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Bill Hait, M.D., Ph.D., global head of Janssen R&D

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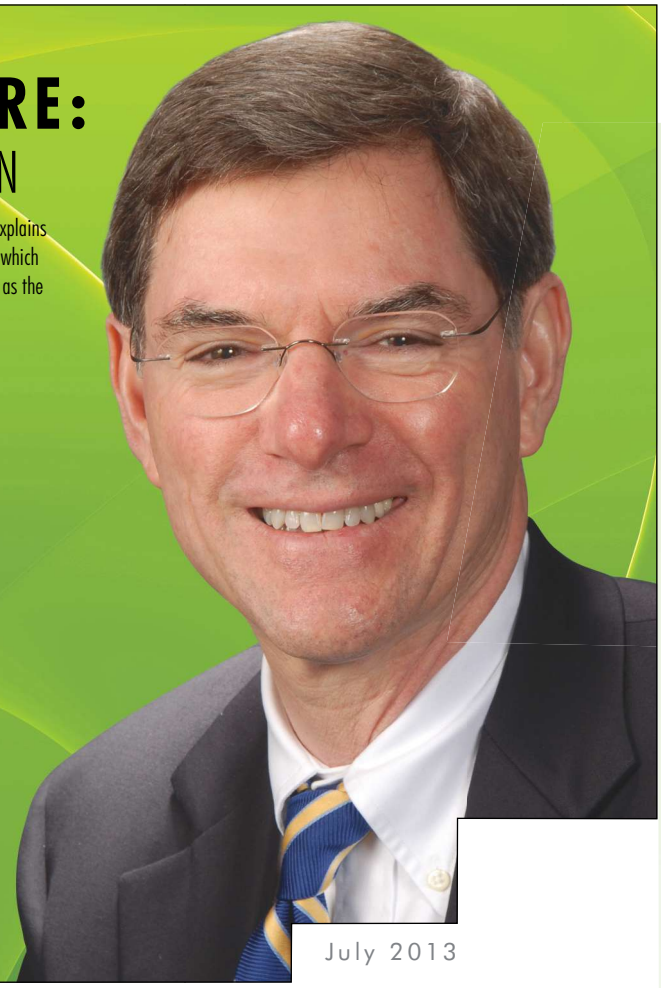
18 FEATURE: J&J/JANSSEN

Bill Hait, M.D., Ph.D., global head of Janssen R&D, explains some of the company's approaches to drug discovery which have resulted in J&J recently being ranked by *Forbes* as the most productive drug firm in the last 10 years.



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EDITOR'S NOTE

Is Closing Your Manufacturing Plant The Best Option?

This year there have been a number of companies announcing pharmaceutical manufacturing plant closures. For example, Catalent Pharma Solutions announced the closing of its Allendale, NJ, facility. Solgar Inc., a subsidiary of NBTY, announced the closing of its plant in Lyndhurst, NJ. These pharma manufacturing plant closings equate to 196 jobs lost for New Jersey. Jeremy Levin, CEO of Teva Pharmaceuticals, is looking at net income being down 26.7%. When income is down, companies look to cut costs. For Teva, one of the cost-cutting solutions is the proposed closure of the company's West Rockhill Township, PA, manufacturing facility, resulting in the loss of 450 jobs. That comes on the heels of Teva's previously announced closing of a plant in Irvine, CA and its 403 jobs. These are tough decisions and have a lasting impact on the families of 1,049 people. Having been laid off before, I know how it feels. You tell yourself it is just business and not to take it personally — this is easier said than done. The business decision to close a plant has a negative ripple effect on the economy as those who are unemployed begin spending less, stop contributing to 401K investment plans, pay fewer taxes, and draw unemployment. But what if you didn't have to close the plant?

In St. Louis, MO, there is a 27-year-old biopharmaceutical manufacturing facility that has been part of Wyeth, Pfizer, and most recently J&J. Had Mark Bamforth (who worked for Genzyme at the time) gotten his way, it would have become part of the Boston-based biotech. Twice he tried to negotiate purchasing the site for his former employer, and twice the decision was made not to proceed with the acquisition. Bamforth was so impressed with the people at the facility he set out to buy it himself, successfully closing the financing to purchase the site in May 2011. Today, Bamforth is the president and CEO of Gallus BioPharmaceuticals, a unique start-up — profitable from day one with a 27-year history. He credits his company's success to the former J&J staff he retained who weren't interested in selling the site but instead wanted to create a sustainable, separate business.

Facing a similar decision of having to close a facility within your company? Perhaps you should consider the option of selling in order to position your business for success. J&J's approach may have required a little more effort, but instead of having 160 employees collecting unemployment, they are now contributing positively to the U.S. economy.

In this month's issue, I interview Dr. Bill Hait, an executive with J&J (see page 18). During our discussion, Hait commented, "Doing good in the world. That's what ethical companies do." For example, J&J developed Remicade, the first drug specifically approved for patients with moderate to severe Crohn's disease, an ailment which affects less than 0.2% of the U.S. population. The company didn't set out to create a blockbuster. It set out to fill an unmet medical need. The drug has since gone on to receive 15 additional indications, and in 2012, generated $6.1 billion in sales. Interestingly enough, Gallus BioPharmaceuticals is one of the facilities which manufacture Remicade, as well as another J&J product, Stelara. As you can see, J&J has a vested interest in Gallus being successful but not just because the J&J family of companies appears on the products label. It's what ethical companies do.

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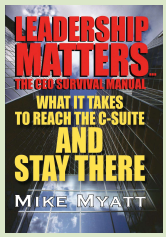

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Q: What is the biggest mistake you have seen a c-level leader make?

One thing I see occur with some regularity is the lack of collaboration in the c-suite. I hold the CEO accountable. The CEO may ask the executive team to work together but does not hold them accountable when they do not. Therefore they drift into their own silos and act more territorially than cross-functionally.

It's the CEO who must insist that senior executives meet formally and informally to share insights and expertise with one another. Naturally there is a hesitation to meddle, but diversity of thought emerges from diversity of discipline. The CEO must follow through and ask the team how they are collaborating and what they have to show from the collaboration. Such a discussion elevates the issue and makes it actionable.

John Baldoni
Baldoni is an internationally recognized leadership development consultant, executive coach, author, and speaker. John teaches men and women to achieve positive results by focusing on communication, influence, motivation, and supervision.

Q: What specifically should pharma do to repair its broken image?

First, use scientists and patients to teach the value pharma brings to healthcare. The R&D of new medicines is a difficult process. No one can teach this better than the scientists who work on these programs. Second, make clinical trial results available in a timely fashion. Industry critics are eroding public trust by complaining that pharma has been slow to make trial results available. The public is becoming convinced the industry is hiding negative data. Greater transparency will show this to be false.

Third, stop the illegal detailing of drugs. There is nothing more demoralizing than to hear that a company has been fined billions of dollars for breaking the law, which further convinces the public that pharma is run by shady operators. Finally, drop the TV ads. Though informative, the problem is most are distasteful with many of the ads discussing side effects.

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

Q: Beyond the typical benefits of centralized data storage and scalability, do cloud-based tools offer any other practical applications for the pharma industry?

Cloud-based tools play a key role as pharma looks to virtual patient communities and the data these communities generate for indicators of patient outcomes in clinical trials. Eventually, the data generated by advanced sensor/actuator technology in the smartphones and other devices used by patients will find its way to the cloud for analysis and mining, perhaps by pharmas again in the context of a trial or related investigation. Finally, the scientific advances in genetics and simulation will be much more powerful when made searchable/analyzable in a cloud-based environment, and we'll see the impact of that in the next couple of years across the broader community.

Angela Yochem
Yochem previously was the CTO at AstraZeneca, where she formed strategic partnerships to drive innovation and business advantage through technology. She also has held senior roles at Dell, Bank of America, SunTrust, UPS, and IBM.

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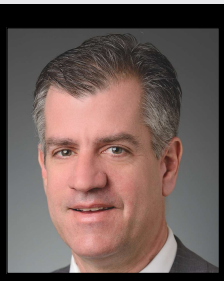
Washington's Baseless Sense Of Complacency On Entitlement Reform

For more than a year, Washington was gripped with the prospects of a grand bargain whereby the country would finally put its fiscal house in order and the two parties would come together on a package of shared sacrifice of entitlement cuts and revenue increases.

But no longer. President Obama lackadaisically issued his budget blueprint two months late. And other than reducing projected inflation updates for Social Security and marginal tax rates, it contained no bold ideas. No fundamental Medicare reform was put on the table, despite bipartisan interest, and no real savings proposed at all from either the burgeoning Medicaid program for the poor or Obamacare itself, which the President's own actuaries had already predicted to be massively more expensive than initially forecast.



John McManus,
The McManus Group
jmcmanus@mcmanusgrp.com

Then in May, the Congressional Budget Office (CBO) observed that the annual deficit will shrink to $642 billion this year, down from the $1 trillion plus annual deficits that the Obama Administration has racked up every year in office. A combination of higher revenue from the fiscal cliff deal, profits from Freddie and Fannie, the budget sequester, which is effectively cutting discretionary spending, and slowing health costs have led to the improved budget outlook.

As a result of these developments, the date when Congress will have to enact an increase to the debt ceiling has been pushed back from May to November, and a feeling of sanguinity has enveloped the capital that all is well with the nation's finances and no further action is necessary at this time.

Nonetheless, the fundamental fiscal challenges that confront the country in the long-term have not changed:

Federal debt held by the public is projected to remain historically high relative to the size of the economy for the next decade at 77% of GDP — a level not hit since the 1940s when the nation had to finance the massive undertaking of World War II.

Both revenues and outlays over the next 10 years are projected to be substantially above their 40-year averages: Revenues will grow from 15.8% of GDP in 2012 to 19.1% of GDP in 2015 compared to a historical average of 17.9%. Although outlays have fallen from their 2009 high of 25.2% of GDP, they will still remain well above the historic average of 21%.

Medicare costs under the U.S. Trustee's current law assumptions will rise from their current level of 3.6% of GDP to 5.8% in 2040 and 6.5% in 2087. Under a more realistic forecast, in which the slated 25% physician-payment cuts are not allowed to go into effect, Medicare costs will rise to 6.1% of GDP in 2040 and 7.2% in 2087.

With 11,000 Baby Boomers aging into Medicare every day, the country still has not fundamentally prepared for the demographic shift of a ballooning aging population living longer and using more Social Security and Medicare resources with fewer workers to support them.

More troubling is that the Medicare Trustees report, which is supposed to inform policy makers on the health of the Medicare program, is entirely detached from the fundamental fiscal strains the country confronts to finance the program. For example, this year's report produced headlines in newspapers across the country of an improving fiscal picture — Medicare's trust fund will go broke in 2026, two years later than last year's projection.

Yet that factoid totally obscures the reality that Medicare is massively underfunded because the Medicare trust fund only records dedicated payroll tax revenue and premiums for Medicare inpatient spending. All outpatient spending — physician services, prescription drugs, hospital outpatient departments, etc. — is financed just 25% through beneficiary premiums and 75% from general revenue. Since healthcare is increasingly migrating to the outpatient setting, the solvency of the inpatient Part A Trust Fund really is not relevant to the financial obligations taxpayers have for financing seniors' healthcare.

A snapshot of 2012 demonstrates the extent of the budgetary sleight of hand in mixing dedicated funding sources with General Fund revenue. In FY 2012, Social Security and Medicare benefits cost $1.32 trillion. Payroll taxes, Medicare premiums, and other fees for these programs equal $920 billion, creating a deficit of $403 billion — $243 billion for Medicare and $160 billion for Social Security. This shortfall has to be covered by general revenue and is a driving force behind the budget deficit.

The Trustee's long-term outlook is even more foreboding with a 50% shortfall for Social Security and Medicare over the next 75 years, where dedicated taxes and premiums will only cover $73.2 trillion of the expected $112.8 trillion of spending.

Things aren't getting better. They are getting worse more slowly.

And what is the administration's answer to this? On "Good Morning America" on March 13, President Obama said, "We don't have an immediate crisis in terms of debt. In fact, for the next 10 years, it's gonna be in a sustainable place."

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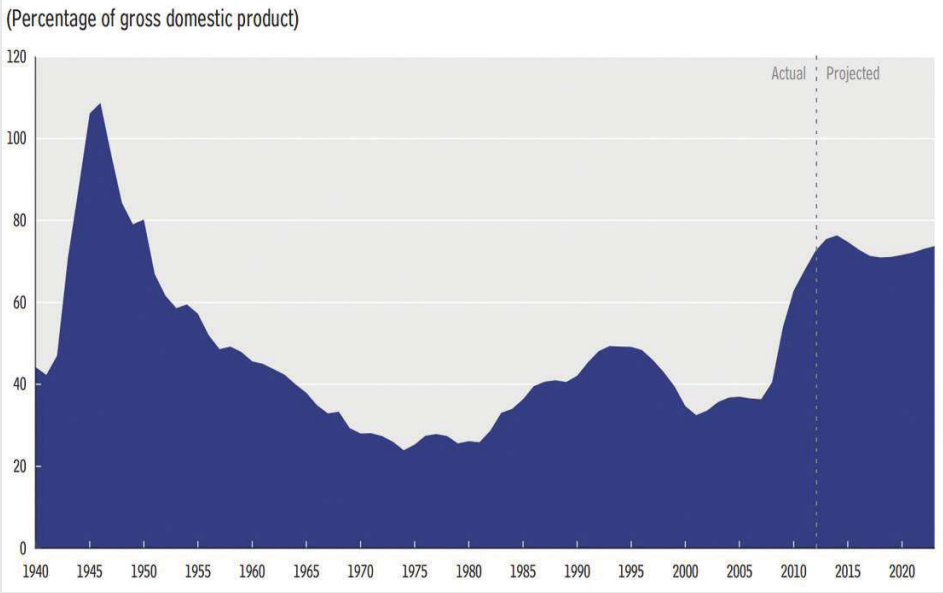


Source: CBO, Updated Budget Projections: Fiscal Years 2013 to 2023 (May 2013)

What is sustainable about the two-pillar entitlement programs for the elderly being underfunded by 50%, to say nothing of his entirely new health program or Medicaid?

WHAT SHOULD BE DONE?

First, we as a country must recognize that although there has been marginal improvement in the fiscal situation, the fundamental problems remain. Second, we must acknowledge today's seniors and future seniors are entitled to and will receive far more in benefits than they ever paid into the system. Third, seniors need to have more skin in the game and become actively engaged in making decisions that will save resources for both the system and themselves.

For Medicare, this means we must move to a more competitive system and away from the command and control of price-by-government fiat. This has been done already to great success in Medicare Part D, where seniors get to choose the prescription drug plan that best fits their needs and share in the savings when they make economical choices through lower premiums. But the entire system should move in this direction. If seniors want to remain in the present government-run system, then they should pay the difference between that system and competing health plans that can offer the same benefits for less.

In addition, the current Medicare fee-for-service program's cost-sharing requirements should be modernized to better align beneficiary choices with costs. For example, healthcare reform made preventive benefits entirely free to beneficiaries, thereby masking massive price differentials for the identical service provided in different sites of care. A Medicare beneficiary does not know that a diagnostic colonoscopy is twice as expensive in a hospital as it is in an ambulatory surgery center.

Similarly, millions of Medicare beneficiaries have Medigap plans which provide supplemental first-dollar coverage, making almost all benefits appear free to the beneficiary. CBO has estimated that simply prohibiting first-dollar coverage of Medigap would save over $50 billion.

But all of these ideas are moot if the President and Congress fall into a false sense of complacency that the fiscal situation is fundamentally sound and no action is necessary.

Skeptics will say that divided government produces paralysis. I say that divided government actually is essential for changes of this magnitude because it requires both parties to offer their ideas and take ownership of the solutions.

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. He can be reached at jmcmanus@mcmanusgrp.com.

By Wayne Koberstein, executive editor

Soligenix

Strong federal support and a unique model centered on biodefense therapeutics and vaccines drive this company — and our interest in it.

SNAPSHOT

Soligenix is a public, biopharma company primarily focused on developing new vaccines and "BioDefense" treatments for public threats such as ricin and radiation, as well as "BioTherapeutics" in cancer and other conditions — with strong federal support. Its product of most current interest is RiVax, a vaccine to protect against ricin poisoning, now entering Phase 2. RiVax has received U.S. federal funding and, if approved, would likely be purchased under government contract. OrbeShield, a therapeutic for GI Acute Radiation Syndrome (GIARS), was also largely funded by the government, which will be its primary customer. In the bigger picture, the company is developing the ThermoVax platform, which could eliminate the cold chain for many vaccines.

Christopher Schaber, Ph.D., Soligenix

LATEST UPDATES

- June 2013: FDA granted Soligenix "fast-track" status for Phase 2 therapeutic SGX942 for oral mucositis in head and neck cancer.
- May 2013: Soligenix and Intrexon announced a partnership to develop therapeutic mAbs for melioidosis.
- Initiated Phase 1 study with SGX203 for pediatric Crohn's Disease.

WHAT'S AT STAKE

I almost feel as if there's no need to say very much about why Soligenix is a company to watch. These days, all I should have to say is "ricin." But I could also say "anthrax, radiation enteritis, GI graft vs. host disease," or any of the key areas addressed by the company's pipeline products — as well as any number of future vaccines that may someday benefit from its heat-stabilizing ThermoVax technology. Aside from the current government interest, its ricin vaccine is not the main thrust of the company, according to its president and CEO, Christopher Schaber, Ph.D. "We are excited about all of our potential development candidates, most notably in the near term, SGX203 [pediatric Crohn's Disease], where we plan on initiating a Phase 2/3 study in the second half of 2013 with primary endpoint data in the second half of 2014, and SGX942 [oral mucositis in head and neck cancer], where we also plan on initiating a Phase 2 study in the second half of 2013 with primary endpoint data available in the second half of 2014." ThermoVax, now being applied to the ricin and anthrax vaccines, along with OrbeShield for GIARS, is further back in the pipeline but easily equal in importance to RiVax.

