Life Science Trends 2017

Value Based Medicine

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About Life Science Trends 2017

Each year, Arris Partners, 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 2017 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 2017 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, big data and Regenerative Medicine are expected to continue as a trend well into the foreseeable future, as is this year's topic; Value Based 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 Arris Partners

Arris Partners, 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 Arris Partners can be found at: www.arris.partners

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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

Ancient Gene Combats Cancer

One would expect that large and long-lived animals – such as elephants – would be more susceptible to cancer due to the fact that their cells need to divide many more times, paving the way for possible mutations. But it turns out that's not the case. According to zoo necropsy records of elephants, less than 5 percent die from cancer, whereas in humans the estimates range up to 25 percent.

Burrus

How Your Supplements Interact With Prescription Drugs
St. John's Wort, lavender, garlic and others can alter drug potency, cause side effects

As millions of Americans consume over-the-counter herbal and botanical supplements in a bid to boost health, there is increasing evidence that these products can interfere with a wide range of prescription medications used to treat everything from cancer to depression to high blood pressure.

Recent studies have found that a greater number of supplements than previously thought may affect the way certain enzymes in the body metabolize drugs. Some supplements may inhibit the enzymes' ability to break down a drug and clear it from the body, causing medication to build up to potentially toxic levels and even cause overdose. Other supplements may increase the rate at which a drug is broken down, clearing it from the body too quickly to be effective.

Botanicals, for example, can interfere with drug-metabolizing enzymes in the liver, stomach and intestines and proteins in the blood that can alter the way drugs are distributed throughout the body.

Wall Street Journal

Interview – Aprea takes aim at new cancer target

A $51m fundraising is an impressive feat for a European company yet to go into phase II trials. But Aprea's lead product, a small molecule p53 modulator, has the potential to treat half of all cancer cases, the Swedish group believes – making the gamble more understandable.

"p53 is by far the most mutated gene in human cancers," Aprea's executive chair Bernd

Seizinger tells EP Vantage. "About 50% of all human cancers have p53 mutations." These mutations inactivate the p53 pathway, which has a role in killing damaged cells – defective p53 allows abnormal cells to grow, leading to cancer.

The idea is that APR-246 could restore this pathway by fixing the mutant p53 protein's conformation and "reactivating all its tumor suppressor function", explains Dr Seizinger.
Identifying those with the mutation in question should be relatively simple with the advent of cheap gene sequencing, he adds.

Evaluate Group

The Pill Robot Is Coming

"The idea that you could repair a human body by swallowing something, instead of making cuts, is amazing," says innovator Daniela Rus.

Form and function
Squeezed into a pill, this robot unfolds like an origami after it's swallowed. It can be guided with a tiny magnet to remove a foreign object from the stomach or treat a wound by administering medication.

Origin
Last summer, Rus and her colleagues began working to adapt an earlier foldable robot for medical use.

Insertion
Rus's team places the accordion-shaped robot into an inch-long, 0.09-ounce pill, which dissolves in the stomach in a minute or two. The robot then expands to 1.4 in. by 0.7 in. by 0.3 in.

Bloomberg

Multiple Virus Vaccine

As we all know, treating viruses is difficult because the same strain can mutate, making last year's vaccines ineffective. And because different viruses are vastly dissimilar, creating a vaccine that combats multiple diseases seems like an impossible task. But a group of researchers has come up with a macromolecule that has the potential to treat several viruses by focusing not on what makes them different but what they have in common.

Multiple Virus Vaccine

'Silicon Valley arrogance'? Google misfires as it strives to turn Star Trek fiction into reality

MOUNTAIN VIEW, Calif. — Google employees, squeezed onto metal risers and standing in the back of a meeting room, erupted in cheers as

newly arrived executive Andrew Conrad announced they would try to turn science fiction into reality: The tech giant had formed a biotech venture to create a futuristic device like Star Trek's iconic "Tricorder" diagnostic wizard — and use it to cure cancer. Conrad, recalled an employee who was present, displayed images on the room's big screens showing nanoparticles tracking down cancer cells in the bloodstream and flashing signals to a Fitbit-style wristband. He promised a working prototype of the cancer early-detection device within six months.

That was three years ago. Recently departed employees said the prototype didn't work as hoped, and the Tricorder project is floundering.

STAT

Digital DNA

In recent years, advancements in storage technology seem to have slowed down, making some experts wonder if Moore's Law has reached its limits with regard to data storage density. But if we've learned anything in this age of accelerated change, it should be that technology will find a way, and the new solutions may be very different than traditional ones. So it appears that storage media of the future will not rely on disks, drives or chips, but on customized strands of organic material.

Microsoft has already begun testing the use of synthetic DNA (also known as long oligonucleotides) as a long term, high density, no-power data storage solution. Why DNA?

DNA strands can remain intact and readable for literally thousands of years. It's estimated that a single cubic millimeter can store one exabyte (that's one million gigabytes) of data. It's also reliable and repeatable; in initial testing, 100 percent of the data encoded could be retrieved. The technology is based on etching methods similar to those used in computer chip manufacturing. The next step is to scale up production through automation, but Microsoft is betting that won't be a problem, since they've already bought 10 million strands.

Burrus

The newest cancer therapies don't work on everyone. Now, doctors have a clue why.

For cancer patients, the promise of new immune-modulating drugs like the one that apparently helped former President Jimmy

Carter comes with a sobering downside: very few get any benefit from them.

But if a new study published on Thursday is right, physicians might be able to figure out which patients those are, sparing others an expensive but useless treatment. The research also offers clues for how to make a promising but unproven treatment, personalized cancer vaccines, more likely to succeed.

The key to both — identifying patients likely to respond to the new immunotherapy drugs and producing tumor-attacking, individualized vaccines — lies in deciphering the crazy quilt of mutations a particular patient has.

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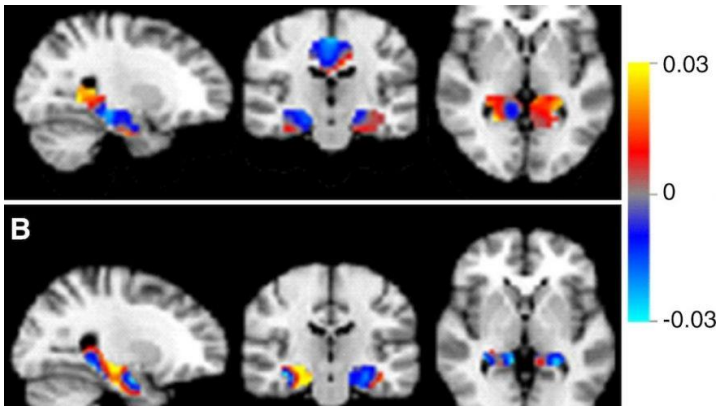
STAT

Artificial intelligence could help catch Alzheimer's early



The devastating neurodegenerative condition Alzheimer's disease is incurable, but with early detection, patients can seek treatments to slow the disease's progression, before some major symptoms appear. Now, by applying artificial intelligence algorithms to MRI brain scans, researchers have developed a way to automatically distinguish between patients with Alzheimer's and two early forms of dementia that can be precursors to the memory-robbing disease.

