Life Science Trends 2016

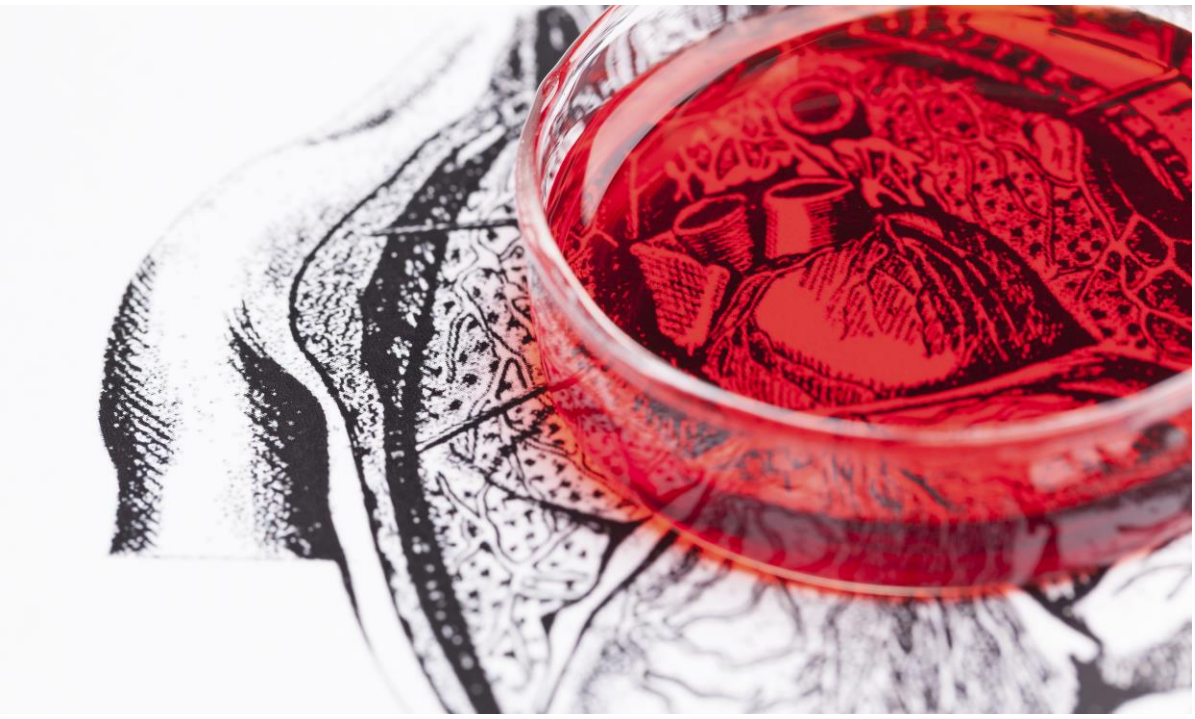
Regenerative Medicine: Past, Present and Future

Featuring Interviews with Thought Leaders in Regenerative Medicine:

Dr. Gail K. Naughton

Dr. Peter C. Johnson

Dr. Chris Mason



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About Life Science Trends 2016

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 2016 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 2016 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, fields covered in previous reports, such as personalized medicine and big data are expected to continue as a trend well into the foreseeable future, as is this year's topic; Regenerative Medicine.

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, founded in 2000 and headquartered near the Research Triangle Park, NC, is an executive and professional search firm focused on the life science, agriculture biotechnology, 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 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

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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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RESEARCH AND INNOVATION

Smartphone Pregnancy Test

A self-contained fiber-optic sensor for smartphones has been developed that could enable users to conduct a wide variety of biomolecular tests, including pregnancy testing or diabetes monitoring. It uses the principle of surface plasmon resonance (SPR) to detect the presence of biomolecules and/or trace gases in basically the same way that a bulky laboratory analyzer functions. However, the new device is a small and robust lab-on-a-chip that is attached to a smartphone and can be designed to monitor a variety of body fluids or gases, such as blood, urine, saliva, sweat and exhaled air.

Burrus

Do Brain Interventions to Treat Disease Change the Essence of Who We Are?

These days, most of us accept that minds are dependent on brain function and wouldn't object to the claim that "You are your brain." After all, we've known for a long time that brains control how we behave, what we remember, even what we desire. But what does that mean? And is it really true?

Despite giving lip service to the importance of brains, in our practical life this knowledge has done little to affect how we view our world. In part, that's probably because we've been largely powerless to affect the way that brains work, at least in a systematic way.

That's all changing. Neuroscience has been advancing rapidly, and has begun to elucidate the circuits for control of behavior, representation of mental content and so on. More dramatically, neuroscientists have now started to develop novel methods of intervening in brain function.

DDDMag.com

Boosting Cancer Immunity

A new protein has been discovered that exploits the innate ability of a person's immune system to kill abnormal cells, offering new hope in the fight against cancer. Although little is known about the molecule or how it works, scientists are hopeful that it will lead to development of more effective treatments, not only for cancer but for viruses and chronic diseases as well.

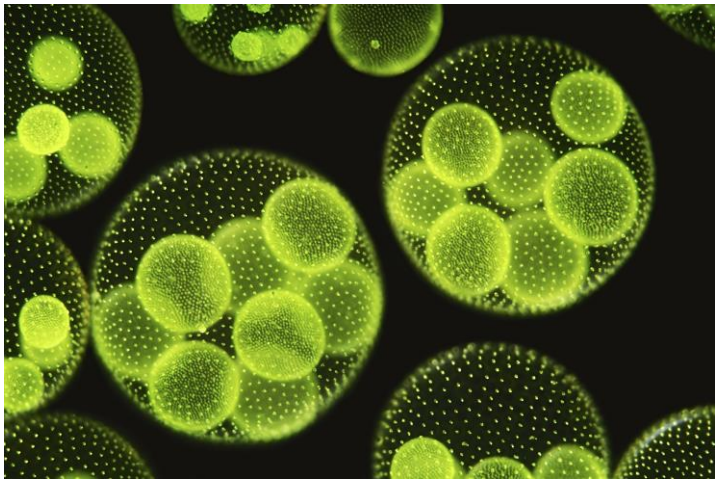
Burrus

How Technology is Transforming Personalized Medicine

These are exciting times. Every day science and technology advancements offer new

insights into the mechanics of human genetics. Maybe more importantly, the space is also rapidly evolving ways to use that information to deliver personalized medicine. Over the next decade, scientists likely will focus on deeply sequencing parts of the genome that prove to have a high degree of clinical utility.

DDDMag.com



Curing Blindness with Algae

The FDA recently approved human clinical trials of a revolutionary new approach to curing blindness caused by retinitis pigmentosa (RP) – a genetic disease in which the photoreceptor cells of the retina die off. The treatment will utilize a light sensitive protein called channelrhodopsin-2, which has been used by neuroscientists for over a decade to make neurons react to light. The protein comes from single-celled green algae that technically can't even see. Instead of an "eye" they have an "eyespot" to seek out the sunlight they need for photosynthesis. It's these same genes which enable algae to detect light that will be transplanted into the retinas of 15 subjects in hopes of restoring their vision.

Burrus

Researchers Find New Code that Makes Reprogramming of Cancer Cells Possible

Cancer researchers dream of the day they can force tumour cells to morph back to the normal cells they once were. Now, researchers on Mayo Clinic's Florida campus have discovered a way to potentially reprogram cancer cells back to normalcy.

The finding represents "an unexpected new biology that provides the code, the software for turning off cancer," says the study's senior investigator, Panos Anastasiadis, Ph.D., chair of the Department of Cancer Biology on Mayo Clinic's Florida campus.

Biotech International

Cleavage Product Shuttled into Mice Brains Reverses Alzheimer's Deficits

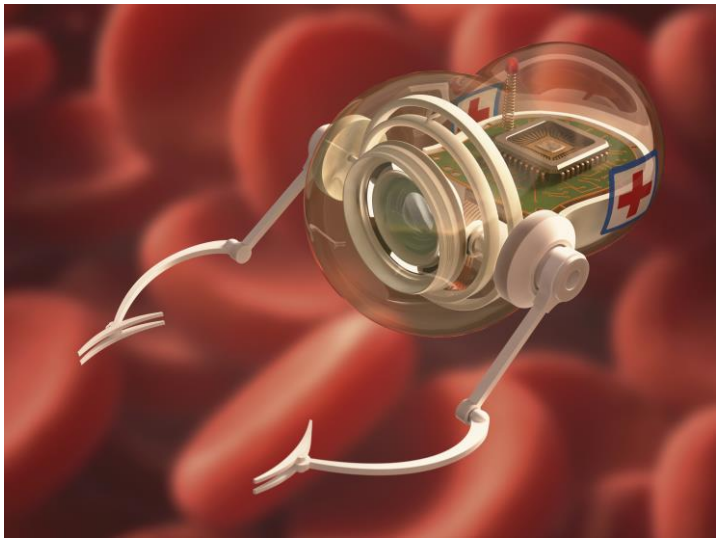
The characteristic synaptic failure and cognitive deficits of Alzheimer's Disease (AD) have been partially mitigated by gene therapy in a mouse

model. By increasing levels of the APP cleavage product, APPsα, researchers from the international ERA-NET NEURON Consortium have demonstrated increased plaque clearance, rescued synaptic connections and improved cognitive functioning in mice with pre-existing AD. This preclinical study suggests that increasing APPsα may be of therapeutic benefit in this degenerative disease.

Bioinsights

Researchers Disguise Drugs as Platelets to Target Cancer

Researchers have for the first time developed a technique that coats anticancer drugs in membranes made from a patient's own platelets, allowing the drugs to last longer in the body and attack both primary cancer tumors and the circulating tumor cells that can cause a cancer to metastasize. The work was tested successfully in an animal model.



DDDMag.com

Alerting the Immune System's Watchmen to Improve Vaccines

As the days get colder and shorter one fall tradition can actually keep you healthy: getting your flu shot. Like all vaccines, the flu shot trains the immune system to fend off infection, but some need help to produce the full effect. In ACS Central Science, researchers report a new way to help improve vaccines using molecules that more effectively direct the immune system.

Some vaccines, like the flu shot, contain a dead or weakened version of the disease-causing pathogen. Other vaccines, like those for hepatitis B and meningitis, contain just a protein, or other molecule (an "antigen") unique to the microbe. When there is a whole pathogen, the innate immune system is strongly activated, which includes alerting cellular watchmen called the toll-like receptors

(TLRs). Antigen-based vaccines do not cause as strong a response, but they produce fewer side effects. Thus, an adjuvant is usually added to antigen-based vaccines to boost their effectiveness. A common adjuvant is a TLR agonist, or activator. In nature, multiple TLR activators work together to effectively direct the immune system.

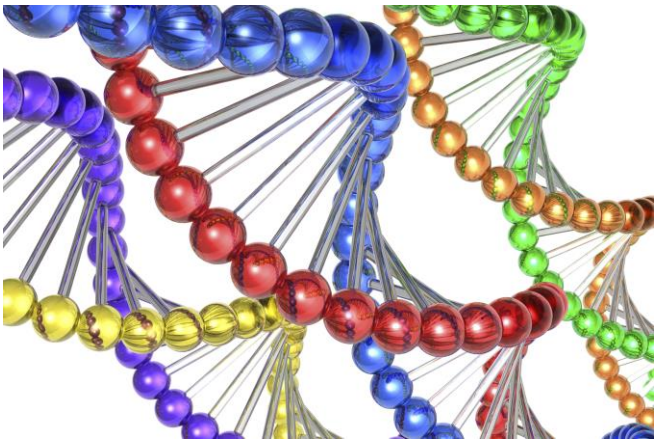
DDDMag.com

Researchers ID Copy Number Changes Associated with Cancer in Normal Cells

Researchers from Uppsala University in Sweden have identified copy number alterations typically associated with cancer in normal cells of breast cancer patients, suggesting that the mutations could be early indicators of disease.

Reporting their work recently in Genome Research, the researchers aimed to look for markers that predict a risk for breast cancer in individuals without a hereditary risk. Approximately 10 percent of women in developed countries get non-familial breast cancer, also called sporadic breast cancer. The disease is heterogeneous and individuals differ in clinical manifestation, radiologic appearance, prognosis, and outcome. Yet, there are no good markers to predict a woman's risk for developing the disease.

GenomeWeb



Gene Summit Organizers Urge Caution on Human Gene Editing

Scientists and ethicists gathered at an international summit in Washington said it would be "irresponsible" to use gene editing technology in human embryos for therapeutic purposes, such as to correct genetic diseases, until safety and efficacy issues are resolved.

But organizers of the International Summit on Human Gene Editing said editing genes in human embryos was permissible for research purposes, so long as the modified cells would not be implanted to establish a pregnancy.

The statement comes amid a growing debate over the use of powerful new gene editing tools in human eggs, sperm and embryos, which have the power to change the DNA of unborn children.

Reuters

Researchers Shed Light on Protein-Related Diseases

Dartmouth researchers have found that some proteins turn into liquid droplets on the way to becoming toxic solids implicated in neurodegenerative diseases and other genetic disorders.