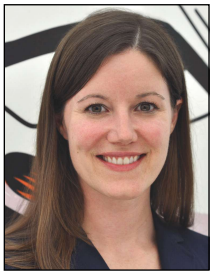
Unmet medical need goes beyond specific conditions or diseases. One significant but more general need in the vaccine area is for greater stability. Like many biologics, vaccines have traditionally faced the hurdle of temperature and, thus, required an expensive and often impractical cold chain, hindering distribution to areas without reliable, or any, refrigeration. Schaber says its ThermoVax-based vaccines can be stored for more than six months at up to 40 degrees Celsius. "With this technology, we can now pursue partnerships with other vaccine companies and nonprofit groups that are looking to take their already marketed or development vaccines out of the refrigerator and stabilize them for room temperature storage."

Soligenix is still in the early stages of partnerships. "A small biotech company like ours must remain opportunistic, looking at all avenues to move the company and our programs forward while maximizing shareholder value," Schaber says. The recently announced alliance with Intrexon adds yet another area to its disease focus — codeveloping a therapy for the potentially fatal infection melioidosis, caused by the gram-negative bacteria burkholderia pseudomallei. He feels confident in the management talent as well as the science Intrexon brings to the table, citing its chairman and CEO, R.J. Kirk, as "a well regarded figure in the life sciences industry for his many successes."

For its unique funding and business model, its novel technologies and products, and for its partnering potential, Soligenix will remain a company to watch well into the future. Whether it remains in the headlines once the ricin scare fades is yet to be determined. But considering the company's orientation toward some of society's greatest recurring terrors and threats, it will not likely stay in the shadows for long.

VITAL STATISTICS

- Employees: 10; Headquarters: Princeton, NJ.
- Finances: Public company (SNGX - NASDAQ) Market Cap: $20 million. No debt or preferred stock outstanding.
- Research partnership funding: More than $25 million in FDA, NIH, DoD and BARDA grants, including a $9.4 million grant from the NIAID to fund ThermoVax.
- Partner: Intrexon Corp.



OUTSOURCING INSIGHTS

Prefilled Syringe Technology Benefits Patients, Healthcare Providers, And Drug Makers

By Kate Hammeke, director of marketing intelligence, Nice Insight

According to the World Health Organization, 1.3 million people die each year from unsafe injection practices such as needle sticks, blood-born pathogens, and the reuse, sharing, and unsafe disposal of syringes. As more parenteral drugs come on the market — driven by the increase in biological drugs that must be injected into the body — it is important that improved safety measures accompany these medications. Technology is playing a part in improving injectable drug safety with the introduction of retractable safety syringes to prevent needle sticks, and prefilled syringes — with or without retractable needles — to improve patient safety and compliance and reduce the likelihood of contamination at the injection site.

According to Visiongain's report, "Prefilled Syringes: World Market Outlooks 2011-2021," prefilled syringes represent one of the fastest growing markets in drug delivery and packaging, with total revenues expected to reach $5.5B by 2025. Prefilled syringes also offer one of the highest growth potentials in the biopharmaceutical industry, with 20% CAGR over the past five years. There is good reason for this growth, as prefilled syringes are arguably a win for all. They offer improved safety for the patient by mitigating dosage errors; healthcare providers have faster access to injectable medications in pre-measured doses, and manufacturers save money through reduced overfill wastage that occurs with vials. In addition to the healthcare benefits, prefilled syringes also offer marketing differentiation for drug makers.

STRENGTH IN REGULATORY AND PRODUCTIVITY

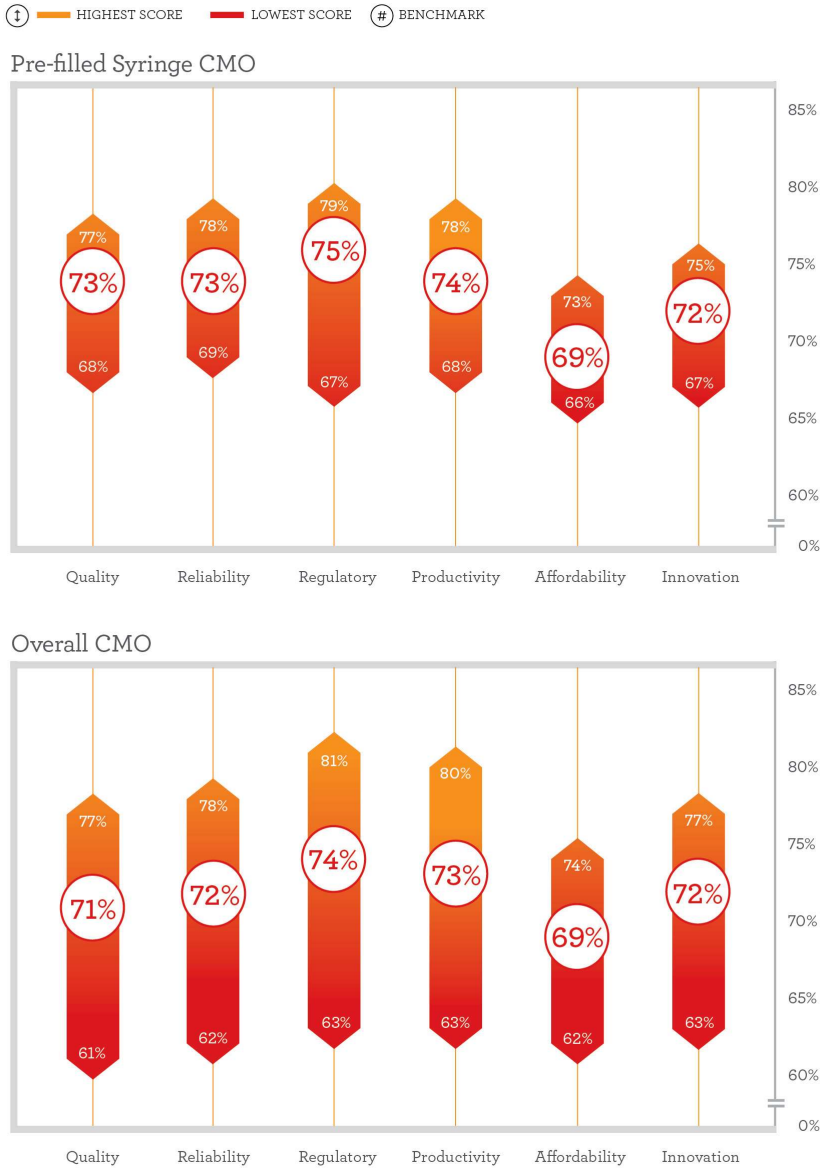
Twenty CMOs included in Nice Insight's annual research offer services for prefilled syringes. We reviewed how the market perceives these brands with respect to the six outsourcing drivers and learned that their strengths lie in regulatory and productivity categories, which were ranked respectively third and fourth in order of importance by buyers of CMO services. On average, regulatory scores among CMOs that offer prefilled syringes were a point higher than the general CMO benchmark for regulatory, 75% vs. 74%. This bodes well for drug innovators concerned about the regulatory challenges that accompany the transition from vials to cartridges. And fortunately for outsourcers, 16 of the 20 CMOs that offer prefilled syringes also provide regulatory support. Productivity was the second highest scoring category for CMOs offering prefilled syringes. Again, we found the average score among these CMOs to be one percentage point higher than the general CMO benchmark for productivity, 74% vs. 73%.

Quality and reliability traditionally score high among buyers of outsourced services. Here, they tied for third place among prefilled syringe CMOs. The two factors were additional areas where these CMOs received higher scores than the typical, broader benchmarks. The average among the prefilled syringe subset was 73% for quality, two percentage points higher than the CMO benchmark of 71%. There was also a single percentage point increase in the reliability benchmark between CMOs offering prefilled syringe services and the broader grouping, 73% vs. 72% respectively.

Innovation often holds sixth place among the outsourcing drivers when ranked by survey respondents, but when viewed from the perspective of CMO performance perceptions, it was ranked one place higher—in fifth. With an average score of 72% among CMOs that offer prefilled syringes, the innovation score was the same as the broader CMO benchmark (72%). The prefilled syringe subset also averaged the same score for affordability as the mainstream CMO benchmark, each at 69%. Affordability tends to be the lowest scoring category regardless of groupings (CMOs, CROs, and service or technology related subsets), which should not come as a surprise since drug innovators are consistently facing cost pressures and the overarching goal of reducing drug development expense.

In this instance, however, poor affordability may be a misconception of sorts, as prefilled syringes have proven to be cost effective for several reasons, including the increased durability of plastic-based prefilled cartridges over traditional glass products that may crack or break, as well as the reduced overfill when compared to vials. The logistics associated with distributing prefilled syringes offer some cost benefit over traditional vials as well. For example, prefilled syringes weigh less and take up less space, which saves on both shipping and storage. In addition to cost efficiencies for drug developers, patients save money by self-administering drugs instead of going to a doctor's office or infusion center — another area where the prefilled technology proves to be a win for all.

NI Drivers that Influence Outsourcing Partner Selection



Survey Methodology: The Nice Insight Pharmaceutical and Biotechnology Survey is deployed to outsourcing-facing pharmaceutical and biotechnology executives on an annual basis. The 2012 sample size is 10,036 respondents. The survey is composed of 500+ questions and randomly presents ~30 questions to each respondent in order to collect baseline information with respect to customer awareness and customer perceptions on 170 companies that service the drug development cycle. More than 800 marketing communications, including branding, websites, print advertisements, corporate literature, and trade show booths, are reviewed by our panel of respondents. Five levels of awareness from "I've never heard of them" to "I've worked with them" factor into the overall customer-awareness score. The customer-perception score is based on six drivers in outsourcing: Quality, Innovation, Regulatory Track Record, Affordability, Productivity, and Reliability.


Walker

If you want to learn more about Nice Insight's CRO/CMO report or to participate in the survey research, please contact Managing Director Nigel Walker of That's Nice at nigel@thatsnice.com. If you have a question about the data or are interested in custom market research, contact Kate Hammeke at kate.h@thatsnice.com.

BIO INNOVATION NOTES

Demand For Innovation In High-Value Bioprocessing

Caution inhibits adoption of new technologies

By Eric Langer, president and managing partner, BioPlan Associates, Inc.

Downstream processing is where drug products in biomanufacturing operations have their highest value. The biologic about to be purified has undergone many prior unit operations, and the costs in material, equipment, and labor can reach well over a million dollars per batch. So this uniquely sensitive area demands careful implementation of changes and improvements. This caution may be one reason that sorely needed innovation in downstream processing continues to be slow in coming.

Results from our 10th Annual Report and Survey of Biopharmaceutical Manufacturers indicate that industry interest in innovation in downstream processing continues. This year, we evaluated dozens of areas of innovation. In downstream operations, for example, innovative, single-use, disposable, tangential flow filtration (TFF) systems are one of the top five new downstream purification technologies under consideration for adoption, cited by 34.9% of respondents to our study. Also seeing strong interest are in-line buffer dilution systems (36.5%), buffer dilution systems/skids (38.1%), and single-use filters (44.4%). But topping the list is interest in high-capacity resins (54%).

Interest in disposable TFF systems appears to have stabilized this year at ~35% of respondents, after rising from 27.8% in 2010. Interestingly, while levels of interest in TFF systems remain, that isn't the case for other downstream technologies we evaluated. For example, in-line buffer dilution systems (36.5% vs. 45.2% in 2010), continuous purification systems (27% vs. 34.8% in 2010), and alternatives to chromatography (20.6% vs. 24.3%) have gradually declined in interest over the years. Conversely, those at the top are seeing steadily increasing consideration, with healthy growth in interest for high-capacity resins (54% vs. 43.5% in 2010) and single-use filters (44.4% vs. 28.7% in 2010).

Some of the decline in interest is the innate conservatism associated with the back end of the process. In addition, the capacity crunch associated with downstream bottlenecks has lifted somewhat as facilities fix bottlenecks in their current systems with incremental improvements.

CMOs LEADING CHANGE

When we sort responses by biotherapeutic developers vs. CMOs, an interesting picture arises, one that may point to future growth for single-use disposable TFF membranes.

In our previous column, we noted that CMOs often act as leading indicators of industry adoption of innovative practices. When looking at innovation in downstream purification, we note that single-use disposable TFF membranes are the top new technologies under consideration by CMOs, cited by half of those respondents, along with use of high-capacity resins and single-use filters.

Notably, the gap in interest between CMOs and biodevelopers was larger for single-use TFF membranes than any other technology. While half of our CMOs demonstrated an interest in innovation in this area, just 32.1% of biodevelopers concurred, a 17.9% point gap. We found a similar discrepancy in last year's study, with CMOs way ahead of the curve in tangential flow filtration demand (55.6% expressing interest, versus 35.6% of biodevelopers). The upshot is that as biodevelopers close the gap with CMOs, we are likely to see greater industry pressure for adoption of these devices.

ADOPTION OF TFF DEVICES HAS GROWN

There are signs that acceptance of disposable TFF devices is already growing. This year, we found that among users of disposables, three-quarters of them report using tangential flow filtration devices at some stage of biopharmaceutical manufacturing. That's the result of a slow, gradual increase from 71.8% in 2007, which in itself came after a big jump from 43.5% in 2006.

And while TFF devices have been one of the faster-growing applications over the past 7 years (+8.1% compound annual growth rate between 2006 and 2013), others have grown faster, with membrane adsorbers, bioreactors, and mixing systems each seeing a ~20% point CAGR in adoption in that time frame. Surprisingly, adoption of TFF devices (at any stage of manufacturing) is slightly higher among biotherapeutic developers (75.6%) than CMOs (71.4%). This result, combined with the finding that CMOs may be more interested in TFF innovation, suggests that biodevelopers are content with existing TFF technologies, while CMOs are the ones pressing for more innovation.

WHERE TO FROM HERE?

Of course, tangential flow filtration devices are but one of many downstream purification innovations that the

industry is seeking. Purification is an area of industry concern in 2013. In fact, the 450 global subject matter experts and industry manufacturers on our Biotechnology Industry Council pointed to aspects of downstream purification as one of their most critical trends of the year.

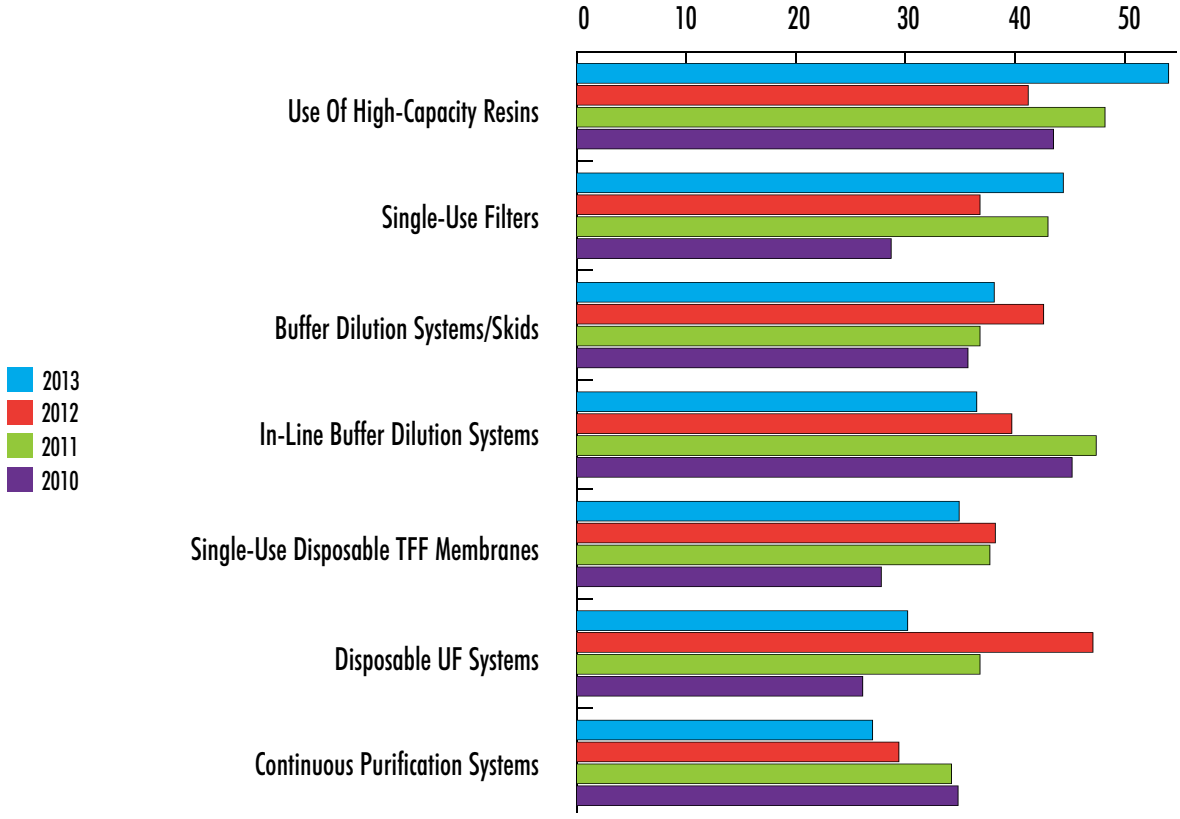
The range of solutions being sought and proposed to downstream purification problems is evident in the responses from our panel. For example, several micro-trends in downstream bioprocessing include:

- alternatives to Protein A
- purification related to impurity profiles in biosimilars
- bioburden control in chromatography columns
- improving overall harvest operations.

As our studies show, some innovations will become integrated over time to resolve chronic problems, while others will fade as the acute urgency for solutions is resolved.

Downstream Purification Technologies Being Considered (%) 2010-2013

Source: 10th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production, April 2013



Survey Methodology: The 2013 10th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production is an evaluation by BioPlan Associates, Inc. that yields a composite view of and trend analysis from 300 to 400 responsible individuals at biopharmaceutical manufacturers and CMOs in 29 countries. The respondents also include more than 185 direct suppliers of materials, services, and equipment to this industry. Each year the study covers issues including 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, 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.