The researchers, from the VU University Medical Center in Amsterdam, suggest the approach could eventually allow automated screening and assisted diagnosis of various forms of dementia, particularly in centers that lack experienced neuroradiologists.

Fox News

Autism Spectrum Disorder Risk Genes Predicted Using Machine-Learning Approach

Researchers at Princeton University have uncovered hundreds of candidate autism spectrum disorder risk genes, many of which are involved in similar biological pathways and are active during particular brain development stages.

Princeton's Olga Troyanskaya and her team developed a machine-learning approach that relies on a brain-specific functional interaction network to predict risk genes for autism spectrum disorder (ASD), which they described today in Nature Neuroscience. The researchers then linked many of these predicted candidate risk genes to certain functions.

GenomeWeb

Google Tries to Spot Eye Conditions With Artificial Intelligence

Google and the U.K.'s government health service have partnered to study whether computers can be trained to spot degenerative eye problems early enough to prevent blindness.

Google DeepMind, the London-based artificial intelligence unit owned by Alphabet Inc., announced a research partnership today with the National Health Service to gain access to a million anonymous eye scans. DeepMind will use the data to train its computers to identify eye defects. The aim is to give doctors a digital tool that can read an eye-scan test and recognize problems faster.

Earlier detection of eye disorders related to diabetes and age-related macular degeneration could allow doctors to prevent loss of vision in many people, according to a statement by DeepMind Tuesday announcing the project with the Moorfields Eye Hospital NHS Foundation Trust.

Bloomberg

DOCTOR READY TO PERFORM FIRST HUMAN HEAD TRANSPLANT

One fall day in 1974, when he was 9, Sergio Canavero visited his regular newsstand on a bustling street in Turin, Italy, to buy a comic book.

As a bullied schoolboy, the man who now claims he can complete the first human head transplant was dismally aware of his pitiable social status—"cookie-cutter nerd"—and sought fictional escape. His attachment to Spider-Man's Peter Parker, another dweeb, lured him deep into the comic book world of Marvel, with its dose of futuristic medicine. That fateful day, he bought Issue 51 of *Marvel Team-Up*, in which Dr. Strange boasts to Spider-Man and Iron Man, "I myself have surgically rejoined severed neurolinkages…. The nerve endings have been fused, the healing process begun." This marked Canavero's first encounter with the idea of spinal cord fusion. And he wanted more.

Three years ago, Canavero, now 51, had his own Dr. Strange moment when he announced he'd be able to do a human head transplant in a two-part procedure he dubs HEAVEN (head anastomosis venture) and Gemini (the

subsequent spinal cord fusion). Valery Spiridonov, a 31-year-old Russian program manager in the software development field, soon emerged from the internet ether to volunteer his noggin. He suffers from Werdnig-Hoffman disease, a muscle-wasting disorder, and is desperate. Canavero likens Spiridonov's willingness to venture into a new medical frontier to cosmonaut Yuri Gagarin's bold resolution to become the first human to travel to space, back in 1961.

Newsweek

Hacking life: Scientists 'recode' DNA in step toward lab-made organisms

Millions of years of evolution gave life on earth a genetic dictionary with 64 words. Harvard University scientists thought they could do better. In an intriguing step toward lab-made organisms, they reported that they created a complete bacterial genome with only 57 of those words — and freed up the deleted seven to have completely new meanings that, one day, could include new biological functions.

At first glance the advance seems abstruse, promising anodyne applications such as making genetically modified bacteria that resist viral infection. (Those infections are problematic for industries that use bacteria to synthesize chemicals and drugs, costing them billions of dollars a year.) But the experiment, published in Science, is also a significant step toward a much grander project: recoding life.

STAT

Paralyzed Monkeys Able to Walk Again With Brain Implant. Human Trials Are Next

Electrodes implanted in the brain and spine have helped paralyzed monkeys walk. The neurologists behind the study reported that the implants restored function in the primates' legs almost instantaneously. The findings are detailed in Nature.

The spinal cord of the subject monkey was partially cut, so the legs had no way of communicating with the brain. To mend the brain-spine interface, electrodes were placed on key parts of the monkey's body. Implants were placed inside the monkey's brain at the part that controls leg movement, together with a wireless transmitter sitting outside the skull. Electrodes were also placed along the spinal cord, below the injury.

Futurism

Summary of EY – Beyond Borders: Biotech Financing

The 2016 Ernst & Young report reflects on the unprecedented financing of 2015 during which time biotech companies have been able to take advantage of the free-flowing capital over 2015 and 2014 to fill (or refill) their coffers.

While the InVentiv Health Consulting report referenced indication of a slowdown in financing in 2016 and beyond, E&Y point to the fact that Biotech is an industry known for cycling between booms and busts. It is therefore not unreasonable that following a period of boom in 2014 and 2015 that a "bust" of some description is due. The key question is not whether the market changed but "how long will this change last for and we see the next cyclical boom"?

The recent turn around in biotech markets is due in part to the retreat of generalist investors that had helped fuel the previous run-up. It's also a reminder that investors' interest in biotech companies can be affected by macroeconomic factors that may spark
worry about, or stimulate interest in, the sector regardless of its fundamentals.
The biotech and broader health care markets do not exist in a vacuum.

E&Y provide substantial evidence for the slowdown taking the US data as a proxy for the global market. For example, in 2015 the US represented 86% of all biotech financing.

The good news is that Biotech's financial reservoirs are full and more importantly the drivers of biotech's overall success remain intact. They include a favorable regulatory environment, public policy tailwinds (such as support for biopharma-friendly Act and development incentives like priority review vouchers), exploring scientific opportunities in the key therapeutic areas such as immuno-oncology, and big pharma's unquenchable desire to acquire innovation. Overall, the vast majority of this capital was raised by development-stage biotech's, many of which are developing cutting-edge science in areas such as gene and cell therapy. Thus, despite signals the bull market was losing steam investors were still willing to back commercially unproven technologies.

Whereas big Pharma was once the main acquirer of younger Biotech established Biotech's now have the balance sheets to also compete for these assets

Whilst public markets are showing lesser appetite for the sector, venture activity looks to remain high, well above the 15 year average of $5.6 billion, again the bulk circa 80% being US based. Reasons for believing VC interest will continue at recent historically high levels include the extraordinary scientific progress underpinning much of the ongoing company creation, see for example, enabling tools like CRISPR in gene editing and new insights into immuno-oncology.