The findings, along with a series of related studies by scientists at other institutions, appeared in the journal Molecular Cell.

The Dartmouth researchers studied proteins that have a massive expansion of a single amino acid, glutamine, typically associated with toxic protein solids. For example, neurodegenerative-linked proteins such as those in Huntington's disease have these amino acids, which makes the protein sticky. The researchers found that proteins like this undergo a transition into liquid droplets on the way to becoming toxic, fibrous solids. These liquid droplets are similar to the ones made when oil and vinegar are mixed to make salad dressing. The researchers suspect that cells use this liquid state for normal physiology, but under certain conditions the proteins transition again from liquid to toxic solids. These kinds of droplets have also been called "membrane-free" organelles because they lack a barrier and are highly dynamic unlike many organelles such as mitochondria or nuclei.

DDDMag.com

FUNDAMENTAL TRENDS

Merck Lowers Cost of Remicade in UK as Biosimilars Enter Market

According to Biosimilar News, during the second quarter of this year, Merck saw a 25% decline in sales of Remicade. This is something that has already happened in various EU countries. As a result, Merck has been offering discounts and rebates. The discount offered to the UK was $73.3 million based on $292 million in Remicade sales. In some Nordic countries, the discounts are as high as 69%.

The writing has been on the wall for a while now, and discounting because of biosimilar competition has been going on for some time now. The question is how this will play out in the U.S. The FDA is currently reviewing a biosimilar version of Remicade from Celltrion, and though approval is not a foregone conclusion, there's a good chance it will happen.

BioPharma Dive

A Nanotechnology-Inspired Grand Challenge for Future Computing

In June [2015], the Office of Science and Technology Policy issued a Request for Information seeking suggestions for Nanotechnology-Inspired Grand Challenges for the Next Decade. After considering over 100 responses, OSTP [was] excited to announce the following grand challenge that addresses three Administration priorities—the National Nanotechnology Initiative, the National Strategic Computing Initiative (NSCI), and the BRAIN initiative:

Create a new type of computer that can proactively interpret and learn from data, solve unfamiliar problems using what it has learned, and operate with the energy efficiency of the human brain.

Fundamental Trends

While it continues to be a US priority to advance conventional digital computing—which has been the engine of the information technology revolution—current technology falls far short of the human brain in terms of both the brain's sensing and problem-solving abilities and its low power consumption. Many experts predict that fundamental physical limitations will prevent transistor technology from ever matching these twin characteristics. We are therefore challenging the nanotechnology and computer science communities to look beyond the decades-old approach to computing based on the Von Neumann architecture as implemented with transistor-based processors, and chart a new path that will continue the rapid pace of innovation beyond the next decade.

WhiteHouse.gov

Deloitte Report - Executing an Open Innovation Model - Cooperation is Key to Competition for Biopharmaceutical Companies

Many biopharmaceutical (biopharma) companies are facing a challenging research and development (R&D) environment and increased competitive pressures. Their heavy reliance on a closed, traditional model of product development might stifle true innovation and may cause biopharma companies to lag behind their more creative peers. Companies in other industries have turned to open innovation (OI) – along a spectrum of openness that ranges from closed/traditional to open/emerging – as one way to successfully overcome many R&D and marketplace challenges by sourcing innovative

ideas, knowledge, and new skills/technologies from outside their organization.

Deloitte's analysis of the current state of OI in biopharma reveals a higher success rate for OI pursuits than for closed-model product development. However, companies have sourced around 80 percent of their R&D pipeline via the more closed end of the OI spectrum. Adoption at the most open end is still infrequent and slow, mainly due to concerns about intellectual property (IP) rights, adopting new OI-based R&D models, and cultural and management style issues. Nonetheless, for biopharma companies, OI seems to be the way forward, as it appears to be a more cost- and time-effective way to bring drugs to market. In fact, several key trends will likely continue to drive the adoption of OI, especially at the most open end of the spectrum.

Deloitte

New Kind of 'Designer' Immune Cells Clear Baby's Leukemia

A baby whom doctors thought almost certain to die has been cleared of a previously incurable leukemia in the first human use of an "off-the-shelf" cell therapy from Cellectis that creates designer immune cells.

One-year-old Layla had run out of all other treatment options when doctors at Britain's Great Ormond Street Hospital (GOSH) gave her the highly experimental, genetically edited cells in a tiny 1-milliliter intravenous infusion.

Two months later, she was cancer-free and she is now home from hospital, the doctors said at a briefing about her case in London.

Reuters

Why 2015 was the Year of the Biopharma Blockbuster

In March of 2015, Thomson Reuters released its annual Drugs to Watch report—an analysis of the biggest new products expected to enter the market this year. The intelligence firm ranked drugs that have just entered or are expected to soon enter the market based on projected 2019 sales. And if the predictions prove correct, then this year has almost four times as many future blockbusters entering the

biopharma fray compared to 2014 (11 in 2015 year versus just three in 2014).

BioPharma Dive

First Trial of Gene-Editing Treatment for Hemophilia

The first attempt to edit the genes of cells inside the human body is about to take place. The technique being trialled aims to cure hemophilia B, a clotting disorder that can result in spontaneous internal bleeding.

The trial was announced in Washington DC in mid-December at the International Summit on Human Gene Editing. Much of the meeting will focus on a revolutionary genetic engineering technique called CRISPR – specifically its application to human beings.

Gene editing refers to the process of deleting, adding or altering DNA in precise spots in a genome. CRISPR is a cheap, easy and fairly precise way to do this, and has the potential to treat numerous diseases. It has not yet been tried in people but older, more expensive forms of gene editing have already been used in cases of leukemia and HIV infection – although cells have been removed from the body first for their genes to be edited.

New Scientist

Why it Matters that the FDA Just Approved the First 3D-Printed Drug

For the first time ever, the FDA has approved a 3D-printed prescription pill for consumer use. This 3D-printed pill, which will sold by Aprecia Pharmaceuticals under the name Spritam, could be used by the more than 3 million adults

and children in America who suffer from certain types of seizures caused by epilepsy.

Washington Post

F.D.A. Approves Zarxio, Its First Biosimilar Drug

The Food and Drug Administration has approved the first so-called biosimilar drug for use in the United States, paving the way for less expensive alternatives to an entire class of complex and costly drugs.

The drug, called Zarxio, produced by Sandoz, is used to help prevent infections in cancer patients receiving chemotherapy. It is a close copy of an existing medication called Neupogen, made by Amgen. It was approved in Europe in 2009 as Zarzio but has not been used in the United States, in part because no regulatory pathway existed to bring biosimilars — approximate copies of drugs in a class known as biologics — to market.

But in January, 2015 an expert panel unanimously recommended that the F.D.A. approve it, and in March, the agency announced that it had taken the panel's advice.

New York Times

Bioinformatics Market to Develop at Robust CAGR of 15.5% Till 2020 with Increasing R&D Initiatives

Transparency Market Research has announced the addition of a market study based on the bioinformatics market. According to the report, the global bioinformatics market is estimated to reach US$30.8 billion by 2020. The study states that the bioinformatics market will develop at a robust CAGR of 15.5% from 2014 to 2020. According to the report, the bioinformatics market had reached a value of US$10.0 billion in 2013. The report is titled "Bioinformatics Market – Global Industry Analysis, Size, Share, Growth, Trends, and Forecast, 2014 – 2020". During the last ten years, the amplified information technology market growth has in turn driven the bioinformatics market.

Bioinformatics helps provide automation of data, accuracy, decreases errors, and reduction in turnaround time (TAT). Bioinformatics has grown due to augmentation of pharmaceutical, bioscience, and life sciences research and development. An upsurge in government support has fueled research and development activities that have resulted in amplified acceptance of bioinformatics in practice.

Medgadget

Selling isn't a Bad Word if it's Done Right

GSK has left the era of the product-centered world of sales far behind, Victoria sees, "A world of change surrounding utilization of a patient-focused model." Indeed, her Sales Managers (who train the medical representatives) now spend more than half their time in the field, observing and coaching frontline sales representatives. She explains, "Their goal is to uncover the needs of patients and doctors; therefore, we tailor the benefits of our medicines to match the needs of the patient."

For Victoria, patient-focused sales is a much more positive approach compared to the traditional product-centered approach. She acknowledges that the transformation is slow-moving, but as employees are trained in the new style, they are finding that doctors are more willing to take the time to discuss products with them, and generally to provide feedback. When doctors feel that they are treated as part of the process, listened to, and can ask questions, they are more willing to purchase new medications because they know the advantages for their patients.

Eyeforpharma

U.S. FDA Accepts First Digital Medicine New Drug Application for Otsuka and Proteus Digital Health

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and Proteus Digital Health (Proteus) today announced that the United States Food and Drug Administration (FDA) has determined that the New Drug Application (NDA) for the combination product of ABILIFY®(aripiprazole) embedded with a Proteus® ingestible sensor in a single tablet is sufficiently complete to allow for a substantive review and is considered filed as of September 8, 2015.

This is the first time an FDA-approved medication (ABILIFY) has been combined and submitted for approval with a sensor within the medication tablet (the Proteus ingestible sensor) to measure actual medication-taking patterns and physiologic response.

Reuters

Tufts Report Evaluates R&D Efforts

To meet the growing demand for innovation, drug developers need to significantly scale up their level of process improvements to reduce the time and cost associated with bringing new drugs to market, according to the Tufts Center for the Study of Drug Development.

"The core challenge is that developing new drugs has become more complex and more expensive than ever," said Tufts CSDD director Kenneth I Kaitin, "It takes an average of $2.6 billion and 15 years to develop and win approval for a new drug, and a typical Phase III protocol now entails an average of 167 procedures, 60% more than at the start of the millennium.

Improving the clinical trial process holds the most promise for enhancing R&D efficiency, he said, including reducing clinical trial complexity, engaging with new partners, and working more closely with regulators. In the longer term, Mr. Kaitin said policy changes, such as shifting some of the U.S. National Institutes of Health grant funding from translational research back to basic research, will improve prospects for developing new drugs to treat an expanding array of medical conditions.

ContractPharma

2016: A Biopharma Market in Flux

William Looney provided a thought provoking and informative view of the Biopharma Market in his article. Starting off with a review of some industry news including; Biopharma accounts for 31 per cent of the profits of Western-based multinationals, compared to 17 per cent in 1999, according to the McKinsey Global Institute and Brand sales increase at double digit rates for 2015, with torrid pace to continue in 2016 due to positive demographic factors, an improving US economy and a bumper crop of specialty biologic products. Worldwide sales of all drugs have surpassed the trillion dollar mark; IMS forecasts a 1.3 trillion dollar market by 2018.

However he moves on to review the arguments that investment dynamics no longer favour organic growth. Amongst the observations included are: As the science of personalized medicine drives drug discovery into progressively smaller niches of treatment, where are the patients going to come from to keep revenue per patient sufficiently high to fuel the requirements of big Pharma for those ever-higher multiples demanded by investors? And the "get big to scale" philosophy driving the trend to consolidation is running counter to an equally significant trend: the shrinking pool of patients available to initiate treatment with new, innovative – and high cost – drugs. Cheap generics now account for 85 per cent of US prescriptions, with the remainder focused on proprietary drugs for smaller, precisely segmented groups of patients, like those with rare diseases or specific types of cancer.

These and other issues raised are developed into arguments as to why the performance bar on the industry is being raised, the increased pressure to define a drug's value and challenges facing the reputational risk of the industry.

Finally there is a review of what is hot (and not), such as M&A action and out-licensing to big Pharma. New drug combinations are another hot area in oncology and investigating the human microbiome, either as a source of new treatments – or the underlying cause – for many common diseases.

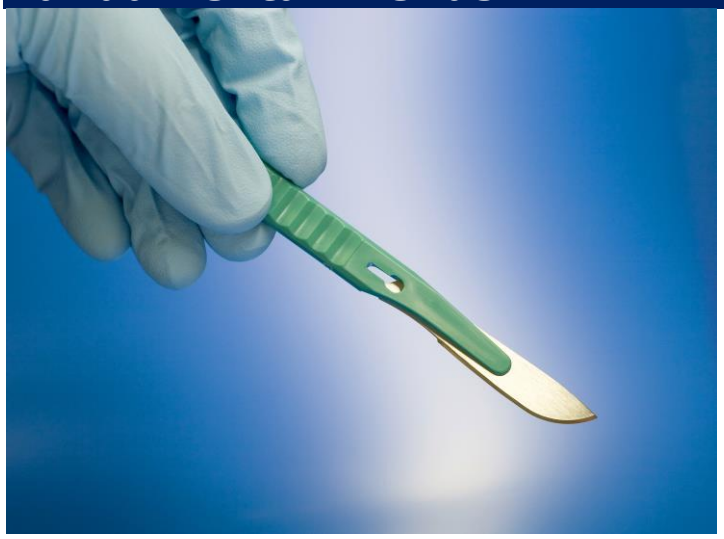
pharmexec

2015 Medtech Approvals Rocket

It's official – 2015 saw the greatest number of novel US medtech approvals in a decade. The FDA granted a total of 51 first-time premarket approvals and humanitarian device exemptions, just shy of the 52 forecast at the half-year point and well above the 33 in 2014.