If you want to learn more about the report, please go to bioplanassociates.com.

Bill Hait, M.D., Ph.D., global head of Janssen R&D

Big Pharma Bets Big On Breakthroughs

J&J's Approach To Drug Discovery

By Rob Wright, chief editor

One year ago, the Food and Drug Administration Safety and Innovation Act (FDASIA) was signed into law. Its most current version includes a provision that allows sponsor companies to request their drug be designated as a "breakthrough therapy." In February, Johnson & Johnson (J&J) became only the second company (behind Vertex Pharmaceuticals) to have a drug receive this designation.

The drug, ibrutinib, is an oral Bruton's tyrosine kinase inhibitor. Thus far, ibrutinib has garnered three breakthrough designations (mantle cell lymphoma, Waldenström's macroglobulinemia, and a subset of patients with chronic lymphocytic leukemia who have a particularly poor prognosis) of the more than 40 requests the FDA has received. In addition to this success, J&J recently won accelerated FDA approval for Sirturo (bedaquiline), the first drug with a new MOA (mechanism of action) for tuberculosis (TB) to be approved in 40 years. It seems J&J's pharmaceutical business is on a roll.

Driven by its R&D engine, Janssen Research & Development, J&J has been capitalizing on FDA initiatives that not only incentivize drug innovation but also reward successful companies. Bill Hait, M.D., Ph.D., is the global head of Janssen R&D. He explains some of the company's approaches to drug discovery that have resulted in J&J recently being ranked by *Forbes* as *the* most productive drug firm in the last 10 years.

FOCUS ON UNMET MEDICAL NEED CAN OFFER BIG WINS

It might seem clichéd in drug discovery to say, "Focus on the unmet medical need as opposed to commercial viability." But being altruistic also can lead to big dividends. For example, in 1998 Remicade (infliximab) was the first drug specifically approved for patients with moderate to severe Crohn's disease, a bowel ailment that afflicts approximately 500,000 Americans. This equates to .16% of the U.S. population. At the time, there were conventional, less-expensive treatments available, including steroids and antibiotics. If Centocor (now Janssen) had not pursued approval of this drug based on the relatively small commercial market (designated fast-track, orphan drug status, priority review), the company would have missed out on significant sales revenue, including $6.1 billion

HOW TO APPLY FOR THE BREAKTHROUGH THERAPY DESIGNATION

Keeping up with global regulatory changes can be a challenge for a small or virtual pharmaceutical/biotech. If you have a drug in development that might qualify for the breakthrough therapy designation, here is what you need to know.

The request for the designation should be submitted concurrently with, or as an amendment to, an Investigational New Drug (IND) application with a cover letter and a completed form 1571 with the following information, which in most cases should be explained in approximately 10 to 20 pages:

If the breakthrough therapy designation request is submitted to the sponsor's IND as an amendment, the cover letter should indicate the submission as a REQUEST FOR BREAKTHROUGH THERAPY DESIGNATION in bold, uppercase letters. If the request is submitted with an initial IND, the cover letter should indicate the submission as both an INITIAL INVESTIGATIONAL NEW DRUG SUBMISSION and a REQUEST FOR BREAKTHROUGH THERAPY DESIGNATION in bold, uppercase letters.

- the name of the sponsor's contact person and the person's address, email address, telephone number, and fax number
- if applicable, the IND application number
- if available, for drug products, the proprietary name and active ingredient and, for biological products, the proper name and trade name
- the division or office to which the IND is being submitted or in which it is active
- the proposed indications
- a concise summary of information that supports the sponsor's breakthrough therapy designation request for the indication being studied, including:
    - the basis for considering the drug as one intended to treat a serious condition
    - the preliminary clinical evidence that the drug may demonstrate substantial improvement over available therapies (A sponsor should describe the preliminary clinical evidence, including, for example, justification for the clinical study endpoint used and a brief description of statistical analyses.)
    - if applicable, a list of documents previously submitted to the IND considered relevant to the designation request, with reference to submission dates. Paper submissions can be resubmitted to FDA as appendices to the designation request.

If you do everything properly, you will find out whether your application has been granted or denied within 60 days. For more information, you can visit the FDA website, which provides contact information for breakthrough therapy coordinators, frequently asked questions, and other useful information at http://goo.gl/Cl13M.

*Information derived from FDA website under Fact Sheet: Breakthrough Therapies

generated by Remicade in 2012. Currently the drug represents nearly 25% of the company's pharmaceutical sales. Since its initial approval, Remicade has received FDA approvals for 15 additional indications, which have not only dramatically increased the commercial viability of the drug, but also more importantly, have benefitted far more patients than the initial single indication. Hait cautions against using potential commercial success as the only criterion for pursuing a drug for approval, pointing to the first new treatment for TB in 40 years.

In December 2012, the FDA granted accelerated approval for Sirturo as part of a combination therapy to treat adults with pulmonary multidrug resistant TB (MDRTB). Presently there are approximately 100 cases of MDRTB annually in the United States and about 500,000 cases globally. If you thought the initial market for Remicade was small, Sirturo's market, by comparison, is downright microscopic. "If commercial success were the only criterion, you probably would not go after a drug for TB," says Hait. "You need to place some bets on drugs you think are going to have a major impact for doing good in the world. That's what ethical companies do." Consider this — globally, one in every three people already carries the germ (bacterium) that causes TB. Once TB becomes active, and if left untreated, as many as half of those afflicted will die. "It's a huge problem," attests Hait. According to Hait, it is important to balance your company's portfolio with commercially viable candidates against those, which on the surface, may have less commercial appeal, yet could prove to be hugely important to humankind and help the company maintain an innovative culture.

Sirturo had been in development for nearly a decade. Yet Hait assures that the drug was neither sitting on a shelf in limbo nor a pet project for which researchers allocated a small percentage of their time. "It was a drug that had a very dedicated small team in our labs in Belgium, who were continuously gaining a fuller understanding of how it was going to work and be used," he explains. If the drug had been killed based on its small potential commercial market, it could have been a devastating blow to the morale of the R&D team. "It's really important for the culture to keep those projects going — when they are working," reminds Hait. Perhaps Sirturo has the possibility of additional indications, or it could lead to other breakthroughs arising from the research. Only time will tell. Although Hait expresses the importance of keeping projects going as they can lead to other research and serve as morale builders, even a company the size of J&J can't fund every project. Sometimes it is necessary to find other opportunities for lower priority projects — thus the development of the J&J innovation incubator.

To prioritize drug development, J&J uses a model that started in Janssen's oncology R&D unit and expanded across all therapeutic areas. "We define the highest-priority diseases within each therapeutic area," says Hait. "For example, in immunology, we define

rheumatoid arthritis, inflammatory bowel disease, and psoriasis as our top areas of investment." Hait uses the following questions to determine which drugs to move forward internally. What is the unmet need? How compelling is the science? How innovative is the product? Does the drug work, and how well? How different is it from other drugs in the space, or those being advanced by other companies? In addition, the company calculates the net present value for all of the company's drug assets to assist in prioritizing. This calculation becomes more precise as the drug develops, as a lot of preliminary calculations are based on the probability of technical and regulatory success (see sidebar "Approaches For Calculating Net Present Value [NPV] For Drug Discovery"). "If the drug isn't highly innovative, differentiated, with high activity early on, it gets killed very early," he attests. "Low activity, a me-too type of drug, all sorts of problems in early development, or preclinical toxicity issues should be red flags to kill a drug quickly." There are other reasons to focus on unmet medical needs as well; namely, the FDA has created incentives for those companies that do and gives rewards for those that are successful.

FDA INCENTIVIZING BREAKTHROUGHS, NOT BLOCKBUSTERS

The FDA's breakthrough therapy designation was enacted to expedite the development and shorten the review time for potential new medicines to treat serious or life-threatening diseases. If preliminary clinical evidence indicates that a drug may demonstrate substantial improvement over existing therapies on one or more clinically significant outcomes, such as substantial treatment effects observed early in clinical development, it may qualify for the breakthrough designation. Janet Woodcock, M.D., director for CDER (Center for Drug Evaluation and Research) at the FDA, remarked in February that it will be possible to win approval based on expanded Phase 1 clinical data. The benefit to a company of getting the breakthrough designation is a quick review, possibly shaving significant time from this traditionally slow process. "It is one of the most exciting FDA incentives for us at the moment," says Hait. "If you are working on a risky project where you think there is the potential to be substantially better than anything that exists for patients in this area, it gives you an incentive to take that risk."

According to Hait, one of the benefits of gaining this designation is the change in the relationship between your company and the FDA — resembling that of a strategic partnership. "The FDA has shown tremendous flexibility in the amount of data you need initially to accelerate getting the drug to patients," he affirms. For example, when ibrutinib first received its breakthrough therapy designation, it was based on Phase 2 clinical data. Such acceleration benefits suffering patients because no longer do they have to wait until the pharmaceutical company completes the traditional three-phase drug development plan to gain access to and potentially benefit from the medication. Hait reminds us that receiving the breakthrough designation does not eliminate the requirement for completing Phase 3 clinical trials and post-marketing analysis, because you still have to show the drug is safe in a large population.

Another FDA incentive J&J capitalized on is related to tropical-disease treatments. As was pointed out previously, TB is a much bigger problem outside the United States. To encourage companies to develop drugs aimed at solving global

IS THE BREAKTHROUGH THERAPY DESIGNATION A GOOD THING?

When I attended the FDA/CMS Summit last December, the ink was still drying on FDASIA and the FDA's new breakthrough therapy designation. One of the event's speakers, Steven Nissen, M.D., chairman of the department of cardiovascular medicine at the Cleveland Clinic Foundation, said that accelerating a drug's approval should be rare and questioned the thinking behind the FDA's breakthrough therapy designation. Nissen's opinion is in sharp contrast to Janssen's global head of R&D, Bill Hait, M.D., Ph.D., who describes the policy as being one of the "most exciting" incentives to encourage pharmaceutical companies to be innovative — rewarding those willing to take chances on what would otherwise be highly risky and expensive projects.

Why the difference of opinion? After all, both Nissen and Hait are physicians who put patients first. My speculation is as follows. Nissen, a cardiologist, witnessed the debacle when one of the most respected drugmakers in the world, Merck, gained FDA approval for Vioxx, a drug that was eventually pulled from the market after being linked to heart attacks and sudden cardiac deaths. Conversely, Hait has 20+ years of experience in cancer research. I imagine he has witnessed his share of heartbroken families losing loved ones while awaiting cures. Both perspectives are valid. However, I side with Hait and view the breakthrough therapy designation as a good thing.

The fact sheet for the process of applying for breakthrough therapy designation is very specific, to the point of requiring that the "REQUEST FOR BREAKTHROUGH THERAPY DESIGNATION," and other points in a company's cover letter and submission to be written "in bold, uppercase letters." This demonstrates the thoroughness with which government agencies leave nothing to chance. So, too, does this language from the FDA: "The Secretary shall, at the request of the sponsor of a drug, expedite the development and review of such drug if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development." Time may prove me wrong. But given the parameters the FDA has placed on applying for and obtaining the designation, I don't anticipate this creating a "gold rush" of unnecessary drug approvals.

"Low activity, a me-too type of drug, all sorts of problems in early development, or preclinical toxicity issues should be red flags to kill a drug quickly."

Bill Hait, M.D., Ph.D., global head of Janssen R&D

health problems that may have little commercial appeal, the FDA developed a voucher program, which falls under the FDA Amendment Act of 2007 (FDAAA). When J&J gained FDA approval of Sirturo, it became eligible to receive a transferrable voucher that allows the bearer to designate a single human drug application (i.e. another drug in the company's pipeline) submitted under section 505(b)(1) or section 351 of the Public Health Service Act, to receive six-month priority review status. By developing a nonrevenue-generating and yet lifesaving drug, J&J has the opportunity to accelerate FDA approval of another drug in its pipeline.

Where is the best place to use these vouchers? "There's no formula," admits Hait. "We look for opportunities. Is there an opportunity to enhance the progression of our internal pipeline by using the voucher? We've thought about this in partnering. It's a very valuable asset to have available and is another great FDA incentive." Conversely, Hait advocates thinking about when not to use a voucher. "You wouldn't want to use it on a project that is already moving quickly," he notes. "When you have complex drug-development issues and are looking for partners to help, a voucher could be very beneficial as you weigh risk versus reward around the asset you think could benefit the most from voucher utilization."

PARTNERING FOR PRODUCTIVITY

There is a saying, "If you can't beat 'em, join 'em." But, when you are a company with nearly 130,000 employees, is it really necessary to partner in order to improve productivity of a drug that's been in development for 13 years? According to Hait, this is exactly what was done with the development of Invokana (canagliflozin), a sodium-glucose co-transporter 2 (SGLT2) inhibitor for adults with type 2 diabetes. The development of Invokana had been strictly internal, but fearing that one of its competitors, Mitsubishi Tanabe Pharma, might be ahead in developing the same type of compound, J&J sought collaboration. Hait describes the collaboration with Mitsubishi as a "receptor ligand issue — we attracted each other." Perhaps this openness to collaboration is one of the reasons J&J has been ranked as the most productive pharmaceutical company in the last 10 years. The collaboration with Mitsubishi allowed the companies to optimize processes and share knowledge — keys Hait attributes to gaining FDA approval of Invokana, an entirely new class of drug, this past March. If you are looking to have similar success, Hait advises you prioritize your pipeline appropriately, capitalize on FDA incentives, focus on unmet medical needs, and don't use the possibility of commercial success as the only criterion for where to invest in R&D.

APPROACHES FOR CALCULATING NET PRESENT VALUE (NPV) FOR DRUG DISCOVERY

According to Bill Hait, M.D., Ph.D., one of the drug prioritization techniques employed by J&J is NPV. "Most companies use similar types of algorithms," states the global head of Janssen R&D. A report produced by consultants McKinsey & Company in which 44 CEOs and the business developers from representative pharmaceutical and biotechnology companies were interviewed does not necessarily agree with Hait's assessment. Of those interviewed, McKinsey found that one-third admitted to not employing any economically valid evaluation method. Of these, 21% used simple cost-plus approaches, and 12% simply made an educated guess. If you fall into one of these categories, you may find the recent article (April 2013) by Andreas Svennebring and Jarl Wikberg, Net Present Value Approaches for Drug Discovery, useful.

Obviously, given the complexity of drug discovery and the high costs of producing reliable data, it is difficult to model the cost of drug discovery. Further compounding this process would be projects requiring major investments, e.g. constructing a building. McKinsey's findings are not surprising if you review the article, the various formulas, the necessary assumptions, and so on. If you are a smaller company and don't have experts in rNPV calculations, you may find a review of Svennebring and Wikberg's work to be insightful and can do so for free by using this link — http://goo.gl/209mP. Another useful tool for those with limited resources is an rNPV Excel spreadsheet developed by the Milken Institute. It is free to download here — http://goo.gl/Tg9Yw. Though you may have a great deal of experience in drug discovery, whether your company is big or small, your investors will require a robust calculation, not an educated guess.

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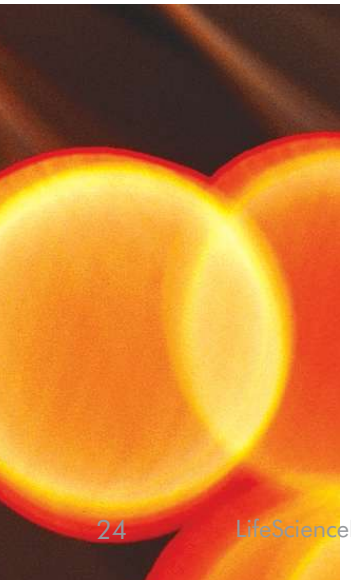


Aptalis — The "Three Ms" Of Specialty Pharma

Mindset, mission, and model are the self-defined keywords guiding a company that applies its novel delivery technology to new and existing drugs.

By Wayne Koberstein, executive editor

General surveys of specialty pharma (SP) are common in the press, but deeper insights sometimes require looking at a specific case. Aptalis Pharma US (Aptalis) serves as both example and exception in shedding light on the SP sector. The company's president and CEO, Frank Verwiel, M.D., coined the "three Ms" — mindset, mission, and model — as organizing keywords for the qualities and goals that distinguish SP from other industry sectors and Aptalis from other SP companies. The keywords triangulate and guide the company in its overall strategic direction:

- **Mindset —** applying the concept of innovation to improve drug delivery, bioavailability, safety, and effectiveness of drugs for targeted populations
- **Mission —** "To improve the health and quality of care by providing specialty therapies for patients around the world." (Meaning: the mission is ambitious and global, but focused on a well-defined sector.)

- **Model —** multiple, complementary businesses — specialty pharma and pharmaceutical technology units create a solid cash flow and partnerships to fund infrastructure and proprietary new-product development

All three Ms have evolved amidst tough conditions and resulting shakeout in the SP sector in the past five years. They reflect practical strategies based on what has worked and what has not in a highly competitive business marked by company failures and consolidation. Here, Aptalis is a case in point. Its combined and markedly different assets result from the well-publicized merger of Axcan and Eurand in 2011. The merger represents a break from the original SP model, where a single company would typically focus on either specialty-drug development or drug-delivery technology. Verwiel views it as a fortuitous confluence, and the resulting cultural mix as a "clinical mindset" that sees a new role for specialty pharma as an innovative force in the industry.

MINDSET: SPECIALTY PHARMA EVOLVES

Not long ago, no pharma company would have used the adjective "specialty" to define itself. From its inception in the 1980s, drug delivery had remained separate from pharmaceuticals as a business — although a few companies, such as the makers of asthma-drug inhalers, distinguished themselves by their delivery technology as well as the drugs delivered.

Technically speaking, all drugs have some form of delivery, even the simplest pill. But when the large pharmas woke up to the potential of extended release (XR) and other "line extensions" for their off-patent drugs, the delivery sector soared — as companies "licensed in" the new technologies, rather than creating them in-house. Even so, the pharma giants let a lot of products go off-patent and compete in their original forms with generics. Specialty pharma was born when new players leapfrogged both pharma and generics by combining the best of both worlds.