The recent renaissance also has its roots in the extended downturn of 2008-2012 which fueled a burst of business models and financing creativity from existing biotech VC's, including asset-centric and tax-efficient LLC umbrella

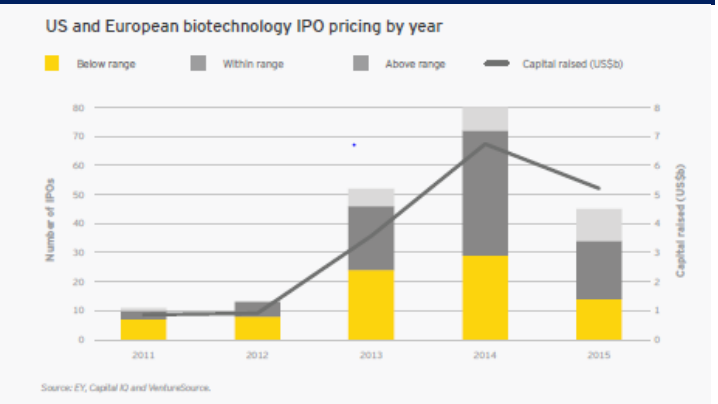
structures. It also expanded and cemented the importance of corporate venture capital as a permanent fixture in biotech financing, whether strategic's invested directly or acted as limited partners in traditional venture funds.

In addition, as a result of recent strong IPO and M&A climates, venture investors have enjoyed atypical successes and importantly, liquidity. This has helped to pull other non-traditional VC investors into biotech deals.

In summary, the E&Y report concludes that however long the current lull in public-market biotech financing the industry is better equipped for the biotech winter than during past downturns in biotech's funding cycle.
The report moves on to provide data on variety of key financing insights, a few of which are highlighted below:

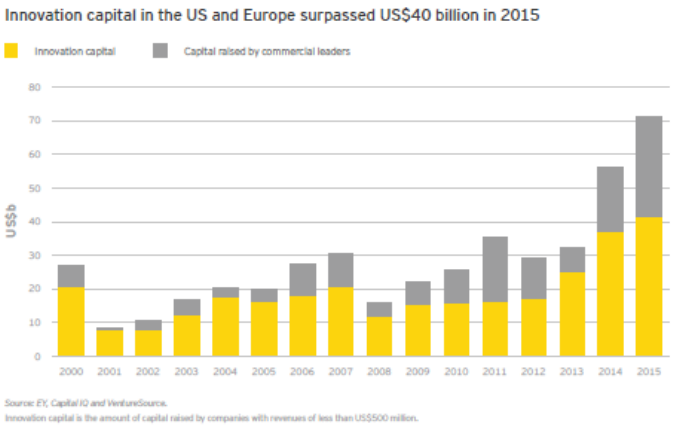
The slowdown in the long-running biotech IPO boom;

Although down on 2014's 95 biotech's going public, a record year, 2015 was still strong with 78 biotech's going public. This matched 2000 as the second best year and compared favorably to the 15 year average of 34. However, the last quarter of 2015 pointed to the beginning of the end of the long-running biotech IPO boom.



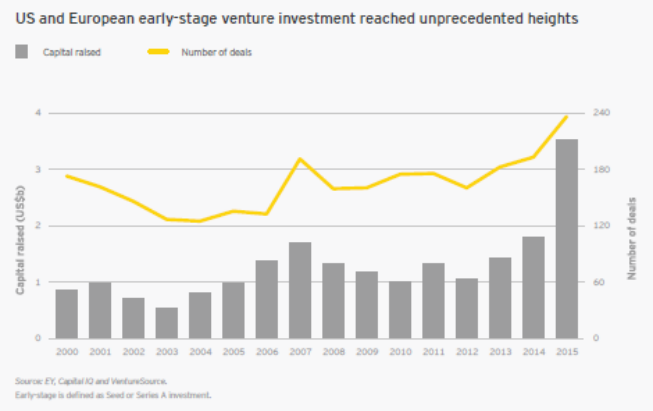
The strong a balance sheets of companies with revenues below $500 million;

Innovation capital — cash raised by companies with revenues of less than $500 million in the US and Europe combined to reach its highest ever total in 2015, eclipsing $41.3 billion. This dwarfs the 15 year average of $17.4 billion) The total included all venture, IPO and nearly all follow-on deals for the year, as well as a smattering of smaller debt offerings. Large debt offerings by Gilead, Celgene, Amgen and Biogen comprised the vast majority of the $29.7 billion raised by the sector's commercial leaders, making innovation capital's share of total financing only 58% for the year.



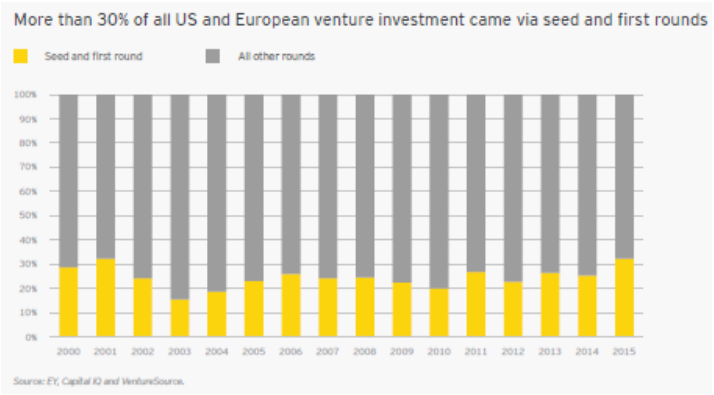
Biotech's in the US and Europe raised $3.5 billion in 235 seed and Series A financing, setting records for both dollars raised and deal volume. Boston Pharmaceuticals raised the largest-ever biotech seed investment, $600 million, from Gurnet Point Capital Gurnet is not an ordinary VC, and Boston Pharma isn't an ordinary biotech. The company is pursuing an alternative search-and-develop model more typical of specialty pharma to bring in early-stage clinical assets and shepherd them through to Phase III.

In Europe, the immuno-oncology start-up Immunocore raised $313 million Series A and earned a valuation of $1 billion in Europe's largest-ever venture round.



The burst of early-stage funding meant the proportion of venture funds going to early-stage biotech companies was greater than any year this millennium, topping 30% for the first time since 2001, with the 15 year average being 24%. This reflects the massive first rounds raised by Denali Therapeutics $217 million, Boston Pharmaceuticals $600 million and Gritstone Oncology $102 million.

In Europe, the early-stage share of venture financing was an incredible 41%, driven by Immunocore's $313 million Series A and $119 million Series A for Mereo BioPharma Group.