The expedited access PMA route, which kicked in in April, seems yet to have an impact – the average time to approval was roughly the same as 2014. But the FDA is saying yes to more devices than ever, and the number and speed of approvals should only increase if the 21st Century Cures bill comes into effect.

Evaluate Group



Cancer Immunotherapy: The Cutting Edge Gets Sharper

Artificially boosting the body's immune response against cancer is the most exciting advance in the treatment of tumors in the past couple of years. But as the jam-packed sessions at a recent scientific conference in New York City made clear, a lot of questions remain to be answered before anyone can declare victory in the war on cancer. Among them: What is the best way to kick the immune system into action? Will immunotherapy work for all sorts of people with all kinds of cancer or just for a lucky few? Is there a way to make the treatments less dangerous or expensive?

It was standing room only for many of the presentations at the first International Cancer Immunotherapy Conference. Speaker after speaker started their talks by disclosing financial ties to a variety of companies ranging from pharmaceutical giants to their own start-ups. The audience consisted primarily of scientists and physicians. But sprinkled among the 1,400 attendees, in addition to the usual smattering of journalists, were a number of industry scouts and finance people seeking to glean the next big investment opportunity or joint project possibility.

Jill O'Donnell-Tormey, chief executive officer of the Cancer Research Institute, proclaimed 2015 "a truly special year for cancer immunotherapy." The U.S. Food and Drug Administration approved two new immunotherapy drugs, she noted, "more than half of the current cancer clinical trials include some form of immunotherapy," several groups are working on possible combination therapies and oncologists around the world are recognizing "a paradigm shift in cancer." But as exciting as these advances are, she continued, "we know that we are only at the beginning" in terms of being able to understand or broadly use them.

ScientificAmerican

Companies Aim to Make Drugs from Bacteria that Live in the Gut

Scientific discoveries in recent years suggest that some serious conditions could be cured by adding “good” bacteria to your digestive tract. Now several companies are racing to develop drugs that do so.

It’s a jungle in there: massive populations of microbes, immune cells, and cells of the gut tissue are interacting and exchanging countless chemical and physical signals. Disruptions to this complex ecosystem, often called the microbiome, have been linked not only to gastrointestinal problems but also to metabolic,

immunological, and even neurological disorders.

One such problem, which occurs when a very common species of bacteria, Clostridium difficile, colonizes the gut and becomes too abundant, can be cured by adding good bacteria to the digestive tract—but the method for doing so requires a transplant of another person's feces, and the reasons it works are not well understood. The next generation of microbiome medicines will instead be "real drugs" that are "easy to take, clean, and safe," says Roger Pomerantz, CEO of Seres Therapeutics.

Technology Review

The US Food and Drug Administration Hit a New Record in its Personalized Medicine Approvals Last Year

Out of 45 new drugs approved by the FDA last year, 13 treatments — or 28 percent —are personalized medicines, the PMC says in a statement. In comparison, in 2014, nine out of 41 new drugs, or 22 percent of treatments, the agency approved were personalized.

The PMC issued the list with input from the FDA. The group considered drugs "personalized" whenever product labeling included a "reference to specific biological markers" that may be gauged by diagnostic tools and which guide decisions or procedures in patients.

GenomeWeb also published a list of 2015 personalized drug approvals, but applied different criteria and considered drugs indicated in labeling for a molecularly defined patient subset and those for which a companion or complementary diagnostic was approved with the drug.

Genomeweb

INVESTING AND DEAL-MAKING

Astrazeneca Taps Crowd Sourcing to Find Cancer Drug Cocktails

Drugmaker AstraZeneca is harnessing the wisdom of crowds to help mix tomorrow's cancer drug cocktails.

The company said its decision to release preclinical data from more than 50 of its medicines was unprecedented in scale and would help accelerate the hunt for synergistic tumor-fighting drug combinations.

The crowd sourcing initiative is being run as part of the DREAM Challenge, an open innovation non-profit biology project in which scientists pool ideas and crunch data.

Reuters

Why the 'Biotech Bubble' is Economic Nonsense

Biotech is a tricky sector. In the mind of many investors and analysts, buying biotech stocks basically means investing in companies which are structurally losing money while taking significant risks relying on complex data releases that are not always easy to interpret. While this might not be an unfair characterization of some biotech investments, there are investors who still have in memory the dotcom bubble of the early 2000's and look upon biotech stocks as if some kind of "sectorial" overvaluation, or bubble, was at play - in other words, biotech investments as a group would be reduced to a bunch of speculative bets based on "hype and smoke and mirrors."

Evidence of that widespread mindset is clear when observing recent massive market reactions such as the one following Hillary Clinton's tweet (in which she promised to act on some drug's exorbitant price) hitting virtually all biotech and pharma companies alike regardless of their specific business model - i.e. does the company rely on a few very expensive drugs or does it have a large portfolio of products covering widespread indications?

The fact is that many financial analysts seem to consider biotech as a kind of market oddity, calling biotech valuations "substantially stretched" and struggling out of their comfort zone when the usual technical indicators fail to deliver any meaningful explanation justifying some companies' substantive market caps. Some other investors may also assimilate an exacerbated sectorial volatility with a lack of fundamental value. From there, there's only one step to claiming that biotechs are just another bubble about to burst sooner or later

Seeking Alpha

Investing and Deal-Making

Biotech IPOs Slow, but Appetite for Size Remains Unsatisfied

Biotech flotations might have slowed last year, but considering the wider performance of jittery equity markets the sector can still be proud of its record. A total of 61 drug developers listed on Western exchanges raising $4.68bn in 2015, by EvaluatePharma's calculations (see tables below).

While both of these tallies fell short of 2014's impressive output, the average amount raised edged 6% higher to $76.7m. This suggests that investor appetite for substantial offerings remained strong in 2015, and raises the question of whether this interest can be sustained in 2016. There are good reasons to be cautious, such as the drop in the Nasdaq biotech index so far this year, and a notable absence of any biotech IPOs on the exchange in December.

Evaluategroup

The FDA is Lukewarm on Those Hyper-Valuable Vouchers for Fast Drug Reviews

Big Pharma has been willing to pay hundreds of millions of dollars for a shortcut to FDA approval, buying up priority review vouchers created to incentivize new drugs for neglected diseases. But the agency seems less than enthusiastic about honoring its end of the bargain, with one top official expressing concerns about how the voucher program might harm the FDA's core mission.

In an interview with Pharma & MedTech Business Intelligence, FDA Office of New Drugs Director John Jenkins said the agency's long-held problems with priority review vouchers have been "amplified" as more and more companies line up to redeem them. And the market value of the vouchers has skyrocketed over the past year, with one going for $350 million in August, suggesting the issue isn't going away.

Fierce Biotech

Healthcare Startup Boom: 2015 Could See More than $12B Invested into VC-Backed Companies

VC-backed healthcare companies in the US have seen a jump in financing, with more than $6B already invested in the first half of 2015 across more than 400 deals, putting 2015 on track to hit a 5-year funding high.

CB Insights used its database to highlight funding trends, exit activity, active investors, and the most well-funded companies to keep you up-to-date with what's happening in the healthcare industry.

CB Insights

Vantage Point – More Consolidation in Medtech, but No Early-Stage Joy

Thanks to biopharma's more onerous clinical trial requirements it takes a vastly larger amount of venture capital to get a biotech concern to the revenue-generating stage than it does a medtech company. But, if a biotech is aiming for a trade sale, it does not need to. Big pharma will buy biotechs pre-revenue, but this is not true of medtech, says Gareth Down, head of European healthcare at the investment bank William Blair.

"The pharma-life science space is driven by formulaic gates: clinical trial outcomes. Once you get to those gates, there is a well-established mathematical rule to determine the success of something that has just concluded phase IIa versus phase IIb," Mr Down tells EP Vantage. "We find that the large buyers of medtech businesses focus on revenue because they don't have that same gating system."

For medtech buyers commercial success is the only solid indicator that a company is worth acquiring. And this is a crucial factor in explaining venture funders' reluctance to invest in medtech start-ups compared with biotechs. VCs know that medtechs will suck in more and more cash before standing an equal chance of an exit. Unlike biotech start-ups they will need to negotiate FDA or at least European approval, hire a sales force and essentially build a business.

A biotech, by contrast, can be a small lab group completing clinical trials, which is an appealing asset in itself, Mr Down says – it does not need to be a business per se.

Evaluategroup

Campbell Alliance 2015 Dealmakers' Intentions Survey

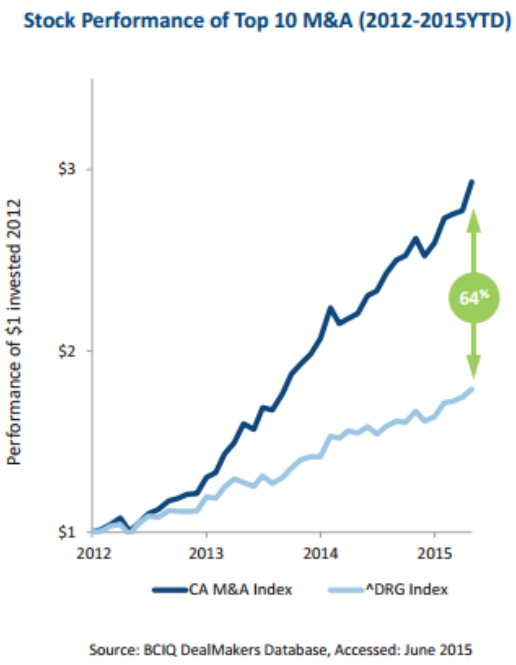
With 2014 being a record year for life science deal making and with more than 180 merger and acquisition (M&A) deals across the pharmaceutical and biotechnology industry, totaling $218 billion in combined M&A, financing, and up-front licensing payments the question coming into 2015 was could this be sustained?

2009 was the last year where deal making was at the same level; however the nature of the deals was very different. 2009 saw a wave of mega-merger contribution to the majority of the deal volume as compared to 2014 when such deals represented less than 40% of activity, with the contribution from mid-to-small caps increasing every year since 2009.

In 2105, this momentum continued. In addition to the availability of cash, a number of other factors were likely influencing the increased M&A trend, including stock performance, the payer environment and tax inversions. Clearly, the market was rewarding companies that engage in M&A. In 2014, the top 10 M&A buyers had a 63% greater return on investment than the overall large-cap pharmaceutical index (DRG, Arca Pharmaceutical Index) from 2012 to May 2015.

M&A Top 10 (Total Deal Value, 2012-2015)

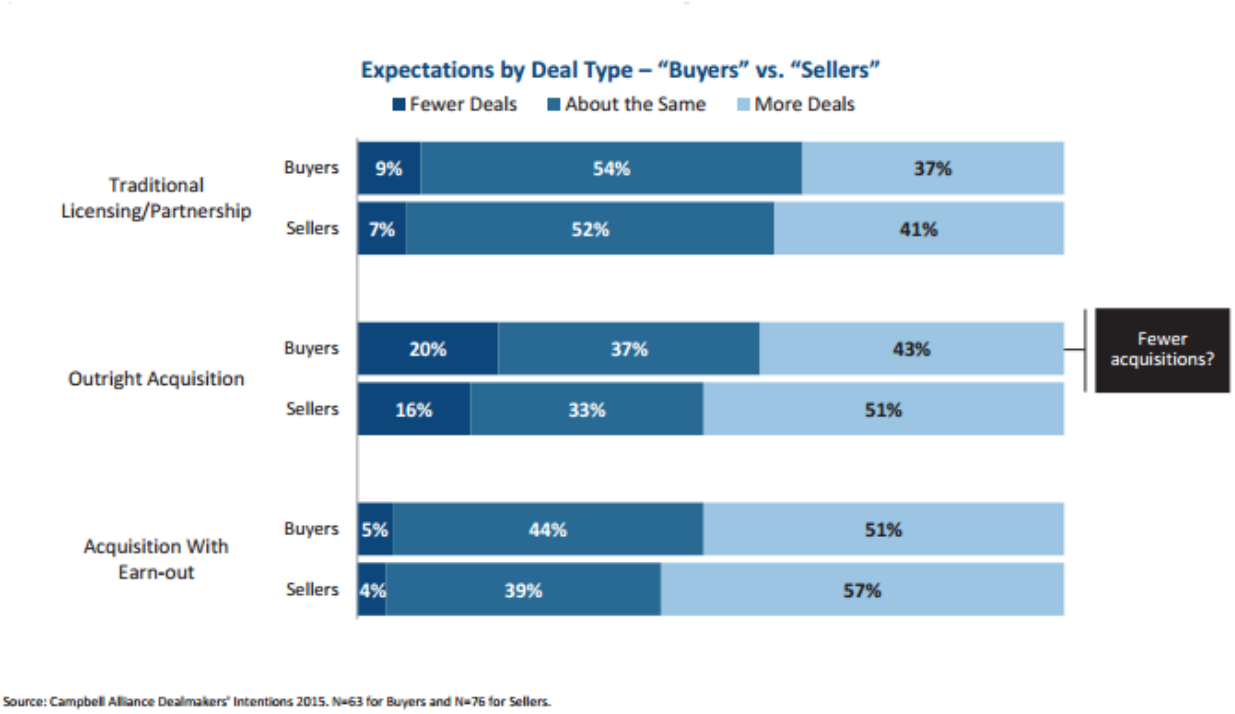
Company	Ticker	Total Deal Value ($M)
Actavis plc	ACT	$ 95,022
Valeant Pharmaceuticals International Inc.	VRX	$ 28,488
Johnson & Johnson	JNJ	$ 22,450
Thermo Fisher Scientific Inc.	TMO	$ 14,525
Merck & Co. Inc.	MRK	$ 13,575
Amgen Inc.	AMGN	$ 13,030
Roche	RHHBY	$ 12,939
Gilead Sciences Inc.	GILD	$ 11,775
Shire plc	SHPG	$ 11,506
Bristol-Myers Squibb Co.	BMY	$ 11,475



Source: BCIQ DealMakers Database, Accessed: June 2015

Investing and Deal Making

Consistent with previous CA surveys, sellers forecast a more optimistic outlook than buyers regarding the extent of deal making in 2015. However, as seen in Figure 4, both groups expected the greatest increase to be in acquisitions with earn-outs (51% of buyers and 57% of sellers), and dealmakers express some bearishness in sentiment with regard to outright acquisitions. 20% of buyers and 16% of sellers expect fewer outright acquisitions, suggesting an expectation of greater risk sharing in the deals that are made.



