

Life Science Trends 2015

Featuring Interviews
with Thought Leaders
in Personalized
Medicine:

**Personalized Medicine
Comes Of Age**

**Dr. Darrin M. Disley
Peter Keeling
Dr. Myla Lai-Goldman
Dr. Ralph Snyderman
Dr. Paul Beresford**



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www.carlyleconlan.com



About Life Science Trends 2015

Each year, Carlyle Conlan, with a focus on North America, and George James Ltd., with a focus on Europe, provide an overview of trends and innovations in the life science industry, encompassing its drugs, biologics, devices and diagnostics sectors. Utilizing a number of in-depth, premium research reports available in the industry, Life Science Trends 2015 summarizes and presents a variety of the most up-to-date industry news under several macro headers: Research and Innovation, Fundamental Trends, Investing and Deal Making, Regulatory and Government, and Healthcare. The result is a meaningful, "quick-read" white paper into which topics our clients, partners and constituents can dig deeper based on their individual interests.

Life Science Trends 2015 captures significant advances in the industry from the past year and makes observations about developments of interest through the year ahead. Of central importance is the understanding that trends do not necessarily change on a yearly basis. For instance, the field of personalized medicine is expected to continue as a trend well into the foreseeable future.

Our report may differ from others in that an early version is sent to CEOs, venture capitalists, and other industry experts for review before its final release. This report was created using both primary and secondary data. Secondary data is highlighted with associated links to further information as available in the public domain or credited to the appropriate source.

We invite you to review the information contained in this report, which we trust you will find interesting and relevant to the sector.

About Carlyle Conlan

Carlyle Conlan, headquartered in the Research Triangle Park, is an executive and professional search firm focused on the life science, agriculture, and applied materials sectors. With a highly dedicated, experienced, and professional team of specialists, we work with small, mid-sized and large companies to secure their most important asset, human capital. Our placement focus is on highly experienced individual contributors through C-level search in a variety of functional position types throughout North America. More information about Carlyle Conlan can be found at: www.carlyleconlan.com



About Life Science Trends 2015

About george james ltd

george james ltd was founded in 1999 to provide a range of both standardised and bespoke recruitment and training service across Europe. As the network of contacts expanded, new services in corporate development were added in 2002.

Founded by two experienced and successful senior industry professionals with global experience across a range of industries now served, they had been frustrated by the level of service they experienced in both sales training and recruitment. As a result the principals' initial focus was to develop and continually optimize services to address the issues they had encountered. Both founders' own career success had been based on the simple understanding that nobody can advance his/her own career, and no company can maximize its success without recruiting, developing and keeping the best talent. Helping their customers achieve this is their core goal and specialization. Other successful, experienced industry professionals who share this vision have joined to strengthen and expand the team. More information about george james ltd can be found at: www.georgejamesltd.co.uk



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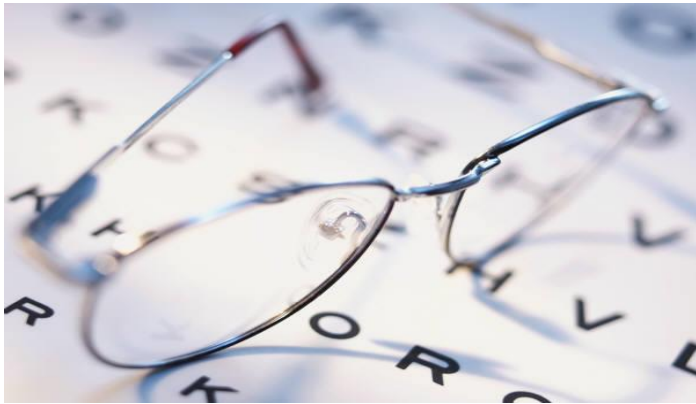


Bacterial Spies

Harvard researchers have fashioned *Escherichia coli* to act as sensors to monitor the gut environment.

Pamela Silver and her colleagues engineered *E. coli* with a two-part system consisting of what they've dubbed a "trigger element" in which the Cro gene from phage lambda is hooked up to a tetracycline-inducible promoter and a so-called "memory element" from the phage cI/Cro region. They then fed these *E. coli* to mice.

GenomeWeb



Cancer Imaging Glasses

Up to 25 percent of breast cancer patients end up requiring a second surgery to remove cells that could not be detected the first time around. But a new wearable technology is being developed that would enable surgeons to distinguish cancer cells from healthy ones, reducing the need for repeat procedures and the associated pain and anxiety.

Burrus

3D Printed Organs Come a Step Closer

For years, scientists have been able to “print” types of human tissue using a 3D printer, but in a significant leap forward by US and Australian researchers they can now make that tissue survive on its own.

Until now a major barrier to them moving from printing tiny sheets of tissue to entire 3D organs is that they hadn't figured out how to develop the blood vessels that provide cells with nutrients and oxygen, and allow them to excrete waste.

The Guardian

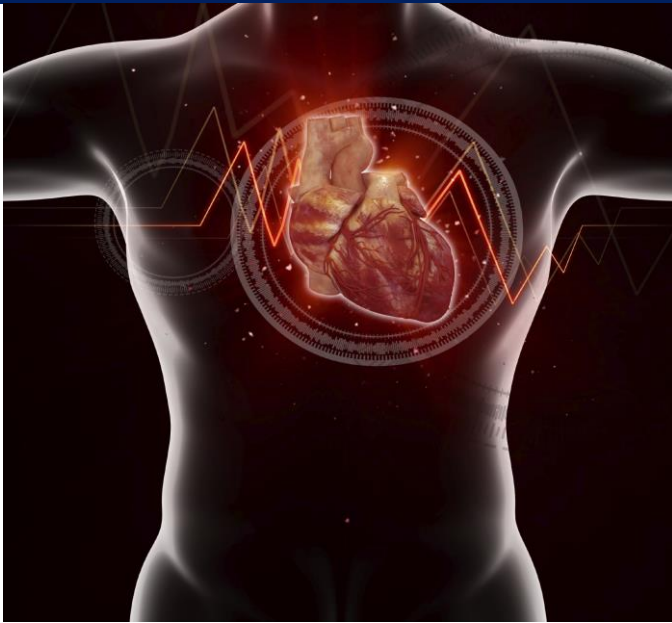
Google[x] Reveals Nano Pill to Seek Out Cancerous Cells

Detecting cancer could be as easy as popping a pill in the near future. Google's head of life sciences, Andrew Conrad, took to the stage at the Wall Street Journal Digital conference to reveal that the tech giant's secretive Google[x] lab has been working on a wearable device that couples with nanotechnology to detect disease within the body.

“We’re passionate about switching from reactive to proactive and we’re trying to provide the tools that make that feasible,” explained Conrad. This is a third project in a series of health initiatives for Google[x]. The team has already developed a smart contact lens that detects glucose levels for diabetics and utensils that help manage hand tremors in Parkinson’s patients.

TechCrunch





Cardiac Pacemaker Powered By Body's Own Muscles Developed

Over the past few decades, cardiac pacemaker technology has improved to the point that pacemakers have become a commonplace medical implant that have helped improve or save the lives of many millions of people around the world. Unfortunately, the battery technology used to power these devices has not kept pace and the batteries need to be replaced on average every seven years, which requires further surgery. To address this problem, a group of researchers from Korea Advanced Institute of Science and Technology (KAIST) has developed a cardiac pacemaker that is powered semi-permanently by harnessing energy from the body's own muscles.

The research team, headed by Professor Keon Jae Lee of KAIST and Professor Boyoung Joung, M.D. at Severance Hospital of Yonsei University, has created a flexible piezoelectric nanogenerator that has been used to directly

stimulate the heart of a live rat using electrical energy produced from small body movements of the animal.

[gizmag](#)

Nobel Laureate: Big Data and Full-Genome Analysis Not All They're Cracked Up To Be

Walter Gilbert won the Nobel Prize in 1980 in Chemistry for his contribution to sequence DNA, or "determination of base sequences in a nucleic acid". Mohit Kumar Jolly, researcher at Rice University and contributor to The Conversation, interviewed him at the 2014 Lindau Nobel Laureates Meeting.

[The Conversation](#)

Researcher Debunks Alzheimer's Development Theory

New research points to tau, not amyloid-beta (Abeta) plaque, as the seminal event that spurs neuron death in disorders such as Alzheimer's disease. The finding, which dramatically alters the prevailing theory of Alzheimer's development, also explains why some people with plaque build-up in their brains don't have dementia.

The study is published online in the journal *Molecular Neurodegeneration*. Neuronal death happens when tau, found inside neurons, fails to function. Tau's role is to provide a structure — like a train track — inside brain neurons that allows the cells to clear accumulation of unwanted and toxic proteins.

[Drug Discovery & Development](#)

Research and Innovation

Revealed: Scientists 'Edit' DNA to Correct Adult Genes and Cure Diseases

A genetic disease has been cured in living, adult animals for the first time using a revolutionary genome-editing technique that can make the smallest changes to the vast database of the DNA molecule with pinpoint accuracy.

Scientists have used the genome-editing technology to cure adult laboratory mice of an inherited liver disease by correcting a single "letter" of the genetic alphabet, which had been mutated in a vital gene involved in liver metabolism.

A similar mutation in the same gene causes the equivalent inherited liver disease in humans – and the successful repair of the genetic defect in laboratory mice raises hopes that the first clinical trials on patients could begin within a few years, scientists said.

The success is the latest achievement in the field of genome editing. This has been transformed by the discovery of Crispr, a technology that allows scientists to make almost any DNA changes at precisely defined points on the chromosomes of animals or plants. Crispr – pronounced "crisper" – was initially discovered in 1987 as an immune defense used by bacteria against invading viruses. Its powerful genome-editing potential in higher animals, including humans, was only fully realized in 2012 and 2013 when scientists showed that it can be combined with a DNA-sniping enzyme called Cas9 and used to edit the human genome.

Independent



Overcoming Antibiotic-Resistance

Overuse of antibiotics has created a number of strains of "superbugs" that are resistant to nearly all forms of treatment. One such threat is a type of tuberculosis (TB), a deadly infectious disease that affects the lungs and which has returned in a resistant state, prompting researchers to seek out solutions that will stop the spread of these diseases once and for all.

Recently, a new compound was patented that is designed to basically "cure" bacteria of their resistance and return them to a primitive, susceptible state. It does this by blocking a mechanism known as an efflux pump, which helps superbugs to ward off antibiotics before they have a chance to work. This enables the antibiotics to remain in the bacteria until they die off.

Burrus

Research and Innovation

Glass Diagnostics

It appears that there may be uses for Google Glass beyond wearing them to attract mates and to make everyone not wearing them feel like outsiders.

In what amounts to a teaser for how Glass and similar tools may one day be used in medicine, an inventive group of UCLA scientists have worked up an app that uses the space-age specs to make it much faster and easier to get the results of medical diagnostic tests.

[GenomeWeb](#)

Top 10 Innovations 2014

The Scientist's annual Top 10 Innovations competition has again turned up some exciting new products that are poised to revolutionize the work of life scientists. Familiar names, such as Illumina and Leica, win again with updates to their sequencing and imaging technologies, while newcomers like Sciencescape, Organovo, and Edico Genome debut with novel products

that caught the eyes of our independent, expert judges.



The Top 5 of this year's winning innovations involve the process of genome sequencing: tools to do the actual sequencing, technologies to make it easier to prepare genetic regions for sequencing, and a processor that can handle the avalanche of data that results from such analyses.

[The Scientist](#)



Fundamental Trends

System Overhaul Needed

The US biomedical research system has "systemic flaws," write four prominent researchers in an editorial in the *Proceedings of the National Academy of Sciences*. They argue that an erroneous assumption that biomedical science would continue its rapid growth has led to a system plagued by hypercompetition that produces too many trainees contending for resources and encourages investigators to stick to well-worn research paths.

