



By Taren Grom

Past, Present, AND FUTURE

PharmaVOICE celebrates 15 years of trends with a look back at the market forces that have defined the industry and what's ahead as the healthcare ecosystem continues to be reinvented.

The world today is much different from when PharmaVOICE began publishing 15 years ago. In the United States, George W. Bush had just taken office, replacing Bill Clinton. Today, Jeb Bush and Hillary Clinton are running for president. Okay, so while some of the names in politics remain the same, the country and the world are very different. Our first issue had gone to press and we were putting the final touches on our second issue when the Twin Towers went down that fateful September 11th morning.

Several other major events punctuated the calendar during 2001, which have or continue to affect the industry:

- ▶ **IN 2001:** Pharmaceutical companies agree to sell AIDS drugs at cost in Africa, a discount of up to 90% to help the fight against AIDS.
- ▶ **TODAY:** New HIV infections have fallen by 35% since 2000 and AIDS-related deaths have fallen by 42% since the peak in 2004.
- ▶ **IN 2001:** The world's first contraceptive patch Ortho Evra, from Janssen, receives market approval.
- ▶ **TODAY:** The Ortho Evra patch, which was made available on U.S. pharmacy shelves in 2002, was discontinued in late 2015 "due to a business decision," according to information on the FDA website. A statement from the company confirms that "Janssen Pharmaceuticals has decided to discontinue its birth control patch Ortho Evra (norelgestromin/ethinyl estradiol transdermal system) in the United States." A generic version of the contraceptive patch is now available.
- ▶ **IN 2001:** The human genome sequence and the preliminary analysis result were revealed on February 12 jointly by scientists from China, Japan, Germany, France, Britain, and the United States, and Celera Genomics, a U.S. company. The human genome was proved to contain some 30,000 to

40,000 genes consisting of 3.2 billion alkali base pairs. This was a major step in exploring the mystery inside the human being. It was estimated that the work of mapping the entire human genome would be finished by the year 2003. In 2001, reports estimated that the cost of sequencing was just under \$10,000.

- ▶ **TODAY:** Through 23andMe, anyone can get a personalized analysis of their DNA and discover their ancestral origins and trace their lineage for less than \$200.
- ▶ **IN 2001:** The most serious economic slowdown in 20 years occurred in most areas of the world. The U.S. economy went into a recession starting in March; affected by the U.S. economic fallout, the 15-member European Union underwent a sharp economic contraction; the Japanese economy experienced a further deterioration; the Asian economy, which was on recovery from the 1996 financial crisis, also slowed its pace of growth; and the Latin American economy plunged into difficulty, with political disturbance breaking out in Argentina owing to the country's economic crisis at the end of the year. The September 11 attacks not only dealt a blow to the U.S. economy, but also severely affected the economies in other parts of the world. The International Monetary Fund estimated that the world economy would grow by only 2.4% that year, 2.3 percentage points lower than the previous year. (Editor's Note: Great time to start a new publication, right?)
- ▶ **TODAY:** The global economy is in a holding pattern in which positive and negative forces offset each other, at least for the immediate future. This characterization of the global economy is unlikely to change in the next 12 to 24 months. After adjusting for China's overstated official growth rate, analysts project a very modest improvement in the growth rate for the global economy to 2.8% in 2016, up from 2.5% in 2015.



For this month's cover story, we asked industry experts from all sectors — from the clinic to commercialization — to provide us with the biggest change they've seen in the past 15 years and what they see on the horizon. By all accounts the biggest trend has been the move to a more patient-centric healthcare model, closely followed by the impact that technology is having on all areas of the life sciences as well as changing business models. Industry leaders also discuss shifts in the cancer category, factors impacting clinical development, global market influences, healthcare delivery, M&A, and other trends.

We hope you enjoy these reflections and projections on the influences shaping the life-sciences industry.

When we began publishing PharmaVOICE in 2001 and using the term life sciences as part of our message and vision, this holistic approach to covering the industry was a nascent concept. Then, as now, we believe life sciences constitutes the companies, organizations, and people involved in moving a pharmaceutical, biopharma, biotechnology, device, product, tool, or service along the continuum of care.