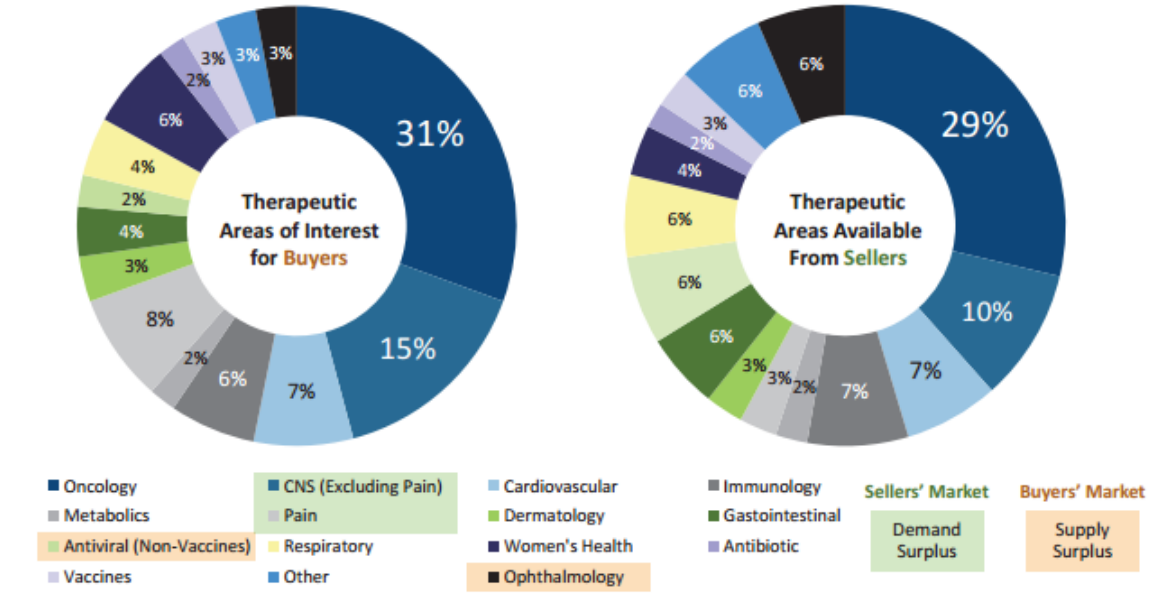
Source: Campbell Alliance Dealmakers' Intentions 2015. N=63 for Buyers and N=76 for Sellers.

Not surprisingly, phase III shows the greatest imbalance with nearly three times more interest in this area than sellers and an inversion of the situation for preclinical assets which is of more interest reflecting potential greater returns for the right picks and the competition to move into hot areas.

Investing and Deal Making

Source: Campbell Alliance Dealmakers' Intentions 2015. N=63 for Buyers and N=76 for Sellers.

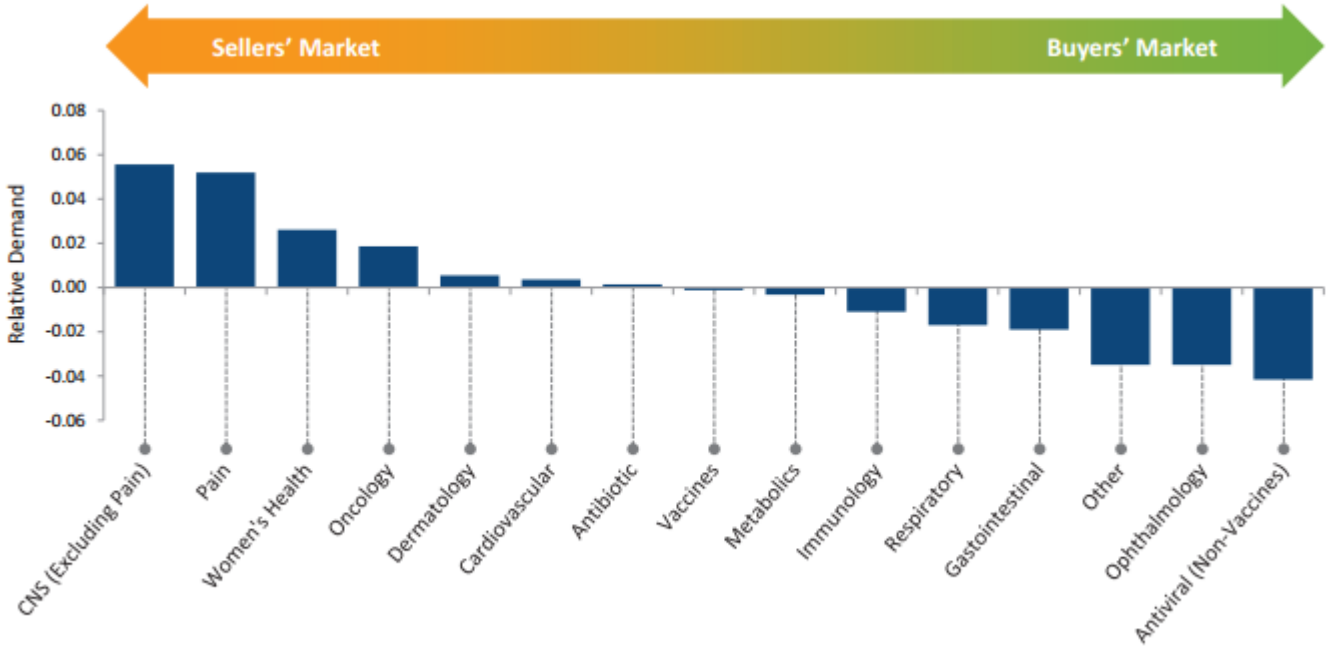
Reviewing therapeutic areas, buyers and sellers share similar interests in what they consider to be key therapeutic areas with deal potential namely. Oncology, central nervous system (CNS) (excluding pain), and cardiovascular are consistent with previous years.



Source: Campbell Alliance Dealmakers' Intentions 2015. N=63 for Buyers and N=76 for Sellers.

Investing and Deal Making

Combining this data identifies areas of demand or supply surplus. Among CNS indications, both excluding as well as including pain, demand exceeds supply, while in the areas of ophthalmology and antivirals that are not vaccine specific we see a relative glut of assets.



Source: Campbell Alliance Dealmakers' Intentions 2015. N=63 for Buyers and N=76 for Sellers. Demand Index is calculated by subtracting the share of respondents with at least one asset to out-license from the share respondents likely or very likely to in-license for at least one therapeutic area for at least one stage of development.

The hottest areas for licensing deals has changed from orphan products to cancer vaccines in part reflecting high profile approvals. The record high gap in discount rates between buyers and sellers of 2013 that financially drove deals collapsed in 2014. However, it has since started to widen again providing an added incentive for deals.

Campbell Alliance

Summary of Ernst & Young – Beyond Borders: Unlocking Value

The EY Beyond Borders Report started by highlighting the recent strength of this sector with nearly all KPI's for revenue, profitability, capital raised reaching record levels in 2014 and continuing into 2015. We saw two of the most successful ever product launches with Gilead Science's Solvadi and Harvoni. With the FDA clarifying the use of new expedited approval channels for breakthrough medicines new product approvals are also reaching new levels. Coupled with expansionary monetary policy/buoyant markets notably the US the biotech industry has a market capitalization of over $1 trillion for the first time. Other key topics covered include:

Europe has nearly half the number of companies as the US employing over half as many people. However, European R&D spend is less than 20% of that in the US. The gap that previously existed between the US and Europe on the EY Survival Index which tracks the amount of cash biotech companies have on hand is closing which should see increased confidence to invest by European companies.

EY Survival Index, 2013-14

	US		Europe		Canada	
	2014	2013	2014	2013	2014	2013
More than 5 years of cash	27%	26%	34%	32%	22%	24%
3-5 years of cash	12%	15%	11%	8%	8%	7%
2-3 years of cash	17%	12%	13%	10%	7%	5%
1-2 years of cash	22%	24%	16%	15%	25%	5%
Less than 1 year of cash	21%	23%	25%	36%	38%	59%

Chart shows percentage of biotech companies with each level of cash. Numbers may appear inconsistent because of rounding.

Source: EY, Capital IQ and company financial statement data.

The Biotech industry continued to enjoy record levels of "innovation capital" with funding in both the US and Europe being robust across the spectrum of IPO's, Venture Capital and Debt Financing. Analyzing the high levels of M&A activity, we see acquirers paying significantly higher premiums and upfront payments. This is in part being driven by greater competiveness as big pharma were eager to acquire commercial-stage biotech's to offset revenue shortfalls reflecting price pressure and slower growth in emerging markets. In addition, licensing deal numbers and value were also historically high.

Further evidence of strong investor sentiment in the sector is the growing number of pre-commercial biotech companies valued in excess of $1 billion.

Investing and Deal Making

Capital raised in the US and Europe, 2000-14
(US$m)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
IPOs	7,838	548	593	484	2,068	1,692	2,091	2,262	119	840	1,325	863	880	3,526	6,802
Follow-on and other	13,415	2,233	1,763	4,904	6,857	6,604	9,286	8,889	4,098	9,226	5,955	5,869	7,616	9,310	13,838
Debt	1,529	1,907	4,472	7,296	6,349	6,030	9,662	10,575	5,776	5,614	12,079	20,587	14,040	12,831	26,049
Venture	4,121	3,694	3,504	4,073	5,277	5,495	6,044	7,930	5,987	5,809	5,805	5,678	5,518	5,948	7,630
Total	**26,903**	**8,382**	**10,332**	**16,757**	**20,551**	**19,821**	**27,083**	**29,657**	**15,980**	**21,491**	**25,163**	**32,998**	**28,055**	**31,614**	**54,319**

Numbers may appear inconsistent because of rounding. Convertible debt instruments included in "debt."

Source: EY, BioCentury, Canadian Biotech News, Capital IQ and VentureSource.

Total revenues for US and European biotech's increased by 610% over the past 14 years. Adjusting for inflation, the revenue generated by the top 10 biotech's in 2014 were 4.6 times greater than the revenues generated by three top 10 in 2000. However, only three of the top 10 US-based and four of the European biotech's in 2000 remain in the 2014 listing, indicating the level of churn in the sector. Seven of those that exited the US list were acquired and two of the entrants in Europe were originally US-based companies that redomiciled via acquisition.

Top 10 changes in European market capitalizations, 2009-14
(US$m)

Company	Market cap at end of 2014	Market cap at end of 2009	US$ change	CAGR (2009-14)
Shire	$41,681	$10,581	$31,099	32%
Jazz Pharmaceuticals	$9,904	$244	$9,660	110%
Alkermes	$8,563	$892	$7,672	57%
Novozymes	$13,014	$6,448	$6,565	15%
Actelion	$12,915	$6,367	$6,549	15%
BTG	$4,720	$721	$3,999	46%
Eurofins Scientific	$3,876	$777	$3,099	38%
Genmab	$3,336	$709	$2,627	36%
Meda	$5,255	$2,726	$2,529	14%
Swedish Orphan Biovitrum	$2,704	$196	$2,508	69%

CAGR: compound annual growth rate. Numbers may appear inconsistent due to rounding.

Source: EY and Capital IQ.

