

Pharmaceutical Executive

WHERE BUSINESS MEETS POLICY



**2016 PHARM SCIENCE
STRATEGIC OUTLOOK**
AN INDUSTRY IN FLUX:
2015–2016 MARKET TRENDS

2016 Pharm Science Strategic Outlook

Market Trends: an Industry in Flux

Still a 21st century growth industry...

- The “idea sector,” where biopharma is a major player, today 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.
- M&A activity will continue to dominate in 2016 as biopharma companies respond to a similar wave of restructuring on the insurance and provider side of health care. Even though the track record for ever-larger combinations is mixed, scaling up remains a compelling proposition for biopharma in an era of growing payer power and the high-cost complexities of drug development.
- Continued progress in the basic science of biology and genomics lead to a cascade of advanced treatments that use the body’s own defenses to attack disease. Oncology, anti-viral and auto-immune disorders are poised for the greatest gains, along with better diagnostic tools to make the delivery of medicines more precise for the individual patient.
- At 45 FDA novel drug approvals, 2015 ranks second only to 1996 on this key marker of innovation. Nearly a third secure the full FDA “trifecta” of breakthrough, fast track and orphan drug status, confirming the quality of the science now emerging from industry labs.
- 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. Generic sales growth is significantly lower, at 3 per cent. Worldwide sales of all drugs have surpassed the trillion dollar mark; IMS forecasts a 1.3 trillion dollar market by 2018.
- Specialty and biologic drugs requiring complex manufacturing protocols will make up half of industry sales by 2020, with oncology drugs dominating at a record high growth rate of more than 10 per cent CAGR up to 2020.
- Specialty and biologics is where the industry will continue to make the bulk of its profits; biosimilar products will begin to play a small but measurable role in US sales by the end of 2016. Therapeutic vaccines are also a significant long-term opportunity.
- Generic drugs now account for 85 per cent of prescriptions written in the US, but margins are increasingly pressed, which will trigger additional consolidation in this segment. Generic

prospects are also impacted by a slowing of brand patent expiries, with 19 brands set to lose coverage [*Crestor*, *Glivec*] in 2016, compared to 48 in the peak year 2012.

- Novartis [see *Pharm Exec's 2015 Pharma 50*] is currently the largest company by overall sales, but consolidation will offer more opportunities for newcomers like Gilead [now ranked 9th, up from 18 in 2014], and Teva [now at 12th] to rise within the top ten. A Pfizer-Allergan combination will immediately vault to the top spot if the merger is approved in 3Q 2016.
- A restructuring of capabilities is emerging as biotech companies capitalize on their increasing status as the primary source of new innovations, while big Pharma looks more toward its competence in global-scale, late-stage development, distribution and marketing. Biotech will benefit from the surge in IPO activity in 2014-2015, with more options to go it alone or partner rather than face outright acquisition by big Pharma.
- New and emerging threats to global health underscore the industry's continued relevance in tackling disease. Eradication of global scourges like polio are within reach, while promising new treatments are on the way against dengue fever and malaria. Solving for one major killer – drug-resistant TB – remains elusive.

But investment dynamics no longer favor organic growth...

- Big Pharma is cash rich and asset poor – and unlocking the promise of the pipeline does not proceed sequentially in a way that recognizes the pressures on short-term quarterly earnings performance. M&A activity is reaching an all-time high, with 37 transactions worth \$200 billion completed through 3Q 2015. Pharma's demand for the few high-quality assets ready to be commercialized will continue to keep biotech valuations high through 2016.
- Smaller biotechs with unique, clinically differentiated assets are driving big Pharma innovation.
- Questions remain about the productivity of in-house R&D: if the model is not “broken,” fixes are needed to control the cash burn rate. Tufts Center for the Study of Drug Development posts estimate of average \$2.6 billion per NCE along with high drug candidate failure rate, especially in costly Phase III studies. While opinions differ as to the amount, there is a consensus that costs of new drug development are increasing.
- 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 scrip, with the remainder focused on proprietary drugs for smaller, precisely segmented groups of patients, like those with rare diseases or specific types of cancer.
- The strategic question for 2016: 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?