GenomeWeb



BIO 2014: An Industry Surrounded by Insurmountable Opportunity

Biotech is riding the crest of a wave of public and private financial interest unparalleled in the 36-years since the founding of Genentech. Since 2012 public markets have committed \$10.3 billion to more than 100 life-sciences IPOs, an industry record. Pharma has been buying/partnering with biotech on an unprecedented scale. Research breakthroughs

from cancer immunotherapy to wearable IT to real-time genomics are generating new business opportunities undreamed of a decade ago. Old technologies like gene therapy and RNAi are showing signs of finally achieving commercial relevance. Demand in the form of unmet medical needs is intense. Led by J&J's Innovation Centers, pharma has suddenly shown an interest in stimulating external discovery/early development. Research continues to generate new hypotheses and targets at such a prodigious rate that commercial development falls further behind every day. The entrepreneurial community overflows with talent from the growth of biotech and the contraction of pharma. As the CEO of one of my portfolio companies once described the challenges he faced, "We are surrounded by insurmountable opportunity."

Xconomy

A Recap On 2014 Outsourcing Trends and What To Expect in 2015

2014 was an exciting year in outsourcing. Several high profile mergers and acquisitions in both the CRO and CMO world will mean some familiar names will go through big changes — Huntingdon acquired Harlan, and PRA acquired RPS in the CRO world; Patheon acquired both DSM and Gallus Biopharma, and AMRI acquired Cedarburg and OsoBio in the CMO world.

Life Science Leader



Fundamental Trends

Global Market for Nanoparticles in Biotechnology and Pharmaceuticals to Reach \$79.8 Billion by 2019

BCC Research (<http://www.bccresearch.com>) reveals in its new report, NANOPARTICLES IN BIOTECHNOLOGY, DRUG DEVELOPMENT AND DRUG DELIVERY, the global market for nanoparticles in biotechnology and pharmaceuticals is expected to reach \$79.8 billion in 2019, with a compound annual growth rate (CAGR) of 22% for the period 2014 to 2019. Drug delivery systems segment is surging at a significant CAGR of 23%.



[PRWeb](#)

Synthetic Futures

The synthetic biology sector is starting to gain steam, as humankind gets closer to achieving its long-held ambitions to hack into the natural world and make it work for us, and more investors start to arrive on the scene, according to *Entrepreneur*.



Developments in recent years have made it more likely that companies can use synthetic biology tools to produce new products like materials, biofuels, flavors, drugs, and fragrances, among others, Britt Wray writes.

[GenomeWeb](#)

Trends and Developments in the European Companion Diagnostics Market

Frost & Sullivan recently released a report entitled "Western European Companion Diagnostics Market." This study provides a global outlook of the companion diagnostics market, specifically focusing on Western Europe. The report discusses the oncology segments in companion diagnostics including breast, lung, and colorectal cancers as well as non-oncology areas such as infectious diseases, central nervous system, and cardiovascular. The study also discusses the reimbursement and regulatory approval pathways for companion diagnostics in Germany, the United Kingdom, France, Italy, Spain, Scandinavia, and Benelux.

Fundamental Trends

According to the report, the companion diagnostics market in Western Europe generated revenues of \$457 million in 2013 and is estimated to reach \$1.3 billion in 2018. The market is expected to grow at a compound annual growth rate of 23.2% from 2013 to 2018.

Medical Design Technology

New System for Classifying Cancer Could Change the Way Drugs Are Developed

Largest cancer genetic analysis reveals tumor subtype correlated to cell type rather than tissue type.

Cancers are traditionally classified depending on the organ of the body where the tumor originates. But a

published study by researchers in the Cancer Genome Atlas Research Network, detailing the largest and most diverse tumor genetic analysis ever conducted, reveals a new approach to classifying cancers that could upend that tradition, revamping traditional ideas of how cancers are diagnosed and treated. It could also have a profound impact on the future landscape of drug development, say the researchers.

The Burrill Report

Exposing Patients to the Bigger Mobile and Digital Health Picture - Did We Forget to Tell Them?

To understand just how far mobile and digital technology can truly influence progress in

global healthcare, we first need to form the foundation of the discussion with a few rudimentary facts.

1. Clinical research ("a branch of medical science in human beings") is critical to healthcare.
2. All patients are human beings.
3. All stakeholders are current or potential patients.
4. All stakeholders therefore have a vested interest in progression of healthcare.

Our current healthcare model is evolving, slowly but surely. How this progression is defined, and how mobile and digital technology can help to speed this along, will be explored in this article.

Applied Clinical Trials

US Hep C, Cancer, Diabetes Med Costs Drive Global Drug Tab Past \$1 Trillion Mark

According to a report from the IMS Institute for Healthcare Informatics, the high cost of novelty hepatitis C and cancer medications (such as Gilead's Sovaldi and Harvoni), especially in the United States, will drive total global drug expenditures past the \$1 trillion mark in 2014.

The biggest drivers of this year's significant rise in drug spending? Hepatitis C drugs, specialty cancer meds (such as Roche's Perjeta and Kadcyra), diabetes medications, and dwindling availability of new, cheap generic versions of branded medications. Hep C and cancer drugs are each estimated to have added \$100 billion to this year's spending tab, while diabetes drugs added another \$78 billion.

BioPharma Dive



Fundamental Trends



Biosimilar Medications Could Create Billions in Savings

The U.S. Food and Drug Administration is developing regulations to govern the approval process for highly similar versions of the already-approved complex, protein-based biologics, which includes drugs such as insulin, monoclonal antibodies and a range of medications to treat other serious conditions.

While expected to produce less-dramatic savings than an earlier generation of less-complex generic drugs, the introduction of biosimilars into the U.S. marketplace is expected to increase competition and drive down prices, resulting in savings for patients, health care payers and taxpayers.

Drug Discovery and Development

2015 Pipeline Report: Burning Bright

Tracking new therapies as they wind their way through development, regulatory approval, and payer acceptance can be like waiting for paint to dry and then repainting in a different color. It's a slow process and far from linear.

This year's pipeline report will check in on these emerging technologies, as well as potential therapies to address metabolic and neurodegenerative diseases. There's a lot to like in the pipeline and more than a little competitive drama to make it really interesting.

PharmExec

Average Cost of Drug R&D? Try \$2.9B On For Size

The Tufts Center for the Study of Drug Development created the industry standard on R&D budgets when it pegged average R&D costs at close to \$1 billion for each new drug. Today, Tufts researchers updated their figures and boosted the total to \$2.9 billion.

Nothing creates an instant controversy in biopharma like a new study on average drug research costs. But before we take up the likely debate, let's look more closely at the figures used by Tufts.



The average out-of-pocket costs on R&D have hit \$1.4 billion. And researchers at Tufts added in \$1.16 billion for what it calls "time costs (expected returns that investors forego while a drug is in development)." Include another \$312 million for postapproval research and the average costs spikes to \$2.9 billion--a megablockbuster figure that would daunt any investor. And that's way up from their \$802 million figure in 2003, a little more than \$1 billion in today's inflation-adjusted figure, which helped get this discussion started.

Fierce Biotech

Supergenerics

The last two decades have seen healthcare costs in most developed countries rise at an unsustainable pace. This is being driven by an ageing population, advances in medical care, a desire to treat more patients with rare diseases, and society's demand for ever-improving medical provision. Healthcare spending in the US accounted for 17.9% of GDP in 2012, while in Sweden the figure is 9.6% and the UK 9.4%. In China, the policy of investing in healthcare is clearly evident, with spending already making up 5.4% of GDP – and estimated to reach 7% in 2020.

In an effort to curb costs, governments around the world have been implementing a broad range of measures. President Obama's Affordable Healthcare Act is the latest in a series of cost-containment measures in the US.

This legislation is designed to provide access to many more Americans, while at the same time saving money via a host of efficiency initiatives.

ScienTex



Inversion Frenzy Rocks Drug Sector

Drug maker Shire PLC of Ireland rejected a \$46 billion takeover bid from U.S. rival AbbVie Inc.

Such so-called inversions have become a popular structure for a wide range of American companies seeking lower corporate tax rates and a way to deploy overseas earnings that would otherwise be subject to stiff U.S. taxes if repatriated.

The tactic has become popular among pharmaceutical companies in recent months as that industry scrambles to reshape itself amid rising pressure on health-care spending and a number of patent expirations that threaten revenue growth.

Wall Street Journal

Therapeutic Licensing and M&A Deals

Licensing deals for therapeutic candidates in 2013 dropped to the lowest volume in at least eight years for deals with disclosed values totaling over \$10M. Total upfront payments to biotechs were also at an eight year low, with only \$1.9B paid to biotechs in 2013. This is a 50 percent drop from peak levels. However, there is a silver lining in the data: Preclinical deal volume saw a slight increase in 2013, and has not dropped by the same extent as the clinical product licensing. This points to the overall trend of large pharma and biotechs emphasizing their commitment to earlier stage deals.

BiotechNow

Biotech Industry Shatters Fundraising Records in 2014

The biotech industry shattered records for venture investment, IPOs, and M&A in 2014 as growing enthusiasm for breakthrough technologies and rising stock prices drove investment. Overall, the global life sciences industry raised a total of \$104.2 billion, up from \$92.9 billion in 2013.

It was the second biggest year for total fundraising in the industry's history, bested only by 2009 when the industry raised \$108.6 billion. The 2009 numbers, though, were driven by a total of \$83.1 billion in global debt financings, much of which was tied to large acquisitions made that year.

The Burrill Report

Investing and Deal Making



Basic Science Spending

US government spending on basic research at universities and colleges was basically flat, and even down a bit in some fields, in fiscal year 2012. That finding, from the National Science

Foundation, is not surprising to anyone who has kept up with how the federal budget has been at the center of a multi-year partisan battle over government spending.

Overall, basic R&D at universities for the life declined by .3 percent between 2011 and 2012. Of the three scientific areas that saw declines, the life sciences took the least of the cut, as it decreased by \$55 million while mathematics research dropped by \$75 million and other sciences fell by \$160 million.

Universities and colleges received 51 percent of all the \$31 billion in federal basic R&D spending in 2012, or \$15.4 billion.

[GenomeWeb](#)