Gene-Therapy Cure Has Money-Back Guarantee

The most expensive drugs in history, or medicine's biggest bargains? Gene therapy could be both.

A gene therapy will be offered for sale in Europe with a money-back guarantee, according to GlaxoSmithKline, the company commercializing it.

The treatment, called Strimvelis, is the first outright cure for a rare disorder to emerge from gene therapy, and its price tag of 594,000 euros ($665,000), announced in early August, 2016, makes it one of the most expensive one-time treatments ever sold by a drug firm.

Now, we've learned, it's also the first genetic fix to come with a warranty.

Technology Review

Humans can only live so long, and we're nearing the limit, researchers say

Humans have squeezed almost as much they can out of their natural lifespans and are approaching the biological limit of how long they can extend their years.

So suggests a paper published in Nature that argues that the human lifespan appears to be fixed. By analyzing demographic data, the authors write that the number of years any one human can live has a natural cap and is restricted by all the biological time bombs that can take us down.

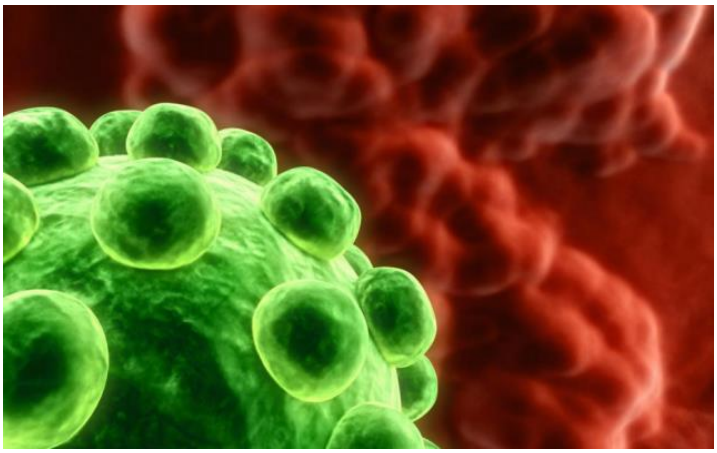
Even if scientists are able to slow some aspects of aging, they say, there are plenty more that can kill us.

STAT

Harnessing the Immune System to Fight Cancer

New drugs and methods of altering a patient's own immune cells are helping some cancer patients but not all – even when standard treatments fail.

Steve Cara expected to sail through the routine medical tests required to increase his life insurance in October 2014. But the results were devastating. He had lung cancer, at age 53. It had begun to spread, and doctors told him it was inoperable.



A few years ago, they would have suggested chemotherapy. Instead, his oncologist, Dr. Matthew D. Hellmann of Memorial Sloan Kettering Cancer Center in New York, recommended an experimental treatment: immunotherapy. Rather than attacking the cancer directly, as chemo does, immunotherapy tries to rally the patient's own immune system to fight the disease.

New York Times

As aging blockbusters come off patent, new opportunities emerge for biosim manufacturers

In a new report, IMS Health predicts biosimilars will play an increasingly important role in the global biologics market as major drugs lose patent exclusivity and new biosimilar versions come online. This could result in cost savings of up to $110 billion in EU and US markets through 2020.

While focusing on the cost implications, the report estimates there are nearly 50 distinct biosimilars currently in development which

could enter the market over the next five years. This will not only ramp up the competition among biosimilar drug makers but will also create new opportunities for drug manufacturing across markets.

BioPharma Dive

The World's Most Expensive Medicine Is a Bust

The most expensive drug in history is a money loser that's not reaching patients. In fact, it's only been paid for and used commercially once since being approved in 2012.

The medication in question is alipogene tiparvovec, better known as Glybera, a medicine widely heralded as the "first gene therapy" in the Western world and whose approval helped ignite an explosion of investment and excitement around treatments that correct DNA.

Technology Review

The 7 biggest problems facing science, according to 270 scientists

"Science, I had come to learn, is as political, competitive, and fierce a career as you can find, full of the temptation to find easy paths." — Paul Kalanithi, neurosurgeon and writer (1977–2015)

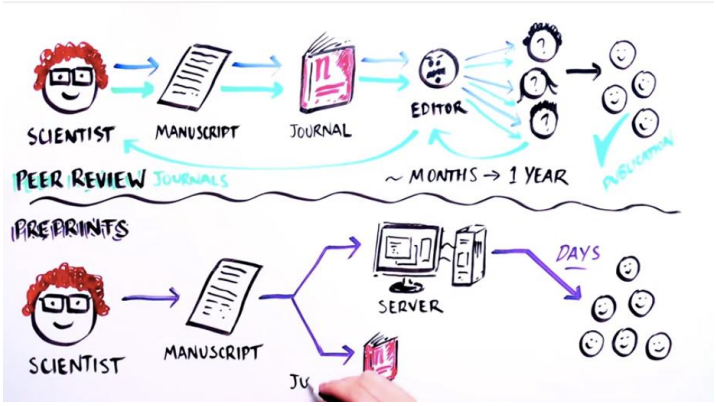
Science is in big trouble. Or so we're told.
In the past several years, many scientists have become afflicted with a serious case of doubt — doubt in the very institution of science.

As reporters covering medicine, psychology, climate change, and other areas of research, we wanted to understand this epidemic of doubt. So we sent scientists a survey asking this simple question: If you could change one thing about how science works today, what would it be and why?

Vox

Handful of Biologists Went Rogue and Published Directly to Internet

On Feb. 29, 2016 Carol Greider of Johns Hopkins University became the third Nobel Prize laureate biologist in a month to do something long considered taboo among biomedical researchers: She posted a report of her recent discoveries to a publicly accessible website, bioRxiv, before submitting it to a scholarly journal to review for "official" publication.



It was a small act of information age defiance, and perhaps also a bit of a throwback, somewhat analogous to Stephen King's 2000 self-publishing an e-book or Radiohead's 2007 release of a download-only record without a

label. To commemorate it, she tweeted the website's confirmation under the hashtag #ASAP bio, a newly coined rallying cry of a cadre of biologists who say they want to speed science by making a key change in the way it is published.

New York Times

Should Heritable Gene Editing Be Used on Humans?

The development of technology that allows human genes to be edited has stirred tremendous excitement about the potential for treating debilitating and life-threatening diseases. The technology could lead to drugs that would treat cancers and other diseases that currently are incurable.

But another facet of this breakthrough has many scientists and others worried: the possibility that the genetic makeup of sperm and eggs could be edited so that diseases that can be inherited won't be passed on to children yet to be born. One concern is that gene editing that affects future generations, not just an individual, is too risky given our still incomplete understanding of the human genome and how changes might affect it. Another is that the ability to edit heritable traits could result in so-called designer babies, with parents choosing traits such as intelligence or physical characteristics.