Investing and Deal Making

Top 10 changes in US market capitalizations, 2009-14
(US$m)

Company	Market cap at end of 2014	Market cap at end of 2009	US$ change	CAGR (2009-14)
Gilead Sciences	$142,207	$38,940	$103,267	30%
Biogen	$80,163	$15,472	$64,691	39%
Amgen	$121,167	$57,257	$63,910	16%
Celgene	$89,343	$25,591	$63,752	28%
Regeneron Pharmaceuticals	$41,471	$1,946	$39,525	84%
Alexion Pharmaceuticals	$36,689	$4,324	$32,365	53%
Illumina	$26,210	$3,838	$22,373	47%
Vertex Pharmaceuticals	$28,574	$8,244	$20,330	28%
BioMarin Pharmaceutical	$13,331	$1,895	$11,436	48%
Incyte Corporation	$12,351	$1,080	$11,271	63%

CAGR: compound annual growth rate. Numbers may appear inconsistent due to rounding.

Source: EY and Capital IQ.

In both the US and Europe, Biotech Stocks outperformed the broader indices, led by mid-sized biotech's in the US and large pharma in Europe.

Investing and Deal Making

US market capitalization relative to leading indices

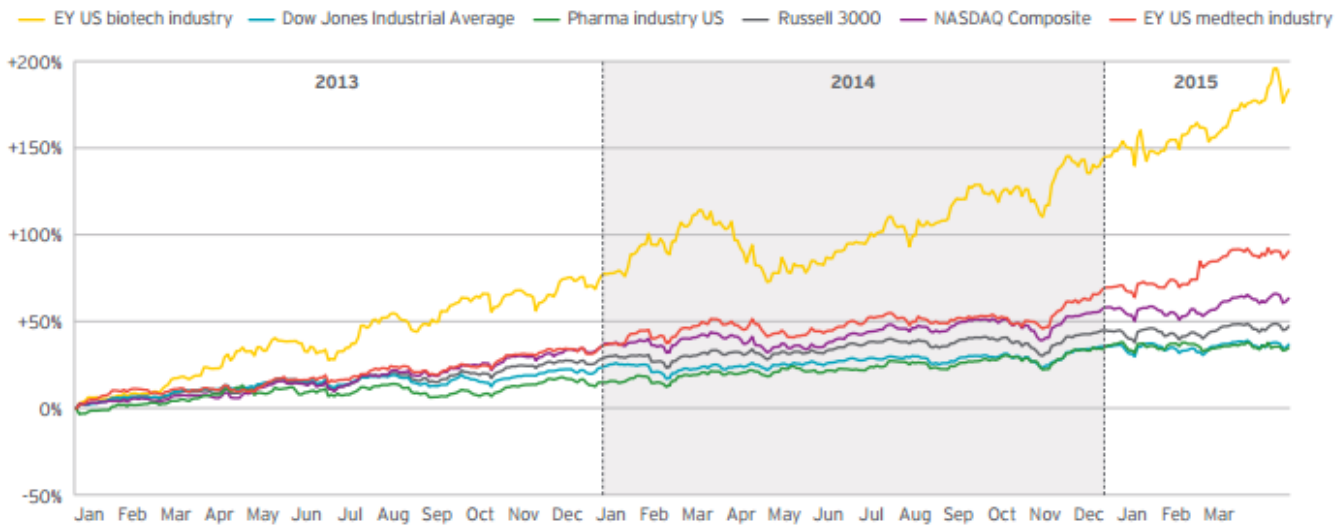


Chart includes companies that were active on 31 March 2015.

Source: EY and Capital IQ.

US market capitalization by company size

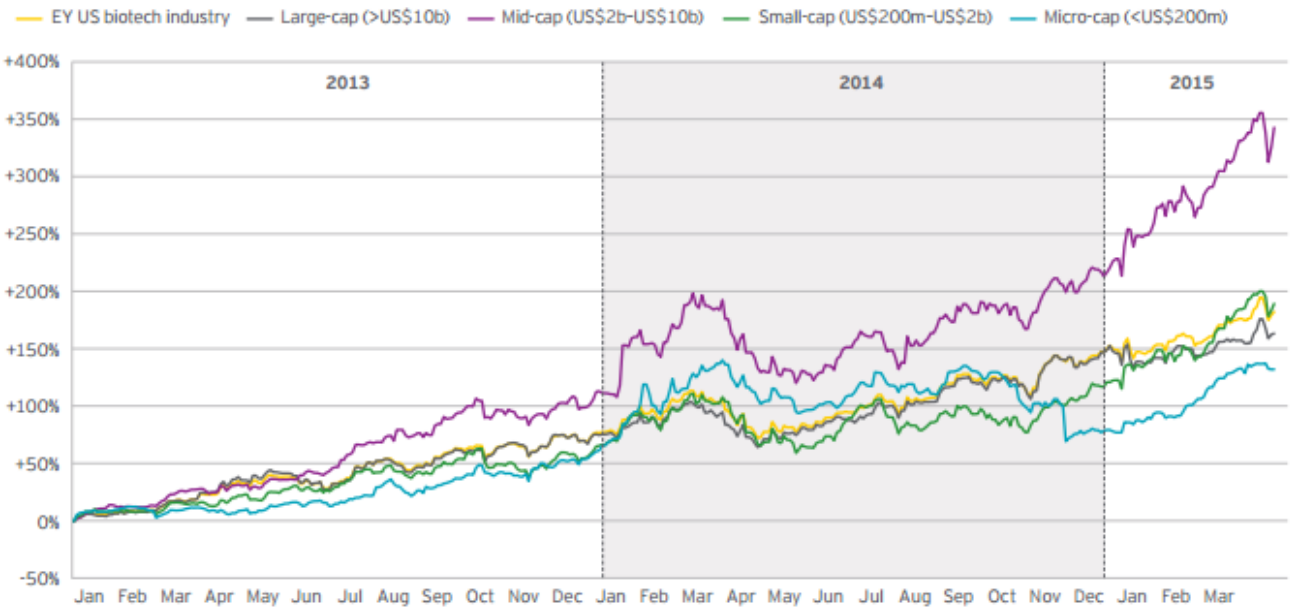


Chart includes companies that were active on 31 March 2015.

Source: EY and Capital IQ.

European market capitalization relative to leading indices

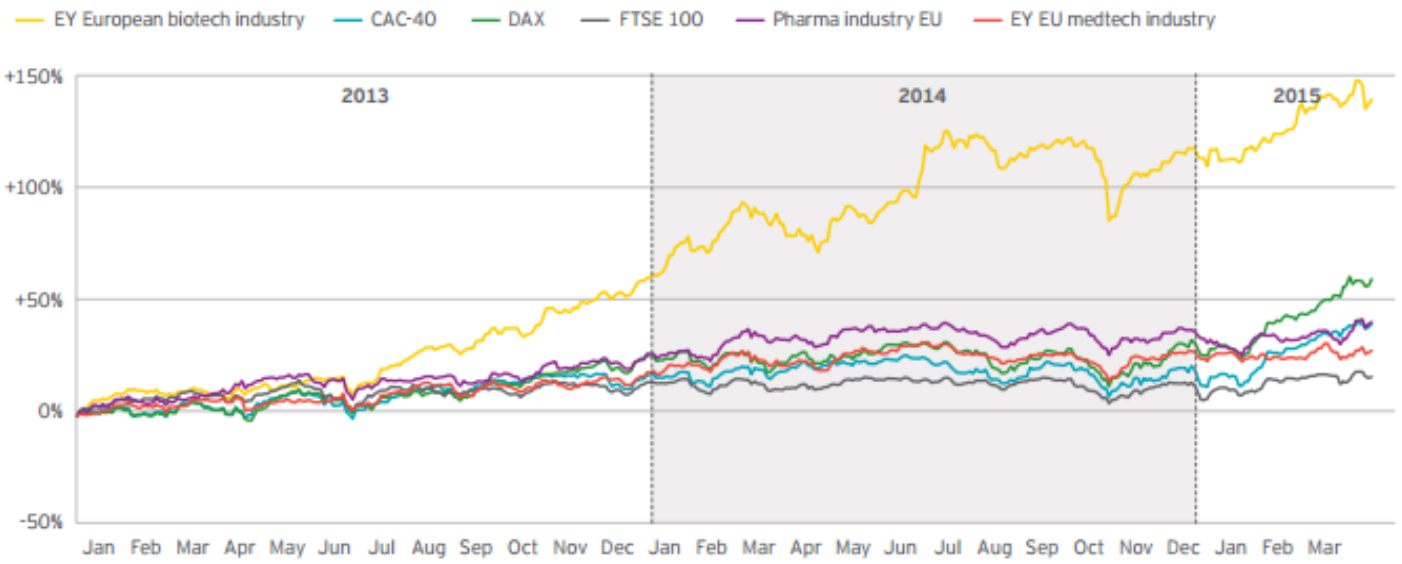


Chart includes companies that were active on 31 March 2015.

Source: EY and Capital IQ.

European market capitalization by company size

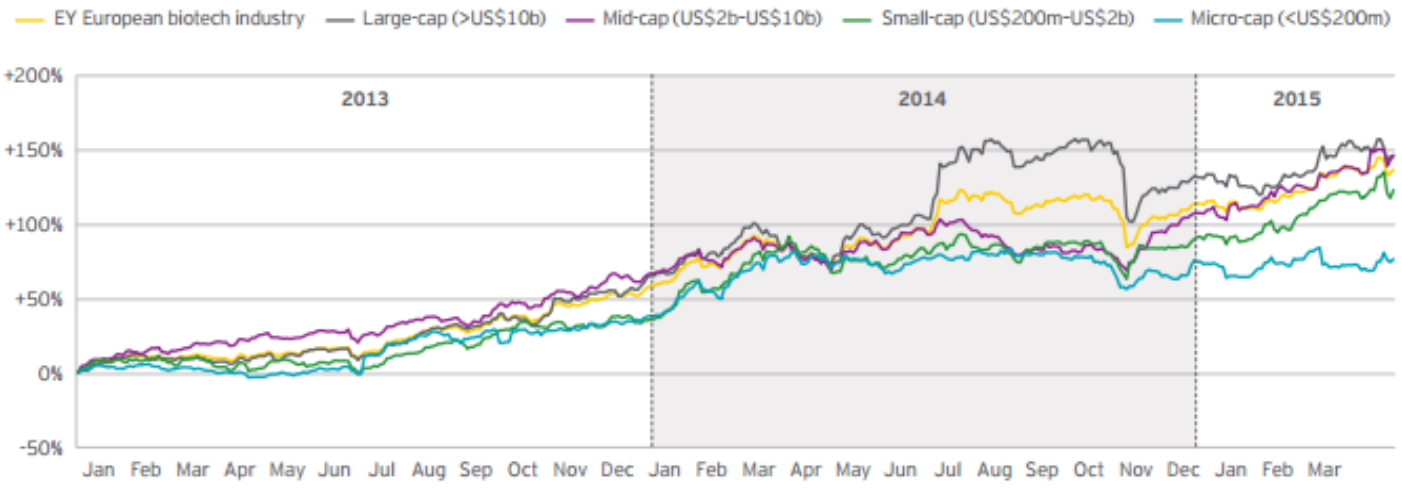


Chart includes companies that were active on 31 March 2015.

Source: EY and Capital IQ.

Investing and Deal Making

The sector is also increasingly appealing to Venture Capital. Recent research by Thomson Reuters shows that one-third of biotech firms go public within five years from initial investment – a higher proportion than for software or other sectors. This represents a significant improvement from a few years ago where the average time to exit extended beyond 8 years, or almost as long as the legal life of a venture capital fund.

E&Y - Beyond-Borders - Unlocking-Value

REGULATORY AND GOVERNMENT

GSK's Asthma Biologic Backed for EU Approval

GlaxoSmithKline's non-inhaled, biologic therapy for a difficult-to-treat form of severe asthma has cleared the last major hurdle before European clearance.

Mepolizumab, which is to be sold under the brand name Nucala, has been recommended for approval by the Medicines and Healthcare products Agency, as an add-on treatment for severe refractory eosinophilic asthma in adult patients.

Pharma Times

Amarin Wins Off-Label Ruling Against FDA

The federal district court in the Southern District of New York has ruled that FDA cannot bar a drug company from marketing a pill for off-label use as long as the claims are truthful. The ruling concerns the Irish company Amarin Pharma and its fish-oil-derived drug icosapent ethyl (Vascepa). The case has been closely watched by the pharmaceutical industry. The ruling means Amarin can give doctors and others truthful accounts of medical studies of the drug for reducing moderately high blood fats even when FDA has not approved it for such use. FDA has contended that such off-label marketing is not lawful, but recent court decisions have held that the First Amendment restricts FDA's power to limit truthful speech.

Wall Street Journal

CMS Plan to Implement Lab Test Pricing Regulation Gets Critical First Response from Industry

The Centers for Medicare & Medicaid Services' preliminary proposal for a massive pricing overhaul for clinical diagnostics to take effect in 2017 has already garnered significant industry criticism.

On September 25, 2015, CMS released a 130-page document laying out its initial plan for how to implement the "Protecting Access to Medicare Act of 2014," which became law in 2014 and seeks to establish a market-based

payment system for diagnostics under the Clinical Laboratory Fee Schedule (CLFS).