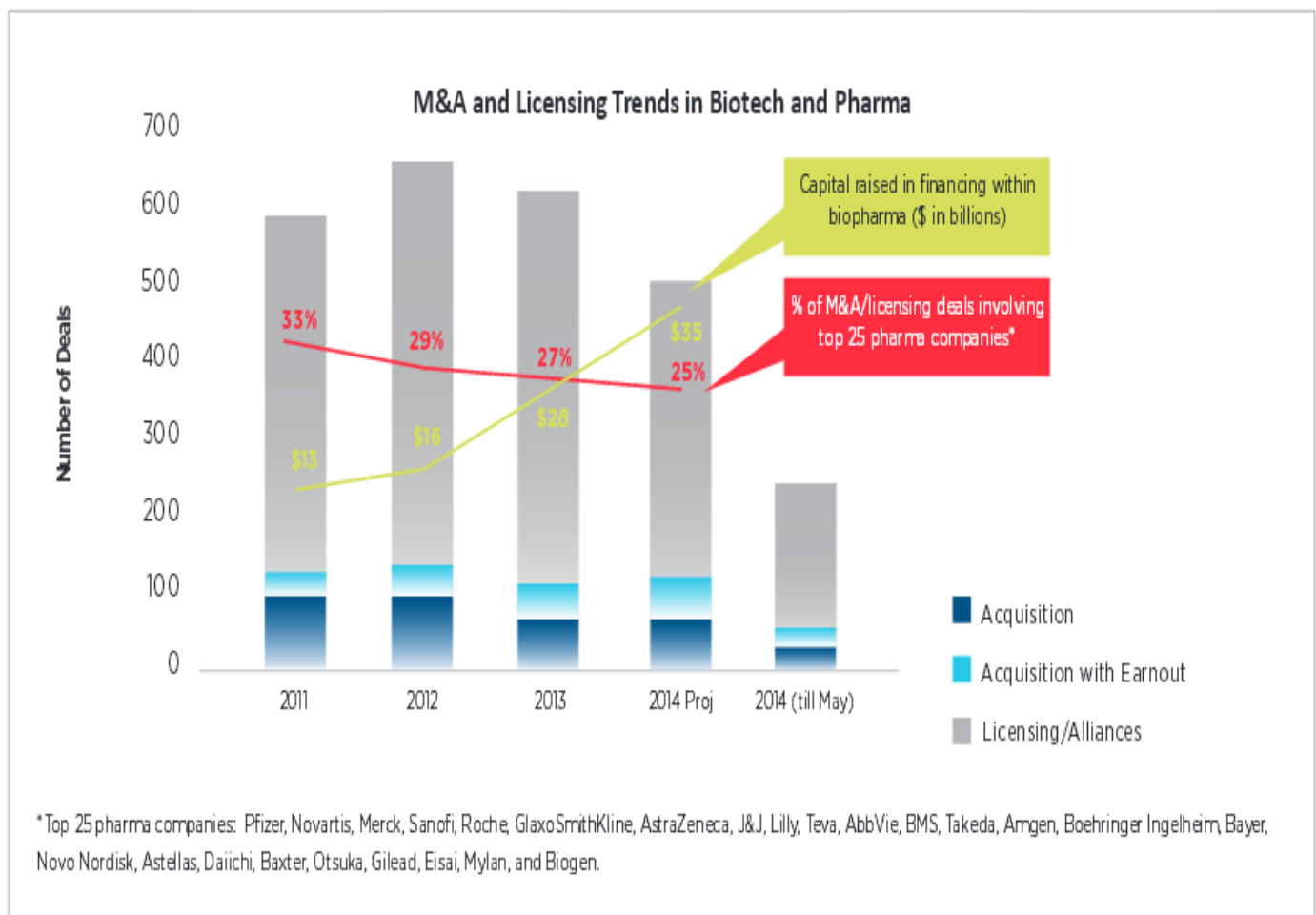


Investing and Deal Making

Campbell Alliance 2014 Dealmakers' Intentions Survey

2013 was described as a "breakout year" for the industry, the NASDAQ Biotech Index ended the year at a record high and follow-on financing was at a record level. This Bull market continued in to the first half of 2014. However this strength in the IPO market and a narrowing in the discount rate gap is tempering optimism for M&A/licencing deal activity.

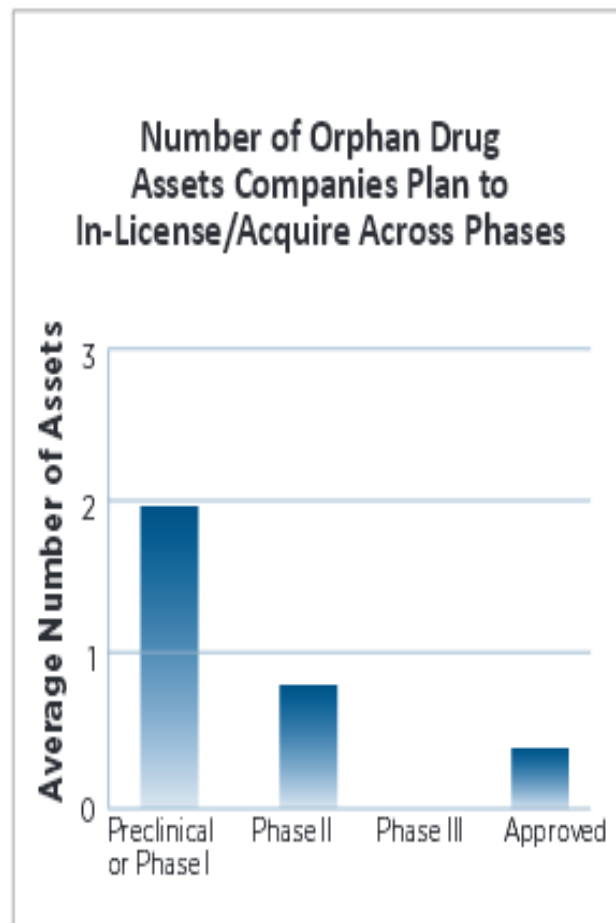
As covered in last years' report the industry relies on a discount rate spread to drive deal-making. This spread has closed significantly reverting to historic norms suggesting a softening of the market for deals, a forecast supported by the fact more financing became available and more options to from a non-traditional, outside the top 25 pharma buyer group has emerged.



Investing and Deal Making

In-licensors report most interest in early-stage assets. As in previous years Oncology remains the area of most activity with Cardiovascular and CNS following. The disparity between supply and demand in these areas is higher than it has been for some years, raising the potential risk of over-valuations.

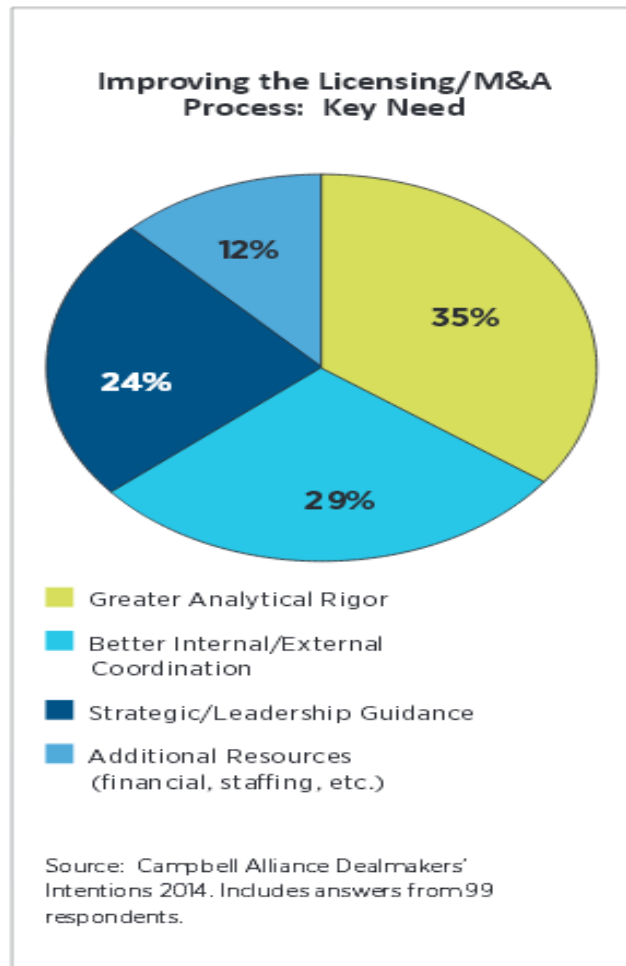
Follow-on biologics, once considered the hottest area for licensing, continue to fall in interest, likely due to the lack of a clear regulatory pathway in the US. Conversely Orphan products continue to be a hot area. Stem Cells despite the relatively high risk associated with this area have moved up significantly in in-licensors interest.



Looking at success rates for licensing, whilst there has been significant improvement to 3.2% of deals considered closing, up from a base level of 1%, this still remains very low.

Investing and Deal Making

When asked “how the licensing/M&A processes could be improved in their companies” respondents’ most common responses were the provision of greater analytical rigour (35%) and better internal /external coordination (29%) Dealmakers on both sides will achieve great success when they are able to work from a shared set of assumptions.



Looking ahead the implications of the responses indicate the commercial success of large IPOs will greatly influence the path of future deal making.

Campbell Alliance

Summary of EY – Beyond Borders: Unlocking Value

As also reported in the Campbell Alliance 2014 Dealmakers' Intentions survey, 2014 came off the back of a strong 2013. This was further explored in the EY – Beyond Borders report. Striking finding included:

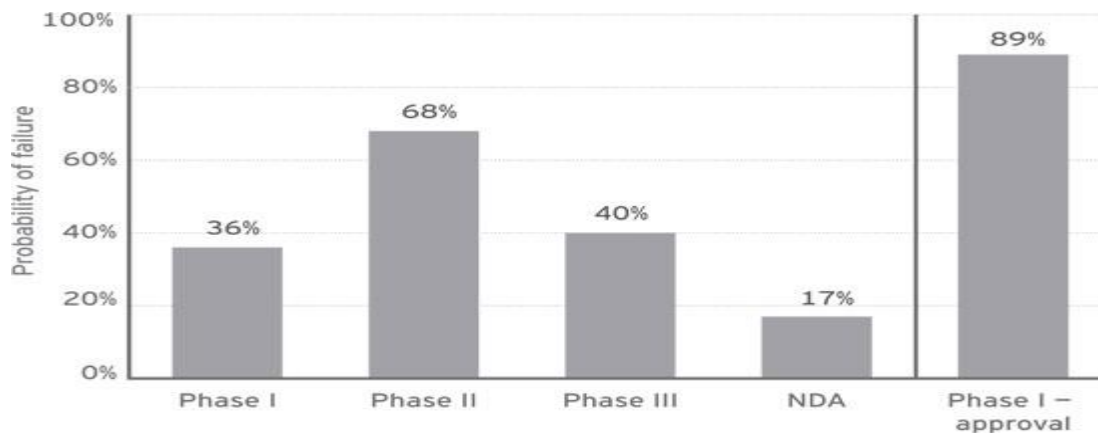
Whilst revenue across the more established markets of the US, Europe, Canada and Australia increased by a healthy 10%, virtually all of this came from 17 US-based companies with revenues > \$500M

R&D spending grew 14% in these geographies, again though this was dominated by a 20% increase in the US.

This larger % increase in R&D as compared to revenues resulted in a slight drop in net income except in Europe where it grew significantly due to an overall 4% drop in R&D spending

This overall double digit growth in revenue accompanies with a slight drop in net income is discussed more fully in the section of the report "The challenge of recognizing value" as the potential for value creation is a key driver in the high risk/reward biotech model.

The central area of value leakage remains R&D, doubling down on R&D has not led to drug launches that meet or exceed investor expectations. Too many drugs continue to fail in Phase III, where R&D spend is highest.



Source: EY, Sagient Research Systems and BIO. Probability of failure was assessed for each stage of drug development, as well as for the entire process (from Phase I to approval).

Investing and Deal Making

Three solutions to unlocking value are reviewed:

Precision medicine – increasing the use of biomarkers and targeted therapies to identify patient sub groups most likely to benefit. This is becoming increasingly important as market entry deals reflecting product performance as opposed to clinic trial results proliferate.

Adaptive clinical trials – Current three phase trials tie up R&D funds for an average of three years and provide few learning opportunities. Adaptive studies enable hypotheses to be refined and hence R&D funds to be reallocated in real time based on trial data.

Comparing a traditional clinical trial to an adaptive design

Trial adaptation	Traditional design	Adaptive design
Study size (number of patients)	459	316
Average time (months)	68	34
Probability of success	59%	59%
Trial costs for initial 24 months	US\$10.0m	US\$18.1m
Overall trial costs	US\$35.7m	US\$26.3m
Adjusted NPV	US\$5.1m	US\$34.9m

Precompetitive collaborations – expand cross-industry collaborations to solve industry-wide problems. As with adaptive clinical trials, these consortia are led by large pharma, the greater involvement of more biotech will benefit all.

The message, especially to Biotechs was:

- Partner early and often
- Empower senior R&D leadership
- Participate in precompetitive consortia
- Prioritize evidence collection initiatives early on

The full report which also covers in more depth the financial trends, review of the biotech bounce, biotech buyers and summary of new product approvals is available via the link,

[E&Y - Beyond-Borders - Unlocking-Value](#)

Investing and Deal Making

Medtech Worth Half a Trillion Dollars in 2020 – with a New Leader in the Offing

In 2020 the worldwide medical device market will be worth \$514bn, topping the half-trillion mark for the first time, *EvaluateMedTech's* World Preview 2014 reveals. The largest company will be Johnson & Johnson, with 2020 medtech sales of \$32.8bn.

But the J&J ranking stands only because Medtronic's purchase of Covidien has not yet closed. Assuming the \$43bn deal – the largest in the sector's history – is completed as planned in the first quarter of 2015, Medtronic will almost certainly take the top spot as the leader of 2020's medical device industry.

Evaluate Group

Dealmaking: Staying Ahead of the Curve

The record-breaking level of dealmaking activity in the pharmaceutical and life sciences (PLS) sector in 2014 is telling us more than it will be a good year for investment bankers' bonuses. There are profound strategic shifts occurring in the PLS business that will change the transactions field for PLS companies out across the next five to ten years.