The term "specialty pharma" holds two clues to its own origin and meaning. One, by the spelling of "specialty" (not "speciality"), the term shows its American roots. Two, in America, at least when coined initially, the term could only mean one thing when applied to companies outside Big Pharma: special forms of existing or generic drugs. Only later did specialty pharma take on the additional meaning of "drugs for special populations" and branch into the development of original specialty drugs. And over time, the sector spread globally.

Nowadays, specialty pharma is outperforming all other industry sectors in growth and profits. But it took a major shakeout of the early pioneers and some aggressive risk management to put the sector in its current shape. Aptalis represents some of the major moves the surviving SP companies have made to ensure their prosperity — consolidation, diversification, and an effective balance of revenue-producing specialty products with original specialty-drug research.

To ensure success, specialty pharma companies such as Aptalis have consolidated, diversified, and created a balance of revenue-producing specialty products with original specialty-drug research.

MISSION: SPECIALTY MEANS NICHES

Once Big Pharma harvested the low-hanging fruit of drug delivery — mainly XR for primary care products such as antibiotics and antihypertensives — it left a sea of smaller markets untouched. Into that sea sailed specialty pharma, and the SP sector is still navigating among the plentiful islands of opportunity to fill the unique medical needs of niche patient populations.

"With specialty pharma products, by targeting smaller populations, you can make very significant breakthroughs in outcomes or quality of life," says Verwiel. "So in our specialty pharma mission, companies are committed to funding research in a very particular, focused area. The same mission gives us the willingness to use innovative technologies and maximize partnering opportunities."

For Aptalis, the main targeted islands are cystic fibrosis (CF) and certain gastrointestinal (GI) conditions. (It also has a line of softgel pediatric vitamins and other OTC nutritional products.) If the mix sounds somewhat odd, it is because the two foci come from a 2011 merger of two quite different companies, Axcan and Eurand.

The merger also accounts for the strategic alignment of the company as a hybrid specialty commercialization/product development model. It melds solid revenue producers such as its SP products division with its pharmaceutical technology (PT) division, which applies proprietary delivery and manufacturing platforms to its own and other companies' products. The company's hybridization makes sense: To compete in SP, you need more than steady income; you need constant technological innovation — a path that inevitably leads not just to the combination of new delivery with existing drugs, but into novel-drug territory. "One of the main reasons for the merger was to leverage the product-development knowledge in the PT division for our own SP products and development pipeline," says Verwiel.

Axcan had a number of products on the market when the merger occurred, including two pancreatic enzymes for exocrine pancreatic

insufficiency, one of which was produced until then by Eurand under contract. Eurand had launched its first market product — Zenpep (pancrelipase) delayed-release capsules, a pancreatic enzyme for the treatment of exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF) or other conditions. Eurand was mainly a supplier and licensor of drug-delivery technology and manufacturing services: the root of Aptalis' pharmaceutical technology unit. But it also came to the merger with its own U.S. sales and marketing group, plus a pipeline of development products for CF and GI, including some new-indication candidates. With the addition of Zenpep alone, the merged company's portfolio continued to expand into the CF area.

Showing market and patient awareness postmerger, Aptalis expanded the usefulness of the pancrelipase line by introducing two additional Zenpep dosages to achieve the broadest range of strength in the class (six dose levels from 3K to 25K lipase units). The expansion was an important strategic as well as therapeutic gain because CF patients must have the right dosage to help them stay active, and each patient's dose must be titrated according to body weight and individual treatment needs.

Beyond such practical but strategic moves, the company has set its sights on larger strategic goals since the merger. One is to follow the implications of the biology displayed in the areas its products now target — the overlapping relationships of the gut, the lung, and the pancreas. Another is to push the envelope in exploring the patient-centric mission of specialty pharma in those areas.

VERWIEL: THE ROAD TO APTALIS

A medical doctor by training, President and CEO Frank Verwiel loved the scientific environment, but felt drawn to the business side of healthcare. Yet his first encounter with industry, a brief marketing internship with a pharmaceutical company, convinced him to finish medical school in his native country, the Netherlands. Thereafter, Verwiel resumed his search in the pharmaceutical industry and landed a job with Servier. He then moved to Merck & Co., starting on the commercial side and moving up the executive management track during the next ten years, where his last position was heading the global hypertension franchise. In 2005, he was approached by Axcan, the predecessor of Aptalis, and soon became the company's CEO.

MODEL: SP INNOVATION TRAILBLAZER

For Aptalis, the CF and GI indications share a common trait. Verwiel says, "Our products target a limited number of patients and physicians, but their impact on the quality of care that physicians give to patients is very significant. Our model combines that focus with the pharmaceutical technology part of our business and allows us to go beyond developing formulations for other companies, to leveraging the technology and expertise for our own pipeline."

For examples, he points to Aptalis' core technologies: taste masking, oral disintegrating tablets, bioavailability enhancement for poorly water-soluble drugs, and customized drug release for targeting delivery to specific parts of the GI tract. All of the platforms can apply to either existing or novel drugs. One application, in fact, follows logically and practically from the other, to paraphrase Verwiel.

"As the company grew, we had more room to develop more innovative products. One reason the two companies came together was that, not only would we have the financial room to innovate but, with the pharmaceutical technology platform, we would also have the capabilities to do it."

Innovation has grown along with the company in the form of new indications as well as novel molecules. More than a decade ago, the FDA stimulated new research into pancreatic enzyme products (PEPs) by requiring NDA (new drug application) approval for continued marketing of PEPs, which until then were "grandfathered" on the market for treating indigestion because they predated the 1962 FD&C Act. Axcan then responded by putting its two existing PEPs through the NDA process for exocrine pancreatic insufficiency — one with time-release delivery; Eurand took the different route of developing its own "specialty" PEP, Zenpep, from scratch. The merged portfolio in Aptalis now accounts for three out of six PEPs on the market.

Postmerger, the company's experience with CF led it to take a look at the pulmonary area. It soon identified a large unmet need for treating recurring lung infections. So in April 2011, Aptalis acquired Mpex Pharmaceuticals, which was developing Aeroquin, (levofloxacin solution for inhalation) for patients with CF and chronic lung infection, an inhaled form of the normally oral antibiotic levofloxacin. In January 2013, Aptalis announced results from its two global Phase 3 trials of Aeroquin for lung infections in CF, and the company is now preparing an EU marketing authorization application. "If you have a foothold in one part of specialty pharma, one of the ways to expand your business is to go into adjacent areas that you already know well," Verwiel concludes.

The company has practiced the same principle of expansion in the GI area, but this time in a marketing rather than research mode. It has licensed in the product Rectiv (nitroglycerin ointment 0.4%), indicated for moderate to severe pain associated with chronic anal fissures, for which there is no other FDA-approved treatment. Before Rectiv, compounding pharmacies supplied the only remedies for the condition, though its introduction in 2012 predated the compounding controversy that year.

Meanwhile, the company branched out on the pharmaceutical technology side as well. Aptalis codeveloped Gilead's pediatric oral-powder form of the antiviral Viread (tenofovir disoproxil fumarate) for the treatment of HIV-1 infection in combination with other antiretro-

viral agents; the product won FDA and EU approvals in 2012. Gilead will commercialize the product, relying on Aptalis to manufacture and supply the oral powder. The product uses the Aptalis Microcaps taste-masking technology in an oral powder form which is easier on the small patients, who may begin therapy as young as age 2.

Aptalis has also continued to expand its market range for Pylera, an oral-capsule combination antibacterial of bismuth subcitrate potassium, metronidazole, and tetracycline. In combination with omeprazole, Pylera is indicated for the eradication of Helicobacter pylori and prevention of relapse of peptic ulcers in patients with active or prior H. pylori-associated ulcers. Pylera gained FDA approval in 2006, and the company has followed the mutual recognition path in Europe and is now launching the product in the first 10 European markets. The elementary method of combining the three most-prescribed drugs for H. Pylori into a patented capsule-in-capsule therapy may simplify treatment for patients.

THREE Ms IN ONE: CENTERED ON THE PATIENT

Whether it is mindset, mission, or model that best describes how Aptalis approaches specialty pharma, according to Verwiel, the uniting principle of development is matching delivery modes to patient needs. "Whenever we talk about development projects, we want to make sure that we understand what we can do to provide the patients with better care."

He describes how the company recently restructured its sales force to create CF account managers, who visit CF centers to deliver supportive information and product offerings for improving patient care. It has also created an award-winning CF patient support program called Live2Thrive, employing an interactive website where members, caregivers, and physicians can get help managing the disease with educational resources, along with access to Aptalis products such as vitamins and nutritional shakes — the patients are often struggling to avoid malnourishment.

But one of the most important patient-centric activities occurs long before products reach the market. Although drug optimization early in drug development is always a good idea, it is especially critical with SP products. Poor formulation — improper concentration, density, aggregation — can defeat the best delivery method. Conversely, the right formulation can help achieve the best, most tolerable, and effective treatment experience. "All of our three main technologies enable product profiles that can be tailored early to optimize drug performance," says Verwiel.

Two engines drive the selection process for SP in-licensing and development: the reliable old standard, "unmet medical need" for new products, and complementary presence in the targeted therapeutic areas for existing products. "We know the GI and CF spaces very well, so we can identify opportunities and have dialogues with the parties that hold the assets. And quite often the dialogue can be long term. For example, we began speaking with ProStrakan Group years before we in-licensed Rectiv," says Verwiel.

The company also maintains a dedicated pipeline group, which he describes as "an experienced team of medical and pharmaceutical scientists whose mission in life is to look at medical need with formulation science and invent, design, and test new concepts that we could develop. These can be new technologies, new applications for existing drugs, new applications for our proprietary technologies, and combinations of all three. The outcomes of this invention feed into our development portfolio and are in the clinic."

BEYOND THE Ms: SPECIALTY PHARMA HEADS ON

These days, in the dearth of new primary-care blockbusters, large pharma companies have ventured into new territories such as biotech, personalized medicine, and premium orphan drugs in the quest for profitable new products. Will they now gobble up specialty pharma as well?

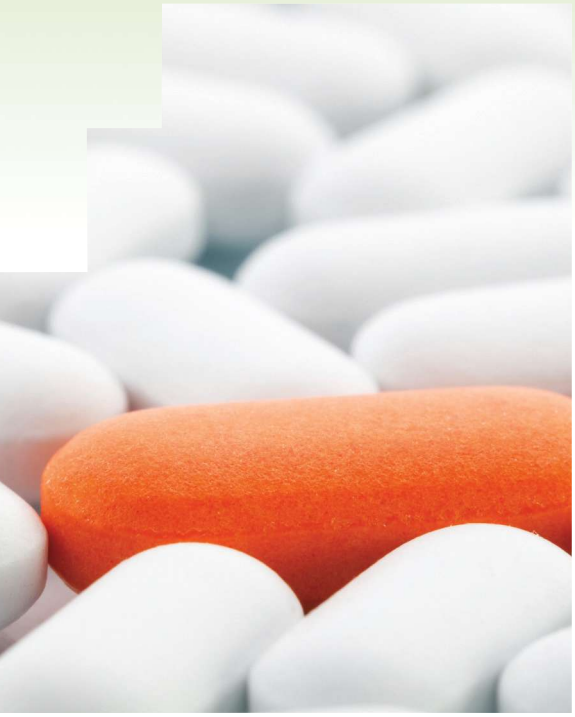
More than an observer, Verwiel still sees the large pharma companies with a somewhat distanced eye. "In specialty pharma, there's still a large unmet medical need, and you can still make significant advances in the medical services you offer. So it's very logical that Big Pharma is entering the space. But specialty pharma demands a different organizational DNA than large pharmas can maintain. Their only recourse may be to buy a successful specialty drug company and let it operate on an independent basis to preserve the special DNA, the special culture needed to be successful in specialty pharma."

It's true that only people can formulate a mission, and mindset, and a model to ensure the continued prosperity of a sector that effectively created itself. Specialty pharma may be one space Big Pharma cannot completely overtake, and its future role in innovation may grow larger than anyone imagines — or could have imagined.

SPECIALTY PHARMA LESSONS LEARNED

President and CEO Frank Verwiel of Aptalis shares some key lessons from his company's experience that may be useful to others in the specialty pharma business.

- It's important to be extremely focused. "We made a very deliberate choice to be in GI and CF and focus on those areas."
- It's important to know what you do — and even more important to know what you don't do. "For an organization of our size, we have a very good understanding of what's in our market. That means that the probability of success is much, much higher."
- You need to have a specific kind of DNA in the organization that recognizes opportunities. "In R&D, the commercial area, or a larger organization active in multiple areas, seeing new opportunities is much more difficult to do."
- Do the basics first, but explore new knowledge. "This is true for everybody but maybe more so for specialty pharma: We were originally only in the GI component of CF, but as our patient-centric SP approach taught us more about the disease and what a patient goes through, we were able to move beyond GI into the pulmonary area of CF."



Biosimilars In Emerging Markets

By Cliff Mintz, Ph.D., contributing editor

To date, 14 biosimilar marketing authorizations have been granted in the EU. Despite their lower cost (20% to 35% less than branded counterparts), the uptake and use of biosimilars in the EU has been less than expected. However, the ongoing global economic downturn, skyrocketing healthcare costs, and patent expiry by 2018 of biologics with annual sales in excess of $67 billion have prompted a renewed global interest in biosimilars, especially in emerging markets.

The growing popularity of biosimilar products in emerging markets can be explained by a number of factors. First, the high cost of branded biologics is placing enormous financial pressure on the nationalized healthcare systems of many emerging countries. Substituting lower-cost biosimilars for branded biologics would help reduce government healthcare costs and lessen the financial burden of insurance companies and third-party payers. Second, countries like China, Brazil, and Russia are extremely dependent upon foreign biologics manufacturers and suppliers for many biologics products. In the past, this has frequently resulted in shortages, rising drug prices, and reductions in patient access to potentially life-saving drugs. Finally, biosimilars represent an opportunity for emerging economies to build domestic biologics and biotechnology capabilities which, in turn, would allow them to penetrate and more effectively compete for a share of the global pharmaceutical and biologics markets.

VARYING FORCES SHAPE BIOSIMILARS' GROWTH

While biosimilar companies in emerging markets share certain advantages over their counterparts in more mature markets, including lower labor costs, cheaper cost of goods, access to large domestic and regional markets, and in many cases, greater government support and involvement, the forces that shape the growth of a biosimilar industry in emerging markets can vary between countries and regions. This certainly is true for the biosimilar industries that have emerged in Brazil, Russia, India, China, and South Korea. Because the market dynamics that shaped the biosimilar industries in each of these countries are different, it is not surprising that their business strategies, practices, and goals are also different.

BRAZIL

Brazil has a population of 205 million and is the second-largest biologics market among emerging countries. Brazilian healthcare is nationalized, and its government is responsible for covering all healthcare and drug costs. "The growing demand for expensive biologics has placed enormous financial stress on the Brazilian pharmaceutical budget," said Kai Wolf, head of Generic Pharma 2.0's Brazilian office. Because of this, Wolf asserted that "the Brazilian government views biosimilar development as a means to improve its domestic biologics capabilities, produce its own biosimilar products, and reduce the country's reliance on expensive, imported, branded biologics and biotechnology drugs."

In 2010, Brazil's regulatory agency, Agencia Nacional de Vigilancia (ANVISA), created a new regulatory approval pathway for biosimilars. Nevertheless, since the early 2000s, biosimilar versions of erythropoietin (EPO), granulocyte colony stimulating factor (G-CSF), and insulin have been available in Brazil. Interestingly, in 2011, almost 20% of biologic drugs prescribed in Brazil were biosimilars.

At present there are as many as 10 Brazilian companies involved in biosimilars' drug development. These include PharmaPraxis, Fiocruz, Cristália, Blausiegel, Eurofarma, Silvestre Lab, Ache, and Prodotti. The focus of almost all of these companies is developing biosimilar versions of blockbuster monoclonals such as Enbrel, Avastin, Herceptin, and others. This is likely because mAbs represent only 1% of the total amount of biologics used in Brazil but represent 32% ($767 million) of the total amount spent

on biologics by the Brazilian government. Recently, the government aided creation of two joint public/private partnerships (PPP); Bionovis (Ache, EMS, Hypermarcas, and Chemical Union) and Orygen (Biolab, Eurofarma, Cristália, and Libbs). Brazil has heavily invested in PPPs as a means to help the country improve its biotechnology and biomanufacturing capabilities and reduce its reliance on high-priced, foreign branded biologics.

While the Brazilian biosimilar market continues to expand and remains attractive, safety concerns persist, and many Brazilian healthcare professionals are not familiar with biosimilars or their use. Further, the Brazilian healthcare market is difficult to navigate, and foreign biosimilar companies will have a challenging time doing business in Brazil unless they partner with domestic biotechnology companies or the Brazilian government. Generic Pharma 2.0's Wolf offered, "Brazil is a vibrant and unique market opportunity. However, if the appropriate relationships are not established locally, then commercial success can be elusive."

RUSSIA

Russia is an emerging pharmaceutical market with a 2011 market size of roughly $25 billion. Moreover, the size of the 2012 Russian generics market was estimated to be $3.5 billion, making it one of the fastest-growing generic drug markets in the world. Finally, according to Roman Ivanoff, VP R&D at Biocad, a Russian biosimilar manufacturer, the size of Russia's 2012 biologics market was almost $2.1 billion.

Like many other emerging countries in the world, Russia's reliance on high-priced foreign biologics is growing and is causing an enormous financial strain on the country's nationalized healthcare system. Because of this, "The Russian government is very open to discussions about substituting lower-cost biosimilars for high-value biologics," offered Ivanoff.