We thank the thousands of industry experts who have raised their voices on the important trends of the past, today, and tomorrow and for helping to move the life-sciences industry forward.

Today, according to Deloitte, aging populations, chronic/lifestyle diseases, emerg-



2016: A Shake Up Year

As the industry copes with the continued influx of the newly insured, the rising burden of medical costs, and a host of new technologies for patients and doctors alike, startups and entrenched companies will look for new ways to reach customers. Patients, meanwhile, will be looking for better methods to manage their medical expenses and their health, according to a new report from PwC. Also, get ready for healthcare to get political.

DRUG PRICING SOLUTIONS.

Concerns over drug prices have reached fever pitch in the U.S. Price increases for branded drugs have outpaced inflation every year since 2006. Even generics prices are inching up, gaining 9% on average since 2014.

One approach that pharma companies may try is an alternative financing model, which spreads out payments for expensive drugs in order to make the cost easier to handle. More than half of consumers polled by PwC said they would be willing to pay for a pricey drug over time rather than bear the full brunt all at once.

There will also likely be more outcomes-based reimbursement agreements struck in 2016. These agreements between pharmaceutical companies and insurers or

health systems link payment for a drug to the health outcome rather than simple volume of product used.

MERGER MANIA WILL CONTINUE.

2015 was a year of massive mergers, from Anthem's \$48.4 billion offer for Cigna to Pfizer's jaw-dropping \$160 billion deal for Allergan. That trend will likely continue in 2016, especially since many of the deals will still be facing regulatory scrutiny over the coming months.

Consolidation will likely beget more consolidation, as smaller companies look to boost their negotiating power when competing with new, larger rivals. As healthcare gets more tech savvy, insurers, health systems, and pharmaceutical companies will be looking for better data analytics and new products to complement existing services.

GET CARE WHEN AND WHERE IT'S CONVENIENT.

Health apps came into their own in 2015 with the telemedicine app Teladoc, making its debut on the public markets. Teladoc's membership has boomed to 8.1 million and continues to expand.

More people are adopting digital health apps to manage their care when and where they want it. Patient adoption of health-related apps nearly doubled over the last two years. About 32% of consumers had at least one health app

on their phones in 2015, up from 16% in 2013, according to the PwC report. Connected devices that go well beyond a fitness tracker — think EKG monitors, glucose trackers, connected pacemakers — will spur greater adoption of apps that help patients better monitor their health. These apps will be especially valuable for sharing information directly with doctors for controlling chronic conditions.

CYBERSECURITY IS GOING TO BE TOP OF MIND.

With more using digital health apps and services, privacy and cybersecurity will be top of mind for both consumers and providers. Insurers have already had a rough go of it recently, facing hacks that have affected hundreds of millions of customers in total. Almost 40% of customers polled by PwC said they would abandon or reconsider using a health organization if it were hacked.

IT'S GOING TO GET POLITICAL.

The election season is well under way, and there's already been a number of healthcare proposals from candidates on both sides of the aisle. With the high-profile tax inversion mergers by pharmaceutical companies, rising medical costs, and high drug prices, healthcare will remain a key issue in 2016.

Source: Fortune's Laura Lorenzetti and PwC Health Research Institute's directors Benjamin Isgur and Trine Tsouderos

ing-market expansion, and treatment and technology advances are expected to spur life-sciences sector growth. But, efforts by governments, healthcare providers, and health plans to reduce costs, improve outcomes, and demonstrate value are dramatically altering the healthcare demand and delivery landscape. It is becoming increasingly evident that the global life-sciences sector is operating in an era of significant transformation.

According to Deloitte, the extended nature of life-sciences product development mandates that sector stakeholders adopt a long-term approach to strategic planning, portfolio management, and market expansion. However, organizations must also prepare for and react to near-term challenges and opportunities. Four major trends are expected to capture the sector's attention in 2015: searching for innovation and growth; changing regulatory

and risk environment; preserving and building shareholder value; and preparing for the next wave. The resulting challenges and opportunities can be both global and market-specific.