Under the law, "applicable laboratories" will report to CMS rates from private payers for each clinical diagnostic lab test and the volumes for each test over a specified period of time. Based on this information, CMS will calculate a weighted median payment amount for each test.

GenomeWeb

Congressional Lawmakers Introduce a Right to Try Bill for Desperate Patients

Yet another legislative effort is under way to expand the ability of terminally ill patients to gain access to experimental medicines. A trio of congressional lawmakers has introduced a bill that would prohibit the federal government, including the FDA, from taking any action to prevent access.

More than a dozen states have already adopted so-called 'Right to Try' laws, which allow patients to leapfrog a drug-development process that takes years before new treatments become available. The laws reflect rising frustration with an FDA program called expanded access, in which people who are seriously ill can obtain a drug under development, even though they aren't enrolled in a clinical trial.

Wall Street Journal

Why the Drug Price Scandal Won't be Enough to Keep Down Prices

A little-known drug called Daraprim captured national attention in September, 2015 when Turing Pharmaceuticals boosted the price of the lifesaving toxoplasmosis treatment by over 5,000%. Overnight, Turing CEO Martin Shkreli became the poster child for bad business in the pharmaceutical industry, skewered for what was seen as price gouging, leaving very ill patients without treatment.

Turing became a tipping point that drew scrutiny from all spheres—patients, doctors, advocates—and made drug makers a prime target of politicians. Presidential candidate Hillary Clinton weighed in with her own proposal to cap drug prices, sending biotech stocks plummeting, and federal authorities targeted Valeant Pharmaceuticals VRX -2.57% with a subpoena demanding more information on its drug pricing strategies.

But despite the uproar, high prescription drug prices in the U.S. are nothing new. The costs of specialty cancer drugs have increased an average of 10% annually since 1995, according to one recent study. Last year alone, brand-name drug prices rose by 14.8%, says

analytics firm Truveris. Price hikes are so routine, in the U.S. in particular, that Credit Suisse CSGKF 0.48% estimates they accounted for 80% of profits last year for the largest drug companies.

Fortune

Allergan Asks SCOTUS to Take a Hard Look at Pharma's Controversial 'Hard Switch' Tactic

New York's Attorney General, Eric Schneiderman's success in his suit against Allergan/Actavis was hailed as a victory by consumer advocates. Many activists and some physicians were riled by Actavis' efforts to promote once-a-day Namenda XR over twice-a-day Namenda IR, especially considering the cost differentials. Also, although Namenda XR appeared to be more convenient, there were issues related to insurance coverage and other factors that made it less convenient for individual patients.

Now, Allergan wants to revisit the issue—with the Supreme Court. On one side, Allergan is defending "innovation" and the need to maximize profits in order to fuel additional ground-breaking R&D. But on the other side, one legal analyst makes the point that reversing the decision could be interpreted as an endorsement of the practice of "product hopping" or "forced switching," which could have adverse effects for patients, the generic drug industry, and competition in general.

This case is certain to be watched closely by the industry and could have broad, sector-wide implications if the Supreme Court decides to take the case.

BioPharma Dive

Congress Reaches Agreement on Budget to Boost NIH Funding by $2B

Congress, late on Tuesday, December 15, 2015, reached an agreement on a tax and spending budget that would give the National Institutes of Health $32 billion in funding in fiscal year 2016, $2 billion more than the agency received the year before and its biggest funding boost in 12 years.

According to government officials, the proposed budget would specifically provide the NIH with $200 million for its planned Precision Medicine Initiative, an ambitious research effort unveiled by President Obama in January that, among other things, seeks to obtaining genome sequence data on more than 1 million Americans and to use that information accelerate the development of personalized medical treatments.

GenomeWeb

The Biggest Winners -And Losers- in the 2015 Race for New Drug Approvals

Let's start with the good news.

In 2015, the FDA by its own account approved 45 new drugs, the largest one-year tally since 1996, which wrapped up with a record 53 regulatory OKs.

The new generational high, easily lapping last year's list of 41 approvals, marks a new peak following a surge by the R&D side of the business, which continues to recover from a lengthy period of marked weakness. The FDA has helped, proving more than willing to come through with faster approvals, particularly in oncology. And the science around drug development has improved markedly as our understanding of the genetic drivers of disease continues to make real progress.

FierceBiotech

HEALTHCARE

Antibiotics: Five Minutes to Midnight

Today, multi-resistant bugs can be found across the globe. Worried governments have set up emergency plans to limit overuse of anti-bacterial medicines in clinics and farms, while the WHO has launched a global action plan that was adopted by G7 leaders in June. Attempts to coax Big Pharma back into the less than lucrative area haven't been very successful so far – but biotech SMEs are rising to the challenge.

Big Pharma deserted the antibiotics market around the turn of the millennium. Since then, bacterial resistance to the around 80 available broad-spectrum antibiotics has only grown. Experts now say that's due to substance overuse and bacterial adaptation. Even though most patients with bacterial infections can still be treated, statistics show that multidrug-resistant (MDR) strains in ICUs and infections with multiresistant microbes are on the rise. Governments all over the world are now trying to coax companies back into the field.

European Biotechnology News

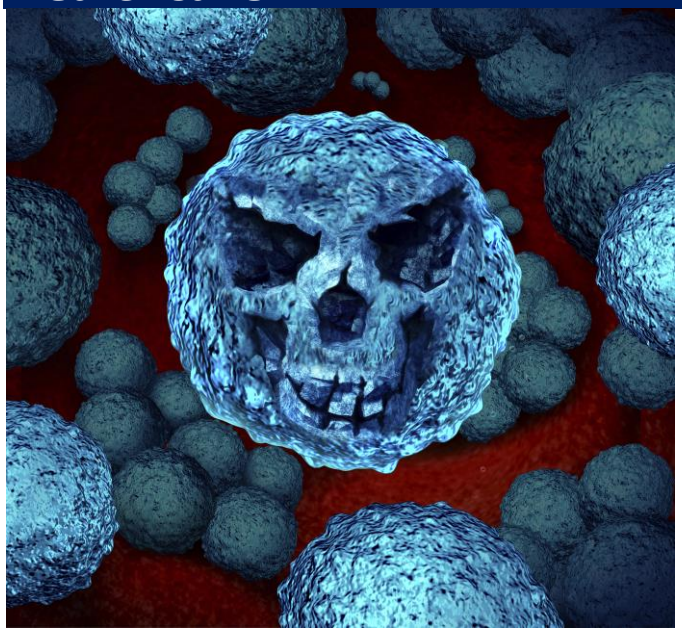
AMA Backs Ban on Direct-to-Consumer Pharma Ads

Spending on drug advertising has risen dramatically in recent years. In 2014, it topped out at $4.54 billion, a 21% increase over 2013. The industry argues patients deserve to be well-informed via print and television advertising.

Now, the AMA says DTC advertising drives patients to request expensive treatments, even when there are other less expensive, equally clinically effective options.

In 2014, AMA's spent $19.7 million lobbying the U.S. government, compared to $16.6 million by PhRMA. Given its financial heft, AMA's push for the elimination of DTC advertisements could realistically impact pharma companies' DTC channels.

BioPharma Dive



Superbug Resistant to Last-Resort Antibiotics Turns Up in UK

Bacteria that resist the most common antibiotic of last resort – colistin – have been discovered in the UK, December 2015. This is following an announcement from Denmark that they had found the same thing, just two weeks after Chinese researchers revealed they had found a similarly resistant strain.

The announcement means the form of the bacteria has spread beyond just one region of the globe. To the surprise of scientists, it has also been circulating in the Scandinavian country for some time. The earliest of the Danish samples showing this resistance gene dates back to 2012. UK doctors thought they had three more years before the colistin-resistant strain would appear in the UK.

Stat News and BBC

Smart Medtech: The Smart Healthcare Environment

Progress in technology, coupled with medical and scientific advances, is expected to significantly change the healthcare environment. Technology companies, healthcare companies, medical device companies, and others are capitalizing on emerging technologies to provide novel healthcare solutions using mHealth, sensors, data analytics, bioinformatics, and advanced software. The result will be a medical environment that takes advantage of "smart" technologies for improved healthcare decision-making and better patient outcomes.

Experts say smart technologies already support individual health monitoring by physicians, but also have the ability to provide data to insurance companies and government agencies on a massive scale.

Pharmavoice

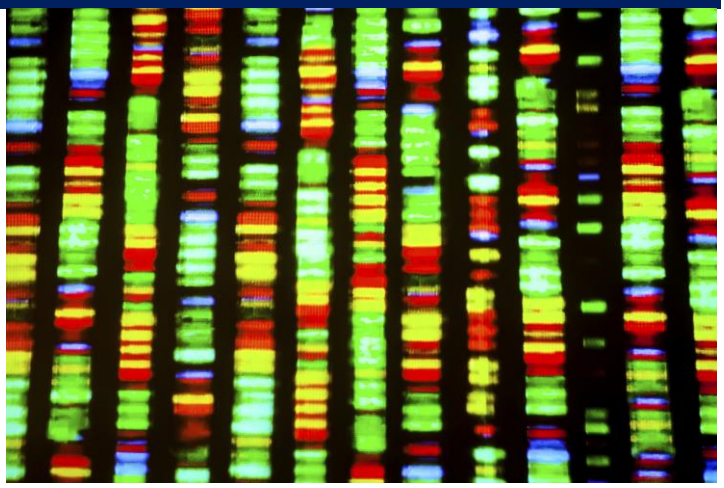
Nation's First Insurance Coverage of Next-Generation Whole Genome Sequencing and Proteomic Diagnostic Platform Announced by Independence Blue Cross and NantHealth in the War Against Cancer

On January 11, 2016 Independence Blue Cross and NantHealth announced the US's first

insurance coverage for a comprehensive whole genome and proteome molecular diagnostic platform (GPS Cancer™) to diagnose molecular alterations in an individual's cancer, and to identify personalized therapeutic regimens. With the announcement, the application of precision medicine in the oncology setting has now emerged from research to the clinical cancer setting – a significant milestone in precision medicine and the war against cancer.

GPS Cancer is a CLIA-certified diagnostic test that combines whole genome sequencing of tumor-normal specimens together with RNA sequencing and quantitative protein analysis to identify the protein pathways active in the individual's cancer. GPS Cancer is the US's first CLIA-certified comprehensive DNA/RNA test with quantitative proteomics to receive reimbursement coverage in the clinical setting. Sequencing the whole DNA of three billion base pairs with over 20,000 genes, as well as RNA to identify those mutated genes which express the proteins from a patient's cancer, provides comprehensive and critical molecular information. Only through this comprehensive test can the physician more accurately identify which of the multitude of molecular alterations that are present in cancer cells translate to abnormal proteins being produced and which are the key targets for many therapeutic interventions. It is anticipated that the commercial launch of the GPS Cancer test will occur by March 2016.

Business Wire



When New Cancer Treatments Fail, Italy Wants Its Money Back

When trying new cancer treatments, Italy's state-run health service is demanding a money-back guarantee. The experiment is being monitored in the U.S. and across Europe, making a country better known for its fashion and fettuccine a leader in innovative strategies to rein in drug spending.

The Italian Medicines Agency has devised deals with pharma companies that set payment based on how well a patient responds to treatment, and in some cases where the medication fails to help, the drugmaker gives a full refund. Italy is signing more such contracts as growing numbers of medications receive regulatory approval after mid-stage trials of fewer than 100 patients rather than awaiting final-stage assessments involving thousands.

Pharmavoice

Regenerative Medicine – Past, Present and Future

– An Introduction by Don Alexander

On February, 15th, 2016, researchers at the Wake Forest Institute for Regenerative Medicine published a paper in Nature Biotechnology entitled "A 3D bioprinting system to produce human-scale tissue constructs with structural integrity." A new method to the challenge of cellular blood flow is articulated in an article in STAT.

While years away from human commercial applications in some cases, the confluence of biology and engineering has enabled exciting breakthroughs that may result in cures for diseases not capable of being treated with small molecules or conventional treatments.

The Regenerative Medicine ecosystem comprised of researchers, pharma, biotech, investors, regulatory agencies, payers and governments have formed non-competitive alliances that will help the field mature at a more rapid rate. More constituent alignment, clinical product success and solutions to larger scale manufacturing issues will further market adoption.

It is with these possibilities in mind that Carlyle Conlan and george james, ltd. are pleased to offer thought provoking views from top global leaders in the field of Regenerative Medicine (RM).

Regenerative Medicine – Past, Present and Future

Dr. Peter C. Johnson
Principal at MedSurgPI and Adjunct Professor at UNC Chapel Hill

Peter C. Johnson, MD, is principal, MedSurgPI, and an adjunct professor of surgery, bioengineering and business at the University of North Carolina at Chapel Hill. He also holds an adjunct professorship at North Carolina State University in bioengineering, and in regenerative medicine at the Wake Forest University School of Medicine. Dr. Johnson graduated from the University of Notre Dame and SUNY Upstate Medical University. After general and plastic surgery training, he practiced reconstructive surgery for 10 years at the University of Pittsburgh, where he founded and was the first president of the Pittsburgh Tissue Engineering Initiative. He went on to serve in business roles; he was the co-founding and CEO of TissueInformatics; executive vice president of life sciences, chief medical officer, and chief business officer of Icoria; executive vice president of Entegrion; and vice president, research and development and medical and scientific affairs, of Vancive Medical Technologies.