At present, Russia lacks a clearly defined regulatory framework for the approval of biosimilars, which has created some confusion among domestic and foreign biosimilar developers. Interestingly, despite the lack of a defined regulatory approval process, biosimilar versions of EPO and G-CSF are currently commercially available in Russia. "Prior to 2010, there were no clear requirements for clinical trials for biosimilars. So, there are biosimilars on the Russian market today that were approved without clinical trials," explained Ivanoff. Surprisingly, once approved, biosimilars are legally interchangeable and substitutable with their branded biologic counterparts that also have received Russian regulatory approval.

The approval of Russian biosimilars without clinical testing has raised safety concerns. This has been complicated by the fact that the Russian government is legally required to accept the lowest tendered

price for all the drugs that it approves. Because approved biosimilars cost less than their branded counterparts, the Russian government has no choice but to purchase them and to instruct healthcare providers to use them in lieu of the more expensive branded biologics. "The Russian government is desperately trying to rein in healthcare costs, and it is regularly substituting biosimilars with questionable safety histories for branded biologics," warned Ivanoff.

Biocad is the major biosimilar manufacturer in Russia and currently sells biosimilar versions of EPO, G-CSF, and interferon-beta-1a as a multiple sclerosis treatment. The company is also developing biosimilar versions of rituximab (Rituxan), bevacizumab (Avastin), and trastuzumab (Herceptin). Several of these products are in late-stage clinical development.

Despite the relative immaturity of the Russian biosimilar industry, Russia is poised for expansive growth in this area. Adoption of clearly defined regulatory guidelines for approval of biosimilars in Russia will help to better define future opportunities for these molecules. However, according to Ivanoff, the U.S. and European biosimilar markets are not a priority for most Russian biosimilar manufacturers. "Generally speaking, we are focused in the short term on Russia's market with Southeast Asia and Latin America as midterm goals," he said.

INDIA

India has the world's second-largest population, and the size of its pharmaceutical market ($14.3 billion in 2012) is growing at an annual rate of roughly 15%. Historically, India has been the world's leading provider of APIs and generic small-molecule drugs. Over the past decade or more, Indian drug manufacturers have turned their attention toward development of biosimilar products. Interestingly, until June 2012, the Indian government had not crafted a formal regulatory approval pathway for biosimilar drugs. Yet, despite this, there are currently more than 50 biosimilar products on the Indian market, including biosimilar versions of EPO (55 brands), interferons (10 brands), G-CSF, insulin, and two mAbs: Reditux (rituximab, Dr. Reddy's Laboratory) and Biomab (nimotuzumab, Biocon).

At present, there are as many as 27 biosimilar manufacturers in India. However, according to Kiran Mazumdar-Shaw, chairman and CEO of Biocon, India's largest biotechnology company, most Indian companies are more interested in competing for a share of India's domestic biosimilar market rather than competing globally. "India's biosimilar industry has taken off in recent years, and opportunities in the domestic market are better than in the U.S. where regulatory confusion and high development costs plague the American biosimilar market," offered Mazumdar-Shaw.

One of the major challenges facing the Indian biosimilar industry is ongoing questions surrounding product quality and safety. Nevertheless, Mazumdar-Shaw believes that the safety and efficacy concerns raised about Indian biosimilar products are more of a "perception issue" fueled by innovator companies and their stakeholders rather than a real issue. But, Mazumdar-Shaw conceded that as a biosimilar company from an emerging market Biocon needs to build its credibility by developing its biosimilar products according to U.S. and European regulatory guidelines. She said, "It may cost us more but it will clearly show that biosimilar products produced by Biocon offer patients the same quality, purity, potency, and safety as those manufactured by Western companies."

CHINA

China has the world's largest population, and its pharmaceutical and biotechnology industries continue to expand despite the country's recent economic slowdown. Healthcare in China is nationalized, and the growing demand for high-priced biologic drug treatments is forcing China's central government to explore ways to cut annual biologics expenditures. According to Steven Lee, CEO of BioGENEXUS, an Asian biosimilar intelligence firm, "Several years ago, China's central government mandated essential healthcare coverage for all of its citizens, which implies controlled-medicine pricing and expenditures by using biosimilars and other generic drugs." To that point, industry analysts expect the size of the Chinese biosimilar markets to reach $2 billion by 2015, which could represent as much as 20% of the global biosimilar market.

To date, China does not have a regulatory framework in place for approval of biosimilar products (although it is expected by the end of 2014). Biosimilars can be approved in China using its traditional biologics approval pathways, which can take many years because of the Chinese regulatory bureaucracy. Recent reports suggest that there may be as many as 18 different biosimilar versions of EPO, 16 versions of G-CSF, 15 versions of interferon alfa, and more than 8 biosimilar versions of human growth hormone that are currently commercially available in China.

H. Fai Poon, R&D Director of Hisun Pharmaceuticals China, estimates that there are over 60 different companies vying for a share of the domestic Chinese biosimilar market. Some of the key players include 3SBio, Shanghai Celgen Bio-Pharmaceutical, Shanghai CP Goujian Pharmaceutical Company (the largest and most advanced), Beijing Four-Rings Pharmaceutical Co., and Xiamen Amoytop Biotech.

Most of these companies are trying to develop biosimilar versions of blockbuster mAbs including Humira, Enbrel, Remicade, and several others. For now, most Chinese biosimilar manufacturers are content to focus on China's domestic biosimilar markets rather than compete globally. "Many companies do not think beyond their local markets," offered Hisun. Consequently he added that "Chinese biosimilar manufacturers that are thinking globally may have a strategic advantage over their Chinese competitors and emerge as a winner in China's domestic market." However, like India, lingering questions regarding the quality and safety of biosimilars manufactured in China will likely impede the ability of Chinese biosimilar developers to export their products and compete on the global biosimilar market.

SOUTH KOREA

In 2009, South Korea created and implemented a regulatory approval framework for approval of biosimilars. Shortly thereafter, the South

Korean government announced an ambitious initiative to attempt to capture 22% of the global biosimilar market by 2020. Unlike India, Brazil, Russia, and China, which are focused on domestic markets, the main objective of the Korean initiative is to become a leading regional and global biosimilar manufacturer and exporter over the next 5 to 10 years. "I think South Korea's strategy is to develop high-quality products to penetrate domestic and regional Asian markets and then attempt to get those products on the more-regulated U.S., European, and Japanese markets. It's a nice, sleek-tiered approach," said Ivo Abraham, a professor at the Center of Health Outcomes and Pharmacoeconomics Research at the University of Arizona.

There may be as many as 25 companies developing biosimilars in Korea. However, the Korean biosimilar industry is dominated by five key players, including Dong-A Pharmaceuticals, Samsung Biologics, LG Life Sciences, Celltrion, and Hanwha Chemical Company. While biosimilar versions of EPO, G-CSF, and several reproductive biologics products are commercially available in Korea (and exported to foreign countries), the main focus of these companies is to develop biosimilar versions of Humira, Herceptin, Avastin, Rituxan, Remicade, Enbrel, and several other mAb-based products. In 2012, Celltrion's biosimilar version of Remicade (infliximab) called Remsima was approved in South Korea. Remsima is currently being evaluated for marketing authorization in Europe, and a decision is expected before the end of 2013.

THE FUTURE

Early biosimilar market entrants included some of the world's largest pharmaceutical and generic companies (e.g. Sandoz, Teva, Hospira, Pfizer, and Merck). Conventional wisdom suggested that these companies had the financial and scientific resources to dominate the global biosimilar landscape. However, missteps with biosimilar product launches, ongoing manufacturing challenges, ill-conceived marketing strategies, and global biosimilar regulatory ambiguity prevented development of a vibrant global biosimilar market.

Instead, it now appears likely that domestic and regional biosimilar companies located in emerging markets will assume leadership roles as the global biosimilar market continues to develop. Unlike the multinationals, these companies have a much better understanding of the regulatory ambiguities, drug pricing and healthcare costs, and the medical needs of the domestic and regional markets that they serve.

Generic Drugs: An Impending Drought?

By Cliff Mintz, Ph.D., contributing editor

Pharmaceutical drug sales in the United States totaled roughly $320 billion in 2011, according to IMS Health. Last year, more than 40 brand-name drugs, including blockbusters like Plavix, Lexapro, and Seroquel — valued at $35 billion in annual sales — lost their patent protection.

This year, an additional $17 billion in branded drugs sales is expected to be lost as other blockbusters are scheduled to lose patent protection and be sold as lower-cost generic drugs. While the patent expiry of so many blockbuster brands — the so-called "patent cliff" — should seemingly be good news for generic drug manufacturers, it is making many generic drug company executives extremely anxious. Recently, Heather Bresch, CEO of Mylan, the second-largest generics company in the U.S., quipped, "I can't go anywhere without being asked about the patent cliff."

A CHANGING GENERIC DRUG LANDSCAPE

Historically, generic drug manufacturers have relied on the lucrative six-month market exclusivity that follows patent expiry of branded drugs as a major revenue driver. During those periods, companies that are first to file an application with the FDA win the right to sell their generic version of a branded prescription drug exclusively or with little competition. However, the patent cliff has forced generic drug companies to reevaluate that business model. Asa Cox, chief executive and founder of Generic Pharma 2.0, a global generic drug manufacturing consulting firm, said, "The patent cliff is over, and generic drug company executives understand that they can no longer rely on six months of market exclusivity as their main revenue driver." He added, "There is simply too much competition for too few brands."

Likewise, Paul Bisaro, CEO of Watson Pharmaceuticals (now Actavis), suggested in a recent article that, while big blockbuster brands like Plavix or Lipitor get a lot of attention when they lose patent protection, patent expiry does not always translate into guaranteed profits for generic drug manufacturers. To that point, generic companies are now scrambling to find creative ways to redefine their business models and reinvent themselves to cope with the impending generic drug drought that is likely to occur over the next few years. Some of these new strategies include selling branded products, specializing in difficult-to-make drugs, and expanding globally into new markets.

NEW BUSINESS STRATEGIES FOR GENERIC DRUG COMPANIES

Many of the top generic drug companies, including Teva, Actavis, and Mylan, are already selling their own branded products (in addition to generics) to ensure growth and maintain revenue streams. Teva is perhaps the best example of this with Copaxone, its injectable blockbuster drug to treat multiple sclerosis. Mylan's and Actavis' sales revenues have also benefited from selling their own branded products including Mylan's antiallergy EpiPen and Watson's branded oral female contraceptives and other women's health products.

Other generic drug makers are going after difficult-to-make products, such as extended-release tablets, patches, creams, and reformulated injectable drugs, based on the notion that with less competition, the prices of these so-called speciality products will not erode as quickly as conventional generic drugs (which can lose as much as 80% of their value once the six-month exclusivity period has expired and the market is flooded with multiple competitors). Scott Tarriff, former CEO of the NY-based generic manufacturer Par Pharmaceuticals and currently CEO of Eagle Pharmaceuticals, believes that specialty pharmaceutical products may represent a major growth opportunity for generic drug makers. "I think the key to success in today's generic industry is to look for the next products that may

be more difficult to develop but will give you a much better return than just developing a simple commodity tablet — it just makes sense," said Tarriff. He added, "The more innovative generic companies have identified areas where they have acquired the requisite expertise, built some type of barrier to entry (cash, infrastructure, etc.) to prevent competition, and possess the knowledge to continue to build value over time."

Companies trying to capitalize on difficult-to-make products include Actavis, Teva, Mylan, and Impax Laboratories. Interestingly, Mylan and Teva are competing with one another to bring generic versions of GlaxoSmithKline's asthma medicine Advair to market. This has been difficult because Advair combines two drugs that are inhaled through a device. Likewise, Actavis is expected to introduce a generic version of Endo Pharmaceuticals' Lidoderm pain patch next year.

Most U.S. and foreign generic companies are also eyeing biosimilar drugs as a new means to bolster revenue and sustain growth. Since 2004, more than 15 biosimilar products have been approved worldwide. In general, biosimilars cost 20% to 40% less than their branded biologic counterparts. While the size of the global biosimilar market continues to grow, these molecules are still not permitted to be approved or sold in the U.S. — the world's largest biologics market. Nevertheless, there are currently as many as 50 generic companies, including, Sandoz, Mylan, Teva, Hospira, Biocon, and others, that are developing biosimilar products. "Biosimilars appear to be the next big thing for generic drug makers," said Kai Wolf, a former Merck Serono executive who helps generic drug manufacturers register their products in Brazil and Latin America. However, Wolf warned, "It's not going to be as easy or lucrative as many generic companies think." Generic Pharma 2.0's Cox agrees, "Biosimilars will require a massive investment in marketing to offset a certain fight by incumbent brands. We've seen some modest successes in Europe, but it is clear that the generic companies have a long way to go to compete in the biosimilar space."

> "We've seen some modest successes in Europe, but it is clear that the generic companies have a long way to go to compete in the biosimilar space."
>
> Asa Cox, chief executive and founder, Generic Pharma 2.0

FOCUS ON EMERGING MARKETS

Another approach being used by generic companies to gain an edge and sustain their growth is expanding into global emerging markets. While generic drug use is pervasive in the United States — recent estimates indicate that roughly 80% of prescriptions are filled with generic drugs — its popularity is growing in other markets including Europe and Japan. In 2007, Mylan bought Germany-based Merck KGaA's generics business, and in 2012 it entered into a strategic partnership with Pfizer to sell generic drugs in Japan.

More recently, Mylan entered into an exclusive strategic collaboration with India-based Biocon for global development and commercialization of Biocon's Glargine, the generic version of Sanofi's Lantus; Lispro, the generic version of Eli Lilly's Humalog; and Aspart, the generic version of Novo Nordisk's NovoLog. Also, last year, U.S.-based Watson Pharmaceuticals purchased the Swiss drug maker Actavis Group for $5.9 billion, increasing its presence in overseas markets. After the acquisition, Watson changed its name to Actavis, which is better known internationally and is likely to provide a better global reach into emerging markets like China, India, Brazil, and elsewhere. "The generic industry is exploding in Brazil and Latin America," said Wolf. However, Generic Pharma 2.0's Cox warns, "While many generic drug companies are focusing on emerging markets, these opportunities often present more challenges than solutions." He recommended that companies seeking to penetrate these markets should proceed with caution to gain a better understanding of regional and national market dynamics before making a final decision.

THE FUTURE IS INNOVATION

The generic drug industry, much like the branded pharmaceutical industry, is in transition and rapidly changing. But, as Eagle Pharmaceutical's Tarriff emphasized, "The generic drug industry is filled with extremely talented people who will continue to innovate and find ways to compete and make money. And I don't think that this industry is going away anytime soon." Cox offered a different perspective. He said, "I think generic companies will be highly marginalized unless they can plot a path to being involved in the service-oriented, personalized-treatment healthcare sector of the future. The rapid evolution of technology, data, and education, combined with the dynamics of funding, fulfillment, and regulation, will create a very different drug industry compared to the one we have today." Nevertheless, both Tarriff and Cox agree that innovation is the key to the future success of the generic drug industry.

Perils And Challenges Of Building A Biotech In Kentucky

By K. John Morrow Jr., Ph.D., contributing editor

Start-up funding for new biotechs has always been a dicey proposition. But today, investment opportunities are even more precarious, both from the private and public sides of the equation. According to Reuters data, venture capital investments in biotechnology declined by 33% in the first quarter of 2013, compared with the previous period in 2012, which had dropped 14% from 2011.

On the public side, NIH will suffer the loss of a trillion dollars over the next 10 years unless the sequestration cuts are reversed. These cuts will dramatically impact the ability of NIH and other government agencies to support small biotech companies through the Small Business Innovative Research (SBIR) program. To date, more than $16 billion has been allocated by the federal government for support of innovative research leading to commercialization, but it is not clear how the program will be affected in the coming years.

BIOTECH START-UPS: WHERE TO LOCATE?

In this climate, biotech start-ups must do everything they can to optimize their chances for success. The path to this goal has traditionally been through the major hotbeds of biotechnology — San Diego, with at least 400 biotechs; the Bay Area, with several hundred; or Maryland, with more than 500 companies. A number of other cities, including Seattle, Boston, and Los Angeles (home to the behemoth biotech Amgen) have welcomed many start-up biotech firms.

The basis for the decision to locate in a recognized biotechnology-friendly environment is guided by the availability of human resources and the proximity to academic centers, hospitals, and private-research institutions. Support services, such as biotech suppliers, are readily available in these zones. Venture capital firms are located nearby, and their management has an excellent understanding of the industry. Finally, these areas are noted for their high quality of life with excellent schools, recreational and leisure time activities, and cosmopolitan lifestyles.

In contrast, the center of the United States has been defined by biotech executives as what they have to fly over in order to get from one coast to the other. Whereas major cities, including Chicago, St Louis, Cleveland, and Kansas City, are home to numerous medical device and major pharma companies, the biotech sector tends to be underrepresented in these regions.

AN OVERLOOKED REGION OFFERS POSSIBILITIES

So it is noteworthy that bioLOGIC, a biotechnology accelerator located in the metropolitan Cincinnati area, has adopted an unconventional approach to initiating small, innovative biotechs. As such, it tests a number of standard assumptions that have guided the industry since its inception. The company was founded in 2006 by Nigel Ferrey and Dr. Ray Takigiku, who were dedicated to building a community of networking researchers. It now provides resources for about 14 companies — among these is Bexion, which seeks to develop a cancer therapeutic. Bexion was also founded in 2006 by Takigiku and rents office and lab space from bioLOGIC.

The most significant factor that entered into bioLOGIC's decision to locate in northern Kentucky was the availability of a unique support vehicle for emerging technologies. The state provides generous sums for SBIR recipients in the form of 100% matching funds. These figures amount to a doubling of up to $150,000 for Phase-1 SBIR awards and up to $1 million matching support for a Phase-2 SBIR. In addition, the Kentucky legislation includes "Phase Zero" and "Phase Double Zero" support programs, which award up to $4,000 to help cover the costs of SBIR proposal preparation. Many other states provide supplements to SBIR awards, but none as munificent as the Kentucky program. While even doubling the size of an SBIR award is not sufficient to fund a biotech company, there is substantial prestige attached to a concept that is approved by a peer-review panel. This provides an

important marketing tool in the recruitment of additional funds from private sources.