Key among those shifts—there's a changing of the guard. Going back several decades, it used to be that household names in the pharma industry, such as Pfizer, Johnson & Johnson, and the like, dominated PLS transactions. While these players continue to be very active, we're

dealing with different companies, many in specialty pharma and biotech, that were small entities ten years ago, but after pursuing mergers and acquisitions (M&A) for growth in the years since, are today major players in the PLS deals space. This includes companies like Valeant, for example.

PharmExec



More Healthcare and Life Sciences M&A Activity Expected In 2015: KPMG Survey

Whether it is dwindling drug pipelines or changes from the Affordable Care Act, mergers and acquisitions in the healthcare and life sciences industries are expected to continue unabated in 2015 as favorable credit markets and cash-rich balance sheets feed deals, according to a survey from KPMG LLP, the U.S. audit, tax and advisory firm.

"We see a convergence of factors facing providers, health plans, and drug and device makers that are forcing them to make tough decisions about strategy and those decisions sometimes entail selling the business," said Bill Baker, an advisory partner who oversees transactional services in the healthcare & life

Investing and Deal Making

sciences practice at KPMG. "Technology, regulation, consumerism and pushback from employers and government payers are reshaping all facets of healthcare, forcing companies to review all of their options. The capital markets – low interest rates and strong valuations – are creating favorable conditions for those considering selling or divesting assets."



In the KPMG M&A Outlook survey of 738 U.S.-based finance officers and M&A professionals covering a variety of industries, one-third said pharmaceuticals/biotechnology will be the most active industry for mergers and acquisitions in 2015, trailing only technology companies (47 percent). In addition, 27 percent saw healthcare providers as being ripe for consolidation, trailing only technology, pharmaceuticals and the oil & gas industry.

Large cash reserves and available credit are the biggest factors driving M&A overall and healthcare is no exception, according to KPMG survey respondents, who work as senior management at companies in an array of industries or as advisors in those sectors, including energy, consumer products, technology.

[PR Newswire](#)

Biotech CEOs Talk JOBS Act and IPO Experiences at 2014 BIO Investor Forum

The JOBS Act has contributed to a dramatic acceleration in new biotech IPOs since its passage, with nearly a tripling in the rate of companies going public in the industry. By changing how entrepreneurs can access and communicate with investors earlier in the process, the JOBS Act has fundamentally shifted how CEOs of discovery-driven companies must spend their time dealing with internal versus external priorities.



At the 2014 BIO Investor Forum, a panel of biotech CEOs discussed new opportunities they have and surprises they encountered in taking their companies public in a post-JOBS Act environment, with implications for future entrepreneurs and policy experts.

Biotech-Now.org



Regulatory and Government

FDA Proposes Early Access Pathway for Breakthrough Medical Devices

The U.S. Food and Drug Administration has proposed a new program to speed access to medical devices that are intended to treat or diagnose patients with serious conditions whose medical needs are unmet by current technology.

The proposed Expedited Access Premarket Approval Application for Unmet Medical Needs for Life Threatening or Irreversibly Debilitating Diseases or Conditions program, also called "Expedited Access PMA" or "EAP" program, features earlier and more interactive engagement with FDA staff, including the involvement of senior management and a collaboratively developed plan for collecting the scientific and clinical data to support approval.

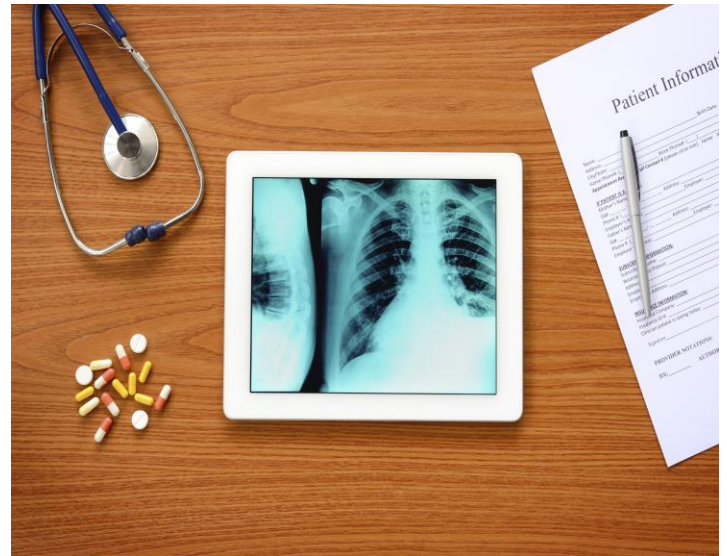
Burrill Report

How European Medtech Companies Might Benefit from TTIP

The proposed free trade agreement between EU and USA, 'Transatlantic Trade and Investment Partnership' (TTIP), stirs up a lot of controversy on both sides of the Atlantic. If it will ever see the light of day medtech companies are likely to be among the beneficiaries.

According to a recent report [in German] from the German trade agency Germany Trade and Invest, the medtech industry will gain from the proposed free trade agreement between EU and USA – Transatlantic Trade and Investment

Partnership (TTIP). The goal of the consultations that started in July 2013 is to reduce the tariff burden and other trade barriers.



The regulatory procedures in both trading blocs differ fundamentally in some areas, which increases the costs of doing business. The discussions between the delegates from the US and Europe with regard to medical devices aiming to harmonize the standards and regulatory requirements "so far have focused on Unique Device Identification (UDI), Regulatory Product Submission (RPS) and Medical Devices Single Audit Programme (MDSAP). Discussions helped to clarify the respective positions and to better understand the functioning of the regulatory systems of both sides, and will continue at technical level," stated the European commission in a recent report.

European Medical Device Technology

Regulatory and Government

Italian Law Permitting Reimbursement of Cheap Off-Label Drugs Could Start EU-Wide Battle

The Eurozone economic crisis has largely passed but many European countries are still cash-strapped in the extreme. So a new law enacted in Italy that effectively mandates the substitution of cheaper, off-label drugs seems like a common-sense plan to save the public purse. It is no wonder that other countries are considering similar moves.

However, the new legislation is in direct conflict with EU law, and could open the way for untested products in Italy and beyond, lawyers believe. "It jeopardizes the system as it was built," says Vincenzo Salvatore, senior counsel at law firm Sidley Austin. "The new Italian legislation says that product is reimbursable if there is evidence that it is safe. The problem is, who assesses this evidence? Who decides that the product is safe outside of the regulatory assessment procedure?"

Evaluate Group

The "Right to Try"- Promoting the Right to Choose Experimental Treatments

String the letters F-D-A together and almost instantly you'll picture the well-recognized scientific safe-haven of the United States. Formed in 1906, the Food and Drug Administration was created to ensure the responsibility and protection of US citizens' interaction with the market of commercial science. From cosmetics to veterinary medicine, the FDA regulates and supervises the

advances that intend to make life more manageable. However, in Colorado terminally ill patients are advocating for a little liberation from this tight hold the FDA so often advocates when regarding human subjects. As of May 17, 2014 Colorado is officially the first state to grant patients access to experimental pharmaceuticals still resting in the developmental pipeline – ones either awaiting or working towards federal approval for lawful commercialization.

iMarc



FDA Outlines to Congress its Long-Awaited Approach toward LDT Regulation

Over the next decade, the US Food and Drug Administration will phase in its risk-based approach toward regulating laboratory developed tests, the agency announced.

The agency provided the US Congress notice of its plans to release the long-awaited draft guidance for LDT regulation, as required by a

Regulatory and Government

provision in the Food and Drug Administration Safety and Innovation Act. The FDA will formally publish its draft guidelines for public comment after 60 days. Simultaneously, the agency also finalized a draft guidance, issued in 2011, on the development, review and premarket regulatory requirements for companion diagnostics – tests that predict whether patients will respond to certain drugs.

GenomeWeb

Eruptions on Europe's Drug-Pricing Horizon

"Better volcano forecasting", the European Union announced with pride in mid-September. The breakthrough was a new EU-funded monitoring scheme for Iceland's volatile geology. What the EU has paid less attention to is the volcano that is soon likely to blow apart its assumptions on the pricing and reimbursement of medicines.

The agenda for the informal meeting of EU ministers of health in the last week in September should have been warning enough. Italy is hosting this six-monthly meeting, in Milan. Exercising its privilege as the current holder of the revolving EU presidency, it has set the agenda – with an eye to pyrotechnics. The centre-piece for the meeting will be a discussion on the price of drugs, driven particularly by concerns over the cost of innovations such as Gilead's hepatitis C treatment, Sovaldi, on which the Italian and French health authorities have been leading the attacks.

A discussion paper circulated in advance to national ministers starts blandly enough, with an outline of the challenges of bringing

innovation rapidly to patients – all that familiar territory of the cost and risk of R&D, and meeting unmet medical need with therapies that "are affordable to the EU healthcare systems", along with calls for closer dialogue with regulators and more capital investment. Similarly, the paper rehearses the range of EU options for speedier marketing authorization – conditional, exceptional circumstances, compassionate use, and the more recent moves to adaptive licensing. But it soon edges closer to controversy with an observation that "some challenges remain since there are still medical needs to be met and patients are demanding faster availability of promising new therapies at affordable prices."

PharmExec



And All Under 140 Characters

The long-awaited US Food and Drug Administration guidance on social media for drug companies has arrived, and it includes information on how to discuss the risks and benefits of drugs on a social media platform like Twitter and how to correct misinformation

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present on websites like Wikipedia, Pharnalot's Ed Silverman writes.

A tweet promoting the benefit of a drug — the brand and generic name of which must be included — needs to also incorporate the top risk associated with it as well as a link to a site that describes all possible harms, Bloomberg reports. FDA offered this as an example of such a tweet: "NoFocus (rememberine HCl) for mild to moderate memory loss-May cause seizures in patients with a seizure disorderwww.nofocus.com/risk." This tweet, which refers to a fictional drug, Bloomberg notes, uses 134 of the 140 characters allowed by Twitter.

[GenomeWeb](#)

Tax-Inversion Hopefuls Balk at New White House Plans to Curb Deals

U.S. Treasury Secretary Jack Lew announced initial regulatory plans to curb so-called "tax-inversion mergers," an increasingly popular tactic being used by biotechs and healthcare companies to lower their effective corporate tax rate by shifting their domiciles abroad.

Several big-name mergers were announced by American companies in 2014, including AbbVie's acquisition of Ireland's Shire and Medtronic's merger with Irish firm Covidien. Elected officials, shareholders, and even some international pharma companies like AstraZeneca have cried foul over the deals.

The regulations will make it harder for U.S. companies to use the deals to lower their tax base by considering certain foreign loans "U.S. property," barring large pre-merger dividend

sales that are used by corporations to "slim down" so that they can qualify for an inversion merger, and disregarding "passive assets" given to (non-bank) foreign partners to make those companies seem bigger.

[BioPharma Dive](#)

Congress Proposes \$30.3B in 2015 Funding for NIH

The US Senate subcommittee that funds the National Institutes of Health yesterday agreed to provide NIH with a budget of \$30.46 billion for the coming fiscal year, an increase of \$605.7 million over the fiscal year 2014 budget of \$29.9 billion.



Although the increase is modest, the budget bump of roughly 2 percent — authorized by the US Senate Appropriations Subcommittee on the Departments of Labor, Health and Human Services, and Education, and Related Agencies (Labor-HHS) — comes at a time when any increase at all is a rarity.

[GenomeWeb](#)

Regulatory and Government

New Patent-Defense Path for Pharma

Just over three years ago, Congress enacted the America Invents Act, hailed as "one of the most significant legislative reforms to the patent system in US history." The Act included several sweeping changes, including advent of *Inter Partes* Review (IPR)—a new litigation procedure held before the Patent Trial and Appeal Board (PTAB) to challenge the validity of patent claims. Designed to be a faster and less expensive alternative to district court litigation, IPRs have taken the patent bar by storm.