- “Frugal innovation” as an emerging theme in R&D, with local champions in China, India and a few other emerging country markets leading the way – but still to be proven as a viable drug development model.
- Collectively, all of these the changes promise a more diverse industry, although the expertise barriers to entry are formidable, particularly in manufacturing the new generation of complex biologics and biosimilars.
- Contract research organizations [CROs] are maturing and now have the scale and size to assume the burden of big Pharma’s drug development and post-marketing obligations – the latter, especially the generation of “real world” evidence, is a lucrative new source of CRO revenues. Exclusive strategic partnerships with big Pharma are becoming commonplace, while CROs from China and India are emerging as competitive rivals to the established US and European players.

Raising the bar on performance...

- Biopharma’s bottom line: future global profits depend on maintaining price freedom in the US, which remains by far the world’s dominant market, accounting for more than one-third of global industry revenues.
- The 2010 Affordable Care Act [ACA] prompts more consolidation in health care and increases payer leverage in pricing and market access. Insurers, PBMs and pharmacy wholesalers that do business with biopharma are now down to two or three players with a dominant share of their respective markets.
- Activist investors continue to apply shareholder arbitrage to force companies to “get lean.”
- Partnering and licensing opportunities are increasingly selective, with less margin for error. Risk protection is advanced through detailed milestones and contingent rights clauses.
- PBMs tighten the screws on drug prices. More drugs are excluded outright from formulary cover while high co-pay tiering placements are used more aggressively to drive the outcome of rebate negotiations. Price protection clauses are becoming standard practice. Expect legal action by PBMs in 2016 to sever the sweetheart arrangements between some manufacturers and specialty pharmacies revealed through activist investor pressures on drug maker Valeant.
- Big distribution wholesaler chains grab a bigger share of the generic compounding business to capitalize on quality issues confronting smaller players tainted by scandal.

- The European Medicines Agency [EMA] moves toward a new registration model: the Adaptive Pathway. A one-time market authorization yields to faster initial approval in return for periodic regulator reevaluation of a product through its life cycle.
- Relentless compliance scrutiny, expanding globally beyond illegal US off-label marketing. Supply chain irregularities a new area of regulator interest.
- Industry responds to a more diverse customer base, with multiple engagement points beyond the physician, especially through integrated care models targeting patients. Costly investments in predictive analytics are required to activate these multiple channels.
- Operational challenges in high-potential emerging country markets: commodity crisis and slowing GDP growth puts more focus on how to turn short-term revenues into sustainable profits.
- Anticipating the reimbursement climate after marketing authorization requires full commercial mobilization of in-house capabilities at a very early stage of drug development. Early investment is a big bet, which in turn incurs big risks.
- China growth engine slows – GDP 14.2% in 2007 vs. 6.5% in 2015 – amidst more government scrutiny of foreign drug multinationals. Health system restructuring creates additional market uncertainties on drug pricing along with a stronger regulatory emphasis on rewarding quality and innovation.
- Greater pricing pressures in Europe amid generalized budget austerity. Treating drugs as a tendering purchase – like band aids – begins to take root in some countries.
- Growing complexity in clinical trial requirements, including big Phase IV population studies extending beyond the patent term. Led by the EMA, pressure increases to make all clinical trial data publicly available, including trials that fail.
- New competitive threats from adjacent industries – Google, GE, Nestle – outside health care. Google uses its data strengths to carve a broader role in lowering timelines and raising efficiencies in drug development, taking it beyond its previous focus on disease mapping and consumer health applications.
- Crowding in key therapeutic categories -- “counter launch” campaigns hype the marketing bill.
- Formal patient group engagement in drug development, regulatory approval, market access. How will the Cystic Fibrosis Foundation spend its \$3 billion royalty windfall from Vertex?
- Social media’s disruptive effect on the patient/physician relationship, data disclosure, privacy and the accuracy of clinical trials – an alternative, open source information stream.