Cincinnati sits on the Ohio River, which forms the border with northern Kentucky. The bioLOGIC facility is located in Covington, KY, a 19th century river community facing the downtown Cincinnati skyline. This location takes advantage of proximity to a major city with two outstanding research institutions, Cincinnati Children's Hospital Medical Center and the University of Cincinnati. The two campuses are adjoining; Cincinnati Children's is recognized as one of the top pediatric hospitals in the world.

Ferrey and Takigiku's decision to locate the biotech accelerator in Kentucky rather than Ohio was based on a number of considerations in addition to the generous SBIR program. Although Covington is a 5-minute drive from downtown Cincinnati, it retains a small-town flavor and, along with it, small-town living costs and an ample range of available commercial real estate. For example, in Covington, current average rates for class A rental space are $15.42 per square foot versus $19.23 in downtown Cincinnati.

In addition to the SBIR matches, Covington offered a small pond for a large biotechnology fish to splash in. City fathers and mothers welcomed bioLOGIC with unbridled enthusiasm, and the Duke Energy Foundation awarded a $100,000 grant to the city, which went to bioLOGIC and was critical in providing the recognition and prestige to build the company in its early days.

bioLOGIC's home sits in stark contrast to the lavish space-age architecture favored by many biotechnology companies. In construction of its wet labs and office space, the company chose to rehab an historic structure, an 1877 livery stable that had been used as a garage and a warehouse over the years. The expansion encompassed 8,000 square feet, and costs ran to one million dollars, bringing the facility's total square footage to 14,000. There is an adjoining 4,300 square feet of unfinished space in the building available for future development. In addition to Bexion, there are six other companies listed on the bioLOGIC website, and numerous negotiations with other start-ups in the works.

The company's location also figures into another tax incentive program not usually available to biotech companies. Both state and federal laws provide for the availability of historic tax credits for the renovation of qualifying structures, subject to guidelines for appropriate exterior preservation. The tax credits can be quite generous, amounting to up to 50% of the costs and can be extended out over a number of years. bioLOGIC is midway between the Covington train

station, now a museum, and the Mutter Gottes Catholic Church, a massive Italian Renaissance revival structure built in the 19th century. BioLOGIC was able to meet the Federal legislative requirements and obtained a substantial boost from this source.

THE SEARCH FOR THERAPEUTIC WINDOWS OF OPPORTUNITY

Takigiku, the CEO of Bexion, is a transplant from the Proctor and Gamble Pharma division, where he was director of core technologies and played a role in the development and marketing of Actonel, an anti-osteoporosis therapeutic, and Asacol, for the treatment of ulcerative colitis.

Bexion's technology is based on the fact that virtually all cancer cells possess the membrane component phosphatidylserine on the outside of the cell membrane, rather than on the inside, as is the case for normal cells. Saposin C is a possible therapeutic agent owing to its ability to interact with the phosphatidylserine present in the cancer cell outer membrane. Bexion has developed Saposin C–dioleoylphosphatidylserine nanovesicles and evaluated their killing potential on malignant and nonmalignant cell lines as well as tumors in experimental animals. The compound, referred to as BXQ-350, targets and treats a broad range of solid tumors without damaging nonmalignant cells. The company anticipates entry into clinical trial later in 2013.

"While our long-term goal is developing treatments for cancer, I am hopeful that we can open a dialog for new approaches that move away from targeting abnormal genes," Takigiku says. "Our strategy is just one of a number of new ways of looking at cancer treatment."

"We don't need to be in San Diego or San Francisco, because Covington, while small, has the benefit of being next to a larger city with amenities and universities."

Dr. Ray Takigiku, Bexion

Bexion's approach is quite different from most therapeutics that target cancer cells, given that it addresses a fundamental property of the cancer cell, without which it cannot flourish. For this reason it seems unlikely that tumor cells could develop resistance to the drug. Moreover, the side effects from its application would be predicted to be much less severe than conventional chemotherapy, which is often accompanied by devastating side effects.

A BUSINESS MODEL THAT FITS THE ENVIRONMENT

Takigiku is enthusiastic concerning his business plan. "Covington has pluses and minuses," he stated. "One disadvantage is that northern Kentucky has no research establishment and no medical school. But weighing all the relevant factors, this was the right choice for Bexion. We have Fortune 500 companies in the area, and we draw from a diverse population whose experience and history motivate us to drive forward. We can create a space in which to work that is accessible and affordable while meeting our needs for a stimulating social and intellectual environment. We don't need to be in San Diego or San Francisco, because Covington, while small, has the benefit of being next to a larger city with amenities and universities. I believe the network of northern Kentucky cities that have a common hunger to be better drives bolder thinking and quicker action on opportunities. That sort of mentality fits in with our idea of a pioneer spirit. We can't afford NOT to get things done."

The companies that are forming under the bioLOGIC umbrella constitute the basis for a community of investigators that are building collaborative agreements with themselves and with other research groups both locally and internationally. "We founded Bexion on the concept of developing new cancer therapies and building our own network for cancer research and expanding our efforts within and beyond the community," Takigiku added. "Similarly, bioLOGIC has a sister company in Ft. Collins, CO, and affiliations with offices in Shanghai, Australia, and France."

THE FUTURE IS NOW

Both Bexion and bioLOGIC have chartered their own respective courses, while taking advantage of the desire of a community to expand its high-tech base and the willingness of the state and local foundations to back up their expansionist goals with solid cash. This game plan could not have succeeded if the region were already thick with high-tech enterprises. As long as the companies within bioLOGIC are able to move their products forward, they will be likely to gather more private and governmental support.

Taking biological inventions from the laboratory to the clinic is a challenging task, requiring years of effort and evaluation. Bexion will need funding and clinical success as it moves its technology forward in the coming years. So far its efforts to confront established wisdom have brought gains that probably could not have been realized if it had followed the conventional routes to biotechnology development. But its eclectic business model is a work in progress that will be judged by the company's success.

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Global Business Update

Norwegian Biotech Faces The Funding Gap

By Suzanne Elvidge, contributing editor

Norway is known worldwide for its offshore industries, including oil, gas, and fishing, as well as mining and forestry, but what is perhaps less well-known is that the country has an emerging biotechnology industry, including biopharma, medical biotechnology, and biorefining (the process of refining products from biomass such as waste from the fishery or timber industries).

"There are quite a large number of biotechnology start-ups in Norway, spinning out from universities and research institutions," says Øystein Rønning, special adviser at the Research Council of Norway. "Most of these are in the biopharma sector, but others include marine biotechnology, such as fish feed and fish genetics."

One of the drivers for the industry is the Norwegian government's national strategy for biotechnology, which is targeting the environmentally sound provision of healthcare, food, clean water, and energy for a growing global population. The strategy runs from 2011 to 2020 and has been designed to balance basic and applied research, innovation, and commercialization in biotechnology. It is backed by the Research Council of Norway and Innovation Norway, an organization that promotes and supports innovation in industry.

A BIOTECH INDUSTRY WITH POTENTIAL

The Norwegian pharmaceutical industry has a long history, growing out of the country's long heritage in the biomedical sciences. However, biotechnology in Norway is still a relative newcomer, only emerging in the 1990s.

"There is a lot of potential, with Norway having plenty of resources for biotechnology, such as biomass from industries such as fishing, agriculture, and timber," says Jan Buch Andersen, who sits on the boards of Industrial Biotech Network Norway, Barents Biocentre Lab, and the BIOTEK2021 Program in the Research Council of Norway, and is also business development director at Tromsø-based ArcticZymes. "Norwegian biotechnology has the basic tools, but the industry is not yet established. There has been phenomenal growth of biotechnology in Denmark, which is a smaller country. If it can be achieved in Denmark, it is also achievable in Norway."

FACING THE FUNDING GAP

One of the key challenges facing biotechnology in Norway is the funding gap. While the country is not alone in this, it is a particular problem for this region because its economics are so tightly focused on high-value and low-risk technologies such as oil and gas. Investors are reluctant to put money into higher-risk projects such as biotech while returns are virtually guaranteed from the offshore industries.

"The offshore oil and gas industries are high volume and high profit, and so private capital and investment is more likely to go to these; so it is hard to get money for other industries such as biotechnology and ICT (information and communications technology). This will be the biggest challenge and will need both governmental and private investment," says Rønning. This gap in funding means that few of the Norwegian start-ups are becoming sustainable, according to Rønning, and those that do become targets of mergers and acquisitions or move away from Norway, further depleting the embryonic industry.

Ole Jørgen Marvik, sector head of health and life sciences at Innovation Norway, has also seen this investment deficit. He says, "We would like to see more projects and could in fact have invested more in the biotech sector. Our grant volumes for healthcare projects have been flat for the past three years, and I suspect that companies are struggling to raise private capital to match the public funding opportunities."

To try to bridge the gap, a number of key sources of financing and support have been put in place recently that could have potential to move the industry forward. These come from both private and public sources.

COMPANIES FINDING THE FUNDING

While finding private funding and venture capital is hard for Norwegian biotech companies, particularly those that are working on early-stage research, there have been some recent success stories. For example, in 2012, Targovax secured NOK18.5 million (around $3.1 million) in public and private

funding for further development of its cancer vaccine TG01 in pancreatic cancer.

Also in 2012, BerGenBio completed an $8.8 million Series A financing round to take its lead oncology compound BGB324 into clinical trials and to develop a companion diagnostic. Lead investors included Sarsia Seed, a Norwegian seed capital fund, and Investinor, a government-funded investment company. This funding will allow BerGenBio to make the step from preclinical to clinical development.

"We see BerGenBio's success as 'seeding' a long-awaited biotech cluster here in Bergen," says Sveinung Hole, CEO of Sarsia Seed.

BIOTEK2021

BIOTEK2021 (Research Programme for Biotechnology for Innovation) is the Research Council of Norway's most recent biotechnology funding initiative. It will run from 2012 through 2021 and follows the completed Functional Genomics in Norway (FUGE) program. The aim of BIOTEK2021 is to help the Norwegian biotech industry to mature and make sure that the knowledge gained from FUGE, which had more of a focus on basic research, isn't lost. The program will have around NOK140 million (approximately $24 million) available each year.

"Until now, Norway has spread its funding rather thin, giving small amounts to many groups of researchers. BIOTEK2021 gives larger grants to consortia with a long-term perspective," says Andersen. "It has industrial relevance written in."

The Research Council of Norway also provides funding for individual projects, awarding up to 50% of total costs for companies, and 100% for universities and research institutions. These grants, which are worth between one and ten million kroner each year, are for early-stage research projects lasting up to three or four years.

THE U.K.-NORWAY COLLABORATION

In February 2011, at the BIOPROSP bioprospecting conference in Tromsø, Norway, the United Kingdom's Technology Strategy Board (the U.K.'s innovation agency) and Innovation Norway signed a five-year memorandum of understanding to support collaboration between industry in Norway and the U.K. in industrial biotechnology and biorefining. While this isn't a new source of funding, it is ongoing and will fund a new group of projects every year of the project.

The collaboration has funded eight projects so far, four in 2011 and four in 2012, at a total value of just over €2 million. Organizations involved have included seven U.K. companies, eight Norwegian companies, and one U.K. university. Merlin Goldman, lead technologist in high-value manufacturing, Technology Strategy Board, confirmed that he expects to see a similar number of new projects supported for 2013.

"The aim of the collaboration is to generate projects and create more high-value chemicals and in the process grow the Norwegian biotech sector, which is still young. Norway has biorefining expertise and access to biomass from the wood, fishing, and agricultural industries, and the U.K. has expertise in industrial biotechnology and specialist areas such as biocatalysis and formulation. Working together, we can drive discoveries toward the marketplace," says Goldman. "The U.K. companies had a free choice as to whether to partner with a U.K. or Norwegian company. We were pleasantly surprised to see how many of them chose a Norwegian one."

Two of the first four funded projects are expected to launch products this year. One of these is a collaboration between Borregaard, Unilever, and Croda to develop alternative sources for cellulose as an ingredient in cosmetics. Borregaard is a Norwegian biorefinery company, making environmentally friendly biochemicals, biomaterials, and bioethanol from sustainable biomass, including waste timber. The second is the result of a collaboration between Aquapharm Biodiscovery in Scotland and Aqua Bio Technology in Norway. The Oban-based company was founded based on discovery of bioactives produced by bacteria found in Scottish rock pools; they now have a culture collection sourced from authorized locations around the world.

The Technology Strategy Board has created a network of organizations from the U.K. and Norway, which currently includes around 250 members and recently launched its Industrial Biotechnology Directory. This is freely available and features U.K. and Norwegian companies and research technology organizations involved in biorefining and industrial biotechnology.

While the sector's future growth will be dependent on continued funding, practical support for the fledgling industry is also important. This needs to include the provision of reasonably priced lab space and services for start-up companies, which allows them to put more of their precious capital into R&D. Barents Biocentre Lab, created through a collaboration among industry, the University of Tromsø, Norut (Northern Research Institute), and Norinnova, provides access to laboratories and equipment. Bioclusters, such as BioTech North, a growing cluster of approximately 30 companies and organizations based in north Norway, or the national parallel — Industrial Biotech Network Norway — can offer support for small companies, as well as shared infrastructure and networking opportunities.

THE FUTURE OF NORWEGIAN BIOTECHNOLOGY

Moving forward, the Norwegian biotechnology sector has potential to supplement and even replace the role of some of the traditional income sources in Norway. These include the oil and gas industries or the small molecule-based traditional pharmaceutical industry. To achieve this will require continued investment, as well as making connections globally.

"These investments have created a foundation for building a biopharma industry," concludes Asbjørn Lilletun, team leader for life sciences at Norinnova Technology Transfer. "Norway has a lot of platforms and services that can help to bring candidates through to the clinic. It needs to realize all these opportunities and build on its reputation, including putting more investment into commercialization, so that its companies can bring products to market."

While biopharma is a vital part, for the Norwegian biotechnology sector to be really significant, Norway will need to exploit its breadth of skills and experience and focus across the whole of the industry.

Shifting Recruitment Patterns In The Pharma Industry

By Suzanne Elvidge, contributing editor

Changing jobs is a big deal at the best of times for both employers and employees, but as the recession continues in many major markets, this really isn't the best of times, even for a growing area like the pharmaceutical industry. So how has recruitment in the pharma industry changed, and who actually has the upper hand?

A number of factors have changed the profile of employment, and therefore recruitment, in the pharma industry. These factors range from macro effects such as the financial downturn, to industry and drug-specific issues including mergers and acquisitions, rising drug-development costs, and the impact of the patent cliff, including the growth of biosimilars and biogenerics. All of these have led to job cuts, explains Victor Kleinman, executive vice president and managing director for the global life sciences practice at the U.S.-based executive search organization DHR International. "The downturn has had an impact on R&D, but mostly on the commercial side — roles in licensing, business development, product management, marketing, and sales have taken the major brunt of the layoffs," says Kleinman.

However, despite all this, some areas are still actively recruiting, such as market access, regulatory affairs, clinical development, and quality assurance, according to Kleinman and Tarquin Bennett-Coles, principal at the United Kingdom- and U.S.-based executive search company Coulter Partners. Newer areas are also growing, such as translational and personalized medicine, as are CROs, as companies are using them more to avoid committing to fixed costs.

THE CHANGING RECRUITMENT PROCESS

As money becomes tighter and staff head counts get smaller, employers are becoming more cautious about hires. As Bennett-Coles explains, "Our clients are asking to see more candidates and needing them to see more people within the organization."

The upside of this is that it allows the comfort of a consensus agreement, a perceived sharing of financial risk, and time to get more background information on individuals. However, it comes with a downside, too. "While time to shortlist has not markedly changed, the length of the client interviewing process has extended considerably and in many cases may take three months or more before reaching offer stage," says Bennett-Coles. "This means that the companies that move the quickest will get the candidates."

FROM THE CANDIDATE'S PERSPECTIVE

There have been changes for candidates as well as for employers. Shrinking teams are actually creating roles that are more interesting and can improve people's employability. "Management teams are smaller and working with fewer resources and so clients want people with a much wider spread of skills," says Bennett-Coles. "This is creating a new layer of candidates with multiple skills who are being stretched more and enjoy the breadth of the role, as each day may be very different."

It's no longer just about the lead candidate either. As the time taken for recruitment into senior roles lengthens, it can be vital to have someone waiting in the wings. "During the past year, clients have looked for more backup candidates. While first-line candidates — often from a competitor — may be the closest fit for the client's recruitment brief, the mere fact that they have been headhunted while not actively looking may make them ask for more from the client. Second-line candidates, who know that they are not the front runners, may be prepared to be more flexible and tend to be more motivated because they have to 'prove' themselves to get to the offer stage," says Bennett-Coles.

However, the longer process can be arduous and stressful for applicants. It can also lead to pharma companies losing good candidates, to the detriment of both parties, and is not sustainable.

"The process could involve up to 15 interviews or more, which can take its toll emotionally on candidates, as well as making it difficult to free up the time needed for travel and interviews. There is more risk of candidates simply having an 'off day' at any individual interview and more risk of the news getting out into the wider market that they are 'looking',"

says Bennett-Coles. "This is not really sustainable; people need to know the length of the process early on and have quick feedback after each meeting."

SHIFTING POWER

With the increasing number of layoffs, as pharma companies merge and downsize, it would appear that the power is entirely in the hands of the employers. However, it's not quite that simple. For a start, it depends on the size and status of the company and its reputation within the industry.

"One of the manifestations of the downturn is the level of due diligence that candidates put clients through, such as career opportunities and pipelines," says Kleinman. "In these times of economic uncertainty, people want certainty."

What happens within companies on a day-to-day basis also has an impact. Breaking news can lead to issues between the client and the candidate. "The market is now so well-connected that, if anything happens, the news gets out almost instantly. We spend a lot of time managing the candidates and looking after them in the process, which can be highly taxing, to make sure they feel good about the process and company," says Bennett-Coles.