Before enactment, the United States Patent and Trademark Office (USPTO) anticipated handling 460 IPR petitions annually. But the response by patent challengers has been overwhelming, with more than 1,750 petitions filed in the first two years, resulting in 114 final decisions through September. In 2013, 87% of the petitions filed met the "reasonable likelihood that the challenger will prevail" standard and progressed to trial. That number has decreased slightly in fiscal year 2014, with trials being

instituted in "only" 76% of the petitions filed. The majority—more than 86%—of the petitions have challenged electrical and mechanical patents, while petitions challenging pharmaceutical and biotech patents account for just over 5%.

PharmExec

FDA Issues Guidelines for Nanotech Companies

Federal regulators want to hear from companies using tiny, engineered micro-particles in their products, part of an effort to stay abreast of the growing field of nanotechnology.

The Food and Drug Administration issued final recommendations for companies using nanotechnology in products regulated by the government, which can include medical therapies, food and cosmetics. FDA regulators want companies to consult with them before launching nanotechnology products, though the decision whether to go to market will essentially rest with manufacturers.

The FDA doesn't make a judgment call on the overall safety of nanotechnology or even define the term.

Inc.

CDER Approved Many Innovative Drugs in 2014

Each year, FDA's Center for Drug Evaluation and Research (CDER) will typically approve more than 100 new medications. A portion of those are novel new drugs, medications that

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have not previously been approved by FDA and are often among the most innovative products serving previously unmet medical needs or otherwise significantly helping to advance patient care and public health.

This year, the news media has been concentrating on the number of novel new drugs – either new molecular entities or new therapeutic biologics – approved by CDER in 2014. And that's understandable because we

approved 41 novel drugs this year, the most in nearly 20 years. But instead of looking at the approval tally, we prefer to focus on the significant benefits that many of these drugs bring to patients and the steps that CDER took to get these products to market in a timely manner while maintaining FDA's standards for safety, effectiveness, and quality.

Blog.FDA.gov



Healthcare

What Will Happen When Biotech Drugs Go Generic?



In a few years, the first blockbusters of the biotech age will begin to face generic competition. Big drugs like Amgen's Epogen and Neulasta, Roche and Biogen Idec's Rituxan, and Erbitux from Eli Lilly and Bristol-Myers Squibb could eventually face cheaper competitors. But they won't be exact substitutions, because these drugs will be so much harder to make. Most will not be true generics but biosimilars — products with a similar profile that are still seen as slightly different from the original. So how quickly will sales erode? It will depend on the disease being treated and whether decisions are being made by physicians and patients or by hospital administrators, according to a new analysis by ZS Associates, a global consultancy.

Forbes

Anatomy of a Drug Price Valuation

There has been a firestorm of criticism surrounding Gilead's decision to price Hep-C

miracle drug Sovaldi (sofosbuvir) at \$1000 per pill. But what is the right way to balance the myriad considerations that go into pricing a drug? The high-cost cystic fibrosis (CF) drug Kalydeco makes for an interesting case study -- especially when juxtaposed against Sovaldi.

Simply put, when a drug works and there is no comparable alternative, chances are it will be relatively expensive, whereas a me-too drug that launches into a crowded therapeutic field will be subject to downward pricing pressure. This is a basic economic reality of supply and demand, and most experts agree it is a fair paradigm that boosts businesses and props up innovative companies that invest time and money into developing lifesaving therapies.



Kalydeco (ivacaftar), an oral, twice-daily medication developed by Vertex Pharmaceuticals, falls into the former camp of drugs with few comparable peers. It was approved in January 2012 as the first-ever treatment to target the underlying genetic mutations that afflict CF patients. But it comes with a daunting price tag: \$307,000 per year for the average individual. That's nearly four

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times the cost of Sovaldi -- even though Kalydeco can be taken by just a tiny fraction of the population that can benefit from the Hep-C drug.

BioPharma Dive

IMS Identifies 10 'Harbingers of Disruptive Change' in Healthcare

As the global market for pharmaceuticals surpasses \$1 trillion this year, a new study has identified 10 "harbingers of disruptive change" which, it says, represent turning points in the role of medicines in advancing healthcare.

These 10 events could be "a threshold reached, a decision made or an action taken," and will have significant long-term impact on the role or use of medicines in the future and will affect all healthcare stakeholders, says the study, published by the IMS Institute for Healthcare Informatics.

PharmaTimes

R&D Pioneer Tackles the Next Hurdle in Gene Therapy: Paying for \$1M-Plus Drugs

Over the last few years, new vector technology has helped inspire a wave of biotech startups involved in developing gene therapies. Now, worried that sticker shock for the \$1 million-plus treatments working their way down the pipeline could wind up poisoning the well for everyone, one of the principal academic investigators behind the new technology has been working on a suggestion for a new payment model for these therapies.

One of the biggest hurdles gene therapies face, writes James M. Wilson, a notable gene therapy researcher at the University of Pennsylvania, is that they may work too well. Where the pharma industry now makes billions off of long-term care for the chronically ill, a one-off gene therapy could partially or completely cure a disease. And with the kind of rare diseases they're focused on, biotechs looking to market these drugs may want to charge millions of dollars to make the economics work.

Fierce Biotech

Study Shows Large-Scale Patient Data Analytics Can Help with Early Interventions for Patients at Risk of Metabolic Syndrome

A study analyzing 37,000 patient healthcare records demonstrated that Big Data analytics of the medical records could predict future risk of metabolic syndrome. Health insurance provider Aetna and big data analytics firm GNS Healthcare conducted the research, which was published in the *American Journal of Managed Care*.

"This study demonstrates how integration of multiple sources of patient data can help predict patient-specific medical problems," says lead author Gregory Steinberg, head of clinical innovation at Aetna Innovation Labs. "We believe the personalized clinical outreach and engagement strategies, informed by data from this study, can help improve the health of people with metabolic syndrome and reduce the associated costs."

More than a third of Americans have metabolic syndrome, a group of five risk factors—large



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waist size, high blood pressure, high triglycerides, low HDL cholesterol, and high blood sugar. When an adult has three or more of these risk factors, he is five times as likely to develop diabetes, and twice as likely to develop heart disease or have a stroke. Combined, these conditions account for almost 20 percent of overall healthcare costs in the United States.

Burrill Report



Market Access: The Impact of HTAs on Strategy

When it comes to Europe and health technology assessments (HTAs), one thing is clear, "The only consistent trend is 'more,' as in more countries are adopting more HTA approaches at a national and regional level," says Steven

Flostrand, pricing and market access director at Creativ-Ceutical.

The increase in HTAs has led to a variety of initiatives at the European level: from industry, through the European Federation of Pharmaceutical Industries and Association's (EFPIA) principles for HTAs; from the European Commission, through its ongoing collaborative work via EUnetHTA; from the industry and the Commission together, through the High Level Pharmaceutical Forum (HLPF).

eye for pharma

Google to Offer Foundation Medicine's Cancer Tests as Latest Health Benefit

Google will soon start covering the cost of Foundation Medicine's DNA tests for employees and their family-members suffering from cancer, as part of its health benefits portfolio.

Foundation Medicine's chief executive Michael Pellini gave a nod to the deal with Google during a corporate earnings call on Wednesday, according to a person who listened in. Pellini said Google employees were made aware of this new benefit.

Reuters

Personalized Medicine Comes of Age

– An Introduction by Don Alexander

On January, 20th, 2015, President Barack Obama presented an initiative directed at Precision Medicine during his State of the Union address in the US. In Europe, the UK government's 100K Genome Project, a public-private collaboration to sequence the genomes of 100,000 infectious micro-organisms, provides a roadmap for more rapid development of tests to identify pathogens and trace their origins. These initiatives, and others, offer the opportunity to accelerate our understanding of Precision Medicine.

The Precision Medicine (a.k.a. Personalized Medicine) ecosystem comprised of pharma, diagnostics companies, payers, governments, providers and patients, has both driven and watched the evolution of Precision Medicine advancements at a significant pace in spite of obstacles and the lack of alignment of the interests of all constituents.

2015 marks a pivotal year, in many respects, for the field. It is with this inflection point in mind that Carlyle Conlan and George James, Ltd. are pleased to offer thought provoking views from top global leaders in the field of Personalized Medicine (PM).



Personalized Medicine Comes Of Age



Dr. Darrin M. Disley
Chief Executive Officer
Horizon Discovery Group

The life sciences experience of Darrin Disley, president and CEO of Horizon Discovery Group, spans the start-up and growth of several business ventures, where he has raised hundreds of millions of dollars in financing from private investors and the public markets. He has also overseen numerous product, service, and licensing deals for Horizon, a genomics company that provides tools and services supporting organizations working in the research and development of personalized medicines. In 2012, Darrin was named Business Leader of the Year at the European Life Science Awards; in 2014, he was Executive of the Year at the Scrip Awards

Under Darrin's leadership, Horizon raised \$113 million in a 2014 initial public stock offering – a record for a life science company. Since that IPO, Horizon has completed several acquisitions, including a deal for CombinatoRx, a Cambridge, MA-based combination screening services company as well as SAGE Labs, a St. Louis company that is a leader in in vivo gene-editing.

Darrin holds a Ph.D. in Biotechnology from the University of Cambridge and has authored numerous papers, patents, and conference abstracts. He has also advised on biotech commercialization strategies around the world. Carlyle Conlan's Don Alexander recently spoke with Darrin about his thoughts on Personalized Medicine (PM).

Don: How is Horizon Discovery contributing to the field of Personalized Medicine (PM)?

Darrin: *We want to make a real impact in elucidating the genetic basis of disease and accelerating the discovery of targeted, or personalized, medicines. Since 2008 Horizon has grown organically, and by acquiring platform technologies, capabilities, and know-how. We now provide products, services and novel pharmaceutical assets – biomarkers, targets, drug candidates – to more than 1,000 customers working in all stages of healthcare, from sequence to treatment. These companies are pioneers and evangelizers of the clinical, economic and societal benefits of personalized medicine, including influencing regulators, policy makers, and clinicians alike. Their scientific founders have been at the center of early case studies changing the genetic basis on which EGFR (Epidermal Growth Factor Receptor) targeted therapies such as Erbitux and Vectibix are prescribed to colorectal cancer*



Personalized Medicine Comes Of Age

patients. These studies led to the formation of the Colon Therapy Research Consortium (Coltheres), a European Union-funded project working toward biomarker-driven clinical trials.

Don: What is driving the growth in PM?

Darrin: *There are two key drivers. First, as sequencing costs have come down since 2008—approximately \$10 million per genome to about \$1,000 in 2014 – now the bottleneck for researchers is the availability of tools, such as IT, informatics, and gene-editing technologies – that enable the understanding of the genetic basis of disease. There is near infinite genetic variation that exists between health and disease states over the course of a life and in a global population, but the technology hasn't kept pace. Horizon's Viral (rAAV) and Nuclease (ZFN, TALEN, CRISPR) gene-editing technologies are platforms for the researcher to determine what functional effect any given DNA sequence variation means in terms of disease prediction, diagnosis, prognosis or even whether a given patient will respond to therapy.*

The second is the area of drug discovery where for many decades the key metric of success has been the peak year sales of a given drug. Bringing a novel drug to market has historically cost between \$3 billion to \$11 billion, according to Forbes. Given a typical 5 to 7 years of patent life after approval, gaining any return on investment requires blockbuster revenue. This places huge pressure on those drugs that do make it to market and leads to dramatic drops in shareholder sentiment and value when drugs fail late, or are found to have only small patient populations based on genetic studies.

Don: So how is Big Pharma changing to adapt to PM?

Darrin: *Big Pharma companies were 50 plus in number and now there are around 10 as they merged pipelines in the hope of maintaining shareholder value. The personalized medicine model of drug development is turning this on its head, focusing on return on investment, shorter development times, smaller patient population, reduced clinical trial costs, defined clinical benefit and reimbursement strategies.*

Pfizer's drug Crizotinib, for example, is administered to 4 percent of patients with non-small cell lung carcinoma who have a chromosomal rearrangement that generates a fusion gene between EML4 (echinoderm microtubule-associated protein-like 4) and ALK (anaplastic lymphoma kinase). Patients with this gene fusion are typically younger non-smokers who do not have mutations in either the epidermal growth factor receptor gene (EGFR) or in the K-Ras gene. The number of new cases of ALK-fusion NSLC is about 9,000 per year in the U.S. and about 45,000 worldwide.