...Leads to more pressure to define a drug's value

- Congress, the courts and the states continue to chip away at key elements of the 2010 Affordable Care Act [ACA], adding to operational uncertainties for business amid cost and coverage concerns for middle-class consumers. The Independent Payment Advisory Board – which carries authority to impose cuts in Medicare, including the Part D drug bill – has yet to convene, and the so-called “Cadillac tax” on high-benefit, high-cost insurance plans has been delayed until 2020, depriving the law of a major source of revenue. Tax penalties for individuals and families that opt out of insurance coverage start to bite, exposing deficiencies in plan design like high deductibles and co-pays.
- 2016 will test the limits of growth in the US insured population. To date, the Obama Administration has enrolled only 38 per cent of the 24 million people eligible to participate with subsidies made available under the law – a rate too low to sustain the program's cost over the long term. Unless enrollments of younger, healthy, middle-class patients currently without insurance step up to broaden the risk pool, commercial insurers that represent the backbone of the exchange-based private insurance market under the law will be compelled to drop out – launching the “death spiral” foreseen by ACA opponents.
- Outcome of the November presidential election will lead to still more legislative debate, with a Democratic president seeking to make exchange-based insurance premiums more affordable to the middle-class, while a GOP administration, assuming support from a GOP Congress, revisits the entire premise of the law beyond that one provision with bipartisan support: no discrimination against pre-existing conditions.
- Drug costs are due to increase as percentage of overall health spending, making the activities of individual drug companies on pricing more politically visible. Scrutiny of double digit price hikes for older, off patent drugs – a practice that continues among the big Pharma majors, not just smaller industry “outsiders” – will add to the debate on what true “innovation” is in medicines. One path to reform is to introduce more competition in the off-patent segment by increasing the pace of FDA approvals of generics through fast-track FDA review.
- The Obama Administration will use its executive authority to test non-legislated approaches to pricing restraint, including reliance on pilot demonstration projects authorized through the ACA. The HHS Center for Medicare and Medicaid Services [CMS] is already introducing a form of European-style “reference pricing” by grouping different biosimilar products intended for use in the same therapeutic category into a single reimbursement code.
- With formal action by government on drug pricing unlikely, PBMs, insurers, professional groups and academia are developing new approaches. Indication-based pricing for cancer therapies – where prices for the same drug might differ depending on its success in treating one cancer versus another – will be implemented by Express Scripts in 2016.

- Patients will pay more out-of-pocket for drug coverage in 2016, resulting in likely lower utilization, less adherence to therapy, and still more pressure for industry to demonstrate “value.”
- Continued phase-in of CMS standards on value and quality to drive more efficiencies in health care, including drugs.
- Outside the US, health technology assessment programs as a supplement or a condition for P&R continue to spread across geographies.
- Heavy industry investments in information systems and technologies are seen as a competitive differentiator in areas as diverse as clinical trial management and market access. Biostatistics grows in importance as a way for industry to meet payer demands for comparative measures of drug cost-effectiveness.

With heightened reputation risks...

- Industry image continues to face challenges – neither elites nor mass opinion believe the industry is a leader in innovation.
- Rogue, price-gouging players in biopharma are disavowed by the big 10 innovator firms – but will the public, in a presidential election year, choose instead to define the entire industry on the basis of the actions of a few “outlier” firms?
- Despite industry claims that it is increasingly a “price taker,” consumers and government payers don’t see it that way – drug makers are aggressively raising prices on existing products, a process largely confined to the US market. Elsewhere, drugs are seen as a “public good.”
- US financial sanctions for deceptive marketing practices, including penalties for violations of an ambiguously defined federal ban on off-label marketing, surpass the \$30 billion mark, as measured over the past five years.
- Industry vulnerability to biased regulatory enforcement in emerging market countries with weak governance standards.
- With more than 80 per cent of API manufacturing now taking place outside the US, industry could be harmed by adulterated or unsafe medicines imported from other countries, especially as FDA oversight in this area is constrained by lack of resources.
- Industry information assets vulnerable to transparency/disclosure pressures.