It also depends on the individuals and how previous companies have treated them, particularly if they have been through redundancy. As Bennett-Coles explains, a lot of these people are not keen on going back into Big Pharma; instead, they are setting up as consultants, or are finding other jobs within smaller organizations.

While executive search is largely global, the balance of power is different in some countries, according to Kleinman. "There are similarities between India and California in the dotcom boom, where the candidates are looking for raises and career advancement at every step. If the employers can't match the conditions that the potential employees want, they will go elsewhere."

PEERING THROUGH THE GLASS CEILING

One of the ongoing issues in pharma recruitment is that of the lack of women in senior-level posts. Despite efforts, this doesn't seem to have changed much in the past few years. "There are a lot of women in the lower rungs of the pharmaceutical industry, but there are fewer at the higher levels," says Kay Wardle, U.K. managing director at RSA, which focuses on global executive search and interim management for the life sciences industries.

This may be because women tend to be more involved with childcare or are more likely to be caring for elderly relatives, and so find it hard to combine these responsibilities with an increasingly demanding job. It is aggravated by the lack of women at higher levels to act as role models. Men and women bring different skills to workplaces and boards, and improving gender diversity can bring some very positive outcomes. Because of this, companies are trying to remedy the situation, increasing the number of women joining at higher levels by revising recruitment practices. However, this practice could backfire by reinforcing the perception that women can only get senior roles based on their gender, not their skills.

"Some companies have a quota system, a mandate for recruitment organizations to have at least one female candidate on the shortlist. However, women want to know that they have the job on merit, rather than being the token female," says Wardle. "There is no quick fix. It needs commitment from the industry and mentors in the business. These would not need to be women, but just people who have seniority, influence, and experience."

There are differences in different parts of the industry; for example, clinical research and regulatory affairs have more women in senior roles, but areas such as manufacturing and engineering are worse, as Wardle explains. However, she cites biotech as a shining example of how things could work, "There are more senior women in biotech, probably because women are involved from the beginning, and this changes the culture of the company, with more open and more flexible business models."

RECRUITMENT IN THE INTERNET AGE

The Internet is becoming a powerful tool in pharma recruitment. While candidates can use the Web to research their chosen company, recruiters and HR departments can also find out a lot about their potential employees through networking sites and online CVs.

"LinkedIn is very useful. You can tell a lot about people through their connections, and you can use these connections to get information about them," says Bennett-Coles.

This is not always as straightforward as it seems. Different sources of information need to be verified and matched up to make sure that people aren't hiding gaps, and there are pitfalls as well as advantages, as Bennett-Coles explains. "Young entrepreneurs use Facebook as a key means of communication, but they need to remember that HR professionals will check their profiles. So think … would you put that picture on your CV now or even in five years?"

IN THE FUTURE

There are changes ahead in the pharma industry, and this will change the kinds of people that companies need to recruit, both in the R&D and commercialization areas. Companies are investing in areas such as translational medicine, with an aim to cut drug development costs and get drugs from the bench to the bedside more efficiently, and in personalized medicine, which will target individual patients with drugs tailored to their disease or genetic makeup, potentially speeding up the drug development process.

"There will be a continued willingness to invest in R&D," says Kleinman. "There will still be a demand for people in regulatory affairs and quality assurance, and companies will need the right kind of professionals in reimbursement and market access to deal with personalized medicine."

New Trends In Pharma/Bio Executive Compensation

By Steve Cornacchia

Over the past several years, the life sciences industry has faced an increasingly challenging environment overall, including stringent regulatory issues, ever-increasing scientific hurdles in new therapeutics R&D, and an increasingly competitive global marketplace. The global hiring pool for life sciences also has become increasingly competitive.

To entice key talent into the fold, companies are offering more aggressive and creative compensation packages.

The structure of executive compensation plans has changed broadly over these last four years. Regardless of company size, there is not only a healthy gain in total compensation, but also a significant change in the mix of cash-vs.-equity and stock-vs.-option awards. Companies need to take note in order to remain competitive in recruiting and retaining their most talented leaders.

NEW CHANGES FOR REWARDING EXECUTIVES

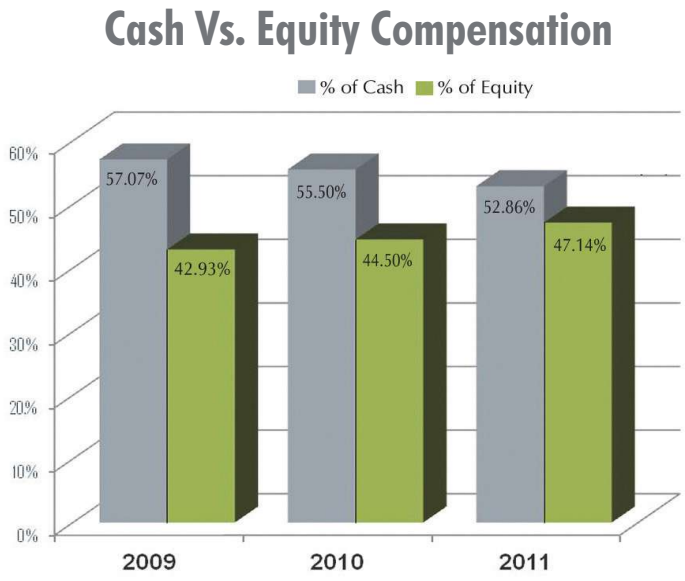
In an analysis of the publicly disclosed executive compensation plans within the U.S. public biotech and pharmaceutical industry, there are several changes that can be tracked in the way executives are being rewarded. These trends can be observed across the spectrum of large corporations with market capitalizations over $10B to small businesses under $250M. Since 2009, these executives have seen an average 20% increase in their overall compensation, mostly driven by increases in variable compensation, including cash incentives and stock and options awards.

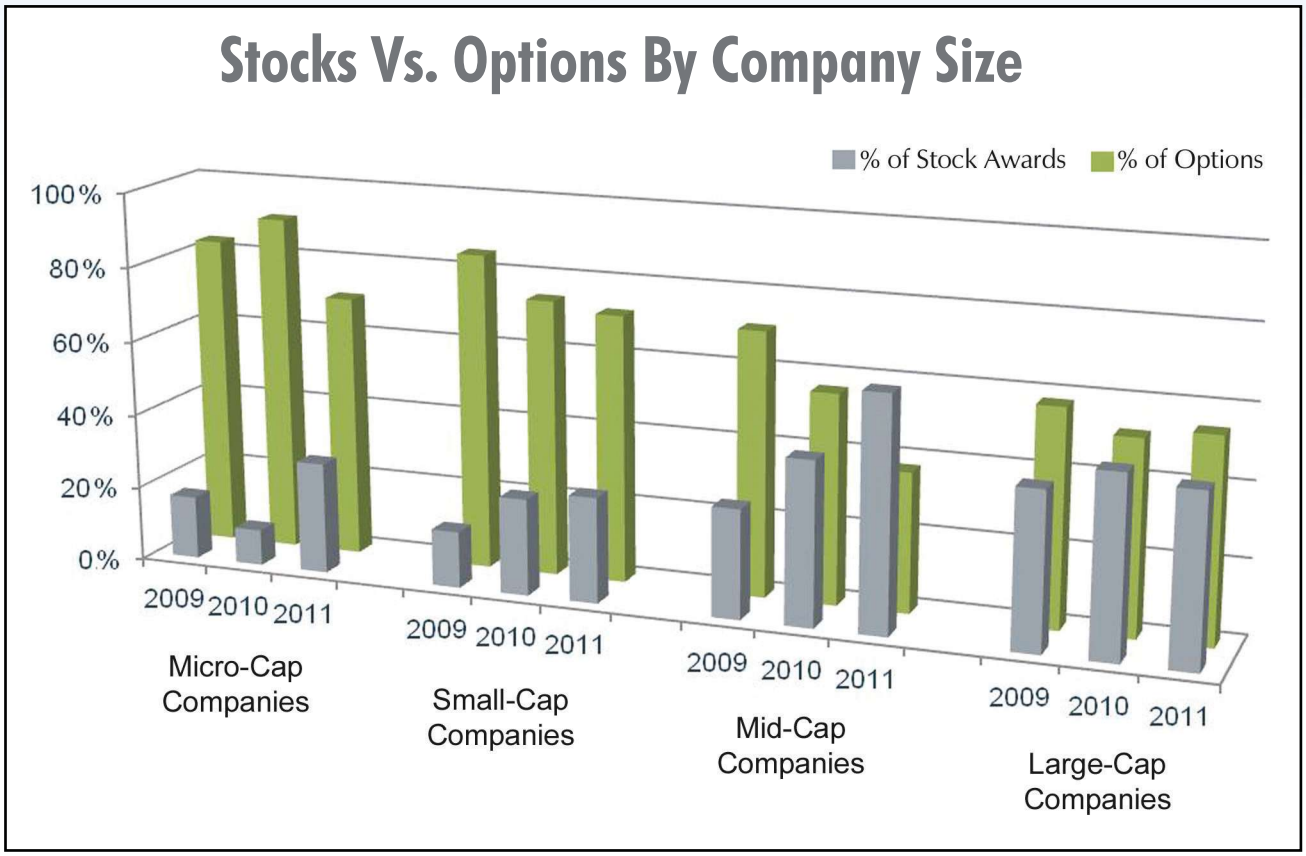
Additionally, it is obvious from the research that life sciences companies are moving away from incentivizing executives with cash bonuses, gravitating much more aggressively towards a mix of equity incentive awards. The percentage of stock to options is increasing, likely reflecting the last several years of stagnant stock performance. Increasing the stock offer in the form of restricted stock units, performance share units, and other nonoption grants in an overall compensation package has become a differentiating offer strategy. These trends are particularly evident with small and midcap companies, organizations that had tended toward stock options as their primary equity driver, but are now moving to stock awards as a major component of their equity incentive.

Even microcap companies with market capitalization under $250M are following suit, despite having historically leveraged significant option awards and lower cash compensation. Today, that same group is now compensating executives with an even mix of cash and equity, and the share of stock awards within that equity package has grown significantly.

WHY COMPENSATION PACKAGES ARE EVOLVING

Fierce competition for skilled, experienced, and successful senior executives is forcing life sciences companies to offer compensation packages that grow





annually at double-digit rates.

The drive behind increased stock awards seems obvious. Over the last decade, candidates have found themselves holding options that inevitably had little or no value after years of service to a company. This is not surprising given the high-risk nature of an industry challenged with difficult scientific hurdles, ever-strengthening regulatory barriers, and issues of broad global market access. Many companies fail, and many therapies do not make it to market. With this sobering view of the market and the odds of success less certain, executives are unwilling to put such a large percentage of their compensation into traditional option awards which — based on recent exits — are less likely to realize the payoffs seen in years past. Until the industry can reinvigorate pipelines and opportunities for significant growth with healthier returns, this trend is certain to continue.

CRAFTING OFFERS TO COMPETE

Base compensation is certainly the foundation of a compelling offer to a candidate for an executive position, but companies can provide some strong lures by paying attention to how they craft their equity offering. The executive search industry is seeing firsthand that a candidate's deciding factor is often the percentages of stock options vs. stock awards in the equity. Prospective candidates are well aware of the market trend, so stock awards have become expected, not just a negotiation strategy.

To remain relevant within the marketplace, biotechnology and pharmaceutical companies will have to remain more cognizant of these trends. Executives and investors will have to evaluate how their own compensation plans may be affecting their ability to attract top talent and then adjust their ongoing strategies accordingly.

About the Author

Steve Cornacchia specializes in the life sciences practice at executive search firm ON Search Partners. He has over a decade of international search experience consulting to multinational biotechnology, medical device, and pharmaceutical companies, including some of the world's foremost companies like Teva Pharmaceuticals, Allergen, and Shire.

Serialization Approval Possible By August

By Gail Dutton, contributing editor

With California's 2015 deadline for serialization looming, Congress is getting serious about crafting a single piece of federal legislation that will prevent a patchwork of legislation crafted by individual states. A bipartisan bill is expected to reach the president's desk in August.

If that occurs, individual states' bills regarding serialization or track-and-trace will be preempted by the federal legislation and set aside. California's serialization regulations contain preemption clauses, ensuring they will not compete with federal legislation and recognizing the benefit of a 50-state solution to address counterfeits.

Nonetheless, the California Board of Pharmacy formed an e-pedigree committee in May to focus upon implementing California e-pedigree law. As Virginia Herold, executive director, says, "We're moving ahead on implementation. If we're preempted, we're preempted." The Board's goal is to ensure that strong track-and-trace protection is in place in the U.S.

While waiting for a federal regulation, Greg Cathcart, CEO of Excellis Health LLC, advises pharmaceutical manufacturers to continue preparing to meet the California requirements. "The California legislation is the most stringent, so if manufacturers meet its requirements, they should meet any other serialization requirements easily."

BILLS READY FOR FLOOR VOTE

According to Chip Meyers, VP of UPS corporate public affairs, "The House version, H.R. 1919, was passed out of committee May 15." Its goal is to prevent duplicative federal and state requirements and "to establish a collaborative, transparent process between the FDA and stakeholders to ensure a reasonable, practical transition to reach unit-level traceability." The current bill requires lot-level traceability as a first step toward unit-level traceability. It establishes national standards for wholesale distributors, while continuing state licensing of wholesale distributors and state fee collection. It also establishes a definition and licensure standards for third-party logistics providers (3PLs) and allows the FDA or the states to collect licensing fees.

The Senate version, S.957, left committee May 22 with no amendments. Like the House bill, it calls for licensing of distributors and 3PLs. In this bill, product labeling is specified as "a human- or machine-readable, two-dimensional data matrix bar code on the package or on the case." As Meyers reports, "As the mark-up concluded, the Drug Supply Chain Security Act was incorporated into S. 959, the Pharmaceutical Compounding Quality and Accountability Act, by unanimous consent. The combined bill was favorably reported out, also by unanimous consent."

Because both bills are similar, industry associations say they each are workable, and Congress foresees no difficulty reconciling them. If the bills are approved by their respective branches of Congress, they will be reconciled. That version will be voted on again and sent to the president for his signature. At that point, it will become law.

The bill that eventually will be approved is intended as a basic framework, allowing the industry and the regulatory communities to build upon what it learns during each phase of implementation. "Lot traceability is a beginning point," according to Elizabeth Gallenagh, VP, government affairs and general counsel, HDMA (Healthcare Distribution Management Association). Whether the final model is track-and-trace or e-pedigree at the unit level is largely a matter of nuance, she adds. The final requirement will create challenges in terms of the enormous amount of data that must be recorded, stored, and passed throughout the supply chain.

TIME FRAMES ARE DIFFERENT

The bills under consideration significantly delay implementation. Initially, the Senate version of traceability legislation called for unit-level serialization and allowed 10 years before the requirements became mandatory. "The House version allowed more time and did

not contain a self-effectuating, date-certain mandate, which thereby requires the FDA to evaluate and promulgate regulations before final enactment," Meyers says. After markup, the Senate bill calls for unit-level traceability within seven years, with an additional evaluation and final enactment in 2027. The California regulation, in comparison, calls for 50% unit level by 2015 and 100% by 2016.

The extended time frames to phase in the federal legislation are included to allow industry leaders and regulators time to analyze the issues associated with each block of implementation process before proceeding to the next. "We need some transition period for the industry to ramp up and decide how to carry out provisions, changes in business practices, and processes," Gallenagh says. Time is needed for education, planning, and technical implementation to ensure that the serialization plan is effective.

"Another difference between bills is the whole concept of e-pedigree. That is a technological choke point, and pedigrees can be counterfeited easier than the drugs. They are not needed with serialization," Meyers says. The difficulty is easily underestimated by those who see the ease with which UPS and other international logistics providers expertly track packages throughout their networks in real or near-real time.

However, he emphasizes, "We're not pushing pedigree information through a pipeline to other users, and our package-tracking systems have taken time and investment to build." The requirement for data to be read and amended at each touch point and accessed by shippers, carriers, or end users creates an enormous database and requires massive standardization, not only of technologies, but of nomenclature. "So far, nobody has an interoperable system that provides a transaction history with a digital signature that does what the California regulation requires."

The ideal system may be a cloud-based portal that would provide a single database from which users could store and access information. "That sounds great on paper, but isn't necessarily the best approach," Meyers says. It would require massive coordination, significant trust, and a huge budget, among other hurdles (such as privacy concerns). Currently, pharmaceutical manufacturers are developing their individual systems to work with internal applications and are hoping to provide connectivity later for distributors and providers.

The closest the industry is coming to standardizing its approaches to serialization is broad agreement to use the GS1 standard for data. GS1 Healthcare U.S. Secure Supply Chain Task Force published a new guideline May 1 to identify and serialize pharmaceutical products using GS1 identification numbers. Called "Applying GS1 Standards to U.S. Pharmaceutical Supply Chain Business Processes to Support Serialization, Pedigree and Track & Trace," the guideline discusses best practices for GS1 deployment.

INDUSTRY IS PLEASED

"We're pleased with overall structure of the bills and the great amount of progress we've seen from Congress. We're very encouraged by that and very committed to continuing this momentum to reach a solution this summer," Gallenagh says. Congressional efforts will streamline the regulations "and make it more difficult for bad actors and products to infiltrate the supply chain. We will build on lessons learned in using new technology to streamline operations to ensure patients get safe products, regardless in which state they reside."

The pharma industry supports the federal efforts. HDMA President and CEO John Gray calls the bills "another step toward finally eliminating the current patchwork of state requirements. Establishing a federal, uniform traceability solution will offer greater regulatory clarity to the healthcare industry and ensure lifesaving medications are delivered safely to those who need them." The Pharmaceutical Distribution Security Alliance (PDSA) is equally supportive, saying, "PDSA strongly supports passage of legislation to protect patient safety and secure the pharmaceutical distribution supply chain through a single, uniform, and national system and urges Congress to enact such a legislative solution as quickly as possible."