Crizotinib was approved in 2011 after only a 7 year development phase and currently generates \$350 million in annual sales. Given the 12-15 year patent life of the drug, the ROI is dramatically higher

Personalized Medicine Comes Of Age

than historical blockbuster models. Drug developers are finding they can generate a greater ROI by targeting smaller populations.

Iressa, AstraZeneca's non-small cell lung cancer drug targeting EGFR, is another example. Originally, 5 percent of patients responded to the drug. Researchers recently found a secondary Caucasian population resulting in about 15 percent of patients responding.

Findings on drugs like Iressa are retrospective, coming years later, versus the emerging PM model with shorter, leaner drug discovery, where one is targeting 3, 5, 10 percent of patient populations. The result is a defined clinical benefit and increased reimbursement per dose. This whole model is driving drug discovery in areas [such as] oncology now.

Don: We know that PM is complex but why is Big Pharma reluctant to take more of a lead in shaping personalized medicine?

Darrin: *In 2008 and '09, EGFR targeted therapies were in clinical trials for treatment of colorectal cancer. Horizon founder Professor Alberto Bardelli and Horizon scientific advisory board member Professor Sabine Tejpar wrote papers showing that 40 percent of patients [who] had the concurrent KRAS mutation would likely not respond to these therapies. The papers were initially ignored by Pharma.*

Pharmas had to do new clinical trials in Europe, which resulted in label changes of these drugs, first by the EMEA in 2009, and then by the FDA in 2010. Initially, pharma was not happy with this retrospective finding. As it turned out, they made more money in the first year of KRAS testing than previously and the healthcare system saved \$740 million, according to estimates from the American Society of Clinical Oncology. Reimbursement came with higher prices and pharma made more money. The economics proved that smaller populations can generate greater revenue. The key, though, is prospective versus retrospective findings. With prospective findings, one can file patents earlier. If you find novel programs, clearly defined patient populations, you can file chemistry patents much earlier.

Don: Oncology is a hot target for PM. What other areas do you view as having good potential?

Darrin: *Infectious disease, irritable bowel, Crohn's. Neurological interest in PM may reflect both prediction and predisposition to various conditions. For instance, associating patterns of SNP's (Single Nucleotide Polymorphisms) with onsets of neurological disorders.*

Don: What are the obstacles to PM adoption?

Darrin: *I see several potential obstacles:*



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- *The cost reduction in sequencing big data, and reimbursement for targeted, but high-priced therapies. On reimbursement, the NICE (National Institute for Health and Care Excellence) provides a framework for health-related assessments. Aspects are a defined clinical benefit and the use of group purchasing power to drive downstream effects. At the moment, there are a relatively small number of personalized medicines with retrospective findings, so Pharma has to front-end load these costs. The payers may put pressure on Pharma to be more flexible. Maybe payment is spread over a number of years as a potential deal structure.*
- *The need to form common practices and standards. There is a real interest to educate patients. There is still work to do on the pathology and physician sides. The people who run clinical trials have bought into genetic biomarkers and are moving into blood-based biomarkers. Providing MDx standards that control the performance of the test is of high importance and key technological/commercial push for Horizon. Multiple tests using different protocols, instruments and assay kits lead to 10 percent of tests being called incorrectly. When you start pushing to the market, people didn't know there was a problem until there were false positives or negatives. The level of physician engagement isn't as high just yet.*

Don: If a disease integration initiative (where multiple stakeholders agree on how to integrate tests, treatments, and education to optimize clinical and cost outcome) demonstrated significant clinical and financial benefit, how will this change industry's perspective?

Darrin: Most historical and current drug discovery is all about helping the next generation. It doesn't help the current people with disease. Drugs approved 8-9 years from now don't help someone today. Adaptive trials are now being pioneered by groups of clinicians like those involved in Coltheres. With rapid, low-cost sequencing, gene editing in vitro and in vivo and combination profiling and biomarker techniques mean in some cancer with long survival time you can go straight back to patients while patients are still living.

Don: How do the regulators deal with this?

Darrin: Bench to bedside's time has not yet come. Regulators may not understand how to regulate PM. They haven't really made a big jump forward on companion or early Dx. For instance, each test on the recently approved Illumina platform will have to be validated separately. The insurance payers and national health systems will need to come to the party for adoption to occur. Patient and industry are on board with this. The system (regulators and health systems) will need to seek ways to move faster. Early detection is critical. Treatments will be co-dependent.

Personalized Medicine Comes Of Age



Peter Keeling
Chief Executive Officer
Diaceutics

As the field of personalized medicine has evolved, Peter Keeling has changed along with it. Peter, CEO of Diaceutics, has transformed his company from a personalized medicine consulting firm into a business that now encompasses consulting and software applications focused on personalized medicine. That transition came from recognition of the importance that companion diagnostics would play in the development and the use of pharmaceuticals.

Peter has more than 24 years of healthcare experience, including the launch of four pharmaceutical companies, seven over-the-counter products, and five diagnostic products. He has also had roles in three joint ventures and two major corporate marketing campaigns. Peter's experience spans the globe, including work in the United States, Germany, the United Kingdom, and Japan. He also has research experience, including one year at the Massachusetts Institute of Technology's Pharmaceutical Program at the Sloan School of Management. Peter took some time to share his thoughts on personalized medicine (PM) with Carlyle Conlan's Don Alexander.

Don: How is your company contributing to the field of Personalized Medicine (PM)?

Peter: *As pharmas move to integrate the complexities of PM into their commercial business model, they need help with planning and implementing novel biomarker technologies alongside their more familiar therapies. More than 50 percent of therapies launched by the top 10 pharma companies in 2017 will require a biomarker strategy. Diaceutics identified this need early on and has been working over the past 9 years to create tools, solutions, and services to help this essential and urgent integration.*

Given that PM commercialization lacks the most basic of infrastructures and is often seen by pharma teams as a barrier to therapy access rather than a benefit, Diaceutics has had to create a suite of innovative services to remove these barriers and better articulate the commercial opportunities that PM creates. Our market analysis, publications, and Convergence meetings are helping to reposition PM in the eyes of our clients from foe to friend.

Don: What, if anything, has surprised you about the field of PM?

Peter: *This is, perhaps, not a surprise but when you start with a view that PM is an obvious way to align everyone's goals – everyone being the stakeholders at the table – a couple of things come to*



Personalized Medicine Comes Of Age

mind. First, there is the realization that PM is very complex. There are complexities with a variety of facets like higher education, genomics, labs, and diagnostics. For asset teams that have been presented with accelerated licenses, there is the idea that, if we put this biomarker in, the track record is 50/50. That is, 50 percent of biomarkers seem to undermine the asset and 50 percent do well.

Then, there is the length of time it has taken to arrive at a junction. Companies are starting to think in a qualitatively different way. There are now instances of accepting complexity, and this is fundamental to the business model. For example, GSK just signed a deal with Clariant [a lab company] for BRAF testing. Adding the laboratory to the diagnostic partnering strategy will be a critical future step versus just partnering with a single diagnostic company.

There is no institutionalized business model for PM. There is some truly integrated thinking going on now with companies [such as] Roche. To date, there has been collaboration but not integration. Diaceutics has developed a scale, internally, to evaluate the types of people they talk to in companies [<http://diaceutics.com/our-new-pm-catch-phrase-it-learn-it-leverage-it>]. Given the challenges, we should be pleasantly surprised that we are at this point.

Don: What about growth rates and the relationship between the drug pipeline and how many drugs are on the market today?

Peter: *50 percent of PM drugs in 2010 made it to market in 2014. What does the pipeline look like? 75 percent is enabled by PM projected through to 2020, when about one third of all drugs on the market will be PM enabled. This will be what is being sold rather than in the pipeline so, roughly, a doubling of the amount of assets. There is a Moore's Law effect now. 2013/2014 may have been a tipping point. 2017 is another tipping point when the FDA will approve more therapies with biomarkers than without.*

Don: We know that PM is complex but why is pharma reluctant to take more of a lead in shaping personalized medicine? What does PM mean for the blockbuster model for pharmaceuticals?

Peter: *Pharmas' reluctance is a commercial issue, not an R&D issue. If anything, the R&D leaders have already identified the clinical and scientific merits of therapeutic targeting. It is the commercial teams who are most uncertain of the complexity of PM. When you explain to commercial asset leaders that there are some 200-300 key business questions that need to be addressed if they wish to optimize their PM strategy, many of which are alien to them, there is a default to PM avoidance. Within oncology this avoidance choice is disappearing as the FDA moves to reward PM drugs with early approval and faster shift to first line treatment, but outside of oncology only the most PM savvy are embracing PM as a way to differentiate them in the market place.*

One of the things that has also been missing in PM is a sense of competitive rivalry. There hasn't been a large amount of competitive heat to leverage PM but we are about to enter an era marked by PD-L1's [the protein Programmed death ligand 1] arrival, where companies are more proactive versus

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doing it if you have to. With the PD-L1 asset class, there are six companies introducing products and there will be competition in biomarkers within the class. This is, in many ways, a game changer as up until now there has been more of a one biomarker, one drug commercial monopoly.

Don: If a disease integration initiative – where multiple stakeholders agree on how to integrate tests, treatments and education to optimize clinical and cost outcome – demonstrated significant clinical and financial benefit, how will this change industry's perspective?

Peter: Our view is that that PM has been positioned, until now, predominantly as a technology play, not a clinical or financial benefit play. If we can prove unequivocally that PM delivers radical clinical and financial benefit to specific disease areas, then we have a Klondike. Proving this will not be easy since it requires levels of cooperation not typically associated with the normal develop then launch therapy model, but it is Pharma's commercial future. We have some early examples, [such as] the Multiple Myeloma Research Foundation [<http://www.themmr.org/>] that are acting as the integrator. However, we believe there is a business model process that can be adopted by Pharma, which makes such PM integration scalable, affordable, and which moves past the current debate that PM medicine is expensive medicine.

Don: Oncology is a hot target for PM. What other areas do you view as having good potential?

Peter: Infectious disease, Hep C. Cardio is another area where we will see reform based on biomarker work that has been done. The willingness of payers to adopt the payment access of biomarkers versus do we really want to give drugs to all patients. Circulating tumor DNA testing may be about as important as NextGen Sequencing. Theoretically, it would have more impact than NGS in the clinic, early on. Point of care testing has been put forward as revolutionizing testing and it hasn't – just 10-15 percent of testing is done at the bedside. But with the advent of smaller, smarter genetic testing equipment, or patient initiatives that have made active investments in PoC platforms, this will change. If one adds in a little Google, Apple, and Amazon, patients will be in a far better position to help manage their own health. We will see a PM director in every board room in the top 10 companies five years from now.

Don: So the definition of PM is changing?

Peter: PM has been, historically, centered on companion testing. Getting the right drug to the right patient at the right time. Add to this, the ability to measure blood pressure and project wearable technology – think FitBit – a few years out, and treatments will become highly relevant to individual patients. Today's definition of PM is far too narrow.

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Don: Tell me about the Integrator Initiative, the Personalized Medicine Convergence Meetings.

Peter: *It's a deliberately different mix of stakeholders brought together to discuss key topics in PM. This last meeting, in October, there were 75 stakeholders representing different interests in the room. They are amongst the most PM-savvy folks in the industry and collectively, we agreed that we needed to move past talk and reflection to building some infrastructure. The Convergence participants voted to set up an integrator proof of concept initiative. Ultimately, someone will need to act as integrator for a period of time. As a proof of principal, the PM CONNECTIVE will be launched and we are in the process of setting this up as a not for profit organization. This initiative will be looking at diseases in two areas in support of an integrator approach and the studies will run about 2-3 years.*

Don: What areas are the initiative looking into and what do you hope to get out of this?