Wall Street Journal

The Drug-Making Process Is Slow and Wasteful—This Machine Could Fix That

A portable assembly line for medicines offers a better way to respond to outbreaks and shortages.

The way drugs are made is dangerously outdated. While many industries have gotten much more efficient at manufacturing, pharmaceutical companies rely on an old-fashioned approach that is slow, inflexible, and prone to breakdowns. A new refrigerator-sized apparatus that can take in a set of ingredients and quickly produce four common pharmaceuticals is the most advanced demonstration yet of a potential new strategy for drug making that is more flexible, efficient, and reliable. Portable drug-making technology like it could be used to more rapidly respond to local drug shortages or spikes in demand, such as in an outbreak.

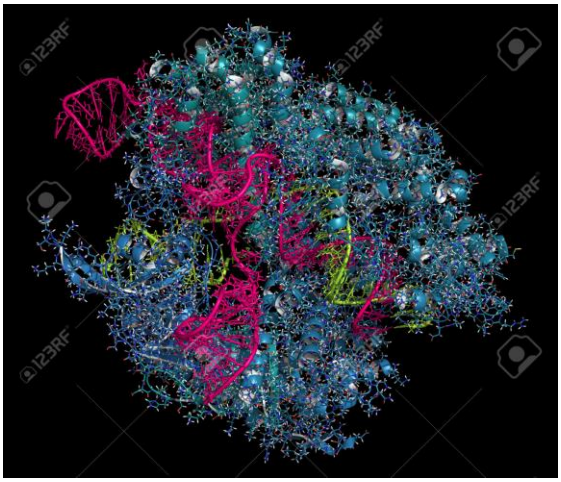
Making pharmaceuticals can take months to a year because the current method entails performing multiple chemical steps, often involving several different manufacturing locations. A single unanticipated plant shutdown can cause substantial supply disruptions.

Technology Review

CRISPR gene-editing tested in a person for the first time

A Chinese group has become the first to inject a person with cells that contain genes edited using the revolutionary CRISPR–Cas9 technique.

On 28 October, 2016 a team led by oncologist Lu You at Sichuan University in Chengdu delivered the modified cells into a patient with aggressive lung cancer as part of a clinical trial at the West China Hospital, also in Chengdu.



Earlier clinical trials using cells edited with a different technique have excited clinicians. The introduction of CRISPR, which is simpler and more efficient than other techniques, will probably accelerate the race to get gene-edited cells into the clinic across the world, says Carl June, who specializes in immunotherapy at the University of Pennsylvania in Philadelphia and led one of the earlier studies.

Nature

INVESTING AND DEAL-MAKING

inVentiv Health Consulting Landmark Study

Now in its eighth year, the inVentiv Health Consulting (formerly Campbell Alliance) Dealmakers' Intentions Study is the only forward-looking measure of deal making activity in the pharmaceutical and biotech industries. While there are many quality sources of information that look historically at past deal trends, this survey offers a prospective view of the partnering and licensing landscape for the year ahead.

In the first quarter of 2016, inVentiv Consulting surveyed 144 licensing professionals, capturing expectations for deal activity, supply and demand for assets at different stages of development, and approaches to valuation. The results of that survey provide a forward-looking view into what dealmakers anticipate will happen in licensing and acquisitions over the upcoming year. The 2016 Dealmakers' Intentions Study notes that buyers' demand for preclinical and phase III assets overshadows supply across several therapeutic areas, which will likely result in significant increase in asset value this year. The study also found that deal making is likely to return to historic norms, or slightly higher. Prices have increased and the margin for error has narrowed, but there are still ample opportunities. Traditional M&A will see slowing growth or be flat, while deals shaped as acquisitions with earn-outs are expected to continue to increase as buyers seek to push more risk onto sellers. For sellers, the market continues to generate options for value creation at different phases of development, with more room for a supply-demand match before phase III. But for buyers, in order to secure the assets they most want, they might need to be more aggressive in crafting acquisitions with earn-outs, creative licensing agreements and more.

inVentiv Health

FDA's Biosimilars Workload: 57 Development Programs, $81M Spent in First Three Fiscal Years

A new independent analysis of the US Food and Drug Administration's (FDA) workload around biosimilars over the first three years shows how biosimilar development has slowly progressed as companies continue to seek more meetings with FDA on specific issues and targeted advice.

As of 30 September 2015, the report says there are 57 programs participating in the

biosimilar product development program (up from 33 in FY 2013 and 48 in FY 2014), and a total of seven Biologics License Applications (BLAs) have been submitted under section 351(k) of the *Public Health Service Act* (known as 351(k) BLAs), one of which (Zarxio) was approved in March 2015.

RAPS

Is The Golden Era Of Pharmaceutical Profits Over?

For decades, the pharmaceutical industry has been highly profitable. The recipe for such profits has been pretty simple for most of the last half-century–discover a chemical or molecule that treats a common problem, like hypertension or diabetes or erectile dysfunction, and make billions of dollars while that product is still under patent protection. But of course, profits were never so simple. It takes billions of dollars to develop one new drug suitable for testing in humans and even then, the drug might turn out to be too toxic or to have too little benefit to make it on to the market. It might take a handful of such drugs before a company finally finds one that works, a single blockbuster that can hopefully make up for all that investment. But the cost of new drug development is rising, and the number of big wins is declining–with the number of common illnesses in need of interventions dwindling–so it is getting increasingly difficult to bring enough blockbusters to market to make up for all those drugs that go bust.

Forbes

Large vs. Small Molecule Success Rates

A recent assessment of R&D success rates reveals that large molecules continue to outperform small molecules, particularly in the early phases of Development.

Overall, from start of GLP Tox to Approval, small molecules have a 5% chance of success compared to 13% for large.

In Preclinical small molecules have a 63% rate of success vs. 79% for large molecules; the difference in Phase I is 41% for small molecules vs. 52% for large. The only phases where there is a statistically significant variance ($p < .05$) in molecule size is in Preclinical and Phase I, but large molecules tend to have higher rates in all phases.

Applied Clinical Trials

Biotech's Resurgence May Cost Big Pharma

An increase in biotech stocks complicates deals and raises risks for would-be acquirers

There are signs that a new wave of deals is brewing in the biotech sector. That is juicing shares and pushing up valuations.

Some likely buyers are Amgen, Gilead Sciences, and Merck, which are among the large drug makers who have said that they are on the hunt for deals.

Among possible sellers are Medivation, which signed confidentiality agreements with several potential acquirers, a precursor to a possible sale. The Wall Street Journal reported earlier in August, 2016 that the biotech giant Biogen has attracted preliminary interest from at least two potential suitors.

