the ring?

18. BREAK BOUNDARIES: Don't let others' limitations apply to you.

19. CULTIVATE AN EXPERIMENTER'S MINDSET: Innovation includes false leads and failures. Today's failure may be the basis of tomorrow's breakthrough.

20. OPTIMISM and alternative mindsets spread fast; it's a leadership decision, not a matter of individual temperament.

21. ENTHUSIASM is the universal spirit that remains compelling.

22. RELENTLESS ADAPTABILITY: The value of your service is determined by your capacity to evolve in rapidly changing circumstances.

23. VITALITY: Your physical, mental, and spiritual health constitutes the foundation of all service.

24. THINK LIKE AN ARTIST: Make every aspect of your experience a part of your evolution.

25. ACHIEVE INTEGRITY: The sum of your parts can be united into a whole that only you can create. L

ARE COLD CHAIN CHALLENGES IMPACTING YOUR COMMERCIAL POTENTIAL?

Coming Soon....

biologistex℠

HELPING CELLS ARRIVE ALIVE

Powered by:

BioLife Solutions®

BIOPRESERVATION TOOLS FOR CELLS, TISSUES, AND ORGANS

3303 Monte Villa Parkway, Suite 310 | Bothell, WA 98021 USA
1.866.4BioLife Phone | **www.BioLifeSolutions.com**

PRESERVATION CHAIN® Media Products

Source Material Cell Products

Get High-Quality Phase I Clinical Trial Materials in as Little as 12 Weeks


Blend in capsule


API in capsule

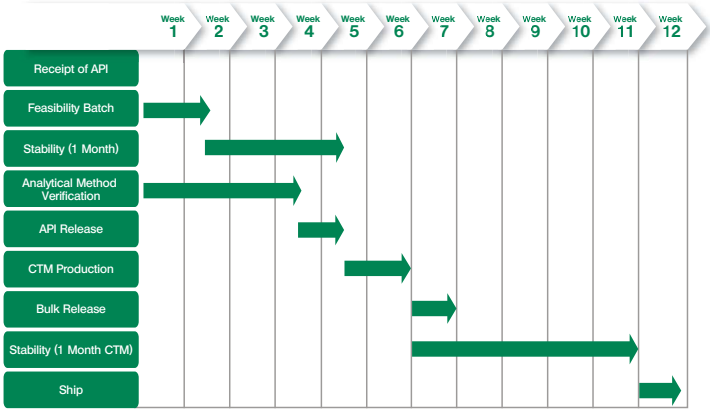

Blend in bottle


API in bottle


Oral liquid


Softgel capsules

More Speed. More Data. More Options.



The Quick to Clinic™ program by Patheon just got quicker. Now in as little as twelve weeks from receiving your API, you can have bulk clinical trial materials for First in Man trials. That's an entire month faster than before and includes clinical trial stability studies. What's more, this accelerated program gives you access to six flexible dosage forms.

Get Your Discovery to Clinical Trials Faster with Quick to Clinic™

Visit us at CPhI/ICSE booth 1H9

+1 866.PATHEON • www.patheon.com • doingbusiness@patheon.com

Patheon®
Performance the World Over®