Peter: *One is in oncology and one outside oncology – yet to be determined. They are considering areas where differences can be illustrated quickly and migrating to areas where there is an acute need. There are three core endpoints. First, evidence that integration has moved the needle in terms of clinical and financial outcomes. You can't have one without the other. The initiative will focus on radical reform rather than mild reform in clinical and financial outcomes in these disease areas. Second, build the integrator process in a way it can be replicated by others. This is what we did, how we did it, what may be done differently, in retrospect. In sum, establishing a business method. Third, a series of future recommendations for moving the model on further. A technical design at the R&D stage, if you will.*

Don: What are your thoughts on adoption factors for PM, such as cost reduction in sequencing, Big Data, etc.?

Peter: *One thinks of Moore's Law as to why we've moved from IBM to laptops to iPads. The technology improvements will be profound but PM will not be driven by tech alone.*

Don: And reimbursement –targeted, but high in price? How should policies cover PM?

Peter: *On reimbursement, sadly, the response has been to price drugs high in the face of smaller, targeted populations. That is not to infer that the right market price shouldn't be charged. The question is how we ensure financial outcomes are assured and prices won't break the system. On the payer side, unless a PM drug is introduced, there is no real payer model yet. Health economics models around PM are still formative. In promoting a holistic program versus a drug, pharma and payers would have a much better pricing contract. Profound financial improvement should be inherent in PM but it requires a behavior change. Also, most novel drugs start in the market dependent on a test. Medics/physicians need to be educated and tests are sometimes not available. Tests will go slower in the market than drugs, unless you drive them. The concept is that one gets to 90 percent of 6 percent of patients, which changes the paradigm. Payers are still sitting on the fence. They respond to data. For a group that could drive the financial benefits, they haven't yet taken the initiative.*

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Don: Is FDA regulation of laboratory developed tests (LDTs), a negative?

Peter: *Companies are asking questions [such as], "Do I only work with Dx companies?" or "Can I work with labs or will the FDA shut me down, ultimately?" The FDA may be taking on LDT regulation prematurely.*

Don: Common processes and standards?

Peter: *Today, we have guideline driven medicine. Guidelines are consensus documents which can take 24 months to discuss and publish. However this is no longer fit for purpose as new biomarkers may arise or combination of markers which outmode the guidelines the day they are published. Instead, we need a new faster Guidance on the use of novel biomarkers in key diseases.*

The other one is litigation. For instance, Plavix court cases and others going on in cardio and monitoring. No doubt, these cases will run their course but the design laws are such that patients could turn around and say, "I was offered a drug and wasn't tested for this scenario. There is a test available. Why wasn't I tested?" This level of litigation will come to the forefront. The FDA has retrofitted 53 drugs. Not many companies have proactive strategies for these safety biomarkers. We see a storm brewing.



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Dr. Myla Lai-Goldman
Chief Executive Officer
& President
GeneCentric Diagnostics

Dr. Myla Lai-Goldman's long diagnostics career spans multiple companies. Currently the CEO and President of GeneCentric Diagnostics, a company developing molecular diagnostics for oncology applications, she had previously served as an executive at Laboratory Corporation of America. Myla's 18 years at LabCorp included 10 years as the company's Executive Vice President, Chief Medical Officer and Chief Scientific Officer. She also served on the company's Executive and Management Committees, where she held strategic and operations responsibilities for three major genomic laboratories comprised of more than 700 people. Her role at the company also included leading all clinical, scientific, and medical activities, including the introduction of more than 400 clinical assays. After leaving LabCorp, Myla worked as a venture partner at Hatteras Venture Partners. Myla recently took some time to speak with Carlyle Conlan's Don Alexander about the role she sees diagnostics playing in Personalized Medicine (PM).

Don: How is your company contributing to the field of PM?

Myla: *GeneCentric is a personalized diagnostics company focused on cancer. We use a novel, capital-efficient business model focused on building bridges between research-based innovation and clinical adoption. By partnering for non-core functions, such as lab services, we can focus effort and funds on clinical development and build the evidence that leads to adoption. Our first area of focus – lung cancer – comes out of the Lineberger Cancer Center at UNC. It brings together the scientific expertise of Drs. Chuck Perou and Neil Hayes, as well as three former LabCorp executives – myself, and Drs. Hawazin Faruki and Christy Ferguson, combining extensive diagnostic commercialization experience with great science.*

Don: What do you see as the barriers to adoption in PM?

Myla: *There are a number of barriers to adoption in PM.*



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Don: For example?

Myla: *Dr Faruki and I published a test adoption model in a paper on a pharmacogenomic marker for hypersensitivity to the HIV drug abacavir [Lai-Goldman, Myla & Faruki, Hawazin. "Abacavir hypersensitivity: a model system for pharmacogenetic test adoption." *Genetics IN Medicine* Vol. 10 No. 12. (2008): 874-878. Print.] and the GeneCentric business model was built with this in mind. The defining gate to test adoption is the demonstration of clinical utility. It's not enough to show that using the diagnostic biomarker is associated with disease. It must also show that using the diagnostic biomarker changes the outcome for the patient. That outcome change could be decreased morbidity, mortality, or cost savings. Reimbursement is the biggest barrier to test adoption, and payers are looking for evidence of clinical utility before agreeing to pay for the test. The hurdle to getting reimbursed is very high and developing the necessary evidence can be very costly. An additional challenge is that diagnostics are paid on a cost versus value basis as is seen for drugs.*

Don: Why is that?

Myla: *We are dealing with a historic view of diagnostics as commodities, such as tests being run on highly automated chemistry analyzers. The U.S. system of payments for diagnostics is based on Current Procedural Terminology, or CPT codes, which are valued on the cost of running the test versus the value that is delivered to the patient. The historical norm doesn't match the new generation of diagnostics-personalized tests that are and will be the gatekeeper of cost control and better therapeutic management. Our challenge is a legacy system that was built for a past generation of test and needs to be updated for PM to be successful for the patient and healthcare system.*

Don: What, if anything, has surprised you about the field of PM?

Myla: *We have been tremendously successful with antivirals and management of patients with HIV and HCV, in particular. People think the implementation of PM has just recently begun and forget that there is, perhaps, no better example than the way we personalized tests and drugs for HIV patients in the 90's. This was an incredible success. People either forget or don't realize that this remarkable success of personalized medicine truly changed the face of HIV in the U.S.*

Don: We know that PM is complex but why has Pharma been reluctant to take more of a lead in shaping personalized medicine?

Myla: *The whole concept is a paradigm shift – responders vs. non-responders and identifying patients where the drug is safe versus not safe. Pharma fears this paradigm shift where having a companion diagnostic – not just being first to market or having a sales force – determines who will get a specific drug, where the addressable market for a specific drug gets subdivided by the test. Moreover, the challenge is compounded by having two very different business models for drugs and diagnostics*



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(timelines for development, risk taking and re-imbursement), which present additional obstacles to successful collaborations.

There have not been many easy or huge successes, yet, for the diagnostics industry. Additionally, most current genomic companion diagnostics tend to be single marker tests that don't fit the emergence of techniques such as next generation sequencing, for detection of mutations and other genetic changes. Nevertheless, it is terrific that we see some early successes such as for EGFR and ALK testing for patients with adenocarcinoma of the lung.

Don: If a disease integration initiative – where multiple stakeholders agree on how to integrate tests, treatments and education to optimize clinical and cost outcomes, demonstrated significant clinical and financial benefit, how will this change industry's perspective?

Myla: *There isn't a one size fits all in PM. We don't need a test for every drug. We need to look at each disease and treatment paradigm and understand how to effect change and, if we do this in a methodical manner, we find the ones that would benefit from disease integration initiatives. The tendency is to jump to a one size fits all approach. When considering a disease integration approach, one is optimizing outcomes and costs that make sense to the patient. The Cystic Fibrosis Foundation is a good example of an organization that has had tremendous success bringing multiple parties together. Additionally, we have had recent successes in orphan indications, particularly for diseases with very strong patient advocates who work hard to bring multiple parties together.*

Don: Oncology is a hot target for PM. What other areas do you view as having good potential?

Myla: *There are many areas but one area that comes to mind is CNS diseases, including neurologic and psychiatric diseases such as Alzheimer's disease, Parkinson's disease, autism spectrum disorders, as well as depression and schizophrenia. With both diagnosis and treatment challenges today, these market segments represent incredible opportunity for precision medicine.*

Don: What are your thoughts on adoption factors for PM, such as cost reduction in sequencing, Big Data, etc.?

Myla: *Making technology available through cost reduction is one part of getting PM into patient care. Ensuring the utility of tests is identified and appropriately reimbursed is also fundamental to patient care.*

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Don: And reimbursement –targeted, but high in price? How should policies cover PM?

Myla: Unfortunately, we are a "sick care" rather than a healthcare system, particularly when it comes to reimbursement. Much of the value of genomics and personalized medicine will come from their ability to identify risk factors and/or disease before the patient gets to a difficult to treat, or untreatable, stage. But, this will require more emphasis on prevention and screening, activities that are not always reimbursed.

Some of the prices on the drug side may not be sustainable. Reimbursement for diagnostics and Pharma has to be aligned with appropriate payments based on outcomes. The diagnostics industry is not, presently, incentivized to take risks to provide the innovation and leadership needed for PM. The incentives have to be better aligned.

Don: Is FDA regulation of laboratory developed tests (LDTs), a negative?

Myla: Most of the time, LDTs have been developed by the clinical laboratory because of the lack of FDA cleared or approved tests. Taking these tests through an FDA process, with significant increased costs, could be a burden that will be challenging for many clinical laboratories, particularly if there is no change in reimbursement. The FDA has discussed their concern around more complex tests, and while this is understandable, we need to keep in mind that any new programs that are put in place need to be aligned with the evolution of knowledge that CLIA labs have been able to integrate into LDTs. Integrating this new knowledge has been critical to patient care, and physicians and patients have relied upon this for decades.

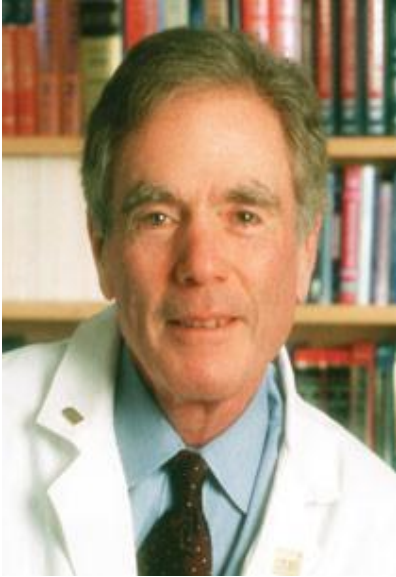
Don: What role does education play in PM?

Myla: Many times it is a lack of understanding of personalized medicine that creates wariness. Educating physicians and patients can create a means to move forward with more comfort.

Don: Common processes and standards?

Myla: People are still a bit wary about how PM will impact them, and their traditional business models. The bottom line is we need to move in this direction and figure it out. Since it is best for patients and the healthcare system, we will continue to break through all of the barriers to recognize the enormous benefit that personalized medicine can bring.

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Dr. Ralph Snyderman
Chancellor Emeritus
Duke University
James B. Duke Professor of Medicine
Duke University School of Medicine

Dr. Ralph Snyderman is Chancellor Emeritus, Duke University and James B. Duke Professor of Medicine in the Duke University School of Medicine. As Chancellor for Health Affairs and Dean of the School of Medicine at Duke University from 1989 to July 2004, he oversaw the development of the Duke University Health System, one of the most successful integrated academic health systems in the country, and served as its first President and Chief Executive Officer. Dr. Snyderman has played a leading role in the conception and development of Personalized Healthcare, an evolving model of national healthcare delivery. He was among the first to envision and articulate the need to move the current focus of healthcare from the treatment of disease-events to personalized, predictive, preventative, and participatory care that is focused on the patient. In 2012, Dr. Snyderman received the David E. Rogers Award from the Association of American Medical Colleges who referred to him as the "father of personalized medicine." Dr. Snyderman recently spoke with Carlyle Conlan's Don Alexander to share his thoughts on Personalized Medicine (PM).