Wall Street Journal

Big pharma's R&D zero-to-hero story

The common narrative of the biotech boom was one of innovative small and mid-sized companies with a single asset or program that ramped up in valuation as investors fell in love with all things pharmaceutical.

A lesser-known story is the sell side appreciation of pipelines throughout big pharma as laboratories and business development came to life amid the biotech boom. Analysts now believe that this cohort 's R&D assets are worth a combined $225bn, representing growth of 53% since EP Vantage last did this analysis two years ago, and more than double in three years.

This analysis looks at the value of R&D pipelines at big pharma by comparing the total NPV of their projects in development – covering those for which analysts have made forecasts – with products on the market, along with company market caps.

It reveals which companies are heavily dependent on their pipelines – the NPV will primarily reflect late-stage assets – and which have balanced or aging portfolios.

Evaluate Group

The Human Body, According to Venture Capitalists

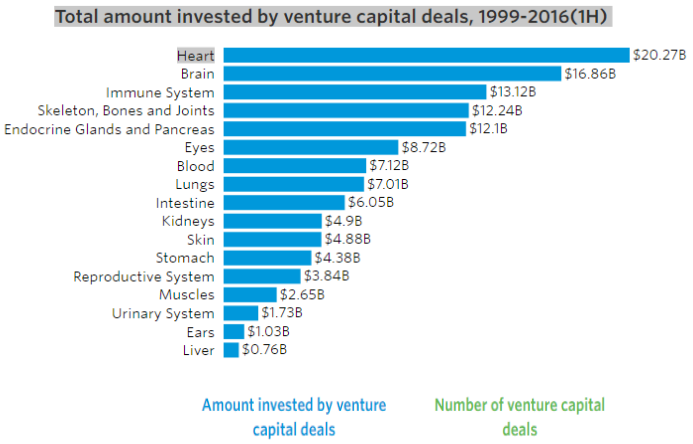
The investors who support emerging medical technologies play an important role in determining which new therapies reach the public. A WSJ Pro analysis of venture investment trends since 1999 reveals which body systems stand to benefit most from their decisions.

Wall Street Journal

Interview – Advamed warns on innovation as the VC crisis bites

The dire effects on device innovation long threatened by the medtech venture financing crisis are beginning to be felt. Recent years have seen a sharp decline in the number of medtech start-ups being formed, according to US industry group Advamed, placing the sector's future at risk. And things are going to get worse before they get better.

"The trend in innovation is going to be perceived to be worse for a little while. Even if the investment starts increasing now, there is a lag of five to six years for some of these



technologies to start seeing the light," says Advamed's chair-elect, Nadim Yared.

An analysis of the US medtech industry conducted by the lobbying group suggests that the formation of new medtech's has declined from a high of more than 2,000 a year in 2006 to around 600 in 2012, the most recent year in Advamed's analysis. And this has come as a direct result of VCs' unwillingness to back these groups.

Evaluate Group

REGULATORY AND GOVERNMENT

F.D.A. Deal Allows Amarin to Promote Drug for Off-Label Use

In a deal that could change the way some companies market their drugs, the Food and Drug Administration has agreed to allow a pharmaceutical company to promote a drug for a use that the agency has not approved, the company said on Tuesday.

The agreement settles a legal case between the agency and the company, Amarin, a small drug maker that sued the F.D.A. last year for the right to promote its only product, Vascepa, to a broader range of patients. In August, a federal district judge in Manhattan ruled that the F.D.A. could not prohibit Amarin from using truthful information to promote its drug, even for unapproved uses, because doing so would violate the company's right to free speech.

The final settlement is still subject to approval by the court.

New York Times

FDA Finalizes Guidance on Adaptive Designs for Device Studies

The US Food and Drug Administration (FDA) finalized guidance that lays out how to design medical device clinical trials that allow for changes based on data, while maintaining study validity and integrity.

FDA says it received 151 comments from seven entities, including the Advanced Medical Technology Association (AdvaMed) and AstraZeneca, on the draft guidance and "incorporated most of them in this final guidance."

RAPS

NIH Awards $55M for Precision Medicine Initiative Cohort Buildout; FDA Releases NGS Draft Guidances

The NIH announced it would provide $55 million in fiscal year 2016 to build and support enrollment of 1 million volunteers into the Precision Medicine Initiative.

Additionally, recognizing that genomic information is critical to delivering precision care, the US Food and Drug Administration released two draft guidances outlining its conceptual framework for establishing the analytical and clinical validity of next-generation sequencing tests.

The latest NIH awards are intended to "support the critical infrastructure we need to build a study of this scale and scope and break new ground in how we engage people in research," NIH Director Francis Collins said during a call.

GenomeWeb

Massachusetts becomes first state to mandate drug take-back

Massachusetts has become the first state in the country to require drug companies to provide a means for consumers to safely dispose unwanted medications. This law comes six months after President Barack Obama signed legislation allowing states to create such take-back programs for prescription and over-the-counter medications.

The law is intended to give the state a way to keep drugs from getting flushed or tossed in the trash, and to ultimately divert from waterways and drinking water as well as prevent drug abuse and accidental drug ingestion-related harm.

Six California counties and one in Washington require pharmaceutical companies to pay for collection of unwanted prescription drugs, and the Massachusetts Department of Public Health will look toward those models to develop its own regulations and means to implement the law.

WasteDIVE

The White House Is Pushing Precision Medicine, but It Won't Happen for Years

For starters, it's too expensive and the science isn't advanced enough.

With the right technologies to collect and make sense of biomedical information, we could speed up the pace of discoveries that lead to a new class of tailor-made drugs. That's the argument behind the White House's push for "precision medicine" (see "A Shot in the Arm for Obama's Precision Medicine Initiative").

The goal of precision medicine is to provide drugs and therapies that are uniquely suited to individual patients based on their genetics and other distinguishing health information. To a small degree, that already is happening.

Dozens of targeted drugs have gotten approval from the U.S. Food and Drug Administration in recent years, and there are particularly successful examples in oncology. But despite the early successes, we are many years from realizing a "new era of medicine" the president described in his 2015 State of the Union address—if we can realize it at all.

MIT Technology Review

Court backs more expansive view of what biotech firms can patent

A federal appeals court's decision in a patent case could give investors more confidence in biotech products. But uncertainty around what can be patented may persist until the Supreme Court weighs in again.

A three-judge panel of the U.S. Court of Appeals for the Federal Circuit ruled in favor of In Vitro, which wanted its patent upheld for a process of repeatedly freezing and thawing a type of liver cell useful for testing, diagnostic and treatment purposes. A lower court had ruled In Vitro's process wasn't patentable because it covered a law of nature and laws of nature can't be patented.