If this bill makes it to the president's desk, "It will get there via compromise. No one sector alone will be popping champagne," Meyers says. "There will be shared pain and, hopefully, a shared sense of accomplishment." Ultimately, however, serialization technology could eventually enable consumers to scan serial numbers for their medication into their smartphones and check a database as assurance against counterfeits.

OTHER NATIONS

Other nations also are advancing their own serialization plans. Globally, serialization efforts began in 2010 with requirements for track-and-trace in Turkey, product codes in Cyprus, traceability in Serbia, and standardized numerical identification in the U.S. Since then, product code requirements have been added by Denmark; batch codes by Canada, France, and Korea; and various traceability requirements by the EU, Spain, and China. Argentina launched an end-to-end serialization system late in 2012.

Going forward, Germany is piloting an end-to-end serialization program late in 2013. The EU is calling for compliance by 2014 and Korea by 2015, Cathcart says. China will begin implementing a national track-and-trace strategy in 2015 and began phasing in revisions to its good supply practices June 1. "The EU is expected to implement a staged approach between 2016 and 2018. Brazil and India, which had put their serialization regulations on hold, are dusting them off."

The message for pharmaceutical manufacturers is clear. Serialization is coming — either through California's regulations in 2015 or through a federal bill this autumn with delayed implementation. Either way, now is the time to prepare.

GDUFA Sheds New Light On Industry's Common Ground

By Wayne Koberstein, executive editor

FDA user-fee programs will now apply to all the competing pharma sectors — and in many ways highlight the interests they share.

Some of my recent work has led me to think of the pharmaceutical industry in a new light — a light that shines broadly. As time goes by, I start to see as many similarities as differences among the industry sectors we commonly define as branded, generic, specialty, bio, and contract pharmaceuticals.

Or, at least, I see more common ground, either because my vision or, more likely, the field itself is expanding. A good example is GDUFA (Generic Drug User Fee Act). Of course it would be logical to think GDUFA is all about generics, but in fact its manufacturing implications for pharmaceuticals tend toward the universal. All of the pharma sectors, even bio indirectly, will feel its effects.

A short pause will ensue for all the cries of "Foul" surely to follow … .

How could I possibly walk onto the battlefield and talk about common ground? Large companies that originally brought their patented products to market — once facilely called the brand name companies — are to generics makers what lions are to jackals, right? All those products going off patent, once firmly in the lion's jaws, are about to be plucked and carried away by the scavengers biting at its heels. How could GDUFA, a program designed to speed the generics feeding frenzy, possibly serve the interests of the originator industry? And if GDUFA reaches its other goal of ensuring manufacturing quality for generics, what will Big Pharma do without its traditional argument that only brands can be trusted?

THE ADVERSE SIDE OF GDUFA

First, I didn't say the effects of the Act would be all good. To the extent that the originators fail to originate, the elimination of ANDA (abbreviated new drug application) backlogs could bring them some tough times. And there will also be pain for pharma when GDUFA inspections tag problems in facilities supplying API or even finished product for on-patent as well as off-patent drugs. On the generics side, there will be a consequent shake-out of manufacturers lacking the resources to comply with the law. But, believe it or not, there is some silver lining in the sub-clauses of this law.

Counterfeiting, drug shortages, uneven product and supplier quality, and post-market safety issues are likely the main Big Pharma concerns GDUFA aims to address. By mandating the FDA's first-ever registry of pharmaceutical manufacturing companies, establishing (by 2017) biannual inspections, and moving toward parity of domestic and foreign inspections, the law may flush out many of the manufacturers who not only produce faulty generics but also counterfeit brands or patent-infringing follow-ons. GDUFA will apply pressure to other plants, many of which supply both generics and brand name API or finished products around the world. It will also supply funding to increase FDA monitoring of post-market safety for generics, which will at least bring a measure of sobriety to the industry's post-patent party.

Whether such measures will favor the large generics companies over the small is debatable, but certainly it will reduce the total number of players and erect new entry barriers. Off-patent brands continuing to compete against generics may thus hold on to somewhat greater market shares — or the innovator companies may find the idea of entering the generics business themselves more attractive. For generics companies and suppliers, the competitive dynamics will shift as they self-identify, pay their fees, and ready themselves for FDA inspections. And there is a wild card: Failure to pay fees on time can result in the loss of "first-to-file" status — a profound strategic and financial blow, to say the least.

Beyond fees, GDUFA will demand a certain amount of capital investment by manufacturers, its size determined by each one's state of repair. The resulting effect on generic-drug pricing is anyone's guess, but if the answer is significantly higher prices, several serious consequences will likely follow. A backlash to the law itself is one, considering its mission of "accessibility." Another is at least a temporary advantage to the bigger players, including the aforementioned pharma companies entering the business they once decried. But, again, not all the consequences will be bad for either side.

GDUFA has long-term implications, good and bad, for biotech and biosimilar drugs as well. The Food and Drug Administration Safety and Innovation Act (FDASIA) of

2012 is the overarching legislation that authorizes user-fee programs for all pharma sectors, including the Bio-Similar User Fee Act (BsUFA) following close on GDUFA's heels. No doubt the FDA will apply some of the lessons learned with GDUFA to the biosimilars program, and there will be numerous analogies between both programs' effects on originator and follow-up manufacturers. Again, the larger CMOs may have the advantage of housing both small-molecule and large-molecule production and applying their experience to one side to the other.

It would be a mistake to assume too many similarities between GDUFA and BsUFA, however; for example, a vast difference in sheer numbers of reviewed products predicates disparate goal structures: "eliminating backlogs" for generics vs. annual review rates for biosimilars. In short, BsUFA seems more closely modeled on PDUFA, the branded pharmaceutical user-fee program, than on its generics equivalent. Still, the simple existence of user-fee programs now established or under construction for all the industry sectors gives them something significant in common and serves to underscore my central point.

FROM COMMONALITIES TO UNITED PURPOSE

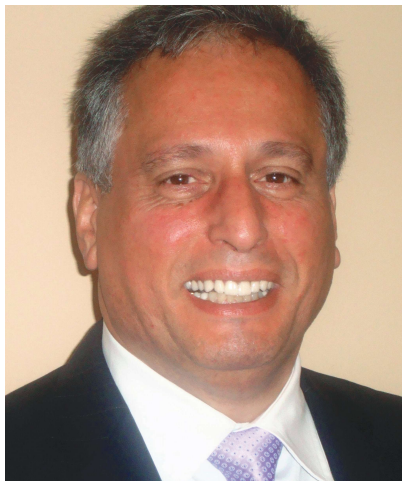
In my mountain-top dream of an industry common ground, I can imagine GDUFA as a great stimulator of technological progress for all companies doing business through the manufacturing of medicines. As in real life, however, the progress will be evolutionary — and, therefore, imperfect. It will take longer than planned, kick up a hive full of inconsistencies and unexpected problems, exalt some players and ruin others, and perhaps never get the credit it deserves. But GDUFA has the potential of breaking the status quo and raising the benchmark for pharma manufacturing technology as a whole.

Some interesting hybrids may result. For example, a large pharma or biotech company might team up with a specialty pharma or generics company to create an entirely original product with superior targeting, potency, and stability. Oh wait … that's already happened, hasn't it? Arguably, one example might be Genzyme and Isis codeveloping Kynamro (mipomersen) for familial hypercholesterolemia, though I invite readers to nominate other candidates. But here is a genuinely unrealized goal: companies from every sector coming together to take a great leap forward in drug efficacy and safety through advanced manufacturing and delivery techniques alone.

This industry, broadly including all life sciences companies and leaders, rarely sees itself as others see it. Patients and people in general hardly ever distinguish between the various sectors or concern themselves with the competitive struggle among them; instead, they look at the industry in the broadest strokes, illuminated by the light of its works. Either they trust you — or they don't. That is the common ground.

Industry Leader

Reformulating Drugs: The Promise For Novel Therapeutics And New Targets



Anthony Giovinazzo

Giovinazzo is president and CEO of Cynapsus Therapeutics, Inc., which is developing the only non-injectable (sublingual) delivery of the only approved drug (apomorphine) to be used as a rescue therapy for "off" motor symptoms of Parkinson's disease.

Finding new formulations for approved drugs continues to produce important therapeutics. In recent years, an increasing number of pharmaceutical development programs have focused on this endeavor.

Depending on the amount of existing human exposure data, reformulating an existing drug has the potential either to eliminate preclinical testing and early clinical trials or cut some of the 10 to15 years and the more than $1 billion it can take to bring a new chemical entity to market. Reformulation also reduces the risk of late-stage product failure from unexpected toxicity or efficacy, and it is breathing new confidence into an industry whose research managers have been trained to "fail fast."

As Fred Olds recently noted in these pages ("Repurposing And Rescuing Pharmaceutical Drugs", May 2013), about 80% of drug candidates fail in Phase 2 trials because they don't reach criteria for efficacy. Reformulating marketed drugs offers entrepreneurs the potential to replenish pipelines with reduced risk and time in drug development. Olds also correctly observed that with reformulation, research starts with defined pharmacokinetic data and a compound already proven safe through possibly millions of human exposures. If an apparent safety issue arises, investigators are more likely to approach it as an anomaly rather than to consider dropping the project.

Reformulating drugs is particularly important in the treatment of central nervous system disorders, cardiovascular disease, metabolic disorders, and cancer. Pathological processes in these conditions are carried out by proteins and processes that differ from their normal counterparts only in a subtle way, such as the level or pattern of expression. Sometimes these subtleties are only discovered by anecdotal observations of patients or by patients reporting unexpected therapeutic benefits, and the reformulating activity depends on improving the formulation or optimizing a treatment regimen. In contrast, molecular target-based screening and rational drug design remain the standard for targeting infectious agents (e.g. HIV and hepatitis C viruses) because the pathogen's targets are either unique or sufficiently different from their human homologues as to increase the likelihood of developing specific inhibitors.

SUPPORT FOR DRUG REFORMULATION

Reflecting the appeal of drug reformulation, 2012 witnessed several conferences for researchers. A few years ago, no such conferences existed. Additionally, initiatives related to drug reformulation are growing. For example, in spring 2012, eight major drug firms joined the National Center for Advancing Translational Sciences (a division of NIH) to create the Discovering New Therapeutic Uses for Existing Molecules program.

Many drug reformulation projects are supported by the FDA's intention to encourage innovation without creating duplicate work under the 505(b)(2) provision. Filing a new drug application (NDA) under the 505(b)(2) provision allows a sponsor to rely, in part, on the FDA's earlier findings of safety and/or effectiveness for the previously approved drug, thereby simplifying the drug development pathway, allowing a less expensive development program and faster access to market.

Drug reformulation holds the promise of delivering new forms of treatment for some of the most intractable CNS disorders, cardiovascular disease, metabolic disorders, and cancer. Reformulated drugs can also provide the tools and understanding needed to develop second-generation drugs. Given the stringent demands of managed care for truly differentiated products, drug reformulation is a beacon of hope to developers of drugs for conditions that have not been improved by molecular target-based design.

In addition to the motivations that have been outlined above, drug reformulation can be instrumental in creating new drug-delivery methods that are better for the patient. For example, a drug that is traditionally available only in an inconvenient and painful injectable form might be reformulated into a sublingual thin-film strip. If pharmacokinetic studies reveal that the latter delivers the drug at a concentration and in a time period similar to that offered by the original form, it can help many patients uncomfortable with the prospect of injection.

Ultimately, a great range of patients with a wide range of conditions may benefit from the class of reformulated drugs that have gone through the regulatory approval process at least once and have an abundance of human experience.

The Advent Of Electronic Source Records In Clinical Trials

Do you remember where you were when you heard the slogan, "cleaner data faster?" That was the promise of electronic data capture (EDC). EDC is now widely embraced and is often the de facto method of data capture in clinical trials. How far can EDC expand? We already have robust processes and services in electronic patient recorded outcomes (ePROs), and this area has combined well with certain types of EDC studies. The question is, "How far are we from the utopian vision that is 'e-Clinical' where data is recorded once and is available directly in the database?" Who is responsible for reviewing the data in an eCRF (electronic case report form) against the source data? What if we didn't have eCRF data — just source data? What if the data recorded in source data were transferred to the database in real time?

EDC studies (i.e. eCRFs) are arguably a contemporary version of a paper CRF with a paper source document. The assessment is recorded in the source at the site, entered into an online EDC application, and then verified by a monitor. It is rare that any development of an eCRF involves the ultimate end users, the investigator, and study nurse in the testing. Therefore, sites often are faced with entering data in a different way from how it was originally captured. Surely there would be greater buy-in from sites if they entered data directly into a repository that replicates the format of the current paper source or electronic medical record (EMR). If this could be accessed and utilized directly at the patient bedside, then data could be accessed in almost real time by the sponsor.

The rise in database variable naming and form structure standards has led to increases in data quality and greater adoption by study teams. As these electronic data standards move into other areas of data capture, we have seen the steady adoption of ePROs as their use negates late patient data entry and allows for reasonably continuous access to patient data via online tools.

We also have seen the integration of data that negates reconciliation. If data that is already captured in an IVRS (interactive voice response system) or IWRS (interactive web response system) is used to populate fields in an eCRF, entry errors and reconciliation can be reduced or eliminated. These processes also can provide a mechanism, through integration, that halts data entry until the patient is acknowledged as randomized within the system, thus negating erroneous entry of screen failures.

INTEGRATING SOURCE RECORDS WITH EMRs

It's often difficult to integrate electronic source records with EMRs because there are two distinct objectives in terms of the data captured. A trial captures data based on a protocol and in a system designed around a CRF. If clinical patient data was collected only as electronic source data, it would be possible to integrate that data with an EMR using healthcare interoperability standards such as Health Level Seven (HL7) data export or, alternatively, printing the electronic source data and adding it to the patient's medical record.

The harnessing of all electronic data could move a trial toward being truly "e-Clinical." However, there are still questions about the legitimacy of data as it is transferred from one location to another through human data entry.

Stuart Cook

Stuart Cook is director of CDM (clinical data management) at Quanticate. During a 13-year career in clinical research, he has been integral to three separate EDC process initiatives and worked extensively in EDC and ePRO-based clinical trials.

With source data verification (SDV) and data management review through edit checks and listings, transcription errors are found throughout trials. If there were no transcription of source data from patient records into the CRF, it wouldn't be necessary to monitor for transcription errors. There would still be a requirement to manage transcription errors, but it would be at the point of initial entry (e.g. checks for future dates, ranges checks). This approach could be harnessed in certain types of trials where there is no other paper-source collection, such as local lab records or paper ECGs, as these would be additional primary source data that would require entry.

Finally, we already have seen attempts to reduce the cost of monitoring visits by increasing central or remote monitoring and targeted SDV. Even so, SDV contributes around 50% of a monitoring visit. The current model of using paper documents or EMRs at the site to record patient source data means that in order for the data to be monitored, the monitor must be able to access the source documents. If electronic source records were used, there would be no need for reconciliation between the source data and the CRF data. Potentially, the frequency of monitoring visits could therefore be reduced.

The Importance Of Succession Planning

Mike Myatt

Succession is a very real concern for every organization — or at least it should be. Here's the thing — when it comes to the topic of succession, it's not a matter of if but when. No leader can lead forever. Failing to plan for the inevitable is irresponsible, but failing to execute the plan is tantamount to leadership malpractice.

Let me be clear — successions fail for one reason: a lack of leadership. Companies, boards, and their advisors who fail to successfully transition a leader (regardless of level) tend to focus more on silly processes than on the need, the people, and the culture. I've seen many corporate succession plans, but rarely does the readiness for succession match the readiness of the planning process.

Many otherwise savvy business people don't understand succession as well as they would have you believe. They focus on optics, politics, and convenience more than on delivering the right outcome. Planning isn't the end game; it's the jumping off point.

In my job, I normally work on 6 to 10 new Fortune 500 CEO succession engagements each year. I've witnessed the best and worst of succession philosophies and practices, and I can assure you that more companies get it wrong than right.

While most organizations have dealt with succession planning at some level, they rarely touch all the necessary constituencies with appropriate timing and care. Succession needs to be part of the values, vision, strategy, and culture of an organization. It must be embraced by leadership, communicated to the workforce, and understood by external stakeholders. It must be viewed as a step forward and not a regression.

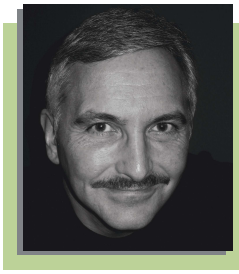
While many will overcomplicate succession, others tend to trivialize it. The truth is, succession is a blending of the art and science of leadership, people, positions, philosophies, relationships, culture, and a certainty of execution. The following are three points to keep in mind as your organization addresses succession.

Internal vs. External — All the leadership development programs in the world won't ensure an internal candidate will be the right person for the job when it becomes available. It doesn't matter whether the succession candidate is internal or external — what matters is whether they are the right candidate to lead the organization.

Process vs. People — A plan doesn't succeed an outgoing leader, a person does. Succession is more than planning, as plans don't develop people, experiences do. The incoming leader must do more than assume a leadership position or title; they must actually be willing to lead and capable of leading the organization through the present and into the future.

Don't Pass the Buck — Succession is not an HR problem; it's a leadership problem. Succession of any position is a complex collaboration between diverse constituencies. It's more complex than recruiting or development. Succession must be a cultural imperative aligned with the core values of the enterprise, or you'll be engaging in little more than a rolling of the dice.

Bottom line — organizations that make succession a priority are more successful than those that don't. I'll leave you with a quote from John Maxwell, "There is no success without a successor."



Mike Myatt is a noted leadership expert and author of *Leadership Matters — The CEO Survival Manual*. As a thought leader and columnist on topics of leadership and innovation, his theories and practices have been taught at many of the nation's top business schools, and his work has been noted in several publications including *Psychology Today, The Washington Post, Entrepreneur,* and *Chicago Sun Times*. He also authors the N2growth Blog, recognized as one of the top leadership blogs on the Internet. For more info go to www.n2growth.com.

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