Don: What, if anything, has surprised you about the field of Personalized Medicine?

Ralph: *I've just returned from the 2015 Personalized Medicine World Congress. The thought leadership at the conference, along with President Obama's announcement of a Precision Medicine initiative and a recent article in The New York Times on the subject, show that the field has really gotten its legs and is taking off. There is tremendous recognition of how PM will lead to transformational change in how healthcare will be delivered, and it is expected to become a dominant force in our healthcare system. There is a confluence of forces happening right now that bode well for its future and for its impact on healthcare.*

Having been involved from inception, it is exhilarating that PM is increasingly changing how healthcare is delivered. The primary area affected thus far has been in therapeutics for cancer. Highly effective targeted therapies and companion diagnostics are becoming more prominent in the clinic and are the wave of the future in the development of new therapeutics. On the other hand, it has been surprising that it has taken so long to get to this point. Even more surprising is how the cost of whole genome sequencing has gone from \$400 million in 2000 to \$1,000 per genome today. If you



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look at Moore's Law and predicted where genomic technologies would be today, the technical capabilities growth has far exceeded Moore's Law projections. The availability of affordable next-generation sequencing (NGS) is bringing whole genome sequencing into the clinic.

Don: We know that PM is complex but why is Pharma reluctant to take more of a lead in shaping personalized medicine?

Ralph: *When I started in this field, drug industry executives talked about nothing other than the development of blockbuster drugs. By 2000, some drug industry executives were aware that one size doesn't fit all, but they were sensitive to the reactions of others in their industry and on Wall Street to challenging the status quo.*

Over the last few years, however, anywhere from 20-40% of all drugs approvals have been PM drugs. There is data indicating that 50% of revenues for the top 20 pharma companies will come from PM drugs by 2020. In addition, the FDA has declared that PM is the wave of the future. The pharma industry has come to accept that PM, companion diagnostics, genomic medicine, and targeted therapeutics will be a big part of therapeutics developed, moving forward. Academics and the NIH have moved into PM, as well. Almost all academic health centers have PM programs, and the NIH is honed to lead the President's Precision Medicine initiative.

Don: What has been the impact of the price of PM therapeutics on the payer community?

Ralph: *There has been some price resistance to PM drugs from payers. For example, Express Scripts recently objected to the high price of Sovaldi and placed AbbVie's Viekira Pak exclusively on its formulary for hepatitis C treatment. In response, for the first time in my recollection, price competition is driving high value drugs. Gilead has offered Sovaldi, at a discount, to United Healthcare to counter Viekira Pak thereby creating market pricing pressures. When thinking about the price/value relationship, the price of treating all hepatitis C individuals would be astronomical. However, it would not be necessary to treat all such patients since only a small percentage develop cirrhosis. It might be best to reserve these new drugs for people who actually develop very early signs of the disease thereby knocking 80-90% off the cost and making it far less expensive than liver transplantation and cirrhosis care.*

This does get to a philosophical question – if we can prevent negative outcomes but it breaks economic fault lines, how far do we go with scarce resources? Cost competition will play a role and segmenting the population to treat the people who really need it, will be necessary. There will be pricing pressure for PM drugs but, I believe the market will support innovation with appropriate pricing and sufficient margin to justify the investment.

Don: What about broader adoption of PM as it relates to prevention as well as treatment?

Ralph: *The provider community has been the slowest to adopt PM as an approach to care. The cultural mind-set of providers is to focus on disease versus prevention. Physicians have not been taught aspects of genomics and the broad capabilities of new technologies to predict and prevent*

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disease. Medical curriculum has to start embracing this. I'm constantly being asked by new medical schools about how to prepare for PM. Physicians are, however, often overworked and don't have a lot of time to adapt to new ways of thinking and, importantly, they are not reimbursed for providing personalized, predictive care. Now that there is a movement in Medicare (2018) to pay for performance, this should facilitate further embracement of PM in the provider community. Traditional reimbursement models have made adoption more challenging. The President's new initiative on enhancing genomics will bring more attention to the potential power of PM to improve disease treatment and hopefully prevent it as well.

Don: Oncology is a hot target for PM. What other areas do you view as having good potential?

Ralph: *Cancer has been revolutionized by PM. Targeted therapies abound. Immunotherapeutic approaches such as targeting PD-1 and PD-L1, checkpoint inhibitors, and several types of antibody drugs are examples. The next area may be autoimmune diseases where therapy will be more highly targeted. These would be areas where one can carefully analyze the patient's specific abnormalities and break from phenotypic descriptions that are caused by multiple different mechanisms. Systemic lupus erythematosus, rheumatoid arthritis, and psoriatic arthritis are examples. Other areas of interest include metabolic diseases such as diabetes. Cystic fibrosis therapy has already benefited by targeted therapies.*

Don: What do you think of LDT regulation by the FDA?

Ralph: *LDTs are very pervasive. There are dozens of tests at Duke as well as many major care providers. People are concerned that FDA oversight may create tremendous bureaucracy and cost, and therefore could limit innovation. The FDA is saying they aren't interested in regulating all LDTs. They want to set criteria for tests that have gone beyond the boundaries of a particular provider system and that may have a very high risk in terms of what the test means regarding clinical decisions. The FDA wants analysis and clinical validation that the test measures accurately what it says it does. The concern is that if the FDA gets involved, approval of important tests will be hindered by uncertainty, the lack of transparency, and the process will be slow and bureaucratic. Some would argue that there is enough regulation via a CLIA approval but this designation only assures analytical validation not clinical validation. The FDA needs to develop and communicate understandable guidance as to what and how LDT regulation will be managed. Oversight must be transparent and agile. One question to ponder is whether the FDA will have the resources to effectively oversee LDTs as there will be so many.*

Don: Common processes and standards for NGS?

Ralph: *Standards for clinical adoption of data from NGS are woefully inadequate. There are no clear-cut common standards or, as yet, broad initiatives to develop them. Illumina recently announced that it has formed collaborations with major clinical cancer centers to develop standards for genomic data for cancer. Foundation Medicine also appears to be working on the development of standards. Standards may be ultimately driven by government initiatives or the NIH.*



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Don: What are your closing thoughts concerning PM?

Ralph: *People tend to consider PM as the same as genomic medicine or precision medicine with a focus on personalized disease treatment. Rendering the right drug for the right individual is an extremely important part of PM, but it is only a small part of the composite power of this approach. The bigger paradigm for PM is its ability to improve health and prevent disease as well as to treat disease better if it occurs. The initial hopes for PM at the time of the initial sequencing of the human genome were for personalized, predictive, preventative care as well as better therapeutics. PM can change our current disease-reactive approach to care when we start with a better understanding of what health is and how to improve it. Health is more than the absence of disease and can be improved by doing the right things. PM in its fullest form is an approach to care that is personalized, predictive, preventative, and patient-driven. At Duke, we call this approach Personalized Healthcare. At its basis is the personalized health plan which is used to assess each individual's health risks and create a plan to mitigate them with actionable goals over a specific timeframe. If disease develops, targeted therapies are used whenever possible.*

Consider that most people have plans for their finances and retirement. We need to plan for our own health, our most important asset, as we do for other things. Personalized Healthcare is a means to do this as well as a way to minimize preventable disease and to make our healthcare expenditures more rational.

While genomics and new technologies will undoubtedly improve our ability to predict an individual's risk for disease, track its development, prevent it more effectively, and treat it better, we already have the tools to practice personalized healthcare. My colleagues and I are developing and honing these capabilities and early indications are exciting.



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Dr. Paul Beresford is the Vice President of Business Development and Strategic Marketing for Biodesix, a company that uses complex data analysis and mass spectrometry to discover and develop novel diagnostics. Paul has held senior management positions at Ventana Medical Systems as well as Roche Diagnostics, following Roche's acquisition of Ventana in 2008. He holds a Ph.D. in immunology from the Sackler School of Graduate Biomedical Sciences at the Tufts University School of Medicine and he was an instructor and junior investigator at the Center for Blood Research at Harvard Medical School. Paul took some time recently to discuss with Carlyle Conlan's Don Alexander his thoughts on Personalized Medicine.

Dr. Paul Beresford
Vice President of Business Development
and Strategic Marketing
Biodesix

Don: How is your company contributing to the field of PM?

Paul: *Biodesix is a fully integrated molecular diagnostic company focused in oncology. Through our discoveries directed at unmet clinical needs, we leverage a number of platforms and move tests through development and commercialization to become the standard of care. While Personalized Medicine is thought to be here today, there are very few companies that have been able to drive to clinical adoption. Biodesix has spanned this gap in lung cancer with VeriStrat, our proprietary test that helps doctors determine if non-small lung cell cancer patients should be treated with the drug erlotinib. We are planning to leverage that infrastructure and knowledge to launch new products this year.*

Don: What have been the critical success factors that have allowed you to do this?

Paul: *First, the access to capital and seasoned investors have been critical to get through significant milestones such as the discovery of a robust test, the development of clinical data and a focused/successful reimbursement strategy. This takes a long period of time. Our first publication of our test was in 2007. Eight years later, Biodesix is in the final throes of driving clinical practice test adoption.*



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The second component is that Biodesix has a diverse group of executives within the company [who] have the experience and knowledge to navigate these hurdles.

Don: What, if anything, has surprised you about the field of PM?

Paul: *What has surprised me is the number of milestones and time to get a product accepted into clinical practice.*

Don: We know that PM is complex but why is Pharma reluctant to take more of a lead in shaping personalized medicine?

Paul: *With the high attrition rate of targeted medicines in unselected patient populations, we have learned that if you don't segment patient populations through diagnostics, the medical system can be very costly. With this understanding, Pharma has taken a more proactive stance in identifying the right patient for the right drug, but there is still a disconnect on the business model. This model has pharma taking all the risk by paying the diagnostics company a fee to develop a test for the drug. Accordingly, the pharma company captures the lion's share of the value and leaves very little value for the diagnostics company to promote the diagnostic solution or reinvest in the innovation of additional tests. Going forward, this value distribution needs to change, if novel companion diagnostics are to be discovered and commercialized. An example of this new type of risk-sharing partnership is the one we executed with AVEO Pharmaceuticals. While each company is focused on the respective drug and diagnostic development, we are driven to work more closely because we share in the risk of the program and the value creation.*

Don: Oncology is a hot target for PM. What other areas do you view as having good potential?

Paul: *Autoimmune disorders are an area with good potential.*

Don: How has the cost reduction in aspects like sequencing helped drive adoption?

Paul: *While cost reductions are part of the commoditization of any product or service, information in medicine and the clinical utility of this information is something that should be valued. We believe that value-based pricing of diagnostics will continue to drive innovation and fuel the payment of costly clinical trials needed to move tests into clinical use.*

Don: What about reimbursement?

Paul: *Strides are being made in the world of reimbursement based on the reimbursement reform started in the Protecting Access to Medicare Act of 2014. Congress is beginning to explore pay-for-performance models for healthcare and they have made massive changes to Medicare reimbursement for all laboratory tests. The new law ties Medicare prices to market rates. Now the importance of clinical data, patient outcomes, and the cost of care will have an even more significant impact on tying Medicare prices to the market adoption of private payers.*



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Don: What about the movement of LDTs to FDA oversight?

Paul: *While Biodesix has pursued the LDT route with VeriStrat, starting early in our company's evolution we adopted a quality system that could evolve with the changing regulatory landscape. In addition, with our pharma relationships our CDx development was always in line with FDA oversight. We held true to that with our AVEO CDx. We are currently engaged with the FDA on this program.*

Don: How does education of PM weigh in?

Paul: *Continuous education is a critical factor in PM. Most physicians see 20 patients a day in the oncology arena. It is difficult for them to keep up with CMEs (*Continuing Medical Education). New technologies can be foreign to them. We have decided to work with community-based oncologists and healthcare professionals in their practice through a multi-touch point approach using a field sales force and medical scientific liaisons to educate them on our new products. We also work through key opinion leaders and patient advocacy groups. It is not an easy process.*



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