The Federal Circuit, however, disagreed saying In Vitro's patent claims in this case involve a "new and useful laboratory technique." The court also said that it doesn't matter that the steps of this new technique were already known; the process is still patentable because it involves putting those steps together in a way that "was itself far from routine and conventional."

Modern Healthcare

FDA should be independent agency, former commissioners say

Six former Food and Drug Administration commissioners, who served under both Democratic and Republican presidents, called for the FDA to become an independent agency rather than part of the Department of Health and Human Services (HHS), Politico reports.

Speaking at the Aspen Ideas Festival in Colorado, the former commissioners advocated for the FDA to be elevated to Cabinet-level status as a way to reduce bureaucracy and increase the agency's profile.

The six commissioners included the recent agency head Margaret Hamburg, as well as Andrew von Eschenbach, Mark McClellan, Jane Henney, David Kessler, and Frank Young.

BioPharma DIVE

FDA's Breakthrough Designation is Working

The good news about FDA's breakthrough drug initiative is that it actually appears to be accelerating clinical development of highly promising new therapies - as opposed to just speeding up the agency's approval process, as with other FDA options for expedited approval. A recent analysis by Friends of Cancer Research (FOCR) finds that pre-market development time for breakthrough-designated drugs is 2.2 years shorter than for those without the BT imprimatur (see http://www.focr.org/news/nature-impact-breakthrough-therapy-designation-cancer-drug-development). FDA has granted BT status to more than 100 experimental therapies since the BT program was established by Congress in 2012, about one-third of the more than 300 BTDRs (breakthrough designation requests) that have been submitted.

Even more important, the program has helped bring some 40 new breakthrough therapies to market, many benefitting from faster development and application review by FDA. That includes a new treatment for a serious form of chronic lymphocytic leukemia (CLL) developed by AbbVie and Genentech, based on a single-arm study that showed an 80% response rate in patients with a specific genetic marker.

Applied Clinical Trials

FDA Holding Off on Finalizing Regulatory Guidance for Lab-Developed Tests

Amid post-election uncertainty, the US Food and Drug Administration has decided to delay finalizing its draft guidance on regulating lab-developed tests, GenomeWeb has learned.

According to multiple sources in Washington, DC, the FDA has been informing stakeholders in policy circles of the decision. GenomeWeb reached out to the FDA for confirmation and received the following statement from a spokesperson:

"The FDA believes that patients and health care providers need accurate, reliable, and clinically valid tests to make good health care decisions — inaccurate or false test results can harm individual patients. We have been working to develop a new oversight policy for laboratory developed tests, one that balances patient protection with continued access and innovation, and realize just how important it is that we continue to work with stakeholders, our new Administration, and Congress to get our approach right."

Genome Web

Why New Drug Approvals Are At A Six-Year Low In The U.S.

Last year turned out to be a disappointing one for new drug approvals with the U.S. Food and Drug Administration clearing just 22 new medicines for sale, the lowest number since 2010 and sharply down on 2015's tally of 45.

Across the Atlantic, the European Medicines Agency recommended 81 new prescription products against a 2015 total of 93. Unlike the FDA, the EMA includes generic drugs in its list. The slowdown suggests the pharmaceuticals industry may be returning to more normal productivity levels after a spike in approvals in 2014 and 2015, when the haul of new drugs reaching the market hit a 19-year high.

The Huffington Post

FDA Finalizes Guidance on Clinical Pharmacology Data to Support Biosimilars

Between Christmas and the beginning of 2017, the US Food and Drug Administration (FDA) finalized guidance from 2014 to help biosimilar sponsors understand what clinical pharmacology data is necessary to support a proposed biosimilar.

The 18-page guidance is one in a series implementing the *Biologics Price Competition and Innovation Act of 2009* (BPCIA) that established a pathway for the approval of such follow-on biologics. Four other final guidance documents and two other draft guidances have been released by FDA so far, and guidance on interchangeability is expected this year (to read more about biosimilars see the *Focus* explainer from last year).

RAPS

FDA to drugmakers: Don't let manufacturing lead to rejection

Only 22 novel drugs passed muster with the Food and Drug Administration in 2016, a sharp drop off from the near two decade-high of 45 new medicines that received approval the year before. The low total, coupled with industry-wide restructuring in R&D, has sparked concerns over the drug development productivity, particularly at large pharmaceutical companies.

A recent report from Deloitte, for example, estimated the annual return on late-stage pipelines among 12 pharmas at a lackluster 3.7% last year — the lowest level in the past seven years. One of the main drivers of that decline, according to the consultancy, is a failure to successfully refill pipelines with promising assets. With M&A muted compared to several years ago, internal R&D appears to be lagging behind historical standards.

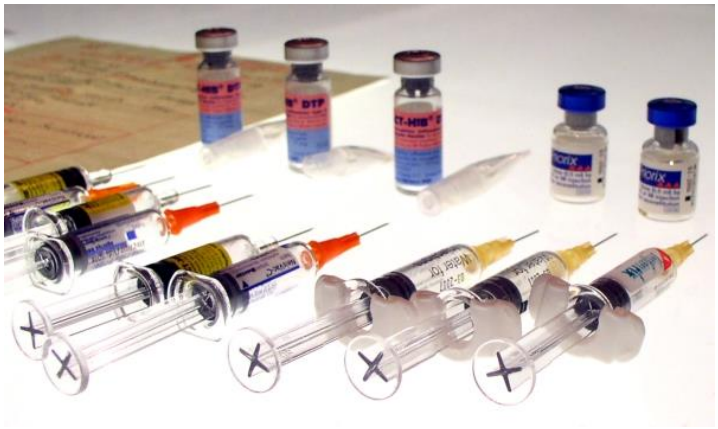
Yet, even as these kinds of structural factors are undoubtedly in play, the explanation for the dip in approvals last year is a bit simpler.

BioPharmaDIV

HEALTHCARE

Overspending driven by oversized single dose vials of cancer drugs

Peter B Bach and colleagues call for an end to contradictory regulatory standards in the US that allow drug manufacturers to boost profits by producing single dose vials containing quantities that increase leftover drug.



Even though reducing waste in healthcare is a top priority, analysts have missed the waste that can be created when expensive infused drugs are packaged containing quantities larger than the amount needed. This is particularly true for drugs for which dosage is based on a patient's weight or body size and that come in single dose packages. These drugs must be either administered or discarded once open, and because patients' body sizes are unlikely to match the amount of drug included in the vial, there is nearly always some left over. The leftover drug still has to be paid for, even when discarded, making it possible for drug companies to artificially increase the amount of drug they sell per treated patient by increasing the amount in each single dose vial relative to the typically required dose.

thebmj

Medical errors cause 250,000 U.S. deaths a year

Medical errors cause more than 250,000 deaths every year in the United States, enough to make them the nation's third-leading cause of death if they were recognized in official statistics, experts say.