Dr. Johnson is the current president of the North Carolina Tissue Engineering and Regenerative Medicine Society (NCTERMS). He has chaired the Plastic Surgery Research Council; was president of both the Pennsylvania Biotechnology Association and the Tissue Engineering Society, International; and is presently the co-editor-in-chief of the three-part journal, Tissue Engineering. He serves on the industry committee of Tissue Engineering and Regenerative Medicine International Society (TERMIS); is a board member of the Transverse Myelitis Association; and is a member of the Industry Advisory Board for the UNC/NC State Joint Program in Biomedical Engineering. Outside of medicine, Dr. Johnson is an avid cook, fly fisherman, artist, and novelist. He took some time recently to speak with Carlyle & Conlan's Don Alexander to share his thoughts about regenerative medicine.

Don: How does one best define regenerative medicine (RM) and has its definition changed over the years?

Peter: RM is the utilization of restorative powers within the body, or components outside of the body, to guide the development of tissues that either develop within or are implanted. As examples, one

can grow skin equivalents, cornea, and bone for implantation, or one can induce the formation of bone within the body using a growth factor and a collagen scaffold.

Don: What areas of RM do you view as having good potential?

Peter: More and more, we are seeing uses of non-hematopoietic (blood forming) stem cells, primarily mesenchymal stem cells (MSCs), which not only differentiate into diverse tissue types but also are being used as immunomodulators to control inflammation. There is a real focus on placing stem cells at various sites in the body where regeneration is desired. Other types of stem cells that are being investigated are capable of growing into additional tissues. These are known as Induced pluripotent stem cells (also called iPS cells or iPSCs). The burning question is how safe are such therapies, and what types of diseases can be effectively treated? There is a great need for additional understanding. Nonetheless, the greatest promise in the field appears to surround these forms of therapy.

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

Peter: Two very different things come to mind. Perhaps the most obvious startling development has been the explosion in our understanding of stem cell biology, especially with regard to the genetic mechanisms underlying tissue differentiation. The second has been the stimulation of advanced bioengineering education and how bioengineering has attracted substantial numbers of women into the regenerative medicine field.

Don: Where do you see the field of RM in 10 years?

Peter: Looking at anatomical prospects from head to toe, companies like Replicel are utilizing stem cells to regrow hair. Hair growth is likely in the near future. Skin equivalents can be made. The other end of the spectrum is organogenesis, whose products release cytokines that optimize wound healing. In that case, one is working with living cells from another donor.

Corneas are being engineered and animal models have proven to be successful. The understanding of brain tissue regeneration via neural stem cells gives us hope that diseases such as Parkinson's disease, where a small volume of cells can be replaced with effect, can be treated. There are other brain diseases being approached but the greatest interest is in spinal cord injury (SCI) where there are attempts to bridge SC defects.

Dental tissue engineering is progressing rapidly. Teeth are now being regrown experimentally, as are oral mucosa, and bone. Bone tissue engineering is one of the most well developed areas in regenerative medicine since one can begin with a firm, avascular scaffold into which cells can grow and remodel the tissue.

The trachea has been bioengineered and implanted clinically. The focus in lung tissue engineering has been on regenerating lung alveolar cells. Almost all organs can be decellularized to the point that one can put normal cells back in. This has been done for lung with experimental success. The clinical utility of lung tissue engineering remains problematic because the lungs are highly vascular, are highly flexible, and must be airtight.

Great attention has been paid to the heart. Engineered heart valves have been successfully constructed and stem cell injections or sheet applications of cardiomyocytes have been shown to strengthen heart function under experimental circumstances. The gastrointestinal (GI) tract regenerates quickly. However, the greatest use of GI tissue has been the use of decellularized small intestinal submucosa (SIS) for repair of ligamentous structures.

The liver has exceptional regenerative capacity. Liver bioreactors have been developed and have been in clinical trials. Kidney tissue has been regenerated in the lab. Long bones, other bone tissue and cartilage have all been engineered. Blood vessels have been engineered and clinical trials of blood vessel extracellular matrices are underway. The idea is to use implanted decellularized vessels that can recruit cells to rebuild a functional structure.

Don: What are the challenges for the field (i.e. manufacturing/scale up)?

Peter: There is always the technical challenge of growing cells at all. An additional challenge is whether autologous cells (one's own) versus allogeneic cells (cells from others) can be used in a regenerative medicine product. Notably, the success of any product will ultimately be dictated by whether it can be approved by the FDA, and be reimbursed. These can be daunting challenges. A whole new field of pharmacoeconomics of RM will be required. This would be a great area of study for students today as the field matures! Lack of awareness of the regulatory process is especially critical amongst students and professors, the earliest generators of these technologies, as has recently been published in Tissue Engineering1.

Don: What about the interplay between the pharma industry and RM, where the industry may find it atypical to cure someone?

Peter: There are some pharma companies that have embraced RM, others that have abandoned it and still others that are considering it. They may be concerned with a "Kodak moment," in which photography, rapidly becoming digital, supplanted film as a product. If RM achieves its promise, you will likely see tissue-based cures emerge that are presently being managed using drugs. Consequently, the pharma industry will likely become more involved as time goes by.

Don: What are your closing thoughts concerning RM?

Peter: Regenerative medicine is a very compelling field and is becoming better organized by the day. Though it will take time before the clinical, technical, industrial, regulatory and reimbursement systems are fully aligned, it seems clear that that day will come, so long as we persist in this effort.

1. Johnson, P, Bertram, T, Hellman, K, Tawil, B, Van Dyke, M, Carty, N, Awareness of the Role of Science in the FDA Regulatory Submission Process: A Survey of the TERMIS-Americas Membership, Tissue Engineering, Part A, 2014, Jun 20(11-12):1565-82.

Regenerative Medicine – Past, Present and Future

Dr. Gail K. Naughton
Chairman and CEO
Histogen, Inc.

Gail K. Naughton, Ph.D., is the chairman and CEO of Histogen, Inc., a regenerative medicine company she founded in 2007. She previously served as dean of the College of Business Administration at San Diego State University from 2002 through 2011, and prior to that, spent more than 15 years at Advanced Tissue Sciences, where she was the company's co-founder and co-inventor of its core technology. During her tenure at Advanced Tissue Sciences, Dr. Naughton held a variety of key management positions, including president, chief operating officer, chief scientific officer, and principal scientist. While serving as an officer and director of the company, Dr. Naughton oversaw the design and development of the world's first up-scaled manufacturing facility for tissue-engineered products. She also established corporate development and marketing partnerships with companies including Smith & Nephew, Ltd., Medtronic, and Inamed Corporation; was pivotal in raising over $350M from the public market and corporate partnerships; and brought four human cell-based products from concept through FDA approval and market launch.

Dr. Naughton holds more than 100 U.S. and foreign patents and has been extensively published in the field of tissue engineering and regenerative medicine. In 2000, she received the 27th annual National Inventor of the Year award by the Intellectual Property Owners Association in honor of her pioneering work in the field of tissue engineering. Dr. Naughton took some time recently to speak with Carlyle & Conlan's Don Alexander to offer her perspectives on regenerative medicine.

Don: How does one best define Regenerative Medicine (RM) and has the definition changed over the years?

Gail: The broad definition is to be able to use either cells or scaffolds, or a combination thereof, to help restore the function and structure of a variety of tissues and organs. In other words, regenerating the organ in vivo. The field really started as two separate fields. In the mid-80s, work in tissue engineering was characterized by growing cells on scaffolds into tissues outside of the body. In parallel, there was work in stem cells alone based on work from Arnold Caplan that, in particular, showed that Mesenchymal Stem Cells from bone marrow can become a variety of tissues in the body. Over the past 10 years, the fields have merged. Some definitions also include the use of different

proteins and cytokines to help induce regeneration, in vivo. So, the definition has become much broader.

Don: What areas of RM do you view as having good potential?

Gail: The ability to have cells regenerate tissues that, right now, have diseases with no cure are the most promising. I was involved early on with skin and tissue re-engineering and we got three products approved at the same time that Organogenesis did. So, we are speaking about the late 1990s to early 2000s when there were good product approvals mostly focused on wound care. Even though products are still on the market, reimbursement has hurt them because there are cheaper alternatives to wound care.

So, we need to find solutions to diseases where there are no good alternatives, such as products that include a focus on genetic diseases, repairing degenerative retinas, curing Parkinson's disease and, ultimately, repairing damaged spinal cords. Basically, to have the body repair vital structures which cannot be treated with small molecules or conventional treatments. This is what will transform the field and prove that this is not science fiction, but fact. The future will be in providing solutions where there are few or no ways of treating patients today.

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

Gail: I expected that there would be far more product approvals on the market by 2015 and 2016. There were some in the late 90s and there has been almost nothing since. A good surprise is what Japan has done recently with their RM law. If, in fact, you can show safety, you don't have to prove efficacy in a clinical trial. In fact, you can have five years on the market before you have to prove efficacy. This is the type of leg up the field needs. Do no harm, but if you have the potential to benefit, get the product out to help people and figure out the rest once you are on the marketplace.

Don: Where do you see the field of RM in 10 years (i.e. 3D printing for solid organs)?

Gail: 3D printing is very valuable as a tool for creating mini organs in the pharmaceutical industry to look at a human effect of drugs in development in ways that animals cannot predict. The big hurdle for 3D printing is that many organs need rapid blood supply after implantation. To print vascular organs that would be functional is the hurdle. Once you get an organ made, the key is how you get it vascularized quickly so that the cells survive for a successful transplant.

Don: Challenges for the field (i.e. manufacturing/scale up)?

Gail: As discussed, early products approved in RM had excellent clinical data but, with cheaper alternatives, reimbursement has twice nearly killed the field. So to focus on aspects like orphan devices or other cures is the lesson. As an example, Dendreon's reimbursement was less than the cost of manufacturing and delivery. Dendreon's subsequent bankruptcy was another hit for the RM field so the key is to have products that address diseases where there is a real quality of life improvement or the product is a cure.

As an example, a company I am associated with, Cytori Therapeutics, is focusing on the use of fat-derived stem cells for the treatment of Scleroderma. Scleroderma is considered an orphan device with nothing that can treat the disease well now. Early results have shown great reversal in debilitating hand constrictions and there is the promise of systemic treatment in the future, also with an orphan focus.

Manufacturing can be a challenge. There are no guidelines for knowing exactly what a cell-based product needs to do outside the body for it to have efficacy inside the body. There are no rules like you have with synthetic molecules or even more traditional biologics like vaccines, where there are clear guidelines on what needs to be shown in terms of product release criteria which correlates well with efficacy. With cell-based material, you don't have this and what the field has seen is that any small change in manufacturing can result in dramatic changes in efficacy. It is not a matter of safety, but a matter of meeting primary and secondary efficacy endpoints. Until we have more predictable bioassays and release criteria for understanding what product attributes the cell-based materials need to have to correlate to efficacy, it is a best guess. In addition, there are regulatory hurdles because the ways that you manufacture and release traditional drugs cannot be applied to living cells. So we are writing the rulebook together along with the regulatory agencies to get a better understanding of requirements.

Don: Interplay between pharma industry and RM (atypical to cure someone)?

Gail: Eight to 10 years ago, Big Pharma said RM is going to be very important and you saw companies starting their own institutes. Most of these do not exist today and Big Pharma did not do much in acquisitions. The model is so different than what they are used to that there are many big question marks. Big Pharma says it sees that RM is important, but they are not investing in it right now.

If Big Pharma leveraged its strengths in non-competitive areas where traditional drugs do not work, this would create a win-win. There are synergies but very different models in terms of manufacturing, regulatory, clinical trials and reimbursement. Most likely, if there is a big home run with an RM

company that becomes large, this may be the first move in Big Pharma getting excited, but I don't see it in the near term. It used to be uncommon for Big Pharma to invest in smaller patient populations but Genzyme changed this years ago, so this is the type of event that needs to occur.

Don: What are your closing thoughts concerning RM?

Gail: In the 1980s, there was no collaboration and, in fact, vast competition between the few groups in the field. We realized that this was not going to get us anywhere and there are groups like the Alliance for Regenerative Medicine (ARM) that have cropped up that are doing tremendous positive change in terms of funding, lobbying for better legislation, and writing white papers for best practices in manufacturing. This will help accelerate the field. The Center for Commercialization of Regenerative Medicine (CCRM) in Canada is positive where other countries may follow suit. The Canadian government has said RM is an important field that we know needs a lot of work but let's figure out how to fund it and get these much needed products to the market. California Institute for Regenerative Medicine (CIRM) is focused on research and paying for clinical studies which is desperately needed. It is tough to raise money with all of the speedbumps and failures.