Adapting business models to account for innovations such as personalized medicine,

► Technology

When PharmaVOICE launched 15 years ago, Facebook was but a twinkle in Mark Zuckerberg's eye and the rest of the social media channels that are dominating our conversations today as they relate to online access to patients, physicians, consumers, and other stakeholders were also still on the drawing boards in living rooms around the country. These media, which started as consumer-based vehicles have morphed into powerful

applying technology innovation to healthcare delivery, talent strategies, and continued expansion and presence in emerging markets will further present challenges and opportunities for companies as they adjust to and meet the needs of this continually changing sector.

mechanisms for life-sciences companies for not only delivering communications, but understanding customers' perspectives on any number of topics. And while final guidelines for online or social media practices have yet to be officially sanctioned, not surprisingly pharma companies — for the most part — still look for solid footing from a regulatory standpoint. Despite continuing hesitation and the full embrace of these vehicles, online



is not only here to stay but growing more powerful every day.

Digital is taking the industry by storm as well. Most people have in their possession more computing power than NASA had to launch the first space capsule in the 1960s, and it fits in our hands. Our cell phones, and who really uses them for talking anyway, have the capabilities that were science fiction-oriented 15 years ago.

As part of the technology revolution, only superseded in the estimation of some experts by the industrial revolution of more than 250 years ago, in terms of a far-reaching impact has been the emergence of the concept of big data and all its associated analytics, segmentation, cloud-based service bells and whistles.

According to various sources, the idea of big data emerged in a 2001 research report by META Group (now Gartner) analyst Doug Laney, who defined data growth challenges and opportunities as being three-dimensional,

i.e. increasing volume (amount of data), velocity (speed of data in and out), and variety (range of data types and sources).

This “3Vs” model continues to be used to describe big data. A dozen or so years later, Gartner updated its definition as follows: “Big data is high volume, high velocity, and/or high variety information assets that require new forms of processing to enable enhanced decision making, insight discovery and process optimization.”

Today, there is no corner of the life-sciences industry immune to the spotlight of technology to improve processes, reduce costs, and enhance efficiencies. From drug discovery to clinical trials to drug delivery to commercial practices, technology innovations will continue to push the industry into uncharted territory.

The software insights company Tableau reports that what’s really going to make big data go mainstream is the ability to connect not just with data scientists and technologists

but business people. And absolutely one of the keys to that is visualization and being able to show people — not just tell people, not just show numbers, or even show charts — but to have those charts and graphs and visualizations come alive.

Tableau also reports that while it is still in its early days, the data from devices in the Internet of Things will become one of the “killer apps” for the cloud and a driver of petabyte scale data explosion. For this reason, they see leading cloud and data companies such as Google, Amazon Web Services, and Microsoft bringing Internet of Things services to life where the data can move seamlessly to their cloud based analytics engines.

And nontraditional companies, such as Google — and its associated alphabet of innovation hub departments — Microsoft, Amazon, GE are changing the life-sciences landscape as they enter into uber-tech deals with the J&Js, Novartis, and Pfizers of our world.

Clinical Development

In 2015, FDA’s Center for Drug Evaluation and Research (CDER) approved 45 novel new therapies – significantly more than the average of 28 approved during the previous nine years of this decade — many of which offer many patients new treatment options for serious and life-threatening conditions.

“During the next five years, we expect to see a surge of innovative medicines emerging from R&D pipelines, as well as technology-enabled advances that will deliver measurable improvements to health outcomes,” says Murray Aitken, IMS Health senior VP and executive director of the IMS Institute for Healthcare Informatics. “With unprecedented treatment options, greater availability of low-cost drugs, and better use of evidence to inform decision making, stakeholders around the world can expect to get more ‘bang for their medicine buck’ in 2020 than ever before.”

In its latest study, the IMS Institute highlights the following findings:

- ▶ By 2020, technology will be enabling more rapid changes to treatment protocols, increasing patient engagement and accountability, shifting patient-provider interaction, and accelerating the adoption of behavior changes that will improve patient adherence to treatments.
- ▶ Every patient with multiple chronic conditions will have the potential to use wearables, mobile apps, and other technologies to manage their health, interact with providers, fellow patients, and family members.