- The best gift to biopharma in 2016 is comprehensive corporate tax reform: the current regime imposes the highest rates in the OECD and dates back to a prehistoric 1986. But prospects for action are nil, and as Congress dithers over a partial fix for *ex-US* domicile changes linked to tax inversion, lessons from the 2014 Pfizer/AstraZeneca takeover fray remain relevant: don't be stateless!

What's Hot...

- The US becomes a fresh source of opportunity now that the bloom on easy profits has faded from emerging country markets, which, with the exception of China, are increasingly seen as a long-term game.
- M&A action and out-licensing to big Pharma remains buoyant: The volume of deals is higher and involve asset swaps and commercialization rights in multiple markets – slowly, biotech is going global.
- Immunology drugs are a \$36 billion market for pharma in 2016, according to investment analysts.
- New treatment options for fibrosis emerge from industry labs.
- New drug combinations are another hot area in oncology.
- More growth in the Injectables segment, with additional delivery innovations.
- Investigating the human microbiome, either as a source of new treatments – or the underlying cause – for many common diseases.
- Cross-institutional consortia to share the burden on infectious disease research, neurocognitive disorders, vaccines and next generation antibiotics. The need for effective treatments against drug resistant “super bugs” garners more international attention.
- Gradual acceptance of biosimilars in the US as regulatory standards on key defining issues like interchangeability are defined in a way that offers a predictable path forward for investors.
- New FDA leadership and a congressional debate on PDUFA reauthorization offer prospects for increased support for streamlined and efficient approvals that keep the US at the front line of biopharma innovation. Heads of major national regulatory agencies initiate a new regular dialogue that will add to the momentum for international rules harmonization.
- Investments continue to expand in digital health products like wearables that allow the patient to track, direct and shape individualized health behaviors – the consumer revolution in health.

- Understanding how the bureaucratic complexities of the US Affordable Care Act will shape future drug utilization patterns, including the effectiveness of the billions of dollars industry spends on patient coupons/rebates designed to block PBM's growing use of formulary access controls to manage drug benefit costs.
- Using new drug delivery platform technologies to create more patient-friendly approaches to tackling poor rates of prescription drug adherence – a \$300 billion annual drain on US health spending.
- Finding efficient and cost effective ways to manage the growing reporting requirements on medicines promotion in the US and internationally.
- Basic research is back. The decade-long drought in National Institutes of Health [NIH] funding is reversed with a FY 2016 budget of \$32 billion funding new Precision Medicine and BRAIN initiatives.
- Boardroom issues and new pressures on the “c suite,” led by the complex politics of previously arcane issues like global tax policy as well as competence in addressing tighter governance oversight requirements. The CFO morphs into COO while the role of Chief Compliance Officer [CCO] assumes more prominence.

What's Not...

- Drug price controls in the US. If Washington could not succeed in granting Medicare the power to negotiate prices with industry under two Democratic presidents with dominant control of both houses of Congress, why expect anything from a divided White House and Congress in an election year estimated to cost an all-time high of \$5 billion – twice what was spent in 2012. Big money always muddies the water.
- “Financial engineering” as a business model for biopharma. Valeant Pharmaceuticals, poster child for this approach, has already crossed the reputational Rubicon with a drip-drip cascade of negatives leading to a restructuring of the business in 2016. Investor sentiment is decisive, swift and unforgiving – everything that government action is not.
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- Backlash against broad-scope patent protections that can be enforced across geographies – one reason why US ratification of the 12 nation Trans-Pacific Partnership [TPP] is far from a sure thing for 2016. The US industry coalition favoring multilateral free trade braced by IP rights has ruptured.
- Big data without the applied analytics that furnish useful insights on commercial strategy.

A final thought for 2016:
The enduring value of science in a chaotic world

“..Science does not stand by itself, but is the creation of very human people. We must continue to work in the humane spirit in which we were fortunate to grow up. If so, we shall help insure that our science continues and that our civilization will prevail..”

James Watson, co-discoverer of DNA and winner of the Nobel Prize for Medicine, 1962 –

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