Regenerative Medicine – Past, Present and Future

Dr. Chris Mason
Advanced Centre for Biochemical Engineering
University College London

Chris Mason, MD, PhD, FRCS is an internationally recognized world leader in cell and gene therapy. A clinician scientist, Dr. Mason was trained at St. Thomas's Hospital London (now part of King's College London), started his research career in gene therapy at St. Mary's Hospital Medical School (Imperial College London), did his PhD in stem cells and tissue engineering at University College London, and has since returned to cell and gene therapy. Today, Dr. Mason is professor of regenerative medicine bioprocessing in the Advanced Centre for Biochemical Engineering, University College London. He is a co-founder and Chief Science Officer at AvroBio, a Boston-based cell and gene therapy company focusing on immuno-oncology and inherited diseases. His areas of expertise include clinical translation, manufacturing, and commercialization of cell and gene therapies.

Dr. Mason sits on a number of national and international committees, working groups, and advisory boards enabling the clinical translation and commercialization of cell and gene therapies including: the UK Ministerial Industry Taskforce on Attracting Advanced Therapy Manufacturing to the UK; the UK-Israel Science Council; the Scientific Advisory Panel of the UK Cell Therapy Catapult, and the Strategic Advisory Board of the Canadian Centre for the Commercialization of Regenerative Medicine. Dr. Mason took some time recently to share his thoughts about regenerative medicine with george james ltd.'s Jayne McLaughlin.

Jayne: How do you define regenerative medicine and has this definition changed over time especially in light of the new dawn for cell and gene therapy?

Chris: The use of the term regenerative medicine has changed significantly over time. The widely used definition that I and Professor Peter Dunnill produced, that "regenerative medicine replaces or regenerates human cell, tissues or organs, to restore or establish normal function" has not changed. The means of replacement or regeneration is independent of any specific technology and includes small molecule drugs, biologics, gene and cell therapies, tissue engineering, biomaterials and medical devices. Unfortunately, the term regenerative medicine was, up until the last few years, used ubiquitously to mean tissue-engineering, and cell and gene therapy, regardless of whether the therapy was regenerative or not. In contrast, cell and gene therapies are platform technologies that can be used to restore of regenerate, however, this is just a small component of their ever-growing repertoire of clinical uses which currently includes immuno-oncology, infectious diseases and single-gene disorders. Cell and gene therapies are powerful approaches to treating a wide range of medical indications, moving from the traditional "pill-a-day" symptom and disease management model, to single treatments with the potential to permanently cure, or at the very least, provide a durable cure lasting many years before a repeat dose is required. The goal is very much to create "once-and-done"

therapies that can treat patients very early in the disease process thus enabling zero, or minimal, reduction in their quality of life.

The power to have durable high-impact responses and cures, whilst welcome by patients and their carers is a challenge for the existing infrastructure, which has evolved to support the pill-a-day for life scenario. The major challenges are regulation and reimbursement. For example, how to cost a once-and-done curative gene therapy that replaces a lifetime of regular drugs, interventions and hospital admissions whilst the patient still suffers with reducing quality of life and increasing burden on carers. What is a cure worth in pure financial terms is a hard question, and one that cell and gene therapy companies, healthcare providers, patients and society are starting to grapple. One thing, however, is certain, there is no simple answer.

Jayne: Where do you see the field of cell and gene therapy in 10 and 20 years?

Chris: With a regulatory pathway that spans well over a decade from initial discovery to regulatory approval before achieving necessary marketing authorization, a 10-year prediction can be be made from a knowledge of what is in clinical trials today. Therefore, provided these trials show today's cohort of cell and gene therapies to be safe and effective, we can expect a number of life-changing once-and-done treatments to be routinely available to patients. These will include immuno-oncology therapies based on the genetic modification of T cells, mono-genetic diseases such as haemophilia, thalassemia, sickle cell and primary immunodeficiences (boy-in-the-bubble diseases), and infectious diseases such as HIV. Twenty years from now, cell and gene therapy will be as big a sector as small molecule drugs, biologics and medical devices and therefore become the fourth and final therapeutic pillar of healthcare. They will not replace the other three pillars, but we will see these different modalities increasingly used in combinations to optimize patient outcomes.

The history of innovation in biotech, in part due to complexity and in part due to the need to comply with regulation to ensure new therapies are safe and effective, is a good predictor of the future. If we look back to monoclonal antibodies following their discovery in the 1970s, it was over decade before the first approved products (e.g. Orthoclone OKT3). It was a further decade before we saw the full power of the technology, initially as a slow stream before becoming a torrent of highly efficacious products, many of which have become billion dollar blockbusters, including Humira, Remacade and Rituxan. For the same underlying reasons, cell and gene therapy will take the same trajectory. The first generation products are now on the market, and whilst making significant improvements to patients' lives are just the tip of a major iceberg. For example, up until now, because of technology limitations, we have only been able to attempt single gene replacement therapy, i.e. leave in the old faulty gene and add a new fully functioning version of that gene that can produce the required protein to affect a cure. Unfortunately, this approach will only work for a limited number of indications. For example, what if the product of the faulty gene is toxic?

Fortunately, a wave of new technologies that edit out faulty genes have just started to appear in the clinic. They work just like cut and paste in a text document but instead of correcting alpha-numeric text, they correct the DNA code. Gene-editing technologies, CRISPR, TALENs and zinc-finger nucleases, all have potential to correct gene defects. The big question is, when should they be

deployed? Adults' bodies are composed of approximately 1013 cells, therefore correcting a faulty gene in every cell that needs it is going to be challenging, hence the current debate over combining the correction of the genetic code and in vitro fertilisation (IVF). The science is not quite yet ready, but undoubtedly will be in the next five to 10 years, judging by the accelerating rate of progress in gene editing. Safety and robustness are paramount, however, overshadowing the science is the important ethical debate over manipulating the DNA of the very early embryo, which could prevent disease in that individual and also remove the faulty genes from the population gene pool, but could have the potential to do a life-time of harm if the unexpected happens and things go badly wrong.

Jayne: What about the interplay with Big Pharma?

Chris: For a long-time the Big Pharmas either stood and watched, or showed no interest in cell and gene therapy. However, today I am pleased to say that just about every Big Pharma is active in the space, either directly with their own teams (for example GSK and Novartis), or via collaborations with cell and gene therapy companies (for example Sanofi/Genzyme and Voyager Therapeutics). The change was undoubtedly due to the spectacular early successes seen using genetically-modified cells including; chimeric antigen receptor T cells (CARTs) in end-stage leukemia (remission rates of 70-80%), and gene therapy to cure fatal boy-in-the-bubble primary immunodeficiencies – some of whom are now living normal lives 15 years after their once-and-done treatment. These results are all the more remarkable in that the successes have been reproduced by many teams all over the world.

The bottom line is, gene and cell therapies now work – the results speak very loudly for themselves. Big Pharmas could therefore no longer be mere spectators and so risk repeating the same error they made with biologics, and thus miss out again on a step-change technology. Does cell and gene therapy fit their business model? The answer is absolutely not. It is going to be a steep learning curve, but for a growing number of Big Pharma there is no doubt about their commitment to cell and gene therapy or in a number of cases, just gene therapy. In the long-term I predict it will all be just 'gene therapy' since cells are now only used as a delivery vehicle until we can more precisely control and target gene therapy to where we want it to go in the body.

Jayne: What are the challenges?

Chris: Like any disruptive technology, the incumbent's supporting infrastructure will not be appropriate. For example, water troughs and oats were not the fuel for the horseless carriage. There are therefore a number of key areas that need to be progressed to enable cell and gene therapy to become the fourth therapeutic pillar of healthcare, including manufacturing, regulation, reimbursement and public perception, and support.

Robust, cost effective, and scalable manufacturing is essential for the ultimate success of any technology. For cell and gene therapy this will span centralized bioprocessing for bulk allogeneic (universal) cell therapies at one end of the spectrum, and distributed (or point-of-care) single-patient bioreactors for autologous (patient-specific cell therapies) at the other end. Current manufacturing technologies for biologics (monoclonal antibodies and recombinant proteins) offer some help, but overall, we are far from having workable solutions.

The traditional regulatory process was designed for small molecule drugs and adapted to accommodate biologics. However, it is no longer fit for purpose with respect for once-and-done cell and gene therapies with their ability to transform patients lives and even cure. The old three phase clinical trial is now slowly being replaced in our sector by first-in-patient-studies, which if they show safety and significant impact, are allowed by many regulators (including in the EU, USA and Japan) to move into a pivotal study. Since the outcomes are often binary, rather than incremental changes, the numbers of patients needing to be treated in a clinical trial in order to demonstrate efficacy is much smaller than for conventional drugs. Hence studies can be completed faster and at lower cost – good news for patients, as well as for the cell and gene therapy companies developing the technologies.

There is a downside for the companies with respect to reimbursement. Usually a Phase 3 study involving many hundreds, or even thousands, of patients takes many years. This enables the necessary health technology assessment to be carried out in parallel, which helps influence the reimbursement level. The challenge is further compounded for once-and-done therapies in that how do you know if you have definitely cured a patient without waiting a lifetime? Reimbursement is going to be a major discussion point for many years, especially given the current high cost-of-goods coupled to the single curative treatments of a pill-a-day for life, and hence, a lifetime of payments to the the Big Pharma companies amounting in total to significant sums of money, but spread over many years. Whilst it is clear what patients want, it is not clear how these advanced therapies are to be reimbursed. Fortunately, in the UK the National Institute for Health and Care Excellence (NICE) has already been commissioned by government to undertake a mock appraisal based on CD19 CART cells for leukemia. The aim is to check the appropriateness of current NICE appraisal methodologies for cell and gene therapy and thus identifying potential areas for improvement. The objective is to be fully transparent to enable cell and gene therapy developers to understand how NICE evaluates both clinical efficacy and cost effectiveness.

Finally, I would like to mention the highly important dialogue with the public and their expectations, and the ongoing debate on the ethics of cell and gene therapy. Gene editing is currently of particular importance, especially with respect to gene editing in the very early stage embryo. If we look back at the prior debates on IVF and on embryonic stem cell research, the latter of which I was very engaged with, it was the informed dialogue with all the stakeholders and responsible media interaction that enabled the building of public trust and support. A similar debate has now begun around a number of topics directly related to the enormous breadth and depth of opportunities for cell and gene therapies. Take, for example, enhancement or performance therapies. There is no denying we can and we will have such capabilities in the very near future. A number of sports medicine experts have suggested that the London Olympics was probably the last Olympics where we could be reasonably certain that the athletes were free of gene therapy enhancement. With the accelerating pace of gene therapy, especially gene editing, the potential for enhancing therapies by Rio de Janeiro in 2016 is a possibility, by Tokyo in 2020 will be a certainty.

Companies will undoubtedly pick therapeutic areas where they can deliver a new therapy in a cost effective manner in a reasonably short period of time, this is especially true for venture capital-funded companies with their five to seven year timelines. In picking off the easy winners, we need to be careful that we do not arrive at a stage where we can enable fully functioning healthy bodies, but not

minds, because the exceptionally challenging issue of dementia and other serious neurological diseases are still rife. This is an unacceptable position in which to arrive and potentially avoidable, but this requires government intervention to help underpin the essential research which is going to need sustained high-levels of funding over decades as well and incentivise company participation. President Obama's $100M BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative is therefore a welcome step in the right direction.

In my lectures to students I always give the analogy of Henry Ford in the 1920s hiring a team to go around the U.S. scrapyards inspecting discarded Ford cars. He was not looking to see what had failed, but rather, at what had not failed, and was therefore over-engineered and could be made in the future at lower cost. Ford wanted his cars to work just like new until the point where everything failed all at once. Surely that is what we want for our own lives?

Jayne: What are your final thoughts?

Chris: Cell and gene therapy, and especially gene editing, will revolutionize both healthcare and the evolution of man and the living environment over the coming decades. The tools are evolving rapidly, their costs are falling, and more researchers can easily use them. Even with the current technologies, the possibilities are endless. However, more step-change gene editing technologies will undoubtedly be discovered. The journey to gene edit embryos has already started in China, and whilst only a few years ago editing one gene was a major challenge, today researchers can quickly manipulate many tens of genes at a time. Just as the information technology (IT) revolution took off exponentially in the late 1990s and has rocketed away ever since, we will look back on the 2010s as the period that the DNA revolution likewise took off exponentially and rocketed away. So where are we heading? Hopefully to a situation where cell therapy, but much more likely gene therapy, will have a major impact on global healthcare equality.

This future is already with us. For example, stem cell therapies to successfully cure blindness in the UK cost ten of thousands of pounds, the same therapy in India, with the same high-level of cure (approximately 80%), using local labor and a lower-cost method of manufacture at a few hundred dollars have already successfully treated thousands of patients. Technology platforms always increase in performance and utility, whilst their cost of goods inevitably falls by orders of magnitude, hence my optimism for the global future of cell and gene therapy.

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