If the statistical rules change, medical mistakes would trail only heart disease and cancer as a leading cause of US fatalities.

"Incidence rates for deaths directly attributable to medical care gone awry haven't been recognized in any standardized method for collecting national statistics," says Martin Makary, professor of surgery at Johns Hopkins University School of Medicine.

Researchers performed their calculations based on eight years of US medical death rate data. The results reflect the fact that national death statistics are derived from a system built for another purpose: generating bills and collecting insurance payments.

Futurity

US prescription drug spending increases to an estimated $457 billion in 2015

US prescription drug spending hit $457 billion in 2015 and continued its recent growth, the Department of Health and Human Services estimated. Projected by the Office of the Assistant Secretary for Planning and Evaluation, the 2015 drug spend represented 16.7% of the overall $2.7 trillion expended on personal health care services.

The brand-name share of retail drug expenditures continued its downward trend, representing about 53% of expenditures between 2013 and 2015, the report said. While the number of brand-name prescriptions has fallen, revenue has remained roughly level.

BioPharma DIVE

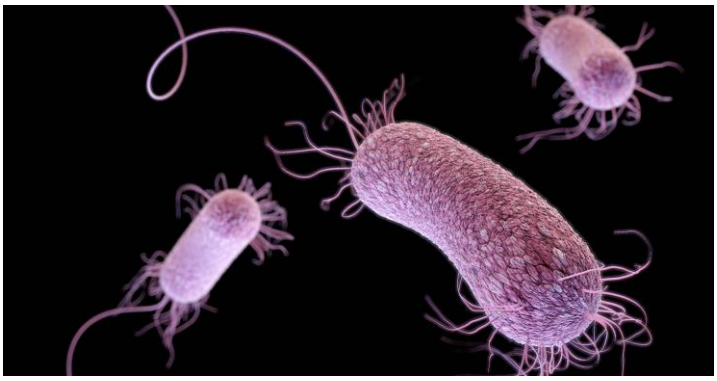
Q&A: Allergan's CEO speaks out on limiting drug prices. 'Somebody had to take the first step'

In a bold move, Allergan chief executive Brent Saunders issued a manifesto promising to avoid "price gouging" as part of a "social contract" with the public. His company will limit price increases on branded drugs to single digit percentages per year in most cases, he wrote. The move comes amid growing national anger over prescription drug prices — most recently fueled by the EpiPen controversy — and ensuing outcries from Washington lawmakers. We spoke with Saunders about his plan and the extent to which it can make a difference.

STAT

'Superbug' scourge spreads as U.S. fails to track rising human toll

Josiah Cooper-Pope, born 15 weeks premature, did fine in the neonatal intensive care unit for the first 10 days of his life. Then, suddenly, his tiny body started to swell. Overnight, he grew so distended that his skin split.



The shock of her son's death came back to her when, after being contacted by Reuters earlier this year about the outbreak, Bowser went to Virginia's Division of Vital Records to get a copy of Josiah's death certificate. The cause of death: "Sepsis due to (or as a consequence of): Prematurity." Sepsis is a complication of infection, but there was no mention of MRSA.

Reuters

Healthcare

Pharmacy benefit managers are restricting access to lots of drugs in 2017

In the latest bid to control prescription drug spending, the nation's largest pharmacy benefits managers are again excluding dozens of medicines from their lists of products that are covered by health insurance, which are known as formularies. PBMs, you may recall, are crucial, behind-the-scenes middleman who negotiate drug prices on behalf of companies, unions, and government agencies.

Express Scripts notified its customers that in 2017, 85 medicines will be excluded from its national formulary, and, as a result, the PBM hopes to recognize about $1.8 billion in savings, up from $1.3 billion in 2016. The number of excluded medicines, by the way, is down slightly from the 88 prescription drugs that were excluded from its 2016 formulary.

CVS Health released its own 2017 formulary that will exclude another 35 medicines, including 10 that were called "hyperinflationary." As a result, CVS is now excluding a total of 131 medicines and boasts such moves have saved more than $9 billion over the last five years, according to a CVS spokeswoman. The PBM did not provide a specific savings estimate, but Barclays analysts forecast about $2.6 billion should be saved in 2017.

STAT

Drug Shortages Forcing Hard Decisions on Rationing Treatments

In the operating room at the Cleveland Clinic, Dr. Brian Fitzsimons has long relied on a decades-old drug to prevent hemorrhages in patients undergoing open-heart surgery. The drug, aminocaproic acid, is widely used, cheap and safe. "It never hurt," he said. "It only helps."

Then manufacturing issues caused a national shortage. "We essentially did military-style triage," said Dr. Fitzsimons, an anesthesiologist, restricting the limited supply to patients at the highest risk of bleeding complications. Those who do not get the once-standard treatment at the clinic, the nation's largest cardiac center, are not told. "The patient is asleep," he said. "The family never knows about it."

In recent years, shortages of all sorts of drugs — anesthetics, painkillers, antibiotics, cancer treatments — have become the new normal in American medicine. The American Society of Health-System Pharmacists currently lists

inadequate supplies of more than 150 drugs and therapeutics, for reasons ranging from manufacturing problems to federal safety crackdowns to drug makers abandoning low-profit products. But while such shortages have periodically drawn attention, the rationing that results from them has been largely hidden from patients and the public.

New York Times

Knockoffs of Biotech Drugs Bring Paltry Savings

Generic drugs have long delivered huge savings over their brand-name counterparts. That isn't likely to happen, though, with knockoff versions of some of the expensive drugs on the market today.

Rival versions of so-called biotech drugs, called biosimilars, are just starting to be released, and health insurers and drug-benefit managers say they expect them to cost nearly as much as the brand-name originals did for years.

One big reason: Pharmaceutical companies have been raising prices on biotech drugs about to lose patent protection to squeeze out more revenue before competition arrives, according to insurers, drug-benefit managers and pharmaceutical industry consultants. And makers of the knockoffs are setting their prices just below those marked-up ones.

Wall Street Journal

Germany's Model For Drug Price Regulation Could Work In The US

Donald Trump and Hillary Clinton agreed on almost nothing during the 2016 presidential campaign — but they did agree that the U.S. needs to address unaffordable prescription drug prices. And the public also supports this idea. A survey released in October 2016 showed that 64 percent of voters, including 52 percent of Republicans, believe that the federal government should place a "limit on how much pharmaceutical companies can increase prescription drug prices."

Further, 73 percent of all voters (68 percent of Republicans) concur that the federal government should be able to negotiate with drug companies to lower Medicare drug prices for seniors. While the November 8 federal election results have dampened prospects for policy change along these lines, does anyone believe that this issue now will disappear? We think not.

Health Affairs

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