▶ The ubiquity of smartphones, tablets, apps and related wearable devices, as well as electronic medical records and exponentially increasing real-world data volumes, will open new avenues to connect healthcare while offering providers and payers new mechanisms to control costs.

Research from the analyst company Dickson states that while estimates vary on how much it costs to bring a new drug to market, a recent study from the Tufts Center for the Study of Drug Development (CSDD) pegs the average total at \$2.9 billion. But, 95% of medicines fail during development, and only two in 10 recoup their research and development costs.

Once drugs lose patent protection, generics siphon off up to 90% of sales. The average annual savings from switching to generic medications is estimated to be \$420 per consumer.

IMS Institute states that generic medicines will continue to provide the vast majority of the prescription drug usage in the U.S., rising from 88% to 91% to 92% of all prescriptions dispensed by 2020. Spending on medicines in the U.S. will reach \$560 billion to \$590 billion, a 34% increase in spending over 2015 on

an invoice price basis.

While drug pricing is commanding significant amounts of attention in Washington, PwC analysts say the life-sciences industry should keep its eye on regulatory reform packages slowly working their way through the halls of Congress and the FDA, which could have wide-ranging impacts on how drug and medical device products are researched, regulated, and even priced.

Some of the most impactful long-term changes to the life-sciences sector in 2016 likely will emerge from the ongoing debate regarding the reauthorization of the FDA’s user fee programs. The programs, which fund much of the FDA’s regulatory activities for drugs (branded, generic, and biosimilars) and medical devices are set to expire in September 2017.

Frequent public negotiations between the FDA and industry over possible changes already are under way and will continue until the end of 2016, paving the way for a 2017 passage. Already at issue: The speed and funding of FDA reviews, the elimination of backlogs of certain applications, and identification of ways to allow patients to participate in the review process.

Cancer

According to PhRMA, since peaking in the 1990s, cancer death rates have declined almost 22%. Approximately 83% of survival gains in cancer are attributable to new treatments, including medicines, as well as other factors.

In 2001, cancer was considered one homo-

geneous disease. Today, the category is now considered to encompass specific diseases, which are now being addressed by targeted cancer therapies designed to interfere with specific molecules necessary for tumor growth and progression.

In 2016, there will be an estimated 1,685,210 new cancer cases diagnosed and 595,690 cancer deaths in the United States.



In President Obama's last State of the Union speech, he announced a national effort to cure cancer with Vice President Joe Biden heading up the initiative.

After the announcement of this moon shot, President Obama stated, "For the loved ones we've all lost, for the family we can still save, let's make America the country that cures cancer once and for all."

Business Models

As the life-sciences industry continues its transformation into a new health ecosystem with a new health economy to address multiple stakeholders, new delivery platforms, and new players entering the arena, business as usual is no longer accepted or acceptable.

Life-sciences companies of all shapes, sizes, and functions are changing how business is done and how they do business. Pricing will remain front and center as a major operational concern as well as the patent loss for several major brands.

According to Matt Zajechowski of Dickson, AstraZeneca is one company in 2016 that is losing two major drugs from patent protection — Crestor and Seroquel XR — worth a combined annual revenue of \$7.34 billion. The top five biggest patent losses in 2016 per holder after AstraZeneca are Daiichi Sankyo, Merck, Abbott, and ViiV.

He says of course, there's room here for consumers to gain. Four major HIV drugs also are going off patent in 2016: Epcicom, Trizivir, Norvir, and Kaletra, with a current cost-per-pill at \$39.57, \$11.07, \$8.83, and \$7.22, respectively.

The good news for consumers is that the costs for generics are 80% to 85% lower on average than those of patented drugs.



JAMES CASTELLO
Executive Director,
Incentive Compensation
Practice, TGaS Advisors

Sales incentive compensation has undergone significant change in the last 15 years as companies have had to administer plans in an increasingly complex environment. The rise of specialty drugs, the dramatic shifts in managed care from traditional managed care organizations to ACO and IDN, and the increased public scrutiny to sales practices have combined to create more distinct selling roles, increased number of smaller, more nimble teams, and an insatiable thirst for motivational and effective compensation plans.

In February, Illumina, the San Diego DNA sequencing company, announced that it is setting up a new company to help create a blood test for cancer detection. Illumina is the majority owner of Grail, which has raised \$100 million in a Series A funding round. Company executives hope that by detecting cancer early before symptoms manifest, this may be mankind's best shot at improving how many sur-



KARL KRAFT
Executive Director, MRL/
Marketing Operations
Practice, TGaS Advisors

Companies are taking a more holistic approach to the medical, regulatory, and legal (MRL) review process and overall promotion development. This critical business process is ripe with opportunity to optimize, including significant cost savings, improvements in time and efficiency, greater adherence, and overall quality and utilization of promotional assets. Operational support has also become less transactional and more strategic, ensuring commercial priorities and strategies are met with timely and productive discussion with the medical, regulatory and legal review teams.



DONNA WRAY
VP, Digital & Multichannel
Marketing, TGaS Advisors

eMarketing centers of excellence were in and out of fashion with the various Internet booms and busts over the past 15 years, but in 2016, we see that the vast majority of pharmaceutical companies have centers of excellence in digital and multichannel marketing that are growing over time. According to our study of pharmaceutical marketers across 19 of the top 50 pharma companies, multichannel campaign management is the top area of importance to successful pharmaceutical marketing and at the core of these groups' responsibilities. What was an "org du jour" is now a crucial part of an effective organization.

Mergers & Acquisitions

Many analysts say the lightening-fast pace of pharmaceutical merger and acquisition activity is only heating up as drug manufacturers seek to shift their headquarters to low tax jurisdictions and take up business

worldwide and that this is a turning point in the war on cancer.

In a statement, Jay Flatley, Illumina CEO and chairman of Grail, said by enabling the early detection of cancer in asymptomatic individuals through a simple blood screen, we aim to massively decrease cancer mortality by detecting the disease at a curable stage.

models that prioritize efficiency over gross R&D spending. Recently, Pfizer and Allergan unveiled an all-stock merger that will allow the combined company, Pfizer PLC, to move its headquarters to Ireland and focus on corporate cost cuts.

The stock deal, which values Allergan at \$363.63 a share, or 11.3 shares in the merged company Pfizer PLC, is the largest merger in the pharmaceutical sector on record. Analysts say the new company is expected to create a biopharma juggernaut with the financial flexibility to make new investments, while also increasing profitability and returns of capital to investors.

2016 kicked off merger mania in style, with Shire's acquisition of the newly spun off Baxalta in a transaction valued at \$32 billion, which creates a giant in rare disease treatments.

The agreement brings together Baxalta's strengths in hematologic and immunologic ailments with Shire's capabilities in lysosomal storage, gastrointestinal, and endocrine diseases.

Just by looking at the top 15 pharma companies in 2001 compared with those in 2015, one needs a score card to tell who the players are — or were. With so many mergers, it takes a pharmaceutical historian to follow the trail of how the new mega-companies came into being.

With Allergan and Pfizer ranking as the biggest-ever pharma merger, per data from Bloomberg, here is a list of the industry's seven largest deals over the past 15 or so years.

1. Allergan announces merger with Pfizer in an all-stock deal valued at \$160 billion
2. Pfizer acquires Warner-Lambert in 1999 in an all-stock deal valued at \$87.3 billion
3. Sanofi buys Aventis SA for \$73.5 billion in 2004 in a cash and stock deal
4. Glaxo acquires SmithKline Beecham for \$72.4 billion in stock in early 2000
5. Allergan acquires Actavis for \$65 billion, in a cash and stock merger that closed in 2015
6. Pfizer acquires Pharmacia for \$64.3 billion in stock in 2002
7. Pfizer acquires Wyeth for \$64.2 billion in cash and stock in 2009 **PV**

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TGaS Advisors
301 East Germantown Pike
East Norriton, PA 19401
www